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Prevalence of Rotavirus, Adenovirus, and Hepatitis A Virus in a Tertiary Care Hospital in Somalia

Somali'de Bir Üçüncü Basamak Hastanesinde Rotavirus, Adenovirus ve Hepatit A Virus Prevalansı

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Abstract

Rotavirus, one of the viral infectious agents that is transmitted mainly through the fecal-oral route and spreads easily in regions with poor sanitation conditions, is the most common causative agent of acute gastroenteritis in children under five years of age worldwide, and enteric adenoviruses are other frequently encountered causative agents of gastroenteritis in childhood. Hepatitis A virus (HAV) is also transmitted in similar routes and is endemic in regions with poor sanitation conditions and limited access to clean water and is usually acquired in early childhood in these regions. In this study conducted in Mogadishu Somalia, rotavirus and adenovirus antigen test (immunochromatographic rapid test) results in patients admitted to a tertiary hospital in the 9-month period between February 2019 and October 2019 and ELISA based HAV antibody test results studied in 2018-2019 were retrospectively examined and it was aimed to determine the distribution of positivity rates of these viruses by age, gender, and year. During the study period, 1136 patients (mean age 6.33±12.36) were tested for rotavirus and adenovirus antigens, and 362 patients (mean age 21.26±18.45) were tested for anti-HAV IgM/IgG antibodies. The positivity rates of rotavirus and adenovirus were found as 17.8% and 5.1%, respectively. The positivity rates of anti-HAV IgM and IgG antibodies were 26.5% and 85.4%. The age group with the highest rotavirus test positivity was babies under one year old (27.3%), positivity rate was also high in children aged 1-2 years old (20.9%), and this distribution was similar for adenovirus. Although a small number of patients were tested in under five years of age, anti-HAV IgG seropositivity was 60% and above in all age groups. The highest anti-HAV IgM positivity rates were observed in children 2-<5 and 5-15 years of age, 52.9% and 44% respectively. Rotavirus antigen positivity was found at high levels in the three-month period covering June, July, and August 2019. In July (2019), it was observed that the number of rotavirus and adenovirus antigen test requests were increased, and also, at the same time the highest positivity rates for both viruses were observed; 31.2% and 9.5% for rotavirus and adenovirus. Rotavirus and enteric adenovirus co-infection was detected in 2.4% (27/1136) of the patients, and 23 (85.2%) of these were under five years of age children. Our study results show that children under the age of two are especially affected by rotavirus and adenovirus infections in Somalia and indicate that HAV infections are

acquired at an early childhood. We can say that it may be useful to review vaccination programs as an important public health measure to reduce the burden of mortality and morbidity associated with HAV and rotavirus, which have a high prevalence and also have protective vaccines.

Keywords: Rotavirus, Adenovirus, Hepatitis A, Somalia.

Özet

Başlıca fekal-oral yolla bulaşan ve sanitasyon koşullarının zayıf olduğu bölgelerde kolay yayılan viral enfeksiyon etkenlerinden rotavirus dünya genelinde beş yaş altı çocuklarda en sık görülen akut gastroenterit etkeni iken, enterik adenoviruslar çocukluk çağında sık karşılaşılan diğer gastroenterit etkenlerindendir. Hepatit A virusu (HAV) da benzer yollarla bulaşır ve sanitasyonun yetersiz olduğu ve temiz suya erişimin kısıtlı olduğu bölgelerde endemiktir ve bu bölgelerde genellikle erken çocukluk çağında edinilir. Mogadişu Somali'de yürütülen bu çalışmada, Şubat 2019 - Ekim 2019 tarihleri arasındaki 9 aylık dönemde bir üçüncü basamak hastaneye başvuran kişilerde rotavirus ve adenovirus antijen test (immünokromatografik hızlı test) sonuçları ve 2018-2019 yıllarında çalışılan ELISA temelli HAV antikor test sonuçları retrospektif olarak incelenmiş ve bu virüsler için pozitiflik oranlarının yaş, cinsiyet ve yıl içerisindeki dağılımının belirlenmesi amaçlanmıştır. Çalışma döneminde 1136 hasta (yaş ortalaması 6.33±12.36) rotavirus ve adenovirus antijenleri için, 362 hasta (yaş ortalaması 21.26±18.45) ise anti-HAV IgM/IgG antikorları için test edilmişti. Rotavirus ve adenovirus için pozitiflik oranları sırasıyla %17.8 ve %5.1 olarak bulundu. Anti-HAV IgM ve IgG antikorları için pozitiflik oranları ise %26.5 ve %85.4 idi. Rotavirus test pozitifliğinin en yüksek olduğu yaş grubu bir yaş altı bebeklerdi (%27.3), pozitiflik oranı 1-2 yaş arası çocuklarda da yüksekti (%20.9), bu dağılım adenovirus için de benzerdi. Anti-HAV IgG için beş yaş altı çocuklarda az sayıda hasta test edilmiş olmakla beraber, seropozitiflik oranı tüm yaş gruplarında %60 ve üzerinde idi. En yüksek anti-HAV IgM pozitiflik oranları ise 2-<5 yaş ve 5-15 yaş grubu çocuklarda görüldü, sırasıyla %52.9 ve %44. Rotavirus antijen pozitifliği 2019 yılı haziran, temmuz ve ağustos aylarını kapsayan üç aylık dönemde yüksek seviyelerde idi. Temmuz (2019) ayında rotavirus ve adenovirus antijen test istemlerinin sayısı artarken, aynı zamanda her iki virüs için de en yüksek pozitiflik oranları gözlemlendi, rotavirus ve adenovirus için sırasıyla %31.2 ve %9.5. Antijen testi çalışılan hastaların %2.4'ünde (27/1136) rotavirus ve enterik adenovirus ko-enfeksiyonu varlığı tespit edildi ve bu hastalardan 23'ü (%85.2) beş yaşından küçük çocuklardı. Çalışma sonuçlarımız Somali'de rotavirus ve adenovirus enfeksiyonlarından özellikle iki yaş altı çocukların etkilendiğini göstermekte, HAV enfeksiyonlarının ise erken yaşlarda edinildiğine işaret etmektedir. Yüksek prevalansa sahip olan, bununla beraber koruyucu aşıları bulunan HAV ve rotavirus ilişkili mortalite ve morbidite yükünün azaltılması için önemli bir halk sağlığı önlemi olarak aşılama programlarının gözden geçirilmesinin yararlı olabileceğini söyleyebiliriz.

Anahtar Kelimeler: Rotavirus, Adenovirus, Hepatit A, Somali.

Introduction

Acute gastroenteritis is a common infectious disease that affects hundreds of millions of people every year and is one of the leading causes of death worldwide [1,2]. Although acute infectious gastroenteritis occurs in all age groups, it mainly affects the pediatric population, and the most affected age group is children under five years of age [3,4]. These infections are common in both developed and developing countries, but overall most deaths occur in low-income and lower-middle-income countries [1,2,5,6].

Viruses, bacteria, and parasites are infectious causes of acute gastroenteritis [6,7]. However, viral pathogens including rotaviruses, enteric adenoviruses (group F viruses; types 40 and 41), noroviruses and other caliciviruses, astroviruses, and enteroviruses cause nearly 70% of acute gastroenteritis in children [6]. With the advances in diagnostic methods, in the last two decades, viral agents, such as rotavirus and adenovirus, have become more frequently identified infectious gastroenteritis agents [3].

Acute gastroenteritis agents are transmitted mainly through the fecal-oral route, as well as contaminated surfaces and water sources [3]. For this reason, limited access to clean water and poor sanitation and hygiene conditions facilitate the spread of the enteric virus infections transmitted via fecal-oral route in communities [8,9]. The fact

that available vaccines (e.g. rotavirus vaccine) have not yet become widespread use and that the desired results have not yet been achieved in research on the development of highly effective antiviral treatments can be considered as other important obstacles to reducing the burden of these infections [10,11].

Rotavirus is the leading cause of diarrhea-related morbidity and mortality worldwide, especially in children under five years of age [1]. Rotavirus causes severe acute gastroenteritis requiring hospitalization and can lead to death if dehydration is left untreated [2]. The inclusion of a rotavirus vaccine in national immunization programs can significantly reduce the rotavirus disease burden [2].

Enteric adenovirus infections are common throughout the world, and almost all individuals are infected with at least one strain by the age of six [12]. Adenoviruses (group F serotype 40 and 41), which cause outbreaks of gastroenteritis, cause infections mostly in children [12,13]. With the possibility of zoonotic transmission and interspecies recombination and lack of approved antivirals or effective vaccines, adenoviruses remain a threat to public health [12].

Hepatitis A is a common form of viral hepatitis. It is usually transmitted by eating food and drinking water contaminated with the feces of an infected person [14,15]. World Health Organization (WHO) estimates that 7,134 people worldwide died from hepatitis A in 2016 (accounting for 0.5% of deaths due to viral hepatitis) [15]. Unlike hepatitis B and C, hepatitis A does not cause chronic liver disease, but can cause debilitating symptoms and, rarely, fulminant hepatitis (acute liver failure), which is often fatal [15].

Although there has been an increase in the number of articles included in the literature in recent years, data on the epidemiology of enteric viruses in Somalia are limited. In this study, it was aimed to examine the positivity rates of rotavirus, enteric adenovirus, and HAV in Mogadishu, Somalia, with the demographic characteristics of the patients, and to contribute to the planning of preventive health policies with the epidemiological data to be obtained.

Material and Method

The study was conducted after obtaining approval from the institutional ethics committee (Ethics Committee of Mogadishu Somalia-Turkey Recep Tayyip Erdoğan Training and Research Hospital, date: 05.12.2019, decision no: 184, number: MSTH/2725).

In this study, the rotavirus and adenovirus antigen test (immunochromatographic rapid test) results in the 9-month period between February 2019 and October 2019 and anti-HAV antibody IgM/IgG test results studied in 2018-2019 were examined retrospectively.

Demographic characteristics of the patients were investigated from the hospital electronic record system. The distribution and positivity rates of the test results in age groups (0-<6 months, 6 months-<12 months, 1 year-<2 years, 2 years-<5 years, 5-15 years, 16-65 years, >65 years), gender, and time were recorded.

Stool samples from the patients were taken into the stool container, and the presence of rotavirus and/or enteric adenovirus antigens were determined with the immunochromatography testing method (Microcult-Rotavirus/Adenovirus Combo, Biotech, China) on the same day.

Anti-HAV serological tests were performed using an Architect HAVAb-IgG chemiluminescence microparticle immunoassay (Abbott Diagnostics, Germany) on the Architect I 2000 SR system (Abbott Diagnostics, USA). The results were interpreted as follows: S/Co≥1.00, reactive; S/Co<1.00, non-reactive.

Statistical analysis

Descriptive statistics are given as mean, standard deviation, frequency, and percentage. Comparisons between groups were analyzed with chi-square test and Fisher's exact test methods for categorical variables. Comparison results were considered statistically significant at $p<0.05$ with a 95% confidence interval. Normality distribution was determined using the Kolmogorov-Smirnov test. Mean comparisons were made with the student's T test for continuous variables with normal distribution, and with the Mann-Whitney U test for variables with non-normal distribution.

Results

1136 patients with a mean age of 6.33±12.36 years (median age of 2, range 1 month-82 years) were tested for rotavirus and adenovirus antigen, and 202 (17.8%) of them were positive for rotavirus and 58 (5.1%) positive for adenovirus.

The rotavirus positivity rate was %18.7 in men and %16.6 in women, the difference was not statistically significant (p=0.359). The adenovirus positivity rate was %5.8 in men and %4.2 in women, and the difference was not statistically significant (p=0.235) (Table 1).

362 patients with a mean age of 21.26±18.45 years (median age of 17, range 1 month-83 years) were tested for anti-HAV IgM/IgG antibodies. The positivity rates for anti-HAV IgM and IgG antibodies were 26.5% (96/362) and 85.4% (309/362). Of these patients, 228 (63.0%) were male and 134 (37.0%) were female. In the patients for whom HAV antibody testing was requested (Table 1), the average age of men (22.25±18.87) was slightly higher than that of women (19.57±17.65), but the difference was not statistically significant (p=0.271). The positivity rates of anti-HAV IgM and IgG were not different by gender, p=0.264 and p=0.671, respectively.

The age group with the highest rotavirus test positivity was babies under one year old (27.3%), the rate was also high in children aged 1-2 years old (20.9%), and this distribution was similar for adenovirus. The highest anti-HAV IgM positivity rates were seen in children aged 2-<5 years and 5-15 years of age, 52.9% and 44% respectively. Anti-HAV IgG seropositivity was 60% and above in all age groups.

Rotavirus antigen positivity was found at high levels in the three-month period covering June, July, and August 2019. In July (2019), while it was observed that the number of rotavirus and adenovirus antigen test requests were increased, and also, at the same time the highest positivity rates for both viruses were observed; 31.2% and 9.5% for rotavirus and adenovirus, respectively. There was also a minor anti-HAV IgM peak during the same period (Table 2 and Figure 1).

Rotavirus and enteric adenovirus co-infection was detected in 2.4% (27/1136) of the patients for whom antigen testing was performed, and 15 (55.6%) of the patients with co-infection were under one year of age, 23 (85.2%) of them were under five years of age. The ages of the remaining four patients were 8, 10, 30 and 46 years.

Table 1. Distribution of rotavirus, adenovirus, and hepatitis A virus test results according to ages and gender.

age groups →			0 - <6 m		6 - <12 m		1 - <2 y		2 - <5 y		5 - 15 y		16 - 65 y		>65 y		Total
results			F	M	F	M	F	M	F	M	F	M	F	M	F	M	
RoV	negative	n	28	43	91	86	92	120	82	133	57	91	43	59	5	4	934
	positive	n	6	17	29	41	19	37	14	16	8	8	3	4	0	0	202
	positive	%	17.6	28.3	24.2	32.3	17.1	23.6	14.6	10.7	12.3	8.1	6.5	6.3	0	0	17.8
AdV	negative	n	32	56	113	115	108	149	92	144	63	93	44	60	5	4	1078
	positive	n	2	4	7	12	3	8	4	5	2	6	2	3	0	0	58
	positive	%	5.9	6.7	5.8	9.4	2.7	5.1	4.2	3.4	3.1	6.1	4.3	4.8	0	0	5.1
HAV IgM	negative	n	3	3	3	7	6	5	11	13	25	26	54	104	1	5	266
	positive	n	0	1	0	0	0	2	8	19	17	23	6	20	0	0	96
	positive	%	0.0	25.0	0.0	0.0	0.0	28.6	42.1	59.4	40.5	46.9	10.0	16.1	0.0	0.0	26.5
HAV IgG	negative	n	1	1	2	2	2	1	5	4	6	1	5	23	0	0	53
	positive	n	2	3	1	5	4	6	14	28	36	48	55	101	1	5	309
	positive	%	66.7	75.0	33.3	71.4	66.7	85.7	73.7	87.5	85.7	98.0	91.7	81.5	100.0	100.0	85.4

F: Female. M: Male. RoV; rotavirus. AdV; adenovirus. HAV; hepatitis A virus.

Table 2. Distribution of rotavirus, adenovirus, and hepatitis A virus test results according to years and months.

years →			2018	2019											Total
months / results				1	2	3	4	5	6	7	8	9	10	11	
RoV	negative	n	-	-	105	135	105	169	208	137	60	14	1	-	934
	positive	n	-	-	23	25	8	21	46	62	16	1	0	-	202
	positive	%	-	-	18.0	15.6	7.1	11.1	18.1	31.2	21.1	6.7	0.0	-	17.8
AdV	negative	n	-	-	126	152	111	179	245	180	70	14	1	-	1078
	positive	n	-	-	2	8	2	11	9	19	6	1	0	-	58
	positive	%	-	-	1.6	5.0	1.8	5.8	3.5	9.5	7.9	6.7	0.0	-	5.1
HAV IgM	negative	n	78	10	11	15	7	13	21	18	25	40	23	5	266
	positive	n	35	2	7	11	5	1	4	8	13	5	5	0	96
	positive	%	31.0	16.7	38.9	42.3	41.7	7.1	16.0	30.8	34.2	11.1	17.9	0.0	26.5
HAV IgG	negative	n	11	2	1	7	2	3	4	4	8	9	2	0	53
	positive	n	102	10	17	19	10	11	21	22	30	36	26	5	309
	positive	%	90.3	83.3	94.4	73.1	83.3	78.6	84.0	84.6	78.9	80.0	92.9	100.0	85.4

RoV; rotavirus. AdV; adenovirus. HAV; hepatitis A virus.

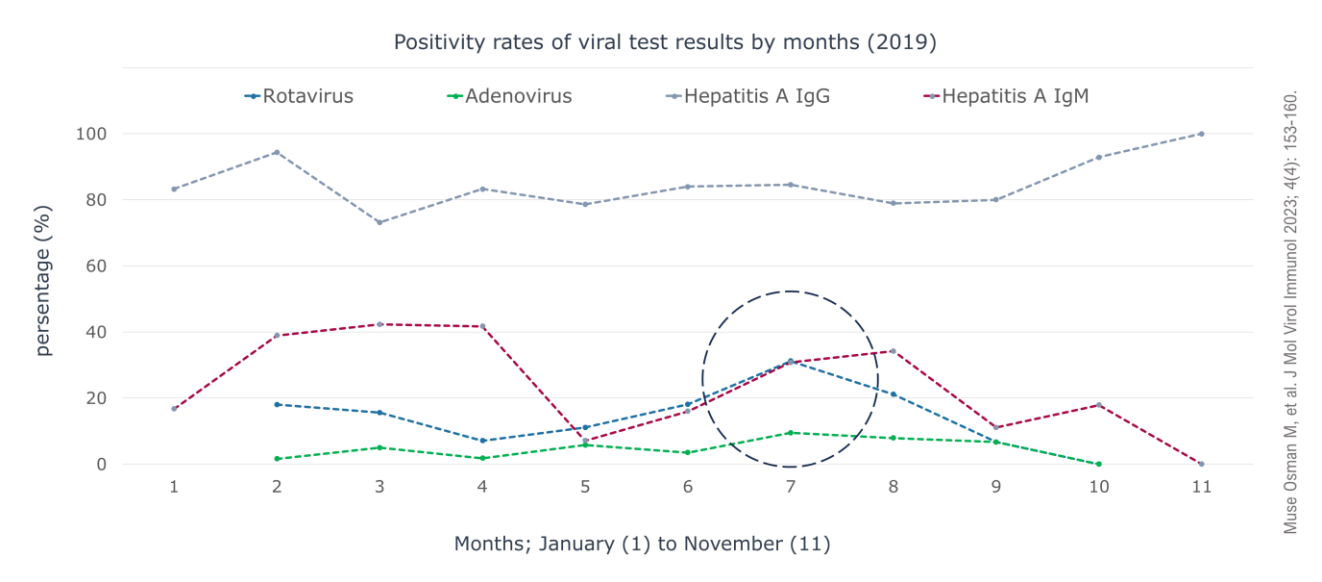

Figure 1. Rotavirus, adenovirus, and hepatitis A virus positive test results by months (2019).

In some months (January and November for rotavirus and adenovirus), the test was not studied because a test kit was not available, and since the study did not cover the period of December 2019, there is no data for this month.

Discussion

At the global level, deaths due to diarrheal diseases have decreased significantly over the last 25 years, although more rapidly in developing countries than in others [1]. Acute gastroenteritis caused by rotavirus causes vomiting and watery diarrhea, which leads to loss of fluid in the body, causing dehydration, which may require hospital treatment in some cases. The number of diarrhea and rotavirus deaths remains high in low-income populations and in developing countries where access to safe water, sanitation, and emergency medical care is poor [1]. Another problem in these regions is the underestimation of the true prevalence of these infections due to inadequate surveillance systems [2].

Accurate and rapid diagnosis of rotavirus infection is important for determining appropriate treatment, preventing unnecessary antibiotic use, and controlling the spread of infection [16]. Immunochromatographic rotavirus antigen tests used in this study are rapid and inexpensive tests that are widely used in the diagnosis of these infections and are of critical importance in low-income countries and regions with limited resources. In a study comparing quantitative reverse transcription polymerase chain reaction (RT-qPCR) results with rapid antigen test results, the overall consistency rate of RT-qPCR and immunochromatographic test was found to be 95.7% (kappa=0.784) [16].

In a systematic review of 165 epidemiological studies published between 1990 and 2017 on rotavirus prevalence, seasonality, vaccination status, and genotype distribution in the WHO-Eastern Mediterranean Region (EMRO), which includes Somalia, it was determined that 76.3% of acute gastroenteritis cases were rotavirus infections that remains the leading cause of acute gastroenteritis in children [2]. In our study, rotavirus infections were more than three times more common than adenoviral infections, 17.8% and 5.1%, respectively.

In a study conducted in Lebanon including 1200 samples, rotavirus was detected in the stool of 204 patients (17.0%), adenovirus was detected in 78 cases (6.5%) and mixed (rotavirus and adenovirus) infections were detected in 26 cases (2.2%) [3]. When we consider mixed infections separately for comparison, these rates were 15.4%, 2.7% and 2.4% in our study. Also, in a study conducted in China, the co-infection rate was found to be 1.11% (35 children) [17].

In a systematic review, it was pointed out that children younger than two years of age in WHO-EMRO countries are at higher risk for rotavirus infections and therefore increased vaccination coverage and surveillance systems are required to reduce the burden of rotavirus-associated gastroenteritis [2]. In our study, the age group with the highest rotavirus antigen positivity was babies under one year old (27.3%), the rate was also high in children between 1-2 years old (20.9%), and in the overall study, 73.8% of the rotavirus antigen test positive cases were children under the age of two and 88.6% were under the age of five. Likewise, in a study conducted in Lebanon, the highest rotavirus prevalence was seen in children aged 12-23 months [3]. In another study conducted in China, the prevalence of rotavirus was highest in children aged 12-24 months (28.6%) [17].

In a research from Brazil where 1012 stool samples were analyzed with TaqMan-based qPCR [13], a higher incidence of adenovirus infections has been reported to be observed in children between the ages of 6 and 24 months, with no apparent seasonality [13]. In a study conducted in China, adenovirus infections were detected in 3.6% of newborns and 5.8% of babies aged 1 to 6 months [17]. In the study conducted in Lebanon, patients infected with adenovirus were mostly 24-35 months old or 4-11 months old [3]. Similarly, in our study, the highest adenovirus positivity rate, was observed in children between 6 months and 12 months (7.7%), and also 25 (43.1%) of the adenovirus infections were in children under one year of age, 36 (62.1%) were in children under two years of age, and 45 (77.6%) were in children under five years of age (Table 1).

Determining the seasonal epidemiology of infections may be important in ensuring that vaccination campaigns are carried out in seasons when relevant viral infections are most prevalent [3]. In general, rotavirus infections peak in the cold winter months, and this situation is stated to be similar for all WHO-EMRO countries except the Gulf region countries [2]. However, it is clear that Somalia, located in the south, differs climatically from most other WHO-EMRO countries. A study conducted in Saudi Arabia showed that rotavirus disease was observed throughout the year, with occasional peaks, regardless of the season, and that rotavirus infections had a common peak with adenovirus infections in April [18]. In our study, which examined narrow-scope data covering only one year, rotavirus antigen positivity was found at high levels in the three-month period covering June, July, and August 2019. Remarkably, a common peak was observed in July, where both rotavirus and adenovirus antigen positivity reached the highest levels. There was also a

minor anti-HAV IgM peak during the same period. This situation may be associated with the common transmission routes of these viruses and spreading together with similar risk factors, such as water contamination. As a result of a common route of transmission, as examples mentioned above, co-infection cases in which both viruses infect a patient at the same time are also observed. In a study conducted in China, located in the northern hemisphere, it was reported that rotavirus had a seasonal cycle that peaked in November and December and decreased in July and August, while no clear seasonal pattern could be found for enteric adenoviruses [17]. In a study conducted in Lebanon, where the monthly distribution of rotavirus and adenovirus infection was found to be more similar to our study, with pattern of two peaks per year, first rotavirus peak observed in January and another peak in July-August, the frequency of adenovirus infection was found to be at its highest level in July-August [3].

Simple but cost-effective interventions such as vaccination against infectious diseases, including rotavirus, have proven to have the potential to prevent significant morbidity and mortality in low-income countries [19]. The majority of WHO-EMRO countries (81.8%) also administer the rotavirus vaccine, while seven countries (Egypt, Iran, Lebanon, Oman, Somalia, Syria, and Tunisia), have not yet administered the rotavirus vaccine in their national programs [2]. According to a systematic review and meta-analysis study conducted by Godfrey et al., evidence from sub-Saharan African countries where the vaccine has been administered indicates significant reductions in rotavirus gastroenteritis and mortality [20]. Currently, 35 countries in sub-Saharan Africa have already introduced the rotavirus vaccine in their national vaccination program [20]. In an analysis examining the costs and benefits of introducing the vaccine for the eight countries, including Somalia, which has not yet included the rotavirus vaccine in the program, for the modeling period between 2021 and 2030, it was concluded that the benefits of introducing rotavirus vaccination outweighed the costs in all eight countries [21].

In a meta-analysis study dated 2022 and including 144 studies, it was determined that the prevalence of HAV was higher in low-income countries (29.0%) and that the prevalence was especially higher in African and Eastern Mediterranean countries [14]. In the same study, it was emphasized that limiting environmental contamination and vaccination is essential for controlling hepatitis A and more effective water/wastewater treatment strategies are needed to limit the environmental circulation of HAV in developing countries. Endemicity is high in low-income countries, mainly due to insufficient safe water and poor sanitation and hygiene. In these countries, most children (90%) are infected with HAV before the age of 10, often without symptoms [14]. This endemic nature of HAV is used to classify age-specific prevalence; such as high (≥90% by age 10 years) and intermediate (≥50% by age 15 years with <90% by age 10) [22]. Somalia is a region with high HAV endemicity according to current literature, and in a recent study, the percentage of anti-HAV IgG seropositivity was found to be high (88.9%) in adults aged ≥41 years and low (29.4%) in children aged 1-2 years [23]. In our study, the positivity rates for anti-HAV IgM and IgG were 26.5% and 85.4%, respectively. The highest anti-HAV IgM positivity rates were seen in children aged 2-<5 years (52.9%) and children aged 5-15 years (44.0%). These data indicate that HAV infections are acquired in childhood, more frequently between the ages of 2 and 15.

Although our study has important limitations such as not including clinical data, making comments based on data that only belongs to one year and some months are missing, lack of confirmation tests, and the study group not being randomly selected. Still, it is considered that it can contribute to the literature as it is compatible with the literature information in many aspects and provides rare epidemiological data of the region.

Conclusion

In this study, we discussed the viral gastroenteritis agents for which access to clean water and sanitation conditions are important for infection prevention. Two of these are vaccine-preventable infections; rotavirus and HAV. We think that the results of our study may contribute to further studies on the burden, trends, and age distribution of these infections.

Conflict of interest: The authors declare that there is no conflict of interest. The authors alone are responsible for the content and writing of the paper. **Financial disclosure:** There is no financial support to this study.

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