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## Prevalence of Rotavirus and Adenovirus in a City Hospital in the Eastern Anatolia Region of Türkiye

## Türkiye'nin Doğu Anadolu Bölgesinde Bir Şehir Hastanesinde Rotavirus ve Adenovirus Prevalansı

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### Abstract

In this study, it was aimed to evaluate the seasonal distribution of rotavirus and enteric adenovirus prevalence and demographic data of patients of all age groups who applied to our hospital with the complaint of acute gastroenteritis. A total of 12,840 patients aged 0-90 years, who applied to our hospital (Elazığ Fethi Sekin City Hospital) with the complaint of acute gastroenteritis between 15 August 2018 and 18 October 2021, were retrospectively analyzed. The presence of rotavirus and adenovirus antigens was determined from stool samples by qualitative immunochromatographic method (Microcult-Rotavirus/Adenovirus Combo, Biotech China) in accordance with the manufacturer's recommendations. Of the patients who applied with the complaint of acute gastroenteritis, 3,507 (27.3%) were infants, 9,087 (70.8%) were children, and 246 (1.91%) were adults. Of all patients, 1,350 (10.5%) were positive for at least one viral agent. Of patients with detected viral agents, 750 (55.6%) were male and 600 (44.4%) were female. Of the samples, 1,099 (8.56%) were positive for rotavirus, 199 (1.55) were positive for adenovirus, and 52 (0.40%) were positive for both pathogens. The positivity rate in men was 10% higher than in women. The positivity rates were highest in patients admitted in 2019 (5,915) for both rotavirus and adenovirus, 10.5% (622) and 2.23% (132) respectively. In the study, rotavirus positivity was highest in winter with 12.2% (270/2,216) and adenovirus positivity was highest with 2.12% (95/4,484) in summer. In the evaluation carried out according to age, gender, and season, the period in which viral gastroenteritis was seen at the highest rate was determined as "childhood". In the evaluation of gastroenteritis cases, it is important to know that viral agents are common, especially in the childhood age group, in addition to bacteriological and parasitological agents in stool samples in acute gastroenteritis infections and considering that there may be seasonal and periodic changes in the frequency of viral gastroenteritis. It was thought that unnecessary antibiotic use would be eliminated or minimized by replacing the lost fluid and electrolytes, which are the basic treatment of viral infections, following the correct identification of the causative agent.

Keywords: Adenovirus, Acute gastroenteritis, Prevalence, Rotavirus.

#### Özet

Bu çalışmada akut gastroenterit şikayetiyle hastanemize başvuran her yaş grubu hastada rotavirus ve enterik adenovirus sıklığının mevsimlere göre dağılımının hastaların demografik verileri ile değerlendirmesi amaçlanmıştır. Akut gastroenterit şikayeti ile 15 Ağustos 2018-18 Ekim 2021 tarihleri arasında hastanemize (Elazığ Fethi Sekin Şehir Hastanesi) başvuran 0-90 yaş aralığında 12.840 hastanın verileri retrospektif olarak incelendi. Rotavirus ve adenovirus antijenlerinin varlığı, dışkı örneklerinden kalitatif immünokromatografik test yöntemi ile (Microcult-Rotavirus/Adenovirus Combo, Biotech China) üretici önerileri doğrultusunda tanımlandı. Akut gastroenterit şikayetiyle başvuran hastaların 3507'si (%27.3) bebek, 9087'si (%70.8) çocuk ve 246'sı (%1.91) yetişkindi. Tüm hastaların 1350'si (%10.5) en az bir viral etken için pozitifti. Viral etken varlığı saptanan hastaların 750'si erkek (%55.6) ve 600'ü (%44.4) kadın hastalardı. Örneklerin 1099'unda (%8.56) rotavirus, 199'unda (%1.55) adenovirus ve 52'sinde (%0.40) iki virüsün birlikte pozitifliği saptandı. Erkeklerdeki pozitiflik oranı kadınlara göre %10 daha yüksek olarak belirlendi. Pozitiflik oranları hem rotavirus hem de adenovirus için 2019 yılında başvuran hastalarda (5915) en yüksek seviyede idi, sırasıyla %10.5 (622) ve %2.23 (132). Rotavirus pozitifliği kış mevsiminde %12.2 ile (270/2216), adenovirus pozitifliği ise yaz mevsiminde %2.12 ile (95/4484) diğer mevsimlerden daha yüksek oranlarda saptandı. Yaş, cinsiyet ve mevsime göre yapılan değerlendirmede viral gastroenteritlerin en yüksek oranda görüldüğü grup "çocukluk dönemi" olarak tespit edildi. Akut gastroenterit enfeksiyonlarında gaita örneklerinde bakteriyolojik ve parazitolojik etkenlerin yanında özellikle çocukluk yaş grubunda viral etkenlerin yaygın olduğunun bilinmesi ve viral gastroenteritlerin görülme sıklıklarında mevsimsel ve dönemsel değişiklikler olabildiğinin dikkate alınması gastroenterit olgularının değerlendirilmesinde önemlidir. Etkenin doğru tanımlanmasını takiben viral enfeksiyonların temel tedavisi olan kaybedilen sıvı ve elektrolitlerin yerine konmasıyla, gereksiz antibiyotik kullanımının ortadan kalkacağı veya en aza ineceği düşünülmüştür.

Anahtar Kelimeler: Adenovirus, Akut gastroenterit, Prevalans, Rotavirus.

#### Introduction

Viral gastroenteritis is an important part of infectious diarrhea. Besides, viruses are the causative agent in 70% of children under the age of 5 who have acute gastroenteritis [1,2]. Rotavirus, norovirus, and adenovirus are mostly encountered pathogens in viral gastroenteritis [3–5]. In a scientific report published in 2012, it was stated that nearly 7 million children under the age of 5 died due to preventable and treatable diseases, and diarrhea was responsible for approximately 10% of these deaths [6]. It has been reported that children under 5 years of age have an average of 3 episodes per year in developing countries, while one (or less) episode of gastroenteritis in developed countries [7–9].

Rotaviruses are non-enveloped, icosahedral, double-stranded RNA viruses from the *Reoviridae* family [10,11]. Rotavirus infection has a wide spectrum of clinical manifestations; it could be asymptomatic but may also present severe disease with dehydration due to severe diarrhea that can result in shock and death [12]. In rotavirus infections (with the incubation period of 1-3 days), viral particles replicate in intestinal epithelial cells (enterocytes) and seriously causes cuboidal changes, blunting, and shortening of the epithelium, resulting in a decrease in the area of villi resorption and loss of electrolyte and water [12–14].

Adenoviruses are non-enveloped, icosahedral and linear double-stranded DNA viruses from the *Adenoviridae* family [10,15]. They can cause eye, gastrointestinal tract, and acute respiratory tract infections [15,16]. Adenovirus serotype 40 and serotype 41 are the most common causes of gastroenteritis in infants and children after rotaviruses [17]. Enteric adenoviruses lead to atrophy of villi by causing damage in enterocytes and secondary hyperplasia in crypts which causes malabsorption and fluid loss [15]. The incubation period of adenovirus gastroenteritis is longer than rotavirus (3-10 days) [13].

Rotavirus and enteric adenovirus associated gastroenteritis are easily transmitted through the fecal-oral route and usage of shared objects [14,17]. Both viruses are relatively resistant to disinfectants and detergents [18]. Rotavirusrelated gastroenteritis leads to hospitalization and malnutrition caused by prolonged diarrhea, vomiting and fluid loss due to fever, especially in children aged 4–23 months [2,19]. Rotavirus gastroenteritis mostly occurs during winter in temperate climate regions; it occurs at an early age, has a more severe clinical course and its mortality rate is higher in developing countries compared to developed countries [14,19,20]. Gastroenteritis due to enteric adenovirus is the second most common cause of prolonged diarrhea requiring hospitalization, but vomiting and fever are rare symptoms in this infection [20]. Adenoviral gastroenteritis are seen throughout the year but are more common in summerautumn as some authors suggest [21].

Our study aims to evaluate the distribution of rotavirus and enteric adenovirus frequency by years in patients who have the complaint of acute gastroenteritis, with the demographic data of the patients, and to compare our data with the literature and to contribute to reducing the consumption of unnecessary antibiotics with early diagnosis.

#### **Material and Method**

Patients between the ages of 0-90 who applied to our hospital with the complaint of acute gastroenteritis between 15 August 2018 and 18 October 2021 were included in the study. Stool samples from these patients were taken into the stool container, and the rotavirus and enteric adenovirus antigen test were quantitatively determined with the immunochromatographic method (Microcult-Rotavirus/Adenovirus Combo, Biotech, China) on the same day. The test results were evaluated retrospectively with the demographic data of the patients according to the seasons and years. For this study, permission was obtained from the Non-Interventional Clinical Research Ethics Committee of Fırat University with the decision no: 2021/12-22 and the date; 18.11.2021, and the study was conducted in accordance with the Declaration of Helsinki.

In this study, the number of samples in the data is shown as "n" and calculated as a percentage. SPSS (Statistical Packages of Social Sciences, SPSS for Windows, Version 18.0, Chicago, IC, USA) package program was used for statistical analysis of the data.

#### Results

A total of 12,840 stool samples of suspected acute gastroenteritis were evaluated. The ages of the patients were in the range of 0-90 years. Of the patients, 3,507 (27.3%) were infants, 9,087 (70.8%) were children, and 246 (1.91%) were adults. Viral agent positivity was detected in 1,350 (10.5%) of all samples (12,840). It was determined that 750 (55.6%) of the patients with viral agents were male and 600 (44.4%) were female. It was found that rotavirus positivity was 8.54% and 8.58% of male and female patients, respectively. It was determined that enteric adenovirus was found in 1.49% of male patients and 1.63% of female patients, co-infection was detected in 0.39% of male and 0.43% in female patients. Of the samples, 1,099 (8.56%) were positive for rotavirus, 199 (1.55%) were positive for adenovirus and 52 (0.40%) were positive for rotavirus and adenovirus. According to age and gender, the highest positivity for both rotavirus and adenovirus was seen in the pediatric age group. The results are shown in detail in Table 1.

Table 1. Rotavirus-adenovirus positivity distribution by age and gender.							
Age	Male	RoV n (%)	AdV n (%)	RoV + AdV n (%)			
Baby (0-24 months)	1,934	149 (7.70)	22 (1.14)	3 (0.16)			
Children (3-18)	5,146	463 (9.00)	84 (1.63)	25 (0.49)			
Adult (19-90)	122	3 (2.46)	1 (0.82)	0 (0)			
Total	7,202	615 (8.54)	107 (1.49)	28 (0.39)			
Age	Female	RoV n (%)	AdV n(%)	RoV + AdV n (%)			
Baby (0-24 months)	1,573	110 (6.99)	19 (1.21)	7 (0.45)			
Children (3-18)	3,941	367 (9.31)	72 (1.83)	17 (0.43)			
Adult (19-90)	124	7 (5.65)	1 (0.81)	0 (0)			
Total	5,638	484 (8.58)	92 (1.63)	24 (0.43)			
RoV; Rotavirus. AdV; Adenovirus.							

According to the seasons, rotavirus positivity was highest in winter with 12.2%, adenovirus positivity was highest with 2.12% in summer. The distribution of rotavirus and enteric adenovirus according to age and season was found to be higher in the pediatric age. Rotavirus and adenovirus positivity was compared according to season and age range in Table 2. When rotavirus and adenovirus positivity were examined by year, the highest level was determined as 10.5% for rotavirus and 2.23% for enteric adenovirus in 2019. In Table 3, the distribution of rotavirusadenovirus positivity and co-infections were compared by years.

Table 2. Rotavirus-adenovirus positivity according to seasons and age.							
	Age	Number of Patients	RoV n(%)	AdV n(%)	RoV + AdV n(%)		
Spring	Baby	603	52 (8.62)	2 (0.33)	2 (0.33)		
	Children	1404	131 (9.33)	6 (0.43)	9 (0.64)		
	Adult	39	3 (7.69)	0 (0)	0 (0)		
	Total	2046	186 (9.09)	8 (0.39)	11 (0.54)		
Summer	Baby	1174	34 (2.90)	19 (1.62)	3 (0.26)		
	Children	3282	183 (5.58)	76 (2.32)	18 (0.55)		
	Adult	28	1 (3.57)	0 (0)	0 (0)		
	Total	4484	218 (4.86)	95 (2.12)	21 (0.47)		
Autumn	Baby	1005	97 (9.65)	15 (1.49)	1 (0.10)		
	Children	2991	327 (10.9)	55 (1.84)	9 (0.30)		
	Adult	98	1 (1.02)	1 (1.02)	0 (0)		
	Total	4094	425 (10.4)	71 (1.73)	10 (0.24)		
Winter	Baby	725	76 (10.5)	5 (0.69)	4 (0.55)		
	Children	1410	189 (13.4)	19 (1.35)	6 (0.43)		
	Adult	81	5 (6.17)	1 (1.23)	0 (0)		
	Total	2216	270 (12.2)	25 (1.13)	10 (0.45)		
RoV; Rotavirus. AdV; Adenovirus.							

Table 3: Rotavirus-Adenovirus positivity distribution by years.								
Years	Number of Patients	RoV n (%)	AdV n (%)	RoV + AdV n (%)				
2018	1,710	97 (5.67)	28 (1.64)	4 (0.23)				
2019	5,915	622 (10.5)	132 (2.23)	16 (0.27)				
2020	1,836	136 (7.41)	14 (0.76)	7 (0.38)				
2021	3,379	244 (7.22)	25 (0.74)	25 (0.74)				
Total	12,840	1,099 (8.56)	199 (1.55)	52 (0.40)				
RoV; Rotavirus. AdV; Adenovirus.								

#### Discussion

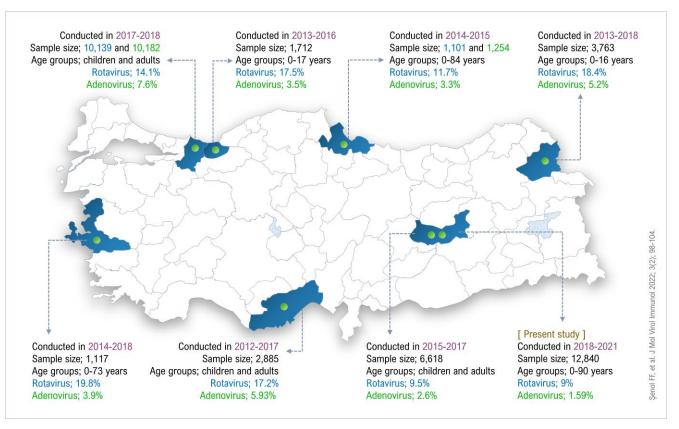
Acute gastroenteritis is an inflammation of the small intestine with sudden onset and has symptoms such as nausea, vomiting, abdominal pain, and diarrhea [22]. Acute gastroenteritis generally transmits via the fecal-oral route, causes epidemics and is responsible for about 2.5 million deaths per year [23]. It especially occurs in countries with dense populations, poor hygienic conditions, shortage of clean drinking water, insufficient and unbalanced nutrition, [7]. In various studies conducted in our country and around the world, it has been reported that rotavirus is responsible for 11-71% of viral gastroenteritis cases and enteric adenovirus for 2-22.2% [24-26]. According to WHO data rotavirus positivity in acute gastroenteritis infections was 34-45% in different countries [27]. In the children who do not receive early diagnosis and treatment in gastroenteritis due to rotavirus and enteric adenoviruses, clinical picture deteriorates rapidly because of high fluid loss with diarrhea and severe vomiting. As a result of this picture, patients need to be hospitalized [19,28].

In a study conducted in the Marmara region, rotavirus positivity was detected as 14.1% and adenovirus positivity as 7.6% in all age groups between June 2017 and May 2018 in more than ten thousand clinical samples from patients with acute gastroenteritis [29]. In another previous study conducted in the same region as our study, but with a smaller sample size; Aytac et al. found that viral gastroenteritis positivity was 9.5% for rotavirus, 2.6% for adenovirus, and 0.3% for rotavirus and adenovirus together [30]. These data are slightly higher than the rates we found. In a study from the northern region of Turkey; Çaycı et al. evaluated 1,101 samples between the ages of 0-84 and found 11.7% positive for rotavirus, 3.3% positivity for adenovirus and two samples were positive for both pathogens [31]. Among antigen positive patients, 70 (11.5%) of the male, and 59 (12%) of the female was positive for rotavirus and 17 (3%) of the female, and 25 (3.7%) of the male were positive for adenovirus infection [31]. Üstebay et al. found that 20% viral antigen positivity was detected in 0-16 years old patients with gastroenteritis, 74% rotavirus, 7% adenovirus and 19% rotavirus and adenovirus were found to be positive together [32], (to compare with other studies conducted in Türkiye, see Figure 1). The study also showed that 48% of the patients with positive viral antigen were female and 52% were male [32]. Aslantas et al. found that 1,712 patients (0-17 years old) admitted to the emergency department had 17.5% rotavirus positivity and 3.5% adenovirus positivity, 56% of positive cases were male and 44% were female, and there was no significant difference between genders in terms of positivity [33]. In our study, 12,840 samples were included to study; 750 (55.6%) of the patients with detected viral agents were male and 600 (44.4%) were female, 1,099 (8.56%) were positive for rotavirus, 199 (1.55%) were positive for adenovirus and 52 (0.40%) were positive for rotavirus and adenovirus. Positivity was found to be higher in male patients.

The incidence of adenovirus does not vary seasonally in temperate climatic regions such as our country, however rotavirus gastroenteritis generally increases in the winter months [14]. Aytaç et al. found that the incidence of rotavirus in the winter was higher and statistically significant than in other seasons, and there was significant no statistically difference for adenovirus [30]. Üstebay et al. found that rotavirus positivity was higher in winter and spring, adenovirus positivity was highest in spring and secondly in autumn [32]. Çaycı et al. reported that rotavirus is most common in spring 18.6% and winter 17%; adenovirus was most common in winter 4.6% and spring 3.4%, and there was no statistically significant difference in seasonal distributions for both pathogens [31]. In our study, rotavirus positivity was highest in winter with 12.2% and adenovirus positivity was highest in summer with 2.12%.

Ozkan et al. examined the distribution of viral antigen positivity rates by age groups; found that rotavirus and adenovirus were seen most frequently between the ages of 6-10 [34]. In the study conducted by Üstebay et al., viral antigen positivity according to age groups, it is found that it was 84% in the 0-2 age group, 9% in the 3-5 age group, and 7% in the 6-16 age group. Also, they found that adenovirus and rotavirus and adenovirus co-positivity were higher in the 0-2 age group compared to other groups [32]. Dinc et al. detected rotavirus antigen positivity was most frequently in children aged 1-2 years and adenovirus antigen positivity was most frequently in children aged 0-1 years, but there was no statistically significant difference between age groups [35]. In our study, it was determined that the childhood age group is higher in all seasons. In the adult age group, rotavirus and adenovirus positivity was lower than the other age groups, but the rotavirus positivity was higher (7.69%) in the spring season.

Every year, 1,5 million children die from vaccine preventable diseases, mostly in developing countries [36]. In all countries, the most important problem is prejudice against vaccines and difficulties in obtaining non-routine vaccines that are not included in the vaccination calendar of governments in developing countries by families in low economic income groups [37]. As we found in our study, there is a decrease in the rates of both rotavirus and adenovirus gastroenteritis compared to previous studies, and it is thought that this may be related to vaccination (Figure 1).



**Figure 1.** Rotavirus and adenovirus positivity in different regions of Türkiye and our results; Sakarya [29], Elazığ [30], Samsun [31], Kars [32], Düzce [33], İzmir [38], Mersin [39].

#### Conclusion

In conclusion, rotavirus and adenovirus gastroenteritis are seen in all age groups, especially in the childhood age group. It has been determined that investigating viral agents along with parasitic and bacterial agents in gastroenteritis cases will give rise to early diagnosis and reduce unnecessary antibiotic use. At the same time, we believe that the dissemination of rotavirus vaccination in early childhood will contribute to both our health system and our country's economy.

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