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Risk assessment of the continuity of essential medications for low socioeconomic patients in Syria: a case study of diabetes mellitus

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Abstract

Objectives During the past decade, the health system in Syria has been devastated due to the ongoing conflict which affected the production of pharmaceuticals as well. Patients of chronic diseases, such as diabetes mellitus, were significantly affected by the shortages of oral anti-diabetic medications, especially those of lower socioeconomic status. The objective of this paper is to study the causes and effects of the shortage of oral anti-diabetic agents in the Syrian market on patients with low socioeconomic status who find difficulties in accessing these medications.

Methods The methodology of the study includes determining the availability of nationally produced oral anti-diabetic agents in different local pharmacies. Then, it studied the effects of this availability on low socioeconomic status patients whose prescriptions were registered in a local NGO and analysed using Microsoft Excel (Microsoft, USA).

Key findings The study shows that many of the anti-diabetic medications included in the study have less than 50% availability in the pharmacies. Metformin, which is considered as a first-line treatment in diabetes has 40% availability. In addition, metformin was the most prescribed medication with about 57% frequency followed by gliclazide with 37% prescription frequency.

Conclusion This study raises concerns about the continuity of supply of some of the oral anti-diabetic agents in the Syrian market. This can impact patient commitment to treatment, where patients from low socioeconomic status can be most affected by medication unavailability in nearby pharmacies or increased pricing due to high demand with low supply.

Keywords: diabetes mellitus; low socioeconomic patients; Syria; medication supply

Graphical Abstract
Introduction

Before the beginning of the Syrian conflict, Syria was a middle-income country with a functioning and comprehensive economic, political, as well as health system. After the war had erupted in 2011, hundreds of medical personnel have been killed or fled out of the country, ambulances have come under fire, and pharmacies have been destroyed, creating a nationwide healthcare crisis. The quality of health care has further been affected by the deterioration in the functionality of medical equipment due to the lack of spare parts and maintenance, shortages of drugs and medical supplies were also present due to sanctions. As a result, many of those injured in Syria’s continued violence cannot be treated or have access to treatment. This becomes more and more challenging in cases of chronic illnesses where thousands of people have been left without access to doctors and essential medications. Living in war-torn Syria means not only coping with the deteriorating living conditions, but for Syrians living with chronic diseases such as asthma, cancer, diabetes, and kidney and heart diseases to be challenged every time they look for treatment.

Globally, chronic diseases are the leading causes of mortality. Approximately 70% of total deaths worldwide are attributed to non-communicable diseases (NCDs), mainly cardiovascular diseases (CVD), cancers, diabetes, and chronic respiratory diseases. Before the outbreak of the pandemic at the beginning of 2020, it was reported by World Health Organization (WHO) that in Syria, NCDs are estimated to account for 45% of premature death including diabetes. The mortality estimates in Syria have a high degree of uncertainty because they are not based on any national NCD mortality data. The data collected by the Institute for Health Metrics and Evaluation (IHME) in 2019 reveal that diabetes mellitus (DM) is one of the top-ranked NCDs in Syria which potentially can lead to death or disability. In Syria, before the conflict began in 2011, the prevalence of diabetes in the city of Aleppo was found to be 14.8% for individuals >25 years of age, and type 2 diabetes was only well controlled in 16.7% of individuals under treatment. In 2017, there were 705 700 reported adult cases of diabetes in Syria, with a prevalence of 12.6% among females and 11.2% among males. It is estimated that there are currently 400 000 Syrians whose survival depends on insulin. The silent progression of diabetes makes it difficult for untreated patients to foresee the side effects of the diseases at older age such as retinopathy.

Preceding the Syrian crisis, insulin was provided free of charge to all registered users with the National Diabetes Programme. With Syria’s only insulin producing facility was damaged stopped production. At present, shortages are common, especially after the pandemic where approximately 60% of insulin-dependent Syrians are at risk due to limited supplies. WHO is the main supplier of insulin in the country. Nevertheless, continuation of insulin supply becomes more difficult due to travel restrictions on people and products. This puts a huge pressure on insulin-dependent diabetes patients. In parallel type 2 patients, where treatment depends on lifestyle changes, blood sugar monitoring, and drugs to regulate glucose blood levels are also affected. Looking at the prescribed medications, shortage of medications is a huge risk of disease management failure and people with lower socioeconomic status are at even higher risk due to limited medications availability and silent nature of the disease.

This paper aims to study the risk of shortage in the supply chain of diabetes medications in the Syrian market.

Aims

The work examines the monthly prescription of patients from low socioeconomic status for prescribed drugs alongside looking into oral anti-diabetic agents in terms of availability in different locations in Damascus pharmacies to assess the risk of medication shortage. This paper highlights the huge risks of treatment failure for low socioeconomic diabetic patients and opens the doors for more studies on the crisis impact on other chronic diseases. The article helps national and international policymakers and stakeholders in understanding the impact of sanctions on the Syrian healthcare system.

Methods

Nationally produced oral anti-diabetic agents supply chain and availability in community pharmacies

During a 3-month period and using random spot checks performed at 2-week intervals, the presence or absence of oral anti-diabetic agents is assessed in 10 pharmacies in Damascus neighbourhood. The list of oral anti-diabetic agents and their doses with the producing company names are collected from the last version of the Syrian Drugs References (SOR) for the year 2018 and used for cross-checks. Data are collected between the years 2020 and 2021, following the pandemic and are limited to oral anti-diabetic agents. Finally, the percentages of availability of medications are calculated using average and standard deviation.

Impact of oral anti-diabetic agents’ availability on low socioeconomic status patient cohort

The list of monthly prescribed oral anti-diabetic agents is collected with the help of Al Tamayo non-governmental organisation (NGO) that provides help for a family with low income in their medication costs. Inclusion criteria are set to be the following: The cohort is patients with only type 2 diabetes mellitus (T2DM) without other medical conditions of ages above 30 years and of both sexes. Furthermore, all patients selected for this study are officially registered with Al Tamayo, as patients in need of financial support to cover medication costs. No indefinable information is given to the authors by Al Tamayo, only gender and age are provided to enable demographic data representation. The prescribed agents are then organised and ordered in terms of their frequency of prescription.

Statistical analysis

Data are organised upon collection using Microsoft Excel (Microsoft, USA) and are subjected to calculations of statistical mean and standard deviation. Percentages and frequencies are used to present the data in the article.

Results

Nationally produced oral anti-diabetic agents supply chain and availability in community pharmacies

Table 1 presents an availability assessment of nationally produced oral anti-diabetic agents from 10 community pharmacies. The frequencies are used to present the data in the article.
pharmacies over a 3-month period collected within a 2-week interval. Except for gliclazide (30–60 mg) and combination tablets containing either sitagliptin or pioglitazone with metformin, the majority of drugs were available in less than 50% of the investigated pharmacies. It is worth noting that sitagliptin/metformin combination is only produced by one pharmaceutical industry in the country. It was also found that meglitinides family members scored only 20% in availability throughout the study period. Metformin, recognised as first-line treatment option was missing in at least 6 out of 10 pharmacies during the study period despite being produced by 14 pharmaceutical industries in the country.

Impact of oral anti-diabetic agents’ availability on low socioeconomic status patient cohort

Demographic data

Table 2 shows the demographic data from 75 patients that are registered as T2DM patients who receive monthly prescription through a local NGO in Damascus neighbourhood. The majority of collected samples are females due to the nature of the NGO support for widows and lone mothers. About 64% of patients are prescribed with more than one oral anti-diabetic agent (N = 48) compared to 36% on single agent (N = 27). The increase in medication followed the age trend with older patients receiving more agents.

Prescribed oral anti-diabetic agents in low socioeconomic status patient cohort

Table 3 presents the most prescribed oral anti-diabetic agent in the patient cohort. It was found that oral anti-diabetic agents prescription followed the order of metformin then gliclazide and finally sitagliptin. The lower doses were more prescribed than the higher ones.

Discussion

DM has become a major public health concern, and its burden has been increasing worldwide, especially in the lower-income countries. This was illustrated by the study of Khan et al., which estimated that around 6% of the world’s population was diagnosed with T2DM in 2007. It is forecasted that the prevalence of the disease could rise to over 7000 case per 100 000 inhabitants by 2040. In Syria, where the healthcare system has been in a dire state in the last decade, there is a major concern about the increasing number of diabetic patients. A study by Al Ali et al. projected that the prevalence of T2DM in Syria may reach to 21% by the end of 2022. This puts DM as one of the most common chronic diseases in the Syrian society. Today and after more than 10 years from the beginning of the crisis in Syria, the healthcare system has been subject to heavy strikes affecting its ability to effectively provide services and medications supply.[17] Again, this highlights that the continuous supply of medications for chronic diseases like T2DM is an area of high impact on public health in the country.

Among the various risk factors that could lead to developing DM, this study looked at age and socioeconomic status when assessing the effects of anti-diabetic agents’ discontinuation in diabetic patients. Kyrou et al.’s study found that elderly patients and those who live in low socioeconomic status were more likely to develop T2DM and suffer from its complications.[18] This is compatible with the sample of
patients we looked at in our study, who are mainly recipients of social support from a damascene NGO. The sample age distribution concluded that about 62% of patients were more than 51 years old, and almost 25% of patients are above the age of retirement (Table 2). These patients suffer from an increased burden of the disease because they cannot afford spending money on a continuous prescription besides their cost of living.

The cohort of the study consists of diabetic patients of low socioeconomic status who depend completely on NGO to receive anti-diabetic agents. The study showed that around 60% of these patients used metformin or gliclazide which had less than 40% availability in the Syrian market (Tables 1 and 3). Having difficulties in purchasing anti-diabetic drugs, the patients try to cope with this situation by skipping tablets, changing their diet habits, or stopping taking their medications until they are available again. All of that will cause serious consequences on their health, and this is especially dangerous with a silent disease like diabetes.[11]

The analysis of the study showed that metformin (500 mg) was the most prescribed drug among all the studied medicines (about 57% of patients) followed by gliclazide (30 mg) with around 37% of patients and sitagliptin (50 mg) with 22.5% of patient’s prescriptions (Table 3). These prescriptions were in line with the NICE guidelines for T2DM treatment and are listed in the WHO Modal List of Essential Medicines.[12, 19] In addition, metformin and gliclazide were suggested by Khan et al. to be part of the emergency kits that should be available in the health centres for the management of T2DM in conflict settings, which is the case in Syria.[9] This puts the three drugs as essential and must be available in continuous manner in the Syrian market to keep supply for DM patients and avoid any adverse reactions from discontinued treatment.

By looking at Table 1, it is noted that there is a significant discontinuation of basic anti-diabetic agents for a long period. For example, metformin (500–1000 mg) was only presented in around 37% of pharmacies included in the study for 14 weeks with 18% standard deviation. This increase in standard deviation reflects the fact that the medicine was either present or absent for a long period in specific pharmacies. Also, gliclazide (30 mg) was only presented in 25% of the included pharmacies with 5% standard deviation. As discussed previously, metformin and gliclazide are considered as first-line treatments in T2DM management, and the absence of these agents in the Syrian market raises a serious concern for diabetic patients, especially for those of lower-income status who struggle to find alternatives to these drugs. On the other hand, the combination formula of pioglitazone and metformin had a higher availability rate (80%) than the other drugs although it was produced by one pharmaceutical company. However, this formula has not been prescribed frequently by doctors in Syria at least for our sample of patients (Table 3).

Based on multiple media reports, the Syrian healthcare sector faces real challenges with providing medications in reasonable prices to patients without affecting the producers’ interests.[20, 21] The producers import most of the raw materials in high prices while, at the same time, they are obliged to sell their products at a lower price, which will eventually lead to a decrease in the supply and discontinuation of many generic medications. This situation shows its sad face with patients of low socioeconomic status suffering from a silent chronic disease like diabetes.

Many reasons lie behind the discontinuation of anti-diabetic agents in the Syrian market. Mainly, the tragic situation since 2011 affected the local pharmaceutical industry and lead to a closure of many factories around the country. According to the WHO report, 90% of local pharmaceutical production was halted due to the armed conflict in 2013.[22] Another important factor is the economic sanctions imposed since mid-2011 and levied gradually since then. Ziad Ghisn in his blog

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**Table 2** Demographic information of low socioeconomic income patient cohort with type 2 diabetes analysed in the study (N = 75)

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age (years)</th>
<th>Total percentage (frequency)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>31–40</td>
<td>41–50</td>
</tr>
<tr>
<td>Females</td>
<td>5.3% (4)</td>
<td>29.3% (22)</td>
</tr>
<tr>
<td>Males</td>
<td>0</td>
<td>2.6% (2)</td>
</tr>
<tr>
<td>Total</td>
<td>5.3% (4)</td>
<td>31.9% (24)</td>
</tr>
</tbody>
</table>

**Table 3** Oral anti-diabetic drugs prescribed to patient cohort expressed by percentage (frequency)

<table>
<thead>
<tr>
<th>Drug (dose)</th>
<th>Age (years)</th>
<th>Total percentage (frequency)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>31–40</td>
<td>41–50</td>
</tr>
<tr>
<td>Metformin (500 mg)</td>
<td>2.66% (2)</td>
<td>20% (15)</td>
</tr>
<tr>
<td>Gliclazide (30 mg)</td>
<td>1.3% (1)</td>
<td>9.3% (7)</td>
</tr>
<tr>
<td>Sitagliptin (50 mg)</td>
<td>1.3% (1)</td>
<td>6.6% (5)</td>
</tr>
<tr>
<td>Metformin (850 mg)</td>
<td>0</td>
<td>6.66% (5)</td>
</tr>
<tr>
<td>Gliclazide (80 mg)</td>
<td>0</td>
<td>6.6% (5)</td>
</tr>
<tr>
<td>Sitagliptin (100 mg)</td>
<td>1.3% (1)</td>
<td>8% (6)</td>
</tr>
<tr>
<td>Metformin (1000 mg)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Gliclazide + Metformin (80/500)</td>
<td>0</td>
<td>1.3% (1)</td>
</tr>
<tr>
<td>Total</td>
<td>6.56% (5)</td>
<td>58.46% (44)</td>
</tr>
</tbody>
</table>
in the LSE Journal suggested that these sanctions have had a great impact on drug manufacturing, importing essential raw materials, pricing, and bank transactions. According to RT Media Agency, and in response to the economic crisis, the Syrian Health Ministry increased the prices of national-produced drugs. This has consequently led to reduced profit margin for community pharmacies and weakened the purchasing power of the patients.

Another important factor that affects the availability of anti-diabetic medications in the Syrian market is the supply chain disruption in small cities and rural areas during the conflict period. The major pharmaceutical factories are located in rural Damascus and Aleppo governorates, and most of them were partially or completely closed due to the conflict. In addition, those factories were facing challenges in transporting essential medications to warehouses and pharmacies in small cities and rural areas around the country. This adds to the list of difficulties that impede a full coverage of anti-diabetic agents in the Syrian market.

This study highlights the importance of treatment adherence in diabetic patients to prevent long-term diabetic complications. Lloyd et al. found in their study that poor glycaemic control can lead to serious long-term microvascular and macrovascular complications of which a mild development of each can significantly affect patient’s quality of life. Besides, Currie et al.’s study showed that non-compliance to anti-diabetic medications increases the mortality rate in T2DM patients. Therefore, more efforts should be done to increase the availability of such drugs in the Syrian market, especially for those who find difficulties in gaining access to them.

This study has the limitation of the small number of patients included in the sample. This is because very few NGOs, including Al Tamayoz, have electronic databases of their beneficiaries which can be used in medical studies. It is now available, and many local pharmaceutical companies are producing it. However, the authors do not have enough information about the availability and the prescription rate of this agent. So, it was decided to defer its inclusion for later studies. Also, there is a noticeable gender imbalance in the sample which is attributed to the fact that most of the NGO’s beneficiaries were widows or dependent females who rely completely on the organisation to cover their living expenses. In addition, this study is limited to Damascus governorate and lacks data from other cities in Syria because the authors had no accessibility to pharmacies or NGOs outside Damascus. Finally, there is a scarcity of resources and peer-reviewed publications that study DM and its complications in the Syrian community, especially in the last decade, which forced the authors to depend on media reports to obtain relevant information.

**Conclusion**

Many classes of oral anti-diabetic agents like metformin, sulfonylureas and SGLT2 inhibitors are available in the Syrian market but were not found in all pharmacies. Some of the medications experienced periods of shortages or absence in some pharmacies. The work highlighted that the three mostly prescribed drugs, such as Metformin, Gliclazide and Sitagliptin should be flagged as essential medications for diabetes and Syria and efforts should be made to ensure their continuous availability in the Syrian market.

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**Author Contributions**

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**Conflict of Interest**

All authors certify that they have no affiliations with or involvement in any organisation or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

**Data Availability**

The data that support the findings of this study are available from the corresponding author, Taher Hatahet, upon reasonable request.

**References**


