# **World Journal of Pharmaceutical**

**Science and Research** 

www.wjpsronline.com

**Research Article** 

ISSN: 2583-6579 SJIF Impact Factor: 5.111 Year - 2025 Volume: 4; Issue: 1 Page: 545-557

# PREVALENCE OF ADENOVIRUS AND ROTAVIRUS IN PATIENTS WITH GASTROENTERITIS: A FIVE-YEAR EVALUATION

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Article Received: 22 December 2024 || Article Revised: 11 January 2025 || Article Accepted: 02 February 2025

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How to cite this Article: Melahat Gürbüz, Cengiz Demir, Selahattin Ünlü and Yeliz Çetinkol (2025). PREVALENCE OF ADENOVIRUS AND ROTAVIRUS IN PATIENTS WITH GASTROENTERITIS: A FIVE-YEAR EVALUATION. World Journal of Pharmaceutical Science and Research, 4(1), 545-557. https://doi.org/10.5281/zenodo.14937084

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## ABSTRACT

Background: Acute gastroenteritis is a leading cause of morbidity and mortality in young children worldwide. Rotavirus and adenovirus have been reported as the primary viral agents associated with this disease. During diarrheal outbreaks, rapid diagnosis is essential to ensure timely implementation of appropriate treatment and control measures. This study aimed to assess the prevalence of rotavirus and adenovirus among patients with acute gastroenteritis and analyze their distribution by sex, age, and season. Methods: This retrospective study evaluated the presence of adenovirus and rotavirus in stool samples sent from different clinics with a prediagnosis of acute gastroenteritis during the five-year period from January 1, 2019, to December 31, 2023 using an immunochromatographic method-based kit (Microcult, Biotech, China). Results: In the study, 1,205 (11.5%) of 10,486 samples were positive for rotavirus and 268 (2.6%) were positive for adenovirus. In the 2-5 age group, rotavirus positivity was detected in 730 (60.6%) and adenovirus positivity in 169 (63.1%) patients. A statistically significant difference was found between age groups (p=0.001). Rotavirus was detected in 79.3% and adenovirus in 69.4% of patients admitted to pediatric emergency department. Co-infection of rotavirus and adenovirus was detected in 57 cases (0.5%). In terms of seasonal distribution, rotavirus was most frequently detected in spring and winter, while adenovirus was detected in summer. Conclusions: This study emphasizes the important role of rotavirus and adenovirus as primary viral agents in pediatric gastroenteritis. The high prevalence of rotavirus infections highlights the urgent need for the integration of rotavirus vaccines into routine immunization programs in Turkey. Furthermore, the use of rapid immunochromatographic tests and molecular diagnostic tools is essential to improve clinical management and outbreak surveillance. These findings support public health strategies focused on vaccination and enhanced diagnostics to reduce the burden of viral gastroenteritis and improve healthcare outcomes.

KEYWORDS: Adenovirus, rotavirus, prevalence, change over years, seasonality.

#### INTRODUCTION

Acute gastroenteritis, most commonly caused by enteric viruses, is a major public health problem affecting hundreds of millions of people worldwide each year. While bacterial infections have traditionally been considered the major cause of gastroenteritis, advances in viral diagnostics have led to the recognition of viruses as the major cause of gastroenteritis over the past 20 years (Malik et al., 2019) Gastroenteritis is a significant infectious disease that impact individuals of all age groups globally, particularly young children who experience acute forms of the disease. Viral infections have been identified as a primary source of gastroenteritis, especially in developing countries. While the majority of infections are self-limiting, they continue to result in morbidity and economic losses (Tate et al., 2016).

The major viral pathogens associated with viral gastroenteritis include rotavirus, norovirus, and adenovirus. Rotavirus is typically the primary etiological agent responsible for acute gastroenteritis in infants and young children globally. It is estimated that rotavirus is responsible for 150,000 to 200,000 deaths in children worldwide each year, with more than 85% of these deaths occurring in low-income countries (GBD 2016 Lower Respiratory Infections Collaborators, 2018). The most common genotypes of rotavirus infection in humans are G1P, G2P, G3P, G8P and G9P, of which G1P accounts for approximately 30% of all human rotavirus strains (Janpanil et al., 2023). The availability of rotavirus vaccines has resulted in a notable decline in the incidence of rotavirus infections and associated mortality rates on a global scale (Cates, Tate & Parashar, 2022).

Following rotavirus, adenovirus represents the most significant etiological agent of acute infantile gastroenteritis. Adenoviruses have been identified as a potential cause of acute diarrhea and gastroenteritis in infants, with an estimated incidence of 2-6% worldwide (Mohammadi et al., 2020). Adenoviruses are non-enveloped icosahedral viruses with 34-36 kb of double-stranded linear DNA. The seven human adenovirus species grouped from A to G include 88 serotypes. Gastrointestinal infections are typically attributed to subgroups A, D, and F. Serotypes 40 and 41 of subgroup F and 31 of subgroup A are predominantly associated with gastroenteritis (Lee, Damon & Platts-Mills, 2020).

Rapid diagnosis of viral gastroenteritis facilitates optimized antimicrobial management and reduces unnecessary healthcare costs. This has been demonstrated in empirical studies to result in a reduction in the number of endoscopic and radiological procedures performed and a shorter duration of hospitalisation (Axelrad et al., 2019). Major enteric viruses have been reported to cause chronic gastroenteritis in HIV-positive and immunocompromised individuals, resulting in prolonged viral transmission that can last for weeks or years (Haessler & Granowitz, 2013). Detection of such cases can prevent community and hospital-based transmission. Detection of enteric viruses in viral gastroenteritis episodes may facilitate timely management of outbreaks.

This study specifically examined the role of two most common viral pathogens, rotavirus and adenovirus, in patients diagnosed with gastroenteritis over a five-year period. The goal of the analysis was to identify patterns to help clinicians consider viral gastroenteritis in their differential diagnosis and optimize their diagnostic approach, focusing on the epidemiology of patients with viral gastroenteritis, age distribution, and changes in the predominant viruses included in the study over a five-year period.

### MATERIALS AND METHODS

In this study, we evaluated the presence of adenovirus and rotavirus in 10,486 stool samples sent to the Medical Microbiology Laboratory of Afyonkarahisar Health Sciences University Health Research and Practice Center with a

preliminary diagnosis of acute gastroenteritis from various clinics over a five-year period (between January 1st, 2019, and December 31st, 2023). The patients were divided into four age-based groups: 0-1, 2-5, 6-13, and 14-18 years old, and over 18 years old. The study cohort included patients presenting with an acute gastroenteritis. Samples positive for bacterial or parasitic pathogens through routine examination, as well as those showing signs of chronic gastroenteritis, were excluded from further analysis. Rotavirus and Adenovirus Combo Rapid Test Cassette (Feces) (Microcult, Biotech, China) kit was used for the qualitative detection of adenovirus and rotavirus in stool samples. The sensitivity and specificity of the immunochromatographic test (ICT) were reported by the manufacturer as 99.9% and 98.4% for rotavirus, 99.9% and 99.0% for adenovirus.

The study was conducted with the approval of the Non-Intervention Scientific Research Ethics Committee at Afyonkarahisar Health Sciences University (Decision: 2024/218).

#### Statistical Analysis

Statistical analysis was performed using SPSS 20.0 package program (IBM, USA) and chi-square test was used. p value <0.05 was considered statistically significant.

#### RESULTS

In total, 1,205 (11.5%) out of 10,486 samples tested positive for rotavirus, and 268 (2.6%) tested positive for adenovirus. Among patients with detectable rotavirus antigen, 691 (57.3%) were male and 514 (42.7%) were female. In a similar manner, among patients with detectable adenovirus antigen, 144 (1.4%) were male and 124 (1.2%) were female. No significant difference was observed between the positivity rates for rotavirus and adenovirus in terms of gender (p=0.348). (Table 1).

The mean age of rotavirus positive patients was  $2.54 \pm 6.99$  (0-75 years), while the mean age of adenovirus positive patients was  $2.77 \pm 7.04$  (0-17 years) (p>0.05). The data revealed that both rotavirus and adenovirus positivity were prevalent among patients aged 2-5 years, with 730 (60.6%) and 169 (63.1%) patients, respectively, testing positive for these viruses. The lowest prevalence of rotavirus positivity was observed in the group of individuals over 18 years of age, while no adenovirus-positive patients were identified in this age group. A statistically significant difference was identified between age groups in the frequency of rotavirus and adenovirus infections (p=0.001) (Table 1).

When the distribution of the clinics the samples were sent was analyzed, it was observed that both rotavirus (79.3%) and adenovirus (69.4%) were the most frequently detected viruses in patients admitted to pediatric emergency departments. In adult patients, both viruses were detected at a frequency below 1%. The list of clinics where the samples were sent is provided in Table 1.

A seasonal analysis of the distribution revealed that rotavirus was most frequently detected in spring and winter, while adenovirus was most frequently detected in summer (Figure 1, Table 2). In our study, 57 patients exhibited co-positivity for rotavirus and adenovirus, representing a prevalence of 0.5%. The highest positivity rate was observed in the 0-1 age group (Figure 2).

		RV n=1205 (%)	AdV n=268 (%)	р	
Age (Mean ± Std)		$2.54 \pm 6.99$	$2.77 \pm 7.04$	0,831	
Candan	Male	691 (57,3)	144 (53,7)	0.249	
Gender	Woman	514 (42,7) 124 (46,3)		0,348	
Age Groups	0-1	326 (27,1)	63 (23,5)		
	2-5	730 (60,6)	169 (63,1)		
	6-13	129 (10,7)	32 (11,9)	0,001	
	14-18	15 (1,2)	4 (1,5)		
	>18	5 (0,4)	0 (0)		
Department of Origin	Child emergency	955 (79,3)	186 (69,4)	- 0,009	
	Pediatric outpatient	116 (0.5)	20 (11 2)		
	clinic	110 (9,5)	50 (11,2)		
	Child service	125 (10,4)	52 (19,4)		
	Adult emergency	6 (0,5)	0 (0)		
	Adult outpatient	2(0,2)	0 (0)		
	clinic	2 (0,2)	0(0)		
	Adult service	1 (0,08)	0 (0)		
	2019	288 (23,9)	102 (38,1)		
	2020	127 (10,5)	24 (9)		
Years	2021	157 (13)	37 (13,8)	0,001	
	2022	279 (23,2)	279 (23,2) 62 (23,1)		
	2023	354 (29,4)	43 (16)		
RV- AdV	Positive together	57 (4,7)	57 (21,3)	0,001	

# Table 1: Distribution of rotavirus (RV) and adenovirus (AdV) antigen positive samples.

 Table 2: Distribution of rotavirus and adenovirus positivity according to months.

	Rotavirus			Adenovirus			
Months	Positive	Number of tests	р	Positive	Number of tests	р	
	n (%)	n		n (%)	n		
Winter	302 (13,8)	2184	-	30 (1,4)	2189	-	
December	63 (9,3)	680	0,005*	10 (1,5)	683	0,857	
January	117 (15,9)	737	0,237	13 (1,8)	738	0,452	
February	122(15,9)	767	0,223	7 (0,9)	768	0,330	
Spring	370 (14,6)	2536	-	71 (2,8)	2537	-	
Mart	134 (16)	836	0,385	12 (1,4)	836	0,030*	
April	109 (13,2)	827	0,381	28 (3,4)	828	0,403	
May	127 (14,5)	873	0,978	31 (3,6)	873	0,275	
Summer	233 (7,6)	3070	-	115 (3,7)	3070	-	
June	66 (8,2)	807	0,606	29 (3,6)	807	0,844	
July	83 (7,8)	1067	0,852	48 (4,5)	1067	0,296	
August	84 (7)	1196	0,556	38 (3,2)	1196	0,386	
Autumn	300 (11,1)	2696	-	52 (1,9)	2690	-	
September	86 (8,6,)	1004	0,040*	26 (2,6)	1004	0,227	
October	105 (12,3)	855	0,411	18 (2,1)	849	0,738	
November	109 (13)	837	0,184	8 (0,9)	837	0,059	
Total	1205 (11,5)	10486	-	268 (2,6)	10486	-	

\*p<0.05 was considered statistically significant.



Figure 1: Monthly distribution of rotavirus, adenovirus and rotavirus-adenovirus co-positivity (n).



Figure 2: Distribution of rotavirus-adenovirus co-positivity according to age groups.

## DISCUSSION

Viral gastroenteritis is a relatively common infectious disease that affects hundreds of millions of people worldwide each year, particularly in low-income countries. It is a leading cause of mortality among children under the age of five. The etiology of viral gastroenteritis includes bacteria, parasites and viruses. Nevertheless, viruses are considered the primary etiological agent in children. The most commonly associated viruses are rotavirus and norovirus, followed by enteric adenovirus, astrovirus, and sapovirus (Gonzalez-Serrano et al., 2020).

Rotavirus, in particular, is the major cause of acute viral gastroenteritis in infants and young children and is transmitted by the fecal-oral route. Clinical symptoms of rotavirus disease include watery diarrhea, vomiting, headache, fever and stomach and abdominal cramps. Rotavirus infection can cause asymptomatic or mild diarrhea in adults, but immunocompromised individuals are more susceptible to infection and may experience severe diarrhea (Bruijning-Verhagen et al., 2017).

Adenovirus infections are a significant cause of acute diarrheal diseases, accounting for 2-15% of cases, particularly in children. They are less prevalent than rotavirus infections, predominantly affecting children under the age of four, and are often indistinguishable from other forms of infectious gastroenteritis based on their clinical presentation. Additionally, it causes persistent and widespread infections in immunocompromised patients (Shieh, 2022).

The primary treatment for patients with gastroenteritis is oral medication or intravenous fluids. The use of antibiotics is inappropriate in the treatment of viral gastroenteritis. Therefore, the accurate and rapid identification of the causative agent may be an effective method of reducing the unnecessary use of antibiotics.

Several diagnostic methods are available for the laboratory diagnosis of rotavirus and adenovirus infections, including ELISA, ICTs, isothermal loop-mediated amplification (LAMP), reverse transcription-PCR, real-time PCR and nucleic acid sequence analysis. Molecular PCR-based methods are the gold standard for detecting these viruses in stool samples. However, this method requires well-trained personnel and expensive equipment. Therefore, rapid, easy and cost-effective tests are preferred to screen for these viruses in clinical specimens. For rapid detection of gastroenteritis-associated viral pathogens, ICT is one of the most useful and accessible diagnostic tools. The majority of commercially available ICT kits are designed for the detection of single or double viruses in a single-lane test (Ushijima et al., 2024).

Kaplon et al. (2020) conducted a study of 160 patient samples to evaluate the sensitivity and specificity of four ICT kits. In their study, the results of these kits were compared with the RT-PCR reference method. It was reported that the sensitivity of these four tests for rotavirus ranged between 93% and specificity between 97.4-100%, while the sensitivity for adenovirus (including all subgroups) ranged between 54.3-58.7% and specificity was 100%.

The patient samples included in our study were analyzed with ICT kits that are capable of detecting both viruses. The sensitivity and specificity of the test were reported by the manufacturer as 99.9% and 98.4% for rotavirus and 99.9% and 99% for adenovirus, respectively.

Increasing severity of gastroenteritis is associated with the rate of rotavirus infections detected in patients. Rotavirus positivity rate is reported to be responsible for 8-10% of all diarrhea episodes and almost 35-40% of diarrhea leading to hospitalization (Bozok & Simsek, 2021).

The prevalence of rotavirus and adenovirus varies significantly across different regions and countries. One important factor that may have influenced the prevalence of rotavirus infection in this study is the implementation of rotavirus vaccination programs. Rotavirus vaccines have been introduced in many countries over the past decade and have shown significant efficacy in reducing the incidence and severity of rotavirus-associated gastroenteritis in children (Patel et al., 2011). In studies conducted worldwide, the prevalence of rotavirus infections was reported as 11%-71% and adenovirus prevalence as 2%-22.2%, while in studies conducted in Turkey, the prevalence of rotavirus infections was found as 8.1%-39.8% and adenovirus prevalence as 1.8%-15% (Coskun & Kasap,2019; Dinc et al.,2012).

In a study conducted in our country, Sert & Erayman (2023) found rotavirus positivity in 4.7% and adenovirus positivity in 9.1% of stool samples of 1,960 patients diagnosed with acute gastroenteritis. Duran & Yucel (2023)

detected rotavirus positivity in 8.9% and adenovirus positivity in 4.4% of 5294 samples studied for acute gastroenteritis. In their study, Üstebay et al. (2019) detected viral antigen positivity at a rate of 20%. Among the patients with viral antigen positivity, rotavirus was found in 74%, adenovirus in 7% and rotavirus-adenovirus co-positivity was reported in 19%.

Cho et al. (2021) detected enteric viruses in 30.1% of 31,750 cases evaluated between 2013 and 2019. In this study, rotavirus positivity was reported as 13.9%, 9.5%, 9.7%, 6.3%, 10.0%, 7.0% and 4.8%, while adenovirus positivity was reported as 1.6%, 3.1%, 1.5%, 4.2%, 2.7%, 3.8% and 1.5%, respectively.

In the present study, a total of 10,486 patient samples from individuals aged between 0 and 75 years were evaluated. The results demonstrated that 11.5% of the samples tested positive for rotavirus, while 2.6% were positive for adenovirus. The higher frequency of rotavirus compared to adenovirus is consistent with the findings of other studies in the literature. The prevalence of rotavirus and adenovirus infections observed in our study aligns with findings from other regions with similar socio-economic conditions, though certain regional differences are noteworthy. In our study, the prevalence of rotavirus infection was found to be 11.5%, which is comparable to rates reported in several middle-income countries, but higher than those seen in regions with established rotavirus vaccination programs. In contrast, low-income countries, particularly in sub-Saharan Africa and Southeast Asia, continue to experience a higher prevalence of rotavirus-related gastroenteritis. Studies report rotavirus prevalence rates as high as 25–40% among children hospitalized with diarrhea. The higher burden in these countries is often associated with limited access to vaccines, poor sanitation, and high population density—factors that facilitate the spread of enteric viruses. Although the overall rotavirus positivity in our study is lower than in these regions, the relatively high rate observed in children under five years old reflects similar socio-economic and healthcare challenges, such as inconsistent vaccine coverage and limited public health interventions (Sarker et al., 2014, Sharif et al., 2023, Manzemu et al., 2024).

In Turkey, although rotavirus vaccines are available, they are not included in the national immunization program, and vaccination coverage remains relatively low. This may explain why the prevalence of rotavirus in our study (11.5%) is higher compared to countries with established national vaccination programs. It has been reported, where national vaccination programs have resulted in significant reductions in rotavirus-related hospitalizations and deaths (Burnett, Parashar &Tate, 2020). The absence of a widespread vaccination program in Turkey, therefore, likely contributes to the ongoing burden of rotavirus gastroenteritis observed in our study.

Although our study did not specifically investigate vaccination status, the importance of rotavirus vaccination cannot be overstated. The implementation of a nationwide rotavirus vaccination program in Turkey could significantly reduce the prevalence of rotavirus infections and associated healthcare costs. Furthermore, surveillance studies like ours provide valuable baseline data that can be used to monitor the long-term effectiveness of vaccination efforts and help shape public health policies aimed at controlling viral gastroenteritis.

In two studies conducted in our country, it was reported that there was no significant difference between genders in terms of rotavirus and adenovirus positivity (Bozok & Simsek, 2021; Tasbent, Gulseren & Ozdemir, 2021). Schmidt et al. (2022) reported that no significant differences were observed in the gender distribution of viral gastroenteritis cases.

In our study, there was no statistical difference between the sexes in rotavirus and adenovirus positivity (p=0.348). Our results are consistent with previous studies showing that viral gastroenteritis affects both men and women equally. This suggests that susceptibility to viral pathogens causing gastroenteritis is not strongly influenced by the sex of the patient.

In a study analyzing viral antigen positivity rates according to age groups, the highest positivity rate was reported in the 13-24 months range with 19.6% for rotavirus and in the 3-5 years range with 5.5% for adenovirus (Genc Bahce, Ozudogru &Acer, 2022). Terzi & Aydemir (2018) found 15.6% of rotavirus cases between 0-12 months and 19.1% between 13-24 months and 10.3% of adenovirus cases between 0-12 months and 7% between 13-24 months in their study. Sert & Erayman (2023) found rotavirus and adenovirus positivity most frequently between the ages of 1 month and 2 years, and rotavirus was most frequently detected in winter and adenovirus in spring. Duran & Yucel (2023) reported rotavirus positivity most frequently between the ages of 13-24 months and 2-5 years, in spring and winter months, and adenovirus positivity most frequently between the ages of 2-5 years and over 18 years, in winter and summer months in their study.

In our study, consistent with the literature, both rotavirus (60.6%) and adenovirus (63.1%) positivity were most commonly detected in the 2-5 age group. This was followed by the 0-1 age group with rates of 27.1% and 23.5% for rotavirus and adenovirus, respectively. While rotavirus was found in 0.4% of patients over 18 years of age, no adenovirus-positive patient was detected in this group. In our study, rotavirus was most frequently detected in spring and winter and adenovirus was most frequently detected in summer (Figure 1, Table 2). When the frequency of both rotavirus (p=0.003) and adenovirus (p=0.003) was analyzed according to all seasons, a statistically significant difference was found. However, when the seasons were evaluated within seasons, a significant difference was found only for rotavirus in December (p=0.005) and for adenovirus in March (p=0.030) (Table 2).

Taşbent, Gulseren & Aydemir (2021) investigated the frequency and seasonal distribution of rotavirus and adenovirus in patients with gastroenteritis and reported that rotavirus positivity was detected most frequently in winter and in samples sent from the emergency department. While adenovirus was reported to be detected frequently in winter and spring months, they found that positive samples were mostly obtained from patients coming from polyclinics.

In our study, both rotavirus (79.3%) and adenovirus (69.4%) were detected most frequently in patients admitted to pediatric emergency department (Table 1). When the positive samples were evaluated in terms of the clinics to which they were sent, a statistically significant difference was found (p=0.009). Five-year data of the patients included in this study were analyzed and the highest rotavirus positivity rate was 29.4% in 2023, while adenovirus positivity was 38.1% in 2019. The positivity rates for both pathogens decreased in 2020, the year of the COVID-19 pandemic (Table 1). During the COVID-19 pandemic, Turkey has implemented comprehensive control measures since the first case was detected in 2020. These control measures included social distancing, mask wearing, travel restrictions, improved hand hygiene practices and temporary closure of daycare centers and schools. The implementation of intensive control measures affected the overall occurrence of infectious diseases, including acute diarrhea. On the other hand, when both rotavirus and adenovirus positivity were evaluated by years in our study, the difference between them was significant (p=0.001).

Co-infections can also be seen in cases of viral gastroenteritis. Tran et al. (2010) reported rotavirus-adenovirus copositivity rate as 16%. Roman et al. reported the rotavirus-adenovirus rate as 25.6% in their study. In studies conducted in our country, adenovirus-rotavirus co-infection was reported at different rates by Ciftci & Machin (2021) (2.3%), Aytaç et al. (2020) (0.3%), Gülbudak et al. (2019) (3.5%-64.9%). In our study, the number of rotavirus-adenovirus copositive patients was 57 (0.5%) in 10,486 patient samples evaluated retrospectively (Table 1).

Risk factors for co-infections in pediatric populations may include a weakened immune system, poor nutritional status, and underlying chronic diseases, all of which are common in resource-limited settings. In regions with inadequate access to healthcare, delayed diagnosis and treatment of viral infections may increase the likelihood of co-infections. In our study, the highest rate of co-infections was seen in children under the age of five, which aligns with global data indicating that younger children, particularly those in daycare settings, are at higher risk for contracting multiple viral pathogens due to close contact with other children (Zhang et al., 2016; Mohammadi et al., 2020).

Given the potential severity of co-infections, early and accurate diagnosis using sensitive diagnostic tools is critical. The use of molecular techniques, such as PCR, could help identify co-infections that may be missed by conventional immunochromatographic methods. Incorporating molecular diagnostics into routine clinical practice may allow for more precise identification of viral pathogens, ultimately improving patient management and outcomes (Tatte & Gopalkrishna, 2019; Makimaa, Ingle & Baldridge, 2020).

In light of these findings, it is important for future studies to further investigate the clinical course of rotavirus and adenovirus co-infections, particularly in different demographic groups and healthcare settings. Understanding the risk factors and clinical implications associated with co-infections could guide more targeted treatment strategies and inform public health interventions aimed at reducing the burden of viral gastroenteritis.

One notable limitation of this study is the exclusive use of ICT for the detection of rotavirus and adenovirus. While ICT methods offer significant advantages in terms of speed, ease of use, and cost-effectiveness, they also have inherent limitations that may have influenced the results of this study. The sensitivity and specificity of ICT kits, although high, are generally lower than those of molecular methods. This may result in underestimation of viral prevalence, particularly in cases where viral loads are low, as is often the case in co-infections or early stages of infection (Kaplon et al., 2020, Tran et al., 2010).

For example, in our study, the co-infection rate of rotavirus and adenovirus was reported to be 0.5%, which may be lower than expected when compared to studies using molecular diagnostics that report higher co-infection rates. The relatively lower sensitivity of ICT tests in detecting multiple viral pathogens could have led to an underreporting of coinfections.

In light of these limitations, future studies should consider incorporating more advanced diagnostic techniques, such as real-time PCR, which allows for the detection of a broader range of pathogens with greater sensitivity and specificity. PCR not only provides more accurate results but also enables genotyping of viral strains, which can offer valuable insights into viral evolution, transmission patterns, and the potential impact of vaccination programs. Additionally, the use of multiplex PCR assays would allow for the simultaneous detection of multiple viral agents, improving the understanding of co-infections and their clinical significance (Tatte & Gopalkrishna, 2019).

While ICTs remain a valuable tool for rapid diagnosis in routine clinical practice, particularly in resource-limited settings, the integration of molecular diagnostics into routine surveillance programs would enhance the accuracy of epidemiological data and inform public health strategies. Future research should also explore the cost-benefit analysis of adopting molecular diagnostic techniques in combination with ICTs to balance speed and precision in the detection of gastroenteritis-causing pathogens.

#### CONCLUSIONS

Our study confirms that rotavirus and adenovirus are key viral pathogens in the etiology of gastroenteritis, particularly in pediatric populations. As demonstrated in this study, the prevalence of rotavirus infections remains high, particularly among young children, underscoring the urgent need for public health interventions that include the incorporation of rotavirus vaccines into routine immunization schedules. Implementing a national rotavirus vaccination program in Turkey could significantly decrease the incidence of gastroenteritis, reduce healthcare costs, and prevent unnecessary antibiotic use. Furthermore, our study suggests that rapid, targeted diagnostic testing is crucial in distinguishing between viral agents and ensuring appropriate clinical management.

Improving the diagnostic capacity for gastroenteritis, especially through the integration of molecular diagnostic methods alongside rapid ICTs, would enable more accurate and timely identification of viral pathogens. This would not only enhance patient outcomes by preventing unnecessary treatments but also contribute to better outbreak management and surveillance of viral gastroenteritis at a national level.

In conclusion, continued investment in rotavirus vaccination, combined with the use of improved diagnostic tools, represents a critical strategy in reducing the burden of viral gastroenteritis. Public health policies must be adapted to reflect the changing epidemiology of viral infections, and surveillance efforts should be strengthened to ensure early detection and containment of outbreaks. The data presented in this study provide a foundation for future initiatives aimed at controlling viral gastroenteritis in both Turkey and other regions with similar public health challenges.

## ACKNOWLEDGEMENTS

The authors received no financial support for this research and declare that there is no conflict of interest.

#### REFERENCES

- Axelrad JE, Freedberg DE, Whittier S, Greendyke W, Lebwohl B, Green DA., Impact of gastrointestinal panel implementation on health care utilization and outcomes. *Journal of clinical microbiology*, 2019; 57(3): e01775-18. DOI: 10.1128/JCM.01775-18.
- Aytaç Ö, Şenol FF, Oner P, Erkmen N, Aslan R, Doğukan M, Toraman ZA., Frequency of Rotavirus and Adenovirus in Patients with Acute Gastroenteritis. *Türk Hijyen ve Deneysel Biyoloji Dergisi*, 2020; 77(2): 179-184. [Article in Turkish] DOI: 10.5505/TurkHijyen.2019.41033.
- Bozok T, Şimşek T., Prevalence and demographic characteristics of rotavirus, enteric adenovirus and enteric parasite infections in a tertiary hospital: A six-year retrospective cross-sectional study. *Mersin University Journal* of *Health Sciences*, 2021; 14(2): 199-207. [Article in Turkish] DOI: 10.26559/mersinsbd.862795.
- Bruijning-Verhagen P, Nipshagen MD, de Graaf H, Bonten MJM., Rotavirus disease course among immunocompromised patients; 5-year observations from a tertiary care medical centre. *The Journal of infection*, 2017; 75(5): 448-454. DOI:10.1016/j.jinf.2017.08.006.

- Burnett E, Parashar UD, Tate JE., Global Impact of Rotavirus Vaccination on Diarrhea Hospitalizations and Deaths Among Children <5 Years Old: 2006-2019. *The Journal of infectious diseases*, 2020; 222(10): 1731-1739. DOI: 10.1093/infdis/jiaa081.
- Cates JE, Tate JE, Parashar U., Rotavirus vaccines: progress and new developments. *Expert opinion on biological therapy*, 2022; 22(3): 423-432. DOI: 10.1080/14712598.2021.1977279.
- 7. Ciftci N, Machin S., Investigation of the frequency of adenovirus and rotavirus gastroenteritis. *Health Academy Kastamonu*, 2021; 6(1): 43-51. [Article in Turkish] DOI: 10.25279/sak.644024.
- Cho SR, Chae SJ, Jung S, Choi W, Han MG, Yoo CK, Lee DY., Trends in acute viral gastroenteritis among children aged≤ 5 years through the national surveillance system in South Korea, 2013-2019. *Journal of medical virology*, 2021; 93(8): 4875-4882. DOI: 10.1002/jmv.26685.
- 9. Coşkun USŞ, Kasap T., Frequency of rotavirus and adenovirus in pediatric patients with acute gastroenteritis. *Journal of Contemporary Medicine*, 2019; 9(1): 85-88. DOI: 10.16899/gopctd.459823.
- Dinç HÖ, Taner Z, Özbey D, Gareayaghi N, Sirekbasan S, Kocazeybek BS., The prevalence of rotavirus and adenovirus childhood gastroenteritis: data of the university hospital of cerrahpaşa medical faculty between January 2013 and December 2018. *Turk Mikrobiyoloji Cemiyiyeti Dergisi*, 2019; 49(4): 206-211. [Article in Turkish] DOI: 10.5222/TMCD.2019.206.
- 11. Duran H, Yücel FY., Frequency of Rotavirus and Adenovirus in Children with Diarrhea. *Journal of Contemporary Medicine*, 2023; 13(5): 724-728. doi:10.16899/jcm.1316829.
- GBD 2016 Lower Respiratory Infections Collaborators, Estimates of the global, regional, and national morbidity, mortality, and aetiologies of lower respiratory infections in 195 countries, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. The Lancet Infect Dis., 2018; 18(11): 1191-1210. DOI: 10.1016/S1473-3099(18)30310-4.
- Genç Bahçe Y, Ozudogru O, Acer Ö., Frequency of Rotavirus and Adenovirus in Gastroenteritis Cases Observed in Siirt Region. *Gevher Nesıbe Journal of Medical and Health Sciences*, 2022; 7(19): 23-28. [Article in Turkish] DOI: 10.5281/zenodo.6974027%20.
- González-Serrano L, Muñoz-Algarra M, González-Sanz R, Portero-Azorín MF, Amaro MJ, Higueras P Cabrerizo M., Viral gastroenteritis in hospitalized patients: Evaluation of immunochromatographic methods for rapid detection in stool samples. *Journal of clinical virology: the official publication of the Pan American Society for Clinical Virology*, 2020; 128: 104420. DOI: 10.1016/j.jcv.2020.104420
- Gülbudak H, Kurnaz N, Tezcan-Ülger S, Vural-Taşdemir E, Bozlu G, Türkegün M, Delialioğlu N., Investigation of the frequency of rotavirus and enteric adenovirus in patients with acute gastroenteritis. *Türk Hijyen ve Deneysel Biyoloji Dergisi*, 2019; 77(2): 185-194. DOI: 10.5505/TurkHijyen.2019.13540
- 16. Haessler S, Granowitz EV., Norovirus gastroenteritis in immunocompromised patients. *The New England journal of medicine*, 2013; 368(10): 971-971. DOI: 10.1056/NEJMc1301022.
- 17. Jampanil N, Kumthip K, Maneekarn N, Khamrin P., Genetic diversity of rotaviruses circulating in pediatric patients and domestic animals in Thailand. *Tropical medicine and infectious disease*, 2023; 8(7): 347. DOI: 10.3390/tropicalmed8070347.
- 18. Kaplon J, Théry L, Bidalot M, Grangier N, Frappier J, Aho Glélé LS, de Rougemont A, Ambert-Balay K., Diagnostic accuracy of four commercial triplex immunochromatographic tests for rapid detection of rotavirus,

adenovirus, and norovirus in human stool samples. *Journal of clinical microbiology*, 2020; 59(1): e01749-20. DOI: 10.1128/JCM.01749-20.

- Lee B, Damon CF, Platts-Mills JA., Pediatric acute gastroenteritis associated with adenovirus 40/41 in low-income and middle-income countries. *Current opinion in infectious diseases*, 2020; 33(5): 398-403. DOI: 10.1097/QCO.00000000000663.
- Makimaa H, Ingle H, Baldridge MT., Enteric Viral Co-Infections: Pathogenesis and Perspective. *Viruses*, 2020; 12(8): 904. DOI: 10.3390/v12080904.
- 21. Malik YS, Verma AK, Kumar N, Touil N, Karthik K, Tiwari R, Bora DP, Dhama K, Ghosh S, Hemida MG, Abdel-Moneim AS, Bányai K, Vlasova AN, Kobayashi N, Singh RK., Advances in diagnostic approaches for viral etiologies of diarrhea: from the lab to the field. *Frontiers in microbiology*, 2019; 10: 1957. DOI: 10.3389/fmicb.2019.01957.
- 22. Manzemu DG, Opara JPA, Kasai ET, Mumbere M, Kampunzu VM, Likele BB, Uvoya NA, Vanzwa HM, Bukaka GM, Dady FS, Dauly NN, Belec L, Tonen-Wolyec S., Rotavirus and adenovirus infections in children with acute gastroenteritis after introducing the Rotasiil® vaccine in Kisangani, Democratic Republic of the Congo. *PLoS One*, 2024; 19(2): e0297219. DOI: 10.1371/journal.pone.0297219
- 23. Mohammadi J, Amini R, Akbari A, Amraei M, Mahmoudvand S, Jalilian FA., Prevalence and Seasonal Frequency of acute viral gastroenteritis in children less than 5 years in Ilam, Iran. *Entomology and Applied Science Letters*, 2020; 7(3): 66-74.
- Öner SZ, Kaleli İ, Demir M, Mete E, Çalişkan A., Rotavirus and adenovirus prevalence in patients with acute viral gastroenteritis in Denizli, Turkey, 2017-2021. *Journal of medical virology*, 2022; 94(8): 3857-3862. DOI: 10.1002/jmv.27834.
- 25. Patel MM, Steele D, Gentsch JR, Wecker J, Glass RI, Parashar UD., Real-world impact of rotavirus vaccination. *The Pediatric infectious disease journal*, 2011; 30(1 Suppl): S1-S5. DOI: 10.1097/INF.0b013e3181fefa1f
- Román E, Wilhelmi I, Colomina J, Villar J, Luz Cilleruelo M, Nebreda V, Del Alamo M, Sánchez-Fauquier A., Acute viral gastroenteritis: proportion and clinical relevance of multiple infections in Spanish children. *Journal of medical microbiology*, 2003; 52(5): 435-440. DOI: 10.1099/jmm.0.05079-0
- Sarker MH, Das SK, Ahmed S, Ferdous F, Das J, Farzana FD, Shahid AS, Shahunja KM, Afrad MH, Malek MA, Chisti MJ, Bardhan PK, Hossain MI, Al Mamun A, Faruque AS., Changing characteristics of rotavirus diarrhea in children younger than five years in urban Bangladesh. *PLoS One*, 2014; 9(8): e105978. DOI: 10.1371/journal.pone.0105978.
- 28. Schmidt MA, Groom HC, Rawlings AM, Mattison CP, Salas SB, Burke RM, Hallowell BD, Calderwood LE, Donald J, Balachandran N, Hall AJ, Incidence, etiology, and healthcare utilization for acute gastroenteritis in the community, United States. *Emerging infectious diseases*, 2022; 28(11): 2234. DOI: 10.3201/eid2811.220247.
- 29. Sert S, Erayman B., Frequency and seasonal distribution of adenovirus and rotavirus in children diagnosed with acute gastroenteritis: A single center experience. *Journal of Contemporary Medicine*, 2023; 13(2): 353-359. DOI: 10.16899/jcm.1259028.
- Sharif N, Sharif N, Khan A, Azpíroz ID, Diaz RM, Díez IDIT, Parvez AK, Dey SK., Prevalence and genetic diversity of rotavirus in Bangladesh during pre-vaccination period, 1973-2023: a meta-analysis. *Frontiers in immunology*, 2023; 14: 1289032. DOI: 10.3389/fimmu.2023.1289032.

- Shieh WJ., Human adenovirus infections in pediatric population-an update on clinico-pathologic correlation. *Biomedical journal*, 2022; 45(1): 38-49. DOI: 10.1016/j.bj.2021.08.009.
- Taşbent FE, Gülseren YD, Özdemir M., Investigation of adenovirus and rotavirus frequencies and seasonal distribution in patients with gastroenteritis. *Ahi Evran Medical Journal*, 2021; 5(3): 218-222. DOI: 10.46332/aemj.826098.
- 33. Tate JE, Burton AH, Boschi-Pinto C, Parashar UD; World Health Organization–Coordinated Global Rotavirus Surveillance Network., Global, regional, and national estimates of rotavirus mortality in children < 5 years of age, 2000-2013. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America, 2016; 62 Suppl 2: 96-105. DOI: 10.1093/cid/civ1013.
- Tatte VS, Gopalkrishna V., Detection of different enteric viruses in children with diarrheal disease: evidence of the high frequency of mixed infections. *Access microbiology*, 2019; 1(2): e000010. DOI: 10.1099/acmi.0.000010.
- 35. Terzi HA, Aydemir Ö., Investigation of Rotavirus and Adenovirus Frequency in Patients with Acute Gastroenteritis; Sakarya *Medical Journal*, 2018; 8(4): 746-752. DOI: 10.31832/smj.473812.
- 36. Tran A, Talmud D, Lejeune B, Jovenin N, Renois F, Payan C, Leveque N, Andreoletti L., Prevalence of rotavirus, adenovirus, norovirus, and astrovirus infections and coinfections among hospitalized children in northern France. *Journal of clinical microbiology*, 2010; 48(5): 1943-1946. DOI: 10.1128/JCM.02181-09.
- 37. Ushijima H, Pham NTK, Hoque SA, Nomura A, Kumthip K, Shimizu-Onda Y, Okitsu S, Kawata K, Hanaoka N, Müller WE, Maneekarn N, Hayakawa S, Khamrin P., Evaluation of a novel triplex immunochromatographic assay for rapid simultaneous detection of norovirus, rotavirus, and adenovirus on a single strip test. *Journal of infection and public health*, 2024; 17(4): 619-623. DOI: 10.1016/j.jiph.2024.02.010.
- Üstebay S, Üstebay DÜ, Ertekin Ö., Frequency of adenovirus and rotavirus in children with acute gastroenteritis. Kafkas Journal of Medical Sciences, 2019; 9(1): 6-10. [Article in Turkish] DOI: 10.5505/kjms.2019.13540
- Yıldız D, Sağlık İ, Hacımustafaoğlu MK, Özakın C, Çelebi S., The Effect of COVID-19 Pandemic on Rotavirus and Adenovirus Prevalence in Bursa Uludag University Hospital. *Turk Mikrobiyoloji Cemiyeti Dergisi*, 2022; 52(4): 299-309. [Article in Turkish] DOI: 10.54453/TMCD.2022.20082.
- 40. Zhang SX, Zhou YM, Xu W, Tian LG, Chen JX, Chen SH, Dang ZS, Gu WP, Yin JW, Serrano E, Zhou XN., Impact of co-infections with enteric pathogens on children suffering from acute diarrhea in southwest China. *Infectious diseases of poverty*, 2016; 5(1): 64. DOI: 10.1186/s40249-016-0157-2.