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Çocukluk Çağında Hangisi Daha Tehlikeli; Rotavirüs mü Adenovirüs mü?

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Hakan ONUR[1a*], Arzu RAHMANALI ONUR[2a]

[1] Memorial Private Diyarbakır Hospital, Department of Pediatric, Diyarbakır, Turkey

[2] Health Sciences University Diyarbakır Gazi Yaşargil Training and Research Hospital, Clinical Microbiology Unit, Diyarbakır, Turkey

[a]*ORCID: 0000-0003-4972-3878,* [b]*ORCID: 0000-0002-7669-9570*

Özet

Amaç: *Hastanemiz Çocuk Polikliniğinde gastroenterit tanısı alan hastalarda Rotavirüs ve Adenovirüs sıklığının immunokromatografik yöntemle belirlenmesi ve etken dağılımının yaş, cinsiyet ve aşılanma durumuna göre değişiminin retrospektif olarak değerlendirilmesi.*

Gereç ve yöntem: *Ocak 2015 - Kasım 2020 tarihleri arasında ishal, kusma, dehidratasyon ve ateş şikayetleri olan ve akut gastroenterit tanısı alan hastalar taze dışkı örnekleri alınarak değerlendirildi. Veriler tanımlayıcı istatistikler kullanılarak sunulmuştur.*

Bulgular: *Çalışmaya dahil edilen akut gastroenterit hastalarının sayısı 1.192 idi. Hastaların ortalama yaşı 18±SD aydı (min: 1 ay, maks: 180 ay). Adenovirüs ve Rotavirüs antijenleri tüm vakaların %10'unda (n=119) tespit edildi. Rotavirüs antijeni tüm vakaların % 6,6'sında (n=78) ve Adenovirüs antijeni % 3,1'inde (n=38) pozitifti. Rotavirüs pozitif vakalarda hastaneye yatış oranı 5.1 kat daha yüksekti (p<0.001). Ateş ve kusmanın Adenovirüs veya Rotavirüs pozitif olan hastalarda istatistiksel olarak daha yüksek olduğu gözlenmiştir. (p=0.001).*

Sonuç: *Rotavirüsün özellikle dehidrasyona yol açan şiddetli kusma/ishali olan çocuklarda akılda tutulması gerektiği gösterilmiştir. Bu nedenle erken çocukluk döneminde Rotavirüs aşılaması çok önemlidir.*

Anahtar Kelimeler: *Rotavirüs, Adenovirüs, Enterit, Çocukluk Çağı, Rotavirüs Aşısı*

Corresponding author: E-mail: drhonur@hotmail.com

Which One Is More Dangerous in Childhood Rotavirus or Adenovirus?

Abstract

Objective: *Determination of the frequency of Rotavirus and Adenovirus in patients diagnosed with gastroenteritis in the Pediatric Polyclinic of our hospital by immunochromatographic method and retrospective evaluation of the change in the distribution of the agent according to age, gender and vaccination status.*

Method: *Those patients with complaints of diarrhea, vomiting, dehydration, and fever as well as those diagnosed with acute gastroenteritis were evaluated by taking fresh stool samples between January 2015 and November 2020. The data were presented using descriptive statistics.*

Results: *The number of acute gastroenteritis patients included in the study was 1,192. The mean age of the patients was 18±SD months (min: 1 month, max: 180 months). Adenovirus and Rotavirus antigens were detected in 10% of all cases (n=119). Rotavirus antigen was positive in 6.6% (n=78) and Adenovirus antigen was positive in 3.1% (n=38) of all cases. The hospitalization rate was 5.1 times higher in Rotavirus positive cases (p<0.001). It was observed that fever and vomiting were statistically higher in patients with Adenovirus or Rotavirus positive. (p=0.001).*

Conclusion: *It has been shown that Rotavirus should be kept in mind, especially in children with severe vomiting/diarrhea leading to dehydration. Therefore, Rotavirus vaccination is very important in early childhood.*

Keywords*: Rotavirus, Adenovirüs, Enteritis, Childhood, Rotavirus Vaccine*

Introduction

In underdeveloped nations, acute gastroenteritis (AGE) is a significant cause of death and morbidity in children under the age of five. It is the third leading cause of death in children under the age of five, after pneumonia and premature birth complications. Gastrointestinal infections are common in developing countries where hygienic conditions and health systems are inadequate.

Increased stool frequency (AGE) is a clinical condition that can occur with or without vomiting or fever. Diarrhea generally lasts for less than seven days and does not exceed 14 days[1]. The most common microbiological causes of infectious gastroenteritis differ according to age, geographic region, and type of diarrhea. Agents can be viral, bacterial and parasitic or infection can be due to multiple agents. Viral agents are responsible for approximately 60% of all gastroenteritis. The peak incidence of the disease is often 3-24 months before weaning, due to a reduction in transplacental antibodies and the development of protective immunity. Viral agents include rotavirus, enteric adenoviruses, astroviruses, noroviruses and caliciviruses[2,3]. Rotaviruses in particular have historically

been the most frequent cause of viral gastroenteritis. Rotaviruses were discovered to be the cause of 30–50% of diarrhea in children under the age of five in Turkish investigations [4,5].

Since the clinical findings of viral gastroenteritis are non-specific, laboratory evaluation is essential to determine the causative agent. By showing the virus' presence in the feces (using electron microscopy or molecular studies) or by identifying it using ELISA tests and other immunological procedures, viral gastroenteritis can be diagnosed [6].

This study was conducted retrospectively and cross-sectionally to determine the frequency of Rotavirus and Adenovirus in children diagnosed with Acute Gastroenteritis between January 2015 and November 2020, and to determine the distribution of the factors according to age, gender, vaccination rates, hospitalization and seasonal variables.

Materials and Methods

Study design

This study is a retrospective and cross-sectional study, and children, who applied to the Pediatric Outpatient Clinic between January 2015 and November 2020 and were diagnosed with AGE, were included. Demographic characteristics of all cases included in the study were noted.

Approval for the study was granted by the Ethics Committee of Memorial Bahçelievler Hospital, dated 08.06.2023 and numbered 102. The study group consisted of children, who were diagnosed with acute gastroenteritis and admitted to the Memorial Private Diyarbakır Hospital, Department of Pediatrics with complaints of diarrhea, vomiting, dehydration and fever between the specified dates. All stool samples were examined in the central laboratory of our hospital, and those with macroscopically watery stools. The study only included samples that were parasite-free under a microscope. Cases with known immunodeficiency diagnosis or in whom parasites (Giardia intestinalis, Entamoeba histolytica etc.) were detected in stool samples and where bacteria grew in stool cultures. were excluded from the study.

The qualitative immunochromatographic test kit (VIKIA BioMerieux SA Rota-Adeno, France) with sensitivity and specificity in fecal material reported as 99.9% and 97.8% respectiviely for rotavirus, and 99.9% and 97% for enteric adenovirus, was used in accordance with the company's working procedures.

Group classification

Children who had rotavirus found in their stool samples and those who had adenovirus were separated into two groups for the research. Apart from these factors, other pathogens were evaluated separately.

Statistical Analysis

The SPSS 25.0 (IBM Corporation, Armonk, New York, United States) program was used in the analysis of the variables. The conformity of the data to the normal distribution was evaluated with the Shapiro-Wilk Francia test Mann-Whitney U test was used together with Monte Carlo results to compare the groups formed according to adenovirus and rotavirus positivity with each other based on the age variable. The comparison of the column ratios with each other was expressed by the Benjamini-Hochberg corrected p-value results. The Odds ratio was used with 95% confidence intervals to show the extent to which those with a risk factor outnumbered those without. While the general distributions of quantitative variables were shown in the tables as Mean (standard deviation) / Median (Minimum -1st Quartile - 3rd Quartile - Maximum) for analysis, they were expressed as Median (1st Quartile - 3rd Quartile). Categorical variables were shown as n (%) in all tables. The variables were analyzed at a 95% confidence level, and a p-value of less than 0.05 was considered significant.

Results

1,402 children were diagnosed with acute gastroenteritis within the specified periods. However, 145 cases were excluded from the study because parasites were detected and 65 cases had another underlying disease. Of the 1,192 patients, who met the criteria, 41.4% (n=493) were female and 58.6% (n=699) were male. The mean age of infants were 31.2 (SD:33.7) Adenovirus or rotavirus antigen were detected as positive in 9.9% (n=119) of the children. Rotavirus antigen was found to be positive in 65.6% (n=78) of cases, adenovirus antigen in 31.9% (n=38), and both rotavirus and adenovirus antigen positivity in 2.5% (n=3).

52.6% (n=20) of the adenovirus positive samples were male, as were 61.5% (n=48) of the rotavirus positive samples; 3 of the samples, which were found to be positive for both rotavirus and adenovirus antigen, were from female patients. Regarding both Rotavirus and Adenovirus antigens, there was no statistically significant gender difference ($p>0.05$).

The relationship between the antigen positivity of both viruses and the season was evaluated separately; both rotavirus and adenovirus antigen positivity was mostly detected in the autumn and winter months ($p>0.05$). The demographic characteristics and seasonal distribution of the cases are summarized in Table 1.

Table 1*. General characteristics of the children*

	Mean (SD) / Median (Min-Q1-Q3-Max)
Age (month)	31.25 (33.67) / 19 (1-8-43-180)
	n (%)
Male gender	699 (58.6)
Seasons Cases	
Spring cases	257 (21.6)
Summer cases	371 (31.1)
Autumn cases	340 (28.5)
Winter cases	224 (18.8)
Vaccine positivity	440 (36.9)
Hospitalization	156 (13.1)
Fever positivity	253 (21.2)
Vomiting positivity	241 (20.2)
Dehydration positivity	57 (4.8)

The cases included in the study were analyzed separately according to the positivity of adenovirus and rotavirus and are shown in Table 2. There was no difference between the two groups according to age, gender and seasonal characteristics ($p>0.05$). The incidence of rotavirus was 4.3 times higher in those who were not vaccinated with rotavirus, and adenovirus positivity was statistically significantly higher in rota-vaccinated cases ($p<0.001$). The rate of hospitalization was higher in rotavirus positive cases, and the rate of hospitalization was 5.1 times higher in rotavirus positivity ($p<0.001$). When it came to fever and vomiting, there was no difference between the groups. The presence of dehydration was higher in rotavirus positive cases. The results are given in Table 2. The distribution by symptoms is shown in Figures 1 and 2.

***Table 2**. Analysis of cases according to Adenovirus and Rotavirus Positivity*

	Adenovirus (n=38)	**Rotavirus (n=78)**	**P**
	Median(Q1-Q3)	**Median(Q1-Q3)**	
Age (m)	19 (11-38)	18 (10-28)	0.528 [u]
	n (%)	**n (%)**	
Male Gender	20 (52.6)	48 (61.5)	0.423 [c]
Season Cases			0.743 [c]
Spring cases	5 (13.2)	13 (16.7)	
Summer cases	7 (18.4)	13 (16.7)	
Autumn cases	15 (39.5)	36 (46.2)	
Winter cases	11 (28.9)	16 (20.5)	
Vaccine positivity	**22 (57.9)**	19 (24.4)	**<0.001** [c]
			4.3 (1.9-9.8) [or]
Hospitalization	6 (15.8)	**38 (48.7)**	**<0.001** [c]
			5.1 (1.9-13.5) [or]
Fever positivity	22 (57.9)	45 (57.7)	0.999 [c]
Vomiting positivity	21 (55.3)	50 (64.1)	0.419 [c]
Dehydration positivity	4 (10.5)	**26 (33.3)**	**0.012** [c]
			4.3 (1.4-13.3) [or]

[c] Pearson Chi Square Test(Monte Carlo),
[u] Mann Whitney U test(Monte Carlo),
[or] Odds Ratio (95% Confidence interval for Odds Ratio),
NS.: Notsignificant, SD. Standard Deviation, Min:Minimum, Max.:Maximum, Q1: 1st Quartile, Q3: 3rd Quartile

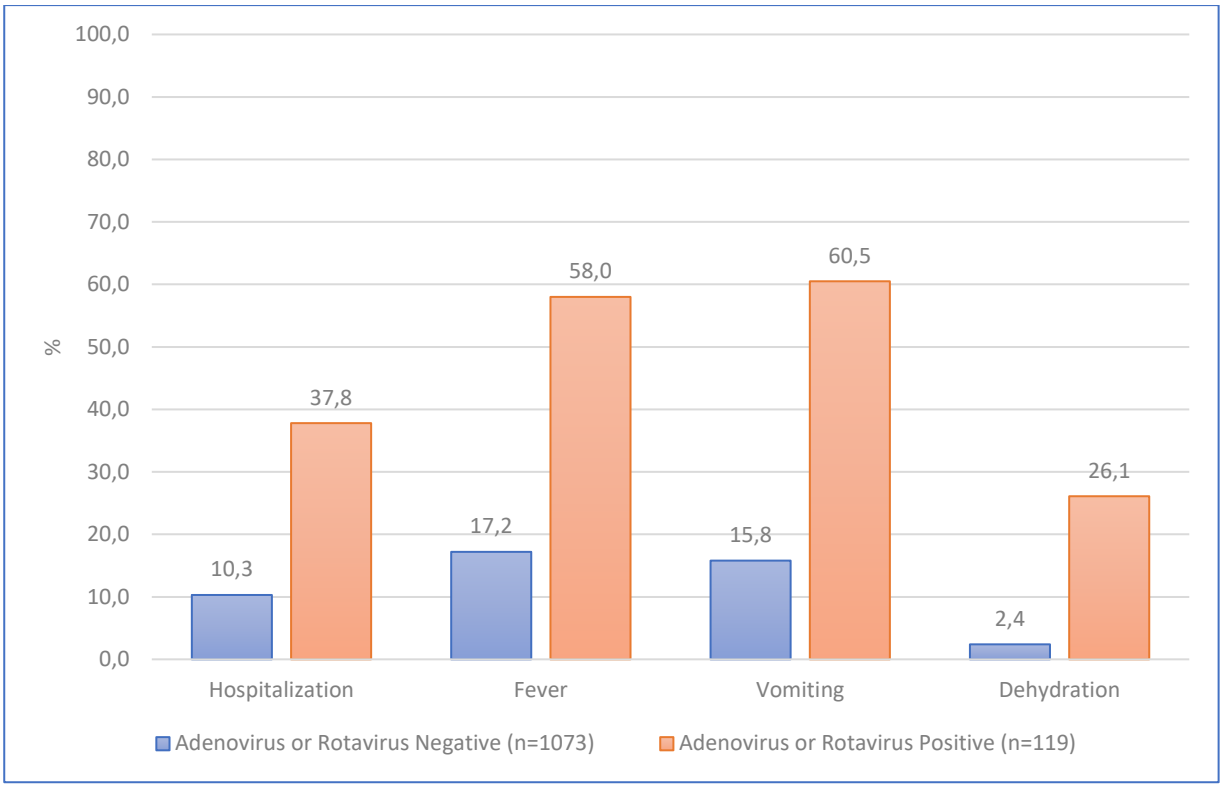

Figure 1. *Distribution of cases according to symptoms*

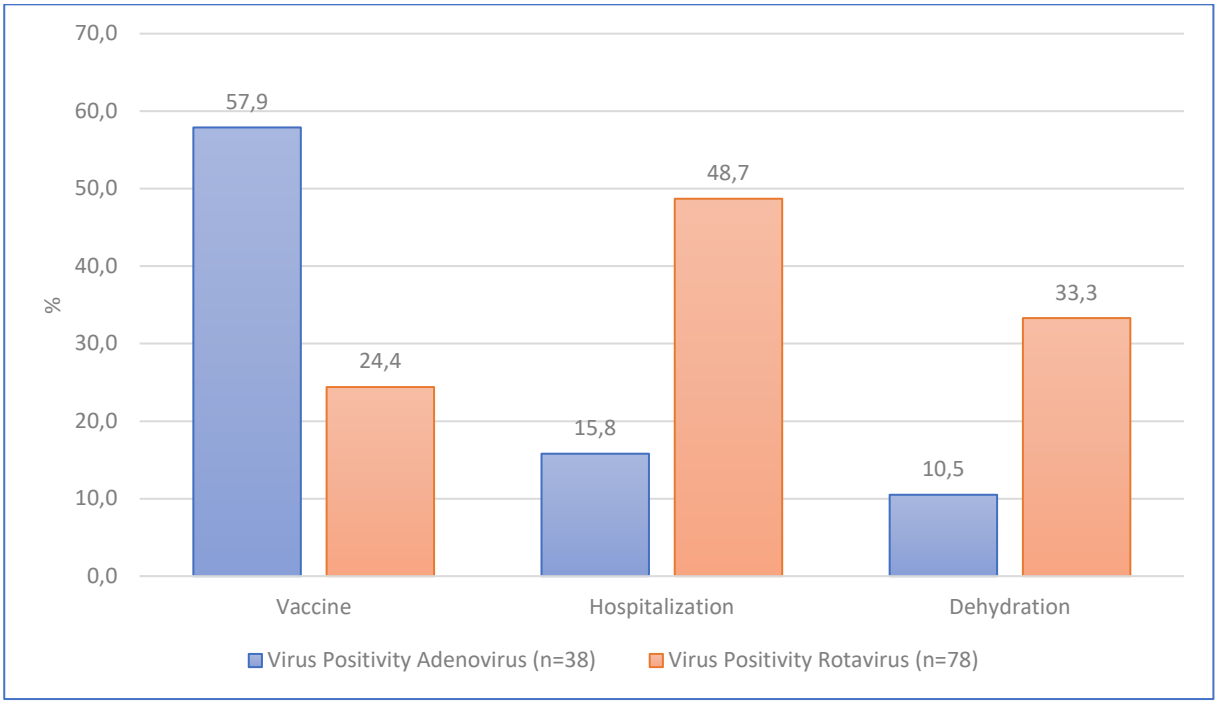

Figure 2*. Distribution of cases according to Adenovirus and Rotavirus Positivity*

The cases included in the study, who were positive for adenovirus or rotavirus and other gastroenteritis agents, are compared in Table 3. The groups did not differ in terms of age, gender, or vaccination rates. Rotavirus or adenovirus antigen positivity was detected most in autumn and winter, with a seasonally significant difference observed between cases with and without rotavirus and adenovirus antigens. ($p<0.001$). Hospitalization was found to be statistically higher in patients, who were found to be positive for adenovirus or rotavirus. ($p=0.001$). According to the analysis, there were 5.3 times more hospitalizations, 6.7 times more fever, 8.2 times more frequent vomiting and 14.2 times more dehydration in adenovirus or rotavirus positive cases. Similarly, fever and vomiting were found to be statistically higher in patients with positive for adenovirus or rotavirus. ($p=0.001$).

Table 3. *Analysis of cases according to viral agents*

	Other Agents (n=1073)	**Adeno and/or Rota Virus Positivity (n=119)**	**P**
	Median(Q1-Q3)	**Median(Q1-Q3)**	
Age (m)	19 (8-43)	18 (11-29)	0.598 [u]
	n (%)	**n (%)**	
Male Gender	631 (58.8)	68 (57.1)	0.769 [c]
Season Cases			**<0.001** [c]
Spring cases	237 (22.1)	20 (16.8)	NS.
Summer cases	**351 (32.7)**	20 (16.8)	**<0.001**
Autumn cases	288 (26.8)	**52 (43.7)**	**<0.001**
Winter cases	197 (18.4)	27 (22.7)	NS.
Vaccine positivity	399 (37.2)	41 (34.5)	0.617 [c]
Hospitalization	111 (10.3)	**45 (37.8)**	**<0.001** [c]
			5.3 (3.5-8) [or]
Fever positivity	184 (17.2)	**69 (58.0)**	**<0.001** [c]
			6.7 (4.5-9.9) [or]
Vomiting positivity	169 (15.8)	**72 (60.5)**	**<0.001** [c]
			8.2 (5.5-12.3) [or]
Dehydration positivity	26 (2.4)	**31 (26.1)**	**<0.001** [c]
			14.2 (8-24.9) [or]

[c] Pearson Chi Square Test(Monte Carlo); Post Hoc Test: Benjamini-Hochberg Correction,
[u] Mann Whitney U test(Monte Carlo),
[or] Odds Ratio (95% Confidence interval for Odds Ratio),
NS.: Notsignificant, SD. Standard Deviation, Min:Minimum, Max.:Maximum, Q1: 1st Quartile, Q3: 3rd Quartile

Discussion:

Although acute gastroenteritis is more common in developing countries, it is a common public health problem that can cause significant issues all over the world. This study investigated rotavirus and adenovirus positivity in childhood according to age, gender, seasons, and symptoms at presentation over a five-year period. Although the data belong to a single center, the rate of hospitalization in childhood, fever, and vomiting were found to be higher in those with gastroenteritis due to adenovirus or rotavirus compared to other factors. In addition, rotavirus-positive cases were compared with adenovirus-positive cases, and it was found that more hospitalizations and more dehydration were found in rotavirus-positive children.

In most temperate areas, acute viral gastroenteritis occurs throughout the year, with an autumn and winter preponderance [7,8]. In our research, we discovered that the fall months were more common for rotavirus and adenovirus positive cases.

The most frequent cause of viral gastroenteritis in children in the past was rotavirus. In nations where newborns are consistently immunized against rotavirus, rotavirus gastroenteritis has significantly decreased. But some older children and adults continue to have rotavirus illness symptoms [9,10]. To better understand the epidemiology of rotavirus infection among children with diarrhea visiting two hospitals in Ankara, Turkey, a prospective research was carried out between September 2004 and December 2005 [11]. Rotavirus was found in 39.7% of the 322 stool samples, and it primarily impacted children between the ages of 6 and 23 months. In another study, Caneriği et al [12] collected a total of 341 stool samples from pediatric patients. They found that rotavirus positivity in stool samples was 23.1%. Most of the cases were detected in the winter months. In another study from Turkey [13], rotavirus positivity was 18.7% (n = 126). 8.9% of those tested positive for adenovirus, and 4.4% also had rota-adenovirus co-infection. In December, January, February, and March, rotavirus positive cases predominated. Regarding vomiting, dehydration, and the cohabitation of diarrhea and vomiting in clinical parameters, there was a substantial difference between rotavirus positive cases and negative cases13. In our study, only 6% of rotavirus-related gastroenteritis cases were detected. We think that the low rate of positive detection of rotavirus in our country may be related to the vaccination rate, which is close to 37%. In the United States, laboratory surveillance during the prevaccine (2000 to 2006) and postvaccine (2007 to 2018) periods demonstrates decreases in rotavirus-positive laboratory tests (from 26 to 6 percent) and rotavirus-positive laboratory tests during the characteristic autumn-winter peak (from 43 to 14 percent) and during the "rotavirus season" (from 26 to 9 weeks) [14]. As a matter of fact, in our study, the incidence of rotavirus was found to be lower in children, who were vaccinated with rotavirus. However, the rotavirus vaccine is not free in Turkey and in many other

countries, so access to the vaccine can be difficult for many families. It shows once again how important the vaccine is in countries where rotavirus is common.

Although most viral enteric infections are asymptomatic, nearly every child experiences more than one episode of symptomatic acute gastroenteritis before the age of two [15,16]. In symptomatic children, illness usually begins 12 hours to 10 days after exposure and lasts 3 to 9 days [17,18,19]. The typical presentation is diarrhea, vomiting, or both; additional symptoms may include fever, abdominal pain or cramps, anorexia, headache and myalgia [20]. Children may experience only diarrhea or vomiting at first, but with progression they may become ill enough to require hospitalization. About 10 percent of children hospitalized for rotavirus infection have only fever and/or vomiting at presentation [21]. In children, vomiting is a prominent feature in both rotavirus and norovirus gastroenteritis [22]. In our study, the most common symptom was vomiting, which was present in 64.1% of rotavirus-positive children. Similarly, it was present in 60% of rotavirus positive and adenovirus positive cases.

In a review of 135 cases of polymerase chain reaction-confirmed gastroenteritis from a tertiary care children's hospital between 2006 and 2009 (during which there was an outbreak of norovirus)[8]. Diarrhea was present in 90% of cases, and vomiting was present in 56%. Abdominal cramping was reported in 12%; abdominal distension in 16%; and abdominal tenderness in 16%[8]. In our study, 57.7% of rotavirus-positive children had fever, similarly, 58% of rotavirus and adenovirus-positive cases had fever. In cases of gastroenteritis due to other agents, fever was present only in 17.2%. This situation makes us think that patients with diarrhea due to rotavirus and adenovirus infections present with a noisier clinical picture. Rotavirus and adenovirus infections should be kept in mind in diarrhea cases that require hospitalization, especially in cases under the age of two. This situation led to a statistical difference in our study.

Dehydration caused by acute viral gastroenteritis necessitating medical treatment is most common in young children, especially those under the age of two[23]. Young children are more prone to dehydration than older kids are because they have smaller fluid stores, a faster metabolic rate, a larger body surface to volume ratio, and a greater reliance on others to deliver fluids. Dehydration may be common, especially due to rotavirus. In our study, it was observed that there was 33.3% dehydration in rotavirus positive cases and this led to a statistical difference. At the same time, hospitalization was found to be higher in rotavirus positive cases compared to adenovirus positivity, this situation was found more in rotavirus positive cases. Rotavirus infection should be considered especially in cases requiring hospitalization and where there is severe diarrhea and vomiting that may lead to dehydration.

Conclusion

In conclusion, increased bowel frequency, with or without vomiting, fever, or abdominal discomfort, is a clinical condition that frequently denotes acute gastroenteritis. Acute viral gastroenteritis is often caused by a viral pathogen. It has been shown that vomiting, fever and hospitalizations may be more frequent in rotavirus and adenovirus infections, and that rotavirus should be kept in mind especially in children with severe vomiting/diarrhea leading to dehydration. Therefore, rotavirus vaccination is very important in early childhood. In terms of both reducing hospitalizations and reducing morbidity, reimbursement of countries by the existing health system can be considered.

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