



Published in final edited form as:

Pediatr Infect Dis J. 2021 March 01; 40(3): 215–219. doi:10.1097/INF.0000000000002989.

Hospital-based Surveillance for Pediatric Norovirus Gastroenteritis in Bangladesh, 2012–2016

Syed M. Satter, MBBS, MPH^{*,†}, Zarin Abdullah, MBBS, MPH^{*,†}, Cristina V. Cardemil, MPH, MD[‡], Meerjady S. Flora, PhD[§], Emily S. Gurley, PhD^{*,¶}, Mahmudur Rahman, PhD^{*}, Muhammad Talha, Msc^{*}, Md D. Islam, Msc^{*}, Mohammad E. Hossain, PhD^{*}, Neha Balachandran, MBBS, MPH^{‡,||}, Benjamin Lopman, PhD^{**}, Mustafizur Rahman, PhD^{*}, Jan Vinjé, PhD[‡], Aron J. Hall, MSPH, DVM[‡], Umesh D. Parashar, MBBS, MPH[‡]

^{*}icddr,b, Mohakhali, Dhaka, Bangladesh

[†] Programme for Emerging Infections, Infectious Diseases Division, icddr,b, Mohakhali, Dhaka, Bangladesh

[‡] Centers for Disease Control and Prevention, Atlanta, GA

[§] Institute of Epidemiology, Disease Control & Research, Dhaka, Bangladesh

[¶] Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

^{||} Cherokee Nation Assurance, Arlington, VA

^{**} Rollins School of Public Health, Emory University, Atlanta, GA.

Abstract

Background: Globally, noroviruses are recognized as an important cause of acute gastroenteritis (AGE), but data from low and middle-income countries are limited.

Aims: To examine the epidemiology and strain diversity of norovirus infections among children hospitalized for AGE in Bangladesh.

Methods: We implemented active surveillance of children <5 years of age hospitalized with AGE at 8 geographically dispersed tertiary care hospitals in Bangladesh from July 2012 to June 2016. We tested random samples of AGE cases stratified by site and age group for norovirus by real-time RT-PCR. Noro-positive specimens were genotyped. Coinfection with rotavirus was assessed based on prior EIA testing.

Results: We enrolled 5622 total AGE cases, of which 1008 were tested for norovirus. Total of 137 (14%) AGE cases tested positive for norovirus (range, 11%–17% by site). Most (94%) norovirus-associated hospitalizations were among children less than 2 years of age. Norovirus was detected year-round, with higher detection from March to June (20%–38%) and November to January (9%–18%). Genogroup II (GII) noroviruses were detected in 96% of cases, and the most

Address for correspondence: Syed M. Satter, MBBS, MPH, Programme for Emerging Infections, Infectious Diseases Division, icddr,b, Mohakhali, Dhaka 1212, Bangladesh. dr.satter@icddr.org.
S.M.S. and Z.A. share the first co-authorship.

No reported conflict of interest. All authors have submitted the ICMJE form for disclosure of potential conflicts of interest.

frequent genotypes were GII.4 Sydney [P4 New Orleans] (33%), GII.3 [P16] (20%), and GII.4 Sydney [P16] (11%). The proportion of norovirus-positive specimens was significantly greater among rotavirus-negative AGE patients compared with rotavirus-positive AGE patients (27% vs. 5%, $P < 0.001$). As measured by the Vesikari severity score, a similar proportion of norovirus and rotavirus positive AGE patients were considered severe (68% vs. 70%, $P = 0.86$).

Conclusions: Norovirus is an important cause of AGE hospitalization in Bangladeshi children with most infections caused by GII viruses.

Keywords

Norovirus; gastroenteritis; surveillance; Bangladesh

In some developed countries, with the decline in rotavirus acute gastroenteritis (AGE) following the implementation of rotavirus vaccines, norovirus has emerged as the leading cause of severe childhood AGE requiring hospitalization.^{1,2} However, in developing countries like Bangladesh, data on the burden and genetic diversity of norovirus as a cause of severe AGE are limited. Such information are essential to assess the need for and value of specific interventions against norovirus, including vaccines that are currently in clinical trials.³

Noroviruses are a genetically diverse group of nonenveloped single-stranded RNA viruses that can be classified into 10 genogroups (G).⁴ Of these, GI and GII viruses cause almost all infections in humans. GI viruses can be further divided into 9 genotypes and GII into 26 genotypes. A dual classification system based on VP1 and RdRp genes has recently been described with at least 49 capsid genotypes and 60 P-types.⁴ Globally, GII.4 viruses have been the most common cause of norovirus illnesses.^{5,6}

In Bangladesh, the prevalence of norovirus among hospitalized patients with AGE ranged from 8.5% to 28% during 2004–2014.^{7–10} Other norovirus data among nonhospitalized children with diarrhea have been obtained from large multicountry studies, such as Malnutrition and Enteric Disease (MAL-ED) and Global Enteric Multicenter Study (GEMS).^{11,12} However, recent data from geographically diverse sites across Bangladesh are lacking.

To better understand the burden of norovirus gastroenteritis in children hospitalized with AGE, we tested a subset of samples from patients previously enrolled in surveillance at 8 geographically diverse and representative pediatric tertiary care hospitals across Bangladesh. The epidemiology of norovirus infections, including clinical features and circulating genotypes, was investigated.

METHODS

Surveillance Sites and Procedures

Surveillance procedures have been previously described.¹³ To describe concisely, an active hospital-based surveillance for AGE in children who were less than 5 years of age, was inaugurated in July 2012; at 8 tertiary hospitals situated in all 7 divisions of Bangladesh

(see Figure, Supplemental Digital Content 1, <http://links.lww.com/INF/E224>). At first, in July 2012, the surveillance has been started at the Rajshahi, Dhaka, and Sylhet sites. Later the surveillance has been extended to Rangpur and Chittagong, in February 2013. The field sites were further extended to Barisal in August 2013 and to Jessore in January 2016. The original surveillance site hospital in Rangpur named World Mission Prayer League hospital was later replaced with Rangpur Medical College Hospital. At surveillance hospitals, every weekday at office hour (8:30 am–4:00 pm), field assistants screened children who are less than 5 years old and admitted to pediatric wards with AGE, defined as ≥ 3 watery or looser-than-normal stools or ≥ 1 episode of forceful vomiting within a 24-hour period with symptoms lasting ≥ 7 days. Each fourth child screened was enrolled by surveillance physicians after meeting case definition. Compared with other sites, the number of AGE-associated hospitalizations at the initial site in Rangpur was low. Therefore, after 3 months, the protocol at this site was modified and every child admitted with AGE symptom was enrolled. Demographic and clinical information of enrolled children was collected by surveillance physicians from the parents and hospital records. A standard questionnaire was used and the extent of dehydration, for example, no dehydration, some dehydration, and severe dehydration, were assessed following clinical criteria in WHO diarrhea treatment guidelines.¹⁴ Stool specimens (4 mL) were collected by field assistants from each child on the day of enrollment and after collection, the specimens were immediately stored in a -70°C liquid nitrogen dry shipper. The stool samples were shipped to the icddr,b virology laboratory in Dhaka every 2 weeks. Stool samples were stored at -70°C at virology laboratory, icddr,b.

From the parents or guardians of the children, written informed consent was sought. Ethical Review Committee of icddr,b was responsible for reviewing and approving this protocol.

Selection of Specimens for Norovirus Test

From July 2012 to June 2016, a total of 5622 stool samples collected from children less than 5 years of age, hospitalized for acute gastroenteritis in surveillance sites were available for our study. Based on studies performed in recent years in Bangladesh, where norovirus accounted for 20%–28% of hospitalizations due to diarrhea among children less than 5 years,^{7,15–18} we determined the need for a sample size of 1000 (18% of total banked samples). Assuming 20% of severe gastroenteritis cases are attributable to norovirus (95% confidence level and $\pm 0.4\%$ absolute precision), this resulted in 200 cases of norovirus annually. To select the 1000 samples, first we stratified the banked samples by site and age group (0–5, 6–11, 12–17, 18–23, and 24–59 months), then we randomly selected the samples from each strata with equal proportion. This allowed us to standardize the prevalence of the original sample distribution. All specimens that tested positive for norovirus were genotyped.

Laboratory Testing

Viral RNA Extraction and Norovirus Real Time RT-PCR

Nucleic acid was extracted from each stool sample using the InviMag Pathogen kit (STRATEC Molecular GmbH, Berlin) on an automatic extractor (KingFisher Flex96).

Nucleic acid was tested by a GI/GII norovirus duplex real-time RT-PCR assay with oligonucleotide primers and probes targeting the ORF1-ORF2 junction region of the genome as described previously.^{19,20} The real time RT-PCR was carried out in a 25- μ L reaction mixture consisting of 5- μ L RNA, 1- μ L of Ag-Path enzyme mix, 12.5- μ L Ag-Path buffer (Ambion Inc., Austin), 0.8 pmol of each oligonucleotide primer and 0.2 pmol of each oligonucleotide probe. Reverse transcription was performed for 30 minutes at 55°C followed by denaturation at 95°C for 30 seconds, and PCR was conducted for 45 cycles at 95°C for 15 seconds and 60°C for 1 minute.

Norovirus Genotyping

For genotyping, nucleic acid of real-time RT-PCR norovirus-positive samples was amplified by conventional RT-PCR using the OneStep RT-PCR Kit (Qiagen, Hilden, Germany) as described previously.^{8,13} For sequencing, the PCR products were purified with the ExoSAP-IT PCR product cleanup kit (Affymetrix, INC, Cleaveland, OH) at 37°C for 15 minutes followed by incubation at 80°C for 15 minutes. The BigDye Terminator kit (Perkin-Elmer Applied Biosystems, Foster City, CA) was used for cycle sequencing on an automated genetic analyzer ABI 3500 \times L (Perkin-Elmer Applied Biosystems, Foster City, CA). Sequences were genotyped using a web-based genotyping tool (<https://norovirus.ng.philab.cdc.gov>).

Data Analysis

The number and proportion of children hospitalized with AGE due to norovirus were determined by site and age group. Coinfection with rotavirus was assessed based on previous EIA testing. Total and site-specific proportions of norovirus-associated AGE hospitalizations were calculated by dividing the number of norovirus-positive stools by the total number of samples tested for norovirus. To estimate the number of norovirus-associated hospitalizations, the overall proportion of norovirus-associated AGE hospitalizations was applied to the total number of AGE admissions during the surveillance period. Duration of AGE was defined as the total days of illness from symptom onset up to the date of enrollment. We obtained a gastroenteritis severity score for each child using the 20-point Vesikari scale calculated from clinical information obtained at enrollment. Mild gastroenteritis was defined by a score of less than 7, moderate was scored as 7–10 and severe gastroenteritis was defined by a score of 11 or more. Clinical data were analyzed to compare severity of illness among children infected with norovirus and rotavirus, excluding children with coinfections. χ^2 and Cochran-Armitage trend tests were used to compare proportions of, that is, sex, having fever [100.4° F or not, dehydration, rehydration, and severity of Vesikari score (mild, moderate, and severe)], and Wilcoxon rank sum test was used for continuous variables, that is, age, greatest number of diarrhea and vomiting per day, length of hospital stay, Vesikari score, and death among rotavirus and norovirus positive patients. *P* values <0.05 were considered statistically significant.

RESULTS

During 48 months of hospital surveillance, 226,795 children less than 5 years of age were admitted to the pediatric wards of the 8 participating hospitals, of whom 22,203

(10%) were hospitalized with AGE. Clinical data and stool specimens were collected from 25% (5622/22,203) of children admitted with AGE. Nucleic acid was extracted from 18% (1008/5622) of these stool samples. Realtime RT-PCR testing identified norovirus RNA in the stools of 14% (137/1008) of the samples (Table 1). Extrapolation of norovirus testing results to the untested AGE cases yielded an estimated total of 3148 norovirus-associated AGE admissions. Thus, an estimated 1.3% (3148/226,795) of all pediatric admissions at participating hospitals was attributable to norovirus-associated AGE during 4 years of surveillance.

The vast majority (94%) of norovirus-associated hospitalizations were among children less than 2 years of age, with children in the 6–17 months age group accounting for three-fourths of cases (see Figure, Supplemental Digital Content 2, <http://links.lww.com/INF/E225>).

Norovirus was detected throughout the year with higher prevalence during the summer months (20%–38% from March to June) and winter months (9%–18% from November to January) and lower prevalence in the intervening months (3%–5%) (Figure 1).

The proportion of norovirus-positive specimens was significantly greater among rotavirus-negative AGE patients compared with rotavirus-positive AGE patients (27% vs. 5%, $P<0.001$) (see Table, Supplemental Digital Content 3, <http://links.lww.com/INF/E226>).

Median duration of illness was significantly longer among hospitalized children infected with rotavirus than norovirus (6 vs. 5 days, $P=0.001$). As measured by the Vesikari score, a similar proportion of norovirus and rotavirus positive AGE patients were considered severe (68% vs. 70%, $P=0.86$). Among the 3 children with AGE that died in the hospital after being enrolled in the study, 2 had rotavirus positive stool samples while the third was negative for both norovirus and rotavirus (Table 2).

The most common genotypes were GII.4 Sydney [P4 New Orleans] (36%), GII.3 [P16] (25%), and GII.4 Sydney [P16] (15%). In the first surveillance year, GII.3 [P16] and GII.4 Sydney [P31] were commonly identified. However, in the second and third years of surveillance, GII.4 Sydney [P4 New Orleans] was the most commonly identified genotype whereas the proportion of GII.3 [P16] was relatively low. In the fourth surveillance year, GII.3[P16] reemerged as the most frequently identified genotype (Figure 2).

DISCUSSION

This comprehensive surveillance in a national network of 8 geographically diverse hospitals clearly demonstrates the burden of norovirus AGE in Bangladeshi children. Norovirus was detected in approximately 1 in 7 children (14%) admitted with AGE to the tertiary care hospitals in our surveillance network. Previous studies showed slightly higher proportion of norovirus infection ranging from 19% to 28% of children seeking care in diarrhea treatment facilities of icddr.⁸ From 2010 to 2014, norovirus was detected in 25% of the hospitalizations due to gastroenteritis in urban Dhaka and rural MATLAB.⁷ Some of these differences might be attributable to secular changes in norovirus prevalence or due to methodological differences in the procedures for collection and testing of specimens among the various studies.

The age distribution of children with laboratory confirmed norovirus was in accordance with previous findings with the highest burden in children between 6 and 23 months of age.^{7,9,21} Although several epidemiologic studies have documented that noroviruses are present year-round in Bangladesh, slightly higher peak activity has typically been observed during March–April.^{7,15–18} Interestingly, rotavirus infections peak during the coldest months (November–March) of the year in Bangladesh.²²

Norovirus infected patients had typical clinical symptoms of severe acute gastroenteritis such as a high number of vomiting events (up to 18 times/day), diarrheal episodes (up to 40 times/day), severe dehydration (64%) and fever (40%). According to Vesikari score, the severity of norovirus AGE patients was similar to that of rotavirus AGE. These findings are different from previous studies in which norovirus AGE patients tended to have milder AGE symptoms.⁸

One in 5 norovirus positive children was coinfecting with rotavirus. The coinfection rate was similar to previous studies conducted among children less than 5 years of age, which shows 10% whereas our study showed 3% of coinfection rate (29/1008).²³ The fact that norovirus prevalence was significantly greater among children who tested negative for rotavirus compared with those that tested positive (27% vs. 5%, respectively) supports the etiologic role of norovirus in severe AGE. If norovirus was merely associated with asymptomatic carriage in the study population and not a causative agent of AGE, then 1 would expect that norovirus prevalence to be similar among children with and without concomitant detection of rotavirus, which is a well-known causative agent of severe childhood diarrhea. However, the fact that the prevalence of norovirus was significantly greater among those testing rotavirus-negative compared with those testing rotavirus-positive supports that the norovirus was likely the etiologic agent in a proportion of the rotavirus-negative AGE cases.

In previous studies among hospitalized diarrhea patients in Bangladesh, viruses from the 3 major genogroups (GI, GII, and GIV) were identified^{7,15–18} with GII.4 and GII.3 viruses as the most prevalent in children <2 years of age.⁷ Similarly, in our study, GII.3 and GII.4 viruses were the most frequently detected genotypes with some fluctuations in the predominant genotype each year.

This study has several limitations. No healthy control children were included which in previous studies has been shown could be as high as the prevalence in AGE cases,⁹ and we also did not test samples for other possible coinfections beyond rotavirus. The Global Enteric Multicenter Study (GEMS) study suggests that bacterial pathogens contribute a substantial burden of AGE among young children.¹² Resources permitting, future studies may consider testing for additional enteric pathogens in both cases and non-AGE controls, which would broaden our understanding of etiologic attribution.

In conclusion, norovirus causes a significant burden among children under 2 years of age hospitalized with AGE and GII.3 and GII.4 viruses cause the majority of these infections. Our findings provide important baseline data before rotavirus vaccine introduction to inform future impact assessments and subsequent changes to the etiology of severe pediatric AGE in Bangladesh. Additional studies, including longitudinal community-based studies and

hospital-based surveillance, that include all age groups will be necessary to understand the full spectrum of norovirus disease burden in Bangladesh.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGMENTS

We thank all the study participants for their time and support. We are also grateful to our implementation partner, surveillance hospital sites and The Institute of Epidemiology, Disease Control and Research (IEDCR) under the Ministry of Health and Family Welfare of Bangladesh Government. Our technical assistance partner, US Centers for Disease Control and Prevention (CDC). The views expressed herein are those of the author(s) and do not necessarily reflect the views of the US Agency for International Development or US Governments.

This work was supported by US Centers for Disease Control and Prevention (CDC); agreement no. 1U51GH001209-01. icddr;b is also grateful to the government of Bangladesh, Canada, Sweden, and the United kingdom for providing core/unrestricted support.

REFERENCES

1. Payne DC, Vinjé J, Szilagyi PG, et al. Norovirus and medically attended gastroenteritis in U.S. children. *N Engl J Med*. 2013;368:1121–1130. [PubMed: 23514289]
2. Puustinen L, Blazevic V, Salminen M, et al. Noroviruses as a major cause of acute gastroenteritis in children in Finland, 2009–2010. *Scand J Infect Dis*. 2011;43:804–808. [PubMed: 21696253]
3. Mattison CP, Cardemil CV, Hall AJ. Progress on norovirus vaccine research: public health considerations and future directions. *Expert Rev Vaccines*. 2018;17:773–784. [PubMed: 30092671]
4. Chhabra P, de Graaf M, Parra GI, et al. Updated classification of norovirus genogroups and genotypes. *J Gen Virol*. 2019;100:1393–1406. [PubMed: 31483239]
5. Lopman B, Vennema H, Kohli E, et al. Increase in viral gastroenteritis outbreaks in Europe and epidemic spread of new norovirus variant. *Lancet*. 2004;363:682–688. [PubMed: 15001325]
6. Siebenga JJ, Vennema H, Renckens B, et al. Epochal evolution of GGII.4 norovirus capsid proteins from 1995 to 2006. *J Virol*. 2007;81:9932–9941. [PubMed: 17609280]
7. Rahman M, Rahman R, Nahar S, et al. Norovirus diarrhea in Bangladesh, 2010–2014: prevalence, clinical features, and genotypes. *J Med Virol*. 2016;88:1742–1750. [PubMed: 27003679]
8. Nahar S, Afrad MH, Begum N, et al. High prevalence of noroviruses among hospitalized diarrheal patients in Bangladesh, 2011. *J Infect Dev Ctries*. 2013;7:892–896. [PubMed: 24240050]
9. Rahman M, Hassan Z, Nahar Z, et al. Molecular detection of noroviruses in hospitalized patients in Bangladesh. *Eur J Clin Microbiol Infect Dis*. 2010;29:937–945. [PubMed: 20467770]
10. Hossain ME, Rahman R, Ali SI, et al. Epidemiologic and genotypic distribution of noroviruses among children with acute diarrhea and healthy controls in a low-income rural setting. *Clin Infect Dis*. 2019;69:505–513. [PubMed: 30351379]
11. Platts-Mills JA, Liu J, Rogawski ET, et al. ; MAL-ED Network Investigators. Use of quantitative molecular diagnostic methods to assess the aetiology, burden, and clinical characteristics of diarrhoea in children in low-resource settings: a reanalysis of the MAL-ED cohort study. *Lancet Glob Health*. 2018;6:e1309–e1318. [PubMed: 30287127]
12. Kotloff KL, Nataro JP, Blackwelder WC, et al. Burden and aetiology of diarrhoeal disease in infants and young children in developing countries (the Global Enteric Multicenter Study, GEMS): a prospective, case-control study. *Lancet*. 2013;382:209–222. [PubMed: 23680352]
13. Satter SM, Gastanaduy PA, Islam K, et al. Hospital-based surveillance for rotavirus gastroenteritis among young children in Bangladesh: defining the potential impact of a rotavirus vaccine program. *Pediatr Infect Dis J*. 2017;36:168–172. [PubMed: 27798545]

14. World Health Organization. The treatment of diarrhoea. A manual for physicians and other senior health workers 2005. Available at: http://www.who.int/maternal_child_adolescent/documents/9241593180/en/. Accessed December 15, 2019.
15. Dey SK, Nguyen TA, Phan TG, et al. Molecular and epidemiological trend of norovirus associated gastroenteritis in Dhaka City, Bangladesh. *J Clin Virol*. 2007;40:218–223. [PubMed: 17881286]
16. Nahar S, Afrad MH, Fahmi T, et al. A novel norovirus recombinant strain GII.4/GII.21 in Bangladesh, 2011. *Virus Genes*. 2013;46:538–541. [PubMed: 23456827]
17. Nahar S, Afrad MH, Matthijnssens J, et al. Novel intergenotype human norovirus recombinant GII.16/GII.3 in Bangladesh. *Infect Genet Evol*. 2013;20:325–329. [PubMed: 24080167]
18. Rahman M, Nahar S, Afrad MH, et al. Norovirus variant GII.4/Sydney/2012, Bangladesh. *Emerg Infect Dis*. 2013;19:1347–1348. [PubMed: 23880583]
19. Cannon JL, Barclay L, Collins NR, et al. Genetic and epidemiologic trends of norovirus outbreaks in the United States from 2013 to 2016 demonstrated emergence of novel GII.4 recombinant viruses. *J Clin Microbiol*. 2017;55:2208–2221. [PubMed: 28490488]
20. Kageyama T, Kojima S, Shinohara M, et al. Broadly reactive and highly sensitive assay for Norwalk-like viruses based on real-time quantitative reverse transcription-PCR. *J Clin Microbiol*. 2003;41:1548–1557. [PubMed: 12682144]
21. Shioda K, Kambhampati A, Hall AJ, et al. Global age distribution of pediatric norovirus cases. *Vaccine*. 2015;33:4065–4068. [PubMed: 26051514]
22. Satter SM, Aliabadi N, Gastanaduy PA, et al. An update from hospital-based surveillance for rotavirus gastroenteritis among young children in Bangladesh, July 2012 to June 2017. *Vaccine*. 2018;36:7811–7815. [PubMed: 29793894]
23. Debbink K, Lindesmith LC, Donaldson EF, et al. Norovirus immunity and the great escape. *PLoS Pathog*. 2012;8:e1002921. [PubMed: 23093932]

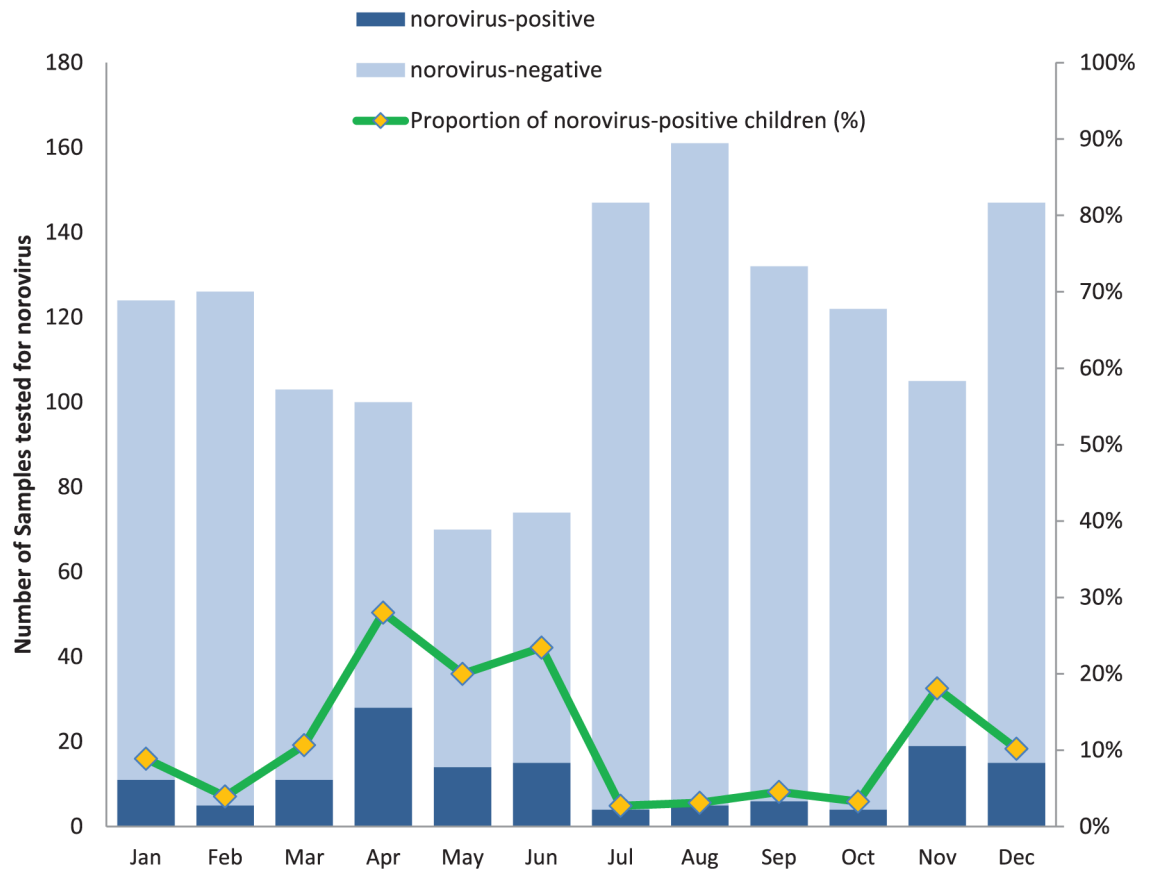


FIGURE 1. Seasonal fluctuations of norovirus gastroenteritis in hospitalized children younger than 5 years of age in Bangladesh, July 2012 to June 2016.

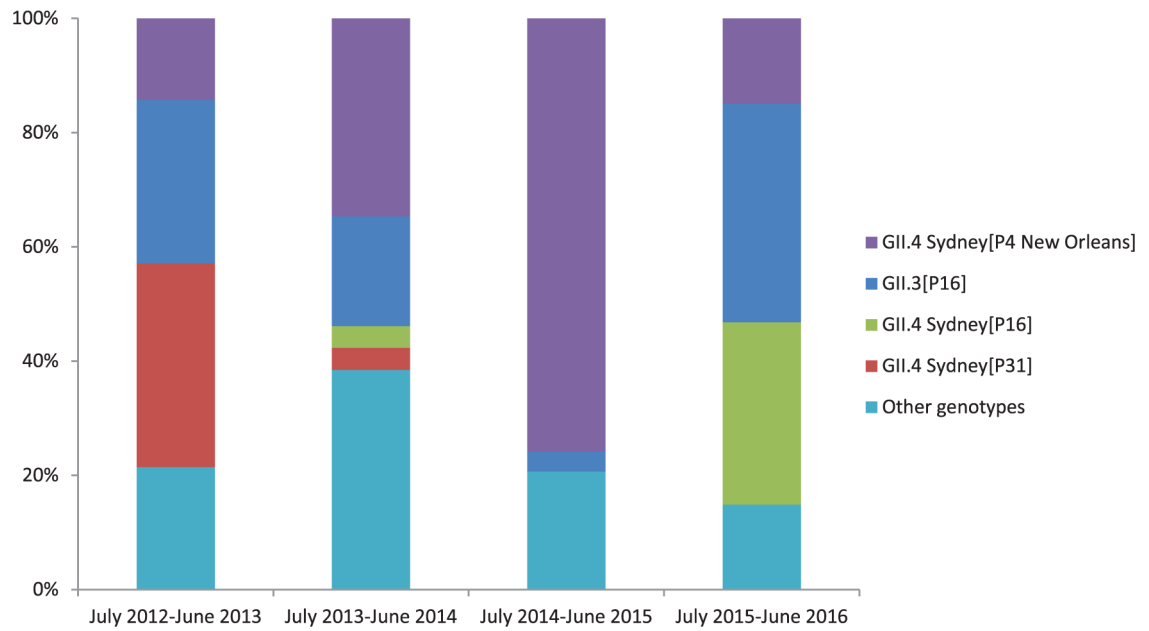


FIGURE 2. Distribution of norovirus polymerase and capsid genotypes detected in samples from hospitalized children <5 years of age with AGE, by season at 8 sentinel hospitals in Bangladesh, July 2012–June 2016.

TABLE 1.

Proportion of Diarrhea Hospitalizations Attributable to Norovirus Infection Among Children Younger Than 5 Years of Age, by Site, July 2012 to June 2016

Site	Surveillance Start Date	Total Number of Children Admitted for AGE	Number of Children Enrolled in AGE Surveillance	Number of Enrolled AGE Subjects Tested for Norovirus	Number (%) Norovirus Positive
Dhaka	July 2012	3195	797	144	20 (14)
Rajshahi	July 2012	6769	1687	301	43 (14)
Sylhet	July 2012	4215	1049	190	20 (11)
Dinajpur	February 2013	178	142	23	4 (17)
Chattogram	February 2013	1318	326	57	7 (12)
Jessore	August 2013	1851	456	82	13 (16)
Barisal	August 2013	4367	1090	196	28 (14)
Rangpur	January 2016	310	75	15	2 (13)
Total		22, 203	5622	1008	137(14)

TABLE 2.
Comparison of Clinical Characteristics in Children with Norovirus and Rotavirus Gastroenteritis

Characteristic	Norovirus Positive (n = 108)	Rotavirus Positive (n = 583)	P ^a
Age in mo (median, range)	12 (3–54)	10 (.6–36)	0.11
Number of episodes of vomiting per day, median (range)	5 (1–18)	5 (1–25)	0.48
Number of episodes of diarrhea per day, median (range)	18 (3–40)	18 (3–40)	0.79
Fever (< 100.4°F)	43 (40%)	290 (50%)	0.06
Duration of illness, in days median (range)	5 (1–12)	6 (2–23)	0.001
Dehydration			
None	39 (36%)	186 (32%)	0.39
Some	0	0	
Severe	69 (64%)	397 (68%)	
Rehydration			
Oral	89 (82%)	502 (86%)	0.32
Intravenous	69 (64%)	393 (67%)	0.48
Vesikari score ^b			
median (range)	11 (4–15)	12 (5–17)	0.30
Mild (<7)	13 (12%)	63 (11%)	0.86
Moderate (7–10)	22 (20%)	111 (19%)	
Severe(11)	73 (68%)	409 (70%)	
Death	0	2 (.34)	0.54

Data are no. (%) of children, unless otherwise indicated; median, range.

^aBy χ^2 or Cochran-Armitage trend tests, unless otherwise noted.

^bVesikari clinical severity scoring system.⁸