

The Incidence of Norovirus, Rotavirus and Adenovirus in Children with Acute Gastroenteritis

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Objective: To investigate the incidence of norovirus, rotavirus and adenovirus in children who presented to the pediatric emergency service with acute diarrhea.

Material and Method: One hundred and twenty-six children among 164 patients who presented to our pediatric emergency department with diarrhea, and gave stool samples between October 2012 and February 2013 were enrolled in the study. Stool samples were analysed for norovirus, rotavirus and adenovirus. The association among frequency, duration of diarrhea, and vomiting, body temperature, age, causative factors of diarrhea, and clinical severity of the disease was evaluated.

Results: Rotavirus, adenovirus, and norovirus were identified in 18.2% (n=23), 10.3% (n=13), and 8.7% (n=11) of the patients, respectively. These three causative agent of diarrhea were most frequently seen in children between 1-5 years of age. Norovirus was more frequent in younger children. Rotavirus infection was more common in January, whereas adenovirus and norovirus were detected in December and January. Any statistically significant difference was not found among three agents of diarrhea in terms of disease severity. However, patients with adenovirus related diarrhea had a higher clinical disease severity score.

Conclusion: In our country rotavirus, adenovirus antijen screening tests are easily performed, however rapid and reliable diagnostic tests for norovirus should be used prevalently. Studies aiming at applicability, and effectiveness of rotavirus vaccination should be conducted

Keywords: Acute viral gastroenteritis, norovirus, rotavirus and adenovirus

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Akut Gastroenteritli Çocuklarda Norovirüs, Rotavirüs ve Adenovirüs Sıklığı

Amaç: Acil çocuk polikliniğine başvuran akut ishallerde çocuklarda rotavirüs, nörovirüs ve adenovirüs sıklığı araştırıldı.

Gereç ve Yöntem: Ekim 2012-Ocak 2013 döneminde, Çocuk Acil Polikliniğine ishalle başvuran, 164 hastadan dışkı örneği alınabilen 126 hasta çalışma grubunu oluşturdu. ELISA yöntemiyle üç virüs tipinin belirlenmesi çalışıldı. Hastaların ishal sayısı ve süresi, kusma sayısı ve süresi ateş düzeyi, ishal etkenlerinin düzeyi ve yaş ile klinik ağırlık arasındaki ilişki değerlendirildi.

Bulgular: Hastaların 23'ünde (%18,2) rotavirüs, 13'ünde (%10,3) adenovirüs, 11'inde (%8,7) ise norovirüs pozitif saptandı. Üç ishal etkeninin de en çok görüldüğü yaş dilimi 1-5'ti. Norovirüs daha küçük yaş grubunda tespit edildi. Rotavirüs enfeksiyonu ocak ayında en fazla görülürken adenovirüs ve norovirüs hem aralık hem de ocak ayında saptandı. Üç ishal etkeninin de klinik ağırlık skorlamasında istatistiksel olarak anlamlı farklılık saptanmadı. Buna karşın adenovirüsün klinik skorlaması daha yüksekti.

Sonuç: Ülkemizde rotavirüs, adenovirüs antijen taramaları kolaylıkla yapılırken norovirüs için hızlı güvenilir tanı tekniklerinin yaygınlaşması gerekmektedir. Rotavirüs aşısının uygulanabilirliğini arttırmaya ve aşısının etkinliğine yönelik çalışmalar yapılmalıdır.

Anahtar kelimeler: Akut viral gastroenterit, norovirüs, rotavirüs ve adenovirüs

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INTRODUCTION

Acute gastroenteritis (AGE) is a common disorder that affects children worldwide. Approximately 179 million episodes of AGE occur each year and result in 600.000 hospitalizations and 5.000 deaths^(1,2).

A specific etiology is attributed to only 20% of AGE cases, although viruses are recognized as the most frequently known agents ^(1,3). Rotavirus, norovirus and adenovirus have been reported as the most common viral pathogens of acute gastroenteritis in children.

Rotaviruses are the most common causes of viral gastroenteritis in children under 5 years of age. Rotavirus gastroenteritis is more frequently observed in winter months under temperate climate conditions ⁽⁴⁾.

Noroviruses are now recognized as the leading cause of epidemics of gastroenteritis and an important cause of sporadic gastroenteritis among children. Norovirus associated AGE is characterized by the sudden onset of intense vomiting and dehydrating diarrhea, typically lasting 1 to 3 days, with high rates of transmission among people of all ages ⁽⁵⁾. Recently, many reports have established the importance of norovirus as a cause of outbreaks.

Enteric adenovirus types 40 and 41 can also cause AGE. The prevalence rate of adenovirus gastroenteritis is not as high as rotavirus or norovirus infections, however it is still very important to monitor these infections for epidemiologic and surveillance studies. Enteric adenoviruses have been related to AGE in variable frequency (ranging from 1.4 to 10%), depending on the geographic setting ⁽⁶⁾.

We investigated the incidence of norovirus, rotavirus and adenovirus in children with the diagnosis of AGE admitted to emergency room of pediatrics.

MATERIAL and METHODS

One hundred and twenty- six children, between 0-18 years of age who had been admitted to our department due to the community- acquired acute viral gastroenteritis between October 2012 and February 2013 were enrolled in the study. Acute viral gastroenteritis was defined as abrupt onset of diarrhea (three or more episodes of watery stools a day) and/or vomiting with or without fever. Informed consents were obtained from both parents. Patients with underlying chronic disorders, diarrhea with confirmed bacterial and parasitic etiologies and the ones with symptoms lasting more than 15 days were excluded.

Patients were divided into 5 subgroups according to age of presentation (0-6 months, 6-12 months, 12-60 months, 60 months - 12 years and >12 years). The severity of gastrointestinal symptoms was evaluated according to Ruuska and Vesikari scoring system ⁽⁷⁾. Rotavirus immunization status of participants was also recorded. For each child, stool samples were collected within 24 hours of admission. Fresh fecal specimens were analysed for rotavirus, norovirus and adenovirus by ELISA kits (R-Biopharm RIDASCREEN, Germany).

Statistical analysis was performed with SPSS program version 21.0. Kruskal-Wallis non-parametric tests were used for evaluation of clinical scoring. The number of variables was given as percentages of descriptive statistics. The study was approved by the Research Ethical Committee of Istanbul University Faculty of Medicine (File no:2009/1914).

RESULTS

One hundred and twenty- six children (68 male, 54%) between the ages of 2-216 months (median 56 months) were enrolled in the study. Viral antigens [rotavirus (n=23, 18.2%), adenovirus (n=15, 10.3%) and norovirus (n=11, 8.7%)] were detected in 40.4% of all specimens (Figure 1). Coinfection (rotavirus and adenovirus) was identified in 2 (1.6%) patients. Four percent of the patients with rotavirus- associated diarrhea had history of rotavirus vaccination.

The incidence of rotavirus, enteric adenovirus and norovirus infections were higher in children between the ages of 12-60 months. The median ages of rotavirus, enteric adenovirus and norovirus infected patients were 53.8 months, 55.1 months and 34.4 months, respectively (Figure 2). The incidence of rotavirus

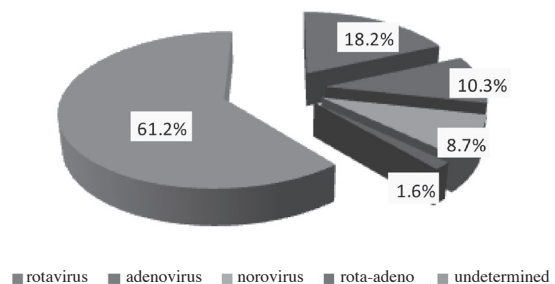


Figure 1. The distribution of viral diarrhea agents.

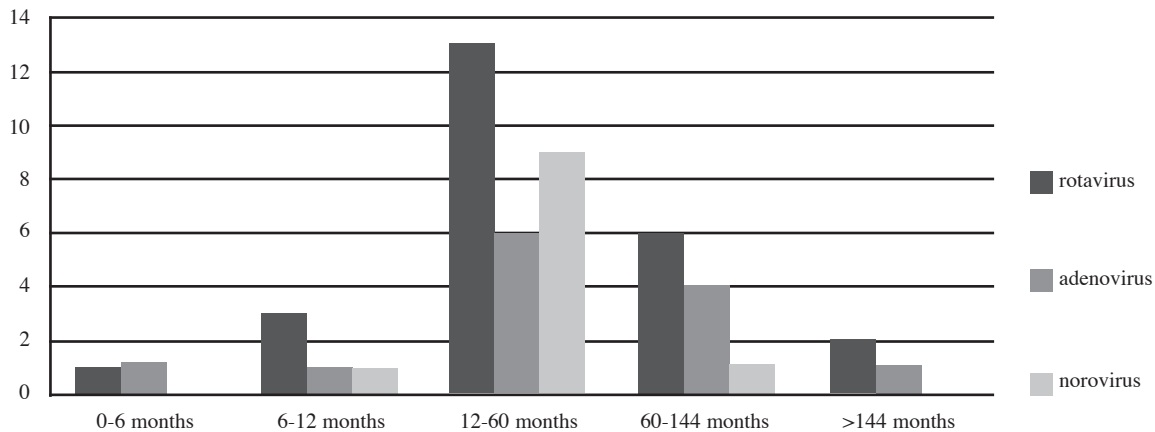


Figure 2. Age distribution of diarrhea agents.

Table 1. Clinical manifestations of rotavirus, adenovirus and norovirus positive cases.

	Rotavirus	Adenovirus	Norovirus	All patients
Fever				
<37 °C	15 (60%)	7 (53.7%)	6 (54%)	73 (57.9%)
37.1 °C-38.4 °C	5 (20%)	5 (38.5%)	5 (46%)	35 (27.8%)
>38.4 °C	5 (20%)	1 (7.7%)	-	18 (14.3%)
Duration of fever (day)				
1	7 (28%)	2 (15.4%)	3 (27.3%)	21 (39.8%)
2	1 (4%)	3 (23.1%)	2 (18.2%)	13 (24.5%)
3-5	2 (8%)	1 (7.7%)	-	19 (35.8%)
Diarrhea (episodes/day)				
1-3	4 (16%)	5 (33.3%)	9 (81.8%)	44 (34.9%)
4-5	8 (32%)	8 (53.3%)	2 (18.3%)	35 (27.8%)
>5	13 (52%)	2 (13.4%)	-	47 (37.3%)
Vomiting (episodes/day)				
1	3 (12%)	3 (20%)	8 (72.7%)	46 (36.5%)
2-4	7 (28%)	9 (60%)	3 (27.3%)	53 (42.1%)
>4	15 (60%)	3 (20%)	-	27 (21.4%)
Abdominal pain				
mild	19 (76%)	10 (77%)	11 (100%)	92 (73%)
moderate	6 (24%)	3 (13%)	-	28 (22.2%)
severe	-	-	-	6 (4.8%)

related diarrhea was highest in January (56%), while adenovirus and norovirus infections were observed more often during December and January.

All of the patients had vomiting and diarrhea. Other clinical symptoms were abdominal pain (58.7%), fever (42.1%), joint pain (9.5%), rash (6.3%), tenesmus (6.3%) and confusion (3.2 %). Fever at the time of presentation was ≥ 38.5 °C in 18 patients (14.2%), between 37.1-38.4 °C in 35 patients (27.8%) whereas 73 patients (57.9%) were admitted without fever. The duration of fever was ≤ 24 hours in 21 patients (39.8%), ≤ 48 hours in 13 patients (24.5%) and between 2-5 days in 19 patients (35.8%). The degree of fever was lower and the duration was shorter in patients with norovirus related diarrhea.

The patients had 1-3 (n=44; 34.9%), 4-5 (n=35; 27.8%) or more than 5 (n=47; 37.3 %) diarrheic episodes a day. Diarrhea lasted for 1-4 days in majority of the patients (n=110, 87.3%). Vomiting accompanied diarrhea once (n=46; 36.5%), 2-4 (n=53; 36.5%), and more than 4 times (n=27: 21.4%) a day (Table 1).

The patients were interpreted as having mild (n=21, 16.7%), moderate (n=82, 65.1%) and severe (n=23, 18.3%) diarrhea according to Ruuska-Vesikari clinical scoring system, which evaluates the combination of parameters such as diarrhea, vomiting, fever and dehydration (Table 2).

Table 2. Ruuska-Vesikari clinical severity scores of patients

	Clinical Severity Scores			Total	P:0.68
	Mild	Moderate	Severe		
Rotavirus (% , n)	16% (4)	72% (18)	12% (3)	25	
Adenovirus (% , n)	7.7% (1)	69.2% (9)	23.1% (3)	13	
Norovirus (% , n)	9.1% (1)	72.7% (8)	18.2% (2)	11	
Rotavirus-adenovirus (% , n)	-	50% (1)	50% (1)	2	
All patients (% , n)	16.7% (21)	65.1% (82)	18.3% (23)	126	

DISCUSSION

The frequency of viral gastroenteritis has been gradually increasing especially in developing countries due to better diagnostic modalities. Rotavirus, which was detected in 18.2% of the patients in our study, is an important etiologic agent of acute gastroenteritis throughout the winter months in our region. Previous studies in other developing countries showed similar results as rotavirus being the responsible agent in 35.4% of the gastroenteritis cases in Taiwan⁽⁸⁾, 43.8% in Germany⁽⁹⁾, 16.3% in Japan⁽¹⁰⁾ and 22.5% in Tunis⁽¹¹⁾. In our country, rotavirus infection rates in diarrheal children vary between 13.7% and 41%^(12,13). Other viral agents like adenovirus and norovirus were detected in 10.3% and 8.7% of the children, respectively. Norovirus was reported as the second most common cause of viral diarrhea in several studies⁽⁸⁻¹¹⁾. However, there is no reliable study regarding the prevalence of norovirus infection in our country. Only a pilot study reported the incidence of norovirus as 17% among hospitalized patients⁽¹⁴⁾. Enteric adenovirus infection rates in acute gastroenteritis vary between 4.3% and 17% in our region. In our study, adenovirus was detected as the second most common cause of viral diarrhea.

Acute viral gastroenteritis is very frequent especially in children under 5 years of age. Chen et al⁽⁸⁾ reported that viral agents were more common in children younger than 3 years⁽⁸⁾. Similarly, in a report from our country, Gultepe et al⁽¹³⁾ found that most cases were below 2 years of age. In our study, rotavirus and adenovirus were common in all age groups of children although most of these cases were between 1-5 years of age. Nakanishia et al⁽¹⁰⁾ reported the median age of children as 46 months in their study. In our study, median ages of children were 53 months, 55 months and 34 months for rotavirus, adenovirus and

norovirus infections, respectively. Norovirus- associated diarrhea occurred most commonly in younger patients.

An extensive surveillance study by Huh et al. revealed that several viral etiologies present peak incidences in different months due to climatic conditions⁽¹⁵⁾. In our study, the incidence of rotavirus- related diarrhea was highest in January (56%), while adenovirus and norovirus infections were observed more often during December and January. These results are similar to those found in many other studies reported from our country⁽¹⁶⁾.

Characteristics and differences in gastroenteritis-related symptoms caused by the most common observed pathogens have been investigated in scarce number of studies. The differentiation of rotavirus and non-rotavirus- associated diarrhea possesses particular importance. Rotavirus infections are known to be more severe and more often associated with a complicated course. Similar results were also found by other investigators such as Chen et al. in Taiwan⁽⁸⁾ and Wiegeling et al. in Germany⁽⁹⁾. In these studies, it is mentioned that, although vomiting was more frequently observed with norovirus infections, the symptoms were relatively milder. In our study, adenovirus infections presented with higher severity scores. According to our observation, rotavirus related infections had higher degree and longer duration of fever with more severe abdominal pain whereas norovirus -related diarrhea generally had a self- limited course. But the differences between these etiological agents as for clinical presentations were not statistically significant.

National rotavirus vaccination programme has not yet been conducted in our country. However, according to recent World Health Organization recommen-

ditions, the introduction of this vaccination in routine practice is being considered ⁽¹⁷⁾. In our study, rotavirus vaccination rate was 20% among children less than five years of age. As shown from our study rotavirus is still being the leading cause of viral gastroenteritis. Introduction of rotavirus vaccines for Extended Program on Immunization could significantly reduce the number of diarrheal cases.

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