Original Article

HEALTH SCIENCES
MEDICINE

DOI: 10.32322/jhsm.1445998
J Health Sci Med. 2024;7(2):213-218

Effect of the COVID-19 pandemic on rotavirus infection frequency in children

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Cite this article as: Nas Y, Gözüküçük S. Effect of the COVID-19 pandemic on rotavirus infection frequency in children. *J Health Sci Med.* 2024;7(2):213-218.

Received: 01.03.2024 ◆ **Accepted**: 23.03.2024 ◆ **Published**: 25.03.2024

ABSTRACT

Aims: During the COVID-19 pandemic, measures such as the wearing of masks, social distancing, enhanced hygiene practices, closures of workplaces and schools, and lockdowns influenced the spread of various infectious diseases. This study aimed to compare the frequency of rotavirus infections during the pandemic to that of the pre-pandemic period.

Methods: This retrospective study included 2912 patients diagnosed with acute gastroenteritis who were admitted to the Pediatric Health and Diseases Department of Hisar Intercontinental Hospital between January 2018 and August 2022. For the diagnosis of rotavirus infection, the Rota-Adeno Ag Rapid Test-Cassette was applied to stool samples as an immunochromatographic method. Patients were divided into two groups based on their hospital admission dates: before the COVID-19 pandemic (1 January 2018 to 10 March 2020) and during the COVID-19 pandemic (11 March 2020 to 30 August 2022).

Results: The prevalence of rotavirus infection in the entire population was 9.5% (n=277). The rate of cases of rotavirus infection was higher among patients during the COVID-19 pandemic compared to the group of patients before the COVID-19 pandemic (10.9% vs. 8.7%, p=0.050). A sharp decline in the frequency of rotavirus infection was observed at the beginning of the COVID-19 pandemic compared to the pre-COVID-19 pandemic period, followed by a sharp increase. In 2022, the frequency of rotavirus infections exceeded the pre-COVID-19 pandemic levels.

Conclusion: The provision of the rotavirus vaccine for free by health authorities, especially for at-risk infants, together with adherence to hand washing, hygiene, and sanitation rules can significantly reduce the frequency of rotavirus infections during both pandemic and non-pandemic periods.

Keywords: COVID-19, pandemic, rotavirus, viral gastroenteritis

INTRODUCTION

Acute gastroenteritis, characterized by the sudden onset of diarrhea and vomiting, remains a significant public health challenge globally, contributing to substantial morbidity and mortality, especially among children under 5 years of age.[1] Among various pathogens, the genus Rotavirus emerges as the primary cause of serious diarrhea in young children on a global scale, leading to significant morbidity and mortality. Vaccines for rotavirus have been available worldwide for more than 10 years, but these infections continue to cause over 200,000 deaths each year, predominantly in countries of lower economic status.[2]

Rotavirus transmission primarily occurs via the fecal-oral route, facilitated by the virus's high infectivity and environmental stability. The persistence of rotavirus in environments frequented by children amplifies its transmission potential, making it a formidable challenge in public health.[3] The onset of the COVID-19 pandemic brought about widespread implementation of non-pharmaceutical interventions such as social distancing, hand hygiene, and the use of masks. These measures, while primarily aimed at curbing the spread of SARS-CoV-2, also affected the transmission dynamics of other infectious agents, including rotavirus.[4-7] Limited studies have shown that the measures taken to control COVID-19 led to significant reductions in the incidence of rotavirus and other enteric viral infections[8-15], highlighting the collateral benefits of such public health interventions. However, comprehensive data on changes in the frequency of rotavirus infections before and during the COVID-19 pandemic are still lacking.

We hypothesized that the public health interventions implemented in response to the COVID-19 pandemic,

aimed at curtailing the spread of the virus, influenced the transmission dynamics of rotavirus, thereby altering its incidence rates. This study aimed to compare the frequency of rotavirus infections during the pandemic to the pre-pandemic period.

METHODS

This retrospective study was conducted with patients who were admitted to the Department of Pediatric Health and Diseases of Hisar Intercontinental Hospital between June 2018 and June 2023. The study was approved by the Hisar Intercontinental Hospital Ethics Committee (Date: 12.01.2024, Decision No: 24-01) and was carried out in accordance with the relevant ethical guidelines and the Declaration of Helsinki (2013 Brazil revision).

A total of 2912 pediatric patients who were admitted to the hospital with a diagnosis of acute gastroenteritis were included in the study. The inclusion criteria were patients being under 18 years of age and diagnosed with acute gastroenteritis. Patients over the age of 18, those with a history of rotavirus, those who had received the rotavirus vaccine, and those diagnosed with co-infections of other enteric pathogens were excluded from the study.

Stool samples were collected from patients for rotavirus infection diagnosis and sent to the hospital's microbiology laboratory. All samples were packaged and stored at -80 °C, and then thawed for processing. Stool specimens were studied using an immunochromatographic method for the presence of rotavirus (Rota-Adeno Ag Rapid Test-Cassette, CTK Biotech, USA) in line with the recommendations of the device's manufacturer. The sensitivity and specificity of this test were reported by the manufacturer as 99.9% and >97.8% for rotavirus. This immunochromatographic assay method relies on identifying rotavirus and adenovirus antigens in feces using an anti-rotavirus antibody (R test line) on the assay membrane. The antigen testing involved blending fecal samples with an extraction buffer and applying three drops (approximately 100 µL) into the kit's sample section. Following 5-15 minutes of incubation at ambient temperature, the appearance of colored lines in the R (rotavirus) and control (C) areas indicated a positive result, while the absence of a colored line in the R area was interpreted as negative.

The demographic and clinical data of the patients were collected from patient files or the hospital's electronic information system. In Turkiye, the first COVID-19 case was detected on 11 March 2020. Subsequently, strict policy measures were introduced to combat the outbreak, including compulsory wearing of masks, social isolation, suspension of air travel, curfews, a transition to online learning, the temporary shutdown of cafes and restaurants, and the cancellation of public events.[16,17] Given the assumption that these measures could influence the transmission pattern of rotavirus and lead to variations in its prevalence, patients were divided into two groups based on their hospital admission dates: before the COVID-19 pandemic (1 January 2018 to 10 March 2020) and during the COVID-19 pandemic (11 March 2020 to 30 August 2022).

Statistical Analysis

All data were analyzed with IBM SPSS Statistics for Windows 20.0 (IBM Corp., Armonk, NY, USA). Numerical data determined to be normally distributed based on the results of Kolmogorov-Smirnov tests are given as mean ± standard deviation while non-normally distributed variables are given as median (minimum–maximum). For comparisons between groups, the Student t-test or Mann-Whitney U test were used in line with the normality of the considered distribution. Categorical variables are given as numbers and percentages, and inter-group comparisons were conducted with chi-square and Fisher exact tests. Significance was accepted at $p<0.05$ (*) for all statistical analyses.

RESULTS

The study population consisted of a total of 2912 pediatric patients, including 1271 girls (43.6%) and 1641 boys (56.4%). The median age of the patients was 3 years (range: 1 month to 18 years), with the majority being between the ages of 1 and 4 years (44.9%). It was determined that the majority of patients (30.6%) presented to the hospital during the spring season. The prevalence of rotavirus infection in the entire population was 9.5% (n=277) (Table 1).

The distributions of sex and age between the groups were similar. In spring, the rates of hospital admissions were higher during the COVID-19 pandemic compared to the group of patients before the COVID-19 pandemic (37.1% vs. 26.7%, $p<0.001$), while admission rates were lower in winter (14.7% vs. 31.4%, $p<0.001$). In summer, the rates of hospital admissions were found to be higher during the COVID-19 pandemic compared to patients before COVID-19 (31.8% vs. 19.5%, $p<0.001$). The rate of cases of rotavirus infection was higher in the group of patients during the COVID-19 pandemic compared to patients before COVID-19 (10.9% vs. 8.7%, $p=0.050$) (Table 1).

The fluctuations in the frequency of rotavirus infection across the years are depicted in Figure. A sharp decline in frequency was observed at the beginning of the COVID-19 pandemic compared to the pre-COVID-19 period, followed by a sharp increase. In 2022, the frequency of rotavirus infections exceeded the pre-COVID-19 pandemic levels (Figure). Prior to the COVID-19

Table 1. Demographic and clinical characteristics of patients				
Variables	**All population**	**COVID-19 pandemic**		**p**
Sex, n (%)	n=2912	Before n=1827	During n=1085	
Girl	1271 (43.6)	790 (43.2)	481 (44.3)	0.566
Boy	1641 (56.4)	1037 (56.8)	604 (55.7)	
Age, years	3 (1-7)	3 (1-7)	3 (1-6)	0.671
<1 years, n (%)	463 (15.9)	290 (15.9)	173 (15.9)	0.072
1-4 years, n (%)	1307 (44.9)	816 (44.7)	491 (45.3)	
5-9 years, n (%)	812 (27.9)	495 (27.1)	317 (29.2)	
10-14 years, n (%)	260 (8.9)	184 (10.1)	76 (7.0)	
15-18 years, n (%)	70 (2.4)	42 (2.3)	28 (2.6)	
Season of presentation, n (%)				
Summer	702 (24.1)	357 (19.5)	345 (31.8)	<0.001*
Autumn	587 (20.2)	409 (22.4)	178 (16.4)	
Winter	733 (25.2)	573 (31.4)	160 (14.7)	
Spring	890 (30.6)	488 (26.7)	402 (37.1)	
Rotavirus infection, n (%)				
No	2635 (90.5)	1668 (91.3)	967 (89.1)	0.049*
Yes	277 (9.5)	159 (8.7)	118 (10.9)	

Numerical variables were shown as mean ± standard deviation or median (IQR). Categorical variables were shown as numbers (%). * P<0.05 shows statistical significance

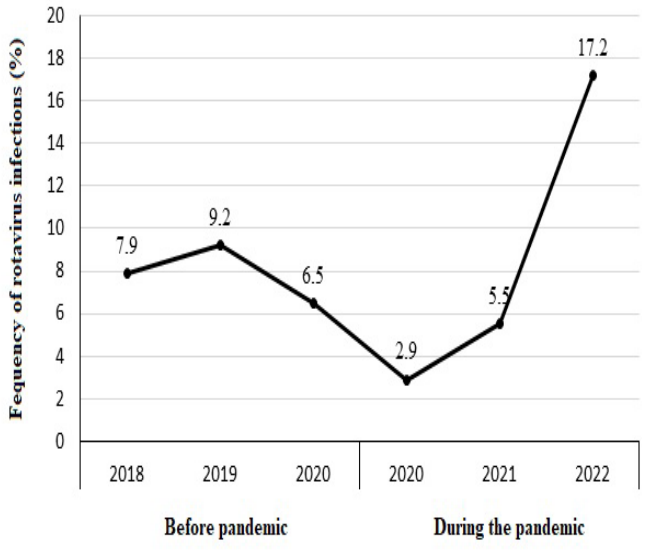

Figure. Yearly distribution of rotavirus infections in children before and during the COVID-19 pandemic

pandemic, peaks in rotavirus infection frequency were noted at the end of winter and during spring, while during the early COVID-19 pandemic period, infection rates peaked at the beginnings of summer and autumn. During the late phase of the COVID-19 pandemic, alongside pronounced surges in winter and spring, there were also notable increases at the end of summer (Table 2).

The frequency of rotavirus infections in girls did not show a significant difference before and after the beginning of the COVID-19 pandemic (9.9% vs. 10.6%, p=0.676). However, a significant increase in the frequency of rotavirus infections was detected in boys after the COVID-19 pandemic began (7.8% vs. 11.1%, p=0.025). Although an increasing trend in the frequency of rotavirus infections was observed in children over the age of 1 year after the beginning of the COVID-19 pandemic, statistical significance was only detected for children aged 1 to 4 years (Table 3).

DISCUSSION

Rotavirus is the leading cause of viral gastroenteritis among newborns and children under the age of 5, representing a major cause of mortality and morbidity within this age group.[18,19] The rates of hospitalization associated with rotavirus range from 7% to 81%, with the average rate of admission being approximately 40%.20,21 On the other hand, the hospitalization rate for diarrhea cases caused by rotavirus varies between 30% and 50%, and it is reported that mortality occurs in 90% of cases in low-income countries.[2] The primary transmission route of rotavirus infection is the fecal-oral route, but it can also spread through contact with contaminated surfaces.[22-24] Therefore, in the prevention of rotavirus, sanitation, hand hygiene, and immunization play significant roles.[25]

In our study, the median age of the patients was 3 years, with the majority of cases being seen among patients aged 1-4 years. The overall prevalence of rotavirus infection

Table 2. Monthly trends of rotavirus infections among children

Months	2018		2019		2020		2021		2022	
	Rotavirus (-)/(+), n	%	Rotavirus (-)/(+), n	%	Rotavirus (-)/(+), n	%	Rotavirus (-)/(+), n	%	Rotavirus (-)/(+), n	%
January	58/2	3.3	58/6	9.4	89/5	5.3	12/0	0	39/4	9.3
February	38/8	17.4	49/21	30.0	57/10	14.9	7/0	0	21/11	34.4
March	47/6	11.3	74/17	18.7	51/6	10.5	15/2	11.8	43/25	36.8
April	42/8	16.0	72/10	12.2	9/2	22.2	12/0	0	97/24	19.8
May	73/12	14.1	64/4	5.9	25/0	0	21/0	0	106/23	17.8
June	52/1	1.9	50/4	7.4	30/0	0	22/3	12.0	75/3	3.8
July	54/8	12.9	55/3	5.2	32/2	5.9	26/2	7.1	64/2	3.0
August	65/4	5.8	57/4	6.6	40/0	0	32/1	3.0	9/2	18.2
September	76/5	6.2	75/0	0	31/1	3.1	39/5	11.4	-	-
October	51/0	0	75/2	2.6	18/1	5.3	43/2	4.4	-	-
November	71/1	1.4	50/3	5.7	11/0	0	26/1	3.7	-	-
December	80/6	7.0	83/3	3.5	12/0	0	52/2	3.7	-	-

among these groups of patients presenting to our hospital was determined to be 9.5% (277/2912). This is similar to the rates of 8-10% reported in the literature.[2,21] Rotavirus can cause nosocomial gastroenteritis in the pediatric wards of hospitals.[26] The prevalence of acute gastroenteritis varies between 25% and 40%, often peaking during winter months.[20] Although a decrease in rotavirus infection frequency towards the summer months is reported in developed countries, seasonal trends may not be observed in developing countries.[27,28]

Rotavirus infections are frequently reported during the winter months, but in our study they were found to peak towards the end of winter. From a seasonal perspective, the rates were significantly higher in the spring months. Moreover, in our study, the rate of rotavirus infection, which was significantly elevated during the COVID-19 pandemic compared to the pre-pandemic period, also exhibited variations in spring. There are limited studies on this topic. In a study conducted in Israel, it was reported that there was an off-season increase in rotavirus cases during the second year of the pandemic.[29] A study in China documented a marked reduction in the incidence of rotavirus infections at the onset of the pandemic, with the greatest disparities noted during

Table 3. Distribution of patient with rotavirus infection by gender, age, and season

Variables	Before pandemic		During the pandemic		p
	Rotavirus (-)/(+)	%	Rotavirus (-)/(+)	%	
Sex, n (%)					
Girl	712/78	9.9	430/51	10.6	0.676
Boy	956/81	7.8	537/67	11.1	0.025*
Age, n (%)					
<1 years	257/33	11.4	162/11	6.4	0.075
1-4 years	745/71	8.7	429/62	12.6	0.023*
5-9 years	457/38	7.7	281/36	11.4	0.076
10-14 years	168/16	8.7	68/8	10.5	0.643
15-18 years	41/1	2.4	27/1	3.6	0.058
Season of infection, n (%)					
Summer	333/24	6.7	330/15	4.3	0.170
Autumn	398/11	2.7	168/10	5.6	0.079
Winter	512/61	10.6	143/17	10.6	0.994
Spring	425/63	12.9	326/73	18.9	0.014*

Numerical variables were shown as mean ± standard deviation or median (IQR). Categorical variables were shown as numbers (%). * P<0.05 shows statistical significance

February, March, and April.[11] Similar results have been observed in another study carried out in China.[30] In a study conducted in Brazil, it was reported that there was a significant increase in the frequency of rotavirus infections during the later stages of the pandemic, and it was shown to peak during the summer months.[7] In a study conducted in Turkiye, it was demonstrated that the frequency of rotavirus infections during the later stages of the pandemic was similar to the rates observed before the pandemic.[12] The possible reasons for these findings may include reduced visits to health facilities for newborn and childhood vaccinations due to the anxiety created by the pandemic in the community, inadequate follow-up of infants and mothers, and the relaxation of measures towards the end of the pandemic. It has been reported that the COVID-19 pandemic caused serious problems in accessing essential health services, such as vaccinations, due to the inadequacies of health systems in responding to the outbreak.[31] Additionally, it has been reported that the reduced circulation of microbial agents during the COVID-19 pandemic, along with disruptions in vaccine supply and administration, may have led to decreased stimulation of the immune system, resulting in adverse outcomes after the pandemic and potentially leading to future outbreaks. It has been emphasized that the implementation of an effective vaccination program is necessary to prevent the resurgence of vaccine-preventable diseases.[32]

The rotavirus vaccine has been shown to significantly reduce hospitalization and mortality rates associated with the infection and indirectly stimulate herd immunity. Therefore, it is recommended to include the rotavirus vaccine in childhood immunization programs, especially in countries with a high prevalence of infection.[24] The rotavirus vaccine is a live oral vaccine and there are two types available: one is the monovalent human rotavirus vaccine, and the other is the pentavalent human-bovine reassortant rotavirus vaccine. The most effective method for preventing highly contagious rotavirus diarrhea is rotavirus vaccination. However, these vaccines are not yet routinely administered in all countries. Since the introduction of rotavirus vaccines in 2006, there has been a significant reduction in disease burden and hospitalization rates.[33] Additionally, although hygiene practices have led to a decrease in rotavirus infection rates, it has been noted that infections can be effectively controlled with the universal rotavirus vaccine.[23] On the other hand, secretory IgA found in breast milk also plays a significant role in the immune response against rotavirus.[34]

Limitations

There are notable limitations to this study. Due to its nature as a retrospective observational study, there was no opportunity to access the long-term follow-up outcomes of the patients. Therefore, clinical data related to patients' long-term clinical courses, rates of recurrent infections, and vaccination statuses could not be obtained. Despite this, our study contributes to the literature by including a large number of patients and determining the prevalence and seasonal occurrence of rotavirus before and after the pandemic.

CONCLUSION

The provision of the rotavirus vaccine for free by health authorities, especially for at-risk infants, together with adherence to hand washing, hygiene, and sanitation rules can significantly reduce the frequency of rotavirus infections during both pandemic and non-pandemic periods. Additionally, it is necessary for doctors to advise mothers with newborn babies to breastfeed their children until at least the age of 2 and to ensure that their vaccinations against rotavirus are up to date to protect against rotavirus gastroenteritis.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Hisar Intercontinental Hospital Ethics Committee (Date: 12.01.2024, Decision No: 24-01).

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author.

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