American Journal of Biochemistry and Biotechnology

Original Research Paper

Clinical Utility of FilmArray Gastrointestinal Panel among Newborn and Infant Patients in a Tertiary Hospital in Korea

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Article history
Received: 21-05-2024
Revised: 05-07-2024
Accepted: 13-07-2024

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Abstract: The rapid and accurate diagnosis of diarrheal pathogens prevents adverse patient outcomes and allows for prompt isolation measures, thereby stopping further transmission. This study aimed to evaluate the clinical utility of the FilmArray GI panel in pediatric patients less than 2 years old, who have rarely been studied. Between July 1, 2021, and July 31, 2022, the Biofire® FilmArray® Gastrointestinal (GI) Panel (BioFire Diagnostics, Salt Lake City, UT) tests were performed for 864 orders from 579 patients with diarrhoea in Dankook University Hospital. We retrospectively evaluated the results of samples (110, 16.1%) from patients aged <2 years. The patients were divided into two groups: group A, children aged <12 months and group B, children aged ≥12 months but under 2 years; their results were compared. Of the 110 samples collected, 30 (41.1%) and 26 (70.3%) in groups A and B, respectively, showed positive results. Seventeen samples (15.5%) contained more than one pathogen. The positivity rate was higher in group B (70.3%) than in group A (41.1%). Multiple pathogens were detected more frequently in group B (29.7%) than in group A (8.2%). The FilmArray GI panel appears to be beneficial for detecting gastrointestinal pathogens in children aged 1-2 years, with a positivity rate reaching 70%, compared with infants under 1 year of age.

Keywords: Newborn, Infant, Diarrhea, Age

Introduction

Diarrheal disease remains a major public health problem and is considered a leading cause of morbidity and mortality worldwide, especially in children aged <5 years (Jo *et al*., 2021; Yoo *et al*., 2021). Differential diagnoses of causative pathogens based on clinical symptoms are often challenging due to their similar presentations, despite a significant correlation between pathogen prevalence and factors such as the child's age and the season (Yoo *et al*., 2021). Therefore, multiplex molecular assays can be used to detect all possible pathogens, including bacteria, viruses and parasites affecting different age groups (Jo *et al*., 2021; Yoo *et al*., 2021). These assays are superior to traditional diagnostic methods, such as stool culture, which requires a longer turnaround time and antigen detection assays, whose sensitivity is limited (Yoo *et al*., 2021). Rapid and accurate diagnosis of diarrheal pathogens is crucial as it prevents adverse patient outcomes and hinders further spread by enabling timely isolation precautions (Yoo *et al*., 2021).

The Biofire® FilmArray® Gastrointestinal (GI) panel (BioFire Diagnostics, Salt Lake City, UT) is a qualitative multiplexed nucleic acid-based in vitro diagnostic test that can simultaneously detect 22 GI pathogens from stool specimens, including bacteria, viruses and parasites and produces results in approximately one h (BioFire® FilmArray®, 2023). Although many studies have evaluated the FilmArray GI panel (Alejo-Cancho *et al*., 2017; Jo *et al*., 2021; Piralla *et al*., 2017; Spina *et al*., 2015; Yoo *et al*., 2021), to the best of our knowledge, few have evaluated age-dependent differences in detection rates in pediatric patients (Jo *et al*., 2021; Spina *et al*., 2015), especially in pediatric patients younger than 2 years old.

Each multiplex Polymerase Chain Reaction (PCR) platform has strengths and weaknesses in detecting GI pathogens (Chhabra *et al*., 2017). This study is valuable in assessing the clinical utility of the FilmArray GI panel in pediatric patients across specific age groups.

The objective of this article is to retrospectively evaluate the clinical usefulness of the FilmArray GI panel in pediatric patients, particularly those under 2 years old, at a tertiary hospital in Korea from July 1, 2021, to July 31, 2022. This evaluation will enhance our understanding of the limitations of this panel and assist clinicians in selecting appropriate diagnostics according to age groups.

Materials and Methods

This study was approved by the Institutional Review Board of Dankook University Hospital (IRB No. 2022-07-011). Informed consent was waived as the analysis was performed retrospectively.

Between July 1, 2021, and July 31, 2022, 684 orders for the GI panel were placed, originating from 579 patients with diarrhoea at Dankook University Hospital. We retrospectively evaluated the results of selected samples (110, 16.1%) from patients younger than 2 years old. We included all the results from those who submitted multiple times during the period. Five patients were tested twice during the study period, and no duplicate-positive pathogens were detected.

Because most reports of diarrheal pathogens show age-dependent differences in detection rates (Jo *et al*., 2021; Spina *et al*., 2015), we categorized the samples into two groups based on age: Group A, children aged <12 months and Group B, children aged ≥12 months but <2 years. Additionally, we focused on the newborn group of less than 1 month regarding the detection rate.

Statistical analyses were performed using Microsoft Excel (Redmond, WA, USA). Detection rates were calculated for each age group. The overall frequency distribution of pathogens detected and frequency distribution of pathogens detected in samples with multiple pathogens were evaluated. Frequency distributions were compared between the two age groups. The chi-square test was used to compare differences in detection rates. Statistical significance was set at $p<0.05$.

Results

Overall, 74 pathogens were detected in 56 samples (50.9%). Of the 110 samples, 30 (41.1%) and 26 (70.3%) in groups A and B, respectively, had positive results. Seventeen samples (15.5%) contained more than one pathogen. Sixteen specimens contained two pathogens, and only one in group B contained three pathogens. In all ages, 283 (41.4%) positive cases were detected, and 59 (8.6%) samples contained more than one pathogen.

The distribution of gastrointestinal pathogens by age is shown in Table (1). The positivity rate was higher in group B (70.3%) than in group A (41.1%). Clostridium difficile toxin A/B was the most commonly identified pathogen in patients younger than 2 years old. Twenty-two cases (20%) were detected, with 10 and 12 patients in groups A and B, respectively. Norovirus GI/GII and Rotavirus followed Clostridium difficile toxin A/B and were detected in 14 cases (12.7%). The positivity rate for Norovirus GI/GII was significantly higher in group B (29.7%; 11/37) than in group A (4.1%; 3/73). Interestingly, six EPEC (Enteropathogenic *Escherichia coli*)-positive cases were detected only in group B. The detection rate of EPEC was significantly higher in group B (16.2%) than in group A (0%). In the case of rotavirus, only one case was detected in group B (2.7%), while 13 cases (17.8%) were detected in group A, showing a significant difference. Additionally, in those patients in the age group of less than 1 month, only one (1/13, 7.7%) case was positive for rotavirus.

Using the GI panel, multiple pathogens were detected in 17 samples from patients younger than 2 years old (Table 2). *C. difficile* toxins A/B were most frequently detected (14/110, 12.7%), followed by Norovirus GI/GII (7/110, 6.4%). The distribution of multiple positive samples varied between the groups. Multiple pathogens were more frequently detected in group B (29.7%) than in group A (8.2%).

Table 1: Number (%) of pathogens according to age groups

Pathogen	Age group		*p*	Total
	A: < 1 yr	B: 1–2 yr		
C. difficile	10 (13.7%)	12 (32.4%)	0.764	22
Salmonella	-	2 (5.4%)	0.168	2
EPEC	-	6 (16.2%)	<0.05	6
STEC	-	1 (2.7%)	0.33	1
Rotavirus A	13 (17.8%)	1 (2.7%)	<0.05	14
Norovirus GI/GII	3 (4.1%)	11 (29.7%)	<0.05	14
Adenovirus F 40/41	6 (8.2%)	1 (2.7%)	0.049	7
Astrovirus	3 (4.1%)	1 (2.7%)	0.291	4
Sapovirus	1 (1.7%)	3 (8.1%)	0.344	4
No. of detected pathogens	36	38		74
No. of positive samples/tested samples (%)	30/73 (41.1%)	26/37 (70.3%)	0.138	56/110 (50.9%)

Abbreviations: EPEC, enteropathogenic *Escherichia coli*; STEC, Shiga toxin-producing *Escherichia coli*

Table 2: Distribution of co-detected pathogens according to age groups

Pathogens	No. of samples according to age groups	
	< 1yr	1–2 yr
C. difficile	5	3
C. difficile, Norovirus	1	4
C. difficile, Sapovirus	1	2
C. difficile, Rotavirus	2	0
C. difficile, Adenovirus	1	0
C. difficile, EPEC	0	1
C. difficile, STEC	0	1
C. difficile, Norovirus, Adenovirus	0	1
Norovirus	2	5
Norovirus, EPEC	0	1
EPEC, Salmonella	0	1
Adenovirus, astrovirus	1	0
Co-detection rate	8.2% (6/73)	29.7% (11/37)

Abbreviations: EPEC, enteropathogenic Escherichia coli; STEC, Shiga toxin-producing Escherichia coli

Discussion

In total, 684 samples were tested using the GI panel during the same period. The total detection rate for all age groups was 41.37% (283/684). This was similar to the detection rate of group A. Group B had a higher detection rate than all age groups, including group A. Interestingly, those less than 1 month old had a very low detection rate (7.7%). Therefore, the GI panel appears to be less useful for patients in this group.

Noninfectious causes or other pathogenic agents not included in the GI panel should be considered. For example, human enterovirus and human parechovirus are major causes of aseptic meningitis, especially in neonates and young infants, gastroenteritis and respiratory infections (De Crom *et al*., 2016; Vollbach *et al*., 2015). Clinicians should be aware that stool samples, as well as other samples from multiple sites, such as the cerebrospinal fluid, can considerably increase the diagnostic yield in this age group (De Crom *et al*., 2016; Vollbach *et al*., 2015).

The detection rate for EPEC was significantly higher in group B than in group A, consistent with a previous study revealing the relation of different types of feeding or attendance at infant schools (Amisano *et al*., 2011). Several false-positive results have been reported, especially for EPEC in GI panels (De Rauw *et al*., 2016; Jo *et al*., 2021). Therefore, the high detection rate of EPEC in group B requires further investigation.

The present study had some limitations. First, the results were limited by the small sample size because the study was conducted in a single tertiary hospital. Second, owing to the retrospective study design, we could not evaluate the diagnostic performance with other syndromic panels. Future studies should compare GI panels with various syndromic multiplex PCR assays, and subsequent discrepancy analysis must be conducted (Chhabra *et al*., 2017; Zhan *et al*., 2020; Schaumburg *et al*., 2021). Lastly, the positivity rate may be different between years.

Conclusion

This study is the first to compare the detection rate of GI pathogens within age groups under 2 years old. We found that the two age groups yielded distinct results. Notably, the FilmArray GI panel is a promising tool for the detection of GI pathogens, particularly within the 1-2 year age groups, exhibiting a positivity rate of over 70%.

Acknowledgement

The authors thank Jae Kyung Kim for advice on experimental design and In Soo Rheem for statistical analysis.

Funding Information

This study received no specific grants from any funding agency.

Author's Contributions

Yoo Na Chung: Responsible for idea presentation, data collection, draft manuscript and subsequent data analysis.

Jae-Sik Jeon: Responsible for presenting ideas, data analysis, proofreading papers and proceeding with the article submission process.

Ethics

This study was approved by the Institutional Review Board of the Dankook University Hospital (IRB No. 2022-07-011).

Conflict of Interest

The authors declare that they have no competing interests.

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