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Accuracy of Point of Care testing for the diagnosis of respiratory pathogens in a Paediatric Intensive Care setting.

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Respiratory tract infections contribute significantly to Paediatric Intensive Care Unit (PICU) admissions. Early diagnosis supports treatment, cohorting and antimicrobial stewardship. Rapid point-of-care (POC) multiplex PCR techniques show promise in improving antimicrobial and investigation stewardship across healthcare settings.(1) However, debate exists regarding their role and accuracy.(2,3) We sought to evaluate the feasibility and accuracy of respiratory pathogen POC testing in our PICU.

All patients admitted to the regional Northern Ireland PICU undergo nasal/nasopharyngeal swab respiratory pathogen POC testing. The BioFire FilmArray BFRP2.1 Panel [Table 1] is utilised which provides results in under an hour. Simultaneously, laboratory-based viral and microbiological testing is performed at clinician discretion. All laboratory testing is undertaken by the Regional Laboratories using standard molecular and non-molecular techniques, with results taking up to 48 hours to result. Herein, we report a retrospective service evaluation of all PICU respiratory pathogen POC testing performed during 2022.

In total, 289 POC tests had contemporaneous laboratory results, taken within 24 hours of the POC test, available for comparison. 44%(127) were negative for pathogens on both techniques and excluded from accuracy analysis. Of all 208 pathogens identified, 57%(118) were detected by both techniques, 36%(75) by POC alone and 7%(15) by laboratory testing alone. POC tests demonstrated sensitivity and specificity of 88% and 63% respectively (using laboratory methods as the reference standard).

Threshold cycle (CT) values for each pathogen were available for 93%(124) of laboratory tests. Mean CT values were significantly higher for detection by laboratory methods only compared to detection on both POC and laboratory testing (25.15, 30.48 respectively) ($P < 0.001$).[Table 2]

Consistent with previously reported epidemiology in PICU, Respiratory Syncytial Virus (RSV), and rhino/enterovirus (RV) were most commonly detected on POC testing. RSV was the most concordant pathogen between testing methods. RV was the most likely to be identified by POC testing alone. Adenoviruses were third most common virus seen overall and the most likely pathogen detected on laboratory methods only. These findings mirror studies showing discordance of pathogen detection and difference of detection thresholds between multiplex and real-time PCR molecular techniques. In particular rhino/enterovirus and adenovirus demonstrate increased discordance.(3,4) One suggestion for this is that rhinoviruses and enteroviruses are a divergent species, between which multiplex PCR techniques fail to distinguish, possibly explaining a higher proportion of RV detected by POC tests only. Moreover, *Pierce et al.* explored the decreased detection of adenovirus through multiplex PCR techniques, identifying discrepancy between specific subtypes.(3)

Our analysis underestimates the "true negatives" which will reduce the reported diagnostic accuracy. Additionally, it is a retrospective study comparing methods which weren't always taken at precisely the same time point.

This evaluation supports POC tests as a screening tool for rapid detection of respiratory pathogens in PICU setting. However, it also highlights the value of more specific, concurrent laboratory techniques which can detect additional pathogens that may be undetected or not included in the panel. While

clinicians and families universally appreciate the benefits of POC testing, awareness of the limitations is essential to ensure appropriate interpretation of these tests.

Viral Pathogens detected by BioFire RP2.1 Panel	*Bacterial Pathogens detected by* BioFire RP2.1 Panel
• Adenovirus; • Coronaviruses HKU1, NL63, 229E, and OC43; • Human metapneumovirus; • Rhinovirus/enterovirus (RV) • Respiratory syncytial virus (RSV) • Influenza A, A/H1-2009, A/H3, • Parainfluenza virus 1, 2, 3, and 4;	• *Bordetella pertussis* and • *Bordetella parapertussis*; • *Chlamydophila pneumoniae*; • *Mycoplasma pneumoniae*

Table 1: 21 pathogens detected by the BioFire RP2.1 Panel [*bioMèrieux, Marcy-l'Étoile, France*]

	TOTAL 208 Pathogens (%)	*Pathogen detected by POC and laboratory testing (%)*	*Pathogen detected by POC test only (%)*	*Pathogen detected by laboratory testing only (%)*
Total		**118 (57%)**	**75 (36%)**	**15 (7%)**
Adenoviruses	**36 (17%)**	11 (9%)	20 (27%)	5 (33%)
Corona viruses	**27 (13%)**	19 (16%)	6 (8%)	2 (13%)
Influenza Viruses	**8 (4%)**	5 (4%)	2 (3%)	1 (7%)
Parainfluenza Viruses	**8 (4%)**	3 (3%)	4 (5%)	1 (7%)
Rhino/Enteroviruses	**74 (36%)**	35 (30%)	34 (45%)	5 (33%)
Respiratory syncytial virus	**47 (23%)**	40 (34%)	6 (8%)	1 (7%)
Metapneumoviruses	**7 (3%)**	5 (4%)	2 (3%)	0 (0%)
Bordatella Parapertussis	**1 (0%)**	0 (0%)	1 (1%)	0 (0%)
Number for which CT VALUES		111/118 (94%)		13/15 (87%)
CT VALUE RANGE		13.68-37.45		24.12-35.8
*CT VALUE MEAN * (range, 0.95 CI)*		25.15 (+/-2.46)		30.48 (+/- 1.20)

Table 2. Pathogens detected in POC testing and relationship to concurrent laboratory testing results. *difference in variance (F test, P=0.03), t-test of differences assuming unequal variance, p<0.001

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Competing interests

There are no competing interests to declare on behalf of any of the authors.