

# Investigation of the Frequency of Rotavirus and Enteric Adenovirus Infections in Patients with Acute Gastroenteritis

## Akut Gastroenterit ile Başvuran Hastalarda Rotavirüs ve Enterik Adenovirüs Enfeksiyonu Sıklığının Araştırılması

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### ÖZ

**Amaç:** Rotavirüs ve enterik adenovirüs ağır klinik semptomlarla seyreden ve sık karşılaşılan viral gastroenterit etkenleridir. Tüm dünyada her yıl milyonlarca insanın ölümüne sebep olan akut gastroenteritlerin %20-40'ına rotavirüsler neden olmaktadır. Bu çalışma hastanemizde akut gastroenterit ön tanısı alan hastalarda rotavirüs ve enterik adenovirüs sıklığını belirlemek ve pozitifliğin yaş grupları, cinsiyet ve mevsimlere göre dağılımını araştırmak amacıyla yapılmıştır.

**Araçlar ve Yöntem:** 5210 dışkı örneği immüno-kromatografik yöntemle analiz edilmiştir. Hastaların verileri retrospektif olarak değerlendirilmiştir. İstatistiksel analizler MedCalc (version 20.009; Ostend, Belgium) istatistik paket programı ile yapıldı.

**Bulgular:** Değerlendirilen örneklerin 261'inde (%5) Rotavirüs pozitifliği saptanmış olup, pozitiflik en sık 25-60 aylık çocuklarda ve yaz aylarında tespit edilmiştir. Enterik adenovirüsler açısından değerlendirilen örneklerin 69'unda (%1.3) pozitiflik saptanmış ve bunların en sık 0-24 ay yaş grubunda saptandıkları belirlenmiştir. Rotavirüs ve enterik adenovirüs pozitifliğinin mevsimlere göre dağılımı incelendiğinde yaz mevsiminde istatistiksel olarak anlamlı bir ilişki elde edilmiştir. Cinsiyet ile viral antijen pozitifliği arasında istatistiksel olarak anlamlı bir ilişki bulunamadı.

**Sonuç:** Sonuç olarak dışkı örneklerinde rotavirüs ve enterik adenovirüs antijenlerinin araştırılması epidemiyolojik verilerin elde edilmesi ve gereksiz antibiyotik kullanımını önleme açısından önemlidir.

**Anahtar Kelimeler:** antijen; dışkı; immüno-kromatografik

### ABSTRACT

**Purpose:** Rotavirus and enteric adenovirus are common viral agents associated with severe clinical symptoms in gastroenteritis. Rotaviruses are responsible for 20-40% of acute gastroenteritis cases worldwide, which result in millions of deaths each year. This study was conducted to determine the frequency of rotavirus and enteric adenovirus infections in patients diagnosed with acute gastroenteritis at our hospital, and to investigate the distribution of positivity based on age groups, gender, and seasons.

**Materials and Methods:** A total of 5210 stool samples were analyzed using the immunochromatographic method. The patients' data were evaluated retrospectively. Statistical analyses were performed using the MedCalc statistical software (version 20.009; Ostend, Belgium).

**Results:** Rotavirus positivity was detected in 261 of the samples (5%), with the highest positivity observed in children aged 25-60 months and during the summer months. Regarding enteric adenoviruses, positivity was detected in 69 samples (1.3%), with the highest positivity found in the 0-24 month age group. When the distribution of rotavirus and enteric adenovirus positivity was examined according to seasons, a statistically significant association was found in the summer season. No statistically significant relationship was found between gender and viral antigen positivity.

**Conclusion:** In conclusion, the investigation of rotavirus and enteric adenovirus antigens in stool samples is important for obtaining epidemiological data and preventing unnecessary antibiotic use.

**Keywords:** antigen; immunochromatographic; stool

Received: 23.05.2024; Accepted: 29.08.2024

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**How to cite:** Kalaycı HÖ, Çalgın MK. Investigation of the frequency of rotavirus and enteric adenovirus infection in patients presenting with acute gastroenteritis. Ahi Evran Med J. 2024;8(3):325-331. DOI: 10.46332/aemj.1488950

## INTRODUCTION

Viruses are responsible for 80% of gastroenteritis cases and there is an increase in the frequency of viral gastroenteritis.<sup>1,2</sup> Rotavirus and adenovirus are clinically important and common viral gastroenteritis agents. While clinical findings of abdominal pain, vomiting and high fever are observed in rotavirus gastroenteritis, hospitalization may be required due to electrolyte losses, severe dehydration and acidosis.<sup>3,4</sup>

Rotavirus gastroenteritis is most commonly detected in temperate climates, during the winter months, and in children under 2 years of age. While it occurs with similar frequency in both developed and developing countries, it tends to manifest at an earlier age, have a more severe clinical course, and result in higher mortality rates in developing countries.<sup>3</sup>

Enteric Adenovirus is the second most common cause of viral gastroenteritis after Rotavirus and is responsible for acute and prolonged gastroenteritis in the 0-3 age group. Adenovirus infections are seen in all months of the year, but are more common in summer months. Although respiratory symptoms such as cough and runny nose are sometimes seen in adenovirus infections, it has a milder course compared to rotavirus gastroenteritis.<sup>3</sup>

Identifying the causative agents of gastroenteritis is crucial for determining the appropriate treatment and predicting the disease's prognosis. Acute gastroenteritis is responsible for one-third of childhood deaths, with rotavirus infections being the most common cause of these fatalities.<sup>5,6</sup> Identification of the causative agents of gastroenteritis is essential for determining the appropriate treatment approach and preventing unnecessary antibiotic use, particularly in children with a severe clinical course.

In this study, stool samples from patients with a pre-diagnosis of acute gastroenteritis, sent to our laboratory, were analyzed using the immunochromatographic method to determine the frequency of rotavirus and enteric adenovirus among viral gastroenteritis agents. Additionally, the study aimed to retrospectively analyze the distribution of these agents according to gender, age, and seasons, contributing to epidemiological data.

## MATERIALS and METHODS

Approval for this study was obtained from the Ordu University Faculty of Medicine Clinical Research Ethics Committee (dated 13.10.2023, number 271). In our study, the records of patients who were admitted to our hospital with a diagnosis of acute gastroenteritis between April 2021 and October 2023 were retrospectively evaluated. The data obtained from the analysis of 5210 stool samples for both rotavirus antigen and enteric adenovirus antigen were assessed.

A total of 2357 stool samples were from female patients, while 2853 were from male patients. The cases were categorized into three age groups: 0-24 months, 25-60 months, and 60 months and older.

Stool samples sent to our laboratory were examined with Adeno-Rota combistrips (Microcult, Biotech, China) which recognize Rotavirus and Enteric Adenovirus antigens by qualitative immunochromatographic method. Stool samples were collected in clean containers and sent to the laboratory before the procedure. After the sample was suspended with buffer solution, it was contacted with the strip and the results were evaluated after 10 minutes. The occurrence of control and test bands together on the strips was considered as a positive result, the occurrence of only the control band was considered as a negative result, and the test was not evaluated if only the test band was formed and not the control band.

Statistical analyses were performed using the MedCalc (version 20.009; Ostend, Belgium) statistical package program. Number, frequency and percentage were used to statistically define the data. Chi-square test was used to evaluate categorical data. Logistic regression analysis was performed for modeling of the study. The results were evaluated according to the significance level as  $p < 0.05$ .

## RESULTS

Of the 5210 patients in our study, rotavirus antigen was positive in 261 (5%), enteric adenovirus antigen in 69 (1.3%), and rotavirus and enteric adenovirus antigens together in 14 samples (0.3%). When rotavirus positivity

was analyzed according to age groups in our study, it was found to be 42.5% in the 25-60 months age group, 31.8% in the 0-24 months age group and 25.7% in the age group over 60 months. Adenovirus antigen positivity was found to be 40.6% in the 0-24 months age group, 34.8% in the 25-60 months age group and 24.6% in the over 60 months age group. When both viral antigen positivities were compared with age groups, no statistically significant difference was found.

Of the 5210 fresh stool samples, 2357 were from female patients and 2853 were from male patients. Rotavirus antigen was found to be positive in 261 patient samples, 121 (46.4%) of which were female and 140 (53.6%) of which were male; Enteric Adenovirus antigen was found to be positive in 69 patients, 35 (50.7%) of which were female and 34 (49.3%) of which were male. There was no statistically significant difference between genders in both groups.

Rotavirus antigen was positive in 4.9% of all male patients and 5.1% of all female patients (Table 1). Adenovirus antigen was positive in 1.2% of all male patients and 1.5% of all female patients (Table 2).

**Table 1.** Distribution of rotavirus antigen positivity rates according to gender, age groups and seasons.

Variables	Number of Cases		Rotavirus Positivity		
	Number	%	Number	%	P
<b>Gender</b>					
Female	2357	45.2	121	5.1	0.7091
Male	2853	54.8	140	4.9	
<b>Age</b>					
0-24 months	1772	34.0	83	4.7	0.3546
25-60 months	1266	24.3	111	8.8	
>60 months	2174	41.7	67	3.1	
<b>Seasons</b>					
Spring	1089	20.9	23	2.1	<0.0001
Summer	2313	44.4	175	7.6	
Autumn	950	18.2	34	3.6	
Winter	858	16.5	29	3.4	
<b>Total</b>	<b>5210</b>	<b>100</b>	<b>261</b>	<b>5</b>	

**Table 3.** Logistic regression table for rotavirus.

Variables	β	SE	Wald X <sup>2</sup>	P	OR	OR (%95 CI)	
Age	-0.020	0.010	4.079	0.043*	0.980	0.961	0.999
Gender"Female"	0.067	0.128	0.269	0.604	1.069	0.831	1.375
Season"Autumn"	0.558	0.274	4.158	0.041*	1.748	1.022	2.990
Season"Winter"	0.503	0.283	3.158	0.076	1.654	0.950	2.881
Season"Summer"	1.347	0.225	35.828	<0.0001*	3.846	2.474	5.978
Model X <sup>2</sup> =66.88, p<0.0001							
Nagelkerke R <sup>2</sup> = 0.01276							
Hosmer & Lemeshow test X <sup>2</sup> =6.77 (DF=8; P=0.561)							
N=5210							

When Rotavirus antigen positivity was evaluated seasonally in our study, the highest positivity was 67.1% in summer, 13% in fall, 11.1% in winter and 8.8% in spring, respectively. Rotavirus antigen positivity in summer was found to be statistically significantly higher than the other seasons (p<0.0001) (Table 1). According to the seasons, Adenovirus positivity was 69.6% in summer, 11.6% in fall, 10.1% in winter and 8.7% in spring. Statistically, a significant relationship was found when adenovirus positivity was analyzed according to seasons (p=0.0009) (Table 2).

**Table 2.** Distribution of adenovirus antigen positivity rates according to gender, age groups and seasons.

Variables	Number of Cases		Adenovirus Positivity		P
	Number	%	Number	%	
<b>Gender</b>					
Female	2357	45.2	35	1.5	0.3690
Male	2853	54.8	34	1.2	
<b>Age</b>					
0-24 months	1772	34.0	28	1.6	0.3546
25-60 months	1266	24.3	24	1.9	
>60 months	2174	41.7	17	0.8	
<b>Seasons</b>					
Spring	1089	20.9	6	0.6	0.0009
Summer	2313	44.4	48	2.1	
Autumn	950	18.2	8	0.8	
Winter	858	16.5	7	0.8	
<b>Total</b>	<b>5210</b>	<b>100</b>	<b>69</b>	<b>1.3</b>	

In the logistic regression analysis for rotavirus, the rate of positivity in summer was 3.846 times (p<0.0001) higher than in spring and 1.748 times (p<0.041) higher in autumn (Table 3). In the logistic regression analysis for adenovirus, the rate of positivity in summer was 3.727 times (p<0.003) higher than in spring (Table 4). There was no significant difference between genders in the logistic regression analysis for rotavirus and adenovirus.

**Table 4.** Logistic regression table for adenovirus.

Variables	$\beta$	SE	Wald $X^2$	P	OR	OR (%95 CI)	
Age	0.008	0.013	0.381	0.537	1.008	0.983	1.034
Gender"Female"	0.212	0.244	0.758	0.384	1.236	0.767	1.993
Season"Autumn"	0.472	0.542	0.759	0.384	1.604	0.554	4.641
Season"Winter"	0.456	0.559	0.665	0.415	1.577	0.528	4.715
Season"Summer"	1.316	0.435	9.148	0.003*	3.727	1.589	8.741
Model $X^2=18,37$ , $p=0.002$							
Nagelkerke $R^2= 0.002$							
Hosmer & Lemeshow test $X^2=6.27$ (DF=8; $P=0.616$ )							
N=5210							

\* Significance at &lt;0.05 level

## DISCUSSION

Acute gastroenteritis is a clinical condition that can affect individuals of all ages, but the severity of the disease varies based on age and season due to different etiological agents. When infectious gastroenteritis is examined according to the causative agents, viral pathogens are the leading cause, accounting for rates as high as 30-70%.<sup>7-10</sup> Studies have shown that Rotavirus and Enteric Adenovirus are the most common causes of gastroenteritis, especially in children younger than 5 years.<sup>2,3,7-11</sup> Viral gastroenteritis is an important cause of morbidity and mortality by causing serious complications especially in young children.<sup>4</sup> In our study, the prevalence of rotavirus and enteric adenovirus in patients admitted with acute gastroenteritis was 5% and 1.3%, respectively. The frequency of rotavirus and enteric adenovirus observed in our study was consistent with the findings reported in the literature.<sup>12-14</sup>

Several agents can coexist in gastroenteritis. While viruses and bacteria may occur together, virus-virus coexistence is more commonly observed.<sup>15</sup> In a study conducted in Spain, where cases under the age of 4 years admitted to the pediatric emergency department with acute gastroenteritis were evaluated, virus-virus coexistence was found more frequently. Specifically, rotavirus-adenovirus coinfection was detected in 1.2% of the cases.<sup>14</sup> In our study, similar to the study by Aytac et al., we found rotavirus-enteric adenovirus association in 0.3% of our cases.<sup>16</sup>

Rotaviruses and adenoviruses have been identified as the most common agents of viral gastroenteritis in children under 2 years of age. In studies conducted in our country, Kurugöl et al. found that rotaviruses were the causative agents of gastroenteritis in 80.7% of cases under 2 years

of age, Akdoğan et al. in 95% of cases under 1 year of age, Oğuz et al. in 58.1% of cases under 2 years of age, Turna et al. in 75.1% of cases under 3 years of age.<sup>10,13,17,18</sup>

When we analyzed rotavirus positivity according to age groups; Gül et al. found the highest rate between 13-24 months (44.7%), 26.3% between 0-12 months and 13.2% between 25-36 months.<sup>11</sup> In a similar study conducted in our country, rotavirus positivity was found to be 19.1% in the 13-24 months age group and 14.4% in the 25-48 months age group.<sup>19</sup> In the study of Barutçu and Barutçu, 46.6% of rotavirus positive patients were frequently seen in the 25-60 month period.<sup>20</sup> In our study, similar to the study by Barutçu and Barutçu, rotavirus positivity was most frequently found in the 25-60 month age group (42.5%).

After rotaviruses, enteric adenoviruses are the most common viral gastroenteritis agents.<sup>3</sup> In our study, adenovirus antigen positivity was detected in 1.3% of the samples, with the highest prevalence observed in the 0-24 months age group (40.6%). However, no statistically significant relationship was found between adenovirus antigen positivity and age groups.

In a study conducted in Konya province, stool samples from patients were examined using the immunochromatographic method to detect rotavirus and enteric adenovirus antigens. The study found that 54.4% of the patients with viral antigen were male, 45.6% were female, and 58.6% of the patients were in the 0-2 age group.<sup>12</sup> In our study, we found that 46.4% of the patients with rotavirus antigen were female and 53.6% were male; 50.7% of the patients with positive adenovirus antigen were female and 49.3% were male; and 40.9% of the patients with positive antigen were in the 25-60 months age group.

Similar to the literature, no significant difference was found between genders in our study ( $p=0.70$ ).

Although rotavirus outbreaks are endemic year-round in warm countries, they are most commonly observed during the winter and early spring in our country and in countries with a temperate climate. However, recent studies in the literature have reported that changes in the epidemiology of rotavirus have occurred, particularly with the introduction of rotavirus vaccines.<sup>21</sup> In studies conducted in our country, rotavirus gastroenteritis was reported by Bulut et al. in September and November, by Kurugöl et al. in Izmir in January and March, and by Oğuz et al. in Ankara in December, January, and February.<sup>6,13,17</sup> In our study, the most frequent rotavirus antigen positivity was detected in August (17.2%) and September (14.2%). When analyzed by seasons, the highest rate of rotavirus antigen positivity was detected in the summer season, with 67.1%. A statistically significant relationship was found between rotavirus positivity and seasonal distribution ( $p<0.0001$ ). In their study, Barutçu and Barutçu observed rotavirus positivity during the winter months, while adenovirus positivity was most common in the spring months.<sup>20</sup> Bozok and Şimşek frequently detected rotavirus positivity during the winter months and adenovirus positivity in both the autumn and winter months.<sup>22</sup> Our rotavirus antigen positivity differs from other studies conducted in our country, and we believe that the statistically significant increase in the frequency of infection during the summer season is due to irregular migration and the increase in the population of the province during the hazelnut harvest season, which is a major livelihood for our region.

Unlike rotaviruses, which exhibit a seasonal pattern, adenoviruses can be causative agents of acute gastroenteritis in all geographical regions, without showing seasonal differences.<sup>23</sup> In our country, although Topkaya et al. detected adenovirus antigen most frequently between June and September, and Gülen et al. observed adenovirus antigen positivity most often between May and October, both studies showed adenovirus antigen positivity throughout all months of the year.<sup>24,25</sup> In a study conducted in Van province, adenovirus antigen was detected most frequently in June (41%), March (33%), July and

November (24%).<sup>3</sup> In our study, we detected adenovirus antigen positivity most frequently in July and August. When evaluated according to the seasons, 69.6% of enteric adenovirus positivity was detected in the summer, 11.6% in the fall, 10.1% in the winter, and 8.7% in the spring. A statistically significant relationship was found between enteric adenovirus positivity and seasonal distribution ( $p=0.0009$ ).

According to the study conducted by Çalgın et al. in 2015, 17.3% rotavirus positivity and 1.3% enteric adenovirus positivity were observed. Seasonally, rotavirus positivity was frequently observed in spring and winter, while no statistical significance was found in the seasonal distribution for adenovirus.<sup>26</sup> In our study, we found rotavirus positivity to be 5% and enteric adenovirus positivity to be 1.3%. The decrease in rotavirus positivity over the years was interpreted as a result of the success of vaccination efforts..

In recent years, as the seriousness of rotavirus infections has become more widely recognized, the number of epidemiological studies providing important data in our country has been increasing. By making a definitive diagnosis of viral gastroenteritis, unnecessary antibiotic use in patient treatment is prevented. Many laboratories providing routine services are unable to perform viral culture methods due to their time-consuming nature and impracticality. Immunochromatographic tests have become routine for detecting rotavirus and enteric adenovirus antigens in stool samples, as they can identify multiple agents in a short time with high sensitivity and specificity (70-100%). Most studies identifying rotavirus positivity have used immunochromatographic and ELISA methods. To achieve optimal performance from these tests, they should be used during the symptomatic period of the patients.<sup>27,28</sup>

In conclusion, in addition to bacterial and parasitic agents, viral agents should also be considered as causative agents of acute gastroenteritis in children under five years of age. In this study, it was observed that rotavirus and enteric adenoviruses are significant agents in the region served by our hospital, particularly during the summer months when our province experiences migration. The frequency of rotavirus gastroenteritis was found

to be higher than that of adenovirus gastroenteritis. We believe that the use of rapid diagnostic tests, such as immunochromatographic tests, will be beneficial in preventing unnecessary antibiotic use and in reducing the risk of serious complications by enabling the correct treatment to be initiated through early diagnosis. Therefore, our study, which includes the distribution of enteric adenovirus and rotavirus agents of viral gastroenteritis according to gender, age, and seasons, will contribute to the epidemiological data of our province.

### Conflict of Interest

The authors declare that there is not any conflict of interest regarding the publication of this manuscript.

### Ethics Committee Permission

Approval for this study was obtained from Ordu University Faculty of Medicine Clinical Research Ethics Committee (dated 13.10.2023 and numbered 271).

### Authors' Contributions

Concept/Design: HÖK. Data Collection and/or Processing: MKÇ. Data analysis and interpretation: HÖK, MKÇ. Literature Search: HÖK. Drafting manuscript: HÖK. Critical revision of manuscript: MKÇ.

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