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Viral Pathogen-Specific Clinical and Demographic Characteristics of Children with Moderate-to-Severe Diarrhea in Rural Bangladesh

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Abstract. Diarrheal disease is a leading cause of childhood morbidity and mortality worldwide, but particularly in low-income countries in sub-Saharan Africa and South Asia. The Global Enteric Multicenter Study (GEMS) examined the infectious etiologies as well as associated demographics, socioeconomic markers, health-care–seeking behaviors, and handwashing practices of the households of children with diarrhea and their age- and gender-matched controls in seven countries over a 3-year period (December 2007–December 2010). Stool studies to determine diarrheal etiologies and anthropometry were performed at baseline and at 60-day follow-up visits, along with surveys to record demographics and living conditions of the children. We performed secondary analyses of the GEMS data derived from the Bangladesh portion of the study in children with diarrhea associated with viral enteropathogens and explored pathogen-specific features of disease burden. Rotavirus and norovirus were the most prevalent pathogens (39.3% and 35%, respectively). Disease due to rotavirus and adenovirus was more common in infants than in older children ($P < 0.001$ and $P = 0.001$, respectively). Height for age decreased from baseline to follow-up in children with diarrhea associated with rotavirus, norovirus, and adenovirus ($P < 0.001$). Based on these analyses, preventive measures targeted at rotavirus, norovirus, and adenovirus will be expected to have meaningful clinical impact. Cost of treatment was highest for rotavirus as well, making it an obvious target for intervention. Association of specific viruses with stunting is particularly notable, as stunting is an attributable risk factor for poor cognitive development and future productivity and economic potential.

INTRODUCTION

Pediatric diarrheal disease is estimated to cause 1.3 million child deaths per year; nearly half a million fatalities annually are in children younger than 5 years, with the highest mortality rates concentrated in sub-Saharan Africa and Southeast Asia.[1] Although this number has decreased by about one-third in the last 10 years, diarrhea remains the fourth leading cause of death in children younger than 5 years, with the burden of this preventable disease concentrated in the poorest children.[1] The Global Enteric Multicenter Study (GEMS) was a 3-year, multicountry, prospective, age-stratified, matched, case–control study to identify the etiology and population-based clinical burden of children with moderate-to-severe diarrhea (MSD).[2] The town of Mirzapur in rural Bangladesh was among the seven sites included in the study. Clinical and epidemiological data, anthropometry, and a stool sample to identify enteropathogens using the most advanced and comprehensive methodology to date were obtained at enrollment; follow-up home visits were made approximately 50–90 days later to determine status, clinical outcome, and interval growth.[2]

Health-care–seeking behavior, handwashing, and costs in Bangladesh have been previously explored, but not in the range of specific viral pathogens assessed in the GEMS: rotavirus, norovirus, adenovirus, astrovirus, and sapovirus.[3–5] This study seeks to evaluate pathogen-specific differences or correlations between clinical and socioeconomic factors and these five viruses. One of the viruses examined in this study, rotavirus, was previously reported to be the highest cause of MSD in infants, both at the Bangladesh site specifically and among the other locations in GEMS.[5] Because of the fecal–oral route of transmission of these viruses, this study focuses specifically on conditions related to water, sanitation, and hygiene (WASH) practices. The GEMS data from the Bangladesh site showed that most households have an improved water source requiring < 30 minutes to obtain, as well as an improved sanitation facility by WHO/UNICEF Joint Monitoring Programme criteria and a handwashing area with some type of cleanser (soap or ash).[3,6] However, the extent to which improved sanitation facilities are protective against viral enteric infection, compared with bacterial infection, remains incompletely defined.[7] In addition, the average health-care costs to families due to treatment of the various viruses were examined. Previous GEMS analysis showed that the average cost per family was the lowest in Bangladesh compared with the other two Asian countries in the study, but the relationship of cost to pathogen etiology has not been examined.[3] Bangladesh census data from 2014 stated that 50.1% of the population living in rural Bangladesh is in the lowest two wealth quintiles, so even a relatively low cost of care is often a barrier to treatment in rural settings.[8] Other variables examined in this study were related to the longitudinal burden of enteric disease on children, including stunting, or low height for age. This is an improving, but continued, problem in Bangladesh, as 36% of children younger than 5 years have been reported to be stunted in growth, although that number has decreased from 51% in 2004.[8] In rural Bangladesh, stunting has been studied in reference to both acute diarrheal disease and environmental enteric dysfunction (EED), or subclinical gut infection, a factor that was able to be tested by GEMS because of the stool sampling in both cases and controls.[9–11] Stunting is a worldwide health issue that has been linked to negative long-term consequences affecting learning capacity and work productivity well beyond childhood. This study attempts to address the lack of viral-specific research as related

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Table 1
Gender, age, and wealth demographics of study children associated with viral pathogen

	Rotavirus		Norovirus		Adenovirus		Astrovirus		Sapovirus	
	n = 293 (%)	*P*-value	*n* = 261 (%)	*P*-value	*n* = 56 (%)	*P*-value	*n* = 57 (%)	*P*-value	*n* = 79 (%)	*P*-value
Gender										
Male, *n* = 2,337	179 (61.1)	–	156 (59.8)	–	27 (48.2)	–	37 (64.9)	–	49 (62.0)	–
Female, *n* = 1,622	114 (38.9)	–	105 (40.2)	–	29 (51.8)	–	20 (35.1)	–	30 (38.0)	–
Age group (months)	–	< 0.001*		0.99*	–	0.001*		0.22*	–	0.70*
0–11	137 (46.8)	–	92 (35.2)	–	32 (57.1)	–	25 (43.9)	–	21 (26.6)	–
12–23	109 (37.2)	–	93 (35.6)	–	15 (26.8)	–	18 (31.6)	–	39 (49.4)	–
24–59	47 (16.0)	–	76 (29.1)	–	9 (16.1)	–	14 (24.6)	–	19 (24.1)	–
Wealth quintile		0.84*	–	0.02*	–	0.69*		0.91*		0.81*
Poorest	62 (21.2)	–	59 (22.6)	–	9 (16.1)	–	10 (17.5)	–	21 (26.6)	–
Lower middle	55 (21.2)	–	52 (22.6)	–	12 (21.4)	–	11 (19.3)	–	11 (13.9)	–
Middle	48 (16.4)	–	62 (23.8)	–	12 (21.4)	–	12 (21.1)	–	14 (17.7)	–
Upper middle	70 (23.9)	–	55 (21.1)	–	11 (19.6)	–	15 (26.3)	–	15 (19.0)	–
Wealthiest	58 (19.8)	–	33 (12.6)	–	12 (21.4)	–	9 (15.8)	–	18 (22.8)	–

* Chi-squared *P*-value for trend.

to pediatric diarrheal disease to develop more appropriate preventive and therapeutic measures to combat this worldwide public health challenge.

MATERIALS AND METHODS

Study area, population, and sampling. Kumudini Hospital is located in Mirzapur, Bangladesh, in the Tangail district, 60 km outside of the capital city of Dhaka, and served as the sole sentinel health center for enrollment in the Bangladesh arm of GEMS. Children aged 0–59 months presenting to this 750-bed, nonprofit, private hospital with MSD during the 36-month period of the study were eligible for enrollment as cases. Moderate-to-severe diarrhea was defined as three or more watery stools in a 24-hour period with one or more of the following variables: sunken eyes, loss of skin turgor, administration of intravenous rehydration, dysentery, or hospitalization. The site maintains a demographic surveillance system (DSS) of approximately 240,000 individuals in 58,300 households, and age-, gender-, and community-matched controls were selected from this database within 14 days of case presentation. The aim was to enroll approximately 333 children in each of the following age strata: 0–11 months, 12–23 months, and 24–56 months. Complete GEMS protocols have been previously described, but a brief overview is presented in the following paragraphs.[2]

Anthropometry. Body weight was measured after rehydration as the recorded enrollment weight, and at follow-up; height was measured on enrollment and at follow-up. Underweight, wasting, and stunting are defined as a weight for age Z-score, height for age Z-score (HAZ), and weight for height Z-score, respectively, of less than −2.0 SD.

Data collection. In 2007 and before initialization of GEMS, baseline data were collected within the DSS by trained interviewers using a standardized questionnaire termed Healthcare Utilization and Attitudes Survey (HUAS), and was followed by an abbreviated survey (HUAS-lite) that was administered three times per year during the last 2 years of the study (2009–2010). Interviews were conducted within the enrolled child's home and all questions were addressed to the primary caretaker in their native language of Bangla. Stool samples were collected from cases and controls on enrollment. Approximately 60 days (range 50–90 days) after enrollment, a follow-up visit was made to the homes of both case and control children to collect vitals, inquire about interim medical events, and reassess anthropometric measurements. Water, sanitation, and hygiene conditions within the home, including water source and handwashing stations, were also observed and recorded during the follow-up visit. Household cost data were obtained at the time of enrollment and again at discharge from Kumudini Hospital, and divided into the following categories: direct medical (payment to medical provider), direct nonmedical (transportation or other cost), indirect costs (time or other cost), and total costs (sum of all categories). Costs were converted from Bangladeshi taka to U.S. dollars and adjusted to 2011 as the reference year.

Data management and analysis. Case report forms were scanned and sent electronically to the central data coordinating center in Perry Point, MD, and maintained in the database there.[12] Quantitative statistical analyses were performed using IBM SPSS Statistics 20.0 (IBM, Armonk, NY) and Epi Info 7.1.1.14.

Ethical considerations. Clinical protocols were approved by the International Review Boards of the University of Maryland, Baltimore, MD, and the Research Review Committee and the Ethical Review Committee of the International Center for Diarrhoeal Disease Research, Bangladesh. Informed written consent was obtained from each participant's primary caretaker before enrollment in GEMS.

RESULTS

Age demographics of viral enteropathogen-positive cases. During the 36 months of the GEMS Bangladesh (December 2007–2010), a total of 3,859 participants were successfully enrolled.[2] These were divided between the three age strata as follows: 1,428 children aged 0–11 months, 1,237 children aged 12–23 months, and 1,194 children aged 24–59 months. Rotavirus caused the highest total number of cases (293), followed by norovirus (261), whereas the other three pathogens were seen in less than 80 cases, for less than 3% of total study participants (Table 1). There was no statistically significant correlation between gender and any of the five viral pathogens. Infants (ages 0–11 months) had the highest percentages of all viruses, with the exception of norovirus, which was slightly greater in children ages 12–23 months (35.6%), and sapovirus, which was also more common in children aged 12–23 months (49.4%) (Table 1). The

TABLE 2
Household water, sanitation, and hygiene conditions associated with viral pathogen

	Rotavirus			Norovirus			Adenovirus			Astrovirus			Sapovirus		
	n = 293 (%)	OR (95% CI)	*P*-value	*n* = 261 (%)	OR (95% CI)	*P*-value	*n* = 56 (%)	OR (95% CI)	*P*-value	*n* = 57 (%)	OR (95% CI)	*P*-value	*n* = 79 (%)	OR (95% CI)	*P*-value
Source of water															
Shallow tube well	142 (48.5)	Ref.	–	106 (40.6)	Ref.	–	23 (41.1)	Ref.	–	29 (50.9)	Ref.	–	33 (41.8)	Ref.	–
Deep tube well	149 (50.9)	1.26 (0.99-1.62)	0.06	153 (58.6)	0.9 (0.69-1.17)	0.43	32 (57.1)	0.93 (0.53-1.65)	0.91	28 (49.1)	1.35 (0.78-2.36)	0.31	46 (58.2)	0.93 (0.58-1.50)	0.85
Type of water treatment															
No treatment	277 (94.5)	Ref.	–	247 (94.6)	Ref.	–	53 (94.6)	Ref.	–	52 (91.2)	Ref.	–	76 (96.2)	Ref.	–
Facility for feces disposal															
Traditional pit toilet	95 (32.4)	Ref.	–	117 (44.8)	Ref.	–	17 (30.4)	Ref.	–	14 (24.6)	Ref.		31 (39.2)	Ref.	–
Pour flush toilet	77 (26.3)	0.98 (0.71-1.35)	0.95	63 (24.1)	1.52 (1.09-2.12)	0.01*	14 (25.0)	0.96 (0.45-2.07)	0.94	17 (29.8)	0.65 (0.3-1.39)	0.31	19 (24.1)	1.30 (0.71-2.41)	0.45
Method handwashing															
Water only	15 (5.1)	Ref.	–	17 (6.5)	Ref.	–	6 (10.7)	Ref.	–	5 (8.8)	Ref.	–	10 (12.7)	Ref.	–
Water and soap	259 (88.4)	0.75 (0.42-1.31)	0.34	222 (85.1)	1.01 (0.58-1.72)	0.92	48 (85.7)	1.66 (0.63-4.09)0.37	0.37	47 (82.5)	1.41 (0.49-3.73)	0.65	60 (75.9)	2.24 (1.06-4.60)	0.03
Type of water container															
Wide-mouthed container	281 (97.1)	–	–	248 (96.1)	–	–	55 (100)	–	–	55 (96.5)	–	–	76 (98.7)	–	–
Container cover															
Uncovered	141 (49.8)	Ref.	–	145 (57.8)	Ref.	–	37 (67.3)	Ref.	–	29 (52.7)	Ref.	–	40 (52.6)	Ref.	–
Covered	128 (45.2)	0.76 (0.59-0.98)	0.03*	104 (41.4)	0.98 (0.75-1.28)0.93	0.93	18 (32.7)	1.45 (0.80-2.66)	0.25	25 (45.5)	0.81 (0.46-1.44)	0.54	30 (39.5)	0.94 (0.57-1.55)	0.88

oldest children (24–59 months) had the lowest percentages of infection for all viruses, and there was a statistically significant decrease in infection with increasing age for rotavirus ($P < 0.001$) and adenovirus ($P = 0.001$). For norovirus, there was a statistically significant decreasing trend in infection with increasing wealth quintile ($P = 0.021$). There was also a statistically significant decreased likelihood of norovirus infection in children in the richest wealth quintile (OR = 0.559, P-value = 0.002).

Household WASH conditions associated with viral pathogens. Most households, regardless of viral status, used a tube well (deep or shallow) for their water source; however, more than 90% do not use any method of water treatment (Table 2). There was no significant correlation between using a deep or shallow tube well with any of the viral pathogens, nor with the lack of water treatment or water filtration. The most common facility for feces disposal associated with all viral pathogens was a traditional pit toilet, except for astrovirus, for which pour flush toilets were slightly more common (29.8% versus 24.6%). The use of a traditional pit toilet versus a pour flush toilet had a statistically significant increased likelihood of norovirus infection (OR = 1.53, 95% CI: 1.09–2.12). Although most households use water and soap, handwashing with water only was also seen in 53 homes with an associated viral pathogen. Sapovirus and adenovirus had the highest percentages of cases associated with water-only handwashing methods at 12.7% and 10.7%, respectively. For sapovirus, use of water-only handwashing increased the likelihood of infection (OR = 2.24, CI: 1.06–4.60). Almost all households, regardless of viral pathogen status, used a widemouthed container to store water, but there was variability in whether these were covered or uncovered; having an uncovered container was more often associated with the presence of viral pathogens. However, there was a decreased likelihood of rotavirus infection associated with use of an uncovered water storage container (OR = 0.76, CI: 0.59–0.98).

Household costs based on specific viral pathogen. The viruses associated with the highest total costs were Rotavirus ($7.54), followed by Astrovirus ($6.60) (Table 3). The highest direct medical costs were associated with Adenovirus ($4.08), whereas the highest direct nonmedical and indirect costs were both associated with Rotavirus ($0.80 and $3.52, respectively). For all viruses, direct costs exceeded indirect costs.

Nutritional variables associated with viral Pathogens in children with and without MSD. For all viruses, percentage of children with stunting increased from baseline to follow-up in both cases and controls, with the exception of those with loss to follow-up (Table 4). The highest percentage of stunting in cases (children presenting with MSD) at baseline and follow-up was seen with sapovirus (42.1% and 47.4%). This was followed by astrovirus (35.3% and 41.2%). However, in controls, adenovirus had the highest percentage at baseline and follow-up (42.9% and 35.0%). There was no significant association between stunting at baseline and at follow-up for any specific viral pathogen (Table 4) nor was there significant correlation between presence of stunting and a given pathogen, either at baseline or follow-up, for cases and controls (data not shown). There was, however, a statistically significant decrease in HAZ (increase in stunting) from baseline to follow-up in children with rotavirus, norovirus, and adenovirus (Table 5).

TABLE 3
Mean household expenditures (U.S. dollars) by type associated with viral pathogens

	Rotavirus		Norovirus		Adenovirus		Astrovirus		Sapovirus	
	n = 217		*n* = 103		*n* = 35		*n* = 17		*n* = 19	
	Cost	Std. Error	Cost	Std. Error	Cost	Std. Error	Cost	Std. Error	Cost	Std. Error
Direct medical	3.96	0.13	3.43	0.46	3.35	0.26	4.08	0.74	2.46	0.19
Direct nonmedical	0.80	0.02	0.01	0.003	0.01	0.07	0.21	0.03	0.03	0.03
Indirect cost	3.52	0.24	2.27	0.46	2.15	0.37	2.49	0.81	1.25	0.62
Total cost	7.54	0.28	5.71	0.75	5.63	0.51	6.60	1.34	3.75	0.67

DISCUSSION

Diarrheal disease is a primary preventable cause of death in children, especially in developing countries. Although declines in mortality and incidence rates have occurred over the last two decades, morbidity has declined less rapidly. The GEMS findings contributed greatly to our knowledge of the diarrheal disease burden in seven distinct regions, particularly by providing demographic data and pathogen identification. It was our goal in the present study to examine this demographic and nutritional data with respect to viral causes of disease, with the aim of identification of modifiable conditions to develop targeted intervention strategies.

Our analysis shows rotavirus and adenovirus rates both decrease with increasing age, and almost all viruses were more common in infants. Efforts to target prevention and early treatment of this group of young children less than 1 year, including through education of mothers and promotion of health-seeking behavior, should be the focus for the greatest reduction in childhood diarrhea morbidity and mortality. With the exception of norovirus, there was no strong association seen with disease incidence and poverty level, leading to the observation that community-wide changes may need to be made in factors unrelated to economic status. With norovirus, however, there is a correlation between increased wealth and decreased infection, pointing to the continued need for increased health care and education for the most impoverished. This study looked specifically at WASH conditions–factors that are often, but not always, related to household wealth–and that have been shown to have direct effects on diarrheal incidence.[13] Of interest, handwashing with soap was only seen to be protective against sapovirus. This may be due to the robust and highly contagious nature of other viruses, allowing them to withstand handwashing, and emphasizes the role of other strategies including immunization, in particular, the rotavirus vaccine. Similarly, the lack of an improved sanitation facility for feces disposal had no correlation with viral pathogen with the exception of norovirus. This was previously studied in an urban setting in India, with the observation that viral pathogens have lower infectious doses and higher titer shedding than bacteria.[7] However, it has also been observed that infants, whom rotavirus disproportionately affects, are not of an age to use the toilet or handwashing facilities, and thus more likely become infected via their caregivers, other infected children, or contaminated food or water.[7] Although most households in Mirzapur have an improved tube well for safe drinking water, most do not use any type of water filtration or chlorination. A study of five tube wells in Matlab, Bangladesh, found bacterial and protozoal species above recommended levels, and other studies of tube wells in Bangladesh have shown similar results; however, these studies did not examine viral contamination.[14,15] Viral contamination of groundwater or surface water wells has not been widely studied in the developing world, but viruses are known to survive for long periods of time and travel long distances relative to their sizes.[16] Our study showed that use of a shallow tube well had a positive correlation with rotavirus infection, and despite the fact that shallow tube wells are improved water sources, in flood-prone areas, which are prevalent in rural Bangladesh, these wells remain at risk of fecal contamination.[15] In addition, ceramic filtration, the most common form of water treatment used in Mirzapur, although highly effective for the removal of fecal bacterial species, is not similarly effective in the removal of viral enteropathogens from water.[16–18] A previous randomized controlled trial in rural Bangladesh showed that safe water storage (defined as having a narrow mouth and tight-fitting lid) alone was effective at decreasing up to 30% of diarrhea cases in children; however, this study again looked only at *Escherichia coli* levels to help evaluate water quality, so the effect of safe storage on viral contamination is unknown.[19] Some of the statistically significant associations found in our analyses are unexpected, given known disease risk factors such as handwashing and covered water containers, and thus may be the result of chance. However, these preventive factors are likely not nearly as effective as newer means of prophylaxis, such as the rotavirus vaccine, and are difficult to standardize in a study such as this.[20] Nonetheless, the study provides important preliminary data that describe these relationships and form the basis to develop future studies to focus on more specific definition and discernment of the clinical and epidemiology implications of these relationships.

The high total cost of rotavirus treatment, as well as the high direct costs of treatment for all viral pathogens, points to the need for preventive measures against viral disease. In households that are poor, rural, or both, a cost of US$7 to treat a diarrheal infection in a child can be devastating to the family, as most of the money used comes primarily from their regular income, which is also needed for food, transportation, clothing, and other basic necessities.[21] The rotavirus vaccine was planned to be introduced in 2018 in Bangladesh, and the effect of that preventive measure on overall disease incidence will be interesting, and hopefully positive. Because rotavirus vaccine is oral, there has been some concern about its efficacy in the developing world, and there is an ongoing clinical trial in Bangladesh to evaluate this (www.clinicaltrials.gov identifier NCT01375647). In addition, the cost of treatment for rotavirus was primarily due to indirect costs (Table 3). This may be because rotavirus more commonly affects children, whereas norovirus and other causes of gastroenteritis affect adults equally; thus, the lost wages for a parent or guardian to miss work or travel costs to

Table 4
Stunting in cases and controls associated with specific virus

	Rotavirus			Norovirus			Adenovirus			Astrovirus			Sapovirus		
Cases	*n* = 219 (%)	OR (95% CI)	*P*-value	*n* = 103 (%)	OR (95% CI)	*P*-value	*n* = 35 (%)	OR (95% CI)	*P*-value	*n* = 17 (%)	OR (95% CI)	*P*-value	*n* = 19 (%)	OR (95% CI)	*P*-value
Baseline	51 (23.3)	Ref.	–	27 (26.2)	Ref.	–	8 (22.9)	Ref.	–	6 (35.3)	Ref.	–	8 (42.1)	Ref.	–
Follow-up	63/210* (30.0)	0.71 (0.46–1.09)	0.14	36/101* (35.6)	0.64 (0.35-1.17)	0.19	11/34* (32.4)	0.62 (0.21-1.8)	0.54	7 (41.2)	0.78 (0.19-3.11)1.00	1.00	9 (47.4)	0.81 (0.22-2.91)	1.00
Controls	*n* = 74 (%)	OR (95% CI)	*P*-value	*n* = 158 (%)	OR (95% CI)	*P*-value	*n* = 21 (%)	OR (95% CI)	*P*-value	*n* = 40 (%)	OR (95% CI)	*P*-value	*n* = 60 (%)	OR (95% CI)	*P*-value
Baseline	21 (28.4)	Ref.	–	45 (28.5)	Ref.	–	9 (42.9)	Ref.	–	8 (20.0)	Ref.	–	18 (30.0)	Ref.	–
Follow-up	24/73* (32.9)	0.81 (0.40-1.63)	0.68	50/155* (32.3)	0.84 (0.52-1.35)	0.55	7/20* (35.0)	1.39 (0.39-4.92)	0.85	8 (20.0)	1.00 (0.33-2.99)	1.00	18/57* (31.0)	0.95 (0.43-2.09)	0.94

* Corrected for number lost to follow-up.

obtain treatment for their child is felt more acutely, whereas these indirect costs are less apparent when the entire household is affected.

The effect of viral infection on stunting was not seen to be pathogen specific. However, the decrease in HAZ observed from baseline to follow-up and the evidence of stunting seen in controls may have important implications for the effects of Environmental Enteric Dysfunction (EED), or subclinical gut infection. Recent studies have pointed to the long-term effects of EED on childhood malnutrition, leading to overall decreased growth.[22,23] It is possible that the children in this study had increased stunting as a result of EED or other confounding factors that were not accounted for. This deserves further study, as stunting has been linked to decreased motor and cognitive functioning, as well as long-term health outcomes and economic stability.[24] A limitation of the study is that we were unable to evaluate for coinfection with multiple pathogens because of our focus only on viral pathogens. Certain reports from the GEMS dataset explored coinfection rates and found this to be significant with variable effects on disease severity. For example, in a Tanzanian study, significant positive and negative interactions were seen with both rotavirus and norovirus in association with another nonviral enteropathogen.[25] Coinfection was not the focus of our study, but this is a potential avenue for future work because of its important effect on treatment and outcomes, particularly in the lower and middle-income settings.

The findings from this viral-focused study, as well as the progressive decline yet still persistent burden of diarrheal disease, indicate viral enteropathogens remain intimately associated with direct and indirect (e.g., stunting) childhood morbidity in lower income countries. Many of the successful preventive measures directed at childhood diarrhea have focused on bacterial causes and severe rotaviral diarrhea, the latter as a relative exception to the challenge of prevention of disease due to other viral etiologies. Our data suggest that successful interventions to prevent viral diarrhea can be expected to decrease not only morbidity and mortality due to diarrhea but also pernicious morbidities attributable to childhood stunting associated with specific pathogens.

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TABLE 5
Mean height-for-age Z-scores at enrollment and follow-up

	Rotavirus		Norovirus		Adenovirus		Astrovirus		Sapovirus	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Enrollment	−1.22	1.3	−1.4	1.2	−1.35	1.3	−1.7	1.8	−1.9	1.1
Follow-up	−1.48	1.2	−1.5	1.2	−1.71	1.3	−1.86	1.8	−1.9	1.0
P-value	**< 0.001**	–	**< 0.001**	–	**< 0.001**	–	0.097	–	0.730	–

Bold values indicate statistical significance.

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