DOCTOR OF PHILOSOPHY

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A mixed methods study

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An exploration of symptom burden and its management in Saudi Arabian patients receiving haemodialysis, and their caregivers: A mixed methods study

Bushra Alshammari, BSc General nursing, MSc advanced professional practice – Critical care

A thesis submitted to the school of Nursing and Midwifery. Queen’s University Belfast for the degree of Doctor of Philosophy (Ph.D.)

December 2019
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<th>Description</th>
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<td>CKD</td>
<td>Chronic kidney disease</td>
</tr>
<tr>
<td>HCPs</td>
<td>Health care providers</td>
</tr>
<tr>
<td>eGFR</td>
<td>Estimated Glomerular filtration rate</td>
</tr>
<tr>
<td>GFR</td>
<td>Glomerular filtration rate</td>
</tr>
<tr>
<td>ESKD</td>
<td>End stage kidney disease</td>
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<tr>
<td>HD</td>
<td>Haemodialysis</td>
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<tr>
<td>HRQOL</td>
<td>Health Related Quality of Life</td>
</tr>
<tr>
<td>KDQOL</td>
<td>Kidney Disease Quality of Life</td>
</tr>
<tr>
<td>RRT</td>
<td>Kidney replacement therapy</td>
</tr>
<tr>
<td>PD</td>
<td>Peritoneal dialysis</td>
</tr>
<tr>
<td>QOL</td>
<td>Quality of life</td>
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<tr>
<td>MMR</td>
<td>Mixed method research</td>
</tr>
<tr>
<td>TOUS</td>
<td>Theory of Unpleasant Symptoms</td>
</tr>
<tr>
<td>CKD-SBI</td>
<td>Chronic Kidney Disease Symptom Burden Index</td>
</tr>
<tr>
<td>DSI</td>
<td>Dialysis Symptom Index</td>
</tr>
<tr>
<td>HG</td>
<td>Haemoglobin</td>
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<tr>
<td>CB</td>
<td>Caregiver burden</td>
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<tr>
<td>POSs</td>
<td>Palliative Outcome Symptom Scale</td>
</tr>
<tr>
<td>mESAS</td>
<td>Modified Edmonton Symptom Assessment System</td>
</tr>
<tr>
<td>ESAS</td>
<td>Edmonton Symptom Assessment System</td>
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<td>PSS</td>
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<td>GRAMMS</td>
<td>Good Reporting of a Mixed Methods Study</td>
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Study conferences and publications

I. The study protocol has been published in BMC nephrology


STUDY PROTOCOL

An exploration of symptom burden and its management, in Saudi Arabian patients receiving haemodialysis, and their caregivers: a mixed methods study protocol

Bushra Abuhammar1,2, Helen Noble1, Helen McAneney3 and Peter O'Halloran4

Abstract

Background: Globally 10% of the population worldwide are affected by chronic kidney disease (CKD), making it one of the most prevalent chronic diseases. Several studies have highlighted that the symptoms of CKD have a significant impact on patients. A number of symptoms, including fatigue and depression, are associated with poor patient health, increased risk of hospitalization and mortality. Physical and emotional symptoms often remain under-recognised and largely untreated. However, patients often create a variety of self-management strategies to meet the challenges of these symptoms. There is a lack of knowledge regarding symptom burden and the experiences of patients receiving haemodialysis (HD) and their caregivers, particularly in Saudi Arabia, therefore, this study aims to explore symptom burden and its management amongst patients receiving HD in addition to caregiver burden.

Method: A mixed methods, sequential, explanatory design consisting of two phases; phase 1 involves a cross-sectional study design with a planned convenience sample size of 141 patients who will be recruited from King Khalid hospital, Saudi Arabia. Thirty-two physical and psychological symptoms will be measured using the Chronic Kidney Disease Symptom Burden Index (CKD-SBI). Additionally, 130 caregivers will complete the Arabic version of the Zarit Burden Interview (ZBI-22) to identify the level of burden in the caregivers of patients on maintenance HD. Phase 2 of the study is a qualitative descriptive design involving semi-structured interviews with 15 eligible patients currently receiving HD. The selection of participants for interviews will be based on the patients’ total CKD-SBI scores with five individuals recruited from the lowest, median and highest percentiles. Additionally, 15 caregivers of the patients to be interviewed, will also be recruited and interviewed.

Discussion: This study focuses on a wide number of physical and psychological symptoms experienced by patients receiving HD. It will also focus on the effective management strategies patients employ to help reduce their perceived symptoms. Burden in caregivers of patients receiving HD will also be explored. Furthermore, the association between symptom burden and caregiver burden will be investigated. Findings from this study will provide evidence to help health care providers to develop effective interventions to assess and manage symptoms in patients receiving HD.

Keywords: Symptom burden, Symptoms, Management, Haemodialysis, Dialysis, End-stage kidney disease, Chronic kidney disease, Caregiver, Burden, Saudi Arabia, Mixed methods research

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II. Findings of the study have been presented “Oral presentation” at the Inaugural Doctoral Collaboration conference 2019
III. Findings from the study have been presented “Poster presentation” at the

UK kidney week conference 2019

Certificate of Presentation

This is to certify that

Bushra Alshammari

Presented a Poster entitled

Burden in patients and their informal caregivers living with haemodialysis in Saudi Arabia: A cross sectional study

at

UK Kidney Week 2019

3rd – 5th June 2019

Sharon Greenwood, British Renal Society President

Graham Lipkin, Renal Association President
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Thanks Allah.
Abstract

Background: Patients receiving haemodialysis (HD) experience substantial symptom burden. These symptoms are associated with reduced physical function, poor treatment tolerance and impaired health-related quality of life. These symptoms are complex and are often undetected by individuals or health care providers (HCPs). A number of symptoms, including fatigue and depression, are associated with poor patient health, increased risk of hospitalisation and mortality. Physical and emotional symptoms are often not diagnosed or treated; however, patients often use a variety of self-management strategies to meet the challenges of these symptoms. There is a lack of knowledge regarding symptom burden and the experiences of patients receiving HD and their caregivers, particularly in Saudi Arabia. Therefore, this study aimed to explore symptom burden, the factors predicting symptoms and the self-management strategies in patients undergoing HD. It also aimed to assess the level of burden in the caregivers of these patients, the relationship between patient and caregiver burden, and the factors that may influence the reported level of caregiver burden.

Method: The study used a mixed-methods, sequential, explanatory design drawing on the three concepts (influencing factors, symptoms experience, and consequences) of the Theory of Unpleasant Symptoms (TOUS) to explore symptoms burden and identify its relationships with influencing factors and consequences. Phase 1 involved a cross-sectional study design, with a convenience sample of 141 patients, who were recruited in King Khaled hospital, Saudi Arabia. Thirty-two physical and psychological symptoms were measured using the Chronic Kidney Disease-Symptom Burden Index (CKD-SBI). Additionally, 61 caregivers completed the Arabic version of the Zarit Burden
Interview (ZBI-22), where 0 indicated low caregiver burden and 88 indicated severe burden, to identify the level of burden in the caregivers of patients on maintenance HD.

Phase 2 of the study was a qualitative descriptive design, involving semi-structural interviews, with 13 eligible patients currently receiving HD. The selection of patients for interview was based on each patients’ total CKD-SBI score, with individuals recruited from the lowest, median and highest percentiles. Additionally, 9 caregivers of these patients were also recruited and interviewed.

Results: The mean age of patients was 53 ± 17 years, while caregiver’s tended to be younger, with a mean age of 36 ± 13 years. 76 (54%) of patients were male and 65 (46%) were female. The majority of caregivers were female (n= 48, 79%) and 90% (n=55) of caregivers lived with the care recipient. Of the 32 measured symptoms, patients reported having a mean of 10 ± 5. The most prevalent symptoms reported were fatigue (72%), followed by itching (63%), bone pain (62%), and muscle cramps (61%).

Being female, unmarried, and having one or more health conditions demonstrated a statistically significant association with increased symptom burden in patients receiving HD. The duration of dialysis and travel time to receive dialysis was not found to be associated with symptom burden. The mean total caregiver burden scores reported by caregivers was 22 ±14. Caregiver burden was positively associated with being older and female, but not with cohabiting with the patient. Cultural beliefs and religion had a significant impact on the levels of reported symptoms, as well as reported caregiver burden. The study also found
a positive correlation between the total number of symptom (symptom prevalence), in patients receiving HD and caregiver burden.

Three overarching themes were revealed from patient interviews, the holistic impact of symptom burden, factors influencing symptoms and symptom management. For caregivers of patients receiving HD, three themes were identified in caregiver interviews: positive caregiving experiences, factors influencing caregiver experience and negative caregiving experiences.

Discussion: This is the first study which explores the experience of symptoms and the impact of symptoms on patients receiving HD in Saudi Arabia. The process of integration between the quantitative and qualitative phases of the study, demonstrated different levels of agreement and understanding of symptoms in patients undergoing HD and burden in caregivers.

In conclusion, future research should consider symptom assessment, effective patient care and the promotion of appropriate symptom management in patients receiving HD. HCPs need to be aware of the interrelation between symptom, which increase symptom burden. A reduction in symptom burden in patients with HD and other chronic illnesses may be achieved if policy makers and clinical staff focus on groups of symptoms and target the main influencing symptom. Early recognition and determining the people at high-risk of experiencing greater symptom burden needs to be undertaken to avoid its impact on patients life and enable early management and referral.
Chapter 1: introduction
1.1. Introduction

Worldwide the incidence of chronic kidney disease (CKD) continues to rise inexorably. The global incidence of CKD increased by 89% from 11.3 million in 1990 to 21.3 million in 2016 (Jha and modi, 2018). CKD has a high global prevalence with a consistent estimated CKD incidence in the population of 11 to 13% (Hill et al., 2016). Living with the advanced stages of CKD creates many challenges for individuals and informal caregivers. At end-stage renal disease (ESRD), patients require renal replacement therapy (RRT), including dialysis. The majority of dialysis patients receive haemodialysis (HD), rather than peritoneal dialysis (PD). Patients receiving HD experience substantial symptom burden. These symptoms are associated with reduced physical function, poor treatment tolerance and impaired health-related quality of life (HRQoL) (Jha and modi, 2018; Goodell and Nail 2005; Haisfield-Wolfe et al. 2012). These symptoms are complex and are often undetected by the individuals or HCPs. In addition, related research has tended to focus on individual symptoms rather than the totality of symptoms and associated burden. Existing research has also focused on the prevalence of symptoms and failed to examine the complex inter-relationship between these various symptoms. This thesis examines the complex experience of symptom burden for patients receiving HD, the factors which affect the symptom experience, and the self-management strategies which patients may use to reduce or relieve symptoms. The thesis will also consider the levels of burden in informal caregivers who often provide care to patients receiving HD.
1.2. Background

1.2.1. Definition of Chronic kidney disease (CKD)

The Renal Association established the definition of CKD as, a condition where kidneys are not functioning normally, with a decrease in the rate of the glomerular filtration of less than 60 mL/min/1.73 m² for at least 90 days, irrespective of the cause (The Renal Association, 2019). According to KDIGO (2013), CKD is defined as abnormalities of kidney function or structure, exist for more than 90 days, with effects for health. In some Western countries, 10-12% of the population is estimated to have CKD, making it one of the most prevalent global chronic diseases (Graf et al., 2009; Nugent et al., 2011). There are five stages of CKD, categorised according to the filtration rate, see (Table 1). Stage 1 of CKD is described as a normal GFR greater than or equal to 90 mL/min/1.73m², and stage 2 CKD as a mild reduction between 60-89 mL/min/1.73m². Stage 1 and 2 cannot be classified as CKD unless there are markers of kidney damage, such as haematuria or structural abnormalities (Kidney Health Australia, 2015; KDIGO 2013). Stage 3 of CKD involves two cases; 3a and 3b, with 3a indicating a mild to moderate reduction in eGFR, and 3b, a moderate to severe reduction in the eGFR of between 30-59 mL/min/1.73m². Stage 4 of CKD represents a severe decrease in renal function with an eGFR of 15-29 mL/min/1.73m². Stage 5 is the advanced stage of CKD with a severe reduction in the eGFR of less than 15 mL/min/1.73m² (KDIGO, 2013). Stage five is the final, permanent and the most advanced stage of CKD, due to the severity of kidneys damage, the kidneys can no longer perform their normal functions properly (The Renal Association, 2019). **End stage renal disease (ESRD)** is the **last stage (stage five)** of **CKD**. A patient with ESRD
requires RRT, either dialysis or kidney transplantation in order to survive (The Renal Association, 2019).

Table 1: Stages of chronic kidney disease

<table>
<thead>
<tr>
<th>CKD Stages</th>
<th>GFR</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>≥90</td>
<td>Normal or high GFR, with other evidence of kidney damage</td>
</tr>
<tr>
<td>2</td>
<td>60-89</td>
<td>Slight decrease in GFR, with other evidence of kidney damage</td>
</tr>
<tr>
<td>3a</td>
<td>45-59</td>
<td>Mild to moderate decreased in GFR</td>
</tr>
<tr>
<td>3b</td>
<td>30-44</td>
<td>Moderately to severely decreased in GFR</td>
</tr>
<tr>
<td>4</td>
<td>15-29</td>
<td>Severe decrease in GFR, with or without other evidence of kidney damage</td>
</tr>
<tr>
<td>5</td>
<td>&lt;15</td>
<td>Established kidney failure</td>
</tr>
</tbody>
</table>

Abbreviations: CKD, chronic kidney disease, GFR, glomerular filtration rate (KDIGO, 2013)

1.2.2. Epidemiology of Chronic Kidney Disease

Chronic kidney disease (CKD) has become a global concern because of the increase in the prevalence of reported cases. The increase in CKD, may be due to the growing prevalence of non-communicable diseases, particularly diabetes mellitus and hypertension (Eggers, 2011; Hill and Fogarty, 2012; Karkar, 2011; Liyanage et al., 2015). Globally, it is estimated that nearly 500 million people have CKD (Mills et al., 2015). It is also estimated that more than 2.6 million individuals require RRT to survive (Liyanage et al., 2015). In Middle Eastern countries, the incidence of CKD is still largely unknown (Alsuwaida et al., 2010; Awad, 2011; Farag et al., 2012; Shaheen and Souqiyyeh, 2010), however, it has been suggested that the incidence of ESRD is approximately at 100 to 140 cases per million of the population (pmp) (Shaheen and Souqiyyeh, 2010). The underreported incidence and prevalence of CKD in
developing countries, may be due to the lack of population based studies (Shaheen and Souqiyyeh, 2010), the limited use of a registry system to record the prevalence and incidence (Barsoum, 2002; Farag et al., 2012; Jedy-Agba et al., 2015) and poor access to health care for early detection of kidney disease (Farag et al., 2012). In a more recent systematic review, the prevalence of ESRD in Middle Eastern countries was reported to be 360 pmp (Malekmakan et al., 2018). It has been reported that the highest prevalence of ESRD is in Saudi Arabia (Abboud, 2006). Therefore, potentially the incidence and prevalence of ESKD may be significantly higher than reported, which could result in underestimating the effects of ESRD (Farag et al., 2012).

1.2.3. Risk factors for Chronic Kidney Disease in Saudi Arabia

Over several decades, there have been a marked rise in the prevalence and incidence of ESRD in Saudi Arabia (Al-Sayyari and Shaheen, 2011). Between 1995 and 2016, the number of individuals receiving dialysis has increased from 3869 to 17687, which is a 457% growth in the dialysis population (SCOT, 2018), see (Figure 1).
Currently, Saudi Arabia and Belgium have the highest estimated CKD prevalence (24%), followed by the UK and Singapore (16%) (Kidney Care UK, 2018). The significant increase in reported CKD in Saudi Arabia, may be due to a number of factors: the change in age demographics, prevalence of diabetes and hypertension, and lifestyle-modifiable risk factors (obesity, lack of exercise and smoking). Some of these factors are shared by other countries, however, some are exclusive to the Saudi population.

1.2.3.1. Age

Currently the population of Saudi Arabia is relatively young see (Table 2), while in the UK the median age of patients who are receiving RRT is 59 years (HD 67 years, PD 64 years, transplant 54 years) (MacNeilla and Ford, 2017). In Saudi Arabia, during the early 1980’s, the mean age of individuals with ESKD was 37.9 years, in the 1990s it was 51.3 years (Jondeby et al., 2001). This change in the age demographics to a larger older population, will contribute to an increase in the incidence and prevalence of ESRD (Hassanien et al, 2012).
It has been reported that the incidence rates of ESRD in Saudi patients who are aged between 15 to 44 years is 199.8 pmp, aged 45–64 years it is 577.7 pmp, and >65 years it is 716 pmp (Al-Homrany and Abolfotoh, 1998). The increased incidence and prevalence of ESRD in older populations is associated with the presence of other chronic illnesses in this age group, as well as age-associated decline in kidney performance, which is not related to any other comorbidities (Prakash and O’Hare 2009). With the anticipated increase of older individuals, it is possible that the incidence and prevalence of ESRD will increase in Saudi Arabia in the future (Al-Sayyari and Shaheen, 2011). This is not consistent with findings from developed countries, were rates of ESRD have declined or stabilized (Foley and Collins, 2007).

Table 2: Renal replacement therapy in Saudi Arabia and age distribution

<table>
<thead>
<tr>
<th>Age distribution (years)</th>
<th>Percentage</th>
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</thead>
<tbody>
<tr>
<td>&lt;15</td>
<td>1.6</td>
</tr>
<tr>
<td>16-25</td>
<td>7.3</td>
</tr>
<tr>
<td>26-45</td>
<td>24.9</td>
</tr>
<tr>
<td>46-55</td>
<td>22.1</td>
</tr>
<tr>
<td>56-65</td>
<td>23.4</td>
</tr>
<tr>
<td>&gt;66</td>
<td>20.7</td>
</tr>
</tbody>
</table>

(Al-Sayyari and Shaheen, 2011)

1.2.3.2. Diabetes Mellitus

The increase prevalence of chronic diseases, particularly diabetes mellitus and hypertension may explain the growing risk of CKD in the population of Saudi
Arabia (Eknoyan and Nagy, 2005; Narres et al., 2016; Karkar et al., 2011; Liyanage et al., 2015). Saudi Arabia has the second highest rate of diabetes mellitus in Middle Eastern countries, and the seventh highest global rate of diabetes, with an estimated 7 million people living with the disease (Alwin Robert et al., 2017). The population living with diabetes mellitus in Saudi Arabia is predicted to increase by 22.3% in 2030, (Whiting et al., 2011). Raised blood sugar damages blood vessels in the kidney, causing an impairment in the function of glomerular cells (Kidney Health Australia, 2015). It has been reported that 42.5% of ESRD cases in Saudi Arabia are directly related to the onset of diabetes mellitus (Al-Sayyari and Shaheen, 2011).

1.2.3.3. Hypertension

Hypertension is an additional risk factor associated with CKD. The prevalence of hypertension in the population of Saudi Arabia was 15% in 1997 (Al-Nozha, 1998), and increased to 26% by 2007 (Al-Nozha, 2007). Hypertension damages renal function by reducing blood flow to the kidney, which reduces the filtration glomeruli rate (Bidani and Griffin, 2004). It is estimated that hypertension is responsible for 24% of ESRD cases in Saudi Arabia (El Minshawy et al., 2014). CKD is common in hypertensive patients in Saudi Arabia, with a prevalence rate of 46.9% (Aldhabi et al., 2018).

1.2.3.4. Lifestyle-modifiable risk factors (obesity, lack of exercise and smoking)

The lifestyle behaviours of the Saudi population, including obesity and smoking, may also lead to an increase in the incidence and prevalence of ESRD. It has been reported that the diet in Saudi Arabia contains high levels
of sugar and fat, some individuals fail to exercise sufficiently and a large proportion of the population smoke (Sami et al 2017). In Saudi Arabia, 37.6% of the population is reported to be obese (Al-Othaimeen et al., 2007). More than half of the population in Saudi Arabia are reported to be insufficiently active (Saudi Gazette, 2018). This may be due to desk-based jobs replacing labour jobs, extremely hot weather, cultural barrier, the absence of female sports program in the schools and using cars to travel (Al-Hazzaa, 2018; Saudi Gazette, 2018). Although, lack of physical activity and obesity are not recognised as a risk factor causing CKD, they can increase the risk of hypertension and diabetes mellitus, which are clearly implicated in the development of CKD (Al-Nozha et al., 2005).

Smoking is also recognised as a significant risk factor in the advancement of CKD to ESRD (Yacoub et al., 2010). The prevalence of smoking in the population of Saudi Arabia, was 12.2% in 2013 (Moradi-Lakeh et al., 2015). The prevalence of smoking in Saudi Arabia is excessive, in the adult population it ranges from 11.6 to 52.3% (median 22.6%), and in the elderly population it is 25% (Mahfouz et al 2013). Smoking increases the production of albumin and protein in the urine, leading to a decline in the rate of glomerular filtration, and the development of CKD (Warmoth et al., 2005). The high prevalence of ESRD will cause an increased need for hospitalizations, greater morbidity, and the need for more individuals to require RRT in the future (Hassanien et al., 2012).

1.2.4. Treatment options for patients with ESRD in Saudi Arabia

There are two treatment options offered to ESRD patients in Saudi Arabia; these are dialysis therapy and renal transplantation (SCOT, 2011).
Conservative management is not offered as a treatment option in Saudi Arabia (MOH, 2014). According to SCOT (2011), HD treatment began in Saudi Arabia in 1971, followed by kidney transplantation in 1979. Peritoneal dialysis (PD) therapy began in Saudi Arabia in 1980. At this time, dialysis centres were created throughout the country. The number of dialysis centres in Saudi Arabia has been increasing substantially which currently reaching the total of 243 dialysis centres (SCOT, 2016) see Figure 2. The most common RRT provided to ESRD patients is HD, with 58% of the population receiving HD and 6% PD. Renal transplantation (Tx) is also a common treatment for ESRD, see Figure 3. In 2011, 36% of patients with ESRD received a kidney transplant (SCOT 2001) (Figure 2). This percentage is predicted to increase in the future, as the Islamic religion continues to encourage the donation of organs (Oliver et al, 2011). However, renal transplantation is not always possible, due to a shortage of professional staff or appropriate medical facilities, long waiting lists or the ineligibility of recipients for kidney transplantation due to their health condition (Patel et al 2011; Abecassis et al 2008). As a result, many patients have to rely on dialysis treatment. Approximately 90% of all dialysis patients are undergoing hemodialysis (HD), see Figure 4(Abecassis et al 2008).
Figure 2: Number of dialysis centres in Saudi Arabia 1971-2016 (SCOT, 2016)

Figure 3: The percentages of the renal replacement therapy provided to patients in Saudi Arabia

Figure 4: Percentages of patients receiving dialysis in Saudi Arabia.
1.2.5. Haemodialysis and Symptom burden

The increasing number of patients with ESRD, has resulted in a substantial rise in the number of individuals receiving HD. HD is one of the most common treatment options provided to patients with ESRD. Haemodialysis is a treatment which uses a special filter, artificial kidney, or a dialyzer, which filters and extracts waste products and additional fluids from the body, see Figure 5 (National Kidney Foundation 2019). This procedure requires access by minor surgery, to blood vessels, usually in the arm, neck or chest. The treatment lasts for up to 4 hours each session, and individuals normally require three dialysis sessions each week. Haemodialysis treatment prolongs the lives of many patients globally. Although dialysis is life-saving, patients on maintenance HD, experience multiple physical and emotional symptoms, which may impact on their well-being (Janssen et al 2008). HD symptoms may be caused by the build-up of waste products in the blood, a side-effects of dialysis or a result of other co-morbidities (Merkus et al., 1999). HD is exhausting for patients who commonly experience a range of symptoms, such as fatigue, depression, anxiety, itching, vomiting and nausea (Murtagh et al 2007; Lowney et al 2015; Weisbord et al 2005). It is estimated that 35-50% of patients receiving HD report having 4 to 10 symptoms, while 25 - 35% report having more than 10 symptoms (Murtagh et al 2007). Patients may view symptoms as more significant than survival, due to the devastating impact of symptom burden on all aspects of their lives (Jhamb et al 2008). Controlling these symptoms is essential and requires comprehensive prior assessment. However, studies claim that HCPs fail to commonly recognise and treat the
physical and emotional symptoms experienced by HD patients (Weisbord et al 2004). Feldman et al (2013) reports that the main barriers to symptom management, is that HCPs are often unaware of many patient’s symptoms. According to Solano (2006), patients with ESRD experience a similar degree of symptom distress to cancer patients. Enhanced assessment and increased awareness of symptom burden in patients at ESRD, may improve the detection and treatment of these symptoms, which will improve the quality of life of individuals (Almutary et al 2016).

**Figure 5**: The process of HD treatment

1.3. **List of Definitions**

1.3.1. **Symptom burden**

Lenz et al. (1997) who established the theory of unpleasant symptoms, defined symptom as “perceived indicators of change in normal functioning as experienced by patients” (Lenz et al. 1997: P15).
Symptom experience is defined as the severity, frequency distress perception when symptoms are expressed and produced (Armstrong et al., 2004). The concept of symptom burden is the sum of the duration, severity, frequency, duration and distress of symptoms experienced by patients (Desbiens et al. 1999). For the purpose of the current study, a more recent definition of “symptom burden” was used, which is “the subjective, quantifiable prevalence, frequency and severity of symptoms placing a physiological burden on patients and producing multiple negative, physical and emotional responses” (Gapstur, 2007, p 673).

Symptom burden can systematically and comprehensively display the experience of symptoms, because it concentrates on various simultaneous symptoms and multidimensional characteristics of symptoms. Yet, symptoms can appear in isolation, commonly, two or more symptoms occur simultaneously (Lenz et al., 1997). Symptom burden has attracted increased research attention, especially in the study of patients with cancer, and more recently in the study of other chronic diseases (Hong et al 2018).

1.3.2. Symptom distress

Symptom distress or bother defines as “the degree or amount of physical or mental upset, anguish, or suffering experienced from a specific symptom” (Rhodes and Watson, 1987, p. 243).

1.3.3. Symptom severity

Symptom severity or intensity defines as “The amount and degree of discomfort from a symptom” (Rhodes & Watson, 1987, p. 242).
1.3.4. Symptom frequency

Symptom frequency or timing defines as “The number of times the symptom occurs within a given time frame” (Rhodes & Watson, 1987, p. 242).

1.3.5. Definition of Self-Management

Self-Management is the ability of individuals to manage symptoms, treatment, physical and psychosocial consequences, and lifestyle changes inherent in living with a chronic condition (Iversen, et al., 2014; Barlow et al, 2002). Self-management is a skill that helps individuals throughout their professional and personal lives. Living with ESRD and receiving HD requires the individual to make lifestyle changes and manage symptoms along with the physical and psychosocial consequences of the disease. Several studies suggest that patients with symptom burden create a self-management strategy to help reduce or, relieve and cope with their chronic disease symptoms (Fu et al 2004; Hsiao et al 2014). The enhancement of self-management and related strategies has been studied and developed mainly in the context of somatic chronic diseases (Barlow et al 2002). This is a neglected area of research study which requires a more rigorous examination and understanding of the day-to-day management of disease symptoms (Hsiao et al 2014).

1.3.6. Informal caregivers

Informal caregivers are generally relatives or close friends of the individual requiring care. Caregivers do not normally receive formal training for this role and this tends to be voluntary in nature. Caregiving includes all assistance required in the home and may range from help with fundamental activities of daily living, ranging from dressing, mobility, organizational needs,
transportation requirements and medication assistance (Grabel & Adabbo, 2011).

1.3.7. Caregiver burden

Burden is one of the most frequently used terms in caregiving research, both as an outcome and as a predictor of the demands of caregiving. Caregiver burden is not well-defined or conceptualized in the literature (Bastawrous 2013). Researchers tend to use this term in association with well-being, stress, problems, and adverse effects (Montgomery et al. 1985). Caregiver burden is a multidimensional experience considering the physical, psychological, financial and social aspects of providing care to a relative (George and Gwyther, 1986). Caregiver burden is defined as the extent to which caregivers perceive their emotional, physical health, social life and financial status, as a result of caring for their relatives and can contribute to changes in life style, which influence health and functioning, socioeconomic status, psychological function, and family interaction dimensions, which all represent quality of life (Zarit 1980; Ferrans and Powers, 1992).

Living with an individual in the advanced stages of CKD and receiving regular HD, can impact on the psychological health and well-being of caregivers (Sherwood et al 2005). Many patients with ESRD who receiving regular HD, are unable physically and emotionally to meet self-care needs and require support from caregivers (Alnazly, 2016). The responsibilities undertaken by caregivers can include: managing the patients’ medical treatments, dietary requirements, and clinic appointments. Patients with ESRD may require lifelong replacement of kidney function, which includes dialysis or
transplantation (NIH, 2018). Patients who are treated with HD causes a substantial burden for their caregivers, who are responsible for balancing dialysis sessions, scheduled three days a week, alongside personal activities and needs such as dressing, preparing an appropriate renal diet, administration of medication and managing other comorbidities (Einollahi et al. 2009). The impact of providing care to patients with ESRD, can be associated with psychological challenges such as depression anxiety, increased use of medication and negative quality of life effects (Etters et al. 2008; Sherwood et al. 2005).

Providing care to a sick family member can have a positive and enhancing relationship between the caregiver and care recipient, and accomplish enhanced family harmony, and promote resilience in caregivers (Hinrichsen et al., 1992). Research should adopt a more holistic approach to burden and focus more on the positive experiences of caregiving, rather than judge caregiving to have a mainly negative outcome. Positive benefits of caregiving, could be used in the development of future appropriate interventions to enhance caregiver well-being. It has been suggested that quantitative measures of ‘caregiver burden’ fail to identify important contextual elements of the caregiving experience and this limitation supports the use of a mixed method approaches to ensure a more comprehensive understanding of caregiver burden (Marina Bastawrous 2013). Unfortunately, limited research about the experience of caregiving for ESRD patients receiving HD in Saudi Arabia, is available.
1.3.8. Social support

The social network that provides psychological and material resources that are designed to assist the caregiver in his or her ability to cope with stress (Cohen, 2004). Social support involves structural aspects of the support network, which include the size of the network and the types of relationships within it, as well as functional social support, which refers to the actual availability of individuals to meet the identified need. It also includes emotional support in forms such as listening, trust, and respect. The nature of the support includes the extent to which it is helpful and the level of difficulty that the caregiver experiences in arranging it (Chang et al., 2001; Cohen, 2004).

1.4. Significance of the study

In Saudi Arabia, the number of individuals with ESRD and receiving HD continues to increase (Al Sayyari and Shaheen, 2011). Patients receiving HD are associated with a high symptom burden, which may lead to a decline in the individual’s HRQoL and poor health outcomes (Yong et al 2009). However, HCPs are mostly unaware of the occurrence of these symptoms in patients requiring HD and underestimate the severity of symptoms (Bossola et al., 2019; Claxton et al., 2010; Weisbord et al., 2007; Raj et al., 2017). Reducing symptom burden is dependent upon focusing on the symptom experience, the factors which increase burden, how these factors influence the symptom experience as well as focusing on the current self-management strategies which individuals use to alleviate symptoms.

Following a review of literature, a majority of published studies were found to have investigated the prevalence of symptoms, or the quality of life of the HD
population, see chapter 3. However, these studies did not provide insights or in-depth experiences of living with symptoms, the interrelationship between symptoms, and the impact of symptoms on the patient’s life. A small number of studies in Saudi Arabia have explored patient receiving HD, however, these studies have only examined individual symptoms, such as depression and sleep disturbance (Al Zaben et al., 2014: Al-Jahdali, 2012). As a result, there is a limited understanding of the holistic experience of symptom burden and the factors which can influence reported symptoms. A study conducted in Saudi Arabia by Almutary et al, (2016) assessing various symptoms of CKD who are receiving dialysis and non-dialyzed using a cross-sectional design. However, there was a lack of the focus on interviewing patients to achieve a range of perspectives in some depth, to explore patients’ views on HD-related symptoms and its management (Cox et al 2017). Symptom assessment and management have been identified as priorities for research on clinical care for patients receiving HD or who are likely to need dialysis in the near term (Davison et al 2015; Manns et al 2014).

Curtin et al., (2002) suggested that one way to understand the interrelationships between symptoms, self-management and functional status is to identify the symptoms which patients experienced and how symptoms are perceived and valued. This study provides an in-depth experience of symptoms as reported by patients receiving HD and assesses the multidimensional nature of symptoms including distress, severity, frequency and duration. It is important to stress that the severity of symptoms in individuals receiving HD, does not always result in the individual reporting
distress (Jablonski, 2007), while on contrary symptom distress often strongly related to symptom intensity (Backer, 2006).

Previous studies have failed to explore symptom burden, its impact and its management, particularly in Saudi Arabia. This study provides a comprehensive understanding of the complex management strategies which patients may use to manage their symptoms, and the potential barriers to symptoms management. This thesis also presents an understanding of the lived experience of individuals receiving HD within a culture setting influenced by unique traditional features and religion principals (Alkahtani et al 2013).

Additionally, limited research about the experience of caregiving for ESRD patients receiving HD in Saudi Arabia, is available. It is generally believed that religion, cultural beliefs, ethnicity may shape the experience of caregiving and contribute to different perceptions of the meaning of this concept (Pharr et al 2014). Saudi Arabia people are influenced by culture (Alkahtani et al 2013), which may influence the levels of perceived caregiver burden (Aranda et al 1997). Although, the caregiving role may be similar across different cultures, the experience and meaning of caregiving between cultures may express differently.

In this study we sought to increase awareness about the nature of symptoms and possible interaction between symptoms that may occur and explain the predictors that influence the levels of symptoms burden and its outcome. This study could add a new knowledge to facilitate the assessment and management of symptom burden in people receiving HD. This study also provides a unique insight into the experience of the informal caregivers who
providing care to the patients receiving HD. Different culture reveals a new point of view as well as new coping strategies to adapt with illness.

1.5. Outline of thesis

This thesis begins with the current chapter, an introduction chapter, which provides an overview of CKD, the epidemiology of renal disease and available treatment options. This chapter also provides a comprehensive overview of the study context, the significant of the issue under investigation and a justification for the study. This chapter also includes research aims and the research questions which framed the development of the study.

Chapter 2. Presents a systematic review and critique of current evidence which explores symptom burden in patients who receive dialysis.

Chapter 3. Contains a systematic review exploring caregiver burden and the factors which may influence burden of caregivers providing care to patients with ESRD. Each systematic review provides an overview of the individual search strategy developed to complete the systematic search, the quality assessment protocol, and study findings.

Chapter 4. Provides a rational for the methodology, sampling approach, ethical considerations, access to participants, data collection and analysis methods used in this study.

Chapter 5. Presents the findings from the quantitative phase of the study, including symptom prevalence, frequency and severity of symptoms and levels of distress. This chapter also outlines the levels of burden reported by
caregivers of patients receiving HD. The correlation between symptom burden in patients and caregiver burden is also identified within this chapter.

Chapter 6. Provides an in-depth analysis of the findings from the qualitative phase of the study, semi-structured interviews with both patients and their associated caregivers. Data were analysed using the thematic analysis framework (Braun and Clarke, 2006).

Chapter 7. The integration chapter presents the integration and synthesis of findings from both the quantitative and qualitative phases of the study. In this chapter a narrative approach using a theme-by-theme method was used (Fetters et al 2013) to help provide insights and explanations for study findings.

Chapter 8. The discussion chapter presents findings from both phases of the study. This chapter compares and contrasts study findings with existing evidence and critically discusses the strengths and limitations of the study.

Chapter 9. The conclusion chapter outlines the implications and recommendations for future research and links study findings to potential education and future research.

1.6. Summary of this chapter

The number of patients receiving dialysis is increasing dramatically in Saudi Arabia due to many risk factors. HD treatment is associated with multiple symptoms with significant impact on their daily life. In Saudi Arabia, little is known about symptom burden in patients receiving HD (Almutary et al., 2016). Using mixed methods design is important to give a holistic picture of the symptoms experience as well as caregivers experience of patients receiving
HD (Marina Bastawrous 2013). In summary, this chapter provides an overview of the study aim, and research question, rationale for the study, and the thesis outlines.
Chapter 2: Symptom burden in patients with end-stage kidney disease receiving dialysis: a systematic review
2.1. Introduction

Patients with ESRD, receiving dialysis, experience multiple symptoms which can negatively impact on all aspects of the individual’s life. This review contributes to the existing body of knowledge, by reviewing recent studies that focus on the assessment of multiple symptoms in patients who are receiving regular dialysis therapy and reviewing the symptom burden in these individuals. Previous reviews have explored symptom prevalence in patients with ESRD, with a focus on end-of-life care (Murtagh et al, 2007) or symptom burden in stages 4 and 5 (Almutary et al., 2013). This review develops and extends the current understanding of symptom burden in patients with CKD, and exclusively considers symptom burden literature in patients undergoing dialysis without any restriction to the date of publication. This systematic review also aims to identify the symptom burden in patients undergoing dialysis and includes all factors which influence symptoms, to help provide a better understanding of the total symptom burden.

2.2. Background

CKD has become a global concern due to its increased prevalence, affecting around 35% of those over 70 years (O’Callaghan et al, 2011) and 10% of people worldwide (National Kidney Foundation, 2015). At the ESRD, patients require a replacement of kidney function, which includes dialysis or renal transplantation (Abecassis et al 2008). Renal transplantation is not always available due to a shortage of donors and medical facilities or the ineligibility of recipients for kidney transplantation due to their health condition (Patel et al, 2011). As a result, patients depend on dialysis treatment to sustain their life (Shah et al 2017). Patients with ESKD who are being treated with dialysis
experience a variety of symptoms which might cause burden (Davison et al 2010). Symptoms were found to be very severe in the advanced stages of CKD, particularly for patients who are undergoing dialysis (Senanayake et al, 2017). Symptom burden has been found to reduce the QoL and increase the mortality and morbidity rates among patients receiving HD (Weisbord et al. 2003).

Studies also suggest that demographic data and clinical variables could potentially influence the individual’s symptom experience in CKD, which need to be investigated (Caplin et al., 2011; Danquah et al., 2010; Yu et al., 2012).

Previous reviews have explored symptom burden in end-stage chronic organ failure, however, the results were presented in conjunction with other chronic diseases, including heart failure and chronic obstructive pulmonary disease (Janssen et al., 2008). The review by Janssen et al., (2008) fails to report any factors which may influence symptom burden. A review completed by Murtagh et al, (2007), in patients with ESRD primarily considered the end-of-life period and it is possible that the higher incidence of symptom burden reported is due to the fact that complex symptoms may exist prior to death.

Almutary et al (2013) conducted a review exploring symptom burden in patients with CKD, managed by dialysis and those on a non-dialysis therapy, in stages 4 and 5 of the disease. The review was limited to those studies from the period between 2006 to 2012, and focused on the available instruments used to assess multiple symptoms in CKD. In this review, a comprehensive overview exploring the symptoms experience by patients receiving dialysis is provided, with no time limit employed to exclude studies, in order to maximise
the number of studies included in the review. This review compares and contrasts study findings with the explanations previously presented in earlier literature. It is important that researchers engaged in the study of renal disease provide HCPs with an insight into symptom burden in patients undergoing dialysis and the factors which may influence these symptoms. With the high incidence of population at ESRD undergoing dialysis, who generally experience a complex range of symptoms, it is important that these symptoms are understood and effectively addressed by HCPs providing care to this population. A literature review is required to explore these symptoms and what has been documented about the dialysis population.

In the current systematic review, we present the currently available peer-reviewed literature that addresses the symptom burden of patients undergoing dialysis and identifies the available factors which affect that experience of symptom burden.

This review seeks to answer the following questions:

- What are the levels of symptom burden in patients receiving dialysis?
- What are the most commonly reported symptoms for patients receiving dialysis?
- What are the factors that influence symptom experiences among patients receiving dialysis?

2.3. Methodology of the Review
Petticrew and Roberts (2006) define an extended systematic review of literature as an evidence review that is directly related to a particular research question, which makes the use of systematic methods essential in order to identify, select and appraise the appropriate primary research topic. According to Okoli and Schabram (2010), developing an advanced plan taking into account the transparency and comprehensiveness of the method is required for an effective systematic review, besides giving significance to high-quality information. The following work presents the review methodology, the eligibility criteria, the methods for data extraction and the data quality appraisal.

2.3.1. Database Search Strategy

This review conducted a systemic search using three important electronic databases, MEDLINE (1975-2019), EMBASE (1975-2019) and CINHAL (1975-2019). According to Moher et al. (2009), the search criteria and the search terms used in a review determine the effectiveness of the review. The search was limited to original research articles published in English and Arabic, using the following key terms: haemodialysis, peritoneal dialysis, end-stage renal failure, renal failure, symptom burden. The PICO framework was used to select keywords and identify relevant studies. A “Boolean search” was also used, which includes using AND, OR, and NOT to structure a term to be able to further produce more relevant results regarding the topic of the review. Table 3, identifies the combination of text terms and medical subject heading terms which were used to maximise the total amount of literature retrieved and Table 4 summarises the Search Strategy output.
2.3.2. Study Selection Process

A three-step selection process was carried out.

- The first stage in the process was an initial search using identified keywords. The relevance of the articles was initially determined using firstly the title, followed by the abstract. In addition, the researcher also ruled out the duplication of data obtained from multiple sources.

- The second stage was the assessment of the full study report. During this stage, the studies were pre-screened for relevance using the complete articles.

- The third stage was data extraction and quality assessment. At this stage, the data were extracted from the relevant studies using a data extraction form created by the researcher. Then the quality assessment was performed on the final studies to check the quality of the evidence included in this review.

2.3.3. The Study Review Process: Quality Scoring

According to Katrak et al. (2004), the key considerations that should be made in a critical appraisal process involve the need to examine its methodological effectiveness, comprising validity, results, and relevance, as well as analytical reliability, including consistency and lack of bias. In this review, the Joanna Briggs Institute Critical Appraisal Checklist was used for the assessment of the analytical cross-sectional studies and cohort studies which were included (Appendix 1) (Aromataris and Munn, 2017). The goal of appraising the included studies was to examine the quality of methodology in each study and
to investigate the extent to which the study has detected the potential for bias, as well as the rigour and analysis of the findings in each study. The quality score was calculated by aggregating the number of yes responses in all individual criteria. Based on the criteria, studies could receive up to 8 points. Less than 3 indicates a low quality study, from 3 to 5 a moderate and more than 5 a high quality study. The quality assessment was performed to guide the interpretation of results. No papers were excluded, in an attempt to provide sufficient data from extensive sources. All studies in this review demonstrated high overall quality with a low risk of bias. 22 studies reported as being of high quality, while 11 were of moderate quality. The majority of the studies had methodological weaknesses according to the criteria set out in the JBI, however, no study reported a low-quality study. The major issues in the included studies were related to the lack of recognition of the potential confounding variables in the design, while some studies have failed to report how they dealt with those variables. A summary of the criteria and the scores which have been given to the studies were presented in Appendix 2.

2.3.4. Ethics in the Literature Review

Vergnes (2010) argues that in order to conduct a systematic review, ethical standards need to be adhered to efficiently. The author further argues that the researcher must assure they consider the work of existing articles objectively and accurately. It is essential that a detailed search be carried out, along with the verifying of details, in addition to follow-ups on potential conflicts of interest, errors and diverse results (Vergnes, 2010). Additionally, it has been argued that prior authorisation should be obtained from researchers of the articles that have not been published in the public domain and that all the research must
be acknowledged (Silverman 2015). It should be noted here that the researchers gave the required consideration to the given ethical principles in the development of the current review.

2.3.5. Eligibility criteria

Inclusion Criteria

The inclusion criteria were, thus, defined as follows:

- Peer reviewed studies of adult patients receiving dialysis: haemodialysis or peritoneal dialysis.
- Studies which explore the prevalence of symptoms, with or without including other symptom dimensions including distress, frequency, severity, or duration.
- Only studies which include both physical and psychological symptoms (ie, no studies which include one of these dimensions).
- Studies in English and Arabic.
- Primary studies.
- No design or time limit to exclude studies.

Exclusion criteria

Exclusion criteria were defined as follows:

- Studies which explore symptoms as a component of HRQOL or other summative score.
- Studies which assess symptoms in patients receiving kidney transplantation or conservative management.
- Studies which assess one symptom, or either physical or psychological symptoms individually.
• Reviews, dissertations, conference abstracts, editorials or researcher opinions were excluded.
Table 3: *Keywords used in to carry out the review search*

<table>
<thead>
<tr>
<th>First key words attached with OR</th>
<th>Combine with</th>
<th>Second key words attached with OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom burden</td>
<td>AND</td>
<td>Renal failure</td>
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<tr>
<td>Symptom prevalence</td>
<td></td>
<td>Renal insufficiency</td>
</tr>
<tr>
<td>Symptom*</td>
<td></td>
<td>Renal disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Kidney insufficiency</td>
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<tr>
<td></td>
<td></td>
<td>Kidney failure</td>
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<td>Chronic kidney disease</td>
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<td>Chronic kidney failure</td>
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<td>Chronic renal disease</td>
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<td>End-stage renal failure</td>
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<td>End-stage renal disease</td>
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<td>End-stage kidney failure</td>
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<td>Haemodialysis</td>
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<td>Hemodialysis</td>
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<td></td>
<td></td>
<td>Peritoneal dialysis</td>
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<td></td>
<td></td>
<td>Dialysis</td>
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</tbody>
</table>

Table 4: *Summarises the Search Strategy output.*

<table>
<thead>
<tr>
<th>Database</th>
<th>until 2019</th>
<th>Initial Results</th>
<th>Total Results</th>
<th>Final Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>EMBASE</td>
<td></td>
<td>30256</td>
<td>50032</td>
<td>33</td>
</tr>
<tr>
<td>CINHAL</td>
<td></td>
<td>3763</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MEDLINE</td>
<td></td>
<td>16013</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Figure 6: PRISMA flowchart diagram
2.3.6. Data extraction

A pre-designed data extraction form was used to analyse data on the design of studies and reported results. For each study, authors, year of publication, country of origin, sample, study design, data collection methods, symptoms reported, and other factors affecting the levels of reported symptoms, was recorded. A full summary of the study findings is provided in Table 5.

2.3.7. Data synthesis and analysis

Given that the main purpose of this systematic review which was to develop a more comprehensive picture and synthesize published studies focusing on symptom burden in patients receiving dialysis and the factors that influence symptom experiences among them, all data extracted from the articles were presented narratively in text and summary tables (Campbell et al 2019). The main aim of this systematic review was to develop a comprehensive understanding and synthesize of published studies, focusing on symptom burden in patients receiving dialysis and the factors that influence symptom experiences in this population. All data extracted from the published studies was presented narratively in text and summary tables, (Campbell et al 2019). This decision was made because narrative synthesis provides a broad overview of relevant information, through a textual approach which is appropriate when studies are too heterogeneous to allow for a quantitative summary (Loannidis et al., 2008). Heterogeneous of studies was assessed according to inconsistencies in across study methodologies, sample characteristics, and the instruments used to measure symptom burden.

The following review questions were answered:
• What are the levels of symptom burden in patients receiving dialysis?
• What are the most commonly reported symptoms in patients receiving dialysis?
• What are the factors that influence symptom experiences in patients receiving dialysis?

When using a narrative summary to describe included studies and their conclusions, the reader may not be able to discern how the evidence was weighed and whether conclusions are biased. Therefore, it is recommended that tables, graphs, and other diagrams are used to emphasize the characteristics of studies and data extracted, to help compare data and to enhance transparency (Munn, 2014). It was judged important to involve two researchers to extract data independently, to ensure accuracy of the findings. To answer review questions, quantitative data was extracted from individual studies, including the prevalence of symptoms experienced by patients receiving dialysis and the factors which influenced the level of symptom burden. A figure was used to present the range in prevalence of symptoms across all of the included studies. Two tables were included, to provide a summary of the factors which influenced the experience of symptoms, as well as the most prevalent symptoms. The use of a narrative summary, and presenting data in table and figure form, was necessary to help promote clarity during data analysis. Specifically, included studies were carefully reviewed and the limitations of each (i.e., quality assessment) was described. Additionally, the entire data extraction and synthesis process was carefully detailed and was independently cross-checked and verified by multiple researchers.
2.3.8. Search outcome

After duplicate studies were removed, a total of 24,539 study titles from all databases were initially screened for eligibility by BA. After initial screening, a total of 421 studies were identified, and were screened for inclusion using the abstract by PO, HN and BA. Finally, 71 full-text articles were read and the content discussed by the review team, to assess the suitability for inclusion and to resolve any disagreements concerning inclusion or exclusion.

Figure 6: presented the PRISMA flowchart diagram. A total of 38 studies were excluded. Studies by the same authors that used similar samples and similar findings were excluded (Jablonski 2007b; Almutary et al 2017; Davison et al 2006a). To prevent repetition, the following studies were only included (Jablonski 2007a; Almutary et al 2016; Davison et al 2006b). A study protocol was excluded (Olagunju et al 2019). Portz et al (2017) were excluded due to the fact that their findings were not separated from other chronic diseases (cancer is the primary diagnosis). Studies focused on patients managed conservatively, or without dialysis were excluded (Pugh-Clarke et al 2017; Saini et al., 2006; Desbiens et al 1999; Ramer et al 2012; Bonner et al., 2008; Murphy et al., 2008; Murtagh et al., 2011; Nobel et al., 2010; Molnar et al., 2007). One review was excluded (Brennan et al 2013). Two studies focused only on the gastrointestinal symptoms without considering psychological and other physical symptoms (Salamon et al 2013; Cano et al 2007). Studies focusing only on symptoms of depression without considering the physical symptoms were excluded (Aldukhayel et al 2015; Drayer et al 2006). Studies that measured symptoms as a part of a summative score for the HRQoL, and/or not providing details in relation to symptom prevalence were excluded.
(Wu et al 2019; Shim and cho 2017; Zamanian and Kharameh 2015; Amro et al. 2014; Hays et al 1994; Sexton et al 2016; Weisbord 2004; Raj et al. 2018; Kimmel 2003; Thong et al., 2009; Chen et al 2017; Joshi et al 2010; Tannor et al 2017). A longitudinal study was excluded due to the fact that symptom prevalence at the baseline and after follow-ups were not provided (Song et al 2017). Dissertations were excluded (Johnson, 2017; Danquah, 2009). Two studies involving patients receiving dialysis and conservative management (not dialysed) were included, as findings separated the data from dialysis and non-dialysed patients (Tan et al 2017; Wan Zukiman et al 2016; Yong et al. 2009). Five relevant studies were identified after checking reference in related reviews and included studies (Zhang 2016; Cao et al 2017; Li et al 2011; Li et al 2015; Myint et al 2013). However, one of these papers was not a primary research study, but a conference abstract (Myint et al 2013). Two studies were not available in English, the Chinese studies by (Li et al 2011; Li et al 2015). Two further studies were not available in search data bases or through inter-library loan (Zhang 2016; Cao et al 2017). In total, 33 studies were considered eligible to be included in the review.
Table 5: Summary of the review findings.

<table>
<thead>
<tr>
<th>Author and year of publication</th>
<th>Aim of the study</th>
<th>Study design and sample</th>
<th>Instrument used and the number of symptoms measured</th>
<th>Mean symptoms reported</th>
<th>Most prevalence symptoms reported in this study</th>
<th>Least reported symptoms</th>
<th>Factors which influence the experience of symptoms</th>
<th>Strengths and limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdel-Kader et al. (2009)</td>
<td>To compare symptoms, depression, and QoL in patients with ESRD and those with CKD</td>
<td>Prospective cohort study. 177 participants.</td>
<td>DSI</td>
<td>11</td>
<td>Feeling tired or lack of energy, Difficulty falling asleep, dry mouth, Difficulty becoming sexually aroused.</td>
<td>Chest pain, vomiting and numbness or tingling in feet.</td>
<td>There were no associations of stage of CKD or type of dialysis with symptoms A correlation between increased symptom burden and depression were identified.</td>
<td>Strengths: Quantitatively considered the connection between mental health and the perceived experience of physical symptoms. Limitations: the sample size was relatively small.</td>
</tr>
<tr>
<td>Almutary et al (2016)</td>
<td>To examine (1) symptom burden at CKD stages 4 and 5, and dialysis modalities, and demographic</td>
<td>cross-sectional design on 436 people with CKD HD n=287; PD, n = 42; 107 = not undergoing dialysis</td>
<td>CKD-SBI</td>
<td>13</td>
<td>Five symptoms were found to be most distressing: fatigue, bone or joint pain, itching, decrease appetite</td>
<td>Depressions, sexual symptoms, nocturia</td>
<td>Psychological distress, stage of chronic kidney disease, being female or older patients were associated with greater symptom burden</td>
<td>Limited generalizability because the sample were young unlike other studies.</td>
</tr>
<tr>
<td>Berman et al. (2013)</td>
<td>To propose a category of Haemodialysis patients at elevated risk for symptom burden</td>
<td>A cross-sectional study using 57 HD patients.</td>
<td>DSI</td>
<td>11</td>
<td>Tiredness, dry skin and difficulty staying asleep.</td>
<td>Headache, vomiting and chest pain.</td>
<td>Those ineligible to transplant reported more bothersome symptoms. Mental symptoms contributed extensively to overall Symptom.</td>
<td>Strength: using Multiple regression analysis. Limitation: Small sample size. The self-reported data were obtained while patients were on dialysis when patients’ reflections on overall symptom burden may be influenced</td>
</tr>
<tr>
<td>Study</td>
<td>Location</td>
<td>Objective</td>
<td>Study Design</td>
<td>Sample Size</td>
<td>Symptoms</td>
<td>Strength</td>
<td>Limitation</td>
<td></td>
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</tr>
<tr>
<td>Caplin et al. (2011)</td>
<td>London, UK</td>
<td>To quantify the burden and duration of dialysis-associated symptoms.</td>
<td>Cohort study using 508 HD patients.</td>
<td>6</td>
<td>Fatigue, light-headedness and cramps.</td>
<td>Symptom burden was associated with being female sex, younger age, longer duration of dialysis sessions, ethnicity (Asian more than Black) and dialysis centre practice</td>
<td>Small number of symptoms investigated.</td>
<td></td>
</tr>
<tr>
<td>Cervantes et al. (2018)</td>
<td>Colorado, USA</td>
<td>To estimate the symptom burden of Latinos with ESRD and access to standard or emergency-only HD</td>
<td>Observational descriptive study using 67 HD patients.</td>
<td>ESAS 7</td>
<td>Fatigue, feeling of lack of wellbeing lack of sleep and depression Anxiety, shortness of breath, nausea.</td>
<td>Symptom burden negatively impacts HRQoL emergency-only HD patients reported experiencing more nausea compared to standard HD patients</td>
<td>Nearly all participants were of Mexican descent.</td>
<td></td>
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<tr>
<td>Cho et al. (2018)</td>
<td>Korea</td>
<td>To develop the Korean version of the DSI in patients receiving HD</td>
<td>Questionnaire study using 230 patients receiving HD</td>
<td>DSI ND</td>
<td>Fatigue, dry skin, itching, Foot (hand) numbness Vomiting, loss of sex interest and being aroused and chest pain.</td>
<td>Symptoms that are experienced by dialysis patients negatively affect their QOL</td>
<td>Culture might affect reported level of sexual symptoms. Limited exploration of factors which increase likelihood of symptoms.</td>
<td></td>
</tr>
<tr>
<td>Curtin et al. (2002)</td>
<td>USA</td>
<td>To use self-reported symptoms to categorise symptoms.</td>
<td>Cross-sectional study using 307 participants.</td>
<td>The SF-36 Physical Component Summary scale, Mental 9</td>
<td>Fatigue, itchy skin and dry mouth Painful urination, hearing loss and pelvic pain.</td>
<td>Symptoms associated with increased age, diabetes, fatigue and reduced mobility.</td>
<td>Strength: large number of symptoms were explored, large sample size and prioritisation for symptom management.</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Objective</td>
<td>Study Design</td>
<td>Measure(s)</td>
<td>Sample Size</td>
<td>Symptoms Assessed</td>
<td>Limitations/Strengths</td>
<td></td>
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<tr>
<td>Danquah et al. (2010) Houston, USA</td>
<td>To determine which symptoms are the most reported, occur most frequently, severity, and cause the most bother for HD patients</td>
<td>Cross-sectional comparative study</td>
<td>DFSSBI</td>
<td>99 HD patients</td>
<td>Tiredness, dry skin, difficulty falling asleep, itching, numbness/tingling, difficulty staying asleep, decreased interest in sex, and bone/joint pain</td>
<td>Being female patients. Age was not a predictor for symptom prevalence. Strength: measuring a wide range of symptoms</td>
<td></td>
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<tr>
<td>Davison et al. (2006b) Canada</td>
<td>To validate the modified Edmonton Symptom Assessment System</td>
<td>Cross-sectional questioner study using 507 dialysis</td>
<td>MESAS</td>
<td>7</td>
<td>Fatigue, lack of appetite, and pain.</td>
<td>Symptom burden of dialysis patients is tremendous and that this burden has a significant negative impact on patients’ HRQoL. Strength: Large sample size. Limitation: Only 10 symptoms assessed and limited exploration of factors which increase likelihood of symptoms.</td>
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<tr>
<td>Davison et al. (2010) Canada</td>
<td>To explore the association between symptom burden and HRQoL</td>
<td>Cross-sectional questioner study using 591 HD</td>
<td>MESAS</td>
<td>7</td>
<td>Fatigue, Anorexia, Pain</td>
<td>No demographic or dialysis related factors are related to symptom burden. Symptom burden is negatively impact HRQoL. Limitation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Figueiredo et al. (2012) UK</td>
<td>To determine the prevalence of symptoms (general and abdominal) in dialysis patients</td>
<td>Cohort study using 41 PD patients</td>
<td>Author-designed 21 symptoms questionnaire</td>
<td>9</td>
<td>Fatigue, lack of wellbeing, itching, cramps, loss of appetite and poor sleep, constipation and abdominal distention</td>
<td>No significant association between symptoms and age, gender, being diabetic or being PD or HD patients. Limitation: small sample size. The study measured 21 symptoms but only 7 symptoms have been provided.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Country</td>
<td>Objective</td>
<td>Design</td>
<td>Methods</td>
<td>Instruments</td>
<td>Symptoms</td>
<td>Strength</td>
<td>Limitation</td>
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<tr>
<td>Gamondi et al. (2013)</td>
<td>Switzerland</td>
<td>To collect information on the frequency and severity of pain and symptom distress among long-term dialysis patients in southern Switzerland</td>
<td>Cross-sectional, observational, multi-centre study using 123 dialysis patients</td>
<td>Visual Analogue Scale, the Brief Pain Inventory and ESAS</td>
<td>ND</td>
<td>Fatigue, pain, and lack of wellbeing, Emotional symptoms including Anxiety, Depression, sad and loss of appetite</td>
<td>Being female and were associated with increasing the reported levels of pain Pain were correlated significantly with other symptoms including asthenia, fatigue, sleep disturbances, dyspnoea, loss of appetite, nausea/vomiting and anxiety</td>
<td>Strength: including patients from multi-centre. Limitation: Only small number of symptoms assessed.</td>
</tr>
<tr>
<td>Goris et al. (2016)</td>
<td>Turkey</td>
<td>To determine the effect of haemodialysis symptoms on marital adjustment</td>
<td>Cross-sectional study using 282 HD patients</td>
<td>DSI</td>
<td>ND</td>
<td>Fatigue, muscle cramps and difficulty sleeping, leg swelling, chest pain, and diarrhea</td>
<td>This study revealed that female and illiterate patients, with low income, being housewife, having comorbid diseases and no support from their spouse had higher symptom burden scores The more symptoms the patients suffered from, the more negatively affected their marital adjustment was</td>
<td>Limitation: excluded single patients</td>
</tr>
<tr>
<td>Jablonski (2007)</td>
<td>USA</td>
<td>To examine the symptoms experienced by patients on HD</td>
<td>Cross-sectional study using 130 HD.</td>
<td>Instrument created by Author</td>
<td>5</td>
<td>Fatigue, difficulty sleeping and cramps, Pain, decreased appetite, changes in taste and restless legs</td>
<td>ND</td>
<td>Strength: explore a multidimensional characteristics of symptoms Limitation: Limited exploration of factors which increase likelihood of symptoms.</td>
</tr>
<tr>
<td>Jeong lee and Jeon (2015)</td>
<td></td>
<td>To identify the relationship between</td>
<td>Cross-sectional questionnair</td>
<td>POSs</td>
<td>ND</td>
<td>Drowsiness, pain, Vomiting, diarrhoea, Young age, having diabetes, low education, not employed patients</td>
<td>Strength: using valid tool</td>
<td></td>
</tr>
<tr>
<td>Location</td>
<td>Study Purpose</td>
<td>Study Type</td>
<td>Patients</td>
<td>Symptoms</td>
<td>QoL Change</td>
<td>Limitations</td>
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<tr>
<td>South Korea</td>
<td>Symptom clusters and QoL study using 143 patients</td>
<td>e study</td>
<td></td>
<td>Constipation, poor mobility, change in skin</td>
<td></td>
<td>Reported increasing of more severe symptoms. Lower QoL associated with perception of symptoms.</td>
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</tr>
<tr>
<td>Lowney et al. (2015) England and Ireland</td>
<td>To describe the symptom profile on a cohort of patients with ESRF.</td>
<td>Cross-sectional study using 893 HD patients.</td>
<td></td>
<td>Weakness, poor mobility and pain, Dry mouth, diarrhoea and vomiting</td>
<td>Symptom burden is associated with poorer QoL. Patients from UK reported higher symptoms than patients from Ireland. The majority of UK patients are black and Asian ethnic.</td>
<td>Strength: Large sample size. Limitations: Absence of co-morbidity indices. Demographic data on Irish non-responders are not presented in this article.</td>
<td></td>
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</tr>
<tr>
<td>Merkus et al. (1999) The Netherlands</td>
<td>To assess the impact of demographic, clinical and dialysis data on symptoms and QoL</td>
<td>Descriptive study using 226 dialysis patients (120 HD and 106 PD).</td>
<td></td>
<td>8 Fatigue, itching and muscle cramps. Lack of appetite, Nausea, and numbness in legs. Higher comorbidity, lower body percentage lean mass were associated with high symptom burden. No differences in symptom prevalence between dialysis modalities.</td>
<td>ND</td>
<td>Strength: Stringent participant selection process. Limitation: Dated research. No details about the validity of the instrument used.</td>
<td></td>
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</tr>
<tr>
<td>Moskovitch et al 2019 Australia</td>
<td>To determine the prevalence, severity, and change in symptoms</td>
<td>Cross sectional observationa l study in 160 dialysis patients</td>
<td></td>
<td>7 Lack of energy (66%) and poor mobility (58%), trouble sleeping (53%), and pain (47.5%). Vomiting, diarrhoea, mouth problems. HD patients experienced pain more commonly. Peritoneal dialysis was associated with an increased risk of</td>
<td>ND</td>
<td>Using POS-renal instead of POS, which is specifically design for renal failure patients.</td>
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<tr>
<td>Study</td>
<td>Country</td>
<td>Objective</td>
<td>Methodology</td>
<td>Symptom Burden</td>
<td>Strength</td>
<td>Limitation</td>
<td></td>
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<tr>
<td>Novak et al. (2008) USA</td>
<td>To evaluate if symptoms improved in the first year of dialysis.</td>
<td>Longitudinal study, 3, 6,9,12-month using 45 PD patients.</td>
<td>PSS 5</td>
<td>Fatigue, difficulty sleeping and difficulty concentrating. Muscle pain, bone pain and itching.</td>
<td>Strength: Data collected over 3 years, designed to assess symptom progression. Limitation: small sample size, limited psychological symptoms.</td>
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<td>Raj et al. (2016) Australia</td>
<td>To investigate the symptom burden in adults on HD</td>
<td>Cross-sectional snapshot observationa l study using 43 dialysis.</td>
<td>POS-renal 5</td>
<td>weakness or lack of energy (in 69%), followed by poor mobility, drowsiness, difficulty sleeping, and shortness of breath</td>
<td>Symptoms better recognised and managed by nurses compared with nephrologists.</td>
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<td>Tan et al. (2017) Australia</td>
<td>To compare the trajectory of symptom burden and functional status in elderly patients manage with dialysis and conservatively</td>
<td>Longitudinal study 6 months follow up Elderly receiving dialysis N=12 (5 HD and 7 PD) and patients manage conservatively n=8</td>
<td>POS ND</td>
<td>Fatigue, difficulty sleeping, poor appetite</td>
<td>Patients receiving Dialysis reported improvement in overall symptom scores, while no improvement in patients conservatively managed. Limitation: very small sample size. The follow-up period of six months may be too short to track the trajectory of symptoms. The dialysis group were younger which might influence the reported symptoms.</td>
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<td>Senanayake et al.</td>
<td>Sri Lanka</td>
<td>To assess the symptom burden and self-perceived severity of symptoms among CKD patients</td>
<td>Cross-sectional study using 1174 participants.</td>
<td>6</td>
<td>Bone pain, fatigue, difficulty sleeping. Changes in skin colour and hiccups.</td>
<td>Symptoms more severe with stage 5 CKD. Being dialyzed and presence of comorbidities, being employed with higher educational were significant predictors of less symptom burden scores.</td>
<td>Strength: Large sample size. Limitation: limit details about the participants such as ethnicity and level of education.</td>
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<td>Son et al. (2009)</td>
<td>Korea</td>
<td>To explore the level of depression experienced by patients receiving HD</td>
<td>Cross-sectional descriptive survey using 146 HD patients</td>
<td>9</td>
<td>Fatigue, Decrease interest in sex, Feeling irritable</td>
<td>Vomiting, chest pain rest leg</td>
<td>Depression was a predictor of more and severer symptoms.</td>
<td>Strength: Widely used and validated questionnaire. Limitation: small sample size limited the power to identify subtle differences between groups.</td>
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<td>Wang et al. (2016)</td>
<td>China</td>
<td>To explore the effect of sleep and QoL on symptom distress.</td>
<td>Cross-sectional survey using 301 HD patients.</td>
<td>14</td>
<td>Dry skin, itching and difficult asleep</td>
<td>Diarrhoea, vomiting and chest pain.</td>
<td>Poor sleep and QoL caused and exacerbated symptoms.</td>
<td>Strength: Widely used and validated questionnaire large sample size. Limitation: Cause and effect were not thoroughly addressed.</td>
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<td>Wan-Zukiman et al.</td>
<td>Malaysia</td>
<td>To investigate the prevalence of symptom burden and severity of ESRD patients and correlate the findings with their psychological status.</td>
<td>Cross-sectional survey using 187 participants.</td>
<td>ND</td>
<td>Fatigue, sleep difficulties, dry skin and loss of sexual drive.</td>
<td>chest pain, anxiety, and leg swelling.</td>
<td>Psychological disturbances were associated with higher symptom burden and severity</td>
<td>Strength: Comprehensive symptoms exploration Limitation: the translated DSI to Malay is not valid.</td>
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<td>Weisbord et al. (2005)</td>
<td>USA</td>
<td>To assess symptoms and their relationship to</td>
<td>Cross-sectional survey using 162 HD.</td>
<td>9</td>
<td>Dry skin, fatigue and bone pain</td>
<td>Shortness of breath, vomiting</td>
<td>Female reported high symptom burden levels. Emotional symptoms were associated with</td>
<td>Limitation: not considering the haemoglobin levels and</td>
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<td>To compare these domains between African American and White patients on chronic HD.</td>
<td>Cross-sectional survey using 160 HD.</td>
<td>DSI</td>
<td>9</td>
<td>Dry skin, fatigue and dry mouth.</td>
<td>No racial differences in symptom burden and severity. Physical and emotional symptoms are prevalent, and are correlated directly with impaired quality of life and depression in maintenance HD patients. No differences in symptom burden levels and patients race (white and black), age or duration of dialysis or being diabetic.</td>
<td>Strength: Consideration of religion and beliefs although, using invalid instrument. Limitation: Relatively small sample size.</td>
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<td>To assess renal provider recognition of symptoms and their severity in haemodialysis patients</td>
<td>Cross-sectional survey using 75 HD.</td>
<td>DSI</td>
<td>ND</td>
<td>Shortness of breath, Fatigue, nausea</td>
<td>Decreased interest in sex Chest pain Difficulty concentrating</td>
<td>No significant risks or influencers found but symptom management was better when renal provider’s awareness was greater.</td>
<td>Strength: Objective measure of provider awareness. Limitation: Relatively small sample size.</td>
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<td>To explore differences in the prevalence</td>
<td>Cross-sectional study 75</td>
<td>DSI</td>
<td>12</td>
<td>Fatigue, dry skin and dry mouth, Itching, Trouble Chest pain, anxiety.</td>
<td>Italian patients receiving chronic HD report a greater burden of comorbidity, which may bias the data.</td>
<td>The demographic and clinical characteristics between the 2 groups</td>
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<td>Yong et al. (2009) Hong Kong</td>
<td>USA and Italy</td>
<td>Prospective cross-sectional study</td>
<td>179 (HD, PD and palliative care)</td>
<td>Fatigue, dry mouth and lack of vitality</td>
<td>Symptoms than American patients, particularly those related to sexual dysfunction and psychosocial distress.</td>
<td>Older age, diabetes and lower socioeconomic status associated with more and severer symptoms.</td>
<td>Strength: High applicability. Limitation: Single centre only.</td>
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<td>Yu et al. (2012) Taiwan</td>
<td>USA and Italy</td>
<td>Cross-sectional survey</td>
<td>117 HD</td>
<td>Fatigue, dry mouth and lack of vitality</td>
<td>Restless leg, hearing impairment, change in taste</td>
<td>Being Female, increased duration of dialysis, greater depression, lower HG levels were associated with more symptoms.</td>
<td>Limitation: HG levels usually abnormal in HD patients, which make it difficult to obtain a strong correlation in relation to symptom burden levels reported. Implicit personality may confound the overall of symptoms reported.</td>
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Table 6: Summary of the symptoms prevalence of the included studies.

ND – Not Documented.

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<th>Itching</th>
<th>Anxiety</th>
<th>Feeling sad or depressed</th>
<th>Bone or joint pain</th>
<th>Muscle cramps</th>
<th>Constipation</th>
<th>Diarrhoea</th>
<th>Swelling in legs</th>
<th>Nausea or vomiting</th>
<th>Difficulty concentrating</th>
<th>Chest Pain</th>
<th>Shortness of breath</th>
<th>Numbness in feet</th>
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2.4. Results

A narrative synthesis approach was used to synthesis the findings in this review. This is one of the most appropriate approaches to help synthesize quantitative research findings from multiple studies, and is only used when meta-analysis is not possible (Popay et al., 2006). In this review, a cross-sectional design was used for 29 studies and a longitudinal design for 4 studies. These studies were conducted in 16 countries including: 11 studies in the USA, 3 in Korea, 2 in Australia, 2 in China, 2 in the UK, 2 in Canada and a single study in the following countries; Sri Lanka, Taiwan, Malaysia, Switzerland, Turkey, Pakistan, Saudi Arabia, Netherlands. While two studies were conducted between two countries; England and Ireland (Lowney et al. 2015), and the USA and Italy (Weisbord et al. 2008).

In this review the most common instruments used to measure symptom burden in patients receiving dialysis were; the Dialysis Symptom Index (DSI) in 12 studies (Weisbord et al. 2004), the Patient Outcome Symptom Scale (POSs) in five studies (Hearn 1999), the Edmonton Symptom Assessment System (ESAS) and its modified version in four studies (Bruera et al. 1991) and the Pittsburgh Symptom Score (PSS) in one study (Novak et al. 2008). Therefore, in six studies, the authors developed questionnaires to measure symptom burden. A summary of the instruments used to measure symptom burden is presented in Table 5.

2.4.1 Symptom experience

Table 6: summaries of the symptoms prevalence of the included studies. The mean/median number of symptoms reported between the studies range from
4 to 14 symptoms. Patients receiving dialysis reported a great number of symptoms concurrently. The results also showed that 32 out of 33 of the studies included in this review reported fatigue as one of the most common symptoms in patients with ESRD undergoing dialysis, with a percentage range from 38% to 96%. Several symptoms were also found to be prevalent including; dry skin (12-90%), bone and joint pain (12-88%), loss of appetite (9-82%), difficulty falling and staying asleep (28-79%), itching (37-78), dry mouth (28-77) and muscle cramp (12-63) respectively, see Figure 7.

**Figure 7:** The symptom prevalence ranges in percentages %

In this review the symptom prevalence ranges were clear and wide differences between the lowest and highest prevalence symptoms reported. In a study conducted in Switzerland in 123 dialysis patients, the percentage of patients reporting anxiety and loss of appetite was 7 (Gamondi et al. 2013). However,
this percentage was higher in Canada, where 591 HD patients were investigated, and anxiety was reported in 65% of patients and loss of appetite in 82% (Davison and Jhangri 2010). Although both studies used the same instrument (ESAS) to measure symptom burden, their findings were significantly different.

The majority of the studies found that depression, or other classified feelings of sadness, were correlated with more significant symptoms (Yu et al. 2012; Son et al. 2009; Abdel-Kader et al. 2009; Weisbord et al. 2005), while several studies found that female and older patients reported a higher number of symptoms and/or greater levels of severity of symptoms (Almutary et al. 2016; Yong et al. 2009). Other, less commonly investigated symptom influencers were lower economic status, co-morbidities, Haemoglobin (HG) levels, level of education, socioeconomic status and degree of marital support. A full summary of the study findings is provided in Table 5.

2.4.2. The Relationship between Symptom Burden and Demographic or Clinical Variables

Several studies in this review reported relationships between symptom burden and clinical variables or the demographic data of patients, such as age, marital status, gender, race, duration of dialysis, and comorbidity. However, some evidence shows no significant differences regarding associations between some of the demographic data and symptom burden. The following are the most common factors affecting symptom burden among patients receiving dialysis:
2.4.2.1. Age

Age was found to be significantly associated with the level of symptom burden in patients receiving dialysis (Almutary et al., 2016; Caplin et al., 2011; Jeong and Jeon, 2015; Curtin et al., 2002; Yong et al., 2009). Elderly patients receiving dialysis reported more symptoms than younger patients (Almutary et al, 2016; Curtin et al. 2002; Yong et al. 2009). This was in contrast to Caplin et al., (2011) and Jeong lee and Jeon, (2015) who reported that younger patients reported more symptom burden. No correlations were identified between age and symptom burden according to some researchers (Danquah et al., 2010; Davison and Jhangri, 2010; Figueiredo et al., 2012; Weisbord et al., 2005).

2.4.2.2. Duration of dialysis or dialysis vintage

Dialysis vintage or duration of dialysis is defined as the duration of time between the first day of dialysis treatment and the day of kidney transplantation (Molner et al, 2012). Duration of dialysis was found to positively associate with symptom distress (Yu et al., 2012). However, Weisbord et al. (2005) reported no correlation between dialysis duration and symptom burden when investigating 162 HD in the USA. The study did not control the confounding variable in that they did not take comorbidity and HG levels into account, which might bias the results.

Additionally, a cohort study exploring symptom burden in 508 HD patients suggested that greater dialysis duration and longer HD session time was associated with shorter dialysis recovery time, describing that with the progress of time, patients may adapt to these treatment changes and could recover more quickly from the consequences of dialysis, which might include
symptoms. In addition, in these circumstances patients may become willing to persist with dialysis therapy (Caplin et al., 2011).

2.4.2.3. Marital status
A study conducted in Turkey on 282 HD patients described that patients with no spousal support had higher symptom burden scores (Goris et al. 2016). The association between marital status and levels of symptom burden was not investigated in the studies included in this review.

2.4.2.4. Education, occupation, income, socioeconomic status
A study indicated that lower socioeconomic status is associated with a greater number of symptoms and more severe symptoms (Yong et al. 2009). Low income patients reported a higher symptom burden (Goris et al. 2016). Patients who are illiterate and housewives reported a higher symptom burden (Goris et al. 2016). Patients with low education and unemployed patients reported higher fatigue, weakness and poor mobility (Jeong Lee and Jeon, 2015). In contrast, Senanayake et al. (2017), who conducted a recent study in a large sample size of 1174 in Sri Lanka, revealed that a high symptom burden is associated with being educated up to advanced Level and being employed.

2.4.2.5. Culture and ethnicity
Several studies explored the associations between various ethnicities and cultural behaviours and reported symptoms (Caplin et al. 2011; Weisbord et al. 2007A; Weisbord et al. 2008). In one cross-sectional study of 75 American and 61 Italian patients receiving in-centre HD in two countries, the USA and Italy, less symptom burden was reported in American patients than the patients from Italian backgrounds, especially symptoms related to sexual dysfunction.
and emotional distress (Weisbord et al., 2008). In a large-scale study of 508 dialysis patients conducted in the UK exploring the symptom burden in three different ethnicities including Black, White, and South Asian, the study found that patients with an Asian subcontinent origin had higher symptom levels than those of African origin (Caplin et al., 2011). Furthermore, a study conducted in the USA including 82 Caucasian and 78 African American HD patients, the findings showed no differences in the overall symptom burden, although black patients reported higher sexual symptoms (decreased interest in sex) than white patients (Weisbord et al. 2007A).

2.4.2.6. Depression

In this review, the studies agreed that greater depression and high psychological distress were associated with greater symptoms (Abdel-Kader et al. 2009; Almutary et al. 2016; Son et al. 2009; Yu et al. 2012; Weisbord et al. 2005).

2.4.2.7. Gender

Women were found to be more likely than men to experience a higher number of symptoms or more severe symptoms (Yu et al. 2012; Weisbord et al. 2005; Gamondi et al. 2013; Goris et al. 2016; Cao et al. 2017; Zhang et al. 2016; Almutary et al. 2016; Danquah et al. 2010; Caplin et al. 2011; Gamondi et al. 2013). Only one study stated that men reported a significant higher level of a sexual symptom (difficulty becoming sexually aroused) than women, and this was constant in two ethnicities investigated in the study (African American and white) (Weisbord et al. 2007A). No significant association was identified between genders in two studies (Danquah et al. 2010; Figueiredo et al. 2012).
2.4.2.8. Co-morbidities

Higher symptom burden levels were associated with higher comorbidity scores (Merkus et al. 1999; Goris et al. 2016; Song et al. 2017; Senanayake et al. 2017) and being diabetic (Curtin et al. 2002; Jeong lee and Jeon 2015; Moskovitch et al., 2019; Yong et al., 2009). On the other hand, no correlation between being diabetic and the levels of symptoms was reported in two studies (Weisbord et al. 2005; Figueiredo et al. 2012).

2.4.2.9. Type of dialysis and CKD stages

The association between the dialysis modalities (HD or PD) and symptom burden was investigated. In some studies, HD patients associated with greater levels of symptom burden (Almutary et al. 2016; Moskovitch et al. 2019), while other studies reported no association between symptom burden and dialysis (HD, PD) (Abdel-Kader et al. 2009; Figueiredo et al. 2012; Merkus et al. 1999) or symptom burden and patients with different stages of CKD (Abdel-Kader et al. 2009). Although a study reported that dialysis patients reported better symptoms than conservatively managed patients (Tan et al. 2017), Senanayake et al. (2017), stated that symptoms were severe with stage 5 patients who are being dialysed. Those ineligible to transplant reported more bothersome emotional symptoms which contributed extensively to increase the overall symptoms reported (Berman et al. 2013).

2.4.2.10 HRQoL and Other factors

Several studies in this review agreed that higher symptom burden was associated with lower HRQoL (Raj et al. 2018; Cervantes et al. 2018; Lowney et al. 2015; Jeong lee and Jeon 2015; Davison and Jhangri, 2010 Davison et al. 2006B; Cho et al. 2018). Lower levels of HG (Yu et al. 2012), lower body...
percentage lean mass (Merkus et al. 1999), higher levels of pain (Gamondi et al. 2013), and reduced mobility (Curtin et al. 2002) were associated with a greater number of symptoms.

2.5. Discussion

This review of the global literature reveals both considerable variation and inconsistencies in the reporting of symptom prevalence across studies and the factors which may influence the reported levels of symptom burden.

The potential reasons for differences in levels of symptom burden between studies, maybe due to differences in study design and instruments used to measure symptom burden. In addition, the time when the survey was completed (before and after dialysis) may have influenced respondents’ perceptions of symptoms. In the studies included in this review, respondents were asked to recall symptoms and complete questionnaires at different times. Several studies requested respondents to recall symptoms during the last week, some studies between dialysis period, while a number of studies failed to record when data when collected.

Patients receiving HD in the USA and Iran reported higher levels of sexual symptoms (Weisbord et al., 2004; Zamanian and Kharameh, 2015) than the patients in Korea, for whom sexual symptoms were the least reported symptoms (Cho et al. 2018). The great variability of symptom prevalence may be due to the fact that age, gender, and cultural differences between these populations can affect the level of reported symptoms. The mean age of patients undergoing dialysis in Korea was 60 (Cho et al. 2018), while it was 51 in the USA (Weisbord et al., 2004), and 48 in Saudi Arabia (Almutary et al.,
Sexual desire is said to be significantly associated with age (DeLamater and Sill, 2005). It is reported that many Korean women find themselves in a difficult position regarding sexual matters after a cancer diagnosis due to the patriarchal nature of Korean culture (Kim and Kim, 2014). Almutary et al. (2016), who reported high symptoms in female patients with CKD, stated that in Middle Eastern countries, male patients possibly report fewer symptoms for cultural reasons (i.e. men should be stronger, more patient and avoid expressing their weaknesses in public). Moreover, Yu et al., (2012) reported lower symptom severity in Chinese patients and suggested that the “implicit personality”, where individuals tend to express their emotions in an implicit way, effects the level of reported symptoms. Chiou, (1998) states that this might be due to the impact of the norms in this culture, where keeping negative emotions to oneself is considered polite. As a result, Chinese people often keep their sufferings within the family instead of talking to others (Chiou, 1998). This suggests that it is important to take cultural differences into consideration, (including age, gender, traditions and cultural values) when assessing symptoms.

Old age is associated with an increased reported symptom burden. This might be due to the health deterioration associated with increasing age, as well as the illnesses associated with aging such as diabetes and hypertension (Zhang et al. 2014; Eckerblad et al. 2015). It was suggested that older kidneys are not as resilient to stress and are not able to regulate their associated physiological systems to the same extent when damaged, which may increase the experience of symptoms (Jeong and Jeon, 2015). Having another comorbidity associated with aging can lead to patients reporting more symptoms which
might not be associated with CKD (Stojanovic and Stefanovic, 2007; Almutary et al., 2016). Studies also suggested a high proportion of older adults suffering from musculoskeletal pain and back pain, which might contribute to an increase in the prevalence of symptoms in this group (D’Astolfo et al 2006). In contrast, Caplin et al., (2011) and Jeong lee and Jeon (2015) reported that younger patients were reporting more symptoms than older ones. This might be due to the fact that younger patients are facing difficulties in adapting to the restrictions imposed by the dialysis treatment as well as changes in their social and financial circumstances compared to friends and peers, whereas older patients are more adaptable to chronic ill-health (Chilcot et al 2013). This was supported by Jeong Lee and Jeon (2015), who reported high emotional instability in patients receiving dialysis as well as high levels of energy insufficiency and weakness in this group. Age was inversely associated with both anxiety and depression (Song et al 2017). It also has been suggested that sexual symptoms are significantly decreased with increasing age, which might contribute to a reduction in the level of some of the symptoms reported in elderly patients (DeLamater and Sill, 2005).

In this review, being female was associated with higher symptom scores. It has been suggested that the higher symptom rate in women could be linked to the higher rate of stress and depression seen in this gender (Aldukhayel et al., 2015; Blake and courts 1996). Depression can often alter the perception of daily stressors and result in symptoms being more severely experienced (Amro et al., 2014). Men receiving HD confronting some stressors may exhibit emotional detachment or a sense of apathy during the treatment. Different behaviour in inhibiting stressors between genders might explain the varied
levels of symptoms reported, particularly the emotional symptoms (Johnson 2017). Additionally, Caplin et al. (2011) conducted a study in 508 HD patients and reported (without explaining the reasons) that men are likely to recover to their baseline a few minutes after dialysis. It has been suggested that the hormonal differences between genders might alter the levels of reported symptoms between them (Lewis et al., 1996; Albert, 2015). Hormonal changes can cause more psychological symptoms in females than in male patients (Albert 2015). The physical structure can affect the differences in reported symptoms between genders, such as the fact that urinary tract infection symptoms are more likely among women than in men, due to women having shorter urethras than men (Eriksen and Ingebretsen, 2006). Men also tend to have larger bodies than women, which makes them less likely to be susceptible to the toxic effects of uraemia (Spalding et al. 2008). This is supported by a study included in this review, which reported that lower body percentage lean mass (the total body weight without counting the fat mass) is associated with more symptoms (Merkus et al. 1999). It has been suggested that gender characteristics and emotional differences should be taken into account when assessing symptoms (Almutary et al. 2016).

A higher level of comorbidity was associated with worse physical functioning (Amro et al. 2014; Stojanovic and Stefanovic, 2007). In this review, various causes for the variance in symptoms were posited. Patients may experience many symptoms at the same time from various sources such as renal failure (restless legs, pruritus), dialysis treatment (cramping, intradialytic hypotension, sleep disturbance) and comorbidities (diabetic peripheral neuropathy) (Brennan et al, 2013). A combination of co-morbidities is a core influencer of
symptoms reported by patients with CKD (Sexton et al. 2016). Diabetes was a common co-morbidity condition investigated as a contributor to symptom burden (Jeong lee and Jeon, 2015). Abnormal sugar levels in diabetic patients can cause nerve damage in limbs, causing the death of cells in the extremities of the body (Brennan et al. 2013). This leads to limb numbness and loss of sensation, which was reported in many of the studies included in this review (Brennan et al. 2013). It has been also stated that diabetes in patients with CKD is significantly associated with skin problems such as pruritus, changes to the skin, mouth problems (Jeong lee and Jeon, 2015), and restless leg syndrome (Moskovitch et al. 2019), while having a cardiovascular disease is associated with lack of energy, poor mobility and pain. (Jeong lee and Jeon. 2015). This outlines the complexities of distinguishing whether the symptom burden experienced by patients receiving dialysis is truly a result of kidney disease or whether other diseases are causing these symptoms.

The review highlights the importance of treating the underlying source of symptoms rather than just the symptom manifestations. According to Cho et al., (2018), the build-up of waste products is also likely to be the reason why itching was prevalent among patients receiving dialysis. The diversity of symptoms observed indicates the broad spectrum of experiences of the examined population. This is particularly apparent in lesser observed symptoms, where the varying medications provided could be the cause of rarer symptoms, such as diarrhoea (Fervenza et al., 2004). This indicates a need for more consistent treatment pathways in practice.

Cultural differences were found to be associated with increased symptoms reported during dialysis. Caplin et al., (2011) reported that Asians are more
likely to be vegetarian. Using a healthy diet supposes to reduce symptoms and the consequences of the disease. However, the study reported that Asian reported greater symptoms than those of African American ethnicity, although the study did not consider the effect of educational background on the result, which might bias the findings of the study (Caplin et al., 2011). Typically, Asians tend to have a smaller body than those of African American origin (Caplin et al., 2011). It has been suggested that smaller patients, as with those of Asian origin, would be more susceptible to the toxic effects of uraemia (Spalding et al. 2008).

No symptom burden differences were reported between the two ethnicities; African American and Caucasian patients, although the study involved a relatively small sample size (Weisbord et al. 2007A). This might suggest that differences in racial background (white and black) might not contribute to differences in symptom burden levels (Weisbord et al. 2007A), and that the life-styles, beliefs and priorities of specific cultures (American and Italian in this particular instance) might be the ultimate influencer of symptom burden (Weisbord et al., 2008). It has been suggested that African Americans were more likely to refer to their religious and spiritual beliefs as very significant aspects in dealing with their symptoms (Song et al. 2017; Weisbord et al. 2007A). Religion and spirituality affect the level of pain reported (Dedeli and Kaptan 2013). It has been suggested that the differences in the lifestyle and beliefs between cultures might contribute to the differences in symptom levels between cultures and need to be considered when measuring symptom burden (Spalding et al., 2008).
Depression was associated with increasing the level of the reported symptom (Davison et al., 2006 b; Abdel-Kader et al., 2009; Yu et al., 2012). It is not clear if depression is comorbid, causing other symptoms, or a symptom leading to other symptoms. According to Amro et al (2014), managing the physical symptoms may help to relieve the depressive symptoms in patients with dialysis. However, this is in conflict with the daily symptoms of ESRD being a source of ongoing depression, which makes identifying an initial cause and treatment more complex. Again, this suggests that a multifactorial cause of symptoms may be at play with a demand for an equally varied approach to treatment.

The effect of marital status on levels of symptom reported has not been identified in this review, although a study described that patients with no spousal support had higher symptoms burden scores (Goris et al. 2016). More studies need to investigate this relationship.

Furthermore, contrasting findings in relation to education level and its relationship to the overall symptoms distress were reported (Goris et al. 2016; Jeong lee and Jeon, 2015; Senanayake et al. 2017). Those who were lower educated reported a more severe experience of symptoms, which could be explained by the fact that the less educated patients might have less knowledge of the disease mechanism and, therefore, the importance of maintaining treatment (Plantinga et al., 2012). Similarly, those with a lower socioeconomic status were also more likely to experience symptoms. This could be because lower socioeconomic status is correlated with a lower degree of education (Kincheloe and Steinberg, 2007). Likewise, certain areas of poverty have been accused of poorer standards of healthcare in what has
been termed the ‘postcode lottery’ (Bailoni, 2011). Alternatively, the cause could be that those with higher socioeconomic status are more likely to seek private healthcare with shorter waiting lists and, subsequently, swifter treatment of symptoms. However, contrasting findings by Senanayake et al. (2017) stated that patients who are employed and with advanced education reported high levels of symptom burden, which might be due to that fact that educated patients are aware of the consequences of leaving these symptoms untreated.

2.6. Strengths and limitations

This systematic review provided a summary of all studies that reported the prevalence of symptoms in patients receiving dialysis. This review involved 33 studies conducted in 15 different countries, which could enhance the generalizability of the review findings.

A few limitations were presented in this review. Some symptoms were not included in the most available instruments used in the CKD population. These symptoms might be prevalent and might need to be highlighted. These less frequently investigated symptoms include poor mobility, hearing changes, voice changes (Lowney et al. 2015; Curtin et al. 2002), backache, and palpitations (Caplin et al. 2011), hiccups, and difficulty keeping legs still, the last of which was reported by 100% of dialysis patients in Sri Lanka and has not been a focus in other studies (Senanayake et al. 2017).

Some confounding variables were not controlled in the studies included. Patients with other comorbidities might have reported symptoms that are not related to the study focus, namely patients receiving dialysis.
Furthermore, some studies explored a limited number of symptoms, and as a consequence, this review may have inaccurately reported some of the less commonly examined symptoms. The studies in this review have been conducted in different countries, which might influence the consistency of the findings. It has been suggested that cultural differences influence symptom experience (Weisbord et al. 2008).

Unfortunately, the heterogeneity and limitations of the study designs as well as the differences between the instruments used make the comparison impossible between the studies. For example, some studies explore the presence of symptoms, while other studies explore the prevalence and the levels of distress between symptoms. Also using different instruments to measure symptom burden makes the comparison unachievable (Murtagh et al 2007), such as the use of different scales from 0 to 10 in the mESAS, and a scale from 0-5 in POSs.

2.7. Conclusion and Recommendations

This review demonstrates the considerable gaps that remain in the understanding of the symptoms which patients undergoing dialysis may experience, and indicates that these patients have a high prevalence of symptoms and considerable symptom burden.

Patients requiring dialysis treatment need to visit hospital three times each week, however, there are inadequate dialysis units in large territorial areas, which requires patients to travel distances to receive RRT (Santos and Arcanjo, 2012). Traveling to dialysis centres may be associated with burden and possibly exacerbate the symptoms experienced by dialysis patients. The
association between distance to dialysis centre and symptom burden needs to be more rigorously investigated.

This review found that patients who receive HD reported greater symptom burden than those requiring peritoneal dialysis or those in other stages of CKD. This suggests that future studies need to focus on HD patients, as this population make-up the majority of individuals requiring dialysis and reporting higher symptom burden.

Patients reporting extremely high total symptom burden associated with dialysis treatments may be more at risk of functional and emotional disability, such as fatigue, bone pain and depression. These disabilities and the need for dialysis treatment may create an additional burden for informal caregivers of patients receiving dialysis. Future research should explore the association between symptom burden and caregiver burden and the impact this may have for informal caregivers.

Additional research is required to help create effective symptom assessment strategies which take into account the factors which influence reported symptom burden. It is also suggested that future research explores and develops evidence-based management strategies to help control the symptoms experienced by patients requiring dialysis (Davison and Jhangri, 2010). Future research needs to focus on those symptoms which require immediate attention, which is dependent on the real impact of symptoms on the HRQoL of patients, especially fatigue and depression (Davison and Jhangri, 2010). This goal can be achieved by exploring the most prevalent and
distressful symptoms, as well as the amount of the negative impact these symptoms may cause to individuals.

The Majority of studies included in the review used a cross-sectional study design, with a small number using a cohort study design (Li et al 2018). This limits understanding of the cause and effect relationship in symptoms experienced and does not provide definite in-depth information related to the symptom experience and how some factors influence reported symptoms. There is a need for more in-depth research; including qualitative research to present a holistic understanding of symptom burden, how factors affect the symptom experiences and how symptoms impact on the lives of patients. This review gives an overview to enhance the understanding of symptom burden experienced by patients receiving dialysis. Future studies examining the impact of demographic characteristics, clinical characteristics, comorbidity and cultural factors will help healthcare providers identify patients who are most likely to be symptomatic in the future.
Chapter 3: Factors associated with burden in caregivers of patients with end-stage renal disease: A systematic review.
3.1. Introduction

The population of patients with Chronic Kidney Disease (CKD) is growing due to the increased prevalence of hypertension, diabetes and obesity. Globally, CKD has a high prevalence of between 11 to 13.4% in the general population, which make it one of the most common worldwide diseases (Hill et al. 2016). More than 500,000 people in the United States live with end-stage renal disease (ESRD) (Benjamin and Lappin 2018). Living with an individual in the advanced stage of CKD and being the main caregiver, can impact on the psychological health and well-being of these caregivers (Sherwood et al. 2005). Many patients with ESRD are unable physically and emotionally to meet self-care needs and require support from caregivers. The major responsibilities undertaken by caregivers include: managing the patients’ medical treatments, dietary requirements, and clinic appointments. Patients with ESRD may require lifelong replacement of kidney function, which includes dialysis or transplantation. Being treated with dialysis causes a substantial burden for caregivers, who are responsible for balancing dialysis sessions, scheduled three days a week, alongside personal activities and needs such as dressing and preparing an appropriate renal diet (Einollahi et al. 2009). The impact of providing care to patients with ESRD can be associated with psychological challenges such as depression, anxiety, increased use of medication and negative quality of life effects (Etters et al. 2008; Sherwood et al. 2005). ‘Caregiver burden’ define as the stresses that individuals experience due to providing care which include the physical, psychological, emotional, social and financial stress (George and Gwyther 1986). In the ESRD population, many
factors are related to caregiver burden (CB), such as the demographic characteristics of both caregivers and care recipients, ethnicity and comorbidity status, cohabiting with the patient, relationship with the patient and duration of caring (Etters et al 2008; Zhang et al 2016; Rodrigue et al 2010; Oyegbile and Brysiewicz, 2017; Sansoni et al., 2013; Caap-Ahlgren and Dehlin, 2002).

Hoang et al (2018), completed a mixed-method systematic review to explore the experiences of family members and friends who provided support for adults receiving HD or PD. This review considered the association between caregiver demographics and feelings of burden. However, this review did not address the holistic factors associated with CB, such as patient characteristics, relationship duration, comorbidity, culture and type of dialysis received by the care recipients.

A comprehensive and comparative overview is necessary to inform researchers and HCPs of the impact these important factors can have on caregiver experiences. The aim of this review is to analyse studies related to the experiences of informal caregivers and to summarise the characteristics associated with CB.

3.2. The review methodology

3.2.1 Eligibility criteria

- Studies including informal caregivers of adult patients with ESRD either undergoing dialysis or not.
- Studies focusing on CB and the factors associated positively or negatively to CB. CB involves the stresses that individuals experience
due to providing care including the physical, psychological, emotional, social and financial stress. The studies that investigated on some or all of these aspects were included.

- Studies including caregivers of patients with renal transplant (Tx) recipients were excluded, unless they included patients undergoing dialysis.
- Studies including caregivers of patients with early stages of CKD were excluded.
- Studies measuring CB in caregivers of patients with both ESRD and other chronic illnesses, which did not report findings for those with ESRD independently were excluded.
- Published in English.
- No time limit employed to exclude studies, to maximize literature included.
- Studies assessing the effectiveness of interventions in CB were excluded.
- Primary studies included. Reviews, conference abstracts, editorials or researcher opinions were excluded.

3.2.2 Search strategy:

This search was not limited to a specific time period. A systematic literature search was conducted in February 2019 assisted by the university librarian. Included studies were identified through searching the following electronic databases; Medline (1982-2019), Embase (1974 - 2019), CINAHL (1982-2019), PsycINFO (1809-2019) and Scopus (1985-2019). The search also included reference lists contained within review studies and other relevant
published reviews. ProQuest RefWorks was used to manage references electronically and to remove duplicate studies. A final assessment was then performed to determine eligibility or exclusion. A Boolean search was used to identify relevant studies in each database, which helped to produce studies relevant to this topic (see Table 7).

Table 7: Full electronic search strategy used

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<td>236,230</td>
<td>168855</td>
</tr>
<tr>
<td>1 AND 2 AND 3</td>
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<td>387</td>
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</tr>
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<td>Limits: Language: English</td>
<td>257</td>
<td>369</td>
<td>56</td>
<td>140</td>
<td>524</td>
</tr>
</tbody>
</table>

3.2.3. Selection of studies

Figure 8: presented the PRISMA flowchart diagram. After duplicate studies were removed, a total of 980 titles and abstracts from all databases were initially screened for eligibility independently by three authors BA, HN and PO, using the inclusion and exclusion criteria. After initial screening, 72 full-text articles were read and the content discussed by the review team, to assess the suitability for inclusion and to resolve any disagreements concerning inclusion or exclusion. A total of 49 studies were excluded for not meeting the eligibility criteria. Of these, 2 studies focused on caregivers in paediatric
patients (Kilis-Pstrusinska et al., 2013; Parham et al., 2016). Two studies examined caregiving in patients following renal transplantation (Wicks et al., 1998; Einollahi et al., 2009). A study which did not clarify the CKD stage was excluded (Park et al. 2018). 11 studies were excluded as they did not either focus on CB or include factors associated with CB (Byers, 2009; Cil Akinci and Pinar, 2014; Ferrario et al., 2002; Dos Santos Pereira et al., 2017; Piening, 1984; Piira et al. 2002; Pomaki et al., 2011; Ekelund et al., 2004; Reiss, 1990; Giacobbo Wachter et al., 2016; wick et al., 2007). Two studies characterized the degree of burden on informal caregivers as perceived by patients (Suri et al., 2011; Suri et al., 2014). Four studies evaluated the effectiveness of interventions aimed at providing support to caregivers (Chan et al., 2016; Ghane et al., 2016; Alnazly, 2018; Farahani et al., 2016). Six conference abstracts were excluded (Antonaki and Xidakis, 2016; Al Wakeel and Bayoumi, 2014; Kang et al., 2014; Kang et al., 2018; Rasmussen et al., 2017; Dorantes 2015). Five studies were excluded as they examined CB in patients with a range of chronic diseases, in addition to CKD (Grapsa et al., 2014; Arora et al., 2015; Faronbi, 2018; Nakken et al., 2015; Magliano et al., 2005). Dissertations were excluded as they may be less scientifically rigorous, than papers which are peer-reviewed and published (Affinito, 2016; Byers, 2008; Cohen, 1996: Harris, 2003; Limpanichkul, 2004; Williams, 2016). However, the reference sections of dissertations were scanned for additional papers. Five studies were not available in English (Abbasi et al., 2012; Arechabala et al., 2011; Gulpak and Kocaoz, 2014; Talebi et al., 216; TeixidoPlanas et al., 2018). Editorial and commentaries were excluded (Gayomali et al., 2008; Cohen and Germain, 2014; Klak et al., 008; Rutkowski and Rychlik, 2011; Nagarathnam.
et al., 2016). Four additional studies were added, as they had been identified in other relevant reviews, dissertations or reference lists of included studies (Bayoumi, 2014: Shakya et al., 2017: Cagan et al., 2018: Zhang et al., 2016).

Due to the heterogeneity of the data and measurement instruments used in this review, a meta-analysis approach was not possible (Impellizzeri and Bizzini 2012). The final phase of the process involved appraising the research quality of the 27 studies selected for inclusion.

3.2.4. Quality assessment tool

The Joanna Briggs Institute (JBI) quality assessment tool was used to evaluate all studies included (Aromataris and Munn, 2017). JBI is designed to be used in systematic reviews and uses appropriate criteria to assess a range of study designs. The goal of appraising included studies was to examine the quality of methodology in each study and to investigate the extent to which the study has detected the potential for bias, rigour and analysis of findings in each study. There are 8-13 questions (depending on study design), each question should be answered as “yes”, “no”, “unclear” or “NA” (not applicable).

The JBI Critical Appraisal Checklist for Analytical Cross Sectional Studies was used to screen the final list of cross sectional studies, across different domains including: inclusion and exclusion criteria, definition, location of the study, validity and reliability of exposure, measurement and outcome measurement, appropriateness of statistical analysis performed, confounding variables and how these have been considered.

We assigned specific ratings to the studies included, and referred to them as high, moderate or low quality study (Table 8). The quality score was calculated
by aggregating the number of ‘yes’ responses in all individual criteria. Based on the criteria, studies could receive up to 8 points. Less than 3 indicates a low quality study, from 3 to 5 a moderate and more than 5 a high quality study. The quality assessment was performed to guide the interpretation of results. No papers were excluded on the basis of their methodological quality, in an attempt to provide sufficient data from extensive sources. The first author (BA) performed the first quality assessment for all included studies, which was reviewed and discussed by the research team (PO, HN & HM). The studies in this review presented an overall moderate to high quality with low risk of bias. Some of the included studies failed to report standard criteria used for measurement of CB as well as to describe the setting (Table 8).
### Table 8: Quality appraisal of the included studies using JBI

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
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<td>Affinito 2018</td>
<td>Yes</td>
<td>Unclear</td>
<td>Yes</td>
<td>Unclear</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Moderate</td>
</tr>
<tr>
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<td>Unclear</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>High</td>
</tr>
<tr>
<td>Alvareza-Ude 2004</td>
<td>Yes</td>
<td>Unclear</td>
<td>Yes</td>
<td>Yes</td>
<td>Unclear</td>
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<td>Yes</td>
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</tr>
<tr>
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<td>Unclear</td>
<td>Yes</td>
<td>Yes</td>
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<td>Moderate</td>
</tr>
<tr>
<td>Avars al 2013</td>
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<td>Yes</td>
<td>Unclear</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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</tr>
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<td>Moderate</td>
</tr>
<tr>
<td>Bardak 2018</td>
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<td>Yes</td>
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<td>Yes</td>
<td>Yes</td>
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</tr>
<tr>
<td>Bayoumi 2014</td>
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<td>Unclear</td>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>High</td>
</tr>
<tr>
<td>Belasco 2002</td>
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<td>Unclear</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<td>Yes</td>
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<td>High</td>
</tr>
<tr>
<td>Belasco et al 2006</td>
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<td>Yes</td>
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</tr>
<tr>
<td>Cagan et al 2018</td>
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<td>Unclear</td>
<td>Unclear</td>
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<tr>
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<td>Unclear</td>
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</tr>
<tr>
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<td>Kilic et al 2017</td>
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</tr>
<tr>
<td>Oyegbile 2017</td>
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</tr>
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<td>Shah et al 2017</td>
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<td>Shakya et al 2017</td>
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<td>Unclear</td>
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<td>Molloaoglu 2013</td>
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</table>
3.2.5. Data extraction

The following data was extracted: identification data (author’s name, year of publication and setting), methodological data (study design, number of participants, aim and measurement tool) and findings (CB level and factors associated with burden) (Table 9).
**Figure 8: PRISMA flowchart diagram**

Number of Records to February 2019

- PsycINFO N=56
- Scopus N=524
- Medline N=257
- EMBASE N=369
- CINHAL N=140

Total Number of records from all databases N=1346

Records after duplicates removed N=980

Records after Initial title and abstract screened N=72

Records after full text analysis N=23

Additional records identified through relevant studies and included studies reference N=4

Total articles included N=27

Records excluded (N=49)
- Including caregivers of patients with other chronic illnesses (N=5)
- The stage of CKD was not identified (N=1)
- Including caregivers of Tx patients (N=2)
- Focused on caregiver of paediatric patients (N=2)
- Assessing the degree to which patients perceive themselves as a burden on unpaid caregivers (N=2)
- Dissertation (N=6)
- Conference abstract (N=6)
- Editorials or commentaries (N=5)
- Not English (N=5)
- No relevant outcomes (N=15).
3.3 Results

Narrative synthesis of study findings was performed. The search identified 27 studies which met the eligibility criteria. Of the included studies, 25 used a cross-sectional design; one study used a quasi-experimental design (Molloaoglu et al. 2013) and a mixed method design (Oyegbile and Brysiewicz 2017). Studies included in the review were completed in a variety of countries including: Seven in Turkey, four in the USA, 2 in Iran, 2 Brazil, 2 Japan, 2 Saudi Arabia and a single study in Canada, Nepal, Pakistan, Greece, Nigeria, Jordan, Spain and China. Studies which have been included investigated CB in relation to a variety of individuals with ESRD including: HD in 14 studies, PD in 1 study, both HD and PD in 4 studies, PD and Tx in 1 study, HD and Tx in 1 study, and PD, HD and Tx in 2 studies. Three studies investigated ESRD without specifying if subjects are dialysis dependent or not, and a single study included caregivers of both dialysis dependent and non-dependent patients. All the reviewed studies had been published between 1997 and 2018.

The most common tools used to measure CB were the Zarit Burden Interview (ZBI) (Zarit et al. 1980) in 19 studies, Caregiver Burden Scale (CBS) (Elmstahl et al. 1996) in 4 studies, and single studies used the Oberst Caregiving Burden Scale (OCBS) (Bakas et al. 2004), Caregiving Stress Appraisal (CSA) (Abe 2007), Novak and Guest Care Burden Questionnaire (Novak and Guest 1989), and the Caregiver Strain Index (CSI) (Robinson 1983).

The literature discussed different factors that influence CB levels, which can be categorised as:
• Caregiver socio-demographical factors (age, gender, ethnicity, marital status, education, employment, income).

• Patient’s socio-demographical factors (age, gender, marital status, education, employment, income).

• Disease related factors (treatment modality, frequency of weekly dialysis sessions, duration of dialysis, duration of illness, comorbidity, level of patient’s dependency, QoL)

• Caregiver situational factors or caregiving related factors (cohabiting status, relationship to the patient, the duration of caregiving, time of contact per week, duration of relationship between caregivers and patients)

• Environmental factors (social support)

• Psychological factors (depression, anxiety)
Table 9: Data Extraction tool: characteristics of included studies

<table>
<thead>
<tr>
<th>Author/Year/Country</th>
<th>Aim</th>
<th>Design/sample</th>
<th>Caregiver burden/measurement tool</th>
<th>Factors associated with CB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Affinito 2018 USA</td>
<td>To explore the association of burden in relation to the positive aspects and self-assessed levels of health experienced by caregivers of patients on HD</td>
<td>Cross sectional study of 89 caregivers of patients on HD</td>
<td>Mean of 29.38 out of a total score of 48 indicating moderate to severe CB using CSA</td>
<td>Caregivers with good level of health, and who viewed their caregiver role positively, experienced lesser degree of CB.</td>
</tr>
<tr>
<td>Alnazly 2016 Jordan</td>
<td>To explore the burden and coping strategies of caregivers of patients receiving HD</td>
<td>Cross sectional study of 139 caregivers of patients on HD</td>
<td>Moderate degree of burden using OCBS</td>
<td>Living with the patient was the only variable positively correlated to CB. Caregivers’ and patients’ age, gender, education, employment status, relation to patient, years of caregiving, caregiving hours per week, were not significantly related to CB.</td>
</tr>
<tr>
<td>Alvarez-Ude et al 2004 Spain</td>
<td>To evaluate the HRQoL and burden of family caregivers of chronic dialysis patients and analyse the factors associated with it.</td>
<td>Cross sectional study of 221 patients/caregivers of patients on HD and PD</td>
<td>Moderate to severe burden using ZBI</td>
<td>CB was higher in caregivers with less social support CB associated with poor physical and mental health of both patients and caregivers. Age of patients, number of caregiving hours, number of comorbid conditions of patients and caregivers, number of medications of patients, correlated positively with CB. No differences in CB were found between caregivers of patients with HD and PD.</td>
</tr>
<tr>
<td>Alwakeel &amp; Bayoumi 2016 Saudi Arabia</td>
<td>To compare the burden on family caregiver between HD and PD in Saudi Arabian population</td>
<td>Cross sectional study of 105 caregivers, 50 caregivers of patients receiving HD and 55 caregivers of patients receiving PD</td>
<td>Mean CB in patient receiving HD was 43.3 (21.7) and 49 (24.5) in caregivers of the PD group. Both reported moderate to severe burden using ZBI</td>
<td>No significant differences between CB in caregivers of patients receiving PD and HD. Caregiver’s age and education level correlated negatively to CB in the HD group. Age and level of education and dialysis duration were not correlated to CB in PD group.</td>
</tr>
<tr>
<td>Avsar et al 2013 Turkey</td>
<td>To examine the relationship between caregivers of PD and Tx patients with regard to sleep quality, anxiety, depression, and overall burden</td>
<td>Cross sectional study of 113 caregivers, 53 Tx recipients and 60 caregivers of PD patients</td>
<td>51 (96.2%) of caregivers of Tx recipients reported low CB and 30 (50%) of caregivers of patients on PD reported moderate CB using ZBI</td>
<td>CB scores were significantly higher in caregivers of PD patients compared with Tx patients The demographic data of caregivers did not significantly affect CB in either group including age, gender, income, educational level. Duration of caregiving in year was not associated to CB.</td>
</tr>
<tr>
<td>Authors</td>
<td>Research Question</td>
<td>Study Design</td>
<td>Sample Size</td>
<td>Results</td>
</tr>
<tr>
<td>------------------</td>
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</tr>
<tr>
<td>Avsar et al 2015</td>
<td>To compare the caregivers of HD patients and caregivers of patients with Tx in terms of anxiety, depression, sleep quality, and CB</td>
<td>Cross sectional study of 133 caregivers, 65 caregivers in the Tx group and 68 in the HD group</td>
<td>62 (95.4%) of caregivers of Tx patients reported low CB. 31 (45.6%) of caregivers of HD patients reported low CB and 27 (39.7%) of them reported moderate CB using ZBI.</td>
<td>CB scores were significantly higher for caregivers in the HD group compared with caregivers in the Tx group.</td>
</tr>
<tr>
<td>Bardak et al 2018</td>
<td>To compare CB, psychological symptoms in caregivers of PD, HD, and Tx, and find out associated factors</td>
<td>Cross sectional study of 127 caregivers caring for 43 PD, 42 HD, 42 Tx patients</td>
<td>Participants reported mild to moderate CB in all caregiver groups (PD, HD, Tx) using ZBI.</td>
<td>CB score was found to be higher in caregivers who reported higher level of psychological symptoms (anxiety and depression). CB score was found to be highest in caregivers of patients receiving HD and it was significantly higher than PD and Tx groups. The gender, age, occupation, marital status, education level of caregivers and patients were not associated with ZBI score. ZBI score was also not associated to caregiver relationships to the patient, living in the same house or whether caregivers take all responsibility alone or not. Longer duration of HD affected the ZBI scores positively.</td>
</tr>
<tr>
<td>Bayoumi 2014</td>
<td>To evaluate the CB of individuals who provide care for patients on maintenance HD</td>
<td>Cross sectional study of 50 caregivers for patients on HD</td>
<td>Moderate to severe burden using ZBI</td>
<td>The total caregiver burden significantly correlated positively with patient age and negatively correlated with caregiver age. Negative correlations were identified between caregivers’ and patients’ levels of education in relation to CB.</td>
</tr>
<tr>
<td>Belasco and Sesso 2002</td>
<td>To describe the characteristics of caregivers of chronic HD patients, assess their perceived burden and HRQoL and the factors influencing this burden.</td>
<td>Cross sectional study of 100 caregivers of HD patients</td>
<td>Moderate CB using CBS</td>
<td>Caregivers of male patients with a low education level (illiterate or primary), with a multiple number of patient comorbid conditions had a higher mean score burden. Caregivers who were female spouses of patients, and caring for long lengths of time, perceived a significantly greater burden than those with other types of relationships.</td>
</tr>
<tr>
<td>Belasco et al 2006</td>
<td>To describe caregivers’ characteristics and evaluate their burden and QoL</td>
<td>Cross sectional study of 201 caregivers, 161 caregivers of HD patients and 40 caregivers of PD patients</td>
<td>Moderate burden for both caregivers of elderly HD and PD patients using CBS</td>
<td>There is a significant difference noted in the environment dimension of CBS, which was better for caregivers of the elderly receiving HD than in younger patients. Caregiver’s mental status score was lower for caregivers of elderly receiving PD than caregivers of patient receiving HD. No significant influence of caregiver sex detected.</td>
</tr>
<tr>
<td>Study</td>
<td>Country</td>
<td>Objective</td>
<td>Study Design</td>
<td>Methods</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>-------------</td>
<td>----------------------------------------------------------------------------</td>
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<td>-----------------------------------------------</td>
</tr>
<tr>
<td>Cagan et al 2018</td>
<td>Turkey</td>
<td>To examine the burden of caregivers of HD patients and some related variables</td>
<td>Cross sectional study of 163 caregivers of HD patients</td>
<td>Moderate CB using ZBI</td>
</tr>
<tr>
<td>Cantekin et al 2016</td>
<td>Turkey</td>
<td>To determine the burden on primary caregivers of patients undergoing dialysis</td>
<td>Cross sectional survey of 114 patients, 54 were relatives of HD patients and 60 were relatives of PD patients</td>
<td>Caregivers of HD patients reported moderate to high burden while caregivers of PD reported low to medium levels of CB using ZBI</td>
</tr>
<tr>
<td>Harris et al 2000</td>
<td>USA</td>
<td>To identify the level of CB reported by African American caregivers of patients with ESRD waiting for Tx and to identify whether subjective burdens varied by caregiver age</td>
<td>Cross sectional survey of 78 African American family caregivers of patients with ESRD</td>
<td>Mean burden score of 18.83 (11.26) indicating little to no burden using ZBI</td>
</tr>
<tr>
<td>Jafari et al 2018</td>
<td>Iran</td>
<td>To determine the level of CB and its relationship with the QoL of caregivers of HD patients.</td>
<td>Cross sectional study 246 caregivers of HD patients</td>
<td>42.7% experiencing moderate CB and 37.4% were experiencing high to severe levels of CB, using the Novak and Guest Care Burden Questionnaire</td>
</tr>
<tr>
<td>Kilic and Kaptanogullari, 2017</td>
<td>Turkey</td>
<td>To evaluate the burden of caregivers who provided care to HD patients in two different communities.</td>
<td>Cross sectional study of 210 caregivers of patients receiving HD</td>
<td>In Turkey (central district), mild CB &amp; in Northern Cyprus (rural area) moderate CB, using ZBI</td>
</tr>
<tr>
<td>Authors</td>
<td>Country</td>
<td>Study Objective</td>
<td>Study Design</td>
<td>Level of CB Using Scale</td>
</tr>
<tr>
<td>-------------------------</td>
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</tr>
<tr>
<td>Mashayekhi et al 2015</td>
<td>Iran</td>
<td>To assess the level of CB in caregivers of HD patients</td>
<td>Cross sectional study of 51 caregivers of HD patients</td>
<td>Moderate to severe levels of CB using CBS</td>
</tr>
<tr>
<td>Mollaoglu, 2013</td>
<td>Turkey</td>
<td>To determine the burden, educational needs, influential factors, and the effects of home care education over CB among primary caregivers of patients undergoing HD</td>
<td>Pre and post-test design including 122 caregivers of HD patients</td>
<td>Moderate to severe, using ZBI</td>
</tr>
<tr>
<td>Oyegbile &amp; Brysiewicz 2017</td>
<td>Nigeria</td>
<td>To explore the CB of family caregivers of ESRD patients in South-West Nigeria</td>
<td>Mixed method study including a cross sectional survey of 96 family caregivers of patients with ESRD</td>
<td>Moderate to severe CB using ZBI</td>
</tr>
<tr>
<td>Paschou et al 2018</td>
<td>Greece</td>
<td>To explore the CB and depression in spouses of patients with CKD</td>
<td>Cross sectional study of 50 spouses of patients; 29 of whom were dialysis dependent and 21 were not dialysis dependent.</td>
<td>Moderate burden using ZBI</td>
</tr>
<tr>
<td>Rioux et al 2012</td>
<td>Canada</td>
<td>To assess CB, QOL, and depressive symptoms and to compare these with their patients’</td>
<td>Cross sectional study of 61 caregivers of HD patients</td>
<td>Low level burden perceived using CBS</td>
</tr>
</tbody>
</table>
| Rodrigue et al 2010      | USA         | To characterise the psychosocial functioning of spouse/partner caregivers.       | Cross sectional study spouse/partner caregivers of HD & PD patients before (n = 33) and after (n = 46) kidney transplantation | High CB before and after transplantation using CSI | CB was not associated with age, sex, or relationship duration even though older females reported high CB but did not reach statistical significance. High levels of patients physical health associated with lower CB. CB was higher when the patient was on HD than not yet on dialysis. Higher CB was associated with worse patient health and lower mental QOL. No differences between CB of patients before and after Tx.
<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Country</th>
<th>Objective</th>
<th>Study Design</th>
<th>Sample Size</th>
<th>CB Description</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shah et al</td>
<td>2017</td>
<td>Pakistan</td>
<td>To determine CB of patients receiving dialysis</td>
<td>Cross sectional study</td>
<td>164 caregivers of patients receiving dialysis</td>
<td>Mild to moderate CB. Using ZBI</td>
<td>A positive correlation was found between the duration of patient on dialysis/year, daily hours of caregiving and the total CB score. Low social class, high level of patients functional dependency associated with high CB.</td>
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<tr>
<td>Shakya et al</td>
<td>2017</td>
<td>Nepal</td>
<td>To assess the burden on caregivers and find out their liability for developing depression</td>
<td>Cross sectional, descriptive study design</td>
<td>164 caregivers of patients taking maintenance HD</td>
<td>The mean CB score was 46.99 ± 14.6 which indicated moderate to severe burden. Using ZBI.</td>
<td>CB increased with increasing caregiver age, decreasing education, low socio-economic status and decreasing social support. Widow caregiver reported high CB then in married and the lowest CB was on single. Relationship to patient were also found to affect burden (spouses and parents having higher CB than in children, siblings, children in laws and grandchildren). CB was significantly positively associated with caregivers depression. However, duration of dialysis, frequency of dialysis, comorbid illness of (patients) were not found to have any significant association with CB.</td>
</tr>
<tr>
<td>Shimoyama et al</td>
<td>2003</td>
<td>Japan</td>
<td>To examine the relationship in Japan between PD patients and caregivers with regard to HRQOL and CB</td>
<td>Cross sectional survey</td>
<td>34 caregivers of PD patients</td>
<td>Mean CB was 14.1 indicated little to No burden. Using ZBI</td>
<td>Caregivers of patient receiving PD reported low CB levels. CB associated with increasing age of patients and decreasing health-related QoL of caregivers.</td>
</tr>
<tr>
<td>Washio et al</td>
<td>2012</td>
<td>Japan</td>
<td>To investigate factors related to burden among caregivers of regular HD patients.</td>
<td>Cross sectional survey</td>
<td>108 caregivers of HD</td>
<td>Mean CB score of 29 indicating mild burden to moderate. Using ZBI</td>
<td>Being spouse, having chronic diseases, long time spent on caregiving is reported to be a related factor to the heavy burden among caregivers</td>
</tr>
<tr>
<td>Wicks et al</td>
<td>1997</td>
<td>USA</td>
<td>To explore QoL and CB reported by caregivers of persons with ESRD and to examine the relationship between these variables</td>
<td>Cross sectional design</td>
<td>96 caregivers of 96 Tx candidates diagnosed with ESRD</td>
<td>Little to no burden. Using ZBI</td>
<td>Neither caregiver race, gender, relationship to the patient, caregivers health level, nor patient gender significantly contributed to CB. CB did not differ by dialysis type (PD, incenter HD) or employment category (full-time, part-time). Caregivers QoL related negatively with CB.</td>
</tr>
<tr>
<td>Zhang et al</td>
<td>2016</td>
<td>China</td>
<td>To assess the burden for caring patients on maintenance HD by primary family caregivers</td>
<td>Cross sectional survey</td>
<td>151 caregiver of HD patients</td>
<td>151 caregivers (51%) reported mild to moderate burden and (25.2%) caregivers was reported moderate to severe burden. Using ZBI</td>
<td>Caregiver age increasing, low educational levels, without job, long caring hours were associated with high CB. CB was lesser degree with high level of caregiver health. CB was significantly increased in patients with more than two comorbidities and patients low income. CB did not associate with duration of HD. Relationship with patients, spouses, parents and adult children felt more stressful than siblings, daughter and son-in-laws.</td>
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</table>

HD=Haemodialysis; CB= Caregiver burden; CSA= Caregiving Stress Appraisal; OCBS= Oberst Caregiving Burden Scale; PD=Peritoneal Dialysis; ZBI= Zarit Burden Interview; Tx= Renal transplant; HRQoL= Health-related quality of life; CBS= Caregiver Burden scale; QoL= Quality of life; ESRD= End stage renal disease; CKD=Chronic kidney disease; CSI= Caregiver Strain Index.
3.3.1. Levels of Caregiver burden

In this review, 27 studies investigated the level of CB in ESRD patients, and reported a variety of contrasting findings. The majority of the studies reported moderate CB in nine studies and severe in three studies while mild burden reported in four studies.

Two studies reported severe levels of burden in England (Rodrigue et al 2010), Nigeria (Oyegbile and Brysiewicz 2017) and Turkey (Mollaoğlu et al 2013). Several studies reported moderate to severe levels of burden in caregivers of patients undergoing HD in different countries: USA (Affinito 2018), Spain (Alvarez-Ude et al 2004), Iran (Mashayekhi et al 2015), Nepal (Shakya et al 2017), two studies in Turkey (Cantekin et al 2016; Mollaoğlu et al 2013) and two in Saudi Arabia (Alwakeel and Bayoumi 2016; Bayoumi 2014). The majority of included studies reported moderate CB (Cagan et al 2018; Belasco et al 2006; Belasco and Sesso 2002; Jafari et al 2018; Paschou et al 2018; Alnazly 2016; Kilic and Kaptanogullari 2017). Two studies reported moderate CB in the caregiver dialysis group and low CB in caregivers of Tx patients (Avsar et al 2013; Avsar et al 2015). Mild to moderate burden was reported in caregivers of patients receiving HD in Pakistan, Japan and China, and patients receiving PD in Turkey (Shah et al 2017; Washio et al 2012; Zhang et al 2016; Cantekin et al 2016; Bardak et al 2018). Several studies reported mild to no burden in caregivers of patients receiving HD in Japan and the USA, and PD in the USA (Wicks et al 1997; Rioux et al 2012; Shimoyama et al 2003). Low burden was also reported in one study in dialysis dependent patients, without specifying whether these patients are HD dependent or PD dependent (Harris et al 2000).
3.3.2. Factors which affect levels of Caregiver Burden, Table 10

3.3.2.1. Caregiver and patient socio-demographical factors

*The impact of age of caregivers and patients, and perceived CB*

Seventeen out of the total twenty seven studies included, have explored the age of caregivers as a predictor of CB (Alnazly 2016; AlWakeel and Bayoumi 2016; Avsar et al 2013; Bardak et al 2018; Bayoumi 2014; Belasco and Sesso 2002; Cagan et al 2018; Cantekin et al 2016; Harris 2000; Jafari et al 2018; Paschou et al 2018; Mollaoglu et al 2013; Mashayekhi et al 2015; Shakya et al 2017; Zhang et al 2016; Rodrigue et al 2010; Kilic and Kaptanogullari, 2017).

Four studies highlighted a negative correlation between CB and caregiver age (AlWakeel and Bayoumi 2016; Bayoumi 2014; Belasco et al 2006; Mollaoglu et al 2013). In contrast, four studies reported that older caregivers tend to struggle more and experience higher levels of burden, than younger caregivers (Jafari et al 2018; Zhang et al 2016; Rodrigue et al 2010; Shakya et al 2017).

Rodrigue et al (2010) reported higher CB with increased caregiver age, although it did not reach a statistically significant result and suggested that further research is required, using a larger sample population to determine if any relationship exists. The remaining studies reported that caregiver age did not influence feelings of burden in caregivers (Alnazly 2016; Avsar et al 2013; Bardak et al 2018, Belasco and Sesso 2002; Cagan et al 2018; Cantekin et al 2016; Harris et al 2000; Mashayekhi et al 2015).

Several studies have explored the levels of CB and the care recipients age as a predictor of CB (Alnazly 2016; Bardak et al 2018; Belasco et al 2006; Bayoumi 2014; Alvarez-Ude et al 2004; Jafari et al 2018; Mashayekhi et al...
2015; Shimoyama et al. 2003). Caregivers of older patients experienced higher CB than caregivers of younger patients (Shimoyama 2003; Alvarez-Ude et al. 2004; Bayoumi 2014), while one study found high scores reported in one CB component (environmental component) in caregivers of younger patients (Belasco et al. 2006). The remaining studies reported that patients age did not influence CB levels (Alnazly 2016; Bardak et al. 2018; Belasco and Sesso 2002; Jafari et al. 2018; Mashayekhi et al. 2015).

Correlation between gender and CB

Gender has frequently been investigated as a factor in CB. Fifteen studies explored the gender of caregivers as a contribution to CB (Alnazly 2016; Avsar et al. 2013; Bardak et al. 2018; Belasco et al. 2006; Belasco and Sesso 2002; Cagan et al. 2018; Cantekin et al. 2016; Kilic and Kaptanogullari, 2017; Jafari et al. 2018; Mollaoğlu et al. 2013; Mashayekhi et al. 2015; Oyegbile and Brysiewicz 2017; Paschou et al. 2018; Rodrigue et al. 2010; Wicks et al. 1997). Many of the studies reported that female caregivers experience greater feelings of burden than male caregivers (Belasco and Sesso 2002; Cagan et al. 2018; Mollaoğlu et al. 2013; Oyegbile and Brysiewicz 2017; Rodrigue et al. 2010). However, two of these studies reported that this association did not reach a statistically significant level (Oyegbile and Brysiewicz 2017; Rodrigue et al. 2010). A number of studies have reported that there is no evidence of a relationship between CB and caregiver gender (Alnazly 2016; Avsar et al. 2013; Bardak et al. 2018; Belasco et al. 2006; Cantekin et al. 2016; Jafari et al. 2018; Kilic and Kaptanogullari, 2017; Mashayekhi et al. 2015; Paschou et al. 2018; Wicks et al. 1997).
The gender of care recipients has been investigated as a contribution to CB (Alnazly 2016; Bardak et al 2018; Belasco et al 2006; Belasco and Sesso 2002; Jafari et al 2018; Mashayekhi et al 2015; Wicks et al 1997). Two studies suggested that providing care to male patients increases the level of reported CB, regardless of the gender of caregivers (Belasco and Sesso 2002; Mashayekhi et al 2015). The remaining studies reported that there is no evidence of a relationship between CB and care recipients gender (Alnazly 2016; Bardak et al 2018; Belasco et al 2006; Jafari et al 2018; Wicks et al 1997).

**The significance of marital status in CB**

Eight studies examined the relationship between caregiver marital status (being single, married, widow or divorced) and reported CB (Bardak et al 2018; Kilic and Kaptanogullari, 2017; Cagan et al 2018; Jafari et al 2018; Mashayekhi et al 2015; Mollaoğlu et al 2013; Oyegbile and Brysiewicz 2017; Shakya et al 2017). Two studies reported that single caregivers experience higher levels of burden when caring for ESRD patients, than married caregivers (Mashayekhi et al 2015; Mollaoğlu et al 2013). These findings are supported by Mashayekhi et al (2015), who reported that being single played a significant role in some CB components, including disappointment, lack of freedom, financial difficulties and the feeling that life is unfair. However, younger caregivers confident in their ability to provide care and cope with patient problems (Mashayekhi et al 2015). Mixed findings were reported by Shakya et al (2017), who demonstrated that widowed caregivers reported higher CB levels, than those who were married, and the lowest CB was in single caregivers.
The remaining studies reported that there was no relationship between CB and the marital status of caregivers (Bardak et al 2018; Cagan et al 2018; Jafari et al 2018; Kilic and Kaptanogullari, 2017; Oyegbile and Brysiewicz 2017). No association between CB and the patient’s marital status was found (Bardak et al 2018; Mashayekhi et al 2015). One study investigated the marital satisfaction levels reported by caregivers, and no relationship was identified (Paschou et al 2018).

**Education, employment and income**

A number of other socio-demographic factors have been explored to determine if they may contribute to CB. Sixteen studies have examined the relationship between CB and caregiver’s educational attainment (AlWakeel and Bayoumi 2016; Avsar et al 2013; Bardak et al 2018; Bayoumi 2014; Kilic and Kaptanogullari, 2017; Belasco and Sesso 2002; Alnazly 2016; Cagan et al 2018; Cantekin et al 2016; Jafari et al 2018; Paschou et al 2018; Mollaoğlu et al 2013; Mashayekhi et al 2015; Oyegbile and Brysiewicz 2017; Shakya et al 2017; Zhang et al 2016). Ten of these studies reported no correlation, while five reported a negative association between CB and the level of caregiver education. The lower the level of educational attainment in caregivers, the higher the level of CB is perceived (AlWakeel and Bayoumi 2016; Bayoumi 2014; Jafari et al 2018; Shakya et al 2017; Zhang et al 2016). In contrast, a single study reported higher CB in caregivers with greater levels of educational attainment, although, this study reported that providing home care education programs to caregivers, was associated with lower perceived CB (Mollaoğlu et al 2013).
The association between CB and patient educational attainment was also investigated by (Bardak et al 2018; Bayoumi 2014; Belasco and Sesso 2002; Alnazly 2016; Mashayekhi et al 2015). Only two of these studies found that lower levels of educational attainment contributed to higher levels of CB (Bayoumi 2014; Belasco and Sesso 2002), while remaining studies reported no relationship (Alnazly 2016; Bardak et al 2018; Mashayekhi et al 2015).

Seven studies examined caregiver income as a predictor of CB (Avsar et al 2013; Cagan et al 2018; Cantekin et al 2016; Jafari et al 2018; Mashayekhi et al 2015; Mollaoğlu et al 2013; Zhang et al 2016). Lower caregiver income was found to be a factor in higher CB (Cagan et al 2018; Mashayekhi et al 2015).

Two studies explored patient’s income as a contributor to CB, one of these studies reported that low patient income was associated with higher CB (Zhang et al 2016), while the other study reported no association (Belasco and Sesso 2002).

Ten studies examined the association between CB and the employment status of caregiver, including employed, unemployed, retired, full-time and part-time work (Bardak et al 2018; Belasco and Sesso 2002; Cagan et al 2018; Jafari et al 2018; Mashayekhi et al 2015; Mollaoğlu 2013; Oyegbile and Brysiewicz 2017; Wicks et al 1997; Paschou et al 2016; Zhang et al 2016). Zhang et al (2016) suggested that CB were greater in unemployed caregivers. However, Cagan et al (2018) reported that higher CB was evident in those who were employed. Three studies examined the employment status in both caregivers and patients and detected no correlation with CB (Bardak et al 2018; Belasco and Sesso 2002; Mashayekhi et al 2015).
Ethnicity, race and religion

A small number of studies have investigated ethnicity and the race of caregivers in patients with ESRD and reported no correlation with perceived CB (Oyegbile and Brysiewicz 2017; Wicks et al 1997). Only one study examined the effect of how caregivers, who identified with a specific religious group, Islam and Christianity, can impact on the level of CB, and reported no correlation (Oyegbile and Brysiewicz 2017).

3.3.2.2. Disease related factors:

Comorbidity, duration of illness, patient’s dependency, health status and QoL:

The physical and mental well-being status of patients and caregivers was found to be negatively correlated with CB. Several studies have investigated caregiver comorbidity as a CB predictor (Alvarez-Ude et al 2004; Belasco and Sesso 2002; Cagan et al 2018; Mollaoğlu et al 2013; Washio 2012). A number of studies have reported that burden is greater in caregivers who experience comorbid conditions or health problems (Alvarez-Ude et al 2004; Mollaoğlu et al 2013; Washio 2012), while two studies reported no correlation (Belasco and Sesso 2002; Cagan et al 2018). A significant positive correlation was reported between patient comorbidity and CB, especially when patients have more than two comorbidities (Alvarez-Ude et al 2004; Belasco and Sesso 2002; Jafari et al 2018; Zhang et al 2016). Limited evidence supports a relationship between the presence of comorbid conditions in patients and CB (Shakya et al 2017; Mashayekhi et al 2015).

CB was likely to increase when a patient’s physical health deteriorates and patient functional independence declines (Alvarez-Ude et al 2004; Shah 2017;
Jafari 2018; Rodrigue et al 2010). In addition, CB was reported to increase when caregivers also experience health problems (Affinito 2018; Alvarez-Ude et al 2004). Two studies investigated the duration of illness, and reported no relationship between illness duration of patients with ESRD and CB (AlWakeel and Bayoumi 2016; Bayoumi 2014). Four studies explore the relationship between CB and HRQoL of caregivers and reported negative correlations to CB. (Jafari et al 2018; Rodrigue et al 2010; Shimoyama 2003; Wicks et al 1997).

*Duration of dialysis, number of dialysis sessions/ week and treatment modality:* Duration of dialysis is the period in which patients have been dialysis dependent. The duration of dialysis in care recipients has been explored and found to be positively correlated with the level of CB (Bardak et al 2018; Cagan et al 2018; Shah et al 2017), while other studies reported no association between dialysis duration and CB (Belasco and Sesso, 2002; Jafari et al., 2018; Mashayekhi 2015; Shakya et al., 2017). The number of weekly dialysis sessions has also been examined and found not to have a relationship with CB (Cagan et al 2018; Mashayekhi 2015; Shakya et al 2017).

Several studies have investigated treatment modality and if patients were dialysis dependent or not, in relation to reported CB (Alvarez-Ude et al., 2004; Bardak, 2018; Cantekin et al., 2016; AlWakeel and Bayoumi, 2016; Belasco et al., 2006; Wicks et al 1997). CB scores were found to be highest in caregivers of patients receiving HD, and it was significantly higher than caregivers of patients within PD and Tx groups (Bardak et al 2018), as well as for patients who were not yet on dialysis (Rodrigue et al 2010). Caregivers of PD patients
had lower levels of burden than caregivers of HD patients, and this was highly significant (Cantekin et al 2016). Two studies reported no differences between HD and PD, and reported CB (Alvarez-Ude et al 2004; AlWakeel and Bayoumi 2016; Belasco et al 2006). CB levels did not also differ by dialysis type (PD, HD, home or in-centre HD, and no dialysis) (Wicks et al 1997) and dependency (dialysis dependent or not) (Paschou et al 2018). Caregivers of patients with Tx reported lower CB than patients receiving dialysis (Avsar et al 2013; Avsar et al 2015; Bardak et al 2018). However, Rodrigue et al (2010), reported no difference between CB in caregivers providing care to patients before and after Tx.

3.3.2.3. Caregiving related factors (situation factors)

Cohabiting arrangements, caregiver relationship to patients, and duration of relationship between patients and caregivers:

Several studies examined the effect of caregiver relationships in patients with CB (Alnazly 2016; Bardak et al 2018; Belasco and Sesso 2002: Cagan et al 2018; Kilic and Kaptanogullari 2017: Mashayekhi et al 2015; Mollaoğlu et al 2013; Oyegbile and Brysiewicz 2017; Washio 2012; Wicks et al 1997; Shakya et al 2017; Zhang et al 2016). Six studies reported that caregiver relationships with the patient, was found to be a factor in CB (Belasco and Sesso 2002; Belasco and Sesso 2002; Kilic and Kaptanogullari 2017; Mollaoğlu et al 2013; Washio et al 2012; Shakya et al 2017; Zhang et al 2016). Caregivers who had relationships with the patient as spouses, parents and adult children, experienced greater stress and burden, than other caregivers including siblings, daughters and son-in-laws (Zhang et al 2016). Belasco and Sesso (2002), reported that female spouses perceived a significantly greater burden, than those with other types
of relationships, including mother, friends and son/daughter. This finding was supported by Shakya et al (2017), who found that spouses and parents, regardless their gender, had higher CB, when compared to other relationships, including children, siblings, children in law and grandchildren. Washio et al (2012) concluded that being a spouse was associated with higher burden, than in non-spousal caregivers. However, this study did not make it explicitly clear what non-spousal relationship was being examined.

Two studies conducted on caregivers of patients receiving HD in Turkey, reported different findings, and claimed that spouses as caregivers, have less burden compared to other family relatives such as sons, daughters, siblings, grandmothers and grandfathers (Kilic and Kaptanogullari, 2017) and of daughters, daughters-in-laws, and siblings (Mollaoğlu et al 2013). A number of studies suggested that the nature of the relationship with the patient did not predict CB (Alnazly 2016; Bardak et al 2018; Cagan et al 2018; Mashayekhi et al 2015; Oyegbile and Brysiewicz 2017; Wicks et al 1997).

Only one study highlighted that caregivers living with patients, irrespective of the relationship, experienced greater burden in caregiving than those relatives who live in a separate residence (Alnazly 2016), while four studies reported no effect (Bardak 2018; Cagan et al 2018; Belasco and Sesso 2002; Oyegbile and Brysiewicz 2017). Place of residency (either city or rural area), has been investigated in patients receiving in-centre HD, and found that those living in a city location, had lower CB scores, whereas caregivers living in a rural area were found to have higher CB (Kilic and Kaptanogullari, 2017; Mollaoğlu et al
2013). However, another study reported no association between residency and CB (Cagan et al 2018).

A single study reported a positive correlation between the duration of the relationship between caregivers and care recipients and caregiving benefits. Caregiving benefits of providing care in informal caregivers may involve gaining a new or different life perspective, a closer relationship with the patient, or determining their inner strength to overcome stress (Rodrigue et al 2010).

Caregiving duration indicates the time when caregivers started to take the caregiving roles (per months or year). Caregiving duration was also examined as a predictor of CB in six studies (Alnazly 2016; Avsar 2013; Belasco and Sesso 2002; Cagan et al 2018; Cantekin 2016; Washio 2012). A positive correlation was identified between the duration of caregiving and reported CB (Belasco and Sesso 2002; Cagan et al 2018; Washio 2012), while the remaining studies reported no relationship.

The time spent providing care (hours per day) has also been investigated. Longer daily hours of caregiving was found to be positively correlated to the level of CB (Alvarez-Ude et al 2004; Shah et al 2017; Zhang et al 2016). No correlation was identified in three studies (Alnazly 2016; Belasco and Sesso 2002; Oyegbile and Brysiewicz 2017). A single study investigated a variety of caregiver variables including: the number of children, smoking habits and alcohol consumption, and reported that caregivers having 3 or more children, have higher CB, with no changes in CB associated with smoking and alcohol consumption (Cagan et al 2018). One study identified positive association
between CB and the number of medications used by patients (Alvarez-Ude et al 2004).

3.3.2.4. Environmental factor:

Social support:
Social support is the any kind of support provided by the family, relatives, and friends to assist primary caregivers in their ability to cope with burden (Cohen, 2004) Social support was also examined and found to be negatively associated with CB (Alvarez-Ude et al 2004; Shakya et al 2017; Alnazly 2016).

3.3.2.5. Psychological factors

Depression and anxiety
All the studies that investigated the relationship between depression and anxiety in related to CB, reported a positive correlation between psychological health and CB (Bardak et al 2018; Paschou et al 2018; Rioux et al 2012; Shakya et al 2017; Washio et al 2012). Higher levels of psychological symptoms, including depression and anxiety are correlated with increased perceived CB.
Table 10: Summary of the factors associated with CB

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HROQoL=Health-related quality of life, HD=Haemodialysis, PD=Peritoneal dialysis, Tx=renal transplant, n= factor explored but did not showed a significant association to CB, s= factor explored and showed a significant association to CB.
3.4. Discussion

Caregivers of patients with ESRD experienced heavy burden. The findings of this review suggests different levels of burden in caregivers supporting individuals with ESRD, regardless of the country of residence. Burden levels experienced by caregivers were associated with a wide range of factors. These factors included; the socio-demographic characteristics of caregivers and patients, disease related factors such as comorbidity, duration of dialysis and dialysis modalities, caregiving situational factors such as cohabiting status, relationship to care recipient and duration of caregiving, environmental factor such as social support, and finally psychological factors such as depression and anxiety.

3.4.1. Consistency between studies

The studies included in this systematic review consistently report that gender, caregiver and patient income, time providing daily care, duration of caregiving, and relationship to patients, and cohabiting arrangements are associated with CB. Being a female caregiver is always reported as a contributor to high CB even in different populations. This finding may be due to a number of factors. For example, due to gender roles, with women still largely regarded as the primary caregiver in social situations (Chappell, et al, 2015). Therefore, women may self-impose the duty of caregiving more readily than their male counterparts. It might it be expected from women to take caregiving role and therefore receive less help and appreciation from others. Alternatively, women may more readily voice their experiences of caregiving versus men, which may be aligned to gender roles that typically result in women being more expressive.
and articulate about their emotions (Akpinar et al. 2011). Accordingly, women are more likely to express negative feelings than men (Chaplin 2015; Kiring and Gordon 1998). In Middle Eastern countries, men are less willing to complain and express weakness due to cultural reasons which portray men as strong and able to tolerate stress (Almutary 2016). If this explanation is accurate, then these findings are simply a confounding reflection of individual responses rather than a true reflection of the CB experienced by those caring for individuals with CKD.

Due to the fact that low education levels, the low income of patients and caregivers and having no job were associated with low socio-economic status, it was also suggested that this would increase the levels of CB. Individuals with a poor socio-economic condition may experience a higher CB due to, for example, the lack of adequate facilities to meet patient requirements, receive suitable care and medication, a lack of transportation, difficult access to medical facilities, and less availability of social support organisations (Belasco and Sesso 2002). Low socio-economic levels have been related to depression in caregivers of patients with dementia (Schulz et al. 1995).

A longer duration of caregiving, being a spouse, living with patients at the same residency were found to be associated with high CB. The duration of the relationship between caregivers and the care recipients and their marital satisfaction were associated positively with caregiving benefits. Living in a peripheral district was associated with increased CB. Notably, studies in this review reported that caregivers living in rural areas might report higher CB, which could be due to the probability of those patients requiring in-centre
dialysis treatment. Travelling to dialysis centres might add physical and financial burdens, which may need to be explored.

Social support was found to reduce burden (Alvarez-Ude et al 2004; Shakya et al 2017; Alnazly 2016). According to Alnazly (2016), in Jordan, spouses, children and siblings are involved in caregiving, which helps to minimise feelings of burden on the primary caregivers. The increased in the number of family members obliged to provide care to patients might contribute to reduce CB to those individuals. More studies needed to identify the association between the numbers of individuals involved in providing care and CB levels.

Spending longer time periods providing daily care is associated with increased CB, which may be due to the poor health status of patients that require more time caring. This is consistent with the findings of Serrano-Aguilar et al (2006) who reported that lower levels of physical and psychological wellbeing in caregivers is associated with a greater number of hours spent providing caregiving. This is supported by Conde-Sala et al (2010), who explained that when patients have lower levels of wellbeing, caregivers would be expected to assist in providing further hours of care.

In this systematic review, studies reported that disease related factors were associated with increased CB consistently. Longer durations of dialysis of care recipients who are receiving HD were significantly higher than caregivers of patients with PD and Tx groups. This review also reported higher numbers of comorbidities in patients and caregivers which were also associated with higher levels of CB. The physical and mental well-being status of patients and caregivers were found to be negatively correlated with CB. Caregiver stress
was likely to increase when a patient’s physical health deteriorates and patient functional dependence increases when their ability to perform daily activity declines.

Psychological symptoms such as depression and anxiety were significant contributors to CB. These findings agreed with previous findings and reported that psychological symptoms were the main factors that contributed to CB (Chiao et al 2015). Negative thoughts and feelings towards the loved one who is suffering, fear and worries may develop to depression and contribute to higher levels of depression and anxiety as a consequence of increased CB.

3.4.2. Contradictions between findings

In this review, some socio-demographic factors reported contradictory findings in relation to CB. Age of caregivers and patient, was the most frequently investigated characteristics, and was found to affect CB both negatively and positively. Younger caregivers might be more vulnerable to the challenges imposed when caregiving results in constraints such as social restrictions and financial insecurities (Kim et al 2017) with fewer problem solving skills (Mollaoglu et al 2013). Furthermore, older caregivers might be limited physically and mentally which may influence their caregiving abilities to provide care (Kim et al 2012). Either explanation makes sense and suggests that these differences may be due to the multinational research which has been included in the review which considers this problem from a diverse range of cultures. It is clear that culture shapes caregiving attitudes and this conclusion is supported by a number of authors (Anngela-Cole and Hilton 2009; Yeh et al. 2006).
This systematic review identified only two studies which explored ethnicity, race and the religious group of caregivers, and found no effect on CB. More studies are needed to examine cultural differences and the effect on CB.

In this review, it has been noted that caregivers of patients with low educational levels had higher CB scores in five studies, except for one study conducted in Turkey, which stated contradictory results and reported that more highly educated caregivers reported higher CB (Mollaoğlu et al 2013). They explained their findings and stated that caregivers with high levels of education might commit to other responsibilities and have higher expectations for their lives rather than dedicating themselves to caring.

This review highlights that single caregivers reported greater feelings of burden, in contrast to one study which suggested that single caregivers reported the lowest CB (Shakya et al 2017). Burnley (1987) reports that married patients will have a spouse who presumably can provide support in times of stress and as a consequence can reduce their feelings of burden. Married caregivers can receive support from their spouse, a resource which single caregivers cannot avail of (Burnley 1987). The author suggests that marriage can be a source of solace and support from partners and can help to reduce burden. In this review, being married was not a predictor of higher CB of caregivers of patients with ESRD, even though it was found to be a strong predictor of high CB in patients with dementia (Vaingankar et al 2016). Marital status has been investigated extensively in literature. However, marital satisfaction levels is the key for positive caregiving outcomes, being more adaptive to illness and having positive management behaviour (Randall and
Spouse perception of marital satisfaction is related to depression levels (Daneker et al 2001; Pruchno et al 2009). In this review, only one study has investigated the relationship between the marital satisfaction and CB, and found no correlation (Paschou et al 2018). This might be due to the low sample size that limited the opportunity to determine any association (Paschou et al 2018). More studies are needed to identify this association between marital satisfaction and CB.

The caregiver relationship to patient reported different findings between the studies. Three studies reported that spouses experience higher CB than other relationships (Belasco and Sesso 2002; Zhang et al 2016; Shakya et al 2017), while two studies conducted in Turkey identified that the lowest reported CB was reported by spouses (female and male) (Kilic and Kaptanogullari, 2017; Mollaoğlu et al 2013). Parent caregivers of adult patients reported high CB in two studies (Zhang et al 2016; Shakya et al 2017).

The findings in this review and in additional studies demonstrate that close family members are more likely to experience higher CB than other relatives or unrelated individuals (Lin et al 2012; Friedemann and Buckwalter 2014). This is because family members are more emotionally involved in their duties as caregivers. They feel obliged to take care of the family member even when their personal well-being is compromised (Friedemann and Buckwalter, 2014). Mollaoğlu et al (2013) suggest that lower CB was reported among spouses. This study illustrates that spouses experience a greater sense of responsibility in relation to adherence to their caregiving role, while offering care in a more emotional way. It is clear from these studies that findings might not be
generalised to different contexts in light of differences in caregiver relationships in different regions. For example, more traditional values make it clear that daughters are the preferred caregivers in Middle Eastern countries (Alshammari et al. 2017; Mollaoğlu et al. 2013), while the spouse is judged to be the most appropriate caregiver in Canada (Riouxi et al. 2012). This suggests that there may be a disparity in CB in patients across a wide range of cultural settings.

3.5. Limitations

This review was conducted to synthesise the current evidence related to CB and the factors which are associated with the CB of patients with ESRD. Informal caregiving research has largely focused on patients with cancer and mental illness, including dementia and Alzheimer’s disease. However, limited research focus has considered caregiving in patients with renal failure. This systematic review included a variety of countries from all around the world. Culture values and social patterns of all those countries were reflected in these review findings which might support the generalisability of this systematic review. However, there are several limitations that should be acknowledged. In this review language bias might be introduced. Some eligible studies were identified from the title and abstract scanning, unfortunately these were unavailable in English in full text (Abbasi et al. 2012; Arechabala et al. 2011; Gulpak and Kocaoz 2014; Talebi et al. 216; TeixidoPlanas et al. 2018). Additionally, the majority of the studies included used a convenience sample. This method may increase the risk of bias as the study participants may not be typical of the population. Moreover, due to different instruments used to
measure CB, a variety of results were reported. Each instrument has different components to measure CB, for example CSA comprises two components; social constraints and physical exhaustion. ZBI includes in addition to the previous components the guilt strain, while CBS contains isolation, disappointment and emotional involvement. These differences in the measurement criteria of CB were due to a lack of a conceptualisation or constant definition for CB in the literature (Chiao et al 2015; Chou et al 2003). These differences in CB concepts and data collection instruments might contribute to the existence of differences in the results reported.

3.6. Conclusion

This review provides evidence to support the work of HCPs, to help professionals understand the factors which may impact on CB when assessing CB. This review will help HCPs to consider the important factors when measuring CB, or targeting caregivers for interventions related to burden. This review includes studies from a range of countries and this feature enhances the generalizability of findings contained within the review.

It has been clearly discussed in published literature that there are negative experiences for caregivers providing care to patients with ESRD. Therefore, future research should adopt a more holistic approach to the study of burden and focus more on the positive experiences of caregiving, rather than judge caregiving to always be a negative experience for caregivers. The positive benefits of caregiving, should be used in the future to assist the development of appropriate interventions by HCPs to enhance caregiver well-being.
The quantitative measures of ‘caregiver burden’ employed in this review, failed to identify important contextual elements of the caregiving experience and this limitation supports the use of mixed method approaches in the future, to ensure a more comprehensive understanding of caregiver burden (Bastawrous, 2013).

Differences between findings in this review and previous studies, may be due to the multinational research which has been included in this review, which considers this problem in a diverse range of cultures. It is clear that culture shapes caregiving attitudes and this conclusion has been highlighted previously by a number of authors (Anngela-Cole and Hilton 2009; Yeh et al. 2006). In the future it is important that burden research explores how cultural beliefs may influence caregiver behaviours toward the experience of providing care to patients with a range of health problems.

The majority of patients with ESRD, receive regular dialysis treatment within hospital settings. Traveling from and to dialysis centres may be a significant source of burden for patients and their caregivers. Further research is required to provide evidence of any association between CB and the distance from home to hospital for dialysis treatment.

A number of studies in this review have reported that burden is greater in caregivers when the patient’s health status declines. Health decline may involve comorbidities and lower level of independence. However, the key element is that the symptom associated with comorbidity might be the main contributor to increase caregiver burden in the informal caregivers. However,
no previous study has explored the symptom burden in care recipient and CB in their informal caregivers.

3.6.1. Rational for the study:
Following a review of literature, a majority of published studies were found to have investigated the prevalence of symptoms, or the quality of life of the HD population. However, these studies did not provide insights or in-depth experiences of living with symptoms, the interrelationship between symptoms, and the impact of symptoms on the patient’s life. A small number of studies in Saudi Arabia have explored patient receiving HD, however, these studies have only examined individual symptoms, such as depression and sleep disturbance (Al Zaben et al., 2014: Al-Jahdali, 2012). As a result, there is a limited understanding of the holistic experience of symptom burden and the factors which can influence reported symptoms. A study conducted in Saudi Arabia by Almutary et al. (2016) assessing various symptoms of CKD who are receiving dialysis and non-dialyzed using a cross-sectional design. However, there was a lack of the focus on interviewing patients to achieve a range of perspectives in some depth, to explore patients’ views on HD-related symptoms and its management (Cox et al 2017). Symptom assessment and management have been identified as priorities for research on clinical care for patients receiving HD or who are likely to need dialysis in the near term (Davison et al 2015; Manns et al 2014).

Curtin et al., (2002) suggested that one way to understand the interrelationships between symptoms, self-management and functional status is to identify the symptoms which patients experienced and how symptoms are
perceived and valued. This study provides an in-depth experience of symptoms as reported by patients receiving HD and assesses the multidimensional nature of symptoms including distress, severity, frequency and duration. It is important to stress that the severity of symptoms in individuals receiving HD, does not always result in the individual reporting distress (Jablonski, 2007), while on contrary symptom distress often strongly related to symptom intensity (Backer, 2006).

In Saudi Arabia the number of individuals with ESRD and receiving HD continues to increase (Al Sayyari and Shaheen, 2011). Patients receiving HD are associated with a high symptom burden, which may lead to a decline in the individual’s HRQoL and poor health outcomes (Yong et al. 2009). However, HCPs are mostly unaware of the occurrence of these symptoms in patients requiring HD and underestimate the severity of symptoms (Bossola et al., 2019; Claxton et al., 2010; Weisbord et al., 2007; Raj et al., 2017). Reducing symptom burden is dependent upon focusing on the symptom experience, the factors which increase burden, how these factors influence the symptom experience as well as focusing on the current self-management strategies which individuals use to alleviate symptoms.

Previous studies have failed to explore symptom burden, its impact and its management, particularly in Saudi Arabia. This study provides a comprehensive understanding of the complex management strategies which patients may use to manage their symptoms, and the potential barriers to symptoms management. This thesis also presents an understanding of the
lived experience of individuals receiving HD within a culture setting influenced by unique traditional features and religion principals (Alkahtani et al 2013).

Additionally, the review reported that living with an individual in the advanced stages of CKD and receiving regular HD, can impact on the psychological health and well-being of caregivers (Sherwood et al 2005). Many patients with ESRD who receiving regular HD, are unable physically and emotionally to meet self-care needs and require support from caregivers and reported high caregiver burden (Alnazly, 2016). Patients who are treated with HD causes a substantial burden for their caregivers, who are responsible for balancing dialysis sessions, scheduled three days a week, alongside personal activities and needs such as dressing, preparing an appropriate renal diet, administration of medication and managing other comorbidities (Einollahi et al 2009). The impact of providing care to patients with HD, can be associated with psychological challenges such as depression anxiety, increased use of medication and negative quality of life effects (Etters et al 2008; Sherwood et al 2005).

Providing care to a sick family member can have a positive and enhancing relationship between the caregiver and care recipient, and accomplish enhanced family harmony, and promote resilience in caregivers (Hinrichsen et al., 1992). Research should adopt a more holistic approach to burden and focus more on the positive experiences of caregiving, rather than judge caregiving to have a mainly negative outcome. Positive benefits of caregiving, could be used in the development of future appropriate interventions to enhance caregiver well-being. It has been suggested that quantitative
measures of ‘caregiver burden’ fail to identify important contextual elements of the caregiving experience and this limitation supports the use of a mixed method approaches to ensure a more comprehensive understanding of caregiver burden (Marina Bastawrous 2013). Unfortunately, limited research about the experience of caregiving for ESRD patients receiving HD in Saudi Arabia, is available.

Additionally, limited research about the experience of caregiving for ESRD patients receiving HD in Saudi Arabia, is available. It is generally believed that religion, cultural beliefs, ethnicity may shape the experience of caregiving and contribute to different perceptions of the meaning of this concept (Pharr et al 2014). Saudi Arabia people are influenced by culture (Alkahtani et al 2013), which may influence the levels of perceived caregiver burden (Aranda et al 1997). Although, the caregiving role may be similar across different cultures, the experience and meaning of caregiving between cultures may express differently.

In this study we sought to increase awareness about the nature of symptoms and possible interaction between symptoms that may occur and explain the predictors that influence the levels of symptoms burden and its outcome. This study could add a new knowledge to facilities the assessment, and management of symptom burden in people receiving HD. This study also provides a unique insight into the experience of the informal caregivers who providing care to the patients receiving HD. Different culture reveal a new point of views as well as a new coping strategies to adapt with illness.

3.6.2. Aim and Objectives of the study:
The main aim of this study is to address the gap in knowledge in relation to the experience of symptom burden of patients with ESRD receiving HD and their caregivers to achieve this aim, the following objectives were presented:

**Phase 1-A: Cross sectional design with patients**
- Measure symptom burden of patients receiving HD using the Chronic Kidney Disease-Symptom Burden Index (CKD-SBI) (Almutary et al., 2015).
- Identify the association between symptom burden scores of patients and the following predictors: age, gender, education level, marital status, income, co-morbidity, employment, distance from hospital, and duration of dialysis.

**Phase 1-B: Cross sectional design with caregivers**
- Measure the burden of caregivers in patients receiving HD using Zarit Burden Index (ZBI). (Zarit et al., 1980)
- Identify the association between caregiver burden scores in relation to the following predictors: age, gender, income, relationship to patients, education level, co-morbidity, and co-habiting status.
- Explore the association between symptom burden and caregiver burden.

**Phase 2: Qualitative descriptive design for patients and caregivers**
- To explore the impact of symptom burden on patients.
- To explore how patients, control and manage their daily symptoms.
- To explore the experience of informal caregivers in providing care to patients receiving HD.

**3.6.3. Research questions**

This study seeks to answer the following research questions:
Phase 1 - A cross sectional design with patients

- What is the level of symptom burden for patients receiving HD?
- What are the factors that predict symptom burden among HD patients?

Phase 1-B cross sectional design with caregivers of patients receiving HD:

- What is the level of caregiver burden?
- What are the factors that predict caregiver burden?
- What is the association between patient symptom burden and caregiver burden?

Phase 2 Qualitative descriptive design - patients and caregivers

- What is the experience of symptom burden for patients receiving HD?
- What is the experience of caregiver burden for caregivers of patients receiving HD?
- What management strategies are used by patients receiving HD to manage symptoms?

Integration question:

- How do the insights gained from the qualitative data help to explain the impact of symptom burden and the factors associated with symptom and caregiver burden identified in the quantitative analysis?
Chapter 4: Methodology
4.1. Introduction
The purpose of this chapter is to describe the methods used in this thesis. This research aims to explore the symptom burden, the factors influence symptom experience and the management strategies used by patients receiving HD. It also aims to assess the level of burden in the caregivers of these patients, the relationship between patient and caregiver burden, and to explore factors that may influence reporting of patient and caregiver burden. The first part of this chapter presents the research aim and objectives. It also provides a description of the study design, theoretical framework, sample, setting, data collection, data analysis and ethical consideration.

4.2. Aim, Objectives and Research questions (Figure 9):
The main aim of this study is to address the gap I knowledge in relation to the experience of symptom burden of patients with ESRD receiving HD and their caregivers to achieve this aim, the following objectives were presented:

**Phase 1-A: Cross sectional design with patients**
- Measure symptom burden of patients receiving HD using the Chronic Kidney Disease-Symptom Burden Index (CKD-SBI) (Almutary et al., 2015).
- Identify the association between symptom burden scores of patients and the following predictors: age, gender, education level, marital status, income, comorbidity, employment, distance from hospital, and duration of dialysis.

**Phase 1-B: Cross sectional design with caregivers**
- Measure the burden of caregivers in patients receiving HD using Zarit Burden Index (ZBI). (Zarit et al., 1980)
• Identify the association between caregiver burden scores in relation to the following predictors: age, gender, income, relationship to patients, education level, co-morbidity, and co-habiting status.

• Explore the association between symptom burden and caregiver burden.

**Phase 2: Qualitative descriptive design for patients and caregivers**

• To explore the impact of symptom burden on patients.

• To explore how patients control and manage their daily symptoms.

• To explore the experience of informal caregivers in providing care to patients receiving HD.

**Research questions**

This study seeks to answer the following research questions:

Phase 1-A cross sectional design with patients

• What is the level of symptom burden for patients receiving HD?

• What are the factors that predict symptom burden among HD patients?

Phase 1-B cross sectional design with caregivers of patients receiving HD:

• What is the level of caregiver burden?

• What are the factors that predict caregiver burden?

• What is the association between patient symptom burden and caregiver burden?

Phase 2 Qualitative descriptive design - patients and caregivers

• What is the experience of symptom burden for patients receiving HD?
• What is the experience of caregiver burden for caregivers of patients receiving HD?
• What management strategies are used by patients receiving HD to manage symptoms?

Integration question:

• How do the insights gained from the qualitative data help to explain the impact of symptom burden and the factors associated with symptom and caregiver burden identified in the quantitative analysis?
Phase I: cross sectional design

Phase I-A Patients
- Measure the symptom burden of patients receiving HD.
- Identify the association between symptom burden scores of patients and the following predictors: age, gender, education level, marital status, income, co-morbidity, employment, distance from hospital and duration of dialysis

Phase I-B Caregivers
- Measure the burden of caregivers in patients receiving haemodialysis.
- Identify the impact on caregivers' burden scores in relation to caregivers' age, gender, income, relation to patients, education level, comorbidity, and whether they live together or not.

- Explore the association between symptom burden and caregivers’

Phase II: Qualitative descriptive
- To explore the impact of symptom burden on the patient’s life
- To explore how patients control and manage symptoms
- To explore the effect of caregiver burden in the informal caregivers of patients receiving HD

Figure 9: Study Aim and Objectives
4.3. Introduction and rational for Mixed Methods research (MMR)

Generally, researchers tend to use either quantitative or qualitative research approaches (Leech and Onwuegbuzie, 2009). However, the use of a single research approach, quantitative and qualitative methods, has a number of obvious strengths and weaknesses (Bamberger, 2012).

Quantitative researchers frequently use a deductive approach, and predominantly use numbers or patterns to provide meaning, patterns of association, deduction of causality and determining the pervasiveness of phenomena (Bryman, 2015). Quantitative research typically works within a positivist paradigm, on the basis that the knower and the known are independent (Teddlie and Tashakkori, 2009). This research approach offers a superficial explanation for a complex cultural or social phenomena of a phenomena, and commonly fail to provide deeper understanding of a phenomenon (Cresswell and Plano Clark 2011; Tikly, 2015; Tariq and Woodman, 2013). Qualitative researchers primarily work with a constructivist or interpretivist paradigm, and consider the knower and known as conjoined (Teddlie and Tashakkori, 2009; Flick 2009: Creswell and Plano Clark, 2011). Qualitative research is mainly inductive, and allows for the exploration of previously unknown processes, explanations of why and how phenomena occur, and the range of these effects (Pasick et al., 2009; Pollock, 2012; Peter, 2015). A strength of qualitative research design is that it concentrates on the context and meaning of human lives and experiences, and helps to understand phenomena deeply and in detail (Cresswell and Plano Clark 2011; Atieno, 2009). Robust qualitative studies are able to produce a strong theory that is appropriate to contexts outside of the study area in question, assisting to lead
policy-makers and HCPs (Murphy et al., 1998). Although this design provides an in-depth detailed description about phenomena, it fails to allocate rates and frequencies to the linguistic features which are identified in the data, consequently rare phenomena obtain similar focus as more frequent phenomena (Atieno, 2009). Results from the qualitative research cannot be extended to larger populations, with the same levels of assurance such as in the quantitative research, which is due to the fact that findings are not examined for statistical significance (Atieno, 2009).

Obtaining an understanding of the strengths and weaknesses of quantitative and qualitative research positions the researcher at a point to combine various research strategies, and to use the fundamental principles of a MMR (Johnson and Turner, 2003). According to this principle, researchers may gather data using various research methods, approaches and strategies, and this can result in complementary strengths and non-overlapping weaknesses (Johnson and Turner, 2003). The use of this principle is a key basis of explanation for MMR, and will be more advantageous than the use of a single design study (Johnson and Onwuegbuzie, 2004). A mixed method approach extends beyond gathering qualitative data from interviews, or collecting several types of qualitative data (e.g., interviews, observations) or several forms of quantitative data (e.g., surveys) (Creswell and Plano Clark, 2011). Analysis of multiple sources of data enable a more holistic awareness of health issue, than can be achieved by the collection of a single data source (O’Cathain, Murphy, and Nichol, 2008; Lewin, Glenton, and Oxman, 2009; Fetters, Curry, and Creswell, 2013).
A mixed-methods research (MMR) design is an alternative to the independent use of either quantitative or qualitative research (Teddlie and Tashakkori, 2009). Mixed methods research is defined as “the class of research where the researcher mixes or combines quantitative and qualitative research techniques, methods, approaches, concepts or language, into a single study” (Johnson and Onwuegbuzie 2004: P17). The emergence of MMR, coincides with the perceived limitations with the use of qualitative and quantitative independently, and now MMR is considered as the third research design, alongside quantitative and qualitative research designs (Doyle et al 2009; Johnson and Onwuegbuzie 2004; Creswell et al 2011). The goal of MMR is not to search for corroboration, but rather to expand researcher understanding (Onwuegbuzie and Leech, 2004). MMR involves the use of a combined quantitative and qualitative design, to merge the strengths of each method and to minimise the weakness of each design. Using a mixed method design enables a holistic understanding of health issues and possible resolutions, as well as helping to bridge the division between quantitative and qualitative research approaches (Onwuegbuzie and Leech, 2004).

Health care research is increasingly moving away from the dichotomies or polarisation associated with qualitative and quantitative research with the mixing of designs providing a better understanding the needs and experiences of patients (Curry et al., 2009). In health science research, there is an incessant need to improve and develop methodological approaches, to enhance the collection, analysis, and reporting of diverse data via new technologies and platforms (Creswell et al., 2011). The diversity of data demonstrates the nature of public health problems, which may influence health
status, such as variances in the population such as; age, ethnicity and culture:
and behavioural factors such as poor adherence to treatment (Creswell et al.,
2011). This diversity of data may need to increase the integration of several
methods, to examine a complicated health issues such as the cultural and
social shapes of illness, patient-provider interactions, and health, and
wellbeing.

Mixed methods research begins with the assumption that researchers collect
data based on the type of health-related question and can address the aim of
research more comprehensively than using a single method (Creswell and
Clark 2007). Research questions benefit from using MMR as they tend to be
more complex and board with several facets that can be achieve more
effectively than using either quantitative or qualitative methods (Tariq and
Woodmen, 2013).

Indications for using MMR are where the phenomena is complex and using
one method will not be adequate (Creswell et al., 2011). Creswell et al., (2011)
and Morse and Niehaus, (2009) suggest that the use of MMR can strengthen
the validity of findings by confirming conclusions from an additional
perspective, which reduces the risk of bias, which can occur when using a
single research method. The five reasons why researchers may use both
quantitative and qualitative methods in a single study include:
complementarity, development, initiation, expansion and triangulation (Greene
et al 1989). Complementarity involves seeking illustration, elaboration and
clarification of findings from one method with the results from the other method.
Development involves the use of findings from a single method study to inform
the development of a further method to study the same concept. Initiation is a process where quantitative and qualitative research approaches are employed to explore areas of incongruence, to help seek new insights into phenomena. Expansion involves examining different aspects of a research question, where each aspect warrants the use of a different research method. Triangulation involves the use of data obtained by quantitative and qualitative research approaches, to reduce bias and corroborate findings (Tariq and Woodman 2013; Crump and Logan, 2008). In this study the purposes for using a MMR design was primarily complementarity, although all other purposes mentioned also applied to this study.

This study involved the exploration of the levels of burden in patients receiving HD and their caregivers, and the association between levels of burden and participants characteristics. The most appropriate research design to explore levels of burden as well as the significance association pattern between the levels of burden and any influential factors was the use of a quantitative research method. While a qualitative semi-structured interview approach was considered to be the most appropriate research method to explore the symptom burden in patients and caregivers. The use of a qualitative approach will also help to provide understanding of any factors and potential cultural influences that may contribute to any detected differences in study outcomes. The quantitative phase of the study enabled the researcher to identify any potentially significant associations in study results. The qualitative phase of the study allowed the researcher to obtain an in-depth understanding of the lived experience of receiving HD and its association with other symptoms which may cause disparities in the experience of burden for different individuals.
The researcher made the decision to use an explanatory sequential design rather than a convergent parallel design, exploratory design or embedded design (Creswell et al. 2011). The mixed-method sequential explanatory approach involved two different study phases, including a quantitative phase followed by a qualitative phase (Ivankova, Creswell and Stick, 2006). In this approach, quantitative data was collected and analysed in phase one, and in phase two the researcher collected and analysed qualitative data to help elaborate or explain quantitative findings obtained in phase one. The qualitative phase of the study partially builds on the quantitative phase and findings from both phases of the study were combined in the intermediate and final stage of the study.

The rationale for this approach is that the analysis of quantitative data provides a general understanding of the research problem including: symptom burden levels, caregiver burden levels, and factors that influence the experience of burden in both samples. The analysis of qualitative data refines and explains statistical results by exploring participants’ experiences and insights in more depth (Rossman and Wilson 1984; Tashakkori and Teddlie 1998; Creswell 2003). The advantage of using a mixed-methods sequential explanatory approach is that it provides an opportunity to explore quantitative results in more detail, especially when the unexpected may arise in quantitative data (Morse 1991; Creswell, Goodchild, and Turner 1996; Creswell 2017). A potential difficulty in using a MMR design is that this approach is time consuming and data collection and analysis will span a considerable period of time (Ivankova, Creswell and Stick, 2006). Figure 10 illustrates the procedure of using MMR in this study.
Figure 10: Visual model illustrating the use of Mixed-Methods Sequential Explanatory Design procedures in this study
4.4. Theoretical framework

Theoretical framework offer structure for a complex investigation of health behaviours, social determinants of health, or patient and family-focused health care, and facilitate translation of research findings into practice (Forthofer, 2003). Using a framework in research could assist to navigate the uncertainty in mixed methods research, help addressing research questions and providing a map for combining the what with the why to obtain additional understanding of the subject (Evans et al, 2011). Following an examination of the literature, two theoretical frameworks were judged to be the best used to guide this study supported by the rational for the selection.

4.4.1. Theory of Unpleasant Symptoms (TOUS)

Theoretically, this study is based on the theory of unpleasant symptoms (TOUS). The main purpose of this study was to measure symptom burden in HD patients and the factors which influenced reported symptoms. TOUS provides a holistic insight into the symptom experience of single or multiple symptoms and the impact on the patient’s life, which may influence a particular outcome (Lenz et al., 1997). TOUS was first published in 1995 (Lenz et al., 1995) and subsequently updated in 1997 (Lenz et al., 1997) to reflect the experience of single or multiple symptoms and how symptoms influence performance and outcome. Lenz et al., (1995) initially focused on the following symptom concepts, dyspnoea and fatigue, and concluded that all symptoms differ from each other, but share similar dimensions including: duration (frequency of symptoms), intensity (level of severity), quality and distress (level of discomfort) (Lenz et al., 1995; 1997). The assumption which underpins
TOUS, is that there are commonalities between symptoms this should guide future research, practice and theory development (Lenz et al., 1997). The TOUS was further developed by Lenz et al (1997), and three main components of symptoms were identified, symptom experience, factors influencing symptoms, and the consequences of the symptom experience.

4.4.1.1. Symptom experience

Symptom experience is defined as, “the perception of the frequency, intensity, distress, and meaning which occurs, as symptoms are produced and expressed” (Armstrong, 2003 P. 602). The TOUS states that each symptom can be measured separately or in a group of symptoms. Each symptom is different and is dependent on its unique characteristics. For example, symptoms which are reported as severe, may not necessarily be reported as distressing (Myers, 2009). Furthermore, it is difficult to measure symptom experience from one person to another, because this evaluation is influenced by individual perceptions and level of tolerance (Rodgers et al., 2013; Lenz et al., 1997). These variations are due to the individuality of the person experiencing symptoms, and maybe influenced by educational level, age, and any perceptual disorder, which may influence individual interpretations of the symptom experience (Lenz et al., 1997). TOUS has been used as a framework to support the study of symptom identification and verification in patients with chronic diseases (Chen and Tseng, 2006). According to Lopes-Júnior (2015), unpleasant symptoms, their interactions, synergy and complexity are experienced daily by patients who receive care. To identify potential factors of influence, this theory provides a framework which helps to determine the factors that may affect the symptom experience.
4.4.1.2. Influencing factors

According to TOUS, influencing factors include physiological, situational, and psychological factors. Physiological factors represent all factors that affect the normal function of the patient, such as age, gender, family history, comorbidity, clinical variables, or variables related to illness(es) (Lenz, 2018). Situational factors are influenced by the physical environment and may include, employment, marital status, and treatment access and resources (Lenz, 2018). Psychological factors also affect the symptom experience and may include depression, anxiety and adapting to symptoms (Myers, 2009) (Figure 11).

![Diagram of Theory of Unpleasant Symptoms (Lenz et al., 1997)]

*Figure 11: Theory of unpleasant symptoms (Lenz et al., 1997)*
4.4.1.3. Consequences (outcome)

According to TOUS, consequences are the impact of the symptom experience on the patients’ health status (Armstrong, 2003). Consequences can be functional or cognitive with functional performance related to the physical and social activities that people undertake, while cognitive performance is the ability to think and solve problems (Lenz et al., 1997). According to Gift et al. 2004, the consequences can be the ability to undertake physical activities. The consequences of symptoms and the performance undertaken by individuals can affect the symptom experience (Liehr 2005). For example, one of the consequences of symptoms is that individuals develop personal strategies to relieve these symptoms. Managing symptoms can improve symptom experience successfully.

Many studies have used or adapted the TOUS to study symptoms in a range of disorders (JablonskiA, 2007; Omran et al., 2017; Tyler et al., 2009; Park et al., 2012; Thong et al., 2009). TOUS was selected for use in this study because of the simplicity of its constructs, its ability to capture a comprehensive overview of symptoms, and the ease with which it can be used to conceptualize the symptom experience (Almutary et al, 2016). In addition, the components of the model are clearly described (influencing factors, symptom experience, and consequence) and the relationships between components are explicitly identified. In previous studies, researchers have demonstrated the flexibility of the model in a range of research studies (Jablonski, 2007A; Omran et al., 2017; Tyler et al., 2009; Park et al., 2012; Thong et al., 2009).
Questions in the patient interview schedule, (appendix 3), were based on the three main components of TOUS. Symptom experience represented by (prevalence, frequency, distress and severity of symptoms) was measured quantitatively by using the CKD-SBI, a rating scale ranging from 0 to 10, and qualitatively by asking questions such as, “Describe what symptoms feel like”, “Describe living with concurrent symptoms” and “Tell me about things that you could do previously, but you are no longer able to do?”.

The influential physiological factors associated with symptoms was addressed in the quantitative phase of the study by exploring the relationship between demographic features individual and clinical characteristics in relation to symptom burden levels and included: gender, age, dialysis duration, HG level, comorbidity. Situational factors were explored by examine all factors which were influenced by the physical environment such as marital status, distance from hospital, cohabiting status and socioeconomic status. Psychological factors were not exploring during the quantitative phase of the study, due to time limitations and the cognitive ability of patients receiving HD, which prevented them from being able to complete an additional survey. In qualitative interviews, a general question was asked to patients about factors that can influence symptom experiences, which addressed the holistic factors including psychological factors: “Can you tell me about things (factors) that negatively or positively affect your symptoms?”

The final component of the model, is the consequences. This component was explored qualitatively by asking patients about the impact of symptoms and what actions or activities they had undertaken to reduce or relieve symptoms,
“What consequences have symptoms had on your life?”, “How do you manage and control symptoms when they bother you?” and “What actions or strategies do you take to reduce or relieve symptoms?”. This theory helped to model the multidimensional nature of the symptom experience and outcomes, which helped to meet the aim of the study.

4.4.2. The Theory of Caregiver Stress (TOCS)

An additional focus of the study was to explore caregiver burden in caregivers of patients receiving HD. In this part of the study, the Theory of Caregiver Stress (TOCS) was also used to guide data collection and provided an understanding of the positive and negative outcomes experienced by caregivers. The Theory of Caregiver Stress (TOCS) was derived from the Roy Adaptation Model (RAM) (Roy, 1984) updated and further developed by Andrews and Roy, (1991). The most recent version of TOCS provides a holistic understanding of caregiver burden and includes three main components: input, control process, and output. Caregivers not only provided insights into the experiences of patients at the time of their illness, they also reflected on their own personal experience as caregivers.

4.4.2.1 Input

Input is the stimuli that can affect caregiver stress. According to Andrews and Roy (1991), each caregiver has a different adaptation ability to deal with their individual problems. The level of adaptation may result in the individual reacting negatively or positively to the environmental stimuli. In this theory, there are three forms of stimulus which may affect the level of burden
perceived by caregiver: focal stimuli, contextual stimuli and residual stimuli (Tasi, 1998; 2003).

Focal stimuli are the amount of duties or responsibilities undertaken by caregivers of patients with chronic illness such as hours of care. These tasks usually impact on all aspects of the caregiver’s life, such as, relationships with others, privacy, or ability to meet other responsibilities such as work or family and may create additional stress for the individual. In the quantitative phase of this study, the association between the duration of caregiving and caregiver burden were measured.

Contextual stimuli includes social support, social roles and stressful life (Tsai, 2003). Social support is defined as how the individual (caregiver), perceives that they are cared and loved, respected and involved in mutual obligations within their network, which reduces the stress they experienced (Tsai, 2003; Cohen and Wills, 1985). Stressful life events are defined as challenging events and cause caregivers to be distressed (Stout and Nemeroff, 1994; Vedhara et al., 2000). Caregivers who experience stressful life events, demonstrate higher levels of stress than caregivers who are not experiencing similar events (Kendler et al., 1999). Additionally, social role within this model is defined as the function in which the caregiver has towards other individuals, in other aspects of their lives, such as being a parent, sister, or supervisor. This component of the model suggests that if a caregiver has multiple roles, this potentially affect caregiver stress reported. In this study, the social role considered to be the employment status of caregivers and therefore the study explored the association between caregiver burden and the employment
status. The stressful life events considered to be the comorbid condition and its influence in caregiver burden.

Residual stimuli are the characteristics that have unclear influences on the levels of caregiver burden (Andrews and Roy, 1991) such as race, age, gender, and relationship to care recipient, see Figure 12 (Tasi, 2003). This study explored the association between the levels of caregiver burden and caregiver’s age, gender, education level, marital status, co-habiting status and relationship to patients. While a number of qualitative questions were used to explore the Residual stimuli in this study population, such as “Can you tell me about things (factors) that you think negatively or positively affect your burden of care” see (appendix 4).

TOCS suggested to explore the influence of race and culture in caregiver burden. Exploring cultural belief and value influences were not one of the main aims of the study, however, they were observed, throughout the qualitative interviews, to be significant influencers to the caregiver experiences. Saudi Arabia has a unique culture based on deeply rooted believes and religious values (Alaoufi et al, 2012), and the influence of this culture was clearly revealed in this study.

4.4.2.2. Control Process

The control process of TOCS links the input to the output section through perceived caregiver stress (Tasi, 2003). The control process represents the level of stress experienced by the caregiver and is measured quantitatively using ZBI.
4.4.2.3. Output

Output is the consequences and the responses that caregivers will experience to caregiver stress (Tsai, 2003). There are two kinds of output: adaptive responses and maladaptive (ineffective) responses (Tsai, 2003). The theory suggested four elements of caregivers responses involve physical function, self-esteem/self-worth, role enjoyment, and marital satisfaction. This study focused on the experiences and the impact of caregiving on caregivers’ life. ZBI was used to measure the level of burden and the impact of providing care to ill patients in the physical function, relationship with other family members, whether they are angry, afraid of the future, able to control life, or feel guilty.

The impact of providing care in the informal caregivers was also explored in the qualitative interviews by asking specific questions such as “How does your life change when you started providing care to your patient? (Social, emotional, physical)”, “What is the most rewarding aspect of being a caregiver?”, “Can you tell me how you cope with caring for your patients?”
This theory designed to predict caregiver burden and its consequences in informal caregivers caring for patients with chronic kidney diseases. The main advantage of this theory is that it acknowledges that caregiving can be a positive experience, and can bring satisfaction, knowledge and promote self-esteem, as much as it brings burden (Figure 12).

4.4.3. Comparison between Theory of unpleasant symptoms and Theory of caregiver stress

TOUS and TOCS are middle-range nursing theories that predict burden and its outcomes in patients and caregivers from a variety of different perspectives.

The following table compares and summarizes both theories (Table 11)

Table 11: Comparison between Theory of unpleasant symptoms and Theory of caregiver stress

<table>
<thead>
<tr>
<th>Theory of unpleasant symptoms (TOUS)</th>
<th>Theory of caregiver stress (TOCS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Published</td>
<td>Published in 1995 and revised in 1997</td>
</tr>
<tr>
<td>Objective</td>
<td>It been used as a framework to support studies for the identification of symptom experience, and consequences. And also, to predict factors influencing symptoms, including physiological, situational, psychological factors.</td>
</tr>
<tr>
<td>Component of Theory</td>
<td>Influencing factors: physiological psychological situational factors</td>
</tr>
<tr>
<td>Symptom experience</td>
<td>Consequences (performance)</td>
</tr>
<tr>
<td>Strengths</td>
<td>Limitations</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Able to account for multiple symptoms</td>
<td>It does not take symptom management into account (Almutary et al., 2016).</td>
</tr>
<tr>
<td>dimension and their interaction</td>
<td>It does not take in to account the changes of symptoms over the time.</td>
</tr>
<tr>
<td>The theory is attributed to the simplicity of</td>
<td>There is confusion between symptoms. For, instant, depression could be</td>
</tr>
<tr>
<td>its concepts.</td>
<td>categorized as a symptom, consequence or influencing factor (psychological</td>
</tr>
<tr>
<td></td>
<td>factors)</td>
</tr>
<tr>
<td>Using this theory in assessment and planning</td>
<td>Only a few studies have used RAM in the context of caregiving for the</td>
</tr>
<tr>
<td>interventions emphasizes the complexity and</td>
<td>chronically ill.</td>
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<tr>
<td>interaction of symptoms and the relationships</td>
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<tr>
<td>between and among symptoms, influencing</td>
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<td>factors, and symptom consequences. It has</td>
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<tr>
<td>has been used extensively and successfully in</td>
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<tr>
<td>previous studies.</td>
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<tr>
<td></td>
<td>Straightforward relationships between the assumptions that developed and</td>
</tr>
<tr>
<td></td>
<td>surrounded the Caregiver Stress Theory.</td>
</tr>
</tbody>
</table>
4.5. Setting

This research was conducted in the dialysis centre at King Khaled Hospital, Hail city, in the northern region of Saudi Arabia. King Khaled Hospital provides free services and treatment to all Saudi nationals who experience health problems in Hail city. The hospital can accommodate up to 284 patients and contains various specialist facilities, including Medical units, Cardiac unit, Burns unit, Department of Ophthalmology, Bone unit, Surgical unit, Paediatric ward, Intensive care unit and a Dialysis centre.

Approximately 280 HD patients attend the dialysis centre each week. The centre is open 6 days a week; there are two shifts each day morning and evening. The unit closes at 5 pm each day and remains closed each Saturday. For any urgent HD cases during Saturday, patients need to go to the emergency department to receive the treatment. Each shift provides HD treatment for approximately 70 patients. This hospital is one of three hospitals in Hail city, but it is the only hospital which provides HD treatment for patients with ESRD.

4.6. PHASE ONE: Cross-sectional design:

The cross-sectional design phase involved exploring burden in two different participant groups; patients and their caregivers. Two questionnaires, the CKD-SBI and ZBI, were used to address the aim of the quantitative phase of the study, the exploration of symptom burden in patients receiving HD and the impact of symptom burden in relation to demographic characteristics and clinical variables. In addition, this phase of the study aimed to explore caregiver burden levels and the factors which influenced burden scores. This phase of
the study concluded with establishing if there was an association between symptom burden and caregiver burden. The self-completed questionnaires were considered the most appropriate way to collect data, as symptom burden in patients and the burden of caregiving for carers is a subjective concept (Gapstur, 2007; Tough et al., 2017), which is best evaluated by the relevant population. Using self-completed questionnaire helped to avoid any bias which may have resulted from researcher effects (Teddlie and Tashakkori, 2009). This strategy also helped eliminate the possibility of any under-reporting of sensitive information (Bryman, 2016), such as sexual symptoms.

After reviewing the literature, a variety of questionnaires were identified to measure symptom burden and caregiver burden in CKD populations. The research team selected the CKD-SBI and ZBI to be used in this study. CKD-SBI was selected as the majority of available instruments were judged by the research team to be not adequate to explore all symptom dimensions, and would not contribute to a more comprehensive understanding of the symptom experience (Cleeland, 2007; Almutary et al 2013). Some measures used to explore symptom prevalence, such as the KDQOL-SF (Thong et al., 2009), which measures the presence of symptoms, without providing any understanding if these symptoms are distressful or not to patients, and will not be demonstrated the actual symptom burden (Cleeland, 2007). The measure of symptom experiences must involve individual perceptions of frequency, intensity and the distress of these symptoms (Armstrong, 2003; Kirkova et al., 2006). Instruments which have been designed to explore a small number of symptoms (N=10), the Modified Edmonton Symptom Assessment (mESAS)
and Pittsburgh Symptom Score (PSS), were discounted as this study aimed to cover a wider range of symptoms in HD patients.

An ideal assessment tool to comprehensively assess the range of symptoms, would target the appropriate populations and would include the following; prevalence, distress, frequency and intensity of symptoms (Almutary et al 2013). The Memorial Symptom Assessment Scale Short Form (MSAS-SF) was used to assess the prevalence of 32 symptoms. However, MSAS-SF included some unusual symptoms for patients with CKD, such as hair loss or difficulty swallowing, which are not beneficial in the case of this study, and there is also no consideration of the level of symptom intensity (Almutary et al 2013). Additionally, the Palliative Care Outcome Scale (POSs), was designed to explore symptom burden in cancer patients and does not take into consideration common symptoms in dialysis population such as itching and bone pain. Although amended versions of the POSs have been developed to create the IPOS-renal, for use with those living with CKD, this version was not available during the preparation of the current study protocol (IPOS-Renal 2017) and has only recently been tested for validity and reliability (Raj et al 2018).

The Dialysis symptom index (DSI) was judged to be the best instrument to measure symptom burden, as it was designed specifically for dialysis patients, to consider a variety of emotional, physical and cognitive symptoms (N=30), that may occur in this population. DSI has been translated into and validated in Arabic, which is the language of the population involved in this study (Almutary et al 2015). Almutary et al (2015), made a number of modifications
to the DSI, to create the CKD-SBI, which enhanced the measurement of a wider range of symptoms of burden. The CKD-SBI offers greater opportunity for patients to report symptoms, by offering three empty fields at the end of the symptoms list, to provide respondents with an opportunity to identify any symptoms not contained within the measure. CKD-SBI includes two further dimensions, to help measure the intensity and frequency of symptoms, which allows a more holistic symptoms assessment (Almutary et al 2015). CKD-SBI was selected because it was designed specifically for dialysis patients, and it is the only measure which evaluates the multidimensional nature of symptoms, including prevalence, distress, severity and frequency of symptoms. Currently, a large number of instruments are used to assess and explore caregiver burden, in a variety of chronic diseases. The literature identified three instruments which were potentially suitable to measure caregiver burden in patients with CKD (Hoang et al 2018). This included; Oberst Caregiving Burden Scale (OCBS) (Bakas et al 2004), Zarit Burden Index (ZBI) (Zarit et al., 1981) and Caregiver Burden Scale (CBS) (Elmstahl et al 1996). All these instruments used similar rating systems, rating burden from 0 to 88, with 0 suggesting low burden and 88 as an extremely high burden. All of these instruments measure the impact for caregivers associated with the levels of disability of patients, including social strain, emotional burden and financial burden. These instruments have been primarily designed to be used to measure caregiver burden in a variety of illnesses such as mental illness and patients with stroke.
Due to the restricted time period to complete the study, the ZBI was selected for use in this study, as it has previously been translated into Arabic, validated and reliability tested for use in caregiver burden (Mapi Research Trust, 2019). The ZBI is easy to use, quick to complete (normally five minutes) and contains a language which easy to comprehend for caregivers (Stagg and Larner, 2015). Therefore, the ZBI is considered an effective instrument for the identification and quantification of caregiver burden, at the initial diagnostic assessment period in patients with chronic illness (Stagg and Larner, 2015).

4.7. PHASE TWO: Qualitative descriptive design

The second phase of the study aims to explore the impact of symptom burden and the effective self-management strategies found to reduce perceived symptoms amongst patients receiving HD through qualitative interviews. It was also focused on the impact of providing care in the informal caregivers of these individuals.

One of the most commonly utilised methods to collect qualitative data is the focus group. This involves the use of in-depth group interviews to engage in a guided discussion subject raised by the interviewer (Rabiee 2004; Morgan 1997). Focus group is useful to create ideas for how participants interact and think (Morgan 1997). However, focus group was not selected in this study for many reasons; participants may be discouraged to provide privet or sensitive information and cannot trust others with sensitive or personal information (Gibbs, 1997). This study involved discussion about the experience of symptoms and the impact of symptoms, which was anticipated to include any sensitive information such as sexual symptoms, depression.
Semi-structured interviews were chosen as the most appropriate method instead of structured interviews to give participants more opportunity to express their feeling freely. The semi-structured interview also gave the researcher the ability to explore significant issues related to the research questions and clarify comments made by participants in an ongoing conversation between the researchers and participants interviewed. The interview questions were originally devised from the literature review with some suggestions from the main researcher followed by the agreement of the research team. Later, and after the quantitative data initially analysed, some questions were added to provide a clarification of unexplained findings. Additional questions “off-script” were asked during the interviews were processed to earn understanding for unclear answers provided by participants. The questions started with icebreaker questions which were used to ease the participants into the interview, followed by main topic questions relating to the aim of the study, and the interviews were concluded with closing questions that provide the participants with the opportunity to raise any issues or concerns.

At the final stage, two interview schedules were prepared for the patients and their informal caregivers. The questions were used in the interview schedule were open-ended and close-ended questions. Questions were developed to ensure that the responses will not be led by these questions. Moreover, mock interviews have been carried out in two Arabic speaker Ph.D. students to test the clarity of the interview questions and improve the researcher interviewing skills. Researchers made the necessary modifications to ensure that the interview questions will encourage participants to share their feelings as if it’s an informal interview.
The interviews were undertaken in the local dialysis centre, in a private clinic room, for caregivers and those patients who received HD on shared treatment room, and based on their preference time (e.g., before or after dialysis). Some interviews were conducted during HD for patients who are in isolation room.

4.7. Instruments

4.7.1. Chronic kidney disease-symptom burden index (CKD-SBI)

Symptom burden was measured using the Arabic version of the CKD-SBI (Appendix 5). CKD-SBI is the modified and translated version of the Dialysis Symptom Index (DSI), developed by Weisbord et al. (2004), and used widely to assess CKD symptoms in ESRD. The Arabic version of CKD-SBI (Appendix 6), demonstrates good psychometric properties, with an excellent internal consistency (Cronbach’s $\alpha = 0.91$) as well as good reliability and validity in CKD population (Almutary et al., 2015). The CKD-SBI was adapted by Almutary et al. (2016) to assess various aspects of symptom burden. This includes assessment of the burden of the disease, and the prevalence, frequency, distress and severity of the symptom. Two more symptoms (depression and nocturia) were added to capture any possible symptoms that were not included in the DSI. A total of 32 CKD symptoms were assessed. Three empty fields were provided, to allow patients to add symptoms not identified on the symptom list (Almutary et al. 2015). The time needed to complete CKD-SBI ranges from 15 to 30 minutes (Almutary et al., 2015). The patients were asked to recall symptoms for a period of one week.

The purpose of the prevalence scale is to assess each symptom’s presence or absence using (Yes/No). Prevalence scores range from 0 to 32. 0 is lowest
prevalence score while a score of 32 is the highest possible score. Three further factors will be measured (distress, severity and frequency) on a scale of 0 to 10 for each respondent’s rating and will be recorded as, Distress: from none to highly distressed; Severity: none to extremely intense; and Frequency: from never to frequent. The highest possible score for each scale (frequency, severity, distress) is 320, which is considered to constitute an extremely high burden. The total CKD-SBI scores are calculated by summing up the four subscales together, (prevalence 0-32 distress 0-320 severity 0-320 frequency 0-320). The total symptom burden scores were converted to percentages by multiplying the final score by 100 and dividing it by 992 (Almutary et al 2016).

4.7.2. Zarit Burden Interview

The ZBI (appendix 7) was developed by Zarit, Reever and Bach-Peterson in 1980 to assess the level of burden for those caring for patients with dementia. It has more recently been used in CKD (Shimoyama et al 2003; Alvarez-Ude et al 2004; Oyegbile and Brysiewicz, 2017). It contains 22 items, which examine five caregiver burden domains: burden on the relationship; loss of control over life; finance; social and family life; and emotional wellbeing. The questionnaire items were rated using a five-point Likert scale, with 0 (rarely) being the lowest, and 4 (nearly always) being the highest. Zarit et al. (1980) suggest summing all response scores from the 22 questions in ZBI to show the level of the caregiver burden, with 0 to 20 showing that no burden or slight burden; 21 to 40 indicating mild to moderate burden; 41 to 60 moderate and severe burden; and 61 to 88 indicating a heavy burden (Zarit et al., 1980). ZBI was translated into Arabic (Appendix 8) and showed good validity (Bachner et al 2013). Reliability of the translated instruments was also tested and found to
be 0.97 (Elmahdi et al., 2011). User agreement required the use of the Arabic version of ZBI, was obtained from the MAPI Institute.

4.7.3. Davies’ comorbidity index

Fried et al. (2003) compared Davies et al.’s (2002) comorbidity index with other comorbidity scales, such as the Charlson Comorbidity Index (Charlson et al., 1994) both of which are well documented in the literature. Both indexes identified similar variance in the health status of people with CKD, indicating that both indices are appropriate for evaluating the comorbidities in this population. However, Davies et al.’s (2002) comorbidity index was chosen for this study due to the simplicity of its constructs and scoring, which is useful for large sample sizes (Van Manen et al., 2003; Fried et al., 2003). Additionally, this index has revealed the potential effect of comorbidity on the quality of life in people with CKD in many other studies (Murphy et al., 2009; Murtagh et al., 2010; Almutary et al., 2016). The Davies Index score assigned 1 score for each condition with a total of 7 (Appendix 9). The scores are graded into three risk groups: grade 0 (zero total scores), grade 1 (score 1-2) or grade 2 (score 3-7). However, the Charlson Comorbidity Index assigns different scores for different diseases, for example: 1 point assigns for heart failure or diabetes, 2 points for leukemia, 3 points for liver disease and 6 points are assigned for AIDS. Charlson Index also requires to add 1 extra point to the score of 7, for every decade over 40 years of age. This makes Charlson Comorbidity Index more complicated when counting the total scores, especially in a large sample size.

4.8. Data resources

Phase 1: Cross-sectional study
One of the primary aims of this study is to measure symptom burden and caregiver burden in patients undergoing HD, which was explored using the CKD-SBI and ZBI. In addition, demographic information was collected from patients and included the: age (years); gender (female, male); marital status (married, divorced, widow, single); education level (primary, secondary, higher education, other); employment status (full time job, part-time job, student, housewife, unemployed, retired, self-employee, others); income (0-5000, 5000-10000, 15000-20000, 20000-25000, 25000-30000, 30000<), distance from home to hospital (per minutes) (Appendix 10). Co-morbidities (0, 1-2, 3-7), the duration of dialysis (per months) and levels of Haemoglobin (HG) (low, normal, high) were obtained from the dialysis charts and hospital records. Co-morbidity was measured using the Davies Co-morbidity Index. Caregiver demographics data and other characteristics were collected using a questionnaire designed by the researcher (Appendix 11). This included age, gender, income, relationship to patient, educational level, comorbidity, and whether they lived together or not. Comorbidity was then measured using the Davies Comorbidity Index (Davies et al., 2002). All instruments that were used in the study have demonstrated validity and reliability (Almutary et al 2015; Zarit et al 1985).

4.9. Sampling

Sampling techniques are complex in MMR, where qualitative and quantitative research methods are integrated either sequentially or simultaneously, than in mono-method research (Onwuegbuzie and Collins, 2007). The major component of sampling involves; sample size and sampling scheme; in which
sample size indicates the number of participants to select, while sampling scheme indicates how to use probability or non-Probability sampling methods to select respondents (May, 2001; Onwuegbuzie and Collins, 2007).

4.9.1. Sampling scheme

If the aim of a study is to generalize findings from qualitative and quantitative phases to the population from which the sample was selected, it is advised to select a random sampling scheme (Onwuegbuzie and Collins, 2007). However, as the aim of our study is not concerned with generalizability, but to gain awareness of the phenomenon and individuals experiences, this required the study to recruit participants and settings purposively, to help expand understanding of the phenomena. As a result of these considerations, a non-random sample scheme was used (Onwuegbuzie and Collins, 2007). In MMR, these are 19 different non-random sampling schemes (Appendix 12) and the decision to select these schemes was based on the research aim, study objectives and research questions (Onwuegbuzie and Collins, 2007). Of the possible 19 different non-random sampling schemes, a convenience sampling method was judged to be most suitable for use in the quantitative phase of the study whereas the qualitative phase of the study utilised extreme cases sampling scheme.

Convenience sampling method was used because it is easy to use, inexpensive and subjects are easy to recruit. If a convenience sampling method is used, it is essential for researchers to illustrate how the sample is varied from other samples that are randomly sampled. It also important when using a convenience sampling, that individual demographic features are not
over-represented in the sample (Etikan et al., 2016). The selection of extreme cases in the qualitative was to identify the variation of the management strategies used by patients with different scores (high, medium and low), and also to determine the common pattern between cases in related to the lived experience with HD and its associated symptoms.

4.9.2. Sample size: a cross-sectional survey with patients and caregivers

In order to complete the sampling phase, MMR also requires to ascertain suitable sample sizes for each phase the qualitative and quantitative. Sample size selection is significant as the selection of choice of sampling scheme (probability or non-probability sampling) since it also identifies the extent to which the researcher can make analytic or statistical generalizations (Onwuegbuzie and Collins, 2007). Sample size decision used to be dichotomized, with large samples being assigned to quantitative studies and small samples being assigned to qualitative research (Onwuegbuzie and Collins, 2007). Previous research suggested to use fundamental guidelines such as the recommendation of using sample sizes of 30 for both designs: causal-comparative and correlational (Creswell 2002; Onwuegbuzie and Collins, 2007). which will lead to insufficient statistical power because they are not based on power analyses (Onwuegbuzie and Collins, 2004). The sample size primarily selected based on the objectives, research questions and subsequently the design of the study (i.e., descriptive, correlational, causal-comparative, experimental). The primary outcome of this study is to measure symptom burden in patients receiving HD. The study will also identify the effect on symptom burden in relation to the following possible predictors: age,
gender, education level, marital status, income, co-morbidity, employment, living distance from dialysis centre, and the duration of dialysis. A power calculation was performed using GPower software (Faul et al., 2007) to help avoid type 11 error and calculate the sample size required. Given a medium effect size ($f^2 = 0.15$), significance level of 5, 90% power and 9 predictors, the sample size required is 141 patients receiving HD (Figure 13). Similarly, for 7 predictor variables include; age, gender, education level, marital status, co-morbidity, employment, cohabiting status, the study needs to recruit 130 caregivers (Figure 14). The number of people available in the hospital who receive HD is 280. A previous study involving CKD population was able to recruit a larger number of participants in Saudi Arabia (Almutary et al, 2016), so this study is likely to recruit the required number of participants to help ensure the credibility of findings.
Figure 13: Sample size calculation for patients: Medium effect size of 0.15, alpha = 0.05, power from 0.8 to 0.95, number of predictors in regression model 9

Figure 14: Sample size calculation for caregivers: Alpha 0.05, 7 predictors, medium effect size (0.15), power is 0.9, sample size is 130
4.9.3. Sample size: interviews with patients and caregivers

Qualitative sample sizes need to be large enough to determine a good understanding of most or all of the research perceptions (Ritchie and Lewis, 2013). Guest et al. (2006) argue that data saturation can be reached within the first twelve interviews after which it is rare for any new information to suggested conducting from five to twenty-five interviews for phenomenological studies. Creswell (2011) suggested that in relation to a sample size that is normally within qualitative research “it is typical to study a few individuals or a few cases” (Page 209). In (2014) Creswell recommended 3 to 10 participants to understand the explored central phenomenon. According to Gonzalez (2009), when undertaking research that is reliant on a phenomenological approach, the sample size is usually driven by the need to uncover all the main variants within the approach. The author suggested that within conditions such as this, small survey samples of less than twenty are common. Creswell (1998) al. (2006) argued that data saturation is reached after 12 interviews, and a minimum of 6 interviews are recommended by Morse (1994).

In a wide number of PhD qualitative researches, the common sample size used is 20 and 30 (followed by 40, 10 and 25) (Mason 2010). It is not clear why the PhD qualitative studies use multiples of five or ten when using the concept of data saturation to guide the qualitative study’s sample size which is more likely to be achieved at any point and at any number, such as 4, 7, 12 (Mason 2010). Mason (2010) explains that PhD researchers understand the meaning of data saturation but prefer to base their sample size on a larger number than that needed.
There are no specific rules when determining appropriate sample size in qualitative research. The concept of data saturation is the best recommendation for achieving a reasonable number of qualitative interviews (Glaser and Strauss, 1967). For the semi-structured interviews, we anticipated a sample of approximately 15–20, participants in both patient and caregiver groups which consider sufficient to achieve data saturation (Johnston and Noble, 2012). Data saturation is reached when no further additional information is added when interviewing further participants. The data emerging from respondent interviews kept under review as interviews progress, and no further interviews completed when it becomes clear that no new themes emerged from subsequent data (Bowen, 2008; Guest et al, 2011). Decision was therefore made prior to coding and thematic development. This sample size we anticipated was supported by Guest, Bunce, and Johnson, (2006) who reported that 12 interviews is the minimum suggested sample size when using the nested sampling scheme, which indicates the samples from one phase of the study represents a subset of those participants chosen for the other facet of the investigation (Onwuegbeuzie and Collins, 2007).

The selection of participants for the interviews was based on patients' total CKD-SBI scores with five from the lowest, median and highest percentiles. This gave the opportunity to obtain different insights into a variety of cases, which was reflected in the variation in symptom experience as well as the variation in the effective management strategies used by the patients.

4.10. Participants
Based on a power calculation, the required sample size needed for this study is 141 HD patients and 130 caregivers. This sample was recruited from the Dialysis Centre in King Khaled Hospital, Hail city, Saudi Arabia. Data were collected between September 2017 and March 2018. Eligible participants were required to meet the following criteria:

**Inclusion criteria for patients:**

- Participants must be:
  - Over 18 years of age
  - Able to communicate in English or Arabic
  - Undergoing regular haemodialysis therapy for more than three months
  - Cognitively able to participate in the study (assessment is based on clinician decision)
  - Consent to participate in this study

**Exclusion criteria**

- Patients receiving peritoneal dialysis or conservative management
- Patients with cognitive impairment.

**Inclusion criteria for caregivers:**

- Aged over 18
- The informal caregiver with the responsibility for the patient’s care for more than three months (identified by the patient as the key caregiver who provides some level of practical help and support during their times of illness)
- Indicated by the patient as his/her primary caregiver
• Their patients must be participated in this study.

• Able to communicate in English or Arabic

• Consent and agree to participate in this study

Exclusion criteria:

• Paid caregivers

• Unable to meet the inclusion criteria (Figure 15)
Figure 15: Flow diagram illustrating study procedures

Phase 1: Quantitative

Haemodialysis patients
(N=141 patients)

Caregivers of HD
(N=130 caregivers)

Patient inclusion criteria
- Over 18 years of age
- Able to communicate in English or Arabic
- Undergoing regular haemodialysis therapy for more than three months
- Cognitively able to participate

Caregivers inclusion criteria
- Over 18 years of age
- Indicated by the patient as his/her primary caregiver (Paid caregivers will be excluded)
- Able to communicate in English or Arabic
- Participants who sign consent

Initial SPSS analysis – To identify patient symptom burden scores for the next phase sampling

Phase 2: Qualitative

In-depth semi-structured interviews

N=15 patients
Sampling will be based on CKD-SBI scores

N=15 caregivers
Associated with the patients interviewed

5 Patients with highest
5 Patients with middle
5 Patients with lowest

Data analysis
4.11. Recruitment

4.11.1. Phase 1: Quantitative phase

*Patients*

A renal unit staff member, acted as a gatekeeper and were involved in the process of pre-screening and the recruitment of patients at the centre. If potential participants who meet the inclusion and exclusion criteria acknowledge interest, the gatekeeper introduced them to the researcher. Participants were provided with an invitation form (Appendix 13) along with an information sheet outlining the study (Appendix 14) and a consent form (Appendix 15), to be returned if they are willing to participate. Participants were given at least 24 hours to consider whether they wish to participate in the study or not. When patients sign the consent form, the questionnaire was distributed and completed by patients during their HD sessions. The researcher provided explanations and assistance to the patients who are unable to complete the questionnaire, due to either a lack of understanding or physical restrictions imposed by the dialysis treatment, such as the presence of cannulas or cuff pressure on the patients arms. To help maximize the response rate, patients who did not return the questionnaire within a three-week period were sent a single reminder directly.

*Caregivers*

Patients were asked to identify the person who is primarily involved in their care, this allowed identification of the most appropriate caregivers to be included in the study. The invitation (appendix 16), information sheet (Appendix 17) and caregiver questionnaire (Appendix 8) were sent to
caregivers in a sealed envelope via the patient. The information sheet included an invitation to contact the researcher when the caregiver has any questions. The sealed envelope also included a separate form asking caregivers whether they are happy to be contacted at a later date to determine if they would like to be interviewed (consent to be contacted form) (Appendix 18). Questionnaires, and (if the caregiver wishes, the consent to be contacted form) were returned to the researcher in the stamped addressed envelope provided to be returned to the dialysis centre by mail or directly to the researcher or gatekeeper. Returning the questionnaire were judged to imply consent. To help maximize the response rate, caregivers who did not return the questionnaire within a three-week period were sent a single reminder via the patients.

4.11.2. Phase 2: Qualitative phase

The researcher identified those patients with the top five highest, median and lowest scores from the CKD-SBI using SPSS and their caregivers. If these patients and their associated caregivers refused to participate in the study, patients with the next highest, median and low scores were recruited. Potential participants were contacted with their preferred way to provide them with an information sheet explaining the nature and purpose of interviews (Appendix 19, Appendix 20) and consent form (Appendix 21, Appendix 22). Between the time of distributing the information sheet and the consent stage, prospective participants were given at least 24 hours to consider whether or not to consent. After 24 hours, the researcher approached the patients to see if they had any questions about the interview, and to ascertain whether they were
willing to participate. Once consent was obtained from patients, the interview was arranged.

In order to recruit caregivers to the qualitative phase of the study, those caring for patients with the highest, median and lowest scores from the CKD-SBI were contacted. Some caregivers were approached directly (those who consented to be contacted) and others through the patients. The caregivers who had previously provided their consent to be contacted were contacted directly by the researcher using their preferred means of communication. They were sent a participant information sheet and after a period of at least 24 hours the researcher contacted them again to check whether they had any questions about the research. Caregivers who agreed to participate were invited to meet with the researcher at an agreed venue to sign the consent form and take part in the interview. Caregivers who preferred a telephone interview were sent a consent form, which could be returned via the patient or by using the supplied stamped addressed envelope. Once consent was obtained the telephone interview were arranged.

If consent to be contacted was not provided by caregivers in the first phase, the information sheet for the interview was sent to caregivers in a sealed envelope via the patient. Caregivers who were interested in taking part were invited to contact the researcher to discuss participating in the research. Caregivers who agreed to participate were invited to meet with the researcher at an agreed venue to sign a consent form and take part in the interview, or to take part in a telephone interview. To help maximize the response rate, caregivers who did not response to the invitation within a three-week period
were sent a single reminder via the patients. Patients and caregivers were interviewed separately to offer sharing information in a confident and accurate way. The interviews took approximately 15-60 minutes’ duration.

4.12. Data analysis

4.12.1. Phase 1: cross-sectional study analysis

Simple descriptive statistics analysis was provided for the scale and categorical variables in the patient and caregiver data sets using the Statistical Package for the Social Sciences 22 (SPSS). For the scale variables, mean standard deviation, as in age, and sometimes median, interquartile range (IQR), and range, such as the total scores of distress, frequency, severity subscale and caregiver burden scores were reported. For the categorical variables, absolute frequency (n) and relative frequency (percentage) (%) of the response, such as gender, education level, marital status, monthly income, and HB level were reported. Independent t-tests were used to compare the means of variables between groups. A one-way analysis of variance (ANOVA) was conducted to compare mean scores across categorical variables with more than two levels. Chi-square was used to explore the differences between two independent categorical variables in two groups. The Pearson correlation was used to identify the relationship between symptom burden, caregiver burden and participant characteristics.

Data preparation:

There are a number of issues to consider in regard to the statistical analysis undertaken in this phase of the study. Data preparation included coding of the data entered, entry of data, cleaning of data and verification. The data were
entered manually by the main researcher into SPSS version 22 to minimise any possibility for data entry errors. In order to ensure the accuracy of data entry and identify any possible errors, several steps were undertaken.

To ensure the accuracy of data entered one of the supervisory researcher team HM was involved in this assessment. Data was checked in terms of logical inconsistencies. For example, when the participants indicated that they had no symptoms, the CKD-SBI questionnaire should not have recorded any value for the level of distress, severity, or frequency of symptoms. There were no inconsistent results identified when checking the data set. Frequencies of all variables were checked for invalid coding and outliers. There were a few invalid codes identified, these were checked and corrected using original questionnaires. The data were also checked for missing values. There was some missing data identified across all the data. Few missing data were reported (less than 5%). Imputation was not performed as there is little disagreement about whether or not to conduct imputation to manage and replace the missing value which may introduce risk of biases (Mittag 2013).

Data collected from patients (symptom burden scores) and (caregiver burden scores) were normally distributed and therefore parametric analysis was performed. Descriptive statistics were reported on demographic and clinical characteristics (marital status (married or other); employment status (employed/unemployed); HG level (normal, abnormal). Additional analysis was performed using Pearson Co-efficient Correlations to identify significant contributors to patient symptom burden and caregiver burden. Multiple linear
regression was used to explore a statistical model to predict symptom burden and carer burden.

4.12.2. Phase 2: Qualitative data analysis

Interviews were analysed using thematic analysis (Braun and Clarke, 2006). Thematic analysis defines as "method of identifying, analysing and reporting pattern themes with in the data" (Braun and Clarke, 2006, p.79). Audio-recorded interviews were transcribed into Arabic by the main researcher and translated by a certified bilingual translator into English. The translator signed a non-disclosure form to assure the confidentiality of the participants’ data (Appendix 23). The validity of the translation was checked by the main researcher BA to ensure the accuracy of the data translated. The data were then stored electronically to allow coding and analysis. Coding was managed using NVivo qualitative data analysis software Version 11 (Richards, 1999).

The analysis was based on six phases: familiarisation with data, coding, searching for themes, reviewing themes, defining and naming the themes and reporting themes (Braun and Clarke, 2006). Part of the interviews were coded by three of the supervisory team PO, HN, and HM, and the main researcher BA independently, to guide the student into achieving of coding extraction. Findings were regularly discussed and verified with the supervisory team at every stage to improve reliability, assess the accuracy of the interpretation, and ensure a rigorous qualitative phase for the research. Using coding researchers can identify trends and patterns in interviewees’ use of words including word frequency, relationships between words, and how communication is structured (Grbich, 2012). Codes can then be displayed or
organised to give greater clarification of the content and allow generating the overarching themes, reviewing and defining those themes, and drawing of conclusions (Braun and Clarke, 2006).

4.13. Integration of the findings from all phases of data collection

In line with using the sequential explanatory mixed-method approach, this chapter will present an integration of the findings from the quantitative and qualitative phases of data collection.

4.13.1. Rationale for Integration

To improve the value of MMR, the integration of quantitative and qualitative phases is essential (Bryman 2006; Creswell and Plano Clark 2011). According to O’Cathain et al (2010), the study can only be considered as MMR, when the integration of both phases happen. Integration permits a more utilization of the data generated from quantitative and qualitative. The quantitative can help clarify the qualitative data or assist in generating the qualitative sample whereas the qualitative data can be utilized to evaluate the validity of quantitative findings (Fetters et al 2013).

4.13.2. Integration approaches

In MMR, several approaches have been identified to integrate findings from qualitative and quantitative research (O’Cathain et al 2010; Creswell and Plano Clark 2011). These approaches can be applied at three different levels: at the design, methods, and interpretation and reporting stages of the research process.
4.13.2.1. Integration at the Study Design Level

Integration at the design stage can be accomplished through three basic approaches and can include; (1) exploratory sequential; (2) explanatory sequential; and (3) convergent designs. In sequential designs, an initial mixed-method phase is used to construct and develop a second phase of a study. In a convergent design, data collection and analysis is completed in a parallel timeframe, so that results can be compared and contrasted. In this study, an explanatory sequential design was used, in which the researcher collected and analysed quantitative data, which was then used to inform qualitative data collection and analysis (Ivankova, Creswell, and Stick 2006).

4.13.2.2. Integration at the Methods Level

Integration in the methods stage of a MMR occurs by linking the methods of data collection and analysis (Creswell et al. 2011). Integration at the methods level, occurs through four approaches: (1) connecting; (2) building; (3) merging; and (4) embedding. Descriptions of each approach are identified in Table 12.

<table>
<thead>
<tr>
<th>Approach</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>Connecting</td>
<td>One phase links to the other through sampling</td>
</tr>
<tr>
<td>Building</td>
<td>One phase informs the data collection approach of the other</td>
</tr>
<tr>
<td>Merging</td>
<td>The two phases are brought together for analysis</td>
</tr>
<tr>
<td>Embedding</td>
<td>Data collection and analysis link at multiple points</td>
</tr>
</tbody>
</table>
In this study integration occurred only through three approaches; connection, building and merging. **Connection** ensued when interview participants were selected from the population of who responded to the survey. **Building** occurred when quantitative findings were used to inform the sample for the qualitative phase of the study. Based on symptom burden scores, in the quantitative phase of the study, patients were selected to participate in semi-structured interviews. Patients with high, middle and low symptom burden scores, were assigned to semi-structured interviews. Building was also implemented when the results from quantitative analysis, informed the qualitative data collection approach. Interview questions were modified based on quantitative findings to meet the aim of the study. **Merging** occurred when the researcher integrated the two databases for analysis and to assist with comparison in the final stage of the study. Both forms of data were collected in a way that facilitates merging both databases. There was commonality at times between the questions used during both phases of the study, to help ensure that findings will be comparable, and to enhance the merging of findings (Castro et al. 2010).

**4.13.2.3. Integration at the interpretation and reporting Level**
Quantitative and qualitative data analysis was completed individually and the integration of findings from each phase of the study was incorporated together in the final stage of the study (integration chapter). Study findings were integrated through a narrative approach which included writing both quantitative and qualitative findings together, on a theme-by-theme or concept-by-concept basis (Fetters et al 2013).
4.14. Ensuring rigour

It is essential to researchers to consider rigour when commencing of research (Plano Clark 2010). In MMR, there are three quality standards when ensuring rigour: qualitative methods standards, quantitative methods, and those for mixed methods. Rigour in quantitative and qualitative research is ensured in various ways (Whittemore et al, 2001); in quantitative research, the criteria for rigour includes validity, reliability, objectivity and generalizability (Bryman et al, 2008; Lincoln and Guba, 1985), whereas in qualitative research, the criteria are credibility, transferability, dependability and confirmability, (Lincoln and Guba, 1985; Smith et al., 2014). Despite the current criteria to ensure rigour of quantitative and qualitative research, there is a lack of agreement regarding the criteria in MMR. Creswell et al. (2011) acknowledge that MMR should illustrate rigour using the same standards used separately in quantitative and qualitative research. To ensure the rigorous of this study, the mixed method rigour the Good Reporting of a Mixed Methods Study (GRAMMS) guidelines was also used (O’Cathain, Murphy and Nicholl 2008). The following criteria were used to establish the rigour of the quantitative and qualitative research (Table 13).

Table 13: Quantitative and Qualitative Appraisal Criteria:

<table>
<thead>
<tr>
<th>Standard</th>
<th>Qualitative Appraisal Criteria</th>
<th>Quantitative Appraisal Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trustworthiness</td>
<td>The credibility is to ensure that the finding of the research is believable and reflected in the data.</td>
<td>Internal Validity: The degree to which the findings represent a “true” reflection of a causal relationship between the variables of interest in the population under study</td>
</tr>
</tbody>
</table>
Applicability | Transferability refers to the degree in which the research can be transferred to other contexts, setting or population | Generalizability The degree to which the study results hold true for a population beyond the participants in the study or in other settings

Consistency | Dependability ensures that the research findings are consistent and could be repeated. | Reliability or replicability The degree to which observations, measures or results can be replicated (for the same participant or in different studies)

Neutrality | Confirmability The degree to which the findings of a study are shaped and supported by the data collected and not researcher bias, motivation, or interest | Objectivity The degree to which researchers can remain distanced from what they study so findings reflect the nature of what was studied rather than researcher bias, motivation, or interest

(Curry and Nunez-Smith 2014)

4.14.1. Trustworthiness

Trustworthiness which is similar to the internal validity in quantitative research while it is credibility in qualitative. The concept means to ensure the findings are measured based on the data, and make the inferences that are believable, credible and trustworthy (Plano Clark 2010). The ability of which a concept is measured adequately and accurately in a quantitative study; in another word, the appropriateness of the tools. The instruments used to collect the data were designed to measure symptom burden and caregiver burden. This study used two well-validated instruments in the CKD population (Almutary et al., 2015; Oyegbile and Brysiewicz, 2017). Both instruments demonstrated good validity and reliability. ZBI has excellent internal consistency $\alpha = 0.83$ (Majerovitz, 1995), and $\alpha = 0.89$ (Zarit et al., 1987; Yap, 2010).
Member checks or participant confirmation is a process of verifying the results with the participants either during the interview or at the conclusion of the study to ensure the accuracy and improve the credibility (Onwuegbuzie and Leech, 2007). In this study, member checking was conducted during the interview process. The researcher repeated and rephrased some of the interview questions during the interview in different ways to clarify and ensure credibility of the participants’ answers. The researcher restated the interviews questions to establish the accuracy of the information obtained (Guba, 1981) such as “What is the impact of symptom in your life?”, “Tell me about things that you can do previously, and no longer be able to do them now?”, and “How does your life change after your disease?”.

Peer debriefing is also another significant technique used in this study to assure the collection of valid data (Lincoln and Guba, 1985; Sandelowski, 1993). This technique required working with other researchers (supervisors) who have impartial experience of the study to ensure the information collected is valid and not biased. The supervisors reviewed the researcher’s transcripts, final report and general methodology. After that, feedback provided to ensure credibility and enhance validity. This process helped the researcher to detect general errors in the data, vague description and recognize biases.

4.14.2. Applicability

The third standard is the applicability which is similar to generalizability in quantitative studies and transferability in qualitative studies. Applicability describes the extent to which research can be transferred to different contexts, settings, cultures or populations that are different from the settings where the
study was previously conducted (Bitsch, 2005). Common similarities between studies can determine the possibility of the applicability of the findings of one research to another (Trochim, 2015). In this study, techniques were undertaken in the quantitative phase to enhance applicability included: providing a clear definition and rationale for inclusion and exclusion criteria, use of validated instruments, assessment of bias, and descriptions of statistical calculation and findings (Curry and Nunez-Smith 2014). Ensuring the transferability in the qualitative phase of the study was facilitated using thick description (Li 2004). Thick description involves collecting the necessary details regarding the research participants, setting, context, which while guide other researchers to decide on whether the findings can be transferable to their particular settings. The amount of information provided is not as important as its clarity (Geertz, 1973). The researcher in this study provided sufficient detailed description of the research participants (chapter 6 table 26, 27), details of the research setting (location of approaching and recruiting participants, location where interview were conducted), methodology approach and data analyses were also being offered in the current chapter (chapter 4). The researcher reported all details sufficiently, avoided general or abstract words; rather, the researcher used examples, descriptions, and quotations to clarify the content to readers. Taking voice recordings and writing notes during the interviews was also significant for capturing small details such as the intonations of voice captured. Thick description may improve the interpretation and definition of the measures, improve matching and subsequent data collection for matched subjects, and enhance the presentation of conclusions.
4.14.3. Neutrality

Neutrality which is the objectivity in quantitative and confirmability in the qualitative. Neutrality is the degree to which researchers can remain distanced from the study findings, and findings of a study should be shaped and supported by the data collected and not researcher bias, motivation, or interest (Curry and Nunez-Smith 2014). Neutrality is most commonly used for establishing the quality of qualitative research, due to the fact that quantitative research are commonly not at a potential risk for bias, as it uses distinct protocols and conducts statistical calculation and randomization to avoid bias (Curry & Nunez-Smith 2014). Although, bias can occur in quantitative research in many other ways; thus, it necessary to consider measuring objectivity (Malterud, 2001).

One of the techniques used to ensure neutrality, data obtained from the semi-structured interviews were coded by the main researcher BA and three of the supervisory team PO, HN, HM independently. Codes emerged were discussed followed by the agreement for the final subthemes and overarching themes. In this study, sufficient detailed information was provided in the methodology to allow the reader to understand all the key design and analysis decisions made. Maximum transparency in reporting key decisions and processes for the study implementation and analysis were explicit addressed.

4.14.4. Consistency

Consistency refers to reliability in quantitative and dependability in qualitative research. Consistency ensures that the research results are repeatable and constant (Guba and Lincoln, 1982). Reliability evidence through statistical
tests for instrument reliability (e.g. Cronbach’s alpha). Both instruments used in this study showed good reliability in English and in Arabic. Reliability of the translated ZBI was also tested and was found to be 0.97 (Elmahdi et al., 2011). CKD-SBI also shows high reliability of $\alpha =0.91$ (Almutary et al., 2015). In addition, a consistent technique was used during the study. The instruments were administered and collected by one researcher. Assistance was provided by the same researcher who read out each item and possible responses. This technique helped to maintain a consistent approach during data collection and ensured that participants received the same instructions.

4.14.5. **Rigour in mixed methods research**

The Good Reporting of a Mixed Methods Study (GRAMMS) framework was used to ensure the study quality and rigours (O’Cathain, Murphy and Nicholl 2008). GRAMMS guidelines are explicitly applied to MMR and giving consideration to each method individually (quantitative and qualitative), which will significantly improve the quality of reporting MMR (Halcomb and Hickman 2015). GRAMMS guidelines are presented in Table 14. All GRAMMS guidelines have been addressed in the current chapter including justification for using MMR, description of the design purposes and sequences, describe sampling and when integration occurs. The description of the insight gained from using MMR was reported in the integration chapter (chapter 6).
Table 14: The GRAMMS guidelines as described by O’Cathain et al. 2008

- describe the justification for using a mixed methods approach to the research question;
- describe the design in terms of the purpose, priority, and sequence of methods;
- describe each method in terms of sampling, data collection and analysis;
- describe where integration has occurred, how it has occurred, and who has participated in it;
- describe any limitation of one method associated with the presence of the other method; and
- describe any insights gained from mixing or integrating methods.

4.15. Ethical Considerations

The study protocol was approved by the Research Ethics Committees at Queen’s University Belfast, UK, in September 2017, reference number 10. B.Alshammari 05.17.M6.V1 (Appendix 24). It has also been approved by the Research, Training and Education Centre at King Khaled Hospital, Saudi Arabia, where the study was conducted (Appendix 25). The study is sponsored by the Ministry of Education, Hail University, Saudi Arabia kindly supported by the School of Nursing and Midwifery, at Queens University Belfast. Access to the dialysis centre had been granted from the date of issue of the approval letter, in January 2017, until the end of the study.

During the interviews, there is a possibility that the participants might be tired, distressed or embarrassed during the interview due to discussing personal issue related symptoms and its impact. Participants were given the right to refuse to participate without prejudice. Participation in this study involved the
completion of anonymous self-reported questionnaires. Plain envelopes were supplied with the instruments to ensure confidentiality. The interviews were also conducted in a private place to ensure confidentiality of the participants. The topic being discussed in the questionnaires and interviews (symptom burden and caregiver burden) are unlikely to cause distress. However, consecrations were taken in the case of a participant become distressed or upset when completing the questionnaire or during the interview. In this case, the procedure has to stop until the participant gives verbal consent to continue. The researcher should then give the participant the opportunity to decide whether or not he/she wants to withdraw completely from the study. The researcher reminded the participants of the fact that they had the right to withdraw from the study at any time without prejudice and without providing a reason. Alternatively, should the researcher consider it too distressing for a participant to re-engage with the interview, the interview would be terminated at that point and the researcher would encourage the participant to contact his/her psychiatric liaison team to provide a psychiatric assessment and any additional support to reduce distress and to ensure a valuable interface between the mental and physical health of participants. Finally, the researcher considered following up any distressed participants with a courtesy call to confirm their well-being and that they have taken action.

Anonymization was used to avoid invasion of privacy of participant. All private, personal and sensitive data were not directly related to participants. All data, such as files with personal or identifiable data and can’t be destroyed were stored securely in safe lockers at QUB if they are hard copies, and in a password-protected file if an electronic copy.
4.16. Confidentiality, Anonymity and Safety

According to Babbie (2015), certain unethical behaviours exist in research, such as misuse of information, violation of privacy, and harming other individuals. While gathering data using the semi-structured interview method, various moral principles will be regarded in order to avoid deception, breach of confidentiality and harm to the respondents. The respondents were informed about the goal of the research before participating in the interview in order to avoid violating any moral code. Participants’ data including names and identification information were tabulated and anonymized. The researcher used a specific code to link the data to the participants securely at the time of data collection in order to remove names or other identifying information. This process ensured that the identity of the participants remained secure. Furthermore, the participants were asked to indicate any specific information that they wished to be kept confidential. During the semi-structured interview, both patients and caregivers were offered privacy by choosing a suitable private place to meet. They were informed that they could skip any questions that they did not feel comfortable answering. Patients were also assured of their right to decline or withdraw from the interview at any point if they felt uncomfortable. Participants were assured that this decision would not affect the level of care they receive routinely. Participants were also informed about how their data would be used and secured, such as the questionnaire and audio recordings.

Regarding the safety of data, the voice recorder and all paperwork generated during these processes (including questionnaires, interview notes and consent forms) were brought back to QUB along with a personal laptop; which is
password protected. These kept in a locked filing cabinet in a secured room. Any information stored electronically kept on a password-protected computer. In addition, a copy of the data saved in the QUB Dropbox to avoid losing data, as insurance against any unexpected damage to the personal laptop. A Participant Identification Number was allocated to each participant, and all documentation was numbered. Access to identifiable information was restricted; only the relevant researchers have access to the list that identifies the code of each participant. At the end of the study, the tape recordings were destroyed, and all paperwork generated were kept securely for five years.

It was also taking into consideration the safety of the researcher, by planning a reasonable steps to promote safety and avoid any threats such as physical violence or inappropriate sexual behaviours (Williamson and Burns 2014). The potential plan was to have one of the researcher family members to drive her to the interview appointments. The family member will not be joining the researcher during the interview but waiting nearby to protect the privacy of the participants. The researcher did not need to do this plan as all participants acknowledged their preferences to do the interviews in the hospitals. A mobile telephone was given to the researcher in case she needed assistance and to ensure her safety. A mobile telephone was given to the researcher in case she needed assistance and to ensure her safety.

4.17. Conclusion
This chapter has discussed the research methodology adopted to meet the objectives of this research. It has provided a discussion and justification for
both phases of the study about the aspects of research design, sampling methods, and instruments applied. The study procedures, statistical methods for data analysis and ethical considerations have been described. The subsequent chapter presents the findings of this research.
Chapter 5, Phase 1: Quantitative results
5.1. Introduction:

Quantitative data was collected between September 2017 and March 2018. This chapter is presented using the following headings: 1) Participants demographics and clinical characteristics; 2) The symptom burden level experienced by patients receiving HD; 3) The level of caregiver burden; 4) The association between patient characteristics and symptom burden 5) The association between caregiver characteristics and caregiver burden 6) The association between symptom burden and caregiver burden; 6) summary of the findings and conclusion.

Response rate

In 280 ESRD patients receiving HD at King Khaled Hospital in Hail city; Saudi Arabia, 231 patients were assessed for eligibility and the patients who were eligible were invited to participate in the study. Only 170 patients met the inclusion criteria and were then approached and asked to complete the CKD-SBI. 141 out of 170 patients invited, completed questionnaires with a response rate of approximately 83%, which is considered high for a survey (Nulty, 2008). The required sample size needed for this study was 141 HD patients and 130 caregivers, to achieve the medium effect size, and to ascertain the medium power of the study. The total required number of patients was recruited (141/141). However, from the 141 caregivers invited to participate, only 61 caregivers completed the questionnaire (61/130), with a response rate of 43%. Although a 43% response rate is low compared to the patient response rate of 83%, it is still sufficiently adequate to avoid nonresponse bias and to ensure reliability and validity of survey study findings (Fincham 2008; Nulty 2008;
Baruch and Holtom 2008). Using the independent samples t-test and chi-square indicated that there were no differences in the demographic characteristics between patients who had caregivers, and those who did not have caregivers participating in this study (see Table 15). A significant higher mean symptom burden scores in the patients whose caregivers participated in this study compared to those patients whose caregivers did not participate was identified. This difference indicated that the caregivers who did not participated are having patients with less symptoms which may indicate that they are less distress.

Caregivers received a questionnaire with a stamped addressed envelope and were requested to return the questionnaire within three weeks. Reminder letters were then sent to the appropriate caregivers by the researcher. Only 21 replies out of 141 questionnaires were received from caregivers through the mail, while the remaining 40 questionnaires were completed in the dialysis centre when caregivers were dropping off, picking up, or waiting for their relatives. Figure 16 shows the flow of patients and caregivers throughout the study. It was difficult to approach caregivers as they often do not present at the dialysis centre, and the only way to contact them was through their patients. Using mail for returning questionnaires may have impacted on the response rate (Sheehan 2001). To detect any recruitment bias, t-test was used to compare the differences in the scores between patients who have caregivers participated and the patients who did not have caregivers participated.
**Table 15:** Demographic differences in patients who had caregivers and patients who did not participate in the study

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patients who had caregivers n=61 (%)</th>
<th>Patients with no caregivers participated in the study n=80 (%)</th>
<th>Test of significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs) Mean, SD</td>
<td>51 ± 16</td>
<td>54 ±17</td>
<td>t=1.22, df=139, P=.223</td>
</tr>
<tr>
<td>Gender n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>37(60)</td>
<td>39 (49)</td>
<td>(\chi^2=1.974, df=1, P=.160)</td>
</tr>
<tr>
<td>Female</td>
<td>24(39)</td>
<td>41(51)</td>
<td></td>
</tr>
<tr>
<td>Education level n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary studies</td>
<td>22(36)</td>
<td>45(56)</td>
<td></td>
</tr>
<tr>
<td>Secondary studies</td>
<td>20(32)</td>
<td>22(27)</td>
<td></td>
</tr>
<tr>
<td>Higher education</td>
<td>18(29)</td>
<td>13(16)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1(2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marital status n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>36(59)</td>
<td>50(62)</td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>10(16)</td>
<td>10(12)</td>
<td></td>
</tr>
<tr>
<td>Widowed</td>
<td>8 (13)</td>
<td>18(22)</td>
<td></td>
</tr>
<tr>
<td>Divorced</td>
<td>7(11)</td>
<td>2(3)</td>
<td></td>
</tr>
<tr>
<td>Employment status n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full time job</td>
<td>11(18)</td>
<td>7(9)</td>
<td></td>
</tr>
<tr>
<td>Part time job</td>
<td>3 (5)</td>
<td>1(1)</td>
<td></td>
</tr>
<tr>
<td>Retired</td>
<td>18(30)</td>
<td>22(28)</td>
<td></td>
</tr>
<tr>
<td>Student</td>
<td>2(3)</td>
<td>5(6)</td>
<td></td>
</tr>
<tr>
<td>Unemployed</td>
<td>11(18)</td>
<td>10(13)</td>
<td></td>
</tr>
<tr>
<td>Housewife</td>
<td>14(23)</td>
<td>32(40)</td>
<td></td>
</tr>
<tr>
<td>Self-employee</td>
<td>2(3)</td>
<td>3(4)</td>
<td></td>
</tr>
<tr>
<td>Comorbidity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>18 (29)</td>
<td>28(35)</td>
<td></td>
</tr>
<tr>
<td>1-2</td>
<td>36(59)</td>
<td>47(59)</td>
<td></td>
</tr>
<tr>
<td>3-7</td>
<td>7(11)</td>
<td>5(6.3)</td>
<td></td>
</tr>
<tr>
<td>Travel time to dialysis centre, min</td>
<td>18 ± 19</td>
<td>16± 14</td>
<td></td>
</tr>
<tr>
<td>Duration of dialysis, months</td>
<td>30 ± 44</td>
<td>41±47</td>
<td>t=-1.37, df=139, P=.171</td>
</tr>
<tr>
<td>Symptom prevalence mean, SD</td>
<td>11.2± 6.4</td>
<td>9.8 ± 5</td>
<td>t=-1.44, df=134, P=.152</td>
</tr>
<tr>
<td>Total symptom burden scores</td>
<td>208 ± 146</td>
<td>160± 110</td>
<td>t=-2.19, df=131, P=.030</td>
</tr>
</tbody>
</table>

SD=standard deviation, df= degree of freedom, n= number, yrs=years, min= minutes, %=percentage; * p<.05
Figure 16: Participants flow diagram

N=231 checked for eligibility

Excluded N=61
- 4 under 18
- 7 were receiving HD for less than 3 months
- 36 were illiterate
- 6 were cognitively impaired.
- 1 could not speak either Arabic or English language.
- 2 deaf patients.
- 1 patient had a tracheostomy making speech difficult.
- 3 unconscious.
- 1 died.

Approached and invited N=170

N=141

Patients completed the questionnaires

N=29
Participants (refused/not interested/did not complete the questionnaires)

Caregivers associated with patients who completed the questionnaires were approached and invited N=141

N=80
Did not return the questionnaire back

Caregivers completed the questionnaires N=61

- 4 under 18
- 7 were receiving HD for less than 3 months
- 36 were illiterate
- 6 were cognitively impaired.
- 1 could not speak either Arabic or English language.
- 2 deaf patients.
- 1 patient had a tracheostomy making speech difficult.
- 3 unconscious.
- 1 died.
5.2. Demographic and clinical characteristics of patients and caregivers

The demographic and clinical characteristics of patients and caregivers are summarized in Table 16. Most of the independent variables related to patient characteristics were normally distributed and have been described using mean and standard deviation for continuous variables, and frequency and percentage for categorical data. However, travel time to hospital and dialysis duration were skewed (Figure 17) so they are described using median and IQR, as both are continuous variables.

The mean age of patients on HD was 53 ± 17 years, while for caregivers it was 36 ± 12 years. Patient age ranged between 18 and 90 years. Caregivers were younger, with age ranging between 18 and 66 years (Figure 18). 76 (54%) patients were male and 65 (46%) were female. Unlike patients, most caregiver participants were female 48 (79%) (Figure 19). Males were less likely to take care of female patients than their counterparts.

Approximately 86 (61%) of patients were married; the remainder had no partner, which included 26 (18%) widowed, 20 (14%) single, and 9 (6%) divorced. 40 (28.4%) of the total number of patients were retired; only 18 (12.8%) patients worked in full-time jobs and 4 (2.8%) in part-time jobs. 70% of female patients were housewives (46 out of 65 female patients). 133 (94%) patients were Saudi nationals, of whom 67 (47%) had studied only to primary school level, 42 (30%) to secondary level and 21 (22%) had received higher education.
94 (67%) of patients receiving HD had normal HG levels. Patients had more comorbidities 95 (67%), compared to caregivers 15 (24%). However, there were no significant differences between both groups in relation to comorbidity condition $\chi^2 (1, N = 61) = 2.502: P = 0.114$. The median journey time for patients to reach the dialysis centre was 15 minutes, ranging between 10-20 minutes.

More than half of the caregivers had attended higher education 34 (55.7%), followed by 16 (26.2%) for secondary education with the remainder receiving only primary school education. Many of the patients were cared for primarily by their spouse 20 (32.8%) and adult children 23 (37.7%). The majority of caregivers lived in the same residence as the care recipient 55 (90.2%).

Parametric test was selected after testing the normality of data of dependent variables (symptom burden and caregiver burden) (Sullivan and Artino, 2013). Significance was set at $p < 0.05$. 
Figure 17: Travel time patients spend to reach hospital and dialysis duration were skewed.
Table 16: Demographic and clinical characteristics of patients and caregivers

<table>
<thead>
<tr>
<th>Variable</th>
<th>Categories</th>
<th>Patients (n=141)</th>
<th>Caregivers (n = 61)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr) Mean (SD)</td>
<td></td>
<td>53.1 (17.3)</td>
<td>36.4 (12.9)</td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td>Male</td>
<td>76 (53.9)</td>
<td>13 (21.3)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>65 (46.1)</td>
<td>48 (78.7)</td>
</tr>
<tr>
<td></td>
<td>Saudi</td>
<td>133 (94.3)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Asian</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>African</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>White</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Patient Nationality n (%)</td>
<td>Egyptian</td>
<td>4 (2.8)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yemeni</td>
<td>2 (1.4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Jordanian</td>
<td>1 (0.7)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sudan</td>
<td>1 (0.7)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Illiterate</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Primary studies</td>
<td>67 (47.5)</td>
<td>11 (18.0)</td>
</tr>
<tr>
<td>Educational Level, n (%)</td>
<td>Secondary studies</td>
<td>42 (29.8)</td>
<td>16 (26.2)</td>
</tr>
<tr>
<td></td>
<td>Higher education</td>
<td>31 (22.0)</td>
<td>34 (55.7)</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>1(0.7)</td>
<td>-</td>
</tr>
<tr>
<td>Marital Status, n (%)</td>
<td>Married</td>
<td>86 (61.0)</td>
<td>37 (60.7)</td>
</tr>
<tr>
<td></td>
<td>Single</td>
<td>20 (14.2)</td>
<td>18 (29.5)</td>
</tr>
<tr>
<td></td>
<td>Widowed</td>
<td>26 (18.4)</td>
<td>2 (3.3)</td>
</tr>
<tr>
<td></td>
<td>Divorced</td>
<td>9 (6.4)</td>
<td>4 (6.6)</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Employment, n (%)</td>
<td>Full-time Job</td>
<td>18 (12.8)</td>
<td>23 (37.7)</td>
</tr>
<tr>
<td></td>
<td>Part-time Job</td>
<td>4 (2.8)</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Retired</td>
<td>40 (28.4)</td>
<td>3 (4.9)</td>
</tr>
<tr>
<td></td>
<td>Full-time student</td>
<td>6 (4.3)</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Part-time student</td>
<td>1(0.7)</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Student (FT &amp; PT)</td>
<td></td>
<td>7 (11.5)</td>
</tr>
<tr>
<td></td>
<td>Unemployed</td>
<td>21 (14.9)</td>
<td>7 (11.5)</td>
</tr>
<tr>
<td></td>
<td>Housewife</td>
<td>46 (32.6)</td>
<td>21 (34.4)</td>
</tr>
<tr>
<td></td>
<td>Self-employed</td>
<td>5 (3.5)</td>
<td>-</td>
</tr>
<tr>
<td>Monthly household income (SA Riyal), n (%)</td>
<td>0-5000</td>
<td>5000-10000</td>
<td>10000-15000</td>
</tr>
<tr>
<td>-----------------------------------------</td>
<td>--------</td>
<td>------------</td>
<td>------------</td>
</tr>
<tr>
<td>n (%)</td>
<td>30 (21.3)</td>
<td>45 (31.9)</td>
<td>51 (36.2)</td>
</tr>
</tbody>
</table>

| Patient Travel time, minutes, median (IQR) | 15 (10-20) |

| Dialysis Duration, month median (IQR) | 20 (8-54) |

<table>
<thead>
<tr>
<th>Comorbidity n (%)</th>
<th>0</th>
<th>1-2</th>
<th>3-7</th>
<th>Low (&lt; 10)</th>
<th>Normal (10 – 12)</th>
<th>High (&gt; 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>46 (32.6)</td>
<td>83 (58.9)</td>
<td>12 (8.5)</td>
<td>38 (27)</td>
<td>94 (66.7)</td>
<td>9 (6.4)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Caregiver relationship to Patient n (%)</th>
<th>Spouse</th>
<th>Sibling</th>
<th>Parent</th>
<th>Friend</th>
<th>Son/Daughter</th>
<th>Grandchildren</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>20 (32.8)</td>
<td>4 (6.6)</td>
<td>9 (14.8)</td>
<td>-</td>
<td>23 (37.7)</td>
<td>2 (3.3)</td>
<td>3 (4.9)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patients and caregiver live together n (%)</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>55 (90.2)</td>
<td>6 (9.8)</td>
</tr>
</tbody>
</table>
Yrs= Years, n=number, %=percentages, SA=Saudi Arabia, SAR= Saudi Riyal, GBP= British pound sterling

Figure 18: Histograms of patients and caregivers age.
Figure 19: Chart presenting the differences in gender percentages between patient and caregivers.

5.3. Symptoms experienced by patients receiving HD

A summary of each symptom dimension including prevalence, distress, severity and frequency, for the patient sample is presented in Table 17. These are listed in order from most to least prevalent. The number of symptoms reported by patients is presented in Figure 20, with an overall mean of 10 ± 5.8 from a total of 32 symptoms presented in the CKD-SBI. The most prevalent reported symptom was tiredness (fatigue) 101 (71.6%), followed by itching 89 (63%), bone pain 87 (62%), and muscle cramps 86 (61%). Difficulty falling asleep 71 (50%) and trouble staying asleep 76 (54%) were also reported by the patient sample. Other prevalent symptoms reported included, headache 70 (50%), light-headedness 67 (47.5%), numbness 62 (44%), and dry skin 61 (43%). A number of less common symptoms were also reported including, decreased interest in sex 5 (3.5%) and difficulty with sexual arousal 4 (2.8%). Missing data was observed in the reporting of sexual symptoms in 5 patients, with a percentage of 3.5%. Less than 5% of missing data in the data set, was
acceptable for valid statistical inferences (Dong and Peng 2013). Depression was one of the least reported symptoms 13 (9.2%). However, patients who reported depression, considered it as very severe, frequent and distressing (mean score was 8 out of 10 in all symptom dimensions). Figure 21 summarizes the prevalence of each symptom reported by patients.

Symptom distress was measured on a Likert scale of 0 (none) to 10 in which 0 was not distressful and 10 was very distressful. Overall symptom distress was moderate with a mean (SD) of 5.37 ± 3.01. The highest reported mean symptom distress was for depression 8.31 ± 2.18, followed by anxiety 7.13 ± 3.36, bone pain 6.48 ± 2.92, sadness 6.72 ± 3.43, irritability 6.42 ± 3.17, worry 6.36 ± 2.49, and nervousness 6.26 ± 3.01. Psychological symptoms clearly caused higher levels of distress than physical symptoms. Two reported symptoms had lower mean distress levels: difficulty with sexual arousal and diarrhoea (mean 3 on the 10-point scale). The severity and frequency of psychological symptoms were notably higher than any physical symptoms, see Table 17. The study showed that the greater frequency and severity of symptoms is associated with higher symptom distress.
### Table 17: Summary for symptom (prevalence, distress, severity and frequency) for patient (N=141) using CKD-SBI

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Prevalence n (%)</th>
<th>Distress mean, SD*</th>
<th>Severity mean, SD*</th>
<th>Frequency mean, SD*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tiredness (fatigue)</td>
<td>101 (71.6)</td>
<td>5.71 ± 3.23</td>
<td>6.46 ± 3.08</td>
<td>6.41 ± 3.22</td>
</tr>
<tr>
<td>Itching</td>
<td>89 (63.1)</td>
<td>5.29 ± 3.38</td>
<td>5.98 ± 3.06</td>
<td>5.64 ± 3.34</td>
</tr>
<tr>
<td>Bone Pain</td>
<td>87 (61.7)</td>
<td>6.48 ± 2.92</td>
<td>6.80 ± 2.62</td>
<td>7.02 ± 3.03</td>
</tr>
<tr>
<td>Muscle Cramps</td>
<td>86 (61.0)</td>
<td>5.16 ± 3.01</td>
<td>5.77 ± 2.85</td>
<td>4.50 ± 2.47</td>
</tr>
<tr>
<td>Trouble Staying Asleep</td>
<td>76 (53.9)</td>
<td>5.32 ± 3.09</td>
<td>6.34 ± 2.82</td>
<td>6.64 ± 3.01</td>
</tr>
<tr>
<td>Trouble Falling Asleep</td>
<td>71 (50.4)</td>
<td>5.42 ± 3.26</td>
<td>6.10 ± 3.04</td>
<td>6.45 ± 3.23</td>
</tr>
<tr>
<td>Headache</td>
<td>70 (49.6)</td>
<td>4.76 ± 2.89</td>
<td>4.97 ± 2.70</td>
<td>4.70 ± 2.75</td>
</tr>
<tr>
<td>Light-headedness</td>
<td>67 (47.5)</td>
<td>4.81 ± 2.71</td>
<td>5.22 ± 2.59</td>
<td>4.63 ± 2.58</td>
</tr>
<tr>
<td>Numbness</td>
<td>62 (44.0)</td>
<td>4.60 ± 2.82</td>
<td>5.45 ± 3.08</td>
<td>5.08 ± 3.29</td>
</tr>
<tr>
<td>Dry Skin</td>
<td>61 (43.3)</td>
<td>4.98 ± 3.13</td>
<td>5.10 ± 3.03</td>
<td>5.26 ± 3.37</td>
</tr>
<tr>
<td>Cough</td>
<td>60 (42.6)</td>
<td>4.38 ± 2.96</td>
<td>4.67 ± 2.83</td>
<td>3.82 ± 2.69</td>
</tr>
<tr>
<td>Nausea</td>
<td>58 (41.1)</td>
<td>4.45 ± 2.84</td>
<td>4.41 ± 2.81</td>
<td>4.21 ± 3.14</td>
</tr>
<tr>
<td>Decreased Appetite</td>
<td>55 (39.0)</td>
<td>5.11 ± 2.62</td>
<td>6.13 ± 2.56</td>
<td>6.53 ± 2.53</td>
</tr>
<tr>
<td>Shortness Breath</td>
<td>53 (37.6)</td>
<td>4.62 ± 2.63</td>
<td>4.30 ± 2.49</td>
<td>4.13 ± 2.39</td>
</tr>
<tr>
<td>Constipation</td>
<td>49 (34.8)</td>
<td>4.96 ± 3.12</td>
<td>5.65 ± 2.88</td>
<td>5.55 ± 2.99</td>
</tr>
<tr>
<td>Dry Mouth</td>
<td>49 (34.8)</td>
<td>4.98 ± 2.93</td>
<td>5.08 ± 2.74</td>
<td>5.22 ± 3.21</td>
</tr>
<tr>
<td>Swelling Legs</td>
<td>43 (30.5)</td>
<td>4.70 ± 2.69</td>
<td>4.49 ± 2.29</td>
<td>4.47 ± 2.69</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>41 (29.1)</td>
<td>3.93 ± 2.57</td>
<td>4.54 ± 2.54</td>
<td>4.44 ± 2.64</td>
</tr>
<tr>
<td>Vomiting</td>
<td>40 (28.4)</td>
<td>4.78 ± 2.94</td>
<td>4.70 ± 3.07</td>
<td>4.15 ± 3.07</td>
</tr>
<tr>
<td>Worrying</td>
<td>36 (25.5)</td>
<td>6.36 ± 2.49</td>
<td>6.06 ± 2.41</td>
<td>6.19 ± 2.91</td>
</tr>
<tr>
<td>Irritable</td>
<td>36 (25.5)</td>
<td>6.42 ± 3.17</td>
<td>6.67 ± 3.25</td>
<td>6.28 ± 3.55</td>
</tr>
<tr>
<td>Nervous</td>
<td>35 (24.8)</td>
<td>6.26 ± 3.01</td>
<td>5.94 ± 3.01</td>
<td>5.89 ± 3.30</td>
</tr>
<tr>
<td>Sad</td>
<td>32 (21.3)</td>
<td>6.72 ± 3.43</td>
<td>6.81 ± 3.52</td>
<td>6.31 ± 3.58</td>
</tr>
<tr>
<td>Muscle Soreness</td>
<td>28 (19.9)</td>
<td>5.29 ± 2.48</td>
<td>5.50 ± 2.30</td>
<td>5.36 ± 2.69</td>
</tr>
<tr>
<td>Chest Pain</td>
<td>24 (17.0)</td>
<td>5.25 ± 2.91</td>
<td>4.92 ± 2.83</td>
<td>4.42 ± 3.06</td>
</tr>
<tr>
<td>Restless Legs</td>
<td>17 (12.1)</td>
<td>6.24 ± 3.46</td>
<td>5.47 ± 2.79</td>
<td>6.18 ± 2.34</td>
</tr>
<tr>
<td>Anxious</td>
<td>16 (11.3)</td>
<td>7.13 ± 3.36</td>
<td>7.00 ± 3.37</td>
<td>6.63 ± 3.52</td>
</tr>
<tr>
<td>Difficulty Concentrating</td>
<td>14 (9.9)</td>
<td>4.93 ± 3.08</td>
<td>4.21 ± 2.86</td>
<td>5.43 ± 3.06</td>
</tr>
<tr>
<td>Nocturia</td>
<td>13 (9.2)</td>
<td>5.77 ± 3.70</td>
<td>4.69 ± 2.90</td>
<td>5.46 ± 3.89</td>
</tr>
<tr>
<td>Depression</td>
<td>13 (9.2)</td>
<td>8.31 ± 2.18</td>
<td>8.31 ± 2.39</td>
<td>8.15 ± 2.38</td>
</tr>
<tr>
<td>Decreased Interest Sex</td>
<td>5 (3.5)</td>
<td>5.20 ± 3.27</td>
<td>5.20 ± 3.27</td>
<td>6.40 ± 2.30</td>
</tr>
<tr>
<td>Difficulty with sexual Arousal</td>
<td>4 (2.8)</td>
<td>3.75 ± 4.27</td>
<td>3.75 ± 4.27</td>
<td>4.75 ± 3.86</td>
</tr>
</tbody>
</table>

*Overall Subscale, mean SD* 10 (5.8)

*The mean and standard deviation of symptoms distress, severity, and frequency were only calculated for those participants who answered yes for the symptom prevalence questions, the scores ranging between 0 (none) and 10*
Figure 20: Number of symptoms reported amongst patients receiving HD

Table 18 presents the mean percentages for overall symptom distress, frequency, severity and prevalence. On average 32% of patients reported the prevalence of 32 symptoms. Patients reported similar mean percentages for symptom frequency and severity of 18 ± 12. Lower overall distressing symptoms percentage was reported as 17 ± 11. The average total symptom burden reported was 19 ± 12.
Figure 21: The prevalence of the individual symptoms for the patients

Table 18: Mean percentages of the Overall symptom Scales for HD patients

<table>
<thead>
<tr>
<th>Scale (symptom dimension)</th>
<th>N</th>
<th>Mean and (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total symptom burden</td>
<td>133</td>
<td>19 (12)</td>
</tr>
<tr>
<td>Total symptom prevalence</td>
<td>136</td>
<td>32 (18)</td>
</tr>
<tr>
<td>Total symptom distress</td>
<td>136</td>
<td>17 (12)</td>
</tr>
<tr>
<td>Total symptom severity</td>
<td>136</td>
<td>18 (12)</td>
</tr>
<tr>
<td>Total symptom frequency</td>
<td>136</td>
<td>18 (12)</td>
</tr>
</tbody>
</table>

The total symptoms burden is the sum-up of all symptom dimensions converted to percentages (chapter 4), SD = standard deviation, N=Number of patients.
5.4. Caregiver Burden levels in informal caregivers

The demographic characteristics of caregiver participants is presented in Table 16. Of the 141 patients receiving HD, who were recruited into this study, only 61 of their informal caregivers completed the ZBI and were included in this analysis.

The mean total caregiver burden scores reported by caregivers was $22 \pm 14$, indicating mild to moderate burden, see Table 19 which presents the interpretation of scores for the ZBI. The majority of caregivers 36 (59%) reported a score of $<21$ indicating little to no burden, 18 (29.5%) mild to moderate and 7 (11.5%) reported moderate to severe. No scores indicated extreme severe burden, see Figure 22.

ZBI was rated using a five-point Likert scale, with 0 (rarely) being the lowest score, and 4 (nearly always) being the highest score. The frequencies of caregivers answers are presented in Table 20. This study found that 47 (75.8%) of caregivers considered that their patients were not dependent on them. Commonly caregivers did not report feeling embarrassed 44 (71%), angry with their patients 48 (77.4%) or any loss of privacy 42 (67.7%). The majority of caregivers 52 (85%) expressed fear for their patient’s future, with 24 (38%) reporting an extreme level of fear. A high percentage of caregivers reported that the time spent caring, would impact on their ability to meet other responsibilities and have negative social life effects.
Table 19: Zarit burden interview and interpretation of Score (Zarit 1980)

Interpretation of Zarit burden interview scores:

0 - 21 little or no burden

21 - 40 mild to moderate burden

41 - 60 moderate to severe burden

61 - 88 severe burden

Figure 22: Pie chart presenting the level of burden reported by caregivers
Table 20: Frequency of ZBI responses.

<table>
<thead>
<tr>
<th>Question</th>
<th>Never n (%)</th>
<th>Rarely n (%)</th>
<th>Sometim es n (%)</th>
<th>Often frequent ly n (%)</th>
<th>Nearly always n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do you feel that your relative asks for more help than he or she needs?</td>
<td>26(42.6)</td>
<td>15(24.6)</td>
<td>10(16.4)</td>
<td>7(11.5)</td>
<td>3(4.9)</td>
</tr>
<tr>
<td>Do you feel that because of the time you spend with your relative you don’t have enough time for yourself?</td>
<td>24(38.7)</td>
<td>13(21.0)</td>
<td>14(22.6)</td>
<td>3(4.8)</td>
<td>7(11.3)</td>
</tr>
<tr>
<td>Do you feel stressed between caring for your relative and trying to meet other responsibilities for your family or work?</td>
<td>19(30.6)</td>
<td>10(16.1)</td>
<td>15(24.2)</td>
<td>10(16.1)</td>
<td>7(11.3)</td>
</tr>
<tr>
<td>Do you feel embarrassed about your relative’s behaviour?</td>
<td>44(71)</td>
<td>12(19.4)</td>
<td>4(6.5)</td>
<td>1(1.6)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Do you feel angry when you are around your relative?</td>
<td>48(77.4)</td>
<td>9(14.5)</td>
<td>4(6.5)</td>
<td>0(0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Do you feel that your relative currently affects your relationships with others in a negative way?</td>
<td>33(53.2)</td>
<td>9(14.5)</td>
<td>14(22.6)</td>
<td>3(4.8)</td>
<td>2 (3.2)</td>
</tr>
<tr>
<td>Are you afraid of what the future holds for your relative?</td>
<td>5(8.1)</td>
<td>3(4.8)</td>
<td>19(30.6)</td>
<td>10(16.1)</td>
<td>24(38.7)</td>
</tr>
<tr>
<td>Do you feel your relative is dependent upon you?</td>
<td>47(75.8)</td>
<td>10(16.1)</td>
<td>3(4.8)</td>
<td>1(1.6)</td>
<td>0(0)</td>
</tr>
<tr>
<td>Do you feel strained when you are around your relative?</td>
<td>41(66.1)</td>
<td>12(19.4)</td>
<td>5(8.1)</td>
<td>2(3.2)</td>
<td>1(1.6)</td>
</tr>
<tr>
<td>Do you feel your health has suffered because of your involvement with your relative?</td>
<td>41(67.2)</td>
<td>8(13.1)</td>
<td>4(6.6)</td>
<td>7(11.5)</td>
<td>1(1.6)</td>
</tr>
<tr>
<td>Do you feel that you don’t have as much privacy as you would like because of your relative?</td>
<td>42(67.7)</td>
<td>12(19.4)</td>
<td>5(8.1)</td>
<td>2(3.2)</td>
<td>0(0)</td>
</tr>
<tr>
<td>Do you feel that your social life has suffered because you are caring for your relative?</td>
<td>26(41.9)</td>
<td>14(22.6)</td>
<td>11(17.7)</td>
<td>2(3.2)</td>
<td>8(12.9)</td>
</tr>
<tr>
<td>Do you feel uncomfortable about having friends over, because of your relative?</td>
<td>38 (61.3)</td>
<td>15(24.2)</td>
<td>6(9.7)</td>
<td>0(0)</td>
<td>2(3.2)</td>
</tr>
<tr>
<td>Do you feel that your relative seems to expect you to take care of him/her, as if you were the only one he/she could depend on?</td>
<td>26(42.6)</td>
<td>9(14.8)</td>
<td>15(24.6)</td>
<td>5(8.2)</td>
<td>6(9.8)</td>
</tr>
<tr>
<td>Do you feel that you don’t have enough money to care for your relative in addition to the rest of your expenses?</td>
<td>39(62.9)</td>
<td>9(14.5)</td>
<td>6(9.7)</td>
<td>0(0)</td>
<td>7(11.3)</td>
</tr>
<tr>
<td>Do you feel that you will be unable to take care of your relative for much longer?</td>
<td>47(75.8)</td>
<td>9(14.5)</td>
<td>1(1.6)</td>
<td>2(3.2)</td>
<td>2(3.2)</td>
</tr>
<tr>
<td>Do you feel you have lost control of your life since your relative’s illness?</td>
<td>41(66.1)</td>
<td>8(12.9)</td>
<td>8(12.9)</td>
<td>1(1.6)</td>
<td>3(4.8)</td>
</tr>
<tr>
<td>Do you wish you could just leave the care of your relative to someone else?</td>
<td>45(72.6)</td>
<td>8(12.9)</td>
<td>6(9.7)</td>
<td>2(3.2)</td>
<td>0(0)</td>
</tr>
<tr>
<td>Do you feel uncertain about what to do about your relative?</td>
<td>24(38.7)</td>
<td>13(21.0)</td>
<td>14(22.6)</td>
<td>6(9.7)</td>
<td>4(6.5)</td>
</tr>
<tr>
<td>Do you feel you should be doing more for your relative?</td>
<td>12(19.4)</td>
<td>9(14.5)</td>
<td>19(30.6)</td>
<td>9(14.5)</td>
<td>12(19.4)</td>
</tr>
<tr>
<td>Do you feel you could do a better job in caring for your relative?</td>
<td>8(12.9)</td>
<td>11(17.7)</td>
<td>21(33.9)</td>
<td>10(16.1)</td>
<td>11(17.7)</td>
</tr>
</tbody>
</table>

**Question**

<table>
<thead>
<tr>
<th>Overall, how burdened do you feel in caring for your relative?</th>
<th>Not at all</th>
<th>A little</th>
<th>Moderately</th>
<th>Quite a bit</th>
<th>Extremely</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>20(32.3)</td>
<td>17(27.4)</td>
<td>11(17.7)</td>
<td>9(14.5)</td>
<td>4(6.5)</td>
</tr>
</tbody>
</table>
5.5. **Association between patient characteristics and total symptom burden**

Prior to performing the regression analyses, a visual inspection of residuals and scatterplots confirmed that the assumptions of normality, linearity and homoscedasticity were all met (Mulhern and Greer, 2011). The association between symptom burden and patient characteristics is presented in Tables 21. Gender, marital status, and comorbidities were associated with symptom burden scores in patients receiving HD. Total symptom burden for single (B=0.190, P=.024), widowed (B=.298, P<.001) and divorced (B=.274, P<.001) was significantly higher than in married patients. Higher symptom burden in patients receiving HD was also significantly associated with being female B=.451 P<.001. Higher symptom burden was observed in patients with one or two comorbidities B=.250, P=.006 and was much more significant in patients with more than three comorbidities (B=.291, P=.001). Patient age was negatively associated with symptom burden, although it did not reach a statistically significant level (B=-.078, P=.396). The duration of dialysis and distance from home to the dialysis centre, did not significantly contribute to any symptom burden (B=.014, P=.874) (B=-.051, P=.583).

5.6. **Association between caregiver characteristics and caregiver burden**

Table 22 outlines the association between caregiver characteristics and caregiver burden, and was found to be positively associated with age, gender and comorbidities. Older caregivers reported higher levels of caregiver burden (B=.553, P<.001) (Figure 23). Being female (B=.266, P=.039) was also associated with increased caregiver burden. Caregivers who are spouses or
parents and caring for patients receiving HD, reported more burden than sons or daughters who provided care (B=.514, P<.001) (B=.355, P=.007). Caregivers with at least three comorbidities reported higher caregiver burden, than those with no comorbidities. There was a negative association between unemployment and caregiver burden (B=-.240; P=.074), however, this did not reach a statistically significant level. No significant influence in caregiver burden was found in relation to whether caregivers lived with their patients or not. There was no significant correlation between travel duration and symptom burden in patients (B=-.051, P=.583), and burden in caregivers (B=-.027, P=.836).

![Figure 23: scatterplot showing the positive correlation between caregivers age and caregiver burden](image)

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Table 21: Association between symptom burden and patients characteristics

<table>
<thead>
<tr>
<th>Predictors</th>
<th>symptom burden scores</th>
<th>Mean/SD</th>
<th>β</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td>-0.078</td>
<td>0.369</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>129 ± 88</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>250 ± 140</td>
<td>.451</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary</td>
<td>192 ± 131</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary</td>
<td>185 ± 120</td>
<td>-0.008</td>
<td>0.932</td>
<td></td>
</tr>
<tr>
<td>Higher education</td>
<td>152 ± 132</td>
<td>-0.132</td>
<td>0.155</td>
<td></td>
</tr>
<tr>
<td>other</td>
<td>136</td>
<td>.119</td>
<td>0.170</td>
<td></td>
</tr>
<tr>
<td>Nationality</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saudi</td>
<td>182 ± 130</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Egyptian</td>
<td>182 ± 158</td>
<td>-0.055</td>
<td>0.955</td>
<td></td>
</tr>
<tr>
<td>Yemeni</td>
<td>202 ± 94</td>
<td>0.040</td>
<td>0.645</td>
<td></td>
</tr>
<tr>
<td>Jordanian</td>
<td>189</td>
<td>0.019</td>
<td>0.832</td>
<td></td>
</tr>
<tr>
<td>Sudan</td>
<td>145</td>
<td>-0.008</td>
<td>0.923</td>
<td></td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>married</td>
<td>150 ± 115</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>213 ± 153</td>
<td>0.190</td>
<td>0.024</td>
<td></td>
</tr>
<tr>
<td>divorced</td>
<td>317 ± 163</td>
<td>0.274</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>widow</td>
<td>231 ± 100</td>
<td>0.298</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Employment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full time Job</td>
<td>182 ± 159</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Part time Job</td>
<td>161 ± 90</td>
<td>0.005</td>
<td>0.951</td>
<td></td>
</tr>
<tr>
<td>Retired</td>
<td>119 ± 78</td>
<td>-0.179</td>
<td>0.138</td>
<td></td>
</tr>
<tr>
<td>Full Time Student</td>
<td>185 ± 192</td>
<td>0.35</td>
<td>0.695</td>
<td></td>
</tr>
<tr>
<td>Part Time Student</td>
<td>156 ± 135</td>
<td>-0.119</td>
<td>0.147</td>
<td></td>
</tr>
<tr>
<td>Unemployed</td>
<td>225 ± 118</td>
<td>0.169</td>
<td>0.120</td>
<td></td>
</tr>
<tr>
<td>House wife</td>
<td>237 ± 126</td>
<td>0.220</td>
<td>0.068</td>
<td></td>
</tr>
<tr>
<td>Self-employed</td>
<td>73 ± 66</td>
<td>-0.188</td>
<td>0.035</td>
<td></td>
</tr>
</tbody>
</table>
## Household income in SAR (1 GBP = 5 SAR)

<table>
<thead>
<tr>
<th>Income Range</th>
<th>Mean ± SD</th>
<th>Ref</th>
<th>Beta</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-5000</td>
<td>175 ± 90</td>
<td></td>
<td>.062</td>
<td>.592</td>
</tr>
<tr>
<td>5000-10000</td>
<td>179 ± 148</td>
<td></td>
<td>.056</td>
<td>.633</td>
</tr>
<tr>
<td>10000-15000</td>
<td>196 ± 127</td>
<td></td>
<td>.048</td>
<td>.631</td>
</tr>
<tr>
<td>15000-20000</td>
<td>168 ± 142</td>
<td></td>
<td>.067</td>
<td>.455</td>
</tr>
<tr>
<td>20000&lt;</td>
<td>102 ± 68</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Comorbidity

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>Mean ± SD</th>
<th>Ref</th>
<th>Beta</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No comorbid</td>
<td>149 ± 142</td>
<td></td>
<td>.250</td>
<td>.006</td>
</tr>
<tr>
<td>One or two comorbid</td>
<td>191 ± 119</td>
<td></td>
<td>.291</td>
<td>.001</td>
</tr>
<tr>
<td>Three or more comorbid</td>
<td>250 ± 108</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## HB Level

<table>
<thead>
<tr>
<th>HB Level</th>
<th>Mean ± SD</th>
<th>Ref</th>
<th>Beta</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low HG Level</td>
<td>189 ± 127</td>
<td></td>
<td>.070</td>
<td>.429</td>
</tr>
<tr>
<td>Normal HG Level</td>
<td>178 ± 130</td>
<td></td>
<td>.047</td>
<td>.595</td>
</tr>
<tr>
<td>High HG Level</td>
<td>191 ± 129</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Duration of dialysis/ In months

<table>
<thead>
<tr>
<th>Duration</th>
<th>Beta</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>.014</td>
<td></td>
<td>.874</td>
</tr>
</tbody>
</table>

## Destination to hospital/ In min

<table>
<thead>
<tr>
<th>Destination</th>
<th>Beta</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>-.051</td>
<td></td>
<td>.583</td>
</tr>
</tbody>
</table>

\( \beta = \) Beta or standardized regression coefficient, Min=Minutes, HG=Haemoglobin, SAR=Saudi Riyal, GBP=British pound sterling
Table 22: Association between total caregiver burden and caregiver characteristics

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Caregivers Burden</th>
<th>Mean SD of caregiver burden level</th>
<th>B</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td>.553</td>
<td>.000</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>13 ±7</td>
<td></td>
<td>Ref</td>
<td>.266</td>
</tr>
<tr>
<td>Female</td>
<td>21 ± 48</td>
<td></td>
<td>.375</td>
<td>.039</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary</td>
<td>18 ± 15</td>
<td></td>
<td>Ref</td>
<td>.105</td>
</tr>
<tr>
<td>Secondary</td>
<td>15 ± 8</td>
<td></td>
<td>-.105</td>
<td>.545</td>
</tr>
<tr>
<td>Higher education</td>
<td>22 ± 13</td>
<td></td>
<td>.127</td>
<td>.465</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>21 ± 13</td>
<td></td>
<td>Ref</td>
<td>.298</td>
</tr>
<tr>
<td>Single</td>
<td>13 ± 10</td>
<td></td>
<td>-.105</td>
<td>.019</td>
</tr>
<tr>
<td>Divorced</td>
<td>19 ± 10</td>
<td></td>
<td>-.061</td>
<td>.619</td>
</tr>
<tr>
<td>widow</td>
<td>38 ± 4</td>
<td></td>
<td>.257</td>
<td>.039</td>
</tr>
<tr>
<td>Employment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full time job</td>
<td>18 ± 10</td>
<td></td>
<td>Ref</td>
<td>.072</td>
</tr>
<tr>
<td>Retired</td>
<td>24 ± 21</td>
<td></td>
<td>.072</td>
<td>.571</td>
</tr>
<tr>
<td>Student</td>
<td>14 ± 10</td>
<td></td>
<td>-.111</td>
<td>.403</td>
</tr>
<tr>
<td>House wife</td>
<td>25 ± 14</td>
<td></td>
<td>.225</td>
<td>.107</td>
</tr>
<tr>
<td>unemployed</td>
<td>9 ± 10</td>
<td></td>
<td>-.240</td>
<td>.074</td>
</tr>
<tr>
<td>Household income</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-5000</td>
<td>21 ± 17</td>
<td></td>
<td>Ref</td>
<td>.194</td>
</tr>
<tr>
<td>5000-1000</td>
<td>16 ± 14</td>
<td></td>
<td>-.194</td>
<td>.275</td>
</tr>
<tr>
<td>10000-1500</td>
<td>20 ± 12</td>
<td></td>
<td>-.038</td>
<td>.833</td>
</tr>
<tr>
<td>15000-20000</td>
<td>19 ± 10</td>
<td></td>
<td>-.074</td>
<td>.644</td>
</tr>
<tr>
<td>Comorbidity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No comorbid</td>
<td>17 ± 12</td>
<td></td>
<td>Ref</td>
<td>.227</td>
</tr>
<tr>
<td>One or two comorbid</td>
<td>24 ± 13</td>
<td></td>
<td>.227</td>
<td>.069</td>
</tr>
<tr>
<td>Three or more</td>
<td>38 ± 4</td>
<td></td>
<td>.304</td>
<td>.016</td>
</tr>
<tr>
<td>Co-habitating status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>20 ± 13</td>
<td></td>
<td>Ref</td>
<td>-.097</td>
</tr>
<tr>
<td>no</td>
<td>15 ± 10</td>
<td></td>
<td>-.097</td>
<td>.458</td>
</tr>
<tr>
<td>Relationship to patient</td>
<td>Value (± Standard Error)</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>----------------------------</td>
<td>--------------------------</td>
<td>-------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Son and daughter</td>
<td>12 ± 8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parent</td>
<td>24 ± 13</td>
<td>.355</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spouse</td>
<td>25 ± 15</td>
<td>.514</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sibling</td>
<td>22 ± 9</td>
<td>.220</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grandchildren</td>
<td>16 ± 9</td>
<td>.057</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other relationship</td>
<td>20 ± 2</td>
<td>.158</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$\beta =$ Beta or standardized regression coefficient, Min=Minutes, HG=Haemoglobin, SAR=Saudi Riyal, GBP= British pound sterling
5.7. **Multiple Regression**

Multiple linear regression analysis was performed to examine the association between patient characteristics, for only those characteristics which had a p-value <0.05, and symptom burden levels. A regression model was tested based on the statistical significance of outcomes from bivariate correlations for patients.

5.7.1. **Patients:**

Three variables were identified and included in the regression model. This multiple regression model was developed to test if there would be a significant prediction of symptom burden in patients receiving HD by gender, marital status and comorbid conditions. Gender and marital status was transformed using dummy codes (gender: male [0] & female [1]; married: used as the reference [1] & single, widowed and divorced [0]). The analysis demonstrated predictors explained 25% of the model ($R^2$ of .246). A significant multiple linear regression was found $F (3,129) = 14.058, p<.001$ (Table 23).

However only gender ($\beta=.409; p<.001$) and comorbid conditions ($\beta =.175$, $p=.027$) added statistical significance to the model. Gender, specifically being female, was the strongest contributor to the model ($\beta = .409, CI = 2.175-5.947, p<.001$). Higher comorbidity levels were also associated with higher levels of patient symptom burden ($\beta = .175, CI = .168 – 2.715, p=.027$).
Table 23: Multiple regression analyses predicting total symptom burden and (gender, marital status, and comorbidity)

<table>
<thead>
<tr>
<th>Predictor variable</th>
<th>B</th>
<th>CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>.409</td>
<td>2.175-5.947</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Marital status</td>
<td>.040</td>
<td>-.663-1.017</td>
<td>n.s</td>
</tr>
<tr>
<td>Comorbidity level</td>
<td>.175</td>
<td>.168-2.715</td>
<td>.027</td>
</tr>
</tbody>
</table>

Cl= Confidence Interval, B= Standardized Coefficients Beta, n.s=not significant

5.7.2. Caregivers:

Multiple linear regression analysis was performed to examine the association between caregiver characteristics, for only those characteristics which had a p-value <0.05, and carer burden levels. A regression model was tested based on the statistical significance of outcomes from bivariate correlations for caregivers.

Three variables were identified and included in the regression model. This multiple regression model was developed to test if there would be a significant prediction of caregiver burden in caregivers of patients receiving HD by gender, age and comorbid conditions. Gender was transformed using dummy codes (gender: male [0] and female [1]). The analysis demonstrated predictors explained 39% of the model (R² of .387). A significant multiple linear regression was found F (3, 57) = 14.058, p<.001 (Table 24).

However only age (β=.566; p<.001) and gender (β =.286, p=.009) added statistical significance to the model. Age was the strongest contributor to the
model ($\beta = .566, \ CI = 352-928, \ p<.001$). Gender, specifically being females, was also significantly associated with higher levels of patient symptom burden ($\beta = .286, \ CI = .2.647-17.598, \ p=.009$).

Table 24: Caregiver multiple regression model outcomes

<table>
<thead>
<tr>
<th>R square</th>
<th>Adjusted R Square</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.387</td>
<td>0.354</td>
<td>14.058</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Predictor variable</th>
<th>B</th>
<th>CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>.286</td>
<td>2.647-17.598</td>
<td>.009</td>
</tr>
<tr>
<td>Age</td>
<td>.566</td>
<td>.352-.928</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Comorbidity level</td>
<td>-.005</td>
<td>-7.356-7.051</td>
<td>n.s</td>
</tr>
</tbody>
</table>

CI= Confidence Interval, B= Standardized Coefficients Beta, n.s=not significant

5.8. The relationship between symptom burden and caregiver burden

One of the main aims of this study was to determine the association between caregiver burden levels and patient symptom burden. Only 61 patients/caregivers pairs were established to explore this relationship. The other 80 patients were excluded from this analysis, as caregiver data was not obtained.

Table 25: highlights the association between caregiver burden scores and symptom burden scores measured by Pearson's Correlation. Symptom prevalence in patients receiving HD was significantly associated with caregiver burden ($B= .256^*; \ P=.049$). The more symptoms the patient had, the higher the level of caregiver burden. Figure 24 illustrates the positive association between caregiver burden in relation to symptom burden and the prevalence using a
A positive correlation between total symptom burden and caregiver burden was observed, although it did not reach a statistically significant level ($B=0.196; P=0.138$). Caregiver burden was also positively related to all other symptom dimensions, including symptom distress, frequency and severity.

Table 25: The association between total symptom burden and caregiver burden

<table>
<thead>
<tr>
<th>Symptom Dimension</th>
<th>Caregiver burden</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$B$</td>
</tr>
<tr>
<td>Symptom burden</td>
<td>0.196</td>
</tr>
<tr>
<td>Symptom Prevalence</td>
<td>0.256*</td>
</tr>
<tr>
<td>Symptom distress</td>
<td>0.215</td>
</tr>
<tr>
<td>Symptom frequency</td>
<td>0.184</td>
</tr>
<tr>
<td>Symptom severity</td>
<td>0.197</td>
</tr>
</tbody>
</table>

*B* = Beta or Standardized Coefficients Correlation is significant at the 0.05 level (2-tailed). *$P<0.05$, **$P<0.01$, ***$P<0.001$
Figure 24: Scatter plot presenting the positive correlation between caregiver burden scores in relation to symptom prevalence and symptom burden
5.9. **Summary of the findings:**

The mean number of symptoms reported by patients was approximately $10 \pm 5.8$ from a total of 32 symptoms. The most-reported symptom was fatigue. Being female, unmarried, and having one or more health conditions demonstrated a statistically significant association, with increased symptom burden in patients receiving HD. However, within the multiple regression model, only being female and having a comorbid condition was significantly associated with symptom burden. Caregiver burden was positively associated with being older, female and having numerous comorbidities. Additionally, symptom prevalence in patients receiving HD was significantly associated with caregiver burden. Caregiver burden was also positively related to all other symptom dimensions, including symptom distress, frequency and severity, although it was not observed to be at a statistically significant level.

5.10. **Conclusion:**

This chapter presented the quantitative findings of the study in three main analyses: identifying symptom burden level, identifying the caregiver burden level and comparing between symptom burden and caregiver burden. Discussion of the significant findings, strengths and limitations of this phase of the study are presented in the discussion chapter. Consistent with the mixed method sequential explanatory design, the quantitative findings were explained by the analysis of the qualitative findings. Chapter 6 presents the qualitative data from the semi-structured interviews.
Chapter 6: Qualitative findings
6.1. Introduction

This chapter presents the findings from the in-depth qualitative interviews carried out with patients receiving HD and their caregivers. The aims of the qualitative interviews of this study included an exploration of the impact of symptom burden on patients’ lives and the management strategies used by patients to control or relieve these symptoms. The study also aimed to explore the impact of caregiver burden on those who provided informal care to patients with HD. In this mixed method study, the qualitative analysis performed an in-depth explanatory role which helped to clarify the quantitative phase findings of the study. The quantitative and qualitative data analysis was completed individually. However, the integration of the findings from each phase of the study were incorporated together in the integration chapter of the study (chapter 7).

There are three key parts to the chapter. Descriptive information of study participants is provided, followed by a presentation of the key themes and subthemes generated from participant interviews. The chapter concludes with a discussion of the main findings of this phase.

6.2. The Study Participants

Recruitment of participants for interviewing took place between September 2017 and March 2018, this process is outlined in detail in Chapter 4. All patients involved in this phase of the study had previously participated in the quantitative phase of the study.

The selection of participants for the interviews was based on patients’ total CKD-SBI scores with five from the lowest, median and highest percentiles.
using SPSS. If any patient refused to participate in the study, patients with the next highest, median and low scores were recruited to the study. This gave the researcher the opportunity to obtain different insights into a variety of cases (patients with high, low and medium burden), which was reflected in the variation in symptom experiences as well as the variation in the management strategies used by patients. Caregivers who are associated with these patients, sample, were recruited. If patients refused to participate, their caregivers were excluded from the interviews. The recruitment of study participants and interviews continued until data saturation was achieved.

There were some initial difficulties recruiting caregivers to the quantitative phase of the study, as they generally did not attend the dialysis centre during HD sessions. However, a number of strategies were developed to overcome this difficulty. Caregivers who completed the questionnaire on the quantitative phase were asked to sign "the consent to be contacted form", to be able to contact them in the second phase (qualitative phase). As there were limited caregiver responses from the mail shot during the quantitative phase of the study, the researcher considered phoning potential participants who provided their phone number during the first phase (quantitative), to determine if they would agree to consent to participate in this study.

A total of 27 participants were approached, 15 patients and 13 associated caregivers. Two patients were not able to participate due to health reasons. 4 caregivers declined to participate as they don’t have to attend for interviews. The final overall participants recruited was 22, including 13 patients and 9 associated caregivers. Following these interviews, data saturation was
achieved, as no new themes or subthemes were identified. The decisions of no further interviews is needed, was made prior to coding and thematic development (Saunders et al., 2018). Interviews were conducted face-to-face and lasted between 15 to 60 minutes. All participants provided written consent prior to interviews. Two patients were interviewed while undergoing dialysis, as they were isolated temporarily in this location due to treatment restrictions associated with Hepatitis C. The remaining patients were interviewed in a location and time of their preference within the dialysis centre, before or after dialysis. All caregivers were interviewed in a private room in the dialysis centre based on their choice. Participants included in the study were heterogeneous in terms of socio-demographic characteristics and symptom burden scores. Using a heterogeneous sample in qualitative research is more likely to achieve greater generalisation of findings than a homogenous sample, especially if the findings can be across a diverse group of cases (Robinson 2014). In this study, the diverse case samples involved patients with different ages, marital status, genders as well as experiencing different symptom burden levels (high, middle, low). Table 26 and 27 provide a summary of the demographic characteristics of participants, the duration receiving HD and the symptom burden level based on the CKD-SBI score recorded during the first phase of the study.
Table 26: Patients demographic information

<table>
<thead>
<tr>
<th>patient ID</th>
<th>Age</th>
<th>Gender</th>
<th>Marital status</th>
<th>Occupation</th>
<th>education</th>
<th>HD Duration</th>
<th>SBL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>45</td>
<td>female</td>
<td>divorced</td>
<td>Full-time - Teacher</td>
<td>higher education</td>
<td>54</td>
<td>Highest</td>
</tr>
<tr>
<td>2</td>
<td>41</td>
<td>female</td>
<td>single</td>
<td>unemployed</td>
<td>secondary school</td>
<td>84</td>
<td>Highest</td>
</tr>
<tr>
<td>3</td>
<td>45</td>
<td>female</td>
<td>married</td>
<td>retired</td>
<td>primary school</td>
<td>3</td>
<td>Highest</td>
</tr>
<tr>
<td>4</td>
<td>19</td>
<td>female</td>
<td>single</td>
<td>full-time student</td>
<td>secondary school</td>
<td>3</td>
<td>Highest</td>
</tr>
<tr>
<td>5</td>
<td>67</td>
<td>male</td>
<td>married</td>
<td>retired</td>
<td>high education</td>
<td>36</td>
<td>Highest</td>
</tr>
<tr>
<td>6</td>
<td>49</td>
<td>male</td>
<td>married</td>
<td>retired</td>
<td>secondary school</td>
<td>13</td>
<td>Middle</td>
</tr>
<tr>
<td>7</td>
<td>65</td>
<td>female</td>
<td>married</td>
<td>housewife</td>
<td>primary school</td>
<td>5</td>
<td>Middle</td>
</tr>
<tr>
<td>8</td>
<td>71</td>
<td>male</td>
<td>married</td>
<td>retired</td>
<td>secondary school</td>
<td>48</td>
<td>Middle</td>
</tr>
<tr>
<td>9</td>
<td>80</td>
<td>female</td>
<td>widow</td>
<td>housewife</td>
<td>primary school</td>
<td>48</td>
<td>Middle</td>
</tr>
<tr>
<td>10</td>
<td>65</td>
<td>male</td>
<td>married</td>
<td>Self-employed</td>
<td>Primary school</td>
<td>12</td>
<td>Lowest</td>
</tr>
<tr>
<td>11</td>
<td>56</td>
<td>male</td>
<td>married</td>
<td>Retired</td>
<td>Higher education</td>
<td>60</td>
<td>Lowest</td>
</tr>
<tr>
<td>12</td>
<td>38</td>
<td>female</td>
<td>single</td>
<td>Unemployed</td>
<td>Secondary school</td>
<td>104</td>
<td>Lowest</td>
</tr>
<tr>
<td>13</td>
<td>33</td>
<td>female</td>
<td>married</td>
<td>Housewife</td>
<td>Primary school</td>
<td>9</td>
<td>Lowest</td>
</tr>
</tbody>
</table>

SBL=symptom burden levels patients with the lowest, median and highest percentiles of CKD-SBI were recruited, HD duration was measured in months
Table 27: Caregivers demographic information

<table>
<thead>
<tr>
<th>Carer ID</th>
<th>Pt ID</th>
<th>Age</th>
<th>Sex</th>
<th>Marital status</th>
<th>Education level</th>
<th>Occupation</th>
<th>Caregiver relationship to patients</th>
<th>Level of CB</th>
</tr>
</thead>
<tbody>
<tr>
<td>C3</td>
<td>P3</td>
<td>21</td>
<td>F</td>
<td>Single</td>
<td>Secondary</td>
<td>Student</td>
<td>Daughter</td>
<td>Mild</td>
</tr>
<tr>
<td>C4</td>
<td>P4</td>
<td>45</td>
<td>F</td>
<td>Married</td>
<td>Primary</td>
<td>Housewife</td>
<td>Mother</td>
<td>Moderate</td>
</tr>
<tr>
<td>C5</td>
<td>P5</td>
<td>65</td>
<td>F</td>
<td>Married</td>
<td>Primary</td>
<td>Housewife</td>
<td>Wife</td>
<td>Moderate</td>
</tr>
<tr>
<td>C6</td>
<td>P6</td>
<td>40</td>
<td>F</td>
<td>Married</td>
<td>Higher education</td>
<td>Housewife</td>
<td>First wife</td>
<td>Mild</td>
</tr>
<tr>
<td>C7</td>
<td>P7</td>
<td>35</td>
<td>F</td>
<td>Divorced</td>
<td>Secondary</td>
<td>Unemployed</td>
<td>Daughter</td>
<td>Mild</td>
</tr>
<tr>
<td>C9</td>
<td>P9</td>
<td>32</td>
<td>F</td>
<td>Single</td>
<td>Higher education</td>
<td>Full time teacher</td>
<td>Daughter</td>
<td>no burden</td>
</tr>
<tr>
<td>C10</td>
<td>P10</td>
<td>43</td>
<td>F</td>
<td>Married</td>
<td>Secondary</td>
<td>Housewife</td>
<td>Daughter in-law</td>
<td>Mild</td>
</tr>
<tr>
<td>C11</td>
<td>P11</td>
<td>25</td>
<td>F</td>
<td>Single</td>
<td>Higher education</td>
<td>Unemployed</td>
<td>Daughter</td>
<td>Mild</td>
</tr>
<tr>
<td>C12</td>
<td>P12</td>
<td>20</td>
<td>F</td>
<td>Single</td>
<td>Higher education</td>
<td>Student</td>
<td>Sister</td>
<td>Mild</td>
</tr>
</tbody>
</table>

Pt=patients, F=female, CB=caregiver burden, Level of burden identified based on ZBI scores in the cross-sectional phase which 0-21 = no burden, 21-40=mild, 41-60=moderate, 61-88=sever burden.

6.3. Themes from Patient Interviews

Using the principles and guidance of the Theory of unpleasant symptoms, three main themes and associated sub-themes were identified. These are presented in Table 28.

All the interview transcripts were coded by three researchers independently using Nvivo 11. Later, a map was drawn to correlate the codes initiated and create the overarching themes (Appendix 26). Three thematic charts were generated for each of the main three overarching themes with their associated subthemes identified. These charts presented all quotations in related to the
participants reporting them. An example of one of these themes is presented in (Appendix 27). A discussion of these themes and sub-themes was provided during the data analysis, which included the identification of any relevant inter-relationships between these themes.
Table 28: List of Overarching Themes, Interpretative Themes and Subthemes from the Semi-Structured Interviews

<table>
<thead>
<tr>
<th>Overarching themes</th>
<th>Sub-themes</th>
<th>Subthemes 2</th>
<th>Quotation examples</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1) Holistic impact of symptom burden</strong></td>
<td>A) Physical Impact</td>
<td>Self-care</td>
<td>I stopped doing housework, I used to install lights and repair things that are not working in the house. But now I am so tired that I can’t even comb my hair or take a bath. My mother helps me do that (P4, female, single, 19y)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Family commitment</td>
<td>“Previously, I was able to take care of my sick mother, give her medicine and help her, but I recently stopped doing so because of the stress, tiredness and symptoms that are always present with me after dialysis sessions.” (P1, female, divorced, 45y) “Previously, I relied on myself, I used to tidy up my room, my clothes and stuff, but now I can’t do much work. My wife helps me get my things ready. I don’t have any daughters only 6 sons and all are married except one who still studies at university.” (P8, male, married, 71y)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sense of being dependent</td>
<td>My mettle got weak. Before, I used to cook and prepare the meals, but now if only I go and bring some water to drink I feel tired. I liked cooking some dishes like stuffed vegetables that take time and effort and need high skill, but now this became impossible. (P3, Female, married, 45y)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Feeling of being restrained (restricted and tied)</td>
<td>“Renal dialysis is controlling my sleep. Even when I return from renal dialysis sessions I feel exhausted and cannot go out again until the next day, because all my energy has been drained. I stopped performing my responsibilities. I have a servant at home but I do not depend on her completely. (P7, female, married, 65y)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Inability to continue working, education, and participating in hobbies</td>
<td>I can’t go camping and spend the night because I have dialysis every other day. My hobbies are hunting, camping and long safari trips. But this disease came over me and pinned us (like when a wrestler pins its opponent making them fall). Now we go out at dawn and come back before it is sunset, I got restricted.” (P8, male, married, 71y)</td>
</tr>
<tr>
<td></td>
<td>B) Psychological and Emotional Impact</td>
<td>Look of pity</td>
<td>“I do not like people feeling pity for me for being unable to walk. Sometimes when I take a taxi and the driver knows that I am going to hospital for renal dialysis, he is compassionate and refuses to take the fare.” (P1, female, divorced, 45y) “I need the society not to look at us as only sick people. Such look of pity is annoying, and some words that show sympathy are hard to us even if showed unintentionally.” (P5, male, married, 60y)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sadness</td>
<td>“Sometimes I hide from my son and mother and cry. I want to sweep out the sadness in my heart, I think of how I can adapt to treatment… I have been unable to adapt for five years. Those who see me never realise that my heart is broken...My heart is severely broken. I feel that I lost the most valuable and beloved thing, which is health. People look at me with pity...&quot; (P5, male, married, 60y)</td>
</tr>
</tbody>
</table>
and this is what bothers and affects me most. They make me feel that I am imperfect and internally fragile like glass. (P1, female, divorced, 45y)

Powerless
I feel that I am like a broken hand that cannot do anything; I exist but cannot do anything for them nor for myself. I am unable to get completely treated nor be of help to them. I exist, but with no benefit. I am completely like a broken hand that cannot carry anything nor be of any help. One day such hand may get cut off or splinted. (P1, female, divorced, 45y)

C) Social impact
Social restriction because of Fear: Fear of losing control and fear from symptoms
"I fear of attending parties and drinking a lot of drinks as this will increase symptoms before the next renal dialysis session. Sometimes I prefer staying alone than leaving home for fear of symptoms that I will suffer from after attending parties, such as tiredness, nausea, headache and depression in some cases. When I return from renal dialysis sessions I usually feel exhausted and cannot go out again until the next day, because all my energy has been drained. How about going to parties?" (P1, female, divorced, 45y)

D) Cognitive impact
Losing memories
"Even my memory was affected; yesterday my daughter took some money from me after I gave her permission, a little later I was asking myself where did the money go? I asked my children and my daughter answered “I took them for the purpose I informed you of. At that moment I remembered!!” (P7, female, married, 65y)

Unable to concentrate
"All the time thinking of the pains I am suffering even when my family members speak to me they say I am not concentrating to what they are saying" (P4, female, single, 19y)

2) Factors effecting symptom experience
Socio-demographic factors
Age
"I am an old woman, and it is good to be in this health condition while suffering from such disease, thank God." (P9, female, widow, 80)
"I am not looking for getting healthier anymore. I don’t want my health to be as before when I was a young man. I am an old man and my current health condition is acceptable for someone of such age" (P10, male, married, 65)

Financial status
“Our financial situation is very poor. We live in a rented house. I have sons and daughters and our salary is not sufficient. People say if one is healthy and peaceful, the money then is not important. This is a lie, a patient has to eat and drink certain foods and drinks. A patient must be physically and psychologically relaxed and sleep well. Sometimes a visiting doctor comes from abroad and I need to travel to Riyadh to see them to check on my condition, but I cannot travel because I do not have money" (P3, female, married, 45y)

Education
“I studied in the primary school while I was sixty five years old so that I can learn reading and writing, learn the correct healthy behaviour and learn what I should avoid, and to be able to read doctor instructions and educate myself about life in general. It is enough that when I read the holy Quran I feel overwhelmingly peaceful to such degree it makes me feel that I have healed from all diseases” (P10, male, married, 65)
<table>
<thead>
<tr>
<th><strong>Situational factors</strong></th>
<th><strong>Life burden</strong></th>
<th>“my commitment to teaching, my son, taking care of my sick mother and my work as a teacher at school tire me and exacerbate the symptoms. Also thinking about my cure and burdens of life increases my sorrow and exacerbates my psychological state which in turn makes me feel that the symptoms are getting worse. For example, headache and dizziness increase with stress, thinking and sadness” (P1, female, divorced, 45y)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Emotional status</strong></td>
<td>“When my mood, psychological or emotional state is bad, I stop eating, drinking and taking care of myself in all aspects, and stay alone, which causes deterioration of my health condition. Psychological relief is half of the treatment” (P3. Female, married, 45y)</td>
<td></td>
</tr>
<tr>
<td><strong>Religious &amp; Spirituality</strong></td>
<td>“I do not object to the will of God, I normally accept what God destined for me. My psychological state is always high and I am satisfied with all that God decides for me. If I had suffered from a disease free from symptoms, I may have been able to adapt to more easily knowing the disease has a treatment. And this is, at first and before all, the willing of The Creator, which I do not object to.” (P3. Female, married, 45y)</td>
<td></td>
</tr>
</tbody>
</table>

| **3) Symptom management** | **A) Self-management strategies utilized in response to symptoms** | **Medication** | “I suffer from sleeping disorder when I am in pain whether it is a headache or bone pain, and if this happens, I take Panadol. The symptom gets relieved that night, and the next night the symptom returns. I need to take another painkiller” (P3, Female, married, 45y) |
| | | **Cognitive strategies** | “I am satisfied with my life and try to keep my mind occupied with anything in order not to think about this symptom as it will be present with me all my life if not treated. So I try, as much as possible, to go out whenever I am physically able to” (P1, female, divorced, 45y) |
| | | **Life style changings** | “I do not drink a lot of the fluids, especially after dialysis directly, because the next day there will be no dialysis session and fluids will accumulate in my body causing me nausea or diarrhoea.” (P3. Female, married, 45y) |
| | | | “I should not tire myself and should stay comforted and away from nervousness, these are the doctor’s tips. Everyone receives such tips as they are very useful.” (P10, male, married, 65) |
| | | **Religious and Spiritual methods for acceptance and healing** | “After all doors were closed in my face, I currently go to a sheikh to recite Quran for me to recover and heal. I feel better, thank God” (P1, female, divorced, 45y) |
| | | | “It is enough that when I read the holy Quran I feel overwhelmingly peaceful to such degree it makes me feel that I have healed from all diseases” (P10, male, married, 65) |
| **B) Sources of knowledge** | **Patient experience and family advice** | “My mother (may God have mercy upon her) taught me that massage relieves the symptoms and used this method to relieve my grandfather’s suffering, may God have mercy upon him as well, as he was suffering from renal failure and was very exhausted. When he suffered joint and bone pain, she used to rub his legs with olive oil then wrap them tightly with some warm cloth so that he could sleep. After that my grandfather would feel far better when he got up.” (P2, female, single, 41) |
“Thanks to my experience I obtained from things happened to me in the centre, I was vomiting and a doctor asked a nurse to measure my blood pressure and it was really high.” (P8, male, married, 71y)

<table>
<thead>
<tr>
<th>HCPs and other resources</th>
<th>“I read scientific publications and books and search on the Internet, but at the end I rely only on opinions of the doctors at the centre. (P1, female, divorced, 45y) “Via YouTube and advice from people who had same problems before.” (P2, female, single, 41)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>C) Barriers for symptom management</strong></td>
<td><strong>Losing trust in HCPs quality of care</strong> “I had a situation, two doctors quarrelled with each other over medicine prescription, and it ended that I took medicines that they both prescribed for me. Such decision of taking medicines they both prescribed had effects on my blood and caused me blood coagulation, and because of this I will have to use Aspirin all my life” (P1, female, divorced, 45y)</td>
</tr>
<tr>
<td></td>
<td><strong>Inadequate time and staff availability</strong> “The problem is that the doctors at the centre do not give us the required attention, perhaps due to time limitations and being busy, I do not know. Sometimes, I feel as if they are doing their job as any other money making job, with no consideration for the feelings of patients as human beings...I lost trust in them as my experiences with them prove that patients are not a priority for doctors. The only times I had to go to hospital for emergency treatment were when I fainted.” (P1, female, divorced, 45y)</td>
</tr>
<tr>
<td></td>
<td><strong>Lack of communication and guidance from HCPs and sense of “not being heard” or “being ignored” by the HCPs</strong> “Someone went to a doctor and told them &quot;When my head was down, my hat fell, and when I lifted my head, I carried my hat and placed it on my head.&quot; The doctor said, &quot;One tablet in the morning and one in the evening.&quot; (P9, female, widow, 80)</td>
</tr>
</tbody>
</table>
6.3.1. Theme 1: Holistic impact of symptom burden in patients receiving HD

As the main aim of this study is to explore symptom burden in patients receiving HD, it is significant to explore the possible impact of symptoms on patients’ lives. While the patients interviewed were constantly experiencing multiple symptoms, this offered an explanation of the feelings associated with their symptoms. This is unique, as historically quantitative approaches have generally been used to explore symptom burden which limits understanding of the cause and effect relationship in symptoms experienced and does not provide definite in-depth information related to the symptom experience and how some factors influence reported symptoms.

Within this main theme, a comprehensive picture of the holistic impact of symptom burden on patients receiving HD is described. The focus is on the major aspects of these experiences, in relation to the way symptoms can affect and disrupt normal life. It embraces a variety of physical, psychological, emotional, cognitive and social effects. These effects represent the subthemes which constitute one of the main themes of the study; holistic impact of symptom burden.

6.3.1.1. Physical Impact

Physical effects refer to a reduction in the function of physical activity (Kaba et al 2007). Patients suggested that the physical effects of symptoms had a significant impact on their daily lives. Patients referred to their symptoms as weakness, pain, lack of health or physical disability.
The patients described daily activities which required physical functioning, as a constant struggle without end. This struggle had a significant constant and negative impact on patients’ daily life routine. Often they could no longer carry out simple daily activities, such as self-care, family responsibilities, and engage in hobbies and interests. Patients could not work, most were unable to continue with education or activities which they had engaged in before the diagnosis of ESRD and the development of associated symptoms. Patients primarily identified fatigue, bone and muscle pain as the main reason why they could not engage in physical activities:

“I feel pain in the bones, joints and muscles. I can only stand with difficulty by resting on something so that I can walk... Later on, it came back and increased even while I was having renal dialysis sessions”

(P3. Female, married, 45y)

“I feel there is numbness in my feet and severe pain. I cannot stretch out my feet very well as they feel convulsionary. Foot bone pain does not let me sleep, in addition to fatigue and exhaustion.”

(P9. Female, widow, 80)

One of the participants reported that she was unable to carry out self-care because of the development of fatigue. She stopped doing housework and was so tired, she had to rely on her caregiver for simple activities, such as combing her hair with negative impact on her self-esteem and mood:

“I stopped doing housework, I used to install lights and repair things that are
not working in the house. But now I am so tired that I can't even comb my hair or take a bath. My mom helps me do that" 

(P4, female, single, 19y)

Poor physical ability deprived patients from meeting the commitments associated with family obligations. Patients indicated that they were no longer able to fulfil the minor responsibilities which they were able to complete previously. Patients wished to have a sense of being normal and being able to contribute to role related tasks within the family. Feeling unable to fulfil family related tasks often leads to frustration:

“Previously, I relied on myself, I used to tidy up my room, my clothes and stuff, but now I can’t do much work. My wife helps me get my things ready ”

(P8, male, married, 71y)

“Before I would participate in housework, such as repair and installation of broken lights, but now unfortunately I do not do so anymore. I am so frustrated. I wish my life would return like before. I hope I can take long trips with my family and feel happy as I used to.”

(P4, female, single, 19y)

Sense of dependence and the impact on relationships

Patients in this study wished to remain independent, however, as physical capacity deteriorated they became unable to perform simple tasks such as getting water to drink. Fear of being dependent concerned patients because they were unable to manage daily activities in the same way as before the
onset of the disease and related symptoms. Patients were concerned that they were putting extra burden on their caregivers and worried about the impact this would have on these individuals and their relationship:

“'My mettle got weak. Before, I used to cook and prepare some meals like stuffed vegetables that take time and effort and need high skills, but now if only I go and bring some water to drink. I feel tired. Everything became impossible.

My concentration and vision got strongly affected. My daughters, who study at university, helps me with housework like cleaning, cooking and laundry and bathing me. I feel being ill is harder on my daughter than it is on me, I don't want to be a source of burden for her”

(P3. Female, married, 45y)

Patients not only have a sense of being dependent on their caregivers, they also reported a dependency associated with dialysis therapy. As patients were dependent on dialysis for their continued survival, the regularity of this treatment constantly reminded them that their situation was beyond their control. The disruption to everyday activities dictates that patients change the pattern of their lives, in a way that is unavoidable.

“'In the past, I was free to choose when I walk, sleep, eat or drink; I was not tied to anything. Now I have to go to bed early if I have a renal dialysis session the next day. Renal dialysis is controlling my sleep. Even when I return from renal dialysis sessions I feel exhausted and cannot go out again until the next day, because all my energy has been drained. I stopped performing my
responsibilities. I have a servant at home but I do not depend on her completely.”

(P7, female, married, 65y)

“being tied to dialysis is difficult. Before renal failure I was free and able to go and come whenever I wanted; I enjoyed unrestricted freedom. Now I am restricted. In the past I used to go on vacations for a period ranging from one week to 10 days, but now it is difficult I have appointments on Saturday, Monday and Wednesday. Most people go out, especially on Saturday because it is the weekend, except us, renal failure patients.”

(P11, male, married, 56y)

**Feelings of being restrained, restricted and controlled**

Placing restrictions on patients imposes further limitations on them, which may result in psychological problems such as depression, anxiety and fear (Klang et al. 1996; Griedman 1977). Patients need to regain the ability to control their lifes and illness, the way they used to, to be able to achieve self-efficacy (Curtin et al. 2002). One patient described being tied to dialysis treatment is similar to a wrestler who pins his/her opponent, making them fall:

“I can’t go camping and spend the night because I have dialysis every other day. My hobbies are hunting, camping and long safari trips. But this disease came over me and pinned me, like when a wrestler pins its opponent making them fall, Now we go out at dawn and come back before it is sunset, I got restricted.”
“(P8, male, married, 71y)

“being tied to dialysis is difficult. Before renal failure I was free and able to go and come whenever I wanted; I enjoyed unrestricted freedom. Now I am restricted”

(P11, male, married, 56y)

“Each renal dialysis session takes me four hours plus an hour before the start of the session, i.e. I waste five hours. In addition to that, doctors sometimes impose four sessions a week not three, and this takes me much time.”

(P7, female, married, 65y)

It was clear from the previous extracts that being able to control as many aspects of life as possible, is important to patients’ and their adjustment to living with HD and associated symptoms. Experiencing constant symptoms, the restrictions resulting from dialysis therapy and the inflexibility and uncertainty about dialysis life, alters the relationship between autonomy and dependence (Curtin et al, 2002; Polaschek, 2003). Being tied to regular dialysis treatment, as well as the dietary restrictions to manage symptoms affects the ways in which patients live their lives. Losing the freedom associated with travelling, eating and drinking and socially engagement had a negative impact on the lives of patients in this study. Due to an inflexible HD schedule (Hagren et al 2001) and following strict dietary and fluid intake restrictions, patients felt that they are restrained.
6.3.1.2. Psychological Impact

Lifestyle restrictions and poor physical ability associated with ESRD, impact on physical and social functioning leading to depression and anxiety, impaired adapting and adjustment (Finnegan-John and Thomas 2013: Christensen and Ehlers 2002). Interview data demonstrated a sense of sadness and powerlessness in some patients while other patients reported feeling annoyance when sensing a sympathy look from others.

Sadness associated with Powerlessness

Being physically disabled overwhelmed patients emotionally. Due to long-term physical health problems and associated symptoms, patients reported a feeling of enduring excruciating sadness. The patients desire to remain independent, may appear as a way to preserve self-value. One participant reported feeling worthless, because of her physical weakness, that prevented her from carrying out her own responsibilities towards her family and herself, this made the patient feel sad. This patient was fearful that constrains and powerlessness associated with physical disability would result in her becoming a burden on her family instead of contributing to reduce that burden. Feeling powerlessness has been associated with depression (Harris 2001). The patient expressed feelings of worthlessness, describing herself as being like a “broken hand” which exists but with no benefit.

“My heart is severely broken. I feel that I lost the most valuable and beloved thing, “health”. I feel that I am like a broken hand that cannot do anything; I exist but cannot do anything for them nor for myself. I am unable to get completely treated nor be of help to them. I exist but with no benefit. I am
completely like a broken hand that cannot carry anything nor be of any help.
One day such hand may get cut off or splinted"

(P1, female, divorced, 45y)

Crying was a possible response to help reduce stress, as coping with current symptoms was no longer an option:

‘Sometimes I hide from my son and mother and cry, I feel comforted when I cry and privately talk to myself. I want to sweep out the sadness in my heart. I think of how I can adapt to treatment. I have been unable to adapt for five years. Those who see me never realise that my heart is broken I feel like I lost the most valuable and beloved thing, which is health”

(P1, female, divorced, 45y)

A look of pity
The psychological effects of living with high symptom burden can cause emotional vulnerability (Lutzen 1993). Patients believed that sympathy from others impacted negatively on their sense of welling. Sympathy has been defined in the healthcare literature as "an emotional reaction of pity toward the misfortune of another, especially those who are perceived as suffering unfairly" (Post et al 2014). Sinclair et al (2017), concluded that expressions of sympathy can lead to a deterioration in a patients well-being. Treating patients with pity, even if not intentional, may lead patients to feel inferior. Feelings of being inferior results in patients feeling demoralized and they may develop the perception that they are untreatable, which may make them discontinue treatment.
‘I need the society not to look at us as only sick people. Such look of pity is annoying, and some words that show sympathy are hard to us even if showed unintentionally.’

(P5, male, married, 60y)

“People’s pity for me impacts my psychological state. But thank God for all what I am in, I am better than many others, some who suffer from cancer. I do not like people feeling pity for me for being unable to walk. Sometimes when I take a taxi and the driver knows that I am going to hospital for renal dialysis, he is compassionate and refuses to take the fare. Even the way I dress has changed as I began to cover my body completely so that no one can see the catheter and pity me. I hate that look of pity people have for me, they make me feel that I am imperfect and internally fragile like glass”

(P1, female, divorced, 45y)

6.3.1.3. Social Impact

Individuals with physical disability often experience a sense of social isolation and loneliness, which can also lead to depression and other mental health problems (Kohner 2017). The symptom burden can affect the patients social life, one common statement from participants was that they preferred being alone, not leaving home for fear of the symptoms. Fear was the main reason for disengagement in and may curtail social activities and this may place a greater strain on family life. Some patients were afraid of losing self-control when attending social events which may require them to drink a lot of fluid or eat food which is not recommended. Patients believed that increased fluid
intake and eating a high potassium diet would increase waste within the blood, causing fluid retention and related symptoms.

“I fear attending parties and drinking a lot of drinks as this will increase symptoms before the next renal dialysis session”

(P1, female, divorced, 45y)

“Sometimes I prefer staying alone than leaving home for fear of symptoms that I will suffer from after attending parties, such as tiredness, nausea, headache and depression in some cases.”

(P1, female, divorced, 45y)

Participants felt that their physical ability to get socially involved was not possible since they developed ESKD. Patients described lack of energy and fatigue as symptoms that controlled their social life negatively. The loss of a sense of social and personal worth frequently accompanies the illness experience (Fife & Wright, 2000). There appeared a clear relationship between the patient's physical health and their ability to enjoy social activities.

“Renal dialysis is controlling me. Even when I return from renal dialysis sessions I feel exhausted and cannot go out again until the next day, because all my energy has been drained.”

(P7, female, married, 65y)
6.3.1.4. The cognitive Impact

Participants were not only impaired physically, socially, and psychologically, their cognitive performance was also affected. Most participants were sometimes unable to remember certain things due to memory impairment associated with poor attention and concentration. Patients reported that being worry, anxious and nervous causing them trouble concentrating and poor memory, which impacted negatively on their ability to communicate with others:

"I feel nervous and irritable, and all the time thinking of the pains I am suffering even when my family members speak to me they say I am not concentrating on what they are saying."

(P4, female, single, 19y)

Patients reported the inability to retrieve the details of events that happened to them, which put them in an embarrassing situation in front of people.

"Even my memory was affected; yesterday my daughter took some money from me after I gave her permission, a little later I was asking myself where did the money go? I asked my children, and my daughter answered "I took them for the purpose I informed you of. At that moment I remembered!!"

(P7, female, married, 65y)

The effect of symptoms on the cognitive ability of patients reached the degree that they were unable to plan, make decisions or solve a problem within the family. This results in a change in the gender roles inside the family, which
might have an influence on their power and the ability to lead the family, which is essential to patients.

“*when my children need something, I send them to their mother to decide, my wife is the leader now*”

*(P11, male, married, 56y)*

### 6.3.1.5. The interact between physical, psychological health and social

The interview data established that the psychological symptoms can impact on the physical and social function. These functions are also inter-related between each other, and the impact of one affects all other functions.

Data revealed that reductions in physical abilities caused a lack of social engagement, which played a significant role in the decline of the psychological wellbeing of patients. Physical symptoms include bone and joint pain and fatigue might cause limitation in the social interaction with others due to disabilities associated with these symptoms. Being weak and isolated from the community might cause additional psychological distress which can include, stress, anxiety, sadness and depression. In reverse, the psychological symptoms can also affect the social functioning as well as physical health. Patients express that fear, worry and bad mood can make patients isolated and avoid interacting with others. Furthermore, Patients reported that psychological symptoms might affect their eating appetite as well as they become less effectively help seeking, which causing deterioration to their physical and health condition.
“When my mood, psychological or emotional state is bad, I stop eating, drinking and taking care of myself in all aspects, and stay alone, which causes deterioration of my health condition. Psychological relief is half of the treatment.”

(P6, male, married, 49Y)

It was also noticed that patients did not experience the same level of distress as a result of muscle cramp. Muscle cramp was a frequently reported symptom, but was less distressing, as many patients only experienced muscle cramp during HD sessions and were, therefore, more manageable. Patients reported that they learned from HCPs that muscle cramp appeared to occur due to the dialysis machine extracting excess fluid and the adjustment of the dialysis machine resolved muscle cramp problems.

“Muscle cramp is not an issue for me, when I have a muscle cramp, they stop drawing fluids from my body and the strain goes away”

(P8, male, married, 71Y)

6.3.2. Theme 2: Factors influencing symptom burden

6.3.2.1. Age of patients

Older participants expressed satisfaction with their health status, as they understood that health was likely to deteriorate with age. Having constant symptoms was acceptable for older participants, who reported acceptance of their health and the belief that some symptoms are characterized as normal by older people; such as bone pain, dry mouth and sleep disturbance. Older participants showed greater appreciation of the level of health they experience,
as they perceived that their current health status would not improve.

“*I am an old woman, and it is good to be in this health condition while suffering from such disease, thank God.*”

(P9, female, widow, 80)

“I am not looking for getting healthier anymore. I don’t want my health to be as before when I was a young man. I am an old man and my current health condition is acceptable for someone of such age”

(P10, male, married, 65)

6.3.2.2. Life burden

Life burden is one of the most constantly reported factor by participants that can negatively impact on symptom experience. The burden of life weighs heavily on patients and creates further psychological distress. This is supported by the following interview extract:

“My commitment to teaching, my son, taking care of my sick mother and my work as a teacher at school tire me and exacerbate the symptoms. Also, thinking about my cure and burdens of life increases my sorrow and exacerbates my psychological state, which, in turn, makes me feel that the symptoms are getting worse.”

(P1, female, divorced, 45y)

Dealing with chronic illnesses (ESRD) and providing care to family and working, resulted in a feeling of burden in patients. Patients believed that
exhausting themselves through their daily responsibilities caused them greater intensity levels of symptoms:

“At the end of the day, and when I am tired and exhausted, my headaches kill me but when I am full of energy I can tolerate them”

(P6, male, married, 49Y)

6.3.2.3. Financial status

Participants believed that financial status had a negative effect on their symptoms. Even though the health care system in Saudi Arabia provides medical services free of charge, participants reported that they struggled financially and this impacted on their health. Participants explained that with a lower income, they have less money to meet the health requirements impose by their illness. This includes purchasing required dietary foodstuffs, or traveling to obtain better treatment in higher quality health care centres. Participants are also aware that stress associated with low financial status can lead to physical and psychological symptoms, including a lack of sleep, frustration, anger, anxiety and depression.

“our financial situation is very poor. We live in a rented house. I have sons and daughters and our salary is not sufficient. People say if one is healthy and peaceful, the money then is not important. This is a lie, a patient has to eat and drink certain foods and drinks. A patient must be physically and psychologically relaxed and sleep well. Sometimes a visiting doctor comes from abroad and I need to travel to Riyadh to see them to check on my condition, but I cannot travel because I do not have money. I only need to get relaxed at all levels,
financially, healthily and family-related matters. These accumulations cause me constant anxiety”

(P3, female, married, 45y)

It was notable that patients always mentioned financial stability as one of the main requirements for good health. Increasing financial difficulties is associated with anxiety, depression, and poor quality of life (Delgado-guay et al 2015). Many patients acknowledge financial stability when they were asked about their health needs.

“Thank God. I eat, drink and sleep, and my pension is enough for me, my family is around me and that’s more than enough for me. Previously, I used to borrow money to pay for my family needs, but currently - thank God - we are immersed in blessings”

(P11, male, married, 56y)

6.3.2.4. Faith and religion

Participants with strong religious and spiritual beliefs tended to express less psychological and physical symptoms. Patients with resilient religious beliefs appeared to be more accepting of their symptoms. They believed its Gods willing and they have to accept their fate. Rejection, complaining or questioning of fate is prohibited in Islam and shows a weak belief in God’s judgment. Religious patients may report less symptom burden than they experience, because of the fear of being complaining or being resistant to the will of God. This might not reflect the real symptom burden levels they experience:
“I rely on God, have faith in him and I accept His fate and destiny. I know someone whenever he finds weather hot or cold would say “What a dreadful weather”, I don’t know why he says that, this weather is from God and we need to be happy with whatever God gives us. When it is hot turn on the air conditioner and when it is cold put on warm clothes but don’t be displeased with what God destined for you.”

(P10, male, married, 65)

“I do not object to the will of God, I normally accept what God destined for me. My psychological state is always high and I am satisfied with all that God decides for me. If I had suffered from a disease-free from symptoms, I may have been able to adapt to more easily knowing the disease has a treatment. And this is, at first and before all, the willing of The Creator, which I do not object to”.

(P3, Female, married, 45y)

Participants believed that symptoms are a test from God, because God loves them and selects them, and they need to show faith and trust in Gods ability to cure them. Their inner strength and belief, gives them the power to overcome their current struggles with unlimited patience. Some participants used positive thinking by looking to the advantages they have, instead of focusing on their loss to conquer illness:

“Thank God, good believers go through ordeals. The faithful person is the one who believes in destiny and in God’s will. If I get frustrated, this means I am not a Muslim and don’t believe in God and what is destined for me. My God
chose me to have renal failure but He gave me the blessings of being able to walk and help myself. God gave me many countless blessings.”

(P11, male, married, 56y)

“It is a blessing from God that we are Muslims and we rely on God. This is our only source of solace and reassurance. What God destines for us is a blessing. Whether we live or die, this is a blessing and that is the best and most useful for us. I am not happy, but I have patience and know that it is a test from God, and I beseech Him for recovery”

(P8, male, married, 71y)

6.3.3. Theme 3: Symptom management
Symptom management emerged as a prominent overarching theme following the analysis of the semi-structured interview data. This theme comprised three related subthemes: **Self-management strategies utilized in response to symptoms** which established different techniques undertaken by patients to relieve or reduce their symptoms. **The Second** subtheme revealed the **sources of knowledge** patients used to create their approaches in management their symptoms. The third subtheme discussed the **Barriers to symptom management** for patients receiving HD.

6.3.3.1. Self-management strategies utilized in response to symptoms
Self-management refers to the "patients' efforts to oversee and participate in their health care to optimize health, prevent complications, control symptoms, marshal medical resources, and to minimize the intrusion of the disease into their preferred lifestyles" (Curtin and Mapes 2001; p. 386). The reported impact
of symptoms in patients receiving HD varied, as did their approaches and adaptations to deal with their symptoms. A number of daily activities, behaviours and functions were impacted by symptoms including; driving, sleeping, cooking and walking. All patients participating in this study described at least one way to reduce or relieve some of their symptoms. Although some patients described these strategies briefly, other patients provided significant details about their experiences and management strategies. Table 29 provides a summary of some of the activities impacted by symptoms and the self-management strategies utilized by patients in response:

*Table 29: Activities, function, or behaviours impacted by symptoms and responsive self-management strategies utilized by patients*

<table>
<thead>
<tr>
<th>Impacted activity, function or behaviour</th>
<th>Symptom</th>
<th>Management strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Losing voice</td>
<td>dryness of mouth</td>
<td>Suck lemon candy instead of drinking fluid</td>
</tr>
<tr>
<td></td>
<td>cough with sputum</td>
<td>Using herbal thyme tea to remove all sputum in chest</td>
</tr>
<tr>
<td>Driving safely</td>
<td>weakness of sight, bone and muscles pain in hands and/or feet, and tiredness)</td>
<td>Arrange for family to drive</td>
</tr>
<tr>
<td>Falling asleep</td>
<td>Stomach and throat discomfort</td>
<td>using of acacia gum</td>
</tr>
<tr>
<td></td>
<td>pain</td>
<td>painkiller tablets</td>
</tr>
<tr>
<td></td>
<td>Feet numbness</td>
<td>massage with olive oil</td>
</tr>
<tr>
<td></td>
<td>Itching</td>
<td>Using itching creams, moisturisers and phosphorus tablets.</td>
</tr>
<tr>
<td></td>
<td>Worries or stress</td>
<td>Listening to Quran</td>
</tr>
<tr>
<td>House work, hobbies, family responsibilities</td>
<td>Fatigue/ lack of energy</td>
<td>Taking rest (taking nap or retiring from work), light duties and take minor responsibilities or ask family member to help</td>
</tr>
<tr>
<td>Engaging in Social life</td>
<td>In ability to walk due to joint pain/fatigue</td>
<td>Ask family and friend to come over to their place, or Drinking turmeric and lemon juice for curing joint pain, and massage joints with olive oil.</td>
</tr>
</tbody>
</table>
A) Medication and symptom relief

Patients reported constantly taking prescribed and non-prescribed medicines in order to manage their constant symptoms. These medicines included; Paracetamol and Aspirin as painkillers, calcium tablets for bone and joint discomfort, phosphorus tablets and ointments for itching. One of the participants believed that this provides a quick solution to maintain their health and to help avoid the consequences of symptoms such as a lack of sleep and pain:

“I suffer from sleeping disorder when I am in pain whether it is a headache or bone pain, and if this happens, I take Panadol. The symptom gets relieved that night, and the next night the symptom returns. I need to take another painkiller”

(P3. Female, married, 45y)

“I feel there is numbness in my feet and severe pain. I cannot stretch out my feet very well as they feel convulsionary after I take a Panadol pill, it begins to improve and the convulsion gradually disappears”

(P9, female, widow, 80)

In contrast, some patient realized that they needed to seek a doctor's advice before taking any medicines. They believed that taking medicine without prescriptions might be harmful for their kidney and their health, as it was the cause for having renal failure in the first place:

“I do not use medicines unless they are prescribed by a doctor because one of causes I suffer from renal failure is that I would take big amounts of drugs
without control. Previously I would take medicines on my own without any prescription or control. Now I’m careful about taking medicines, I am afraid it makes my symptoms worse”.

(P3. Female, married, 45y)

B) Lifestyle changes

A number of patients decided to control the way they drink and eat in order to reduce the amount of fluid entering into their bodies and to avoid the consequence of symptoms of fluid overload and subsequent breathlessness. Having stringent dietary and fluid restrictions is important to simultaneously achieve the highest level of functioning and the lowest level of symptoms given the severity of the disease (Clark, 2003).

“ I do not drink a lot of the fluids, especially after dialysis directly, because the next day there will be no dialysis session and fluids will accumulate in my body causing me nausea or diarrhoea. ”

(P3. Female, married, 45y)

Participants became aware that due to their lack energy and high levels of fatigue, they needed to reduce their physical exertion. The awareness come from doctors advices that they need to take enough rest when needed. Most patient decided to change their routine life and take more hours to sleep and some decided to retire from work to face energy difficulties and engage in normalizing activities. This fatigue is likely due to the intensity of their dialysis treatment, their fluid and food limitations, losing their blood during HD
sessions; rest was an effective strategy for them to overcome tiredness and power themselves.

“I should not tire myself and should stay comforted and away from nervousness, these are the doctor’s tips. Everyone receives such tips as they are very useful...Previously I worked on my dump truck, but now I quit because my body can’t bear it. I feel tired quickly sometimes, the vehicle is high and I should climb and get down to put loads on it ... I asked doctors, and they advised me to retire and have rest!”

(P10, male, married, 65)

Adherence to HD treatment was commonly reported as a key reliever of symptoms. One of participants believed that HD is only solution for reliving symptoms. He mentioned that when he finishes his dialysis he feels no symptoms at all and before the next dialysis session he has the worse level of symptom. He is aware that those symptoms are often due the increase of fluids and wastes in his blood. Non-adherence to dialysis sessions is associated the increase of uraemia and the build-up of toxins in the blood (German and McCarthy 2004) which increases the risk of mortality and morbidity (Bernardini, Nagy and Piraino, 2000)

“Sometimes I feel that I weigh a lot but when I weigh myself before the dialysis session I find myself not gaining much weight. The doctor told me that I have this feeling because of high potassium and toxin level in the blood. I believe that all the physical symptoms that renal failure patients suffer from are due to
the high proportion of toxins in the blood, which can only be treated by renal dialysis.”

(P12, female, single, 38)

One of the patients decided to move from her small house to a farm to be able to socially engage with her family and friends. She wanted to have a larger space to accommodate all her visitors. She was not physically able to go and visit them so she decided to make some modifications in her life to be able to become closer to her people.

“After I started dialysis I became unable to walk at all I sometimes want to go to camps but that is difficult due to my use of wheelchair. I decided to move from my house to farm so that I may not feel bored due to staying at home. Although my children refused the idea at the beginning but after I moved, their visits became daily and sometimes they sleep here at the farm. It is something funny”.

(P9, female, widow, 80)

C) Cognitive strategies

Some patients spoke about how distracting themselves from thinking about symptoms, helped them to tolerate symptoms:

“I am satisfied with my life and try to keep my mind occupied with anything in order not to think about this symptom as it will be present with me all my life if not treated. So I try, as much as possible, to go out whenever I am physically able to”
This patient tried to focus on other things rather than her symptoms. This helped her to feel calm, relaxed and reduced her level of stress to help her manage and live with her symptoms. This concept of distraction is similar to mindfulness meditation techniques used by people who try to live and appreciate the present moment rather than re-living stressful past events or expecting stressful future (Noonan 2014).

It was also observed that the religious patients have their own ability to change the negative thoughts to a positive one. Focusing on the blessings they have such as family, love, children, and money, instead of thinking about their lost (health), was a technique to remain grateful and overcome suffering.

“Thank God. I eat, drink and sleep, and my pension is enough for me, my family are around me and that’s more than enough for me…. thank God, we are immersed in blessings”

D) Religious and spiritual methods for acceptance and healing:

Spirituality and religious beliefs are often quoted as essential components of coping with CKD. For patients in the study, their spiritual faith and beliefs provided comfort and help during the difficult times they have endured. Literature describes spirituality as a strong coping mechanism, and the influence it can have over an individual’s ability to deal with stress and negative events must be acknowledged (Walton 2002, Tanyi and Werner 2008). One of
the patients stated that recourse to God is the sanctuary to empower her during her illness journey:

“After all doors were closed in my face, I currently go to a Sheikh to recite the Quran for me to recover and heal. I feel better, thank God.”

(P1, female, divorced, 45y)

Seeking spiritual support to manage and cope with their symptoms and illnesses and practicing religion such as praying and reading the Quran was a source of relaxation and helped to overcome any kind of pain and stress experienced by patients. Reading the Prophet’s stories in the Quran while confronting the challenges of their illness and facing different tests of life, was a motivation for patients to trust in the support of God and to be patient.

“It is enough that when I read the holy Quran I feel overwhelmingly peaceful to such degree it makes me feel that I have healed from all diseases”

(P10, male, married, 65)

6.3.3.2 Sources of knowledge

To manage symptoms patients tended to use all available information sources, which in turn led to differences in knowledge and behaviour responses. This study illustrated the variety of sources used by patients receiving HD. The majority of patients reported that advice from friends and their experiences are the most important source of their knowledge to manage their symptoms. While only one patient reported gaining their information from the internet which might point to the fact that this population have inadequate online
research skills or languages barrier to reach the sufficient information required.
Some patients reported learning from their doctors and nurses although they reported a limitation to those resources.

“My mother (may God have mercy upon her) taught me that massage relieves the symptoms and used this method to relieve my grandfather’s suffering, may God have mercy upon him as well, as he was suffering from renal failure and was very exhausted. When he suffered joint and bone pain, she used to rub his legs with olive oil then wrap them tightly with some warm cloth so that he could sleep. After that my grandfather would feel far better when he got up.”

(P2, female, single, 41)

“Thanks to my experience I obtained from things happened to me in the centre, I was vomiting and a doctor asked a nurse to measure my blood pressure and it was really high.”

(P8, male, married, 71y)

6.3.3.2. Barriers to symptom management

Patients receiving HD were asked to ascertain their perceived barriers to symptom management and they reported many factors: losing trust in the HCPs, limitation of doctor’s time provided to them or inadequate availability of nurse staff, lack of knowledge and losing hope that there is a cure.

Losing trust in the HCPs is a major factor that prevents patients from sharing their symptoms experience and management with Doctors. Patients demonstrated several reasons for why they had stopped involving doctors in
their health plans. Some patients reported that experiences with doctors were unsatisfactory and reported that they were unqualified in their field:

“One of my nephews had a herd of sheep and he had a Sudanese man to take care of the herd. The Sudanese man asked for permission to spend a vacation with his family. Later on, my nephew took his diseased daughter for treatment and found out that the Sudanese shepherd is a doctor!!! One day I will be a doctor, it is easy!!!”

(P9, female, widow, 80)

In the previous extract the patients reported that one of the shepherds who worked for her family became a doctor suspiciously. He travelled back to his country with the intention of taking a holiday and he did not return. Later they discovered him treating patients as a doctor in the local hospital. After this situation the patient was no longer able to trust doctors to give her any treatment.

“When I was complaining of Leishmania in my leg, the nephrologist summoned the dermatologist to check my leg, but I did not like the medicine the dermatologist prescribed to me. The dermatologist asked me to treat the inflammation until the wound heals and then he would perform a surgery to me to remove the egg that is causing the disease in my leg. Why does not the dermatologist perform the surgery whilst my leg is semi-open as a result of inflammation, why do they need my leg to heal first, then open it surgically and I should have to wait again for healing?!?! Frankly, I do not trust them and their efficiency as doctors.”
From the previous extract, the patient reported an inability to trust the doctor’s decision to treat the inflammation in her leg and then perform the surgery. Her suggestion was to do the operation and then treat the inflammation because she did not want to go through the process of healing twice. Probably the fear of taking this path of treatment was due to the limited explanations provided by the doctor when he shared the health care plan with her as well as a lack of rational provided from the doctors for that treatment decision. There was no discussion happening between the patients and HCPs in regard to the treatment plan suggested by the patient and the consequences accompanied with that decision. It was evident that she was unconvinced by her doctor’s decision.

Lack of commination between patients and HCPs were also reported. One of the patients did not know why she was receiving HD. Apparently, she had not received any information regarding why she needed to perform the dialysis treatment, even when she felt healthy if she skipped a HD session. Basic and initial information were not adequately provided to this patient, which was essential to support making an appropriate treatment decision. It seems that even the decision of receiving dialysis might not be based on patient chose.

“Doctors don’t tell us what our problems are. I feel I am normal. I don’t have many symptoms even if I skipped dialysis sessions. Doctors say my tests are fine; I do not know why they put me on renal dialysis machine.”

(P13, Female, married, 33y)
Some patients reported their symptoms to the renal specialists in the centre. However, they did not seem to receive satisfactory outcomes which caused them to give up seeking a treatment to alleviate suffering.

“When I go to hospital symptoms worsen because waiting for long exhausts me and increases problems, and at the end, they prescribe me some painkillers that temporarily relieve the symptoms and do not treat the disease. So I prefer to treat myself at home on my own”

(P2, female, single, 41)

One patient reported having more complications after she received treatment for her symptoms from her doctor, which caused her to experience a permanent side effect of blood clotting:

“I had a situation, two doctors quarrelled with each other over medicine prescription, and it ended that I took medicines that they both prescribed for me. Such decision of taking medicines they both prescribed had effects on my blood and caused me blood coagulation, and because of this I will have to use Aspirin all my life”

(P1, female, divorced, 45y)

One of the patients reported a sense of “not being heard” or “being ignored” by the HCPs when reporting symptoms. The following extract explains that doctors do not listen to patients and commonly prescribe the same medicine to all patients:
"Someone went to a doctor and told him "When my head was down, my hat fell, and when I lifted my head, I carried my hat and placed it on my head." The doctor said, "One tablet in the morning and one in the evening."

(P9, female, widow, 80)

In this extract, the patient used a humorous and anecdotal story to explain their experiences during their encounter with HCPs. This method of explaining the world using humor and anecdotal stories, is a feature of many interactions within the culture of Saudi Arabia. Rather than patients openly being critical of doctors, patients use humor as an indirect way to reflect their true feelings about the limitations of their contacts with HCPs. The anecdotal story talked about a person who complained that when he/she bend downward his/her hat falls from his/her head, and he/she keeps lifting the hat to its place every time he/she needs to bend. His/her problem was not even related to a health condition that need doctor interventions to be undertaken, However, the doctor prescribed a medicine to him/her using the most repetitive sentence used by them "One tablet in the morning and one in the evening". In this extract, the patient has used humor to reflect how doctors ignored her complaines and concerns, and avoided providing her with clarification and resorted only to the use of prescribed medication.

Due to the limitation of the doctor's time or the inadequate availability of nursing staff as expressed by patients, they were unable to receive the required care when they needed it. Patients expressed not being a priority to be treated by HCPs:
The problem is that the doctors at the centre do not" give us the required attention, perhaps due to time limitations and for being busy, I do not know. Sometimes, I feel as if they are doing their job as any other money making job, with no consideration for the feelings of patients as human beings….’I lost trust in them as my all experiences with them prove that patients are not a priority for doctors. The only times I had to go to hospital for emergency were when I fainted.”

(P1, female, divorced, 45y)

Losing hope that there is a cure for their continuous symptoms was one of the causes leading patients to not consider the management of their symptoms. Patients reported that symptoms are simply an unavoidable outcome of HD and cannot be separated. And to treat those symptoms, they need to treat their renal failure.

“There is no hope to manage these symptoms alone. They come as a package with renal failure. Once we cure the disease, the symptoms will also disappear.”

There is agreement between participants about the insufficient education provided to the patients to manage and live with their illness. Receiving the information from HCPs were described as one of the least reported source of knowledge in those patients. Patients were unsatisfied with the education acquired after being diagnosed with renal failure and receiving HD. Patients reported that doctors, and nurses providing a brief information unintentionally and incompletely, which leaves the patients lost. Patients expressed that
education is essential in the process of treatment and not aside voluntary work to do. Patient believed that providing a proper health education could help them to overcome their illness and improve their health.

These barriers to symptoms management identified in this study may contribute to leaving symptoms untreatable, causing lower health-related quality of life as well as high levels of distress and depression (Ludman et al., 2004). Lack of trust of HCPs, losing hope that there is a cure, the sense of being ignored by HCPs, insufficient health education provided, might lead to negative consequences such as seeking out alternative treatment and therapies which could be unreliable and unsafe. Some patients self-prescribe medicine when needed, instead of returning to the renal specialist which might cause serious consequences to their health.
6.4. Themes of Caregiver Interviews

In the interview data, caregivers reported extremely positive experiences in relation to providing care to their patients. Caregivers were always cautious about the way they described their patients such as trying to avoid using the word “burden”. They felt that they are not entitled to complain about providing care to their patients, as this could be perceived as selfish behaviour and would distract attention away from the real one who is suffering, namely the patient. Three themes were identified: positive caregiving experience, negative caregiving experience and factors influence caregiver burden.

6.4.1. Positive caregiving experience

Positive outcomes of providing care to patients have been acknowledged in this study and defined as the rewards and satisfaction derived from the caregiving relationship (Tarlow et al., 2004; Kramer, 1997; ). In this study, caregivers expressed that providing care has a positive effect on them including: feeling satisfied and delighted, building a feeling of confidence and reducing feelings of guilt regarding the care they give to their loved one. Caregivers who are wives in particular expressed their feelings of love towards their husbands and dedication to their commitments and responsibility to their marriage. Adult children caregivers acknowledged gratitude they felt towards their parents for the love and care they have received from them and reported sentiments of wanting to return this favour to their parents until they die.

“Because she is my mother. I owe my parents all my life, and whatever I do for them until my death will not return their favour and efforts”
Feeling delighted and satisfied

Children caregivers reported being emotionally delighted and useful when providing care and being able to help their patients. A daughter caregiver reported that seeing her mother satisfied was a great source of satisfaction for her and energy to continue providing care.

“I have changed for the better. My belief that taking care of my mother is the right thing I should do has been strengthened. Just seeing my mother smiling and satisfied with me makes me feel that I own the whole world.”

A wife caregiver expressed being happy to provide care to her husband as she could not have this time to spend time with him previously. She reported that after he started the dialysis treatment, her husband had to retire from work and she was finally able to spend time with him.

“My husband has retired and I can see him more than before. We became able to spend a lot of time with each other. We live far away from the dialysis centre, so I accompany him for a long distance and spend much time with him during treatment sessions. Every cloud has a silver lining. May God help him recover soon.”

Some caregivers demonstrated a feeling of being useful and appreciated when providing care to the patients. They reported providing care filled their free time...
and gave them a sense of being worthy. Providing care was also a source of motivation to succeed in all aspects of life.

“Usually I spend the time I would spend with my father doing useless things, like sleeping during the afternoon, watching television or playing on my phone, instead of taking care of my father. … In fact, providing care to my father has strengthened my diligence and motivation to be better. “

(C11, 25Y, single, daughter)

Most females in Saudi Arabia are unemployed due to the limitation of work in the job market, as well as limited employment options for women which would be acceptable for them within the constraints of Saudi Arabian culture (Doumato 1999). Finding jobs for women in the work force without violating Saudi Arabia's prohibition of unrelated men and women working together is one of the challenges confronting women (Doumato 1999). Women in Saudi Arabia would typically will be supported financially by their father and later by a husband. As all caregivers in this study were women, mostly they might not be working and therefore have a lot of free time, especially if they are single. Providing care is one of the ways they use to feel productive and worthy, which may increase their levels of satisfaction. Providing care was a source for positive emotional outcome instead of being a source of stress.

6.4.2. Factors influencing caregiver burden

6.4.2.1. Social support and cultural acceptance

It was notable that the caregivers were receiving social support from family and work which may contribute to reduce care burden. One of the participants
reported that she was sharing the responsibility of taking care of her husband with two other wives.

‘I have a lot of time for myself. I sometimes wish to spend more time with him. We (three wives) share in taking care of him.’

(C6, 40Y, first wife)

Muslim culture allows men to be married to multiple women up to four any one time. The culture acceptances and behaviours could influence the levels of caregiver burden reported.

Providing care was a collaboration process between sister, brother and mother to one of the patients. The brother does the travelling role including; accompanying his sister to the dialysis centre and to the follow up appointments in and out of the city. The elder sister of the patient carries out all the activities that need physical and emotional effort, with the mother who covers all the time in the morning when the sister and brother are in school.

“When my sister needs to be subjected to some medical checks in another city my brother travels with her as I am tied to my university studies.”

(C12, 20Y, single, sister)

Informal work support was also provided to caregivers of patients receiving HD. Daughter caregivers reported that this voluntary work support involved cooperation between colleagues and managers to afford a flexible work arrangement, which could help her to present with her mother during her afternoon HD sessions. The managers and co-workers at the school where
she worked knew about the demands of her caregiving role and were able to assist caregivers by granting flexible teaching schedules and classes with no extra after-school activities, based on their needs. This cooperation enabled them to reduce the strain of working to be able to provide care for a relative more effectively.

“My employer and colleagues support me. My work schedule is arranged in such a good way where I do not teach the last classes and do not take any school activities at the time when my mother has dialysis sessions, So I am able to leave early and accompany her”

(C9, 32Y, single, daughter)

6.4.2.2. Being normal

The burden on patients reflected on caregivers. The interview data showed that when patients feel normal and independent, this clearly reflected on the individuals providing care to them. Seeing the patients acting normally, provided as source of emotional comfort while facing any distress related to the illness.

“I do not feel that he is a burden on me nor feel angry with him because love makes one forgive others for a lot of things. My husband makes me feel that life is normal and convey this impression to me, as a result, this is reflected in my own life. I sometimes forget that we have a patient at home”

(C6, 40Y, first wife)
“I think that taking care of patient who is active and seemingly healthy, as in the case of my husband, who gives the impression that he is healthy and not diseased, especially if he does not stay at home much”

(C5, 65Y, wife)

6.4.2.3. Transition stage

Providing care seemed to be a transition stage to most caregivers. The daughter took care of her father then when she got married her sister continued this journey. Later, the daughter-in-law and the grandchildren became involved, and so on. This transition period experience reduced the feeling of being trapped in the role of caregiving which contribute to lower levels of emotional strain.

"My patient is not the kind of person who always complains. He is reticent. His daughters, when she was taking care of him, were able to know his condition once she sees his face. After his daughters married I began to take care of him. I am able to know if he is good or not once I see his face. This depends on gained experience and practice."

(C10, 43Y, married, daughter-in-law)

6.4.2.4. Religion

It was clear in the interview data that caregiver religious and cultural beliefs shaped their experiences of caregiving and contributed to influencing their reported levels of caregiving distress. Family members who are more religious feel more positively about their role as caregivers and experience better
relationships with those they care for (Picot et al 1997; Chang et al 1998). Most children caregivers reported providing care to their patients from a religious commitment.

“First this is my mother, and I do not do anything worthy of praise. This is my duty and sometimes I feel a bit negligent in this regard. I take care of my mother because our true religion commands us to do so, and because “paradise is under the feet of mothers”. Taking care of my mother brings me luck and success in every step I take. Her satisfaction is an important and essential thing in my life. She needs my help a lot now and I should be beside her.”

(C9, 32Y, single, daughter)

Religion was an important matter for those providing care to their parents. Caregivers undertook tremendous personal sacrifices in order to meet the expectations of their religious beliefs regarding achieving the satisfaction of God who could help them to live in peace and assurance. They believed that God would return their sacrifices with even more joy and blessings.

“I got divorced from my former husband because I wanted to stay beside her and take care of her. So it’s likely that I will think about marrying again as long as she is in such a difficult condition, all the tiredness I feel vanishes at a mile from my mother or some prayer for me from the depth of her heart wishing me something beautiful to happen. Now I feel inner peace and reassurance I have never felt before”

(C7, 35Y, divorced, daughter)
“I rejected the marriage proposals of a lot of men only to take care of my mother. I asked my brother and sisters who are younger than me to marry and not to wait for me because I don’t want to stand in their way to marry. I have the conviction that my mother is the most important of all and everything, even myself. She is the cause of my existence and I have to stand by her now. I believe that God hides and saves the most beautiful things for me”

(C9, 32Y, single, daughter)

6.4.2.5. Culture

The culture was also contributing to shaping the experience of caregiving and the reported care distress levels. In this study all the caregivers interviewed were women, in Saudi Arabia, the culture imposes some social restrictions on women which makes going out limited for them. Being socially restricted was not reported by caregivers in this study, as no differences were reported before and after being caregivers.

"My social life has not changed much. We are from a conservative family that does not allow girls to go out with their friends so much."

(C12, 20Y, single, sister)

"Typically, I’m not a social person. I meet my friends at work in the morning and just that."

(C9, 32Y, single, daughter)

Cultural influences were observed in the patient’s behaviour of avoiding complaining about their relative or thinking about leaving the care to someone...
else. According to the values of Middle-Eastern countries, providing care should be at their home by a family relative and consideration would never be given to moving them to a nursing home even if it is next door (Hussein and ismail, 2017; Al-olama and Tarazi 2017). People in Saudi Arabia believe that complaining or leaving their relative in the time of need, would bring scandal and shame to those caregivers, this will cause them to be reviled by society and will bring misfortune to them.

6.4.3. Negative caregiving experience

Although caregivers reported a highly positive caregiving experience, some caregivers reported a few difficulties associated with providing care to patients receiving HD. Caregivers reported that unlike other chronic illnesses, renal failure has a difficult and unique treatment that requires them to visit the hospital regularly. This link to dialysis treatment hinders their freedom and makes their lives less flexible.

“The most difficult thing in her illness is that she has a disease that necessitates her to go to the hospital periodically, and that means it cannot be treated at home like other diseases such as diabetes and bold pressure”

(C12, 20Y, single, sister)

Travel has become impossible due to the association with treatment

“Our lives have become different from the past. We used to travel and go out a lot. I love to travel to Mecca to perform minor pilgrimages from time to time, but after my husband fell ill with this terrible disease and we got tied to treatment plans, I could never go.”
Fear was commonly a negative emotional response by caregivers in this study. Female spousal caregivers reported being worried about the future of their husbands, and were fearful of taking new responsibilities they were not obliged to take before.

“I am afraid that my husband’s condition has worsened. He is my husband and the breadwinner of the family - I am so worried about him”

Fear of losing the patients through death was also reported. Caregivers were afraid of losing their loved one which made them provide the best care they could to avoid feeling guilty. Putting themselves under the strain of providing excessive care increased their anger and may have contributed to increasing their levels of care stress.

“Sometimes she does not stick to her specific meals or refuses to take some medicines, which makes me feel a bit worried about her and her health condition, in general I rarely get angry and do not even like to consider the idea of being angry in connection with my mother. I do not get angry with my mother, but I am just worried about her and fear living without her.”
6.5. **Summary of the main theme:**

This chapter sheds light on the experience of patients receiving HD and living with high symptom burden. The overarching themes identified from this study are

- The Holistic impact of symptom burden
- The factors influence symptoms
- Symptom management

For caregivers of patients receiving HD, three themes were identified:

- Positive caregiving experience
- Factors influence caregiver burden
- Negative caregiving experience.

The next chapter will include the integration of the findings from the quantitative chapter and this chapter (qualitative semi-structured interview), which assists in providing clarity and explanations to the study findings.
Chapter 7: Integration and synthesis
7.1. **Integration of the findings from all phases of data collection**

In line with using the sequential explanatory mixed method approach, this chapter will present an integration of the findings from the quantitative and qualitative phases of data collection. Quantitative and qualitative data analysis was completed individually and the integration of findings from each phase of the study was incorporated together in this chapter. Study findings were integrated through a narrative approach which included writing both quantitative and qualitative findings together, on a theme-by-theme basis (O’Cathain et al 2010). In what follows, first patient symptom burden and the factors influencing the levels of burden will be considered, using a theme by theme approach. Subsequently caregiver burden and the factors effecting the experience of providing care will be presented. For each theme reported, quantitative findings will initially be presented and qualitative findings will be subsequently interrogated to help-seeking insights and explanations of study findings.

7.2. **Patient experience of burden**

    7.2.1. **Symptom experience:**

The most prevalent symptoms identified during the quantitative phase of the study were fatigue and muscle cramps. However, although these symptoms were the most prevalent, they were not the most distressing for individuals. The interviews uncovered fatigue as a devastating symptom for patients, impacting on their physical ability to remain independent, and causing social restrictions as well as emotional distress. However, patients did not experience the same level of distress as a result of muscle cramp. Muscle cramp was a
frequently reported symptom, but was less distressing, as many patients only
experienced muscle cramp during HD sessions and was therefore more
manageable. Patients learned from HCPs that muscle cramp appeared to
occur due to the dialysis machine extracting excess fluid and the adjustment
of the dialysis machine resolved muscle cramp problems.

7.2.2. The relationship between symptoms
The mean symptom prevalence was 10, which was extremely high. In the
qualitative interviews, patients reported that some symptoms were caused by
the presence of other symptoms and as a consequence this increased the
number of symptoms reported. For example, patients reported that bone pain
prevented sleep, which often resulted in fatigue and as a consequence, led to
emotional symptoms. Emotional symptoms and poor sleep were commonly
related to any potential symptoms. Emotional symptoms such as worry,
anxious and sadness can cause cognitive symptoms such as trouble
concentrating and poor memory. Cognitive symptoms such as the inability to
retrieve details of events that happened can cause embarrassment which
leads to emotional symptoms such as sadness and depression.

The interaction between these symptoms may worsen the experience of
symptoms and may increase the number of symptoms as well as the level of
severity, and lead to greater functional disability. Some patients reported being
in low mood which impacted on their appetite, causing limited motivation to
self-care, leading to a further deterioration in health. Others patients reported
being physically disabled, which had a negative impact on their psychological
health. This relationship between symptoms contributed increased prevalence
of some symptoms, such as fatigue, which was reported as the most prevalent symptom in this study at 71%. Study findings suggested that all possible symptoms could be associated with fatigue, this is demonstrated in Figure 25.

Figure 25: How symptoms can cause fatigue

These findings highlighted that fatigue may be a result of other symptoms and not initiated only by the experience of HD. The study also found no correlation between HG levels and fatigue. Fatigue might also exacerbate the feeling of other symptoms figure 26.
7.2.3. Factors associated with symptom burden

7.2.3.1 Gender

Being female was associated with a higher symptom burden. This was reasonable, in light of the differences between the roles of men and women within the family, in Islamic countries (Walther 1981). Women in this study expressed highly distressing levels of burden especially when they were unable to meet the needs of their families. In the qualitative interviews, the role of women was predominantly focused on taking care of home responsibilities, and the needs of children and partners. If women were unable to fulfil these responsibilities, caregivers ensured that these responsibilities are met. However, the feeling of not being able to meet family responsibility and being a burden created a sense of not being worthy in the family leading to additional emotional symptoms. In contrast most men perceived that they achieved their responsibilities associated with providing a suitable income for their family. Many male working patients in this study were offered early retirement after they began HD sessions, which ensured that they were financially secure and this helped to reduce the level of burden for these individuals and their families. Men acknowledged financial stability, as one of the main requirements for good health, when they were asked about their health needs which might contribute to reduce their level of burden.

Women also seemed to be more vulnerable to stress increases the sorrow and exacerbates their psychological state, which as a consequence make them reported higher symptom burden:
“Thinking about my cure and burdens of life increases my sorrow and exacerbates my psychological state, which, in turn, makes me feel that the symptoms are getting worse”.

(P1, female, divorced, 45y)

It was observed that the amount of data generated by female participants during qualitative interviews is larger than male participants'. This suggests that women are more likely to express their feelings when asked to describe burden problems compared to men. See Figure 27.

![Data generated from patients interviews](image)

**Figure 27:** Differences between genders in relation to the average number of words generated from each gender of patients interviews

In this pie chart, the differences in data generated from male and female interviews were significantly clear. Five male patients and eight female patients were interviews. It was not possible to compare the differences in caregivers as all caregivers who participated in the interviews were female.
7.2.3.2. Age

Increasing age of patients was not found to be a contributing factor to symptom burden. There was a negative correlation between age and symptom burden in this study, although it did not reach statistically significant levels. Qualitative findings in the study suggested that older participants were more satisfied with their health status, as they believed that health was likely to deteriorate with age. Having constant symptoms appeared more acceptable to older participants, who believed that some symptoms were probably associated with age, such as bone pain, dry mouth and poor sleeping. Older participants also demonstrated a greater appreciation of their health status, and appeared accepting of the fact that their current health status might not improve.

7.2.3.3. Cultural and religious beliefs

Cultural and religious beliefs were found to impact on symptom reporting. For example, while other studies have identified depression as one of the most prevalent symptoms associated with patients receiving HD (Kimmel, 1993), in this study depression was found to be one of the three least reported symptoms. All participants were born and lived in Saudi Arabia, in a traditional Muslim society where any questioning of fate is unacceptable. Fate is defined as the occurrence of events outside a person's control, regarded as predetermined by a supernatural power (Riggan 1979) and in Islam the superpower is God. Patients reported that they accepted their illnesses and associated consequences and believed illness was God’s will. They accepted their fate and faced it through religious coping strategies (Koenig and Al Shohaib, 2014). Rejection, complaining or questioning fate is prohibited in Islam and shows a weak belief in God’s judgments. When patients became
depressed, they believed that this is a sign for a lack of their faith in God and a loss of trust in God's ability to cure them. Patients frequently repeated the following sentences when depression was discussed "May Allah avoid me this fate" "Heaven forbid" "I seek refuge in Allah" "God protect us".

However, some patients reported some emotional symptoms such as sadness, powerlessness and depression in the interviews, even though they did not report any of them in the survey. This demonstrated that some patients might be fearful of reporting depression as a symptom because of the perceived and the stigma attached to symptoms of depression. This could also be due to the fact that patients did not realise they have these emotional symptoms, and the interviews conducted might give them the opportunity to explore themselves. The majority of quotations taken from the patients were not saying directly the word sad or depressed and instead they used different expressions. The researcher was able to distinguish these emotional symptoms because of the opportunities that face to face interviews give, where participants are more likely to express their experiences in detail (Roberts 2007). The researcher interpreted the psychological symptoms indirectly through analysing the interviews quotations such as “I am like a broken hand with no benefit” expressing a feeling of worthlessness and powerless, “I wish I could enjoy my life like before” feeling sad, “This makes me feel that I am imperfect and internally fragile like glass” showing feelings of inferiority and inadequacy.
7.2.3.4. Income

During quantitative analysis, low income was not identified as a contributor to symptom burden. However, the income of patients was identified as a contributing factor in high symptom burden, throughout the qualitative interviews. Participants who had a low income, had less money to meet the health requirements imposed by their illness. This included purchasing required dietary foodstuffs, or traveling to obtain superior treatment in higher quality health care centres. Participants were also aware that the stress associated with a low income could complicate existing physical and psychological symptoms, such as poor sleep, stress, anxiety and depression. There may be a number of explanations for these contrasting findings within the quantitative and qualitative phases of the study. Income information was collected by categorical data, which may limit the correlation pattern which was explored using a scatterplot. It was decided to use categorical data to collect income information as individuals in Saudi Arabia are often reluctant to report their precise monthly income.

7.2.3.5. Employment

Being unemployed was not related to an increase in the symptom burden. The qualitative interviews determined that some patients might have retired or resigned from work after being diagnosed with ESKD, which might reduce their level of burden. Many male working patients in this study reported being offered early retirement from the government after they began HD sessions, which ensured that they were financially secure and this helped to reduce the stress associated with leaving their jobs because of the treatment (dialysis) leading to reduce the level of burden for the individual and family.
7.2.3.6. Marital status

During the quantitative phase of the study and using simple regression, patients who were divorced, widowed or single experienced greater symptoms of burden than married patients, particularly emotional symptoms, such as sadness, depression and anxiety. The majority (84%) of unmarried patients were women, and 70% of depressed patients were unmarried. Throughout the qualitative interviews, one patient (a divorced female patient), reported that the burden of life weighed heavily on her and created further physical symptoms and psychological distress such as worry, anxiety, lack of sleep and depression. She explained how she was unable to manage family responsibilities, further exacerbating her symptoms. Additionally, patients who are single, expressed greater distress associated with their constant symptoms. Single patients expressed higher symptom burden because they are more likely to delay day-to-day plans, and are unable to fulfil the necessary daily responsibilities to an unknown future date. For the most part single patients considered future plans such as marriage, studying, building a future career, and nurturing relationships with others as an impossible outcome for them, while married patients were mostly at a stage where they finished studying, married and having career. Experiencing physical symptoms; such as fatigue, loss of concentration, limited patient’s ability to make future plans. Experiencing constant symptoms, restrictions resulting from dialysis therapy and the inflexibility and uncertainty about dialysis life, caused a negative impact on the psychological status of patients, which was further exacerbated by symptom burden.
7.3. Caregiver burden experience

In the quantitative phase of the study, caregiver burden levels were low when compared to other studies which have examined similar populations, individuals receiving HD. Throughout the qualitative interviews, caregivers reported only positive and therapeutic benefits of caregiving. They reported being satisfied with providing care to their family member, which helped to reduce any feelings of guilt, and ensured a positive relationship with their patients. Caregivers were reluctant to criticise their relative even when they were experiencing burden providing care. They believed that the illness is overwhelming for patients and as a result they believed that they did not have the right to complain about meeting the patient's care needs. Caregivers demonstrated sympathy to their patients and were reluctant to say anything which may be offensive to the patients in their care. These findings are supported by caregiver responses to the survey used in this study. Many caregivers could not understand why the survey used questions that suggested caregiving could be perceived as demanding, such as “Do you feel strained when you are around your relative?” “How burdened do you feel in caring for your relative”. Some caregivers stated that this survey should not be seen by patients, as this would be upsetting for patients, as they may think they are a burden on their relatives. Caregivers always prioritised patient wellbeing and believed that they should focus on the needs of the patients, not on their personal needs. Caregivers believed that if they reported burden to HCPs this may result in HCPs spending time meeting their needs and potentially limiting the care provided to patients.
7.3.1 Factors influencing caregiver burden

7.3.1.1 Social support

During the recruitment phase of the study, the researcher observed that patients were unsure who their primary caregiver was, and reported that they received care from several people. Patients stated that individuals who drive them to the dialysis centre, are often different from those who cook for them, or help to manage health needs. Social support played a significant role in reducing physical and psychological burden in caregivers. Family support is often available in Saudi Arabia as family size is quite large, with a mean family size of 6.4, with a range of 5.5 to 8.4 (Salam 2014). A large family size, increases the opportunities for family members to collaborate and contribute to providing care, which can help reduce caregiver burden. The strong family bond and collectivism in the Saudi Arabian culture (Al-zahrani 1993) may also contribute to the facilitation of this support. Members of the extended family such as grandchildren, son/daughter in law, were also involved in providing care. Spreading caregiving tasks by a group of family members, reduced the burden on the potential primary caregiver. One of the caregivers interviewed during the study, reported that she was one of three wives providing care to one patient, which suggested that unique cultural characteristics and social acceptance can also help reduce the perceived burden experienced by caregivers (Atagun et al., 2011). Religion was also reported as a factor which motivated caregiving, as this was perceived to be a positive function which may enable individuals to be rewarded by God.
7.3.1.2. Age and comorbidity
The age and the number of comorbidities of the caregiver were found to be positively associated with caregiver burden in this study. Throughout the qualitative interviews, caregivers reported high levels of satisfaction when involved in providing care to their relatives. Caregivers expressed feelings of guilt when they were busy or unable to provide the necessary care to their relatives. Caregiving offered the opportunity to provide feelings of personal self-worth which helped to minimise and reduce caregiver distress. With increased age, the physical health of caregivers will deteriorate, which may reduce the quality of care provided to relatives. This may create feelings of guilt, and lead to increased caregiver burden. Having fewer physical, social, and financial resources associated with additional comorbidities was a contribution to a greater caregiver burden.

7.3.1.3. Cultural impact on the reported burden
The spiritual activities associated with the participant’s religion, significantly influenced their general happiness and life satisfaction and helped reduce depression and anxiety (Moreira-Almeida et al 2008). The cultural background has been identified as a factor which can affect the pain experience (Callister 2003). Based on cultural differences and social acceptance, caregiver burden was found to be low in this study. However, it is possible that participants in this study may have experienced symptoms of burden and underreported these symptoms.

In this study patients appeared reluctant to report depression, they tended to express satisfaction and frequently thanked God and suggested that they were
“blessed” for their personal circumstances. In the Muslim religion, symptoms need to be endured and the duration of symptoms is perceived to be a form of atonement. Although it is unclear if religion acts to encourage individuals to report their symptoms or it helps to limit their ability of patients to report their symptoms.
Integration – Mixed Methods Matrix

The following three tables (Table 30, 31, 32) were designed to systematically integrate the findings from Phase 1, quantitative questionnaires, and Phase 2, semi-structured qualitative interviews. These tables were developed based on the method explained by O’Cathain (O’Cathain et al 2010). In the current mixed methods matrix, each row represents each individual participant (patient or caregiver), that was involved in both phases of the study. Quantitative results, including symptom burden scores and caregiver burden scores (numeric) were presented in the first column, followed by a narrative description of each score presented (high, low or medium). The next 2 columns presented qualitative results, using a selection of quotes from each participant. These quotes were allocated to either the agree or disagree column, based on the results in phase 1 of the study. This allowed the researcher to explore both datasets and integrate them in a more transparent way, than would be achieved with only narrative discussion (O’Cathain et al 2010). Surprises and paradoxes between types of data were considered on a single case and then the patterns across all cases were summarized in the last row.
Table 30: Symptom burden in patients - QUANTITATIVE AND QUALITATIVE DATA INTEGRATION

<table>
<thead>
<tr>
<th>Participant ID</th>
<th>Quantitative results</th>
<th>Qualitative findings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Symptom burden scores out of 992</td>
<td>Agree</td>
</tr>
<tr>
<td>P1</td>
<td>552 High</td>
<td>“I was able to take care of my sick mother, give her medicine and help her, but I recently stopped doing so because of the stress, tiredness and symptoms that are always present with me after dialysis sessions”</td>
</tr>
<tr>
<td>P2</td>
<td>365 High</td>
<td>“I suffer from fatigue after renal dialysis and it exhausts me and makes me unable to do anything. My strength now is not like the last year, and that of the last year is not the same as before. My health is deteriorating and this makes me unable to find solutions for myself.” “I stopped doing any housework, such as sweeping and doing the dishes, but I still cook”</td>
</tr>
<tr>
<td>P3</td>
<td>332 High</td>
<td>“My mettle got weak. Before, I used to cook and prepare the meals, but now if only I go and bring some water to drink I feel tired. I liked cooking some dishes like stuffed vegetables that take time and effort and need high skill, but now this became impossible”. “I am feeling weak and being unable to visit friends and afraid even</td>
</tr>
</tbody>
</table>

278
from taking a hot bath because of the catheter. My daughter is the one who bathes me.”

| P4  | 227 | High | “I delay all matters of life. Everything in my life is postponed to an unknown date.” “I stopped doing housework, I used to install lights and repair things that are not working in the house. But now I am so tired that I can’t even comb my hair. My mom helps me do that.” |
| P5  | 525 | High | I need the society not to look at us as only sick people. Such look of pity is annoying, and some words that show sympathy are hard to us even if showed unintentionally. |
| P6  | 177 | Medium | “I became physically weak, my skin got affected, my weight decreased and I became very lean. My memory became very weak and I am no longer able to travel and drive like before. Though I go out more than before, I return on the same day to take my medicines. I became more nervous, and my vision became weak. Therefore I retired from work.” |
| P7  | 145 | Medium | “Even when I return from renal dialysis sessions I feel exhausted and cannot go out, until the next day, because all my energy has been drained. |
| P8  | 120 | Medium | “Previously, I relied on myself, I used to tidy up my room, my clothes and stuff, but now I can’t
<p>| | | | |</p>
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<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>P9</td>
<td>136</td>
<td>Medium</td>
<td>After I started dialysis I became unable to walk at all. I sometimes want to go to camps but that is difficult due to my use of a wheelchair.</td>
</tr>
<tr>
<td>P10</td>
<td>31</td>
<td>Low</td>
<td>“Previously I worked on my dump truck, but now I quit because my body can’t bear it. I feel tired quickly sometimes, the vehicle is high and I should climb and get down to put loads on it etc. I don’t know whether exhaustion is because of the renal failure or because I am getting older.”</td>
</tr>
<tr>
<td>P11</td>
<td>45</td>
<td>Low</td>
<td>Before I would participate in housework, such as repair and installation of broken lights, but now I do not do so anymore”</td>
</tr>
<tr>
<td>P12</td>
<td>23</td>
<td>Low</td>
<td>I postponed my studies until the time comes to resume them. Fatigue and tiredness I get make me unable to be productive as a student. Also stress and high blood pressure I suffer from are enough for me; I don’t want to increase these by thinking about my studies. Even my relationship with my friends is now different. I tend to be alone more</td>
</tr>
<tr>
<td>P13</td>
<td>0</td>
<td>Low</td>
<td>I feel I am very normal; I don't know why they put me on a dialysis machine. Even if I skipped sessions I don't feel bad. And I feel that I will get better soon.</td>
</tr>
</tbody>
</table>
Symptom burden summary:
The Quantitative high scores were supported by the narrative descriptions in qualitative interviews. However, quotes of patients with low scores disagreed. Quotes of the patients with low symptom burden scores indicated that even patients with less prevalent symptoms will experience the same level of symptom burden as the patients with high scores, impacting on their physical ability to remain independent, and causing social restrictions as well as emotional distress. Fatigue symptoms (low energy, tiredness) had the highest impact in patient’s life.

Table 31: (Depression and sadness, anxiety, irritable, anger) in patients (QUANTITATIVE AND QUALITATIVE DATA INTEGRATION)

<table>
<thead>
<tr>
<th>Patients ID</th>
<th>Quantitative results</th>
<th>Qualitative findings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Depression and sadness scores out of 10</td>
<td>Agree</td>
</tr>
<tr>
<td>1</td>
<td>10 High</td>
<td>“My heart is severely broken. I feel that I lost the most valuable and beloved thing, which is health. People look at me with pity and this is what bothers and affects me most. They make me feel that I am imperfect and internally fragile like glass.” “I feel that I am like a broken hand that cannot do anything; I exist but cannot do anything for them nor for myself. I am unable to get completely treated nor be of help to them. I exist, but with no benefit. I am completely like a broken hand that cannot carry anything nor be of any help. One day such hand may get cut off or splinted”</td>
</tr>
<tr>
<td>2</td>
<td>7 high</td>
<td></td>
</tr>
</tbody>
</table>
|   |   |   | "My disease is accompanied by permanent and annoying symptoms, which sometimes makes me lose control of myself, my life and my psychological state. I suffer family problems along with my disease, which makes me feel that I suffer from two diseases."

“I got adapted to the symptoms I suffer from, but sometimes when I am alone I feel very upset. I think about how I can get completely treated and how I can end my suffering. It is like a psychological state that comes and goes; sometimes I encourage myself until I become calm and sometimes I feel depressed. “

“I feel anxious, sad and depressed, depending on the circumstances and problems in my home”

“I am stressed and irritable all the time. I always feel inactive, introvert and lazy.”

“I am so frustrated. I wish my life would return like before. I hope I can take long trips with my family and feel happy as I used to.”

I need the society not to look at us as only sick people. Such look of pity is annoying, and some words that show sympathy are hard to us even if showed unintentionally

When my mood, psychological or emotional state is bad, I stop eating, drinking and taking care of myself in all aspects, and stay alone, which causes deterioration of my health condition. Psychological relief is half of the treatment." |
<table>
<thead>
<tr>
<th>Page</th>
<th>Column 1</th>
<th>Column 2</th>
<th>Column 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>0</td>
<td>low</td>
<td>I suffered from a psychic shock at the beginning when I was informed that I have renal failure. I refused the renal dialysis until the last moments. The daily renal dialysis is hard for me and the symptoms associated with it are tough. My daughter helped me at the beginning. She insisted that I must go for sessions, but now, thank God, I am completely convinced and willing to do so. I do not know whether I have become accustomed or surrendered!!</td>
</tr>
<tr>
<td>8</td>
<td>0</td>
<td>low</td>
<td>“I can’t travel because I have dialysis every other day. You can’t go camping and spend the night. My hobbies are hunting, camping and long safari trips. But this disease came over me and pinned us; like when a wrestler pins its opponent making them fall. Now we go out at dawn and come back before it is sunset, I got restricted.”</td>
</tr>
<tr>
<td>9</td>
<td>0</td>
<td>low</td>
<td>I suffered from a psychic shock at the beginning when I was informed that I have renal failure. I refused the renal dialysis until the last moments. The daily renal dialysis is hard for me and the symptoms associated with it are tough. My daughter helped me at the beginning. She insisted that I must go for sessions, but now, thank God, I am completely convinced and willing to do so. I do not know whether I have become accustomed or surrendered!!</td>
</tr>
<tr>
<td>10</td>
<td>0</td>
<td>low</td>
<td>It is a blessing from God that we are Muslims and we rely on God. This is our only source of solace and reassurance. I am not happy, but I have patience and know that it is a test from God, and I beseech Him for recovery...</td>
</tr>
<tr>
<td>11</td>
<td>2</td>
<td>low</td>
<td>My psychological state changes before sessions only, but it gets better afterwards.</td>
</tr>
<tr>
<td>----</td>
<td>----</td>
<td>-------</td>
<td>-------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>12</td>
<td>1</td>
<td>low</td>
<td>I tend to be alone more. I also feel annoyed that all my colleagues are ahead of me in school, which makes me think of never going back to school. In short I cannot live my life as before. I became trapped by the condition.</td>
</tr>
<tr>
<td>13</td>
<td>5</td>
<td>Medium</td>
<td>I don't feel bad. And I feel that I will get better soon.</td>
</tr>
</tbody>
</table>

**Summary:**
Quotes did not support the quantitative findings. The majority of patients reported some emotional symptoms such as sadness, powerlessness and depression in the interviews, even though they did not report any of them in the survey. This demonstrated that some patients might be fearful of reporting depression as a symptom because of the perceived and the stigma attached to symptoms of depression. This could also be due to the fact that patients did not realise they have these emotional symptoms, and the interviews conducted might give them the opportunity to explore themselves. Depression was reported as being a sign of weakness and lack of belief and trust in God which might also contributed to the disagreement between phase 1 and 2 findings.
<table>
<thead>
<tr>
<th>Carer ID</th>
<th>QUANTITATIVE</th>
<th>QUALITATIVE</th>
<th>DISAGREE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CAREGIVER BURDEN</td>
<td>AGREE</td>
<td></td>
</tr>
<tr>
<td>C3</td>
<td>Mild</td>
<td>23</td>
<td>“My mother goes to the dialysis centre on Sunday, Tuesday and Thursday, and luckily has no dialysis sessions at the weekend. I try to go out with my mother if she is able to spend some time together”</td>
</tr>
<tr>
<td>C4</td>
<td>Moderate</td>
<td>42</td>
<td>“When I see her suffering and I am unable to help her. She has a small tumour next to the catheter in her hand. Sometimes I feel helpless as I cannot do anything for her”</td>
</tr>
<tr>
<td>C5</td>
<td>Moderate</td>
<td>45</td>
<td>My patients is not such a demanding person who increases the burden on me, but on the contrary I continuously try to ask her if she wants anything. A person can do millions of things if they plan their time and consider some order.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>“I think that taking care of patient who is active and seemingly healthy, as in the case of my husband, who gives the impression that he is healthy and not diseased, especially if he does not stay at home much”</td>
</tr>
<tr>
<td>ID</td>
<td>Age</td>
<td>Burden</td>
<td>Statement</td>
</tr>
<tr>
<td>-----</td>
<td>-----</td>
<td>--------</td>
<td>------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| C6  | 26  | Mild   | “My husband has retired and I can see him more than before. We became able to spend a lot of time with each other. We live far away from the dialysis centre, so I accompany him for a long distance and spend much time with him during treatment sessions. Every cloud has a silver lining”

“I have a lot of time for myself. I sometimes wish to spend more time with him. We (three wives) share in taking care of him.” |
| C7  | 21  | Mild   | “I have changed for the better. My belief that taking care of my mother is the right thing I should do has been strengthened. Just seeing my mother smiling and satisfied with me makes me feel that I own the whole world.”

“Sometimes she does not stick to her specific meals or refuses to take some medicines, which makes me feel a bit worried about her and her health condition, in general I rarely get angry and do not even like to consider the idea of being angry in connection with my mother. I do not get angry with my mother, but I am just worried about her and fear living without her.” |
<p>| C9  | 12  | No burden | “My employer and colleagues support me. My work schedule is arranged in such a good way where I do not teach the last classes and do not take any school activities at the time when my mother has dialysis sessions, So I am able to leave early and accompany her” |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>C10</td>
<td>Mild</td>
<td>25</td>
<td>I do not consider this a burden whatever happens. He is my children's grandfather, he loves me and my children. When he was in good health condition, he did us everything and took care of us. Now I take care of him with all love and respect, and I am sure God will reward me for this good deed.</td>
</tr>
<tr>
<td>C11</td>
<td>Mild</td>
<td>22</td>
<td>“Usually I spend the time I would spend with my father doing useless things, like sleeping during the afternoon, watching television or playing on my phone, instead of taking care of my father. .... In fact, providing care to my father has strengthened my diligence and motivation to be better.”</td>
</tr>
<tr>
<td>C12</td>
<td>Mild</td>
<td>27</td>
<td>“My social life has not changed much. We are from a conservative family that does not allow girls to go out with their friends so much.”</td>
</tr>
</tbody>
</table>

**Summary:**
Quotes from qualitative interview supported the quantitative results indicating that caregiver burden levels were low. Caregivers who reported moderate caregiver burden levels, contradicted themselves and reported that caregiving was not a burden for them mostly. This was due to the social support associated with culture and religious beliefs which reduce the level of burden they were facing. Some caregivers reported of being delighted and satisfied to provide care to their patients associated with the feeling of being worthy.

Level of burden identified based on ZBI scores in the cross-sectional phase which 0-21 = no burden, 21-40=mild, 41-60=moderate, 61-88=sever burden.
Chapter 8: Discussion
8.1. Introduction

This study examined symptom burden experienced by individuals with ESRD receiving HD in Saudi Arabia. In this chapter the outcome of the study will be reviewed to determine if it was achieved. The aim and objective of the research will be also reviewed by considering the current evidence available related to the experience of symptom burden in patients receiving HD and their caregivers. This chapter will close highlighting the strength and limitation of the study.

8.2. Outcome of research

The study outcome outlined at the commencement of this study research was to provide an overview of the symptom burden experience by patients with ESRD receiving HD in Saudi Arabia, along with an exploration of the levels of burden of caregivers who informally providing care to those patients. The outcome was considered to be completely achieved, even though in this study, data was collected from patients from one cultural background which might limited the generalisability of study findings. The findings from this study provides a unique insight of the experience of symptoms, the impact of these symptoms as well as the factors influencing the levels of burden in these individuals. This study is unique in that is explores the caregiving experience and any negative and positive effects of providing care to those individuals requiring HD. Using this research design, provided a comprehensive and explanatory insight into burden from the patient and caregiver perspective, within the unique culture of Saudi Arabian.

The overall aim of this study was to address the lack of understanding
concerning symptom burden experienced by people with ESRD, receiving HD, and caregiver burden in Saudi Arabia. A number of research questions were framed to help answer the aim of the study.

8.3. Answering the Research Questions

This study seeks to answer the following research questions:

- How does the understanding gained in the qualitative phase of the study help to explain the impact of symptom burden and the factors associated with symptom and caregiver burden support quantitative results?

The following discussion supports the answering of this research question.

- What is the level of symptom burden for patients receiving HD?

This research question was addressed in Chapter 4. Patients in this study reported experiencing a wide range of symptoms, with a mean of 10 ± 5 from a total of 32 symptoms, presented in the CKD-SBI. The most prevalent reported symptom was fatigue 101 (71.6%), followed by itching 89 (63%), bone pain 87 (62%), and muscle cramps 86 (61%). Difficulty falling asleep 71 (50%) and trouble staying asleep 76 (54%), was also frequently reported by the patient sample. These reported symptoms were consistent with study results presented in the systematic review (Chapter 2; Figure 7). However, in this study a number of symptoms were reported to be less frequent, depression 13 (9.2%), decreased sexual interest 5 (3.5%) and difficulty with sexual arousal 4 (2.8%). These reported less frequent symptoms related to sexual practices maybe due to personal preferences not to answer question regarding sexual practices. Although sexual symptoms were the least reported symptom in this
study (3%), our results were consistent with Almutary et al (2016) who reported sexual symptoms as the second least reported symptoms in patients with CKD, in Saudi Arabia. Cultural norms and the sensitivity of sexual topics may play a role in the non-reporting of these symptoms. In the Middle Eastern culture, discussing sexual issues is prohibited (Baazeem, 2016). These differences between patients beliefs make patients reluctant to provide information on the subject, failing to provide an answer or possibly giving false information in order to avoid further discussing in this subject on the second phase leading to shame. It is essential that HCPs appreciate that people are not all the same and must recognise that a better understanding of other cultures and cultural barriers may help promote a greater degree of assessment accuracy (Ekelman, et al 2003).

Fatigue was the most reported symptom in this study and has the highest impact on the patient’s physical, social and emotional life. Internationally, a number of studies reported HD patients experienced fatigue as the most prevalent symptoms, by 82% of HD patients in the UK (Caplin et al., 2011), 77% in the USA (Jablonksi, 2007A), 73% in China (Yong et al., 2009) and 92.2% in Canada (Davison and Jhangri, 2010)

Previous studies have reported that patients with normal HG values have significantly less fatigue, and better physical and functional well-being (Blair et al 2008; Holzner et al 2002). In this study 66.7% of patients had a normal HG level, yet 71% reported fatigue as the most frequent and severe symptom. This study found no correlation between HG levels and fatigue, which is supported by Figueiredo et al (2012) and Chang et al. (2001), who reported similar
findings. According to Holzner et al. (2002), fatigue can be present even in cancer patients with normal HB values. This study found that fatigue can be caused by other potential symptoms, such as poor appetite and a lack of sleep, which can be caused by other physical and psychological symptoms, such as depression, sadness, anxiety or pain. According to (Gamondi et al 2013) pain often coexists with depression, anxiety and insomnia and fatigue. This is also supported by Artom et al. (2014) and Sakkas and Karatzaferi, (2012) who reported that a lack of sleep and dietary restrictions, for patients receiving HD, can be additional reasons for fatigue. Fatigue is an important issue and HCPs team and researchers must become more aware of this problem, its impact and treatment. Many patients may benefit from a more comprehensive evaluation of fatigue and more effective interventions to resolve dialysis-related fatigue (Jhamb et al., 2008). The management of fatigue is an important clinical priority for patients receiving HD, to help enhance the QoL of patients (Lee et al 2007), and to minimise the impact of fatigue on the patient’s physical, social and psychological life.

Study findings also demonstrated that the mean symptom prevalence was 10, which was high for patients receiving HD, and consistent with the symptom prevalent score of 9.8, reported in study by Weisbord et al (2004) in USA, 9.3 reported in study by Yong et al. (2009) in China, and 7.4 in Canadian study by Davison and Jhangri, (2010). This study also found that there is an interrelationship between symptoms, with some symptoms exacerbating of other symptoms, leading to increased symptom prevalence. Published literature reports that dialysis patients typically endure several complex symptoms for a prolonged period of time, which is similar to symptoms
prevalence in patients with cancer (Solano et al 2006). When symptoms of a specific illness are more diverse, the delay in seeking medical care is a common outcome (Taber, Leyva, and Persoskie, A., 2015: Andersen et al 1995). The number of symptom in patients receiving HD may be reduced significantly, if the interrelationship between symptoms is investigated more rigorously. However, the causes of these symptoms and their interactions, as well as the association between them, has received limited research attention.

The interaction between psychological, physical and social health, has been investigated in a number of studies. According to Naylor et al (2016), a deterioration in mental health may lead to eating disorders, self-harm, social isolation, higher rates of maladaptive behaviours, such as smoking, alcohol misuse, as well as a reduced ability to self-motivate necessary to manage physical health issues. Also People with functional limitations or bodily impairments are generally disadvantaged in their opportunities to participate in social life (Veen et al 2011: Bickenbach et al 1999). This study demonstrated that psychological symptoms have a significant impact on physical health and social wellbeing and vice versa. Sadness can lead to poor appetite, which will impact on physical wellbeing, any physical dysfunction may cause patients to experience sadness and depression or may lead to be socially confined. It has been suggested that people under psychological stress, are more likely to have an impaired immune system and, as a result, experience more frequent illness (Khansari et al., 1990). These findings establish that researchers should not underestimate the effects of psychological symptoms on physical and social wellbeing. HCPs need to develop a comprehensive care package which addresses the physical, psychological and social needs of patients, to ensure
that these individuals adapt and manage their health more effectively. To facilitate the appropriate care and necessary interventions, HCPs should identify the causes and consequences (physical symptoms causing psychological symptoms), and vice versa, to be able to target the most significant problem, which may help to relieve any associated symptoms. A failure to provide holistic care, may lead to poor health outcomes and advance the progression of disease (de Ridder et al 2008). Pain and physical discomfort such as cramps, aching bones and headaches are associated with sleep disturbances (Danquah et al 2010). It has also been suggested that treating of sleep disturbance could potentially improve the daytime fatigue and serve to improve overall QoL (Clarke et al 2017). The complex association between symptoms and consequences, needs to be investigated to ensure that patients receive appropriate and effective help. Treating one symptom effectively, may assist in alleviating other symptoms and as a result reduce overall symptom prevalence.

Bone pain was the second most prevalent symptom found in this study, which accounted for 62% of the total number of patients who participated in this study. These findings are consistent with similar studies by Weisbord et al. (2005) and Davison (2003), who found that at least 50% of patients receiving HD experience bone and joint pain. A recent study in Sri Lanka by Senanayake et al. (2017), involving 1174 CKD participants, reported that 87.6% of this population experienced bone and joint pain, which was the most prevalent symptom. This may be due to the increasing number of elderly patients with ESRD, who are beginning dialysis (Kurella et al., 2014). The study by Tieland et al. (2018) people of advanced age experience declining of physical functions
due to the loss of skeletal muscle mass and arthritis. However, in this study, patients tended to be younger and only 30.5% of participants were over 65 years. It was noted in this study that 92% of the patients who expressed bone pain, had at least one comorbid condition. It is possible that bone and joint pain maybe the result of other underling diseases such as cardiovascular, hypertension or diabetic complications (Fidan et al 2016). For example, diabetic neuroarthropathy is a complication of diabetes mellitus with spontaneous bone and joint destruction, developing in diabetics with unstable metabolism (Chantelau et al 2007; Forgasc 1977, Johnson 1967). One of the main barrier reported by HCPs to manage symptoms, is that they feel some symptoms are unrelated to dialysis and should be considered by other specialist (Feldman et al 2013). The treatment of symptoms should not rely only on the HD team, this should be a shared responsibility between chronic illness specialists (diabetic, cardiovascular, cancer etc), mental specialist in addition to the dialysis team.

- **What are the factors that predict symptom burden among HD patients?**

In this study, the factors influencing symptom burden levels in patients receiving HD included age, gender, marital status, financial status, comorbidity, and culture and spirituality.

**Age**
The systematic review (chapter 2) reported that older patients experienced higher symptoms than younger due to the deterioration of health associated with aging (Almutary et al. 2016; Curtin et al. 2002; Yong et al. 2009).

In this study increasing age contributed to fewer reported symptoms because patients believed that their health was likely to deteriorate with age, which makes symptoms more acceptable to older patients. Older participants demonstrated a greater appreciation of their health status and appeared accepting of the fact that their current health status might not improve. This might result in fewer reported symptoms in the elderly than what they really experience. The elderly might underestimate the real number of symptoms associated with HD treatment and possibly report only those which they believe are not related to their aging symptoms. The literature suggests that people with CKD reported only the symptoms that they believe most serious to HCPs in order not to disturb them (Curtin and Mapes, 2001). This suggested the significant of identifying the factors associated with underreporting symptoms to ensure accurate assessment.

**Gender**

Current literature reported that being female was associated with higher symptom scores. It has been suggested that the higher symptom rate in women could be linked to the higher rate of stress and depression seen in this gender (Aldukhayel et al., 2015; Blake and courts 1996). Depression can often alter the perception of daily stressors and result in symptoms being more severely experienced (Amro et al., 2014). Men receiving HD confronting some stressors may exhibit emotional detachment or a sense of apathy during the
treatment (Johnson 2017). Different behaviour in inhibiting stressors between genders, might explain the varied levels of symptoms reported, particularly the emotional symptoms (Johnson, 2017). Caplin et al. (2011) men are likely to recover to their baseline a few minutes after dialysis. It has been suggested that the hormonal differences between genders might alter the levels of reported symptoms between them (Lewis et al., 1996; Albert, 2015). Hormonal changes can cause more psychological symptoms in females than in male patients (Albert 2015). The physical structure can affect the differences in reported symptoms between genders, men tend to have larger bodies than women, which makes them less likely to be susceptible to the toxic effects of uraemia (Spalding et al. 2008).

Our findings were consistent with the literature, showing that female patients experienced a significantly higher symptom burden than men. In addition to the explanations provided in the literature, and in light of the differences between the roles of men and women within the family in Islamic countries (Walther, 1981: Gonsoulin, 2005), this was reasonable. Women in this study expressed highly distressing levels of burden especially when they were unable to meet the needs of their families. The role of women was predominantly focused on taking care of home responsibilities, and the needs of children and partners. Feeling of not being able to meet family responsibility and being a burden created a sense of not being worthy in the family leading to additional emotional symptoms. In contrast, most men perceived that they achieved their responsibilities associated with providing a suitable income for their family. Many male working patients in this study were offered early retirement after they began HD sessions, which ensured that they were
financially secure and this helped to reduce the level of burden for these individuals and their families. Men acknowledged financial stability, as one of the main requirements for good health, when they were asked about their health needs which might contribute to reduce their level of burden. Our study also confirmed that women are more likely to express their feelings when asked to describe burden related problems. This was evident when we measured the data generated from the interviews data and found that the length of the data provided by female were greater than male participants. This suggested that gender characteristics and emotional differences should be taken into account when assessing symptoms (Almutary et al. 2016).

Marital status

In the study systematic review (chapter 2), the association between marital status and levels of symptom burden was not investigated, although a study described that patients with no spousal support had higher symptom burden scores (Goris et al. 2016).

In the qualitative interview, we were not able to explore the insight of unmarried male patients as all the men interviewed were married. Our findings revealed that being divorced, widowed or a single patient was associated with a higher degree of symptom burden, when compared to married patients, particularly emotional symptoms, such as sadness, depression and anxiety. Marital status was independently associated with the levels of symptom burden when performing the linear regression (chapter 5). However, when multiple regression conducted, marital status did not show a significant association in
the final model. In this study, the majority of unmarried patients were women 84%, and 70% of patients who reported depression were unmarried. Women in Saudi Arabia commonly rely on their male partner for financial and emotional support which helps to reduce life burden and stressors. However, in this study women who did not have a partner, reported an increase of daily responsibilities and demands which added to feelings of burden. When a woman loses this support, as a result of divorce or death of a partner, especially when there are children, this leads to increased levels of anxiety, depression and burden (Inaba et al. 2005).

Single patients expressed higher symptom burden because they are more likely to delay day-to-day plans, and are unable to fulfil necessary daily responsibilities. Single patients considered future plans such as marriage, studying, building a future career, and nurturing relationships with others, as an impossible outcome for them, because of the burden of their condition. Experiencing physical symptoms; such as fatigue, loss of concentration, limited their ability to make future plans. Experiencing constant symptoms, restrictions resulting from dialysis therapy and the inflexibility and uncertainty about dialysis life, caused a negative impact on the psychological status of single patients, which was further exacerbated by symptom burden. It has been suggested in literature that single patients are more likely to report a greater number of psychological symptoms, due to the lack of support from a partner (Inaba et al., 2005). Even though, it has been suggested that being married might be associated with greater responsibility in terms of providing
economic, care and social support to family members (Cantekin and Tan 2011) which supposed to increase patients burden.

**Financial status**

One study indicated that lower socioeconomic status is associated with a greater number of symptoms and more severe symptoms (Yong *et al.* 2009). Low-income patients reported a higher symptom burden (Goris *et al.* 2016). Patients with low education and unemployed patients reported higher fatigue, weakness and poor mobility (Jeong lee and Jeon, 2015). In contrast, Senanayake *et al.* (2017), who conducted a recent study in a large sample size of 1174 in Sri Lanka, revealed that a high symptom burden is associated with being educated up to advanced Level and being employed.

This study anticipated that there would be an increase in symptom burden when patients being unemployed, which was reported in other studies (Jeong lee and Jeon., 2015; Winkleby *et al* 1992). The proportion of patients who are employed prior to dialysis, decreases significantly after the start of hemodialysis treatment (Tsutsu *et al* 2017). Being employed was reported as a source of financial security to patients with chronic disease, and leaving their jobs increases the burden of disease, particularly mental illness (Herbig *et al* 2013). However, in this study, there was significant financial support from the state provided to individuals who are leaving their work because of illness. The Saudi government provides early retirement settlements to patients with chronic illness, whose performance is affected as employees. This creates feelings of being financially secured for these individuals, which may reduce
the emotional burden. Financial stability was reported by patients to be significant for health stability.

**Cultural impact on reported burden**

Religion has been found to significantly influence general happiness and life satisfaction and helps reduce depression and anxiety (Moreira-Almeida et al 2008). Cultural background has been identified as a factor which can affect the pain experience (Callister 2003). Based on cultural differences and social acceptance, burden may be reported as low. However, it is possible that participants in this study experienced symptom burden and caregiver burden and may have under-reported burden.

In this study, depression was one of the three least reported symptoms. This contrasted with the findings of two other studies (Turk et al 2006; Son et al 2009). The rate of psychiatric disorder in the population of ESRD patients is considerably higher than in populations with other chronic medical conditions (Kimmel et al 1998). The systematic review of studies conducted in Saudi Arabia, reported that depression is less likely to be reported in the population of this region (Alibrahim et al 2010). Even though, Almutary (2016) reported high levels of depression in patients with ESRD, in western Saudi Arabia, however, participants in this study might not be Saudi nationals, and may not reflect the characteristics of the Saudi population. The western region of Saudi Arabia is a destination for all international pilgrims, some may choose to remain there because of the presence of Makkah (the centre of Islam) and some were transient. In this study, patients were found to be reluctant to report
depression, as often they tended to express satisfaction and frequently thanked God and suggested they were “blessed” for their personal circumstances. In the Muslim religion, symptoms need be endured and the duration of symptoms is perceived to be a form of atonement. The torment that patients experienced during illness, helps to erase sins and cleanse individuals, ensuring that they are ready to enter heaven. However, in different cultures, for example the USA, pain is perceived as bad, not to be endured, and should be eliminated (Nayak et al., 2000). HCPs must recognise the confounding effect of cultural differences in reporting symptoms, to enable an accurate assessment and effective interventions for individuals experiencing the symptoms of burden. It is unclear if religion acts to encourage individuals to report their symptoms, or if it inhibits patients reporting symptoms.

Study findings suggest that depression and the number of symptoms reported by patients, may be interpreted in different ways. Patients may be depressed and experience a range of symptoms, but they may suppress adverse feelings associated with symptoms. The suppression of feelings may be due to the cultural inability to accept them, rather than the fear of rejecting God’s will. Depression was reported as being a sign of weakness and lack of belief and trust in God. In Arab countries, it is also common for individuals with depression not to access psychological therapies provided by health care professionals (Gilat et al. 2010). This may be associated with cultural beliefs, and the fear of stigma which may result, if they are perceived to utilise these services (Abbey et al., 2011). The fear of stigma associated with depression, may also contribute to the under-reporting of depression. Stigma may result
in limiting career opportunities in their future, as people assimilate the stereotypes and prejudices of society, in a manner that is detrimental to their success in the workplace (Krupa et al. 2009; Caltaux 2003). If there is a reluctance to discuss depression resulting from feelings of shame, HCPs need to provide education to promote depression as a legitimate health problem. HCPs also need to encourage patients to seek the psychological support services available, if required.

A further explanation of why patients may not report depression is that they interpret their situation differently from others. The religious activities and behaviour based on acceptance rather than rejecting, significantly influenced the patients’ general happiness and life satisfaction and helped reduce symptom burden and caregiver burden. A review conducted by Almutary et al. (2013) suggested that differences in cultural background can affect significantly the symptom burden levels in patients with ESRD. In addition, the wider social support surrounding them, and positive expectations and thoughts related to their health help to improve perceived levels of burden. If that is the case, then the use of positivity may help to reduce the psychological symptoms not only in patients with HD and but also for other chronic conditions. This attitude had been promoted by Khansari et al. (1990) who reported that old anecdotes describes resistance of some people to severe disease using the power of the mind and their thought processes. People who were more positive and exposed to less stress are less likely to have cancer (Reiche et al., 2004). Helping people to interpret their symptoms in a different and positive way, involving the wider family in providing care may be used as an intervention to
reduce symptom and caregiving burden. HCPs should be encouraged to create therapeutic methods to resolve symptom burden and caregiver burden using cognitive approaches which could incorporate greater religious involvement and social support.

- What is the level of caregiver burden for caregivers of patients receiving HD? (Chapter 5)

In the systematic review (chapter 3), the majority of the 27 studies included reported moderate to severe caregiver burden in caregivers providing care to ESRD patients.

In our study, the mean total caregiver burden scores reported by caregivers was 22 ±14, indicating mild to moderate burden. The majority of caregivers 36 (59%) reported a score of <21 indicating little to no burden. This study reported low caregiver burden which could be interpreted in two ways. It was observed that caregivers avoided complaining about their relative patients or thinking about leaving the care to someone else. According to the values of Middle-Eastern countries, providing care should be at their home by a family relative and consideration would never be given to moving them to a nursing home even if it is next door (Al-Olama and Tarazi 2017). People in Saudi Arabia believe that complaining or leaving their relative in the time of need, would bring scandal and shame to those caregivers, this will cause them to be reviled by society and will bring misfortune to them. The second interpretation which is more likely to be true is that the social support associated with culture and religious beliefs reduce the level of burden they are facing. Literature reported that social support helps to reduce caregiver burden in patient receiving
dialysis (Alvarez-Ude et al. 2004; Alnazly 2016; Shakya et al. 2017). The family structure for most Muslims is patriarchal and based on the extended family (Dhami, S. and Sheikh, A., 2000; Ahmed, 1988; Ali, 1996; Henley, 1982). The large family size with the strong family bond and collectivism in the Saudi Arabian culture (Alamri, Cristea, and Al-Zaidi, 2014; Al-zahrani 1993) contributed to involve more family member to provide care and reduce burden. Also the religion belief provided a motivated to provide care to the disease family member, as this was perceived to be a positive function which may enable individuals to be rewarded by God.

- What are the factors that predict caregiver burden?

Age, gender, culture, comorbidities, and social support.

The age and the number of comorbidities of the caregiver were found to be positively associated with caregiver burden in this study. This was consistent with the findings in the systematic review (chapter 3). Caregivers in this study expressed feelings of guilt when they were busy or unable to provide the necessary care to their relatives, as a result of health deterioration associated with aging or illnesses. In addition, providing care in this sample seemed to be a transition stage to most caregivers. This transition period related to the culture nature in Saudi Arabia reduced the feeling of being trapped in the role of caregiving which contribute to lower levels of emotional strain. It was also noticed that patients reported feelings of being restricted socially. However, the majority of caregivers expressed that social restrictions were not an issue for them. As all caregivers interviewed were female, and the culture in Muslim traditional countries imposes social restrictions for these women (Sfeir 1985),
caregivers reported no differences before and after their patients started HD. This suggested that possible cultural differences and traditions can affect the level of reported burden. Burden can be defined differently in diverse cultures, social restrictions might not be a burden for those female caregivers in Saudi Arabia, but could be a possible burden for caregivers in the Canada (Beanlands et al 2005).

- **What is the association between patient symptom burden and caregiver burden?**

The systematic review (chapter 3), reported that the burden is greater in caregivers when the patient’s health status declines. Health decline may involve comorbidities and lower levels of independence. However, the key element is that the symptoms associated with comorbidity might be the main contributors to increasing caregiver burden in informal caregivers. However, no previous study has explored the association between symptom burden in care recipient and caregiver burden in their informal caregivers.

In our study the number of symptoms was significantly associated with symptom burden. This suggests that symptom occurrence is a significant contributor to caregiver burden in patients with ESKD who require HD. This suggests that treatment optimisation in patients receiving HD will not only contribute to improved patient wellbeing, but it may also reduce the level of burden in caregivers.

- **What is the experience of symptom burden for patients receiving HD?**
Living with concurrent symptoms associated with the regular HD treatment impacted patients’ lives in all aspects, physically, socially, psychologically and cognitively.

The level of distress varied between symptoms reported by patients in this study. Knowing the reason for symptoms and symptom management, made them feel more comfortable with these symptoms. Health education can play a significant role in reducing the level of distress which individuals experience when they develop a new disease (Patnaik et al 2105: Telch and Telch 1985). It is important that HCPs are aware of the influence of health education in stress reduction. It is also significant that HCPs need to be aware of the causes of each symptom, treatment options and the impact of symptoms on patients, to help prioritise effective interventions provided and also to enable reductions in the level of symptom distress and occurrence.

Delivering competent professional assessment and treatment might reduce the symptom burden reported. In this study patients reported that muscle cramp was frequently caused by an inappropriate adjustment to the required extracted amount of fluids while being treated via an HD machine. Nonetheless, occurrence of cramps in our study decreased over time, perhaps due to a better understanding of volume management, which is consonant with the findings from Figueiredo et al (2012).

The HCPs need to have a high level of awareness of the potential presence of any mental health symptoms. In the quantitative phase of the study, some patients failed to report their emotional symptoms or did not realise that they were experiencing psychological symptoms. False perceptions made patients
expect that they were well, when in actual fact they were experiencing a clinical symptom of depression. The face to face interviews gave the patients the opportunity to explore themselves. Participants are more likely to express their issues in detail within an interview rather than through a survey (Roberts 2007). Patients reported sense of being worthless, inferior, uselessness and powerless.

It has also been suggested that experiencing symptoms such as fatigue, low energy and mood, in addition to the changes to body image, intrude on relationships and make them difficult to sustain, and subsequently add to the distress experienced by patients (John and Thomas 2013; Hagren et al 2001). Feeling like a burden can influence the quality of life of chronically ill patients in a negative way (McPherson et al., 2007). Patients were concerned that they were putting an extra burden on their caregivers and worried about the impact this would have on these individuals and their relationship. This suggests that HCPs should be mindful that those with physical problems may also have subsequent mental health symptoms and careful, comprehensive and detailed exploration of these issues must be a part of any assessment. To provide effective care to this population, HCPs need to receive comprehensive training on mental health assessment, delivering appropriate routine treatment (dialysis), and managing psychological distress. It is also important that HCPs refer patients with psychological distress to specialised psychological service providers when needed, to help prevent the development of complications associated with symptoms.
The patients reported that the experience of symptoms associated with HD caused their cognitive ability to be impacted. Patients stated that continually thinking about their situation, and the stress and worry they were experiencing affected their memory and ability to concentrate. High concentrations of stress hormones can cause declarative memory disorders (Lupien and Lepage, 2001). It has been suggested that being exposed to stress can cause pathophysiologic changes in the brain, and these changes can be manifested as behavioral, cognitive, and mood disorders (Li et al., 2008). This demonstrates that the cognitive impact experience by patients receiving HD could lead to psychological symptoms and vice versa. It has been suggested that the effect of stress in memory is highly dependent on the time, intensity, and duration of exposure to the stressful events and, in terms of the timing of the imposed stress, memory can be either better or worse (Schwabe et al., 2012). More studies are needed to explore the effect of the duration of HD, stress and levels of memory.

Experiencing constant symptoms, restrictions resulting from dialysis therapy and the inflexibility and uncertainty about dialysis life, alters the relationship between autonomy and dependence (Curtin et al, 2002; Polaschek, 2003). It is clear that being able to control as many aspects of life as possible, is important for patients’ and their adjustment to living with HD and associated symptoms. Being tied to regular dialysis treatment and dietary restrictions to manage symptoms, affects the way in which patients live their lives. Losing freedom associated with travelling, eating and drinking had a negative impact on the lives of patients in this study. Due to a regular HD schedule (Hagren et al 2000) and following strict dietary and fluid intake restrictions, patients felt
that they are restrained. Placing restrictions on patients imposes further limitations on them, which may result in psychological problems such as depression, anxiety and fear (Mausbach et al 2011; Griedman 1977, Klang et al. 1996). Patients need to regain the ability to control their lives and illness, in the way they used to, to be able to achieve self-efficacy (Curtin et al 2002).

- What is the experience of caregiver burden for caregivers of patients receiving HD?

Providing care to patients with HD was not only associated with negative outcomes but also provided some positive outcomes. Caregivers reported of being delighted to provide care to their patients associated with the feeling of being worthy. Culture, religion and traditions impose a sense of commitment and obligation to caring in Saudi Arabia, which was supported in a study conducted in Jordan that reported religion practice and beliefs as one of the main coping strategies with caregiving (Alnazly and Samara, 2014). Providing care to a sick family member can have a positive and enhancing relationship between the caregiver and care recipient, and accomplish enhanced family harmony, and promote resilience in caregivers (Chan, 2011; Hinrichsen et al., 1992). Research should adopt a more holistic approach to caregiver experiences and focus more on the positive experiences of caregiving, rather than judge caregiving to have a mainly negative outcome. Positive benefits of caregiving, could be used in the development of future appropriate interventions to enhance caregiver well-being (Whittier et al., 2002).

- What management strategies are used by patients receiving HD to
**manage symptoms?** Chapter 6 presents the management strategies suggested by patients receiving HD to control their symptoms.

Limited research has been explored the self-management strategies for patient with ESRD (Curtin *et al.*, 2005). In this study patients reported four commonly strategies to manage symptoms including; religious and spiritual methods for acceptance and healing, lifestyle changes, using medication and cognitive skills. Interventional studies have explored the effectiveness of lifestyle modifications and using medication as a treatment to manage CKD (Peng *et al.*, 2019). Additionally, using cognitive skills and religious and spiritual methods for acceptance and healing has not been effectively investigated. Religious beliefs and practice were associated with higher levels of satisfaction in patients receiving HD (Berman *et al* 2004). Future interventional research is needed to explore the effectiveness of these strategies in improving the experience of symptoms and overall satisfaction.

**Symptom management barriers**

According to Davison *et al* (2003), while approximately 50% of patients undergoing HD who experienced pain received treatment for the pain, 5% of them reported ineffective treatment. Likewise, it has been reported that 16% of patients receiving HD who reported depression were receiving psychiatric treatment, including pharmacologic treatment or counselling (Watnick *et al* 2003). Patients who live with multiple symptoms on a daily basis may not even consider reporting these symptoms they think nothing can be done to alleviate (Jablonski 2007A). Patients reported a sense of being ignored and lack of communication with HCPs which lead to lack of trust in their treatment
decisions. In this study, some patients express lack of hope in treating symptoms associated with dialysis, which results in them not trying to seek professional help. This might lead to deterioration of their health and exacerbate the symptoms experience. According to Feldman et al. (2013), the commonly reported reason for the lack of HCPs knowledge about symptoms is the patient resignation leading to underreporting symptoms. Encouraging patients to share their complaints as a part of their treatment is necessary for complementary and successful care. Effective communication between patients and HCPs is essential in building a collaborative therapeutic relationship (Ha and Longnecker, 2010; Ong et al 1995). Building good communication between patients and HCPs will facilitate better understanding of patients needs, adherence to prescribing treatments and following advices (Ong et al 1995; Ha and Longnecker, 2010).

There is an agreement between participants about the insufficient education provided to the patients to manage and live with their illness. According to the descriptions given by these patients, receiving the information from HCPs was one of the least reported sources of knowledge. Patients were unsatisfied with the education they received after being diagnosed with renal failure and started receiving HD. Patients reported that the information that doctors and nurses provided was too brief, ad hoc, and it left the patients lost. Patients expressed the opinion that education is essential in the process of treatment and not non-essential voluntary work. Patients believed that providing a proper health education could help them to overcome their illness and improve their health.
These barriers to symptom management identified in this study may contribute to leaving symptoms untreatable, causing lower health-related quality of life as well as high levels of distress and depression (Ludman et al., 2004). Lack of trust in HCPs, losing hope that there is a cure, the sense of being ignored by HCPs, insufficient health education provided, might lead to negative consequences such as seeking out alternative treatment and therapies which could be unreliable and unsafe (Radeos et al., 2001). Some patients self-prescribed medicine when needed, instead of returning to the renal specialist, which might cause serious consequences to their health.

The data also showed that the majority of patients reported that advice from friends and their experiences are the most important sources of their knowledge to manage their symptoms with limited information gained from their doctors and nurses. This showed that patients were not receiving enough education in relation to their disease and how to manage symptoms. According to (Feldman et al 2013), some HCPs feel symptoms are unavoidable in HD patients. This suggests that further research is needed to better understand the relative contribution of disease states versus iatrogenic symptoms to overall symptom burden in this population and to develop effective symptom management strategies (Feldman et al 2013). These barriers to symptoms management identified in this study may contribute to leaving symptoms untreatable, causing lower health-related quality of life as well as high levels of distress and depression (Ludman et al., 2004).

8.4. Strengths and limitations of the study
• This is the first study that explores the experience of symptoms and their impact on patients receiving HD in Saudi Arabia using a qualitative research approach. This study is unique in that is explores the caregiving experience and any negative and positive effects of providing care to those individuals requiring HD. Using this research design, provided a unique insight into burden from the patient and caregiver perspective, within the unique culture of Saudi Arabian.

• The generalisability of study findings to the total ESRD population receiving HD, may be limited, as the study collected data from a sample which consisted of 94% Saudi nationals. This study did not recruit participants from all the diverse ethnicities who live in Saudi Arabia. In addition, study findings can be generalized to the total population, as data was collected in a single region of Saudi Arabia. The sponsors of this research indicated that they would only support this study if data collection was restricted to a single location within Saudi Arabia. Data was collected from patients from one cultural background. Although, other patients’ characteristics were representative of this population.

• Symptom burden levels may not reflect real burden, as there were a high number of illiterate patients who were excluded from the study, see inclusion criteria Chapter 4. As education was not previously seen as a priority within the Saudi population, older individuals in the population are more likely to be illiterate. There was found to be a strongly negative (Caplin et al 2011) and positive association with symptom burden (Almutary et al 2016; Sanathan 2014; Horigan 2012; Bossola et al 2011; Jhamb et al., 2008; Peng et al., 2007). In this study, the age profile of the sample, may not be an accurate representative sample of the age of patients attending the dialysis centre.
Although the mean age of patients with CKD in a previous study conducted in Saudi Arabia was 48 years (Almutary 2016), which is younger than the population in this study, mean age 53 years.

- Even though the CKD-SBI demonstrated good reliability and validity and had been used previously in a CKD population (Almutary 2016 some participants found it difficult to complete. This may be due to the low level of educational attainment of patients or the effects of HD on their cognitive ability. The researcher in this study explained and assisted patients to accurately answer CKD-SBI questionnaires.

- In this study only 61 patient/caregiver pairs participated, to explore the relationship between symptom burden and caregiver burden, which is considered a small sample for the purpose of identifying a correlation between variables (Filho et al 2011). Small sample size may reduce the transferability of study findings, and may also limit the opportunity to determine if any association or correlation exists between variables.

- The generalisability of findings from caregiver interviews, may also be limited due to the small sample of female caregivers and the non-recruitment of male caregivers to the study. Therefore, this study does purport to represent of the experiences and perceptions of male caregivers of patients receiving HD.

- The study used a convenience sample, which has a number of limitations, which includes the risk of bias, as the sample may not be representative of the total population. The gatekeeper also could limit access to certain individuals. Convenience sample was commonly associated with cross-sectional and
qualitative research and it was the suitable sampling for this study. The time given to data collection was limited (six months), this sampling technique would enable the gathering of data in a much shorter time compared to other methods.

- Caregiver burden was low when compared to other studies. Less than half of the caregivers returned questionnaire. Caregivers who did not participate may have been experiencing higher levels of burden compared to those caregivers who participated. If this is true, the sample may not be representative of populations experiencing varying levels of burden. However, in this study caregivers who did not participate, are more likely not to be stressed as their relatives reported low symptom burden when compared to patients who had caregiver participating.

- Our data was limited to patients, HCPs were not included in interviews. Interview with HCPS may have provided further insights and a different perspective regarding management strategies and barriers to symptom management which was suggested by patients.

- Findings from the interview phase of the study were translated from Arabic to English. It is possible that the real meanings of Arabic words might have been misinterpreted from real and accurate meanings following translation. Participants often used metaphorical expressions and idiomatic language in Arabic, to relate experiences of their illness, and the subsequent impact of suffering on their lives. The complexity and the differences between cultures may make understanding these expressions confusing with translation into the target language. The researcher attempted to maintain real meaning by
checking the quality of the translated work independently by asking another bilingual translator to confirm the transcription. The researcher also provided an explanation of the metaphorical and idiomatic language as much as possible in order to translate the emotions and ideas expressed in the patient’s mother language into the principal language of this study which was English. This assisted the reader to engage fully with the patient and their explanations of their experiences in their first language.

While this study provides comprehensive information related to burden, it has a number of methodologic limitations, which include

A) There is potential confusion in relation to reported symptoms. Patients might have reported symptoms as being related to dialysis, however these symptoms may in fact be related to other physiological variables, such as comorbid condition or aging. This confusion may have increased the number of symptoms reported and in turn influenced study findings. In an attempt to address this important issue, the researcher made it clear to patients that the data collected was only related to symptoms associated with HD treatment.

B) The small sample size for regression analysis for caregivers may result in the model overfitting the data, which fits the sample data well, but does not generalize to the entire population. Caregivers sample size was also low for the minimum sample size needed for accurate predictions.

C) There is a lack of a non-renal failure comparison group and/or lack of comparison group of renal patients not receiving HD. Patients in this study reported high levels of fatigue, however, fatigue was not
measured after the diagnosis of renal failure and before HD treatment is initiated. Fatigue in this population might be significantly high, even before patients received HD treatment. This may result in high rates of fatigue which are not directly related to HD treatment.

D) Although the TOUS framework has been used extensively to measure symptom experiences in patients with chronic illnesses, TOUS does not take into account the interventional aspects of symptom management. The lack of a symptom management component within the TOUS model, limits the identification and evaluation of effective management strategies used by patients to alleviate symptoms and may impact on study findings. Management strategies are described as the “what, where, why, how much, to whom, and how,” which help researchers to explore and select suitable management strategies to alleviate the symptom experience (Linder, 2010). However, in this study the only question asked to patients was “what are the most effective symptom management techniques used to reduce or relieve your symptoms?” However, the amount of the effectiveness of the management techniques and the side effect of using the, for example, were not explored in this study. The lack of a management component, may have impacted negatively on the achievement of the study aim.
Chapter 9: Conclusion
9.1. Introduction to chapter

This chapter summarises the key findings from the study and outlines the implications of study findings for theory, nursing practice, health policy, public and professional education. The chapter concludes with a number of recommendations for future research.

9.2. Summary of the key findings

This is the first study which has been completed in Saudi Arabia using an explanatory sequential design. This study has added to current knowledge and understanding of living with renal disease symptoms and the experiences of informal caregivers in Saudi Arabia.

One of the main aims of the study was to identify the level of symptom burden in patients receiving HD. The study has demonstrated that there is a high prevalence of symptoms and burden in patients receiving HD in Saudi Arabia. The study established that the interrelationship between these symptoms may increase the number of symptoms, as well as the severity of symptoms and will lead to greater functional disability. The study highlighted that fatigue may be a result of other symptoms, which may contribute to the high prevalence of this symptom in the study population. This study also demonstrated that psychological symptoms have a significant impact on physical health and social wellbeing and vice versa. The psychological symptoms also have impact the cognitive ability of patients undergoing HD. Understanding the interaction between symptoms may contribute to a reduction in symptom burden in this population. Detecting the central symptoms which can contribute and lead to other symptoms is essential in the assessment process and treatment plans.
This study found that the most prevalent symptoms are not necessarily distressful for patients receiving HD. Patients reported fatigue as a devastating symptom, impacting on their physical ability to remain independent, and causing social restrictions as well as emotional distress. Patients who experienced muscle cramp did not experience the same level of distress as a result of this symptom. Patients understand that muscle cramp occurs only during dialysis sessions, due to extracting excess fluid and the adjustment of the dialysis machine resolved muscle cramp problems. It is important to understand the treatment priority as perceived by patients, when planning treatment for these individuals.

Being female, unmarried and having a comorbid condition contributed to an increase in levels of symptom burden. Additionally, religion and cultural beliefs significantly influenced the way patients view their illness and symptoms, such as seeing symptoms as a test from God and a sign of God’s love to erase their sins.

The study found that patients appeared reluctant to report sexual symptoms due to personal embarrassment issues which were closely associated with culture. Patients were also reluctant to report depression symptoms, they tended to express satisfaction and frequently thanked God and suggested that they were “blessed” for their personal circumstances. Patients may be reluctant to report depression as a symptom, because of the perceived stigma attached to mental illness symptoms. The suppression of feelings may be due to the cultural inability to accept them, rather than the fear of rejecting
God’s will. The way patients interpret symptoms, influences their reported symptom burden evaluations.

Caregiver burden was found to be mild in the population studied. Social support played a significant role in reducing physical and psychological burden in primary informal caregivers. The role of family, relatives and friends is significant and positively contributes to a reduction in burden. A large family size and strong family bonds increase the opportunities for family members to collaborate and contribute to provide care, which can help reduce caregiver burden. Interventions involving the promotion of social support to help reduce burden in informal caregivers is an important strategy which should be utilized by HCP’s. Social support not only involved family and relative support, but also included work and government support. Caregivers were able to receive support within work organisations to allow them to provide the required care and support to family members. Patients were also offered an early retirement package, which secured them financially and emotionally for the future. Religion was also reported to be a factor which motivated caregiving, as this was perceived to be a positive function which may enable individuals to be rewarded by God. Cultural structures and acceptance, such as the collectivism and the acceptance of multiple marriages, reduced the burden in the primary caregivers.

The study highlighted the impact of living with multiple symptoms associated with HD treatment. This affected all aspects of patients lives, including physical, social, emotional and cognitive ability. The literature reviewed identified how living with dialysis treatments and the restrictions imposed by
these treatments, such as dietary and fluid restrictions, impacted patients lives. However, the impact of restrictions caused by symptoms experience were not clearly identified. It is necessary for HCPs to manage symptoms, as a core process to help achieve the best symptom control and optimum HRQoL.

Patients reported a variety of self-management strategies to manage their daily symptoms including; using medications, lifestyle changes, using cognitive strategies, and religious and spiritual methods for acceptance and healing. This study identified the potential barrier to effective symptom management by patients. HCPs were found not to recognise or value symptom management or education as one of the main treatment priorities. Limited information and training in relation to symptom management is available to HCPs. In addition, a lack of communication and trust between patients and HCPs, seemed to have a negative effect on the process of symptom managements and satisfaction as expressed by patients.

9.3. Implications and recommendations of the findings

9.3.1. Implications for theory

The Theory of Unpleasant Symptoms (TOUS) was used to inform the development of this study whereby symptoms are conceptualised as multidimensional constructs that have the ability to interact with each other (Lenz et al., 1997; Lenz & Pugh, 2014). The TOUS has been used extensively to guide symptom research in oncology and is now being used in a variety of other chronic diseases. The main focus of the study was to explore symptom burden in patients receiving HD and the factors which influenced the
experience of symptoms. This theory provided a framework to help navigate data collection and analysis within the study. Although TOUS provides a range of components covering all aspect of symptoms assessment, (see the methodology chapter, page (128-132)), the theory may need future modification if it is to be used to support effective symptom management. As a result of this study, the TOUS model was refined to include symptom management as an outcome or consequences which needs to be included to measure symptom experiences. It has previously been suggested by Lenz et al (1997) that with the numerous symptoms experience by patients, this is likely to lower functional health status, lead to less effective role performance and poor health outcomes. However, patients who experience symptoms, may react positively to these symptoms, by using self-management strategies to effectively live with these symptoms.

Although TOUS suggested that situational factors could influence the incidence of symptoms, there is a need to emphasis the significant influence of culture in individual attitudes toward symptoms and how they are perceived. The systematic review in this thesis has also highlighted differences in symptom experiences across different cultures. The significance of culture in the reporting and perception of symptoms is supported by the findings of this study. As a result of study findings, it is suggested that the TOUS model should be refined to include cultural and religious factors in future assessments of the symptom experience. Figure 28 presents the TOUS components and figure 29 demonstrates the modifications and recommendations required to improve the theory.
Physiological factors:
- Gender
- Age
- Dialysis duration
- HG level
- Comorbidity

Psychological factors:
- Psychological status

Situational factors:
- Marital status,
- Socioeconomic status
- Cohabiting status
- Distance from hospital.

Culture
Religion

Symptom experience (prevalence, distress, frequency, severity)

Performance/Consequences after symptom experience
Including the impact of the symptoms on cognitive, social, emotional and physical status

Positive outcome and responses of symptoms
Self-management strategies to relieve symptoms

Figure 28: TOUS components

Figure 29: Recommended Theoretical Framework.
9.3.2. Implications for practice and policy

- Health professionals need to be aware that physical, physiological, and sexual symptoms occur in CKD and all require ongoing comprehensive assessment. The symptoms experienced by patients receiving HD are interrelated to each other, which increase symptom burden. A reduction in symptom burden in patients with HD and other chronic illnesses may be achieved if policy makers and clinical staff focus on groups of symptoms and target the main influencing symptom.

- Future research needs to provide a more comprehensive understanding of dialysis-related fatigue and support the implementation of evidence-based interventions (Jhamb et al., 2008). These interventions may involve: the use of exercise, dietary restrictions, life-style changes, the therapeutic use of positive thinking as a cognitive strategy to help reduce burden. Appropriate intervention strategies should be developed to target fatigue and other multiple symptoms.

- There is a need to create a workforce able to support and address the integration of mental and physical health needs to patients with HD. Given the high burden due to psychological symptoms in patients, psychologists and or counsellors should also be involved in multidisciplinary teams, to plan and provide treatment to patients with HD. Strategies to assist patients to manage living with HD physically and emotionally and its consequences, may improve the HRQoL of these individuals, and promote treatment adherence and the well-being of patients.
- Early recognition and determining the people at high-risk of experiencing greater symptom burden needs to be undertaken to enable early management and referral.

- Health care expenditure and planning in the Saudi Arabian health system has generally concentrated on providing the required treatment (HD) to patients with ESRD to ensure survival. The Health care system in Saudi Arabia needs to address all of the issues arising from this study for HD patients and include providing appropriate symptom assessment and treatment as part of routine care to help promote patient health. This can be achieved by promoting cooperative working between doctors, nutritionist, nurses, psychologists and physiotherapists. This integrated supportive care framework will facilitate the design of appropriate care suitable to each individual patients needs with a focus on symptom management, and its causes, to provide optimal care, managed symptoms and improved HRQoL (Davison et al., 2015).

- Currently there is limited funding for research aimed at the continued development of health care services in Saudi Arabia. Policy makers need to provide the necessary expenditure to support future research, with a focus on management and development plans to improve the HRQoL and satisfaction in patients receiving HD in Saudi Arabia.

**9.3.3. Implications for education**

- This study highlighted the impact of stigma in limiting the reporting of psychological symptoms and the reluctance to seek professional, psychological support and treatment. There is an urgent need to provide education programmes to the Saudi public, in order for them to understand the
importance of psychological treatments and the consequences of neglecting one’s mental health. This may lead to the prolonged presence of symptoms for the individual and a delay in receiving the necessary treatment. There is a need for significant investment in public health to help resolve the stigma associated with mental health, to help ensure that individuals seek prompt psychological help when required. HCPs need to provide better education to the public, to ensure that depression is accepted as a legitimate health problem. HCPs should not only be involved in providing these educational programmes, but the Saudi government also needs to offer a comprehensive public mental health education program, via leaflets and the media, to help minimise the stereotypical attitudes towards mental health. The media can represent these mental issues which can contribute to shape the public opinion. This may involve individuals with mental health problems telling their personal story, either through film clips or face to face in workshops, or by providing key messages including that mental health problems are common and affect people of all ages. This might encourage the community to discuss their issues bravely without being afraid of being prejudiced or discriminated. The government could also benefit from offering mental health drop-in centre services. This service can provide informal walk-in advice and information services which can assist individuals with their psychological problems. Education can also be offered to primary school children to develop their positive attitude in relation to psychological problems early in life. Educational strategies in general education is significant to help this younger age group to know how to obtain psychological support when they need it without feeling
shame. This behaviour can grow with them and would help to change the perceptions of the future generation toward mental health problems.

9.3.4. Implications for research and recommendations

- Research needs to explore symptom clusters, and the mechanism of symptom interactions, and how to identify cause symptoms and any resulting symptoms needed. This interrelationship between symptoms will facilitate the development of more effective intervention strategies.

- There is need to develop a measure to identify the main symptoms which may influence the presence of other symptoms. The current measures available, only list symptoms and fail to prioritise symptoms which need to be treated. The development of a more effective instrument will facilitate the better targeting of symptoms, and more efficient management of these symptoms. This will help reduce the number of symptoms which patients experience and enhance the HRQoL of these individuals and reduce the cost of treatment especially if the risk of ineffective treatment is reduced.

- Research should consider the experiences of male caregivers of patients with ESRD, receiving HD. It is important that we better understand the attitudes, behaviours and beliefs of males who provide care to patients with ESRD. The global study of the burden experienced by male caregivers, has received very limited research attention.

- There is a need to conduct intervention studies, and qualitative and quantitative studies supported by policy makers, to identify suitable and effective interventions to control symptoms and reduce fatigue in patients receiving HG. These interventions may support improvements in self-
management and ensure that patients maybe moreable to cope adaptively with their illness. Future research should be targeted at developing the use of a range of self-management strategies suggested by patients in this study. In this study, patients reported a number of individual strategies to manage living with their symptoms, such as the action of sucking on hard boiled sweets to avoid dryness of the mouth during HD sessions, instead of drinking fluids, which is restricted in this population. Some patients used herbal thyme tea to remove all sputum in the chest, while others used acacia gum to increase the energy and reduce fatigue (AlMosawi 2007) for stomach and throat discomfort. For feet numbness, patients reported using massage with olive oil (Cunningham et al 2011), and drinking turmeric and lemon juice to help alleviate joint pain. Some patients used cognitive abilities to reduce emotional and physical symptoms. Spirituality and religious involvement in symptom management may also be investigated and could also become a therapeutic intervention.
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Appendix 1: Critical Appraisal Checklist of the cross-sectional studies

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**JBI Critical Appraisal Checklist for Analytical Cross Sectional Studies**

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
<th>Unclear</th>
<th>Not applicable</th>
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<tr>
<td>1. Were the criteria for inclusion in the sample clearly defined?</td>
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<td>2. Were the study subjects and the setting described in detail?</td>
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<td>3. Was the exposure measured in a valid and reliable way?</td>
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<td>4. Were objective, standard criteria used for measurement of the condition?</td>
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<td>5. Were confounding factors identified?</td>
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<td>7. Were the outcomes measured in a valid and reliable way?</td>
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<td>8. Was appropriate statistical analysis used?</td>
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Overall appraisal:  
- Include [ ]  
- Exclude [ ]  
- Seek further info [ ]

Comments (including reason for exclusion)

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379
Appendix 2: Quality appraisal of the included studies using JBI (Chapter 2)

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<td>Was there a control group?</td>
<td>Were the participants included in any comparisons receiving similar treatment/care?</td>
<td>Were there multiple measurements of the outcome both pre and post the intervention?</td>
<td>Were follow up complete or were differences between group's description and analysis?</td>
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Appendix 3: The patients interview schedule

1) Warm up
   • Could you introduce yourself...?
   • Name, professional role?
   • How long have you been treated with haemodialysis?

2) Symptom experience
   • Can you tell me about the symptom that is occurred frequently and bothering you most recently?
   • Can you describe what the symptom feels like?
   • What life was like, living with the concurrent symptoms and what consequences the symptoms had on your life?

3) Influencing factors
   • Can you tell me about things (factors) you think negatively or positively affect your symptom?
   • What things make your symptoms worse?
   • What things make your symptoms better?

4) Symptom consequences and management
   • What action do you take to reduce or relieve this symptom?
   • How do you manage and control symptoms when they bother you?”
   • Does that minimize or relieve your symptoms, how?
   • Where did you learn to do that?
   • What other ways do you use to reduce or relieve this symptom?
   • Which kind of services do you use as renal failure patients to manage any of your complaining? How those services help you in your complaining?
5) **Understanding the challenges, barriers and needs.**
   - Can you tell me about the barriers and challenges you face managing your symptoms?
   - Tell me about the transportation to the center, does that make any obstacles for you to attend your routinely haemodialysis appointments? If yes, how is that?
   - Can you tell me about your needs?

6) **The impact of symptom burden in the patient’s life and their expectation.**
   - Tell me about things that you could do previously, but you are no longer able to do?
   - How does your life change after your disease?
   - What consequences have the symptoms had on your life
   - What is your expectations and priority as patients on dialysis treatment?

*Anything else you would like to add to the discussion which we have not covered*
Appendix 4: interview schedule for caregivers

Warm up:

- Name.
- Age, Education level, marital status, Professional role.
- How long have you been caring for your patient?
- What is your relationship to patients?
- Why do you take care of this patients?

Knowledge:

- What do you know about CKD?
- What is your source?
- From your knowledge, how do you describe a healthy renal failure life style (nutrition, self-care, medicine)?
- What health support do you receive from hospital? (Formal health education related to how to take care of CKD)?

Caregiving experience and impact

- Can you talk about your daily routine in taking care of the patient?
- Can you tell me about things (factors) you think negatively or positively affect your burden of care?
- How does your life change when you started providing care to your patient? (social, emotional, physical)
- How dose your social life changed after you started providing care to your patient?
- How does this experience impact your life?
- Tell me about caring for your family member and how you meet all your work and family responsibilities?
- Can you tell me how you cope with caring for your patients?
- What is the most rewarding aspect of being a caregiver? What is the most challenge and barrier that face you during providing care to your patient?
- Can you tell me about your needs?

Anything else you would like to add to the discussion which we have not covered
**Appendix 5: Chronic Kidney Disease Symptom Burden Index (CKD-SBI)**

**Supplementary Material 1: CKD-Symptom Burden Index**

**CKD Symptom Burden Index (CKD-SBI)**

**Instructions**
Below is a list of physical and emotional symptoms that people with chronic kidney disease may have. Read each one carefully. If you have had the symptom during the past four weeks, let us know how **OFTEN** you had it, how **SEVERE** it was usually and how much it **DISTRESSED** or **BOthered** you by circling the appropriate number.

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<th>If YES</th>
<th>If YES</th>
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<td>How severe was it usually on a scale of 0-10? 0 = none 10 = very severe</td>
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<td></td>
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<td>IF YES</td>
<td>IF YES</td>
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During the past 4 week:
Did you experience this symptom?  |  If YES  |  If YES  |  If YES
|  NO  | How much did it distress or bother you on a scale of 0-10? 0 = none 10 = very much | How severe was it usually on a scale of 0-10? 0 = none 10 = very severe | How often did you have it on a scale of 0-10? 0 = never 10 = constant

14. Dry mouth
- NO
- Yes

15. Bone or joint pain
- NO
- Yes

16. Chest pain
- NO
- Yes

17. Headache
- NO
- Yes

18. Muscle soreness
- NO
- Yes
During the past 4 weeks:

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19. Difficulty concentrating

20. Dry skin

21. Itching

22. Worrying

23. Feeling nervous

0 = none
10 = very much
0 = never
10 = constant
### During the past 4 weeks:

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<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td><strong>25. Trouble staying asleep</strong></td>
<td>NO</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td><strong>26. Feeling irritable</strong></td>
<td>NO</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
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<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td><strong>27. Feeling sad</strong></td>
<td>NO</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td><strong>28. Feeling anxious</strong></td>
<td>NO</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
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<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td>During the past 4 weeks:</td>
<td>If YES</td>
<td>If YES</td>
<td>If YES</td>
</tr>
<tr>
<td>-------------------------</td>
<td>--------</td>
<td>--------</td>
<td>--------</td>
</tr>
<tr>
<td>Did you experience this symptom?</td>
<td>NO</td>
<td>How much did it distress or bother you on a scale of 0-10? 0 = none 10 = very much</td>
<td>How severe was it usually on a scale of 0-10? 0 = none 10 = very severe</td>
</tr>
<tr>
<td>29. Depression</td>
<td>NO</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td>30. Decreased interest in sex</td>
<td>NO</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td>31. Difficulty becoming sexually aroused</td>
<td>NO</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td>32. Nocturia</td>
<td>NO</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
</tbody>
</table>
### Appendix 6: Arabic version of the Chronic Kidney Disease Symptom Burden Index (CKD-SBI)

**Additional file 1: Arabic version of CKD-SBI**

<table>
<thead>
<tr>
<th>النظريات</th>
<th>إذا تعتبر</th>
<th>التي أي إبراز أو تشخيص أو ملاحظة أي من هذه الأعراض:</th>
<th>حالة الأعراض الأربعة المتضمنة:</th>
</tr>
</thead>
<tbody>
<tr>
<td>إذا كنتا في الحادثة، في المقياس،</td>
<td>21</td>
<td>لا يوجد</td>
<td>لا</td>
</tr>
<tr>
<td>أو مرتين بشكل مستمر</td>
<td>20</td>
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<td>لا</td>
</tr>
<tr>
<td>أو مرتين بشكل مختلف</td>
<td>19</td>
<td>لا يوجد</td>
<td>لا</td>
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<tr>
<td>أو مرتين بشكل مختلف</td>
<td>18</td>
<td>لا يوجد</td>
<td>لا</td>
</tr>
<tr>
<td>أو مرتين بشكل مختلف</td>
<td>17</td>
<td>لا يوجد</td>
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</tr>
<tr>
<td>أو مرتين بشكل مختلف</td>
<td>16</td>
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<td>لا</td>
</tr>
<tr>
<td>أو مرتين بشكل مختلف</td>
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<tr>
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<tr>
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<tr>
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<td>0</td>
<td>لا يوجد</td>
<td>لا</td>
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</table>

<table>
<thead>
<tr>
<th>النظريات</th>
<th>إذا تعتبر</th>
<th>التي أي إبراز أو تشخيص أو ملاحظة أي من هذه الأعراض:</th>
<th>حالة الأعراض الأربعة المتضمنة:</th>
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<tbody>
<tr>
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<td>لا يوجد</td>
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<tr>
<td>أو مرتين بشكل مستمر</td>
<td>20</td>
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<td>لا</td>
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<tr>
<td>أو مرتين بشكل مختلف</td>
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<td>لا</td>
</tr>
<tr>
<td>أو مرتين بشكل مختلف</td>
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<tr>
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</tr>
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<tr>
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<td>لا</td>
</tr>
<tr>
<td>إذا تعلم:</td>
<td>خلال الأسباب الأربعة المعادية:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>---------------------------------</td>
<td>---------------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>كم مرة تكررت تلك على المقياس صفر؟ 0 = أبداً 10 = تقريباً بشكل مستمر</td>
<td>هل عانيت من هذا العرض؟</td>
<td></td>
<td></td>
</tr>
<tr>
<td>كم مرة كانت شدتها في الغالب على المقياس صفر؟ 10 = لا يوجد 0 = تدريجياً 1 = كثيراً</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>إلى أي درجة أعركت أو ضاقت على المقياس صفر؟</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>10 = كثيراً</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<p>| 14 - جفاف اللام | لا |
| 15 - كم العظام أو المفاصل | لا |
| 16 - أم في السدير | لا |
| 17 - السدا | لا |
| 18 - رجع المصدات | لا |
| 19 - الصعدة في التكرير | لا |
| 20 - جفاف الجلد | لا |
| 21 - الحكة | لا |</p>
<table>
<thead>
<tr>
<th>إذا تقم:</th>
<th>خلال الأسابيع الأربعة الماضية هل عانت من هذا العرض؟</th>
</tr>
</thead>
<tbody>
<tr>
<td>كم مرة ينقر ذلك على المقياس صفر-٠؟ ١٠ = لا يوجد ≤ ٥ صفر-٠ = لا يوجد ٥ ≤ صفر = لا يوجد ١٠ = تقرير بشكل مستمر</td>
<td>لا</td>
</tr>
</tbody>
</table>

| 33- التشمر بالترتر | ١ |
| ١٣- صموبة في اللومة | ١ |
| ١٣- صموبة في البقاء دائماً | ١ |
| ١٦- التسمير بسرعة الانفعال و العصب | ١ |
| ١١- التشمر بالحزن | ١ |
| ١٨- الأزماس عند الالتباس | ١ |
| ٢١- الاكتئاب | ١ |
إذا نعم:

<table>
<thead>
<tr>
<th>كيف كانت تくなりました في الغلابة على المقياس صفر - 10</th>
<th>إذا كنت تشعر في الغلابة على المقياس صفر - 10</th>
</tr>
</thead>
<tbody>
<tr>
<td>صفر = لا يوجد</td>
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</tr>
<tr>
<td>1 = شديدة جداً</td>
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</tr>
<tr>
<td>2 = كثيراً جداً</td>
<td></td>
</tr>
<tr>
<td>3 = بعض الشيء</td>
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</tr>
<tr>
<td>4 = لا يوجد</td>
<td></td>
</tr>
<tr>
<td>5 = تقريباً بشكل مستمر</td>
<td></td>
</tr>
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<td>6 = تقريباً</td>
<td></td>
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<td>7 = قليلاً</td>
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</tr>
<tr>
<td>8 = قليلاً</td>
<td></td>
</tr>
<tr>
<td>9 = مثالي</td>
<td></td>
</tr>
<tr>
<td>10 = تقريباً</td>
<td></td>
</tr>
</tbody>
</table>

خلال الأسابيع الأربعة الماضية:
هل عانيت من هذا العرض؟

- نقص الرغبة الجنسية
- صعوبة في الإثارة الجنسية
- كل شيء تكرار الذل في الليل (انتهاء النوم)

إذا كان لديك أي أعراض أخرى خلال الأسابيع الأربعة الماضية، من فضلك اذكرها أدناه:

| أخرى:
<table>
<thead>
<tr>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>------------------------------------------------</td>
</tr>
<tr>
<td>------------------------------------------------</td>
</tr>
<tr>
<td>------------------------------------------------</td>
</tr>
</tbody>
</table>

شكرًا لمشاركتك في إكمال هذا الاستبيان.
The Zarit Burden Interview

Please circle the response the best describes how you feel.

<table>
<thead>
<tr>
<th>Question</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1  Do you feel that your relative asks for more help than he/she needs?</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>2  Do you feel that because of the time you spend with your relative that you don't have enough time for yourself?</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>3  Do you feel stressed between caring for your relative and trying to meet other responsibilities for your family or work?</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>4  Do you feel embarrassed over your relative's behaviour?</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>5  Do you feel angry when you are around your relative?</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>6  Do you feel that your relative currently affects our relationships with other family members or friends in a negative way?</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>7  Are you afraid what the future holds for your relative?</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>8  Do you feel your relative is dependent on you?</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>9  Do you feel strained when you are around your relative?</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>10 Do you feel your health has suffered because of your involvement with your relative?</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>11 Do you feel that you don't have as much privacy as you would like because of your relative?</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>12 Do you feel that your social life has suffered because you are caring for your relative?</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Question</td>
<td>Score</td>
</tr>
<tr>
<td>-------------------------------------------------------------------------</td>
<td>-------</td>
</tr>
<tr>
<td>13 Do you feel uncomfortable about having friends over because of your relative?</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>14 Do you feel that your relative seems to expect you to take care of him/her as if you were the only one he/she could depend on?</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>15 Do you feel that you don’t have enough money to take care of your relative in addition to the rest of your expenses?</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>16 Do you feel that you will be unable to take care of your relative much longer?</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>17 Do you feel you have lost control of your life since your relative’s illness?</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>18 Do you wish you could leave the care of your relative to someone else?</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>19 Do you feel uncertain about what to do about your relative?</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>20 Do you feel you should be doing more for your relative?</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>21 Do you feel you could do a better job in caring for your relative?</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>22 Overall, how burdened do you feel in caring for your relative?</td>
<td>0 1 2 3 4</td>
</tr>
</tbody>
</table>

Interpretation of Score:
- 0 - 21 little or no burden
- 21 - 40 mild to moderate burden
- 41 - 60 moderate to severe burden
- 61 - 88 severe burden
مقابلة حول العباء الذي تشعر به

لم تشعر بأن قريبك يطلب مساعدة أكثر مما يحتاج؟
أحيانا كثيرة 4 تقربيا دائما 3 أحيانا 2 نادرا 1 لا أبدا 0

هل تشعر أنه بسبب الوقت الذي تقضيه مع قريبك لم يعد لديك وقت كاف لنفسك؟
أحيانا كثيرة 4 تقربيا دائما 3 أحيانا 2 نادرا 1 لا أبدا 0

هل تشعر بضغوط بسبب محاولتك الإعناء ب قريبك وقيام بمسؤوليات أخرى تتعلق بعائلتك أو عملك؟
أحيانا كثيرة 4 تقربيا دائما 3 أحيانا 2 نادرا 1 لا أبدا 0

هل تشعر بالإرهاق بسبب تصرف قريبك؟
أحيانا كثيرة 4 تقربيا دائما 3 أحيانا 2 نادرا 1 لا أبدا 0

هل تشعر بغضب حين تكون قريب من قريبك؟
أحيانا كثيرة 4 تقربيا دائما 3 أحيانا 2 نادرا 1 لا أبدا 0

هل تشعر بأن حالة قريبك تؤثر سلبا على علاقاتك مع أفراد العائلة الآخرين أو الأصدقاء في الوقت الحالي؟
أحيانا كثيرة 4 تقربيا دائما 3 أحيانا 2 نادرا 1 لا أبدا 0

هل تشعر بالخوف مما يخبئه المستقبل لل قريبك؟
أحيانا كثيرة 4 تقربيا دائما 3 أحيانا 2 نادرا 1 لا أبدا 0

هل تشعر بأن قريبك عالة عليك؟
أحيانا كثيرة 4 تقربيا دائما 3 أحيانا 2 نادرا 1 لا أبدا 0

هل تشعر بالضيق عندما تكون ملفوفة قريبك؟
أحيانا كثيرة 4 تقربيا دائما 3 أحيانا 2 نادرا 1 لا أبدا 0

Appendix 8: Arabic version of Zarit Burden Interview
<table>
<thead>
<tr>
<th>السؤال</th>
<th>الافتراض</th>
</tr>
</thead>
<tbody>
<tr>
<td>هل تشعر أن إعتناقت ب قريبك أمر سلبا على صحتك؟</td>
<td>لا أبدا</td>
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<td>4. تقريبا دائما</td>
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<td>هل تشعر أنك لا تملك مصداقية كافية كما كنت ترغب ب قريبك؟؟</td>
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<tr>
<td>هل تشعر أن إعتناقت ب قريبك أمر سلبا على حياتك الاجتماعية؟؟</td>
<td>لا أبدا</td>
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<tr>
<td>1. نادرا</td>
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<td>4. تقريبا دائما</td>
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<tr>
<td>هل تشعر بعدم الارتاح في حال دعوة أصدقاء لقضاء الوقت عندك ب قريبك؟</td>
<td>لا أبدا</td>
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<tr>
<td>1. نادرا</td>
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<td>4. تقريبا دائما</td>
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<td>هل تشعر بأن قريبك يبدو وكأنه يتوقع منك أن تعتني به كما لو أنك الشخص الوحيد الذي يمكنه الاعتماد عليه؟</td>
<td>لا أبدا</td>
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<td>1. نادرا</td>
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<td>4. تقريبا دائما</td>
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<td>هل تشعر بأنك لا تملك ما يكفي من المال للعناية ب قريبك، إضافة إلى بقية مصاريف؟</td>
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<td>4. تقريبا دائما</td>
<td>تقريبا دائما</td>
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<tr>
<td>هل تستطيع أن تعلم أنك بإمكانك ترك العناية ب قريبك لشخص آخر؟؟</td>
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<tr>
<td>هل تشعر أنك غير متأكد بالنسبة لما يمكن فعله بخصوص قريبك؟؟</td>
<td>لا أبدا</td>
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<td>1. نادرا</td>
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<td>2. أحيانا</td>
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<td>4. تقريبا دائما</td>
<td>تقريبا دائما</td>
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<td>هل تشعر بأن علوبك القوي بالمزيد تجاه قريبك؟؟</td>
<td>لا أبدا</td>
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<td>2. أحيانا</td>
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</tr>
<tr>
<td>4. تقريبا دائما</td>
<td>تقريبا دائما</td>
</tr>
</tbody>
</table>
### Davies Comorbidity Index

#### Davies comorbidity index

<table>
<thead>
<tr>
<th>Co-morbid Conditions</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Malignancy (active, non-cutaneous);</td>
<td></td>
</tr>
<tr>
<td>2. Ischaemic heart disease (as evidenced by myocardial infarction, angina pectoris,</td>
<td></td>
</tr>
<tr>
<td>positive coronary angiography, or other diagnostic procedures);</td>
<td></td>
</tr>
<tr>
<td>3. Peripheral vascular disease (distal aortic, renovascular, lower limb, and cerebro</td>
<td></td>
</tr>
<tr>
<td>vascular disease, either symptomatic or significant stenosis on imaging);</td>
<td></td>
</tr>
<tr>
<td>4. Left ventricular dysfunction (clinical evidence of pulmonary oedema not attributable to errors in fluid balance and/or moderate to severe left ventricular dysfunction on echocardiogram);</td>
<td></td>
</tr>
<tr>
<td>5. Diabetes mellitus (type 1 or 2);</td>
<td></td>
</tr>
<tr>
<td>6. Systemic collagen vascular disease; or</td>
<td></td>
</tr>
<tr>
<td>7. Other significant pathology (which must be severe enough to impact on survival</td>
<td></td>
</tr>
<tr>
<td>in the general population</td>
<td></td>
</tr>
</tbody>
</table>

**Total score**
Appendix 10: Patient Demographic characteristics

1. Age
   
2. Ethnicity/ Nationality
   
3. Gender
   - Male
   - Female

4. Distance from hospital
   (Time in minutes)

5. Marital Status
   - Married
   - Single
   - Divorced
   - Widowed
   - Other

6. Education level
   - Illiterate
   - Primary studies
   - Secondary
   - Higher education
   - Other

7. Household monthly income/ Saudi Riyal
   - 0-5000
   - 5000-10000
   - 10000-15000
   - 15000-20000
   - 20000-25000
   - 25000-30000
   - >30000

8. Employment level
   - Full-time
   - Part-time
   - Retired
   - Full-time student
   - Part-time student
   - Unemployed
   - Housewife
   - Self-employed
   - Other

Thanks for completing this form
Appendix 11: Caregiver Demographic characteristics

9. Age

10. Ethnicity/ Nationality

11. Gender
   - Male
   - Female

12. Do you live with your patient?
   - Yes
   - No

13. Marital Status
   - Married
   - Single
   - Divorced
   - Widowed
   - Other

14. Education level
   - Illiterate
   - Primary studies
   - Secondary
   - Higher education
   - Other

15. Household monthly income/ Saudi Riyal
   - 0-5000
   - 5000-10000
   - 10000-15000
   - 15000-20000
   - 20000-25000
   - 25000-30000
   - >30000

16. Employment level
   - Full-time
   - Part time
   - Retired
   - student
   - Unemployed
   - Housewife
   - Self-employed
   - Other

17. Relation to the patient
   - Spouse
   - sibling
   - Parent
   - Son/daughter
   - Grandson/grand daughter
   - Other specify

18. State any comorbid condition you have

Thanks for completing this form.
## Appendix 12: Non-probability Sampling Schemes in Mixed Methods Research

<table>
<thead>
<tr>
<th>Sampling Scheme</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum Variation</td>
<td>Choosing settings, groups, and/or individuals to maximize the range of perspectives investigated in the study.</td>
</tr>
<tr>
<td>Homogeneous</td>
<td>Choosing settings, groups, and/or individuals based on similar or specific characteristics.</td>
</tr>
<tr>
<td>Critical Case</td>
<td>Choosing settings, groups, and/or individuals based on specific characteristic(s) because their inclusion provides the researcher with compelling insight about a phenomenon of interest.</td>
</tr>
<tr>
<td>Theory-Based</td>
<td>Choosing settings, groups, and/or individuals because their inclusion helps the researcher to develop a theory.</td>
</tr>
<tr>
<td>Confirming Disconfirming</td>
<td>After beginning data collection, the researcher conducts subsequent analyses to verify or contradict initial results.</td>
</tr>
<tr>
<td>Snowball/Chain</td>
<td>Participants are asked to recruit individuals to join the study.</td>
</tr>
<tr>
<td>Extreme Case</td>
<td>Selecting outlying cases and conducting comparative analyses.</td>
</tr>
<tr>
<td>Typical Case</td>
<td>Selecting and analyzing average or normal cases.</td>
</tr>
<tr>
<td>Intensity</td>
<td>Choosing settings, groups, and/or individuals because their experiences relative to the phenomena of interest are viewed as intense but not extreme.</td>
</tr>
<tr>
<td>Politically Important Case</td>
<td>Choosing settings, groups, and/or individuals to be included or excluded based on their political connections to the phenomena of interest.</td>
</tr>
<tr>
<td>Random Purposeful</td>
<td>Selecting random cases from the sampling frame and randomly choosing a desired number of individuals to participate in the study.</td>
</tr>
<tr>
<td>Stratified Purposeful</td>
<td>Sampling frame is divided into strata to obtain relatively homogeneous sub-groups and a purposeful sample is selected from each stratum.</td>
</tr>
<tr>
<td>Criterion</td>
<td>Choosing settings, groups, and/or individuals because they represent one or more criteria.</td>
</tr>
<tr>
<td>Opportunistic</td>
<td>Researcher selects a case based on specific characteristics (i.e., typical, negative, or extreme) to capitalize on developing events occurring during data collection.</td>
</tr>
<tr>
<td>Mixed Purposeful</td>
<td>Choosing more than one sampling strategy and comparing the results emerging from both samples.</td>
</tr>
<tr>
<td>Convenience</td>
<td>Choosing settings, groups, and/or individuals that are conveniently available and willing to participate in the study.</td>
</tr>
<tr>
<td>Quota</td>
<td>Researcher identifies desired characteristics and quotas of sample members to be included in the study.</td>
</tr>
<tr>
<td>Multi-Stage Purposeful Random</td>
<td>Choosing settings, groups, and/or individuals representing a sample in two or more stages. The first stage is random selection and the following stages are purposive selection of participants.</td>
</tr>
<tr>
<td>Multi-Stage Purposeful</td>
<td>Choosing settings, groups, and/or individuals representing a sample in two or more stages in which all stages reflect purposive sampling of participants.</td>
</tr>
</tbody>
</table>
Appendix 13: Letter of Invitation (for patients)

Dear Sir/Madam,

I am a PhD student in the Nursing and Midwifery School at Queens University Belfast, UK, currently working on my PhD project. It is with great pleasure that I am inviting you to participate in my research.

The aim of my research is to explore the symptom burden amongst patients receiving haemodialysis and their caregivers. The purpose of this letter is to ask you to participate in completing a self-reported questionnaire. In order to increase our understanding of symptom burden experience, you may be invited to participate in a face to face interview with the researcher in a later stage. The interview takes around 30 minutes and it is very informal. Your responses to the questions will be kept confidential.

There is no compensation for participating in this study. However, your participation will be a valuable addition to our research and findings could lead to greater public understanding of symptom burden. Please read the enclosed information sheets which provide more details on the study and may help you decide if you would like to take part. If you are willing to participate please suggest a day and time that suits you. If you decide that you do not want to participate in the study you can withdraw at any time. If you have any questions, please do not hesitate to ask.
Best Regards,

Bushra Alshammari
Appendix 14: Participant Information Sheet (for patient- questionnaire)

Study title.
Symptom burden and its management in Saudi Arabian patients receiving haemodialysis, and their carers.

Invitation paragraph.
You are being invited to take part in a research study. Please take time to read the following information carefully and discuss it with others if you wish. Please ask if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Purpose of This Study.

- To explore the symptom burden and experience of health service provision amongst patients receiving haemodialysis and their carers.
- To explore the impact of living with the symptom burden with patients and their family caregivers.

Why have I been chosen?
You have been selected to take part in this study because you have renal failure treated by haemodialysis which is suitable for the inclusion criteria we are looking for. The information you provide will help to improve the future care provision among chronic kidney diseases patients under haemodialysis and enable the development of understanding symptom burden.

Do I have to take part?
No, you don’t have to take part. Also if you decide to take part you are still free to withdraw at any time and without giving a reason and all the information and data collected from you, will be destroyed and your name will be removed from all the study files. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

What will happen to me if I take part?

If you decide to take part you will be asked to sign a consent form. Then you will be asked to answer a questionnaire about the presence, distress, severity and frequency of physical and emotional symptoms caused by hemodialysis. Completing the questionnaire will not take more than fifteen minutes. We will also ask you to allow us to look at your medical records so that we can collect information on your medical condition.

What are the possible disadvantages of taking part?

There are no anticipated risks or discomfort to you from being in this study. You will be required to give up approximately 15-30 minutes to complete the questionnaire. The topic being discussed in the questionnaire (symptom burden) is unlikely to cause distress. However, if any participant becomes distressed while answering the questionnaire, the process will be put on hold until the participant gives verbal consent for it to continue or withdraw. Alternatively, if the researcher feels it would be distressing for the participant to complete, the process will be terminated at this time, and the researcher will encourage the participant to contact their psychiatric liaison team to provide psychiatric assessment and any additional support required to reduce stress.

What are the possible advantages of taking part?

It is necessary that understanding of symptom burden be increased in order to provide timely and appropriate multidisciplinary renal health care. The main priority for healthcare providers should be symptom burden and how it affects the quality of life of people receiving haemodialysis. Treatment priorities and choices can be based on an enhanced understanding of symptom burden in the future.
Will my taking part in this study be kept confidential?

All information that you give will be anonymized. This means that your name will not be used in any report or publication. The electronic data will be stored securely on a password protected computer known only by researcher. After the questionnaire have been used in this study, the hard copies will be destroyed. You will not be identified in any report or publication from this study. In the unlikely event of disclosure of practice which does not meet the standards expected by patients, it is the professional responsibility of the researcher to refer this on appropriately. Therefore, you are encouraged to be as honest and open as you can. Therefore, you are encouraged to be as honest and open as you can.

What will happen to the results of this study?

The results of this study will be published after the completion of the research. The results may appear in journals or be presented at conferences. A copy of the published results will be available in the library at the Queen’s University Belfast. You will not be identified in any report or publication from this study.

Who is organising and funding this research?

Funding has been provided by the ministry of higher education, University of Hail, Saudi Arabia

Who has reviewed this study?

Ethical approval for the study has been obtained from the education centre at King Khaled Hospital in Hail City Kingdom of Saudi Arabia. Also, The Research Ethical Committee of the Queen’s University Belfast has reviewed all aspects of this study and given approval for it to proceed.

What do I do if I want to take part?

Sign the ‘consent form’ and ‘The consent to be contacted form’ and return the envelope to the researcher or the gatekeeper on the dialysis center, you will be contacted by the researcher in the way you prefer such as phone, email, face to face..etc.
Contacts for Further Information.

If you have any further questions about this study the person to contact for further information:
The main researcher: Bushra Alshammari
Telephone number: 00966559715427
Email: blshammari01@qub.ac.uk

What will happen with my data if I choose to withdraw from the study?

If a participant chooses to withdraw from this study, we will ask their permission to use the data up until that point. If they do not give permission, their data will be removed and discarded.

Who do I contact if I have a complaint about the study?

If you have a complaint about any part of this study, you should contact the manager of the Dialysis center or the manager of King Khaled Hospital who will deal with your complaint.

Manager of Dialysis center Name: Fahad Alaslmi
Phone number +966 16 532 8888.

THANK YOU FOR TAKING TIME TO READ THIS INFORMATION SHEET
YOUR PARTICIPATION IN THIS STUDY IS GREATLY APPRECIATED
Appendix 15: consent from (for questionnaire-patient)

Title: Symptom burden and its management in Saudi Arabian patients receiving haemodialysis, and their carers: A mixed methods study

Name of PhD student: Bushra Alshammari

Name of supervisors:
Dr. Peter O’Halloran, Dr. Helen Noble, Dr. Helen McAneney

Please initial the boxes below:

1. I confirm that I have read the information sheet for the above study. I have had the opportunity to consider the information, ask questions and have had my questions fully answered.

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason.

3. I have been informed that the confidentiality of the information I provide will be safeguarded.

4. I understand that my medical records will contain details needed in this study. I give permission to access my records for this purpose.

5. I understand that the results of the research will be published but will not include information that might identify individuals taking part.

6. I agree to take part in the above study.

--------------------------------------------------------  -----------  ------------
Name of Participant                               Date           Signature

--------------------------------------------------------  -----------  ------------
Researcher                                      Date           Signature

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Appendix 16: Letter of Invitation (for caregivers)

Dear Sir/ Madam,

I am a PhD student in the Nursing and Midwifery School at Queens University Belfast, currently working on my PhD project. It is with great pleasure that I am inviting you to participate in my research.

One of the aims of my research is to explore caregiver burden in the informal caregivers providing care to patients receiving haemodialysis.

The purpose of this letter is to ask you to participate in completing a self-reported questionnaire. In order increase our understanding of the effect of caregiving, you may be invited to participate in a face to face interview with the researcher. The interview takes around 30 minutes and is very informal. Your responses to the questions will be kept confidential. Each interview will be assigned a number code to help ensure that personal identifiers are not revealed during the analysis and write up of findings. There is no compensation for participating in this study. However, your participation will be a valuable addition to our research and findings could lead to greater public understanding of caregiver burden.

Please read the enclosed information sheets which provide more details on the study and may help you decide if you would like to take part. If you are willing to participate please suggest a day and time that suits you. If you decide that you do not want to participate in the study, you can withdraw at any time.
Study Title.

Symptom burden and its management in Saudi Arabian patients receiving haemodialysis, and their carers

Invitation Paragraph.

You are being invited to take part in a research study. Please take time to read the following information carefully and discuss it with others if you wish. Please ask if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Purpose of this study.

- To explore the symptom burden and experience of health service provision amongst patients receiving haemodialysis and their carers.
- To explore the impact of symptom burden with patients and their family caregivers through qualitative interviews.

Why have I been chosen?

You have been selected to take part in this study because you are the primary caregiver for patient with chronic kidney disease. The information you provide will help inform future care provision for people with chronic kidney disease receiving haemodialysis and enable the development of understanding of carers burden in future.

Do I have to take part?
No, you don’t have to take part. If you decide to take part you will be asked to sign a consent form. Also if you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you relative is receiving.

**What will happen To me If I take part?**

If you agree to take part you will be asked to answer 12 questions about the burden you experience while taking care of your sick relative. Completing the questionnaire won’t take more than 10 minutes.

**What are the possible disadvantages of taking part?**

There are no anticipated risks or discomfort to you from being in this study. You will be required to give up approximately 10 minutes of your time to complete the questionnaire.

**What are the possible advantages of taking part?**

The information you provide is necessary to help inform future care provision for chronic kidney diseases under haemodialysis and enable the development of understanding caregiver burden in future. Treatment priorities and choices can be based on enhanced understanding of the symptom burden and carer burden as well.

**Will my taking part In this study be kept confidential?**

All information that you give will be anonymised this means that your name will not be used in any report or publication. After using the information in the questionnaires, the hardcopies of them will be destroyed. Therefore, you are encouraged to be as honest and open as you can. In the unlikely event of disclosure of practice which does not meet the standards expected by patients, it is the professional responsibility of the researcher to refer this on appropriately. Therefore, you are encouraged to be as honest and open as you can.

**What will happen to the results of this study?**
The results of this study will be published after the completion of the research. The results may appear in journals or be presented at conferences. A copy of the published results will be available in the library at the Queen’s University Belfast. You will not be identified in any report or publication from this study.

Who is organising and funding this research?

Funding has been provided by the ministry of higher education, University of Hail, Saudi Arabia.

Who has reviewed this study?

Ethical approval for the study has been obtained from the education centre at King Khaled Hospital in Hail City Kingdom of Saudi Arabia. Also The Research Ethical Committee of the Queen’s University Belfast have reviewed all aspects of this study and given approval for it to proceed.

What do I do if I want to take part?

Sign the ‘consent form’ and ‘The consent to be contacted form’ and leave them in the front desk in the dialysis center, you will be contacted by the researcher in the way you prefer ex, phone, email, face to face ... etc.

Contacts for further information.

If you have any further questions about this study please contact:

PhD student: Bushra Alshammari
Telephone number: 00966559715427
Email: blshammari01@qub.ac.uk

What will happen with my data if I choose to withdraw from the study?

If participant chooses to withdraw from this study, we will ask their permission to use the data up until that point. If they do not give us permission, their data will be removed and discarded.

Who do I contact if I have a complaint about the study?
If you have a complaint about any part of this study, you should contact the manager of the Dialysis center or the manager of the hospital who will deal with your complaint,

Manager of Dialysis center Name: Fahad AlasImi

Phone number +966 16 532 8888.

THANK YOU FOR TAKING TIME TO READ THIS INFORMATION SHEET YOUR PARTICIPATION IN THIS STUDY IS GREATLY APPRECIATED
Appendix 18: Consent to be contacted form

Please return this form to the front desk in the dialysis centre in the envelope provided.

Note: this is not consent to take part in the research. It is asking you to indicate your willingness to be contacted to discuss participation.

I am willing / not willing (delete as appropriate) to be contacted by Bushra Alshammari to discuss my participation in a research study: Symptom burden and its management in Saudi Arabian patients receiving haemodialysis, and their caregivers

Name: __________________________________________

Preference way to be contacted i.e. phone. Email

_____________________________________

Provide contact details ___________________________________________
Appendix 19: Participant Information Sheet (for patient interview)

Study Title.


Invitation Paragraph.

You are being invited to take part in a research study. Please take time to read the following information carefully and discuss it with others if you wish. Please ask if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Purpose of This Study.

- To explore the symptom burden and experience of health service provision amongst patients receiving haemodialysis and their carers.
- To explore the impact of symptom burden with patients and their family caregivers through qualitative interviews.

Why Have I Been Chosen?

You have been selected to take part in this study because you have renal failure treated by haemodialysis which is suitable for the inclusion criteria we are looking for. The information you provide will help to improve the future care provision among chronic kidney diseases patients under haemodialysis and enable the development of understanding symptom burden.

Do I Have To Take Part?

No, you don’t have to take part. Also if you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

What Will Happen To Me If I Take Part?
If you decide to take part you will be asked to sign a consent form. You will be asked to attend face to face interview along with the researcher. During the interview the researcher will be present only to ask questions and observe and take notes. This individual interview will last for approximately 30 minutes and it will take place in a suitable and private place agreed with the interviewer. The interview will be digitally recorded and there is a possibility of anonymous direct quotation being used in publication from this research.

**What Are The Possible Disadvantages Of Taking Part?**

There are no anticipated risks or discomfort to you from being in this study. You will be required to give up approximately 30 minutes of your time to allow the individual interview take place. The topic being discussed in the interviews (symptom burden) is unlikely to cause distress. However, if any participant becomes distressed during the interview, the interview will be put on hold until the participant gives verbal consent for it to continue. Alternatively, if the researcher feels it would be distressing for the participant to re-engage with the interview, the interview will be terminated at this time, and the researcher will encourage the participant to contact their GP for additional support, as required.

**What Are The Possible Advantages Of Taking Part?**

It is necessary that understanding of symptom burden be increased in order to provide timely and appropriate multidisciplinary renal health care. A main priority for healthcare providers should be symptom burden and how it affects the quality of life of people with CKD. Treatment priorities and choices can be based on enhanced understanding of symptom burden in future.

**Will My Taking Part In This Study Be Kept Confidential?**

All information that you give will be anonymized. This means that your name will not be used in any report or publication. The electronic data will be stored securely on a password protected computer known only by researcher. After the interviews have been transcribed, the tape will be destroyed. You will not be identified in any report or publication from this study. In the unlikely event of disclosure of practice which does not meet the standards expected by patients, it is the professional responsibility of the researcher to refer this on appropriately. Therefore, you are encouraged to be as honest and open as you can. Therefore, you are encouraged to be as honest and open as you can.

**What Will Happen To The Results Of This Study?**

The results of this study will be published after the completion of the research. The results may appear in journals or be presented at conferences. A copy of the published
results will be available in the library at the Queen’s University Belfast. You will not be identified in any report or publication from this study.

**Who Is Organising and Funding This Research?**

Funding has been provided by the ministry of higher education, University of Hail, Saudi Arabia.

**Who Has Reviewed This Study?**

Ethical approval for the study has been obtained from the education centre at King Khaled Hospital in Hail City Kingdom of Saudi Arabia. Also, The Research Ethical Committee of the Queen’s University Belfast have reviewed all aspects of this study and given approval for it to proceed.

**What do I do if I want to take part?**

Sign the ‘consent form’ and ‘The consent to be contacted form’ and return the envelop to the researcher or the gatekeeper on the dialysis center, you will be contacted by the researcher in the way you prefer such as phone, email, face to face.

**Contacts for Further Information.**

If you have any further questions about this study please contact:

PhD student: Bushra Alshammari

Telephone number: 00966559715427

Email: blshammari01@qub.ac.uk

**What will happen with my data if I choose to withdraw from the study?**

If participant choose to withdraw from this study, we will ask their permission to use the data up until that point. If they do not give us permission, their data will be removed and discarded.

**Who do I contact if I have a complaint about the study?**

If you have a complaint about any part of this study, you should contact the manager of Dialysis center or the manager of the hospital who will deal with your complaint,

Manager of Dialysis center Name: Fahad Alaslmi
Phone number +966 16 532 8888.

THANK YOU FOR TAKING TIME TO READ THIS INFORMATION SHEET

YOUR PARTICIPATION IN THIS STUDY IS GREATLY APPRECIATED
Appendix 20: Participant Information Sheet (for caregiver-interview)

**Study Title.**


**Invitation Paragraph.**

You are being invited to take part in a research study. Please take time to read the following information carefully and discuss it with others if you wish. Please ask if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

**Purpose of This Study.**

- To explore the symptom burden and experience of health service provision amongst patients receiving haemodialysis and their caregivers.
- To explore the impact of symptom burden with patients and their family caregivers.
- To identify the managements strategies patients used to relieve their symptoms.

**Why Have I Been Chosen?**

You have been selected to take part in this study because you are the primary caregiver for patient with chronic kidney disease. The information you provide will help inform future care provision for people with chronic kidney disease receiving haemodialysis and enable the development of understanding of carers burden in future.

**Do I Have To Take Part?**

No, you don’t have to take part. If you decide to take part, you will be asked to sign a consent form. Also if you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you relative is receiving.
What Will Happen to Me If I Take Part?

If you decide to take part you will be asked to sign a consent form. Then you will be asked to attend a face-to-face interview along with the researcher. During the interview the researcher will be present only to ask questions and observe and take notes. This individual interview will last for approximately 30 minutes and it will take place in a suitable and private place (any place suits you). The interview will be digitally recorded and there is a possibility of anonymous direct quotation being used in publication from this research.

What Are The Possible Disadvantages Of Taking Part?

There are no anticipated risks or discomfort to you from being in this study. You will be required to give up approximately 30 minutes of your time to allow the individual interview to take place. The topic being discussed in the interviews (symptom burden) is unlikely to cause distress. However, if any participant becomes distressed during the interview, the interview will be put on hold until the participant gives verbal consent for it to continue. Alternatively, if the researcher feels it would be distressing for the participant to re-engage with the interview, the interview will be terminated at this time, and the researcher will encourage the participant to contact their GP for additional support, as required.

What Are The Possible Advantages Of Taking Part?

It is necessary that understanding of symptom burden be increased in order to provide timely and appropriate multidisciplinary renal health care. A main priority for healthcare providers should be symptom burden and how it affects the quality of life of people with CKD. Treatment priorities and choices can be based on enhanced understanding of symptom burden and caregivers burden in future.

Will My Taking Part in This Study Be Kept Confidential?

All information that you give will be anonymized. This means that your name will not be used in any report or publication. The electronic data will be stored securely on a password-protected computer known only by the researcher. After the interviews have been transcribed, the tape will be destroyed. You will not be identified in any report or publication from this study. In the unlikely event of disclosure of practice which does not meet the standards expected by patients, it is the professional responsibility of the researcher to refer this on appropriately. Therefore, you are encouraged to be as honest and open as you can. You will not be identified in any report or publication from this study.

Who Is Organising and Funding This Research?
Funding has been provided by the ministry of higher education, University of Hail, Saudi Arabia.

**Who Has Reviewed This Study?**

Ethical approval for the study has been obtained from the education centre at King Khaled Hospital in Hail City Kingdom of Saudi Arabia. Also, the Research Ethical Committee of the Queen’s University Belfast have reviewed all aspects of this study and given approval for it to proceed.

**What do I do if I want to take part?**

Sign the ‘consent form’ and ‘The consent to be contacted form’ and return the envelop to the researcher or the gatekeeper on the dialysis centre, or by mail to the dialysis centre address. You will be then contacted by the researcher in the way you prefer such as phone, email, face to face. etc.

**Contacts for Further Information.**

If you have any further questions about this study, the person to contact for further information is:

Main researcher: Bushra Alshammari  
Telephone number: 00966559715427  
Email: blshammari01@qub.ac.uk

**What will happen with my data if I choose to withdraw from the study?**

If participant choose to withdraw from this study, we will ask their permission to use the data up until that point. If they do not give us permission, their data will be removed and discarded.

**Who do I contact if I have a complaint about the study?**

If you have a complaint about any part of this study, you should contact the manager of Dialysis center or the manager of the hospital who will deal with your complaint,

Manager of Dialysis centre Name: Fahad Alaslmi  
Phone number +966 16 532 8888.

THANKYOU FOR TAKING TIME TO READ THIS INFORMATION SHEET  
YOUR PARTICIPATION IN THIS STUDY IS GREATLY APPRECIATED
Appendix 21: Consent form (for interview-patient)

Project Title.
Symptom burden and its management in Saudi Arabian patients receiving haemodialysis, and their caregivers.

Researcher: Bushra Alshammari

Please initial the boxes below

1. I confirm that I have read the Participant Information Sheet which is attached to this form. I understand what my role will be in this research and have had the opportunity to ask questions. ☐

2. I understand that my participation is voluntary and that I am free to withdraw from the research at any time, for any reason and without prejudice. ☐

3. I have been informed that the confidentiality of the information I provide will be safeguarded. ☐

4. I understand the interview will be tape-recorded and there is a possibility of anonymous direct quotations being used in publication from this research ☐

5. I agree to take part in this research.

Name of Participant Date Signature

Researcher Date Signature

425
Appendix 22: consent form (for interview-caregiver)

Project Title.

Symptom burden and its management in Saudi Arabian patients receiving haemodialysis, and their carers: A mixed methods study

Name of PhD student: Bushra Alshammari

Please tick the boxes below

1. I confirm that I have read the “participant information sheet” which is attached to this form. I understand what my role will be in this research and have had the opportunity to ask questions.

2. I understand that my participation is voluntary and that I am free to withdraw from the research at any time, for any reason and without prejudice.

3. I have been informed that the confidentiality of the information I provide will be safeguarded.

4. I agree to be audio recorded by the researcher and I understand the possibility of using anonymous direct quotations in publication from this research.

5. I agree to take part in this research.

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Name of Participant                               Date                 Signature

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Researcher                                             Date                Signature

---------------------------------------------------------------------
Appendix 23: Non-Disclosure form

Non-Disclosure form (for Translator)

Project Title:

Name of Researcher:
Bushra Alshammari

For the purpose of confidentiality of this research I agree to the following points:

- I agree to translate the researcher interviews by myself. [X]
- I will not discuss the interviews contents of the participant’s transcriptions with anyone. [X]
- I sign this non-disclosure form to ensure the confidentiality of the participant’s data. [X]

Signed on behalf of: Docsbase Translations Tel: +44 207 936 9896

Date 6 August 2018 Signature [Signature]

Appendix 24: School Research ethics committee QUB
28 February 2018

Ref: 10.BAlshammari05.17.M6V1

Bushra Alshammari
School of Nursing and Midwifery
Queen's University Belfast
Medical Biology Centre
97 Lisburn Road
Belfast
BT9 7BL

Dear Bushra,

SCHOOL RESEARCH ETHICS COMMITTEE

RE:

An exploration of symptom burden and its management in Saudi Arabian patients receiving haemodialysis, and their carers: A mixed methods study

Thank you for your recent submission to the School of Nursing and Midwifery Research Ethics Committee. I wish to advise you that your application has been approved and you can now commence with your study. This approval has been given by Chair’s Action as agreed at the last meeting.

To complete the Research Governance process, you should complete the Gov 3 form (request for sponsorship of a research project) and forward this along with your protocol to Ms Louise Dunlop at the Research Governance Policy Office. In addition, please ensure the project is recorded on the PURE system.

Yours sincerely

Dr Oliver Perre
Chair, School Research Ethics Committee
School of Nursing & Midwifery

cc File copy

Appendix 25: Ethics approval from the education center King Khaled hospital
Ethical Approval Letter

Dear Medical Manager,

Dear Manager of Dialysis Center,

Based on the letter, addressed to us from the University of Hall and the approval of the Assistant Director for Planning and Development and the guidance of the Manager of King Khaled Hospital regarding a study which will be conducted by the researcher from the Nursing and Midwifery Ms. Buthra Alshammari,

We pleased to inform you that the research project titled “study of symptom burden and its management in Saudi Arabian patients receiving haemodialysis and their carers” has been approved. This study will be conducted on the Dialysis center at King Khaled Hospital Saudi Arabia. This approval is given for three years starting from the date of issuing this letter (10 Jan 2017).

Please inform us when the project has been completed.

Yours sincerely,

Pr. Zamel A. Alshammari
The Manager of The Education Center
Appendix 26: Model demonstrating how codes were correlated to create subthemes and overarching themes.
Appendix 27: An example of one of the overarching themes with its associated subtheme’s quotations

<table>
<thead>
<tr>
<th>Participants number</th>
<th>Theme 1: Holistic impact of symptom burden in patients receiving HD</th>
<th>Physical impact</th>
<th>Psychological &amp; emotional impact</th>
<th>Social impact</th>
<th>Cognitive impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1</td>
<td>“I was able to take care of my sick mother, give her medicine and help her, but I recently stopped doing so because of the stress, tiredness and symptoms that are always present with me after dialysis sessions”</td>
<td>“I fear of attending parties and drinking a lot of drinks as this will increase symptoms before the next renal dialysis session.”</td>
<td>“My heart is severely broken. I feel that I lost the most valuable and beloved thing, which is health. People look at me with pity and this is what bothers and affects me most. They make me feel that I am imperfect .and internally fragile like glass”</td>
<td>Sometimes I even lack concentration while teaching my students; I sometimes feel dizzy because of anemia. It became easier for diseases to attack me because of the general weakness of my body and immune system. I got cautious and restricted in enjoying my normal life.</td>
<td>“I feel that I am like a broken hand that cannot do anything; I exist but cannot do anything for them nor for myself. I am unable to get completely treated nor be of help to them. I exist, but with no benefit. I am completely like a broken hand that cannot carry anything nor be of any help. One day such hand may get cut off or splinted”</td>
</tr>
<tr>
<td>P2</td>
<td>“I suffer from fatigue after renal dialysis and it exhausts me and makes me unable to do anything. My strength now is not like the last year, and that of the last year is not the same as before. My health is deteriorating and this makes me unable to find solutions for myself.”</td>
<td>“I stopped doing any housework, such as sweeping and doing the dishes, but I still cook”</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P3</td>
<td>“My mettle got weak. Before, I used to cook and prepare the meals, but now if only I go and bring “My disease is accompanied by permanent and annoying symptoms,”</td>
<td></td>
<td>“I became a non-social person; my daughters attend family events”</td>
<td>My concentration and vision got strongly affected. I</td>
<td></td>
</tr>
<tr>
<td>Page</td>
<td>Statement</td>
<td>Response</td>
<td>Implications</td>
<td></td>
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</tr>
<tr>
<td>P4</td>
<td>“I delay all matters of life. Everything in my life is postponed to an unknown date.” “I stopped doing housework, I used to install lights and repair things that are not working in the house. But now I am so tired that I can’t even comb my hair. My mom helps me do that.”</td>
<td>“I am stressed and irritable all the time. I always feel inactive, introvert and lazy.” “I am so frustrated. I wish my life would return like before. I hope I can take long trips with my family and feel happy as I used to.”</td>
<td>“I hope I can take long trips with my family and feel happy as I used to.” “I feel nervous and irritable, and all the time thinking of the pains I am suffering even when my family members speak to me they say I am not concentrating to what they are saying.”</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P5</td>
<td></td>
<td>I need the society not to look at us as only sick people. Such look of pity is annoying, and some words that show sympathy are hard to us even if showed unintentionally.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P6</td>
<td>“I became physically weak, my skin got affected, my weight decreased and I became very lean. My memory became very weak and I am no longer able to travel and drive like before. Though I go out more than before, I return on the same day to take my medicines. I became more nervous, and my vision became weak. therefore I retired from work.”</td>
<td>When my mood, psychological or emotional state is bad, I stop eating, drinking and taking care of myself in all aspects, and stay alone, which causes deterioration of my health condition. Psychological relief is half of the treatment.</td>
<td>“Though I go out more than before, I return on the same day to take my medicines. I became more nervous.” “My memory became very weak and I am no longer able to travel like before.”</td>
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<tr>
<td>P7</td>
<td>I suffered from a psychic shock at the beginning when I was informed that I have renal failure. I refused the renal dialysis until the last moments. The daily renal dialysis is hard for me and the symptoms associated with it are tough. My daughter helped me at the beginning. She insisted that I must go for sessions, but now, thank God, I am completely convinced and willing to do so. I do not know whether I have become accustomed or surrendered!!</td>
<td>“Even when I return from renal dialysis sessions I feel exhausted and cannot go out, until the next day, because all my energy has been drained.. Not only lack of energy but also lack time. Each renal dialysis session takes me four hours plus an hour before the start of the session, i.e. I waste five hours. In addition to that, doctors sometimes impose four sessions a week not three, and this takes me much time”</td>
<td>Even my memory was affected; yesterday my daughter took some money from me after I gave her permission, a little later I was asking myself where did the money go? I asked my children and my daughter answered “I took them for the purpose I informed you of. At that moment I remembered!!</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P8</td>
<td>“Previously, I relied on myself, I used to tide up my room, my clothes and stuff, but now I can’t do much work. My wife helps me get my things ready. “I was a civil servant. When I first retired and before I was diagnosed with renal failure and its complications, I decided to keep myself busy and buy a farm where I can practice my hobbies. I gathered various animals such as sheep, rabbits, chicken and pigeons. I also planted palm trees which I bought at SR 50 thousands and further planted beautiful trees. I worked in this farm for five years. I sold it after I had renal failure, I couldn’t take care of it and preferred to have rest.”</td>
<td>“I can’t travel because I have dialysis every other day. You can’t go camping and spend the night. My hobbies are hunting, camping and long safari trips. But this disease came over me and pinned us; like when a wrestler pin its opponent making them fall. Now we go out at dawn and come back before it is sunset, I got restricted.”</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P9</td>
<td>After I started dialysis I became unable to walk at all. I sometimes want to go to camps but that is difficult due to my use of a wheelchair.</td>
<td>I decided to move from my house to farm so that I may not feel bored due to staying at home. Although my children refused the idea at the beginning, after I moved, their visits became daily and sometimes they sleep here at the farm. It's something funny</td>
<td></td>
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<tr>
<td><strong>P10</strong></td>
<td>“Previously I worked on my dump truck, but now I quit because my body can't bear it. I feel tired quickly sometimes, the vehicle is high and I should climb and get down to put loads on it etc. I don't know whether exhaustion is because of the renal failure or because I am getting older.”</td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>P11</strong></td>
<td>Before I would participate in housework, such as repair and installation of broken lights, but now I do not do so anymore</td>
<td></td>
<td>Before renal failure I was free and able to go and come whenever I wanted; I enjoyed unrestricted freedom. Now I am restricted. In the past I used to go on vacations for a period ranging from one week to 10 days, but now it is difficult I have appointments on Saturday, Monday and Wednesday. Most people go out, especially on Saturday because it is the weekend, except us, renal failure patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>P12</strong></td>
<td>I postponed my studies until the time comes to resume them. Fatigue and tiredness I get make me unable to be productive as a student. Also stress and high blood pressure I suffer from are enough for me; I don't want to increase these by thinking about my studies. Even my relationship with my friends is now different. I tend to be alone more. I also feel annoyed that all my colleagues are ahead of me in school, which makes me think of never going back to school.</td>
<td>I tend to be alone more. I also feel annoyed that all my colleagues are ahead of me in school, which makes me think of never going back to school. In short I cannot live my life as before. I became trapped by the condition.</td>
<td>I suffer from fatigue and lethargy, I cannot walk or move, and do not eat or drink; even getting out is difficult. In short I cannot live my life as before. I became trapped by the condition.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>P13</strong></td>
<td></td>
<td></td>
<td>I postponed my studies until the time comes to resume them. Fatigue and tiredness I get make me unable to be productive as a student</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>