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Frequency of Rotavirus and Adenovirus in Children with Diarrhea

İshal Şikayeti ile Hastaneye Başvuran Çocuklarda Rotavirus ve Adenovirus Sıklığı

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Abstract

Aim: The aim of this study is retrospective evaluation of the frequency of rotavirus and adenovirus in stool, and their distribution according to gender, age and seasons in children with diarrhea admitted at outpatients or hospitalized in our hospital.

Material and Method: Stool samples of patients aged between 0-18 years received at the Medical Microbiology Laboratory between2021–2022 were evaluated for rotavirus–adenovirus. Rotavirus and adenovirus antigens were determined qualitatively by immunochromatographic cassette test method. Chi-square test was used in the statistical analysis.

Results: A total of 1148 stool samples of pediatric patients were received by our laboratory during these two years for rotavirus and adenovirus antigen test. Of 1148 patients, 8.6% were positive for rotavirus, 5.1% for adenovirus, and 0.6% for both rotavirus and adenovirus antigens. Rotavirus and adenovirus was positive in 7.2% and 5.6% of males, respectively, and 10.6% and 4.5% of females, and there were no statistically significant differences. Rotavirus was most frequently found in the age group 3-5 years (11.6%) and adenovirus was most frequently found in the age group 6-9 years (8.4%), with no significant difference. Rotavirus was most frequently detected in spring (12.9%) while adenovirus was found most frequently in winter (8.1%), without significant differences. Antigen positivity was 4.1% and 4.9% in outpatients for rotavirus and adenovirus, respectively, and 15.1% and 5.5% in hospitalized patients. Rotavirus positivity was significantly higher in hospitalized patients than outpatients, and adenovirus positivity did not show a significant difference.

Conclusion: We found that rotavirus and adenovirus were significant agents causing diarrhea in children, especially those younger than 5 years old, and that its frequency increased in winter and spring, and as rotavirus is a cause of hospitalization, implementation of rotavirus vaccine into routine vaccination programs seem to be beneficial for patients.

Keywords: Rotavirus, adenovirus, diarrhea, children

Öz

Amaç: Bu çalışmada, hastanemize ishal şikayetiyle ayaktan başvuran ya da yatış yapılan çocuk hastalarda rotavirus ve adenovirus sıklığının belirlenmesi, cinsiyet, yaş ve mevsimlere göre dağılımının retrospektif olarak irdelenmesi amaçlanmıştır.

Gereç ve Yöntem: Tıbbi Mikrobiyoloji Laboratuvarına, 2021-2022 tarihleri arasında gelen, 0-18 yaş aralığındaki hastalara ait gaita örnekleri rotavirus-adenovirus açısından değerlendirildi. Rotavirus ve adenovirus antijenleri immünokromatografik kaset test yöntemi ile kalitatif olarak saptanmıştır. İstatistiksel analizde Ki-Kare testi kullanıldı.

Bulgular: İki yıllık sürede rotavirus ve adenovirus antijen testi birlikte istenen toplam 1148 çocuk hastaya ait gaita numunesi laboratuvarımıza ulaşmıştır. 1148 hastanın %8,6'sında rotavirus, %5.1'inde adenovirus, %0,6'sında hem rotavirus hem de adenovirus antijeni pozitif saptanmıştır. Rotavirus ve adenovirus pozitifliği erkeklerde %7.2 ve %5.6, kızlarda %10,6 ve %4,5 oranında saptanmış, istatistiksel olarak anlamlı fark bulunmamıştır. Rotavirus en sık 3-5 yaş (%11,6), adenovirus ise 6-9 yaş (%8,4) grubunda tespit edilmiş, istatistiksel olarak anlamlı fark saptanmamıştır. Rotavirus en sık ilkbaharda (%12,9) saptanırken adenovirus kış (%8,1) aylarında tespit edilmiş, istatistiksel olarak anlamlı fark bulunmamıştır. Antijen pozitiflik oranı rotavirus ve adenovirus için sırasıyla ayaktan hastalarda %4,1 ve %4,9, yatan hastalarda %15,1 ve %5,5 olarak tespit edilmiştir. Rotavirus pozitiflik oranı yatan hastalarda ayaktan hastalara göre istatistiksel olarak anlamlı yüksek bulunmuş, adenovirus için iki grup arasında istatistiksel olarak anlamlı fark saptanmamıştır.

Sonuç: Çalışmamızda çocuklarda, özellikle beş yaşın altında, rotavirus ve adenovirusun önemli birer ishal etkeni olduğu, kış ve ilkbahar aylarında sıklıklarının arttığı, rotavirusun hastaneye yatışlara neden olduğu için aşısının rutin aşılama programına dahil edilmesinin hasta yararına olacağı tespit edilmiştir.

Anahtar Kelimeler: Rotavirus, adenovirus, ishal, çocuklar

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INTRODUCTION

Inflammation of the stomach and intestines due to various causes is termed acute gastroenteritis. Most frequent symptoms of acute gastroenteritis include diarrhea, nausea, vomiting, fever and abdominal pain. Diarrhea is the second most frequent cause of death globally among children younger than 5 years of age. While a considerable number of deaths occur especially in developing countries, diarrhea is still an important cause of death and public health problem in developed countries. Acute diarrhea is caused by viral, bacterial, parasitic or fungal agents. Most important agents causing serious gastroenteritis in especially in children are viruses (75-90%). Determination of the frequency of viral etiology is important both for avoiding unnecessary use of antibiotics and also for implementation of preventive measures.[1-7]

Rotavirus is the most frequent agent causing diarrhea especially among children younger than 5 years of age globally. Rotavirus infections are seen more frequently during winter in milder climates. Rotavirus infects especially children, while causing a mild illness in adults. The cause of less frequent rotavirus gastroenteritis in adults may be antibodies developed against rotavirus in 95% of children during rotavirus infections in the first 5 years of life. Implementation of necessary hygienic conditions in the hospitals and childcare facilities is especially important for avoidance of infection transmission. Orally administered vaccines against rotavirus infections are very important in fighting gastroenteritis. Considerable decreases were obtained in hospitalizations due to rotaviral diarrhea with the use of these vaccines. While many countries have included rotavirus vaccination in their national vaccination programs, this is not yet present in our routine vaccination program of our country.[2,4,6,8,9]

Adenovirus is the second most frequent cause of diarrhea in children after rotavirus, and unlike rotavirus, it may cause diarrhea in children during the whole year. Infections are most commonly seen in children younger than 2 years old. Symptoms are milder than those seen in rotavirus infections, but the duration of infection is longer.[10]

Fast and accurate detection of diarrhea causes is important for the clinical course and effective treatment. Determination of antigen in stool samples with immunochromatographic method is frequently used in routine diagnosis in gastroenteritis due to rotavirus and adenovirus. A quick result obtained in a short time such as 5-10 minutes, ease of use in the laboratory and low cost are among factors for preferring this test.[11,12]

Our aim in this study was to determine retrospectively the frequency of rotavirus and adenovirus in outpatients or patients, aged between 0-18, hospitalized at our hospital with a complaint of diarrhea, and investigate the distribution of pathogens according to gender, age and seasons.

MATERIAL AND METHOD

The study was carried out with the permission of Tekirdag Dr. I. Fehmi Cumalıoglu City Hospital Clinical Investigations Ethics Committee (Date:14.04.2023, Decision No: 35). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Stool samples of patients aged between 0-18 years received between January 2021 – December 2022 at the Medical Microbiology Laboratory were evaluated in terms of rotavirus–adenovirus. When more than one sample was received from the same patient, only the first sample was included. Samples evaluated for both adenovirus and rotavirus were included, and those that were only evaluated for one agent was excluded.

Rotavirus and adenovirus antigens were determined qualitatively by immunochromatographic cassette test in which specific antibodies were used. Rotavirus–Adenovirus Combo Rapid Cassette Test (CITEST DIAGNOSTICS INC, CANADA) kit was used according to the manufacturer's instructions. This is a rapid test where a colored line occurs at the test site in 10 minutes as a result of the reaction of antigen-antibody complex. Presence of these colored lines at the test line means positive result, while absence of them means a negative one. A colored line is seen, showing that an appropriate amount of sample is put on the control line region, and membrane wicking is done. The manufacturer have reported that sensitivity and specifity of the test is 97.3% and 97.1% for rotavirus, and 95.2% and >97.7% for adenovirus.

Demographic data on patients age, gender and seasonal distribution was obtained from the hospital's automation system, and evaluated retrospectively.

Statistical Analysis

Statistical analysis of the data obtained was evaluated by SPSS 22.0 (SPSS Inc, Chicago, IL, USA). Categorical data was presented as percent. Chi-square test was used in the comparison of independent groups with categorical variables. P values below 0.05 were considered as a statistically significant.

RESULTS

A total of 1148 stool samples of pediatric patients were received by our laboratory during these two years for rotavirus and adenovirus antigen test. Demographic data of these patients included 657 males (57.2%) and 491 females (42.8%), with a mean age ± standard deviation of 3.41 ± 4.04 years. There was no significant differences between the patients in terms of gender ($p>0.05$).

Rotavirus antigen was positive in 99 of 1148 patients (8.6%), and adenovirus was positive in 59 (5.1%). Both rotavirus and adenovirus antigens were positive in 7 patients (0.6%). Rotavirus and adenovirus was positive in 7.2% and 5.6% in males, 10.6% and 4.5% of females, and there were no

statistically significant differences (p=0.323 for rotavirus and p=0.756 for adenovirus). Rotavirus was most frequently found in the age group 3-5 years (11.6%), which was followed by 1-2 years (11.2%), and adenovirus was most frequently found in the age group 6-9 years (8.4%) and 1-2 years (6.3%). There was no significant difference between the age groups for both agents in terms of frequency of presence (p=0.219 for rotavirus and p=0.209 for adenovirus) (**Table 1**).

Table 1. Distribution of rotavirus and adenovirus antigen positivity according to age groups

Age	Patients	Rotavirus positive		p value	Adenovirus positive		p value
	n	n	%		n	%	
0 year	331	16	4.8	0.219	13	3.9	0.209
1-2 years	304	34	11.2		19	6.3	
3-5 years	251	29	11.6		13	5.2	
6-9 years	154	15	9.7		13	8.4	
10-17 years	108	5	4.6		1	0.9	
Total	1148	99	8.6		59	5.1	

In the evaluation of distribution of antigen positivity according to seasons, rotavirus was most frequently detected in spring (12.9%) and winter (12.2%) while adenovirus was found most frequently in winter (8.1%) and autumn (5.4%) (**Figure 1**). There were no significant differences in terms of antigen positivity and season relationship (p=0.086 for rotavirus, and p=0.400 for adenovirus) (**Table 2**).

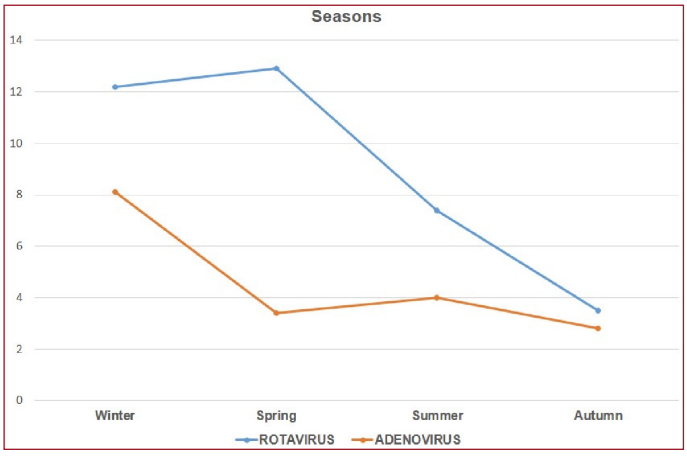

Figure 1. Distribution of rotavirus and adenovirus antigen positivity according to seasons

Table 2. Distribution of rotavirus and adenovirus antigen positivity according to seasons (n/%)

Season	Patients	Rotavirus positive		p value	Adenovirus positive		p value
	n	n	%		n	%	
Winter	246	30	12.2	0.086	20	8.1	0.400
Spring	263	34	12.9		9	3.4	
Summer	324	24	7.4		13	4.0	
Autumn	315	11	3.5		17	5.4	
TOTAL	1148	99	8.6		59	5.1	

When the 1148 patients were grouped according to outpatients and hospitalized patients, 677 (59.0%) were outpatients and 471 (41.0%) were hospitalized ones (clinics / intensive care unit). Antigen positivity was 4.1% and 4.9% in outpatients for rotavirus and adenovirus, respectively, and 15.1% and 5.5% in hospitalized patients. Rotavirus positivity was significantly higher in hospitalized patients than outpatients, and adenovirus positivity did not show a significant difference (p=0.008 for rotavirus, and p=0.756 for adenovirus) (**Table 3**).

Table 3. Distribution of rotavirus and adenovirus antigen positivity according to clinics (n/%)

Clinic	Patients	Rotavirus positive		p value	Adenovirus positive		p value
	n	n	%		n	%	
Outpatients	677	28	4.1	0.008	33	4.9	0.756
Hospitalized patients	471	71	15.1		26	5.5	
TOTAL	1148	99	8.6		59	5.1	

DISCUSSION

Rotavirus and adenovirus are important acute gastroenteritis agents among children younger than 5 years old worldwide.[13,14] While the frequency of these two agents differ between countries and cities, rotavirus is most frequently found as viral gastroenteritis causes, with adenovirus in the second place.[15,16] There are many studies on the frequency of rotavirus and adenovirus presence in stool from Turkey and other countries worldwide. In studies of foreign countries, rotavirus frequency is reported as 11-71% and adenovirus frequency as 2-22.2% while in studies from Turkey showed a frequency of rotavirus infections as 8.1-39.8%, and adenovirus infections as 1.8-15%.[17-19] We evaluated children aged between 0-18 years, and found the frequency of rotavirus presence as 8.6%, frequency of adenovirus as 5.1%, with a higher frequency of rotavirus in comparison with adenovirus, similar to other studies in the literature.

Tokak et al.[20] have found rotavirus frequency as 10.7%, adenovirus frequency as 3.3% in patients with a working diagnosis of acute gastroenteritis, with a significant difference in rotavirus frequency (9.8% in males, 11.7% in female patients), but not in adenovirus frequency. Rotavirus was more frequently found in female patients, and adenovirus was more frequent in males in our study, but there was no significant differences in terms of genders.

In a study evaluating 517 stool samples in Senegal, rotavirus positivity was 6.9%, adenovirus positivity was 3.1%, and co-infection rate was reported as 1.9%. Prevalences of rotavirus and adenovirus were found to be 12.2% and 4.8%, respectively, in children aged between 0-12 months. In an evaluation of seasonal distribution, rotavirus was more frequently detected during September (12.3%) and February (14.9%), while adenovirus was more frequently detected between June-December.[6]

In a study from Poland, where stool samples of 1411 patients aged between 1 month–5 years hospitalized at the Pediatric Gastroenterology Section due to acute gastroenteritis, rotavirus infections were found to be significantly more frequent during winter and spring months, while adenovirus infections were not found to show a significant relationship with seasons.[9]

In a study from the eastern part of Turkey (Siirt), stool samples of 16689 patients were evaluated, in whom rotavirus was positive in 13.6%, adenovirus was positive in 4.9%, and 0.5% was positive for both rotavirus and adenovirus. Rotavirus was most frequently detected in autumn, adenovirus was most frequently detected in summer, and the difference was found to be significant. In the evaluation of positivity rate of viral antigen according to age groups, rotavirus positivity rate was the highest one in 13-24 months age group with 19.6%, and adenovirus positivity rate was the highest one in 3-5 years age group with 5.5%. Also, 89.7% of patients positive for rotavirus and 83.8% of patients positive for adenovirus were found to be younger than 5 years.[10]

In two separate studies from Inner Anatolia Region, Bayrak et al.[1] have found rotavirus positive in stool samples in 25.8% of pediatric patients, and these patients were most frequently (28.6%) at breastfeeding age, and during spring months (34.9%). Sert et al.[21] have found rotavirus positive in 4.7%, and adenovirus positive in 9.1% of stool samples of 1960 patients with a diagnosis of acute gastroenteritis in Konya city, both rotavirus and adenovirus were most frequently found in the age group 1 month–2 years, rotavirus was most frequently detected in winter months, and adenovirus is detected in spring months.

Gür Vural et al.[22] have rotavirus positivity in 8.9% and adenovirus positivity in 4.4% in 5294 stool samples sent to the Microbiology Laboratory with a diagnosis of acute gastroenteritis in Black Sea Region (Samsun). Rotavirus positivity was most frequent between 13-24 months and 2-5 years, in spring and winter months; and adenovirus positivity was most frequent in 2-5 years and over 18 years, in winter and summer months.

Aydın et al.[7] have detected the most frequent rotavirus positivity in 2-3 years and 4-5 years age groups, and the most frequent adenovirus positivity in 12-18 years age group and those younger than 1 year in their study from Aegean Region (Kutahya). In the evaluation of patient distribution according to seasons, adenovirus was most frequently detected in fall, and rotavirus was most frequently detected in winter, spring and summer.

When we evaluated age and antigen positivity in our study, rotavirus was detected most frequently in 3-5 years age group (11.6%), which was followed by 1-2 years (11.2%), and that 79 of 99 patients found to be positive was in the 0-5 years age group. Adenovirus was most frequently detected in 6-9 years (8.4%) and 1-2 years (6.3%), and 45 of 59 positive patients were in 0-5 years age group. Although there were no significant differences between the age groups for these two agents in terms of presence frequency, a great majority of positive patients are under 5 years of age, similar to other studies.

We evaluated the distribution of antigen positivity according to seasons, and found that rotavirus was most frequently detected in spring and winter months, showing a decrease in frequency in summer and autumn. This change was not found to be statistically significant, but p value is near 0.05. As may be seen from other studies mentioned above, rotavirus is not seen frequently only in winter, but also in spring. We are inclined to think that the change in seasons and spring being colder like winter may have caused this. Adenovirus positivity is slightly more frequent in winter, is seen in similar rates, in accordance with other studies.

Use of orally administered vaccines against rotavirus infection have resulted in considerable decreases in hospitalizations due to rotavirus diarrhea.[23] Rotavirus positivity is 4.1% in outpatients and 15.1% in hospitalized patients in the present study, which is an important finding showing a clinical picture requiring hospitalization. Many countries have implemented rotavirus vaccinations into their national vaccination programs, while it is still not part of the national vaccination program in our country.[24] The data of our study supports the belief that inclusion of rotavirus vaccination into the national vaccination program may be beneficial for patients.

Determination of the prevalence of viral agents causing diarrhea is important for avoiding unnecessary use of antibiotics.[25] Many studies were conducted in Turkey in many regions on the frequency of rotavirus and adenovirus frequency. The present study is the first one aiming to determine the frequency of adenovirus and rotavirus in patients younger than 18 years old admitted with a complaint of diarrhea in Thrace Region. Therefore, it is valuable in terms of contributing to the literature. In addition, the retrospective design of our study is a limitation.

CONCLUSION

We have found that rotavirus and adenovirus are important agent causing diarrhea in pediatric patients, especially those younger than 5 years of age, that their frequency increases in winter and spring, and that as rotavirus causes hospitalizations, implementation of rotavirus vaccine into the national vaccination program will be beneficial for patients.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Tekirdag Dr. I. Fehmi Cumalıoglu City Hospital Clinical Investigations Ethics Committee (Date:14.04.2023, Decision No: 35)

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

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