



A Retrospective Analysis of Rotavirus and Adenovirus Infections in Pediatric Population Admitted to Emergency Department with Acute Gastroenteritis

Akut Gastroenteritle Acile Başvuran Pediatrik Popülasyonda Rotavirüs ve Adenovirüs Enfeksiyonlarının Retrospektif Analizi

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Abstract

Objective: Acute gastroenteritis (AGE) is a frequent reason of morbidity and mortality in children in both developed and underdeveloped countries. It is mostly caused by infectious agents which differ according to age groups and seasons. We aimed to review the frequency, and the age, gender, season of admission, characteristics and rate of hospitalization of rotavirus and adenovirus infections in pediatric population admitted to emergency department with AGE in which stool analysis was performed.

Material and Methods: The records of 5526 patients aged between 0-16 years who were admitted to pediatric emergency unit with AGE in a year and in which stool analysis were performed were reviewed. Frequency of rotavirus and adenovirus cases, gender and age distribution and hospitalization data were analyzed.

Results: A total of 5526 patients with AGE, 2303 females and 3223 males, with a mean age of 5.21 ± 3.40 were included. Adenovirus was detected in 3.1% and rotavirus was detected in 22.4% of all cases. There were no significant differences between genders in adenovirus and rotavirus cases. Rotavirus infection was significantly high in children aged between 7 months-2 years and 3-6 years while adenovirus infection rate was similar in all age groups except adolescence. Rotavirus detection was significantly higher in winter months whereas adenovirus infections are seen throughout the year. Among rotavirus cases (n= 1240); 344 (27.7%) patients were taken under observation and 73 (5.9%) patients were hospitalized. For adenovirus cases (n= 169); 50 (29.6%) patients were taken under observation and 10 (5.9%) patients were hospitalized.

Özet

Giriş: Akut ishaller, gelişmiş ve gelişmekte olan ülkelerde çocuklarda morbidite ve mortalitenin sık görülen nedenlerindedir. Çoğunlukla yaş gruplarına ve mevsimlere göre farklılıklar gösteren enfeksiyöz ajanlar tarafından oluşturulur. Biz bu çalışmada Çocuk Acil Polikliniğimize akut gastroenterit nedeniyle gelen ve gaita tahlili yapılan pediatrik hasta grubunda rotavirüs ve adenovirüs sıklığını, bu enfeksiyonlar için mevsim, cinsiyet, yaş özelliklerini ve gözleme alınma, hastaneye yatış üzerine etkilerini araştırmayı amaçladık.

Gereç ve Yöntemler: Çalışmamıza 0-16 yaş grubunda, akut gastroenterit şikayeti ile bir yılda Çocuk Acil'e başvuran ve gaita tahlili yapılmış olan 5526 hasta alındı. Tüm olgularda rotavirüs varlığı, adenovirüs varlığı, yaş, cinsiyet, geliş mevsimi, gözleme alınma ve hastaneye yatış durumlarına ait bilgiler analiz edildi.

Bulgular: Çalışmamıza ortalama yaşları 5.21 ± 3.40 olan, 2303'ü kız, 3223'ü erkek, toplam 5526 akut gastroenteritli olgu alınmıştır. Tüm olguların %3.1'inde adenovirüs, %22.4'ünde rotavirüs etken olarak saptanmıştır. Adenovirüs ve rotavirüs saptanan olgularda cinsiyet anlamlı bulunmamıştır. Yaş gruplarına bakıldığında rotavirüsün en sık 7 ay-2 yaş ve 3-6 yaş dönemi çocuklarında, adenovirüsün ise adolesan dönemi hariç eşit oranda görüldüğü saptanmıştır. Rotavirüs enfeksiyonlarının kışın daha sık, adenovirüs enfeksiyonlarının ise yıl boyunca görüldüğü saptanmıştır. Rotavirüs olguları (n= 1240) içinde; 344 (27.7%) hasta gözleme alınmış ve 73 (5.9%) hasta hospitalize edilmiştir. Adenovirüs ol-

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Conclusion: Our study consists of a remarkable number of patients. Rotavirus has a seasonal pattern and is more frequent in younger children and requires more hospitalization. Describing the characteristics of the infections may help to eliminate unnecessary tests and inappropriate diagnoses especially in emergency settings.

Keywords: Adenovirus, rotavirus, acute gastroenteritis, hospitalization, child

Introduction

Acute gastroenteritis is one of the common important infectious diseases which causes epidemics all over the world and in Turkey as well. Gastroenteritis causes mortality and morbidity during childhood (1,2). Viral factors are the most frequent causes of acute gastroenteritis in children under five years of age (1,3). Rotaviruses are the main agents for gastroenteritis in children under five years of age in our country and all around the world and they are followed by enteric adenoviruses (2,4,5). Rotaviruses and enteric adenoviruses cause 150 million acute infectious gastroenteritis attacks and approximately 800.000 deaths in the world each year. In literature, the incidence of acute infectious gastroenteritis caused by rotaviruses is reported as 1% to 8% in industrialized and developed countries, while this rate is reported as 2% to 31% in developing countries (1,2,6). In a study conducted in the Southeastern Anatolia region of Turkey, it was reported that rotavirus frequency is 16.7% and adenovirus frequency is 1.0% in children with gastroenteritis under five years of age (2). Rotaviruses are responsible for 30% to 50% of severe diarrhea cases in children and approximately one-third of hospitalizations (1,6). Moreover, severe dehydration related to diarrhea and vomiting caused by rotaviruses are important mortality reasons. Adenoviruses cause 3% to 5% of all infectious diseases in children in 2-4 age group and they are known as the second most frequent reason for infantile gastroenteritis (7,8). Among rotaviruses, which are classified as serogroups from A to G, Group A rotaviruses are of epidemiological importance (1). A limited number of adenovirus strains caused childhood diarrhea, only two different adenovirus serotypes were determined in stools of children with gastroenteritis as type 40 and type 41. Enteric adenovirus 40/41 is responsible for 4%-10% of the hospitalized and ambulatory pediatric diarrhea cases (9). Although rotavirus infections may occur in every month of the year they are more common in cooler months and especially in winter (1).

Electron microscopy (EM), immune EM, cell culture, enzyme-based immunological methods (EIA, ELISA), latex ag-

gluları (n= 169) içinde ise 50 (29.6%) hasta gözleme alınmış ve 10 (5.9%) hospitalize edilmiştir.

Sonuç: Çalışmamız oldukça yüksek sayıda hastayı kapsamaktadır. Rotavirüsün mevsimsel paterni vardır, süt çocuklarında daha sıktır ve hastaneye yatışa daha çok gerek duyulur. Akut gastroenterit etkenleri hakkında yeterli epidemiyolojik bilgi sahibi olunursa uygulanmakta olan birçok gereksiz tetkik ve antibiyotik tedavisinden kaçınılmasının mümkün olabileceği görülmektedir.

Anahtar Kelimeler: Adenovirüs, rotavirüs, akut gastroenterit, hospitalizasyon, çocuk

glutination (LA) and polymerase chain reaction (PCR) based methods are used in the diagnosis of gastroenteritis viruses (10).

It is beneficial to directly indicate the virus with EM which is a traditional method; however, the references are restricted to laboratories. Cell cultures are not recommended in the diagnosis of these viruses since they are time-consuming and technically inconvenient (1).

Therefore, direct antigen tests are most commonly preferred in the routine diagnosis nowadays. Rotavirus antigens are quickly detected from the stool with commercial ELISA and LA kits in most laboratories (11). There are sensitive and specific commercial EIA tests in which monoclonal antibodies are used to indicate adenovirus and astrovirus from the stool (12).

The aim of this study is to identify the frequencies of rotavirus and adenovirus antigen using the ELISA method in the stool samples of children with acute diarrhea and to examine the risk factors associated with viral agents in terms of age, gender and season.

Materials and Methods

This single-center study was conducted in a general tertiary state hospital. Patients are admitted to the hospital without a referral chain. The Department of Pediatrics has 40 beds and receives a large number of patients with low socioeconomic status. The records of acute gastroenteritis cases caused by rotavirus and adenovirus were reviewed retrospectively. A total of 5526 pediatric patients aged 0-16 years who were admitted to Hospital Pediatric Emergency Unit in 12 months (April 2011-April 2012) with acute gastroenteritis were included in this study. Age group, gender, season of admittance and the Rotavirus and EIA antigen test results in fresh stool specimens were analyzed. It was considered that December, January and February are in Winter; March, April and May are in Spring; June, July and August are in Summer and September, October and November are in Autumn.

The children were divided into 5 groups according to their ages as 0-6 months, 7 months-2 years, 3 to 6 years, 7 to 12 years and 13 to 16 years. AGE is defined as presence of diarrhea, which is ≥ 3 loose in 24 hours, with or without vomiting and having a duration of less than 7 days (9).

The cases in which acute gastroenteritis was considered a stool analysis was conducted and adenovirus and/or rotavirus were identified. The children with a diagnosis of rotavirus or adenovirus who were taken under observation in the pediatric emergency department or hospitalized in the pediatric clinic of the hospital were compared.

In stool specimens, rotavirus and adenovirus antigens were identified with RIDA Quick combi-strip Test.

The study was approved by the Hospital Ethics Committee on the 05.06.2012 with the project number 2012/35.

Statistical Analysis

The variables of the study were evaluated by statistical analyses. Tests of normality, the chi-square test; the Mann-Whitney U test and the Wilcoxon test were used where necessary. The descriptive statistical methods (average, standard deviation and frequency) were used while evaluating the data. The results were evaluated at 95% confidence interval and $p < 0.05$ significance level.

Results

For 5526 patients, who were admitted to the pediatric emergency unit with acute diarrhea, stool analysis were conducted. Due to AGE 1586 patients were taken under observation in the emergency unit and 348 patients were hospitalized. Rotavirus was identified in 1240 (22.4%) patients and adenovirus was identified in 169 (3.1%) patients.

The Seasonal Distribution of Rotavirus-Adenovirus Cases

The seasonal admissions of the patients and the rotavirus and adenovirus detection rates are indicated in Table 1 and Table 2. The number of stool samples of admitted patients with

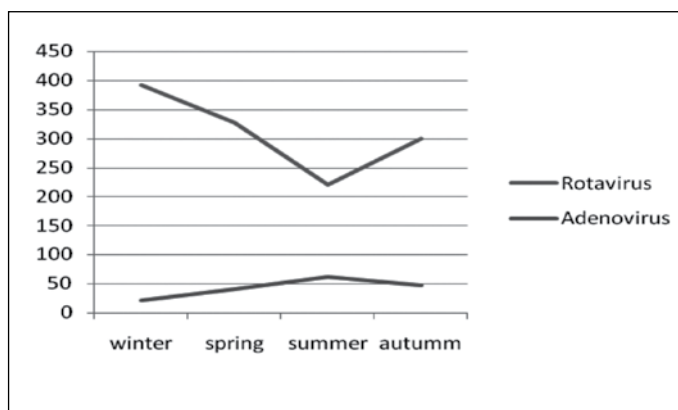


Figure 1. The seasonal distribution of rotavirus (n= 1240) and adenovirus (n= 169) cases in a year.

* Rotavirus cases were (n= 1240,100%); 31.6% in winter; 26.4% in spring; 17.8% in summer and 24.2% in autumn. Adenovirus cases were (n= 169, 100%); 12.4% in winter, 23.7% in spring; 36.1% in summer and 27.8% in autumn.

acute gastroenteritis and the rate of rotavirus detection in gastroenteritis were significantly higher in winter months ($p= 0.001$). The number of stool samples of gastroenteritis cases and the rate of rotavirus detection in gastroenteritis were significantly lower in summer months ($p= 0.001$) (Table 1).

The number of stool samples and the rate of adenovirus detection due to gastroenteritis were significantly lower in winter months ($p= 0.004$). The number of stool samples and the rate of adenovirus detection due to gastroenteritis were significantly higher in summer months ($p= 0.003$) (Table 2).

Among rotavirus cases; the rate of patients in winter months was significantly high, 31.6% (392/1240) ($p= 0.001$). In summer months, the rate of patients was 17.8% (221/1240) and it was significantly lower than the rates of rotavirus in the other seasons (Figure 1) ($p= 0.001$).

Among adenovirus cases, the rate of patients in summer months was significantly high, 36.1% (61/169) ($p= 0.001$). In winter months, the rate of patients was 12.4% (21/169) and significantly lower than the rates of adenovirus in the other seasons (Figure 1) ($p= 0.001$).

Table 1. The distribution of rotavirus according to seasons among acute gastroenteritis cases

Seasons	Acute gastroenteritis cases (AGE) (n)	Rotavirus cases (n)	Rotavirus cases among AGE cases; (%)	p
Spring	1394	370	23.5	0.05
Summer	1458	221	15.2	0.001
Autumn	1478	300	20.3	0.005
Winter	1196	392	32.8	0.001
Total	5526	1240	22.4	

Table 2. The distribution of adenovirus according to seasons among acute gastroenteritis cases

Seasons	Acute gastroenteritis cases (AGE) (n)	Adenovirus cases (n)	Adenovirus cases among AGE cases; (%)	p
Spring	1394	40	2.9	0.05
Summer	1458	61	4.2	0.003
Autumn	1478	47	3.2	0.006
Winter	1196	21	1.8	0.004
Total	5526	169	3.1	

Table 3. The age distribution of the cases of rotavirus

Age groups	Acute gastroenteritis cases (AGE) (n)	Rotavirus cases (n)	Rotavirus cases among AGE cases; (%)	p
0-6 months	370	71	19.2	0.056
7 months-2 years	1804	465	25.8	0.001
3-6 years	2003	539	26.9	0.001
7-12 years	1044	136	13	0.063
13-16 years	305	29	9.5	0.001
Total	5526	1240	22.4	

Table 4. The age distribution of the cases of adenovirus

Age groups	Acute gastroenteritis cases (AGE) (n)	Adenovirus cases (n)	Adenovirus cases among AGE cases; (%)	p
0-6 months	370	14	3.8	0.063
7 months-2 years	1804	63	3.5	0.056
3-6 years	2003	66	3.3	0.067
7-12 years	1044	23	2.2	0.057
13-16 years	305	3	1	0.001
Total	5526	169	3.1	

The Gender Distribution of Rotavirus-Adenovirus Cases

Among 5526 patients who were admitted to the pediatric emergency unit within a year, who were considered to have acute gastroenteritis and the stool analysis were conducted, 2303 (41.7%) were female and 3223 (58.3%) were male.

Among rotavirus cases (n= 1240); 544 (44%) were female and 694 (56%) were male. No significant difference was identified between females and males regarding gender when they were evaluated in terms of the presence of rotavirus (p= 0.056).

Among adenovirus cases (n= 169); 82 (48.5%) were female and 87 (51.5%) were male. There was no significant difference

in terms of gender among the cases in whom adenovirus was detected (p= 0.067).

The Age Distribution of Rotavirus-Adenovirus Cases

The number of admissions according to age groups of 5526 patients and the distribution of rotavirus and adenovirus in the stool samples are presented in Table 3 and Table 4.

The rate of rotavirus in 7 months-2 years children group is 25.8% and it is 26.9 % in 3-6 years age group, it was significantly higher than the rates of rotavirus in the other age groups (p= 0.001). The rate of rotavirus was 9.5% in 13-16 years age group and it was significantly lower than the other age groups (p= 0.001) (Table 3).

Adenovirus was significantly lower in 13-16 years age group than the other age groups (p= 0.001) and there was no significant difference between the other age groups (Table 4).

The Observation and Hospitalization Rates of Rotavirus-Adenovirus Cases

Among the patients in which rotavirus was detected within a year 344/1240 (27.7%) of them were taken under obser-

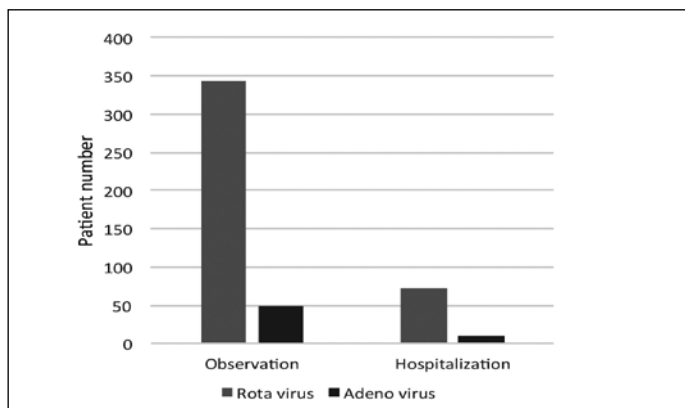


Figure 2. The rotavirus and adenovirus cases which were under observation or were hospitalized.

vation and 73/1240 (5.9%) patients were hospitalized.

Due to AGE, 1586 patients were taken under observation in the emergency unit and 348 patients were hospitalized. The rate of hospitalization and observation for both viruses are presented in Figure 2.

Among the patients in which adenovirus was detected within a year 50/169 (29.6%) were taken under observation and 10/169(5.9%) patients were hospitalized for treatment.

In the relationship between age and hospitalization in the patients in which rotavirus and adenovirus were detected, it was observed that the rate of hospitalization due to rotavirus is the highest in the 7 months-2 years age group. As the age increased, the rate of hospitalization decreased. The relationship between age and hospitalization is presented in Table 5. There was no significant relationship between hospitalization due to rotavirus and age (p= 0.074).

The rate of hospitalization due to adenovirus was the highest in 7 to12 years age group. As the age increased, the rate of hospitalization decreased. The relationship of age and hospitalization is presented in Table 6. There was no significant relationship between hospitalization due to adenovirus and age (p= 0.73).

Table 5. The relationship of hospitalization due to rotavirus and age

Age groups	n	Hospitalized patients (n)	% *	p
0-6 months	71	1	1.4	0.074
7 months-2 years	465	34	7.3	
3-6 years	539	28	5.2	
7-12 years	136	6	4.4	
13-16 years	29	4	3.8	
Total	1240	73	5.9	

* Hospitalized rotavirus cases among all hospitalized cases due to AGE.

Table 6. The relationship of hospitalization due to adenovirus and age

Age groups	n	Hospitalized patients (n)	%*	p
0-6 months	14	0	0.0	0.73
7 months-2 years	63	5	7.9	
3-6 years	66	3	4.5	
7-12 years	23	2	8.7	
13-16 years	3	0	0.0	
Total	169	10	5.9	

* Hospitalized adenovirus cases among all hospitalized cases due to AGE.

Discussion

In this retrospective study, we investigated the demographic features of 5526 children who were admitted to the pediatric emergency unit of our hospital for acute gastroenteritis and in which presence of rotavirus and adenovirus were found positive. Acute gastroenteritis is an infectious disease affecting children, which is seen often both in underdeveloped and developed countries of the world. In studies investigating the etiology of gastroenteritis, information about the clinical and demographic features of the patients with viral infections are obtained. Viral infections may be treated by symptom management and viral etiologies at certain ages and seasons are needed to be considered especially at emergency units.

Frequency

In one year, in children aged from 0 to 16 years, rotavirus was detected in 1240 children (22.4%) while adenovirus was detected in 169 children (3.1%) of all cases which is similar with reported studies. Izuddin et al, have detected rotavirus as the most frequent agent (22%) followed by bacteriologic agents in their study consisting of 393 pediatric cases with acute gastroenteritis in a year (13). Fodha et al, have found rotavirus (20%) as the most common infectious agent for viral gastroenteritis followed by astrovirus (7%) and adenovirus (6%) (14).

In a recent study in Turkey, rotavirus antigens were present in 797 samples (17.0%), adenovirus antigens were present in 113 samples (2.4%) (15). Both adenovirus and rotavirus were detected in 28.3% of 1154 cases in a retrospective study in Turkey. Frequency was 73.7% for rotavirus and was 26.2% for adenovirus (16).

In recent literature, norovirus is also reported to be frequent in acute gastroenteritis cases. In a multicenter Chinese five-year surveillance study in children up to 5 years of age, the most common pathogen was rotavirus(29.7%) followed by norovirus (11.8%). Adenovirus was detected in 4.8% of cases in 32.189 samples throughout 4 years (17). In Japanese pediatric patients with acute gastroenteritis, 2381 stool specimens were tested in 4 years and norovirus was detected mostly (39.3%) followed by rotavirus (20.1%) (18). Chen et al., detected viral agents in 1055 (37.5%) of 2810 subjects with AGE, with rotavirus (21.2%) being the leading cause of disease, followed by norovirus (14.9%) (19).

In a retrospective analysis of acute gastroenteritis in children in Turkey, the detection rate reported for rotavirus, norovirus and adenovirus were 12.7% (75/588), 9.8% (51/520) and 4.9% (28/575), respectively and it is claimed that norovirus is the leading pathogen in 0-2 years and rotavirus is most frequent pathogen in 2-5 years and > 5 years (20). In another

recent study in Turkey, in children with AGE the viral agents were detected in 54.6% of 240 samples; norovirus and rotavirus were the most common agents (21).

Adenovirus, norovirus and rotavirus were identified in 20.8%, 20.3% and 21.6% of reviewed cases of pediatric diarrhoea in Sydney (22). After rotavirus vaccinations have become frequent detection rates for norovirus may have increased. Jin et al, claimed that due to effective rotaviral vaccination the most common cause of acute pediatric viral gastroenteritis had changed from rotavirus to norovirus (23). Reports about norovirus may have increased due to the utilization of the detection tests for norovirus.

Seasonal Pattern

In our study among all 5526 patients, rotavirus was mostly detected in winter (32.8%) and in spring (23.5%). We observed a slight increase in adenovirus cases in summer. A seasonal variation for rotavirus infection in early spring and adenovirus infection in late summer was observed in a recent study (23). Rotavirus cases were found to be more frequent in the first four months of the year (20). Lee et al have detected rotavirus in winter the most in their two-center study in Malasia (24). In China, rotavirus was observed mostly in winter in children under 5 years of age (17). A seasonal pattern was observed for rotavirus however adenovirus was detected throughout the year without an association with a particular season (15,19,22,25).

Filho et al. have reported that in children between 0-5 years adenovirus had a low prevalence throughout the year and slightly increased in late summer and early autumn (26). Rotavirus had its peaks in the cooler months and had the lowest rates in warm months in another study (22).

Gender

In our study among all 5526 patients, rotavirus was 56% positive in males and 44% positive in females whereas adenovirus was detected in 51.5% males and 48.5% in females. Rotavirus and adenovirus detection rates according to sex were not different in our study group.

Rotavirus immunization was reported to be a protective factor against rotavirus infections. Rotavirus and norovirus are the 2 most important viral agents of childhood AGE in Taiwan with partial rotavirus immunization (19).

Age Factor

In our study, when we grouped the 5526 patients according to the age groups, rotavirus was the most frequently observed infectious agent between 3-6 years (26.9%; 539/2003) and 7 months-2 years (25.8%; 465/1804) similar to other reported studies in literature. Frequency of adenovirus was 3.5% (63/1804) in 7 months-2 years and 3.3% (66/2003) in 3-6 years of age. Rotavirus was detected mostly (57.1%) under 2

years in a study conducted in Turkey (16). Rotavirus was frequently present between 6-12 months (55.9%) in a Congolese study conducted in children less than 60 months (27). It was reported that the prevalence for rotavirus was highest in 12 to 24 months old (28.6 %) children and prevalence for adenovirus was 12.0-13.8 % of children over 6 months (25).

Hospitalization

In our study, overall 1586 (28.7%) children with AGE were taken under medical observation in the emergency department for viral infection. Medical observation was needed for 344 cases of rotavirus, the rate was the highest in summer (42%) even higher than the winter in which rotavirus infection has been detected the most. For adenovirus cases medical observation rate was 29.6% (n= 50) and among them school age children were the most (39.1%). In adenovirus infections no seasonal change was not observed.

In China, in 3147 hospitalized children there was a seasonal variation for rotavirus. Rotavirus infection made peaks in November (33.7 %) and December (31.3 %). Adenovirus was detected throughout the year with no seasonal pattern (25).

In our study, 348 patients were hospitalized for further treatment. The hospitalized rotavirus cases were 21% and were mostly in 0-2 years (46.6%) and were hospitalized mostly in summer (34.2%). Hospitalization rate for adenovirus cases was 5.9% and there were not any seasonal changes. School age patients were hospitalized mostly (8.7%).

There was no difference between the decisions to be taken under observation in the emergency unit due to rotavirus (27.7%) and adenovirus (29.6%) infections.

In our study, rotavirus cases needed more hospitalization (21%) than adenovirus cases (5.9%) because the clinical status of the patients needed closer monitoring. Similar to our study, in 3147 hospitalized children, rotavirus was positive for 22% of cases while adenovirus was positive for 10.3% cases in China (25). Also in a recent review, it is concluded that a common cause of diarrhea in children in both developed and developing countries is rotavirus and rotavirus diarrhea may be cost-effectively prevented by rotavirus vaccination (28).

In our study for rotavirus cases, the hospitalization rate for 0-6 months age group was lower than the rate for 13-16 years age group. Breastfeeding may be an important factor in this result as in a systematic review it has been suggested that exclusive breastfeeding throughout first 6 months of infancy is beneficial in prevention of Rotavirus diarrhea among children (29).

After vaccinations for rotavirus have been in practice there are epidemiologic variations. In our country at the time of the data, rotavirus vaccination was not frequent. Rotavirus vaccination is a recommended vaccination in our country.

Limitations of the study

This study is retrospective and the subgroups of rotavirus and adenovirus have not been analyzed. Prospective studies to detect the regional subgroup analyses of especially rotavirus are needed for vaccination procedures.

Conclusion

In this study, frequency of presence of rotavirus and adenovirus in cases with AGE in a year and risk factors associated with rotavirus and adenovirus were evaluated. Our study consists of a remarkable number of patients. Among these huge number of AGE cases, we have found rotavirus and adenovirus as the most frequent causes. Rotavirus has a seasonal pattern, is more frequent in younger children and requires more hospitalization. Describing the characteristics of the infections may help to eliminate unnecessary tests and inappropriate diagnoses.

Ethics Committee Approval: The study was approved by the Hospital Ethics Committee on the 05.06.2012 with the project number 2012/35.

Informed Consent: Patient consent was not received since this required archival studies.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – MÇ, ME; Design – ME, ÖY; Supervision - ME, ÖY, DK; Data Collection and/or Processing - MÇ; Analysis and/or Interpretation – MÇ, ME, DK; Literature Review – MÇ, DK; Writing – MÇ, DK, ME; Critical Review - All authors.

Conflict of Interest: The authors have not reported a conflict of interest.

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