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Original Article

Frequency of Rotavirus Infection in Children Less than 5 Years Old with Transudative Diarrhea Refer to Bouali Hospitals in Ardabil

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Abstract

Background and Aims: Despite the widespread introduction of rotavirus vaccinations more than a decade ago, rotavirus infections continue to cause over 200,000 deaths annually, disproportionately affecting low-income countries. This highlights the ongoing need for surveillance and monitoring of rotavirus spread. Study of the frequency of rotavirus infection in children under 5 years of age with transudative diarrhea referred to Bouali Hospital in Ardabil city in the period of 2019-2020

Material and methods: This study investigated children hospitalized for diarrhea over a 12-month period, collecting data on age, sex, hospital stay duration, and discharge reasons. Samples were tested for rotavirus group A using the ELISA method.

Results: This study analyzed 116 samples, with 45.7% testing positive. The research primarily focused on children aged up to one year. While boys showed a higher infection percentage, the study found no significant link between rotavirus infection and gender. Additionally, the study indicated no correlation between rotavirus infection and the duration of hospitalization.

Conclusions: The presence of a high frequency of rotavirus among patients underscores its significant impact. Further investigation into rotavirus is crucial, as it can aid healthcare systems in reducing economic and social burdens.

Keywords: Gastroenteritis, Transudative diarrhea, Rotavirus

Introduction

Rotaviruses was introduced for the first time in 1973 in the epithelial cells of the duodenum of a child with diarrhea by electron microscopy, and now it is known as the main cause of diarrhea in children, especially infants, as well as in animals such as cows and pigs around the world (1). The name rotavirus is derived from the Latin word "rota" (which translates to "wheel"), which was attributed to this newly discovered virus due to its distinctive morphological appearance (2).

Rotaviruses can be classified into A-E groups based on antigenic groups on VP6, the main capsid antigen. Only group B, A, and C rotaviruses have been shown to infect humans, and most human rotavirus diseases are caused by group A viruses (3). These are classified into G and P types based on the identification of antigens on the outer capsid proteins, VP7 and VP4, respectively. Most severe infections in young children are caused by genotypes G1-4, and in the last two decades, G1 infections seem to have predominated worldwide. In general, more populous countries show the most complex patterns of genotypes occurrence (4). The disease related to rotavirus appears in certain seasons and is known as winter diarrhea in

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some parts of the world. Globally in temperate regions, rotavirus is certainly more common in colder months, but seasonal peaks of infections can vary widely and occur (5). Rotavirus has a short incubation period of 1-3 days. Virus shedding starts before symptoms appear, and children may shed the virus up to 48 hours before symptoms appear. People infected with rotavirus shed high concentrations of rotavirus in their feces. This disease is transmitted from one infected person to another through Fecal Oral. This virus is persistent and may remain in the environment for weeks or even months if not disinfected (6) Rotavirus primarily infects enterocytes and causes diarrhea through destruction of absorptive enterocytes (which causes malabsorption) and stimulation of intestinal secretion by rotavirus NSP4 protein and activation of intestinal nervous system (7). Rotavirus infects almost all children up to the age of 5 years, but severe gastroenteritis and dehydration occur mainly in children aged 3-35 months (8). The primary consequence of rotavirus infection is acute gastroenteritis. Its clinical features range from subclinical infection and mild watery diarrhea to severe diarrhea with vomiting and fever (9), which in severe cases can be up to 20 bouts of diarrhea or vomiting per day with loss of fluids and electrolytes, and these conditions last for 2 to 7 days and lead to severe dehydration with shock and electrolyte imbalance (10).

Each year, rotavirus is responsible for approximately 25 million clinic visits, two million hospitalizations, and 180,000 to 450,000 deaths in children under 5 years of age world-wide. Although rotavirus infection is common worldwide, most deaths from this infection occur in developing countries (11). Rotavirus gastroenteritis is usually self-limiting.

However, even if the patient does not receive medical services, it is better to maintain his oral hydration (12). After a natural infection, 40% of children are protected against subsequent rotavirus infection, 75% are protected against subsequent rotavirus gastroenteritis, and 88% are protected against severe rotavirus gastroenteritis. Second, third, and fourth infections provide progressively greater protection against severe disease (8). Improvements in sanitation significantly reduce the burden of rotavirus disease. The incidence of hospita-lization due to diarrhea in high-income and low-income countries before the introduction of rotavirus vaccines was 40%.

Therefore, vaccination against rotavirus is the best measure to prevent a rotavirus patient. In the present study, considering the need to monitor the control of this infection and preventive programs, based on the registration of the patients hospitalized in Bouali Hospital of Ardabil city, and frequency of rotavirus gastroenteritis in children under 5 years of age has been investigated.

Methods and Materials

The current study was descriptive-analytical cross-sectional. This study was sponsored by Ardabil University of medical science by ethic code (IR.ARUMS.MEDICINE.REC.1400.034 during 2019 to 2021. All children aged 5 years and under who were admitted to the Bu-Ali Hospital in Ardabil city due to diarrhea and who meet the criteria for entering the study were selected, and among them, children who, based on the laboratory report (Stool Exam) had transudative diarrhea" Transudative diarrhea occurs when fluid leaks into the intestinal lumen due to increased pressure or decreased protein levels in the blood, causing the body to release excess fluid into the intestines, resulting in watery stools" Transudative diarrhea by less than 5 RBC and WBC in stool sample (13) and bacterial negative test, were included in the study considering other inclusion criteria. Patients using immunosuppressive medications, those with secondary immunodeficiency, or those who have undergone organ transplantation or radiotherapy were often excluded from studies. Finally, 116 cases were included in the study. In the hospital, a sub-specialist of pediatric infectious diseases as the main focus of the project supervised the registration of children included in the study. For each child, a questionnaire containing information such as name, age, gender, type of nutrition, having or suspected of having COVID-19, clinical manifestations at the time of admission, and laboratory information was prepared.

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A new stool sample was prepared from each child for rotavirus laboratory testing. The collected samples were kept at a temperature of 4℃. . An ELISA test was performed weekly to determine group A antigen on the sample. From all the samples, a 10% suspension solution was made by using sample diluent. The diagnostic kit for this was Rotavirus antigen test (ProSpecT Rotavirus Test, Oxoid, UK) which uses the competitive ELISA technique. The sensitivity of this kit is 100% and its specificity 99.2%. In this kit, polyclonal antibodies of rotavirus antigen are attached to the bottom of all the wells of the plate kit. 100 microliters of the homogenized suspension sample were placed in the bottom of the wells. Positive control and negative control were determined at the same time. 100 microliters of conjugation solution were added to each well and incubated for one hour at room temperature (20-30°C). According to the kit instructions, the wells were washed five times with phosphate buffered saline (PBS) to wash away any unbound antibody. Then 100 microliters of the substrate solution was added and the plate of the kit was covered. They were incubated again for 10 minutes at room tem-perature. Finally, by adding 100 microliters of stop solution, the samples were read by ELISA reader at a wavelength of 450 nm. The positive and negative cut off numbers obtained from the optical absorbance of the wells corresponding to the positive and negative control were considered.

The optical absorbance of any well that was greater than the cut-off value of the negative control by adding 0.5 was considered positive. In other words, it confirms the presence of rotavirus antigen in the samples. The results were first collected in EXCEL file and then analyzed with SPSS version 26 software using Chi-square tests, t-test and Fisher's exact test. The significance level was considered 0.05 in all analyses.

Results

According to the results of this study, the frequency of positive cases for rotavirus among 116 samples was 63 cases (45.7%) (Figure1).

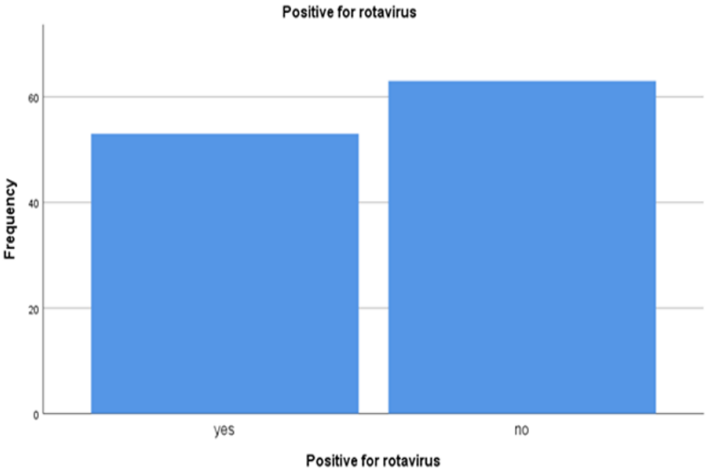

Fig.1 Frequency of positive cases for rotavirus among samples

The maximum age range of rotavirus diarrhea cases was between 0 and 1 year, with 26 positive cases out of the total number of 116 samples. Also, in the age range of 1 to 2 years, 16 samples, in the age range of 2 to 3 years, 8 samples, in the age range of 3 to 4 years, 3 samples were reported positive. In the age range of 4 to under 5 years, no positive case of rotavirus has been reported. According to the chi-square test, there was no significant relationship between age and rotavirus infection. (p-value = 0.347) (Figure. 2).

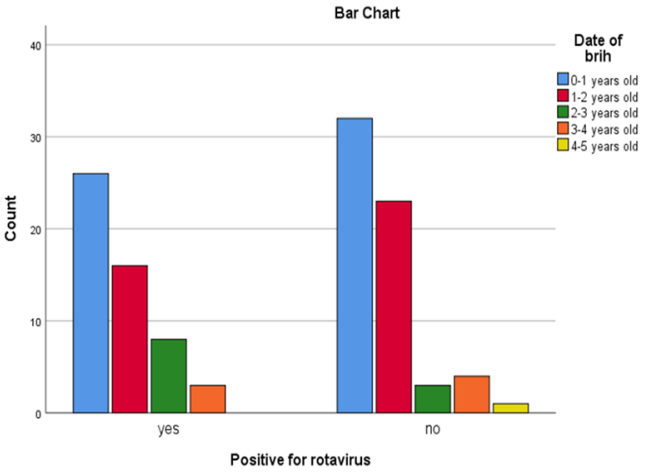

Fig. 2 Frequency positive cases in all age group

Out of 116 cases, 67 cases related to male gender with 33 positive cases in terms of rotavirus and 49 cases related to female gender with 20 positive cases in terms of rotavirus were reported. According to the chi-square test, there was no significant relationship bet-

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ween gender and rotavirus infection. (p value: 0.368) (Figure 3).

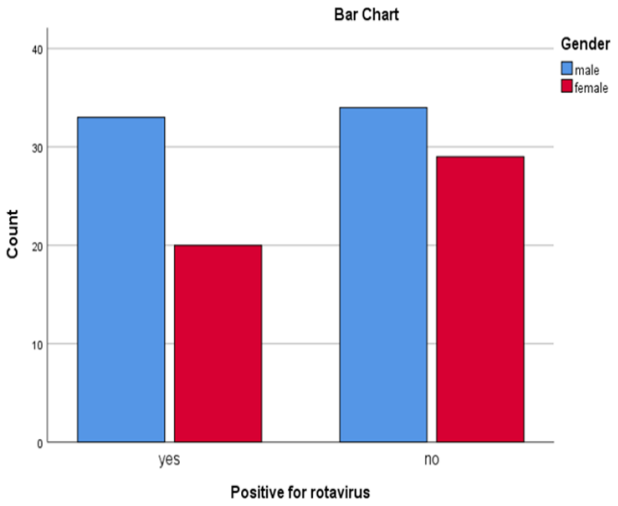

Fig. 3 Frequency positive cases according gender

Out of 116 hospitalizations, the highest number of hospitalizations is related to the age range of 0 to 1 years with 58 cases. We have hospitalized 39 cases in the age range of 1 to 2 years, 11 cases in the age range of 2 to 3 years, 7 cases in the age range of 3 to 4 years, and 1 case in the age range of 4 to 5 years (Figure 4).

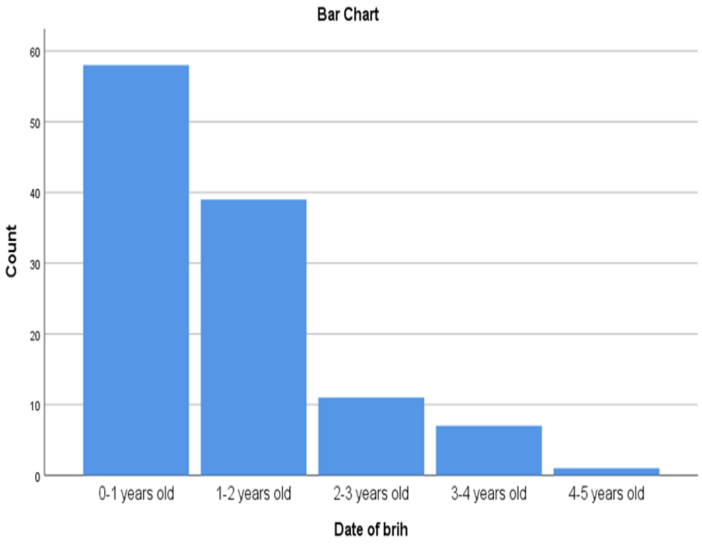

Fig. 4 Frequency positive cases according age range

Among the 53 positive cases for rotavirus, 19 cases were reported with 3 days of hospitalization for treatment, the highest frequency among the number of days required for hospitalization and also the lowest number, 1 case corresponding to 12 days of hospitalization.

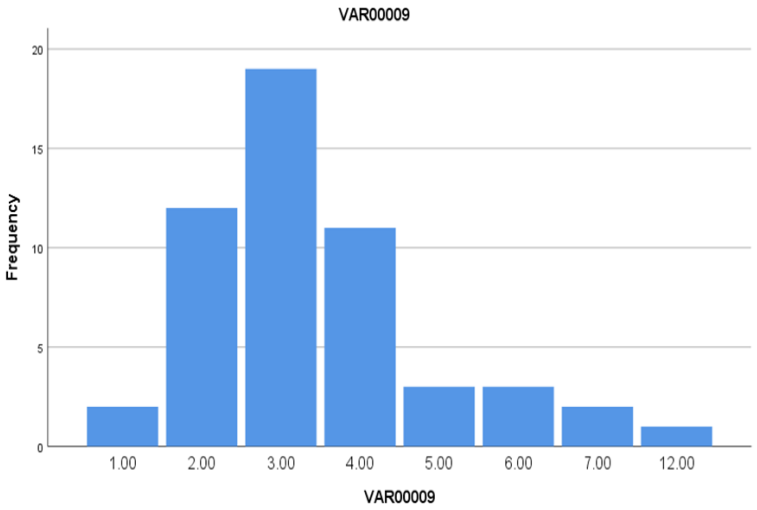

Fig. 5 Frequency positive cases according average number of hospitalization days

The average number of hospitalization days was 3.5 days (Figure 5). No case of child death was recorded in any of the age ranges. Among the total 116 cases, 3 cases were discharged with personal consent and the rest with recovery and under the supervision of the attending physician. The highest number of reasons for disch arge

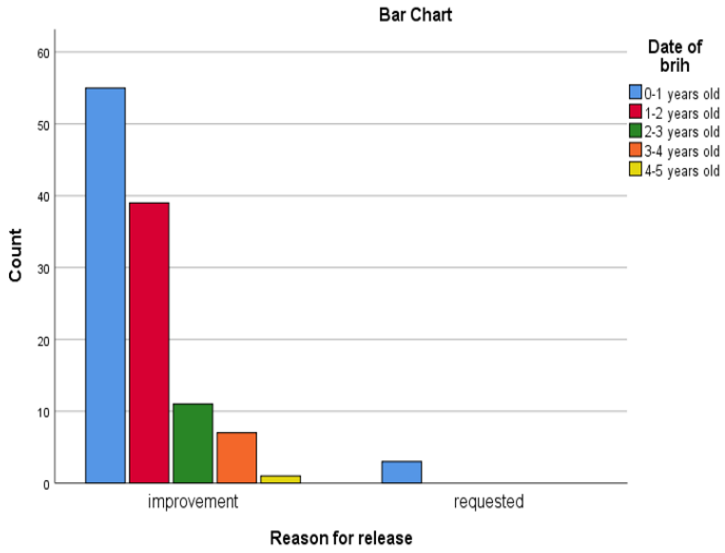

Fig. 6 Frequency number of reasons for discharge

arge related to recovery have been reported in the age range of 0 to 1 year. No cases of death were recorded in this study (Figure 6). No case of child death was reported in either gender.

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Among the 67 male cases, 1 case was discharged by personal consent and the rest recovered and were discharged under the supervision of the attending physician. Also, among the 47 female cases, 2 cases were discharged with personal consent and the rest with recovery (Figure 7).

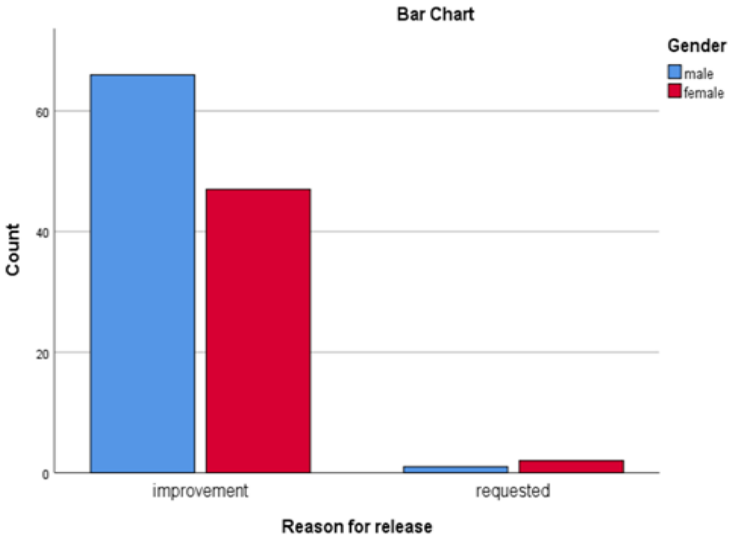

Fig.7 Frequency number of reasons for release

DISCUSSION

In the present study, the frequency of rotavirus diarrhea was 45.7%. In the study of Ornwalan Maiklang in Thailand (14), this percentage is 44.5%, which is almost consistent with our findings, and in the study of A. Karadag in Turkey (15), 36.8% was reported, which is less than our findings. In general, all the results are based on the not very low frequency of rotavirus in children's gastroenteritis, which should be considered in the management of patients in order to avoid indiscriminate prescription of antibiotics. But the differences in the prevalence rate can be related to the sampling time (season) for the test or the geographical area and various other causes, including the sanitation of the sewage and drinking water in the area, as well as the compliance with the hygiene of disposal and the principles of proper hand washing by the family.

In our study, 67 out of 116 samples were boys and 49 were girls. However, no significant relationship between gender and rotavirus infection was observed. According to the studies conducted by several researchers in the 1980s, there is no correlation between gender and rotavirus infection, and the prevalence of this infection is similar in both sexes. So far, none of the studies conducted in the world have reported the superiority of a particular gender in suffering from rotavirus diarrhea (16).

The results of the present study showed that the most age range of affected children was 0 to 1 year (44.8%), but there is no significant relationship between the age range and rotavirus infection.

According to the results of most studies, it can be concluded that children aged 6 to 24 months are one of the most important populations at risk of rotavirus. This finding can be related to the lack of formation of relevant antibodies during repeated infections during the first years of a child's life, or in other words, the lack of development of the immune system of children under 2 years of age. Also, the low rate of infection in children less than 6 months old can be due to the mother receiving antibodies before birth, which protects the baby until 6 months old. Because the mother transmits the antibodies acquired during rotavirus infection to the baby. Recent research shows that the increase in the infection rate in children under 2 years old is due to the decrease in the level of protease in the digestive tract and also the lack of mucin in the intestines of children. As a result, rotaviruses enter the intestinal enterocytes more easily and cause rotavirus infection (17).

In the study of Parshar UD (12), the annual death rate due to diarrhea in children under 5 years of age was reported to be 440,000 on average. Also, several studies have been conducted on the mortality rate due to rotavirus infection, most of which have reported an annual mortality rate of more than 200,000 people, mostly in low-income countries. However, in our study, the death rate among 116 samples was zero. This finding can depend on various causes, including the high level of health in our studied society compared to low-income countries, such as the availability of health care centers or the high level of awareness of parents in early referrals and pre-hospital care. A study's limitation is the inability to conduct molecular testing

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on ELISA-positive samples due to cost and time constraints. This likely restricts the depth of analysis possible, potentially preventing confirmation of ELISA results or further characterization of the positive samples. Thus, it is recommended that PCR-ELI-SA is a sensitive and rapid method. The high sensitivity and specificity of PCR-ELISA may be a good alternative in future studies when resources are limited.

Conclusions

A study found a high frequency of rotavirus among patients, highlighting the importance of detailed examinations to reduce economic and social burdens on healthcare systems.
Typically, rotavirus peaks in winter, but in Ardabil, Iran, it peaks in spring, suggesting a shift in the disease's pattern due to local weather. This necessitates strict control and prevention measures. The research also implies that implementing rotavirus vaccination could be cost-effective, and further research into rotavirus biology is important for control.

Acknowledgment

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Disclosure

None

Conflict of Interest

No conflict of interest is declared.

Funding

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Ethics Approval and Consent to Participate

This study was approved by Ethics Committee of the Ardabil University of Medical Sciences by ethic code (IR.ARUMS.MEDICINE.REC. 1400.034)

Data Availability Statement

All data generated or analyzed during this study are included in this article.

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