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Epidemiological Surveillance of Norovirus Diarrhea in Hospitalized Children with Acute Gastroenteritis in South of Iran

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ABSTRACT

Background: Noroviruses are one of the most common causes of acute diarrhea in both developed and developing countries. They are responsible for more than 50% of all gastroenteritis outbreaks around the world.
Objectives: This study was conducted to assess the prevalence, seasonality and clinical characteristics of norovirus infection in hospitalized Iranian children.
Patients and Methods: Between 2008 and 2010, a cross-sectional descriptive study was conducted on 375 stool samples from children under 7 years of age, who suffered from acute gastroenteritis and who were admitted to the Pediatrics Unit of the 17 Shahrivar Hospital in the city of Borazjan. Acute gastroenteritis was defined as > 3 loose watery stools every 24 hours. All the stool specimens were tested for norovirus antigens with enzyme immunoassays (EIA). Demographic and clinical data were analyzed using SPSS software.
Results: Of the total collected samples, noroviruses were detected in 47 out of 375 (12.53%). The highest infection rate was among children under two years of age (76.6%) (P = 0.001). Diarrhea (95.74%), vomiting (87.23%) and fever (82.98%) were the most frequently reported clinical symptoms in children with norovirus gastroenteritis. The highest prevalence of the virus was observed in autumn (63.83%) and the lowest in summer (6.38%) (P = 0.015).
Conclusions: Regarding the emergence of noroviruses as a relevant cause of acute diarrhea in Iranian children, there is a great need to introduce a routine norovirus testing of hospitalized patients with gastroenteritis, particularly in children under 2 years old during the cold season.

Keywords: Epidemiology; Norovirus; Gastroenteritis; Iran

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Implication for health policy/practice/research/medical education:
This study improves our knowledge about the significance of noroviral gastroenteritis among hospitalized children in south of Iran.

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1. Background

Noroviruses are a group of non-enveloped, single-stranded RNA viruses classified into the genus Norovirus of the family *Caliciviridae* (1). Recent studies have demonstrated that noroviruses are the second most frequent causative agents of viral diarrhea in young children after rotaviruses (2-4). A systematic review of 31 community, outpatient, and hospital-based studies estimated that noroviruses accounted for 10 to 15% of acute gastroenteritis episodes in children less than 5 years old in both developed and developing countries (5). Current estimates of annual global childhood mortality associated with norovirus infections are up to 200,000 deaths (5, 6).

The clinical symptoms of norovirus gastroenteritis are characterized by acute onset, non-bloody diarrhea, vomiting, nausea and abdominal cramps (1). These characteristics are the same as those observed in patients with rotavirus gastroenteritis (7, 8). Studies have shown that outbreaks of norovirus infections occur throughout the year, although there is a seasonal pattern of increased infection rates during the winter months (9-11). Despite the importance of norovirus infections in child morbidity and mortality rates in developing countries, very few studies have investigated the prevalence of norovirus gastroenteritis among hospitalized Iranian children with acute gastroenteritis (12-14).

2. Objectives

The present study aimed at assessing the frequency of norovirus infections in hospitalized children under 7 years old with acute gastroenteritis in Borazjan, Iran. In addition, we examined the age and seasonal distribution, as well as the clinical manifestations associated with norovirus in the same patient population.

3. Patients and Methods

From October 2008 to September 2010, a cross sectional descriptive study was conducted on 375 stool samples collected from hospitalized children under 7 years old with acute, sporadic gastroenteritis in the 17 Shahrivar Hospital in Borazjan City. Acute gastroenteritis was defined as >3 loose watery stools every 24 hours. All the fecal specimens were collected within 24 hours of admission. These specimens were sent to the virology laboratory of the Bushehr University of Medical Science and stored at -70°C until the time of assay.

In our study, patients were removed from the described patient population if they showed symptoms of gastroenteritis with a duration of more than 7 days, antibiotic treatment before diagnosis, or confirmed bacterial diarrhea. Demographic (age and sex) and clinical data (days of hospitalization, diarrhea, vomiting, fever, convulsions, abdominal cramps and severity of dehydration) were collected for each case by using a standard structured questionnaire.

According to the WHO's recommendation, all the children with gastroenteritis were classified in specific age groups (e.g. 0-2, 3-5, 6-8, 9-11, 12-17, 18-23, months) so that age-specific incidence rates of hospitalization can be calculated (15). All the fecal specimens were tested for the presence of the norovirus antigen by using the commercially available enzyme immunoassay (EIA) kit (IDEIA™ Norovirus EIA, Oxoid, Ely, United Kingdom), according to the manufacturer's instructions.

Data was statistically analyzed using SPSS version 17 (SPSS Inc., Chicago, IL, USA). Also, $\chi 2$ test was used to analyze the data obtained for the age groups, sex and seasonal distribution of the noroviruses. Fisher's exact test was used to analyze the clinical symptoms. P value < 0.05 was considered as statistically significant. The study was approved by the Research Ethical Committee of the Medical University of Bushehr.

4. Results

Noroviruses were detected in 47 (12.53%) of all the evaluated stool samples. The distribution of gender in norovirus positive cases was 26 (55.32%) in males and 21 (44.68%) in females (P = 0.08) (*Table 1*). All the patients with acute diarrhea had ages between 1 and 83 months with a median age of 22 months. Children less than 24 months of age accounted for 76.6% of the infected patients, with those children who were between 12 and 17 months of age being the most affected (29.78%) (*P* = 0.001).

Table 1. Distribution of Age Groups in Children With Norovirus Gastroenteritis

Age Groups, Mo	Norovirus Group (n= 47), No.	Non-norovirus Group (n = 328), No.	Global Number (n= 375), No.
0-2	-	6 (1.83)	6 (1.6)
3-5	7 (14.89)	32 (9.76)	39 (10.4)
6-8	5 (10.64)	40 (12.19)	45 (12.0)
9-11	9 (19.15)	39 (11.89)	48 (12.8)
12-17	14 (29.78)	75 (22.87)	89 (23.73)
18-23	3 (6.38)	37 (11.28)	40 (10.67)
24-35	4 (8.52)	30 (9.15)	34 (9.07)
36-47	2 (4.25)	27 (8.23)	29 (7.73)
48-60	2 (4.25)	14 (4.27)	16 (4.27)
61-83	1 (2.13)	28 (8.54)	29 (7.73)

The highest prevalence of noroviruses (63.83%) was identified in autumn, while the corresponding prevalences in winter, spring and summer were 17.02%, 12.77% and 6.38%, respectively ($P = 0.015$). *Figure 1* shows the monthly distribution of noroviruses in patients with acute diarrhea.

The survey of clinical symptoms showed that diarrhea, vomiting and fever were present in 95.74%, 87.23% and 82.98% of all patients with norovirus infections (*Table 2*). In terms of severity of dehydration, moderate dehydration with 55.32% was the most common type among children with gastroenteritis.

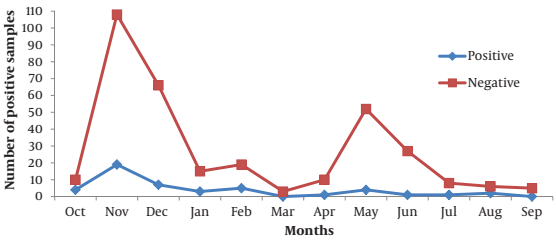

Figure 1. Monthly Distribution of Norovirus Gastroenteritis Among Children Less Than 7 Years

Table 2. Distribution of Clinical Manifestation in Children With Norovirus Gastroenteritis

Norovirus Group (n= 47)	Non-norovirus Group (n = 328)	Global Number (n= 375)	P value	Clinical symptoms
Diarrhea	45 (95.74)	269 (82.01)	314 (83.73)	0.534
Vomiting	41 (87.23)	139 (42.38)	180 (48.0)	0.316
Abdominal pain	27 (57.45)	152 (46.34)	179 (47.73)	0.118
Convulsion	-	10 (3.05)	10 (2.66)	0.427
Fever	39 (82.98)	86 (26.22)	125 (33.33)	0.04
Dehydration severity				
Severe	15 (31.91)	47 (14.33)	62 (16.53)	0.153
Moderate	26 (55.32)	173 (52.74)	199 (53.07)	0.728
Mild	6 (12.77)	108 (32.93)	114 (30.4)	0.06

5. Discussion

Despite considerable advances in current public health services and hygiene control, diarrhea still remains a potential risk to human health, especially in infants and young children worldwide (16). Recently, many studies have demonstrated the importance of noroviruses as one of the most common leading causes of viral epidemic diarrhea in both developed and developing countries (17-19). In our study, the incidence of noroviruses (12.53%) is in agreement with those reported in previous studies in Iran (13, 14) and in other countries (10, 17, 18).

The occurrence of norovirus infections that were observed in the first 24 months of life (76.6%) is greater than in the older age groups, as also found in studies conducted in Spain (10), Taiwan (11) and Vietnam (20). The high frequency of norovirus in this age group indicates that children under 2 years of age, are at greatest risk for developing acute gastroenteritis from norovirus. Norovirus positive cases were detected in males more often than in females, as was found in other investigations (9, 21).

In the present study, norovirus-induced gastroenteritis episodes were observed during the whole year, with the exception of March and September. We also observed a peak wave from November through December. These results are consistent with previous studies that have identified the highest prevalence of norovirus infection during the cold months of the year (11, 13, 19, 21). In the current study, most commonly reported symptoms were diarrhea, vomiting and fever. These findings are in accordance with those studies conducted in Iran (14), Spain (10), Hungary (9) and Venezuela (22).

Because of some limitations in sensitivity and specificity, EIA cannot be a considered as a reliable method for the detection of the infectious pathogens in stool samples. In recent years, molecular methods have rapidly found their way into virological studies. Generally, different studies have considered the PCRs as specific and sensitive techniques used to detect enteric viruses, such as norovirus and rotavirus, in samples (23). For this reason, we suggest using PCRs methods to assess the presence of noroviruses in upcoming surveillance studies.

One limitation of the current study is that the true frequency of norovirus infections could be higher than estimated in the present study (12.53%), because only hospitalized children with moderate to severe gastroenteritis were included, and the proportion of norovirus infections in children with only home care or outpatient visits has not been evaluated. Another possible limitation is that the results in this study may not be representative for all 0 to 7-year-old Iranian children. Since we identified the prevalence of norovirus-induced gastroenteritis

from only one city in Iran, in order to have a comprehensive picture of the disease burden of noroviruses in this country, it is necessary to conduct the same studies in other regions of Iran.

In conclusion, our results provide information on the epidemiology and the prevalence of noroviruses in children with acute gastroenteritis in Borazjan, a city in the south of Iran. We conclude that noroviruses are frequent causes of acute sporadic gastroenteritis, requiring the hospitalization of Iranian children under 7 years of age. It affects mainly children who are less than 2 years old and is more predominant during the cold seasons. Regarding the emergence of noroviruses as a relevant cause of acute diarrhea in Iranian children, there is a great need to introduce routine norovirus testing among hospitalized children with gastroenteritis in order to recognize the real disease burden of viral intestinal infections in the Iranian child population.

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Authors' Contribution

None declared.

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None declared.

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