Burden of Viral and Bacterial Pathogens in Pediatric Patients in Southwest Ohio, United States

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Abstract

Background: Viral gastroenteritis is a leading cause of morbidity worldwide. Evolving epidemiology, in part due to vaccines, has made identifying specific stool pathogens more relevant for clinical and public health providers. Molecular testing for gastrointestinal viruses is sensitive and effective for rapid identification of viruses from stool samples. In this study we report the prevalence of key viral pathogens in diarrheal stool specimens from a pediatric population.

Methods: From February 2014 to March 2017, remnant stool samples from patients presenting to a healthcare provider with diarrhea were examined for both bacteria (*Salmonella* species, *Shigella* species, *Campylobacter* species, and Shiga toxins 1 and 2) and viruses (norovirus, sapovirus, astrovirus, adenovirus, and rotavirus). Detection of targets was performed using an FDA-approved platform (BD Max™) with PCR/sequencing serving as the reference method.

Results: Of the 386 samples tested, at least one potential pathogen (viral and/or bacterial) was detected in 41.2% of specimens. 136 (35.2%) samples tested positive for at least one virus; 34 (8.8%) samples tested positive for at least one bacterium. There were 28 dual infections.

Conclusion: The most commonly detected targets were viruses. Norovirus and sapovirus were the most prevalent stool pathogens, especially in very young patients. *Shigella* species was the most prevalent bacteria and third most detected target overall. Rotavirus prevalence was low, but still detected in 15 (3.9%) of the samples. This may indicate that while vaccine has reduced its prevalence, it should still be considered in clinical evaluation of this population. Of note, the majority (59%) of samples were negative for viral pathogens. Providers should also consider parasites and noninfectious causes such as inflammatory bowel disease when evaluating diarrhea in a pediatric patient.

Keywords: Gastroenteritis; Diarrhea; Norovirus; Rotavirus; Burden; Molecular testing

Introduction

Diarrhea is the primary symptom of gastroenteritis, while dehydration because of electrolyte and fluid loss is the number one complication. According to the World Health Organization, there are 1.7 billion cases of gastroenteritis every year and approximately 1.5 million children deaths [1]. Health care utilization of children <5 years of age for diarrheal illnesses in the United States for 2010-2019 included 58,195 hospitalizations, 308,536 emergency room visits, and 2,426,159 outpatient visits for a total cost of approximately 537 million dollars [2].

When calculating the financial burden of gastroenteritis, productivity loss must be considered along with health care costs. Parental absenteeism from work was reported in 15.8% of the child cases of gastroenteritis [3]. Loss of productivity also includes missing work due to parents contracting the illness themselves. Parents of children with acute gastroenteritis had a 4-fold increased acute gastroenteritis risk, with 3.6% child-parent pairs experiencing gastroenteritis within the same 4-week period and 29.8% of parents missing work due to their own illness [3].

Viruses cause approximately 70% of infectious gastroenteritis, while bacteria cause between 10% to 20% and parasites <10% [4]. Worldwide, the most common viruses causing diarrhea are norovirus and rotavirus [4]. However, with the implementation of the rotavirus vaccine in 2006, that may be changing. According to a recently published national study, the prevalence of viruses was norovirus 7.3%, sapovirus 4.5%, astrovirus 3.5%, rotavirus 2.4%, and adenovirus 1.2% [5].

In the not-too-distant past, identifying the cause of viral gastroenteritis was time consuming and had little clinical impact. However, the advent of multiplex molecular testing has produced a variety of assays for quickly identifying stool pathogens. Rapid diagnosis allows for isolation of the child to prevent nosocomial infection and provide treatment when warranted [4]. In an effort to understand the prevalence of enteric viruses and bacteria in children in our region, we examined stool samples from patients presenting to a healthcare provider with diarrhea for both bacterial and viral enteric pathogens.

Methods

Stool specimens received by the laboratory from both inpatients

and outpatients suspected of gastroenteritis, enteritis, or colitis from November 15, 2016-March 1, 2017 were included in the study. Stools were received either unpreserved or in Cary-Blair preservative. Samples were excluded if formed stool, submitted on swabs, submitted only for *Clostridium difficile,* or were collected from patients with previous positive enteric bacteria results. Each specimen was tested for bacterial and viral stool pathogens using an FDA-cleared platform (BD MAX™ Enteric Bacterial Panel and BD MAX™ Enteric Viral Panel (Becton, Dickison and Company, Sparks, MD)) following manufacturer's guidelines.

Results

Over the course of the study, 386 specimens were received from predominantly pediatric patients, although 7.5% of patients were over 18 years of age. Specimens were largely from outpatients and had a slight predominance of male patients over female patients: 293 (75.9%) outpatients versus 93 (24.1%) inpatients and 210 (54.4%) males to 176 (45.6%) females (Table 1).

At least one potential pathogen (viral and/or bacterial) was detected in 41.2% of specimens (Table 2). Of the 28 patient samples with multiple pathogens detected, 16 were dual viral infections, 10 were viral-bacterial infections, 1 was a dual bacterial infection, and 1 sample contained two viruses and a bacterium.

Viral pathogens were detected in 35.5% of all specimens (Table 3). Norovirus was the most commonly detected virus. Sapovirus was the second most common virus. Rotavirus and sapovirus had the highest detection rates in the 0 to 1 age group, while norovirus had the highest detection rate among 5 to 8-year old children.

Bacterial pathogens were detected in 8.8% of all specimens (Table 4). *Shigella* was the most commonly detected bacteria followed by *Campylobacter*. *Shigella* was most commonly detected in the 0 to 1 age group, followed by the 2 to 4 age group. Only one dual bacterial infection, which was in an adolescent patient, was detected.

Discussion

The proportion of samples positive for viruses compared to bacteria was unexpected. Viral targets were detected 4 times more than bacterial targets. Although a pathogen was detected in fewer than half

Total Specimens	386
Age Group (in Years)	**Number of Specimens**
0 to 1	88
2 to 4	78
5 to 8	60
9 to 12	52
13 to 17	79
18+	29
Gender	**Number of Specimens**
Female	176
Male	210
Admission Status	**Number of Specimens**
Inpatient	93
Outpatient	293

Table 1: Patient demographics.

Patient Age Group (in Years)	Number of Specimens (Percent of specimens in age group)		
	Negative	Single Potential Pathogen Detected	Multiple Potential Pathogens Detected
0 to 1 (n=88)	33 (37.5)	40 (45.5)	15 (17.0)
2 to 4 (n=78)	39 (50.0)	32 (41.0)	7 (9.0)
5 to 8 (n=60)	31 (51.7)	26 (43.3)	3 (5.0)
9 to 12 (n=52)	39 (75.0)	13 (25.0)	0
13 to 17 (n=79)	64 (81.0)	13 (16.5)	2 (2.5)
18+ (n=29)	21 (72.4)	7 (24.1)	1 (3.4)
Total (n=386)	227 (58.8)	131 (33.9)	28 (7.3)

Data is presented as number of specimens (percent of all specimens collected from age group).

Table 2: Viral and bacterial pathogen detection rate by patient age group in years.

Patient Age Group in Years	Number of Specimens (Percent of Specimens in Age Group)						
	Negative	Rotavirus	Norovirus	Adenovirus	Sapovirus	Astrovirus	Dual Viral Infection
0 to 1 (n=88)	36 (40.9)	7 (7.8)	13 (14.8)	4 (4.5)	14 (15.9)	3 (3.4)	11 (12.5)
2 to 4 (n=78)	45 (57.7)	4 (5.1)	13 (16.7)	1 (1.3)	7 (9.0)	5 (6.4)	3 (3.8)
5 to 8 (n=60)	38 (63.3)	1 (1.7)	11 (18.3)	1 (1.7)	4 (6.7)	3 (5.0)	2 (3.3)
9 to 12 (n=52)	42 (80.8)	2 (3.8)	4 (7.7)	0	3 (5.8)	1 (1.9)	0
13 to 17 (n=79)	67 (81.0)	1 (1.2)	4 (5.1)	1 (1.3)	4 (5.1)	1 (1.3)	1 (1.3)
18+ (n=29)	21 (72.4)	0	4 (13.8)	2 (6.9)	0	1 (3.4)	0
Total (n=386)	249 (64.5)	15 (3.9)	49 (12.7)	9 (2.3)	32 (8.3)	14 (3.6)	17 (4.4)

Table 3: Viral burden by patient age group in years.

Number of Specimens (Percent of Specimens in Age Group)						
Patient Age Group (in Years)	Negative	*Salmonella*	*Shigella*	*Campylobacter*	Shiga Toxin	Dual Bacterial Infection
0 to 1 (n=88)	80 (90.9)	0	8 (9.1)	0	0	0
2 to 4 (n=78)	68 (87.2)	0	6 (7.7)	4 (5.1)	0	0
5 to 8 (n=60)	52 (86.7)	1 (1.7)	3 (5.0)	1 (1.7)	0	0
9 to 12 (n=52)	49 (94.2)	1 (1.9)	0	1 (1.9)	3 (5.0)	0
13 to 17 (n=79)	76 (96.2)	0	1 (1.3)	1 (1.3)	1 (1.9)	1 (1.3)
18+ (n=29)	27 (93.1)	0	0	2 (6.9)	0	0
Total (n=386)	352 (91.2)	2 (0.5)	18 (4.7)	9 (2.3)	4 (1.0)	1 (0.2)

Table 4: Bacterial burden by patient age group in years.

of all samples (41.2%), some age groups had a higher positivity rate. For example, infants had the highest proportion of positive tests, as well as the highest proportion of multi-pathogen results. This may be because an infant's enteric microbiome undergoes significant changes during the first year of life and does not begin to mirror that of older children or adults until at least 12 months after delivery [6]. This finding may also suggest that infants are more susceptible to viral gastroenteritis due to lack of previous exposure, higher exposure due to day care, and/or immature immune system. The positivity rate decreased as the age group increased. The samples that tested negative could indicate that the children tested had a non-infectious etiology, such as Crohn's disease or irritable bowel disease, or that there may have been a pathogen not detectable by the assays used.

Advantages of molecular panels are the shorter time to result and the broader group of pathogens that can be detected. This can enable more rapid identification of and response to diseases of public health import and those that require antimicrobial therapy. In children, identification of stool pathogens is especially important in the context of childcare and schools, where the risk of outbreaks is well documented [7-15]. Obtaining rapid results can also be helpful in vulnerable populations such as the immunocompromised, where prolonged more debilitating disease can occur, and treatment is more often indicated [12].

For most children in industrialized nations, viral gastroenteritis is a self-limited disease that does not lead to hospitalization. Because clinicians were previously unable to identify the pathogens in a timely manner, they were forced to treat symptoms, and research to identify effective therapies and vaccines was not feasible. Diagnostic and therapeutic advancement could have significant impact not only in industrialized countries, but in developing countries like sub-Saharan Africa and South Asia where 90% of global diarrheal deaths occur [8].

Our study is subject to a number of limitations. As a convenience sample, our cohort is subject to selection bias and may not be representative of the general population. Furthermore, we were unable to collect data on clinical factors such as duration and severity of illness, and the rationale for testing. A more thorough understanding of the context within which a patient is tested could help determine its clinical utility. Our results provide the basis for further study, particularly to combine clinical management information with molecular testing results.

Conclusion

Molecular viral testing would yield more positive results, and, thus, should be considered a first line test. There may be an opportunity to both reduce costs and accelerate evaluation for noninfectious conditions such as inflammatory bowel disease. Additionally, differences in presentation, clinical course, and outcome could be identified to enable more effective management sooner.

Competing interests

The authors declare that they have no competing interests

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