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Original Article

Microbiology Section

Epidemiology of Rotavirus Diarrhoea in Children and Adults Presenting with Acute Gastroenteritis at a Tertiary Care Hospital in Northern India: A Cross-sectional Study

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ABSTRACT

Introduction: Rotavirus is an important cause of severe diarrhoea in children under five years of age, accounting for approximately 78,000 deaths annually in this age group. The magnitude of acute gastroenteritis caused by rotavirus is often underestimated due to the lack of investigations into these cases. Although rotavirus disease is less common in adults, it can occur, possibly because of contact with children who have rotavirus gastroenteritis.

Aim: To assess the current trend of the disease in both children as well as adults presenting with acute diarrhoea.

Materials and Methods: This cross-sectional study was conducted over a period of one year (January 2023 to January 2024). A total of 185 stool samples were collected from children under five years of age and adults over 18 years presenting with acute diarrhoea at the outpatient and inpatient departments of Guru Nanak Dev Hospital (GNDH), Amritsar, Punjab, India. Commercially available Enzyme Linked Immunosorbent Assay (ELISA) kits were used to detect the VP6 antigen of Group A rotavirus in the stool samples of the patients. The data collected were analysed using Statistical Package for the Social Sciences (SPSS), and relevant conclusions were drawn.

Results: Out of the 185 samples collected, 32 samples (17.3%) tested positive for rotavirus antigen. Vaccinated children experienced milder disease compared to unvaccinated ones. Non breastfed infants showed a higher detection rate of rotavirus, with 20 children (80%) testing positive compared to their breastfed counterparts. The rural-urban distribution indicated a greater burden in rural areas, with 16 children (64%) affected.

Conclusion: This study identifies the risk factors, clinical profile, current burden and seasonal variation of rotavirus diarrhoea. It will be helpful in evaluating the impact of the rotavirus vaccine on the severity of the disease.

Keywords: Rotavirus in children, Rotavirus in adults, Rotavirus antigen, Rotavirus vaccine

INTRODUCTION

Diarrhoea is the leading cause of death among children in the under-five age group and is accountable for half a million deaths worldwide [1]. In India alone, diarrhoea is responsible for an estimated 300,000 deaths in children under five years of age [2]. Rotavirus infection accounts for 30% of all hospitalisations due to diarrhoea in young children [3]. This virus is highly contagious and easily transmissible through the faecal-oral route. In developing countries, because of poor sanitation, hygiene and undernourished children, are particularly affected. Most children are infected by this contagious virus by the age of five, although the symptoms may differ in terms of severity. The magnitude of Rotavirus Acute Gastroenteritis (RVGE) is often underestimated because not all cases undergo investigation. Rotavirus was discovered by Ruth Bishop in 1973 through electron micrograph images. It belongs to the family *Reoviridae* and is a double-stranded Ribonucleic Acid (RNA) virus with 11 discrete segments. Each RNA segment encodes a single viral polypeptide, including six structural proteins (VP1, VP2, VP3, VP4, VP6, VP7) that compose the core, inner shell, and outer shell, as well as six non structural proteins (NSP1 to NSP6) that play important roles in viral replication and growth [4]. Ten distinct Rotavirus groups (or species), designated A through J, have been identified in humans, other mammals and birds on the basis of serological reactivity and the amino acid sequence of protein VP6. Groups A-J can be differentiated using VP6 polyclonal and monoclonal antibodies through immune fluorescence, ELISA and immunoelectron microscopy.

Most childhood gastroenteritis is caused by Group A rotavirus [5]. With a short incubation period of two to four days, this virus can produce a wide spectrum of clinical presentations, ranging from asymptomatic subclinical infection to severe, life-threatening dehydration with diarrhoea, fever and vomiting. Although rotavirus disease is less common in adults, it can occur, possibly because of contact with children who have rotavirus gastroenteritis [6]. Anderson EJ and Weber SG classified rotavirus infections in immunocompetent adults into four categories: endemic disease, epidemic outbreaks, travel-related gastroenteritis and infections transmitted from children to adults [7]. In developing countries, endemic disease and transmission from children to adults tend to be the most common epidemiological forms of Group A rotavirus infections [4]. Limited information on the true prevalence of rotavirus infection in older age groups in India may be due to a lack of testing.

The World Health Organisation (WHO) has recommended the introduction of the rotavirus vaccine in countries with a high burden of diarrhoeal diseases [8]. A total of 96 countries have introduced the rotavirus vaccine into their immunisation programmes to date [9]. India launched the rotavirus vaccine in 11 states in 2016 under its National Immunisation Schedule, and it was introduced in Punjab in a phased manner in 2019. There is limited data on the prevalence and epidemiology of rotavirus diarrhoea in children and adults in Punjab,

India, especially after the introduction of the rotavirus vaccine. This study aims to highlight the prevalence, risk factors, vaccination status and clinical profile of rotavirus diarrhoea in children and adults presenting to the outpatient department as well as hospitalised patients at a tertiary care centre in Amritsar, Punjab, India. While most studies focus solely on children, present study also included the adult population, making it a novel study in this region of India.

The aim of the study was to determine the current trend of the disease in both children as well as adults presenting with acute diarrhoea. The primary objective was to estimate the prevalence of acute gastroenteritis caused by rotavirus in children and adults. The secondary objectives were to study the risk factors, vaccination status and clinical profile of patients with rotavirus diarrhoea.

MATERIALS AND METHODS

This cross-sectional study was conducted in the Department of Microbiology, Government Medical College and Guru Nanak Dev Hospital (GNDH), Amritsar, Punjab, India from January 2023 to January 2024, following approval from the ethics committee of the college (number 10750/D-26/2021 batch).

Inclusion criteria: Patients presenting to GNDH with acute diarrhoea (lasting less than 14 days) seeking treatment and those who produced a stool sample within the first 24 hours of presentation, if admitted, were included in the study.

Exclusion criteria: Patients who did not consent or had diarrhoea due to other chronic ailments were excluded from the study.

Sample size: Sample collection was performed from various wards and outpatient departments of the hospital for cases of acute diarrhoea after obtaining consent. The sample size for the study was 185. This was a time-bound study, and all subjects available during the study period were considered. The clinical and epidemiological profiles were retrieved from the patients using a structured proforma.

A patient was considered to be suffering from acute gastroenteritis if they had experienced at least three episodes of diarrhoea (characterised by stool that is less formed than usual in terms of volume, consistency, or change in bowel habits) within a 24-hour period, less than a week before visiting the health facility, which was not related to any associated health problem [10].

Data collection: A structured proforma was used to gather information, including socio-demographic details (including urban/rural set-up and source of drinking water), medical history, symptoms of the current illness and treatment procedures. Hospital records and treatment charts were used to retrieve information on the duration and frequency of diarrhoea and vomiting. Birth history, birth weight, breastfeeding practices and vaccination status (specifically the rotavirus oral vaccine) were also collected. In case of adults, history of travel and contact with children was noted. The severity of diarrhoea was assessed using the Clinical Dehydration Scale [11]. A score of 1-4 was considered mild, 5-8 moderate, and greater than 8 severe dehydration [11].

Sample collection and processing: A freshly passed stool sample was collected in a wide-mouth, sterile container and transported to the microbiology lab immediately. An aliquot was stored at -70°C, and further testing was conducted using a commercially available ELISA kit (Serazym rotavirus detection-an in-vitro diagnostic device for direct detection of rotavirus in faecal samples, utilising polyclonal antibodies to the group-specific VP6 antigen, the major protein of Group A rotaviruses) [12].

STATISTICAL ANALYSIS

Data entry was performed in Microsoft Excel, and the final analysis was conducted using the SPSS software, IBM manufacturer, Chicago, USA, version 20.0. Various statistical tests like Chi-square, odds ratio, and t-test, were used to infer relevant results.

RESULTS

A total of 185 stool samples were collected and tested (70 adults, 37.84%, and 115 children, 62.16%) over a period of one year. Out of the 185 patients tested, 32 (17.3%) were positive for rotavirus antigen in stool samples. Among the 115 children, 25 (21.7%) tested positive for Group A rotavirus antigen, while 7 out of 70 adults (10%) were positive. Among the 25 children who tested positive for rotavirus antigen, only 7 (28%) had received the oral rotavirus vaccine, while the remaining were unvaccinated [Table/Fig-1]. In children, the number of patients presenting with acute gastroenteritis was highest among those aged 2 to 5 years (41 patients, 35.65%), but the positivity rate was highest in the 12 to 23 months age group (14 patients, 46.67%).

The socio-demographic profile is provided in [Table/Fig-2]. A total of 113 (61.08%) of the enrolled patients were male. Among the 27 patients with rotavirus diarrhoea, 20 (62.5%) were from rural areas. The clinical profile is provided in [Table/Fig-3]. Diarrhoea was experienced during the first four days, with an average of 4 to 5 episodes per day in patients affected by rotavirus. The time trend indicates that cases of rotavirus diarrhoea in children were more prevalent during the winter and spring seasons, while they were fewer during the summer. In adults, the peak was observed only during the winter season [Table/Fig-4].

Age group	Tested	Positive	Vaccinated (out of positive cases)	Not vaccinated (out of positive cases)
0-5 months	16 (13.91%)	3 (18.75%)	1 (33.33%)	2 (66.67%)
6-11 months	28 (24.35%)	5 (17.85%)	2 (40%)	3 (60%)
12-23 months	30 (26.09%)	14 (46.67%)	3 (21.43%)	11 (78.57%)
2-5 years	41 (35.65%)	3 (7.31%)	1 (33.33%)	2 (66.67%)
Total	115 (100%)	25 (21.74%)	7 (28%)	18 (72%)*

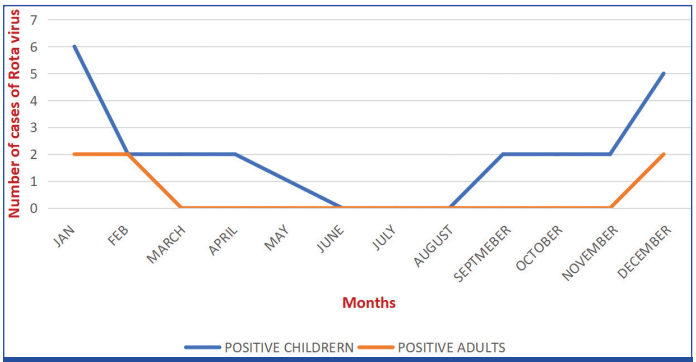
[Table/Fig-1]: Age-wise distribution of children tested for Rotavirus and their vaccination status.
*p-value- 0.032- vaccinated children have less association with Rotaviral diarrhoea; Statistical test- Chi-square test applied and p-value <0.05 was considered significant

Characteristics		Rota virus positive children N=25	Rota virus negative children N=90	Rota virus positive adults N=7	Rota virus negative adults N=63	Chi-square value	p-value
Gender	Male	20 (80%)	47 (52%)	5 (71%)	41 (65%)	7.4743	0.058223
	Female	5 (20%)	43 (48%)	2 (29%)	22 (35%)		
Locality	Urban	9 (36%)	72 (80%)	3 (42%)	42 (67%)	19.8403	0.0001
	Rural	16 (64%)*	18 (20%)	4 (58%)	21 (33%)		
Literacy of mother	Literate	10 (40%)	65 (72.2%)			8.9551	0.002767
	Illiterate	15 (60%)	25 (27.8%)				

[Table/Fig-2]: Sociodemographic profiles of patients.
Statistical test- Chi-square test applied and *p-value <0.05 was considered significant

Clinical symptoms	Duration of diarrhoea in days	Rota positive children N=25	Rota virus negative children N=90	Rota virus positive adults N=7	Rota virus negative adults N=63	Significant p-value
Duration of diarrhoea	0-4 days	18 (72%)	72 (80%)	4 (57.1%)	56 (89%)	0.001#
	5 to 7days	5 (20%)	13 (14.4%)	2 (28.6%)	6 (9.5%)	
	8 to 14 days	2 (8%)	5 (5.6%)	1 (14.3%)	1 (1.6%)	
#Chi-square value=67.13, Degree of freedom=6, CI=0.0064-16.9655 p-value=0.001 (Statistically significant- duration of diarrhoea- most patients present with acute diarrhoea of 0-4 days)						
Number of diarrhoeal episodes per day	3	4 (16%)	71 (79%)	2 (28.6%)	59 (94%)	0.0455
	4-5	18 (72%)	13 (14%)	4 (57.1%)	4 (6%)	
	6 or more	3 (12%)	6 (7%)	1 (14.3%)	0	
^Chi-square-65.322, odds ratio- 2.500, Confidence interval- 1.0186-6.1358, p-value- <0.0455, P significant, Number of episodes- most patients have 4-5 episodes per day						
Experienced vomiting	Yes	14 (56%)	70 (78%)	5 (72%)	27 (43%)	0.0336*
	No	11 (44%)	20 (22%)	2 (28%)	36 (57%)	
*Vomiting- Odds ratio (0.3636), its standard error and 95% Confidence interval- 0.1430-0.9245 are calculated according to Altman 1991- p-value=0.0336- Statistically significant						
Experienced fever	Yes	18 (72%)	57 (63.3%)	5 (72%)	21 (33%)	0.0003**
	No	7 (28%)	33 (36.7%)	2 (28%)	42 (67%)	
**Fever- Odds ratio (6.0000), its standard error and 95% Confidence interval- 2.2891- 15.7267 are calculated according to Altman 1991- p-value=0.0003- Statistically significant						
Dehydration-	Mild	2 (8%)	77 (85.6%)	5 (72%)	54 (86%)	0.00001***
	Moderate	18 (72%)	10 (11.1%)	2 (28%)	6 (9%)	
	Severe	5 (20%)	3 (3.3%)	0	3 (5%)	
***Chi-square value 57.34, p-value=0.00001 (Statistically significant- Confidence interval- 0.0380-0.1771 Dehydration was found to be associated with rota virus patients						
Breastfed till 6 months of age	Yes	5 (22%)	76 (84%)			<0.0001****
	No (includes top feeding)	20 (80%)	14 (16%)			
****Breast feeding- Odds ratio (21.71), its standard error and 95% Confidence interval -6.9883-67.4713 are calculated according to Altman 1991- p-value <0.0001- Statistically significant						
IPD		16 (64%)	76 (84%)	3 (42.9%)	43 (68%)	0.02*****
OPD		9 (36%)	14 (16%)	4 (57.1%)	20 (32%)	
*****OPD/IPD odds ratio (3.0536), its standard error and 95% Confidence interval- 1.1279-8.2668 are calculated according to Altman 1991- p-value=0.0280- Statistically significant						

[Table/Fig-3]: Clinical profiles of patients tested for Rotavirus diarrhoea.



[Table/Fig-4]: Seasonal variations in Rotavirus diarrhoea.

DISCUSSION

In this study, we reported the magnitude of rotavirus diarrhoea in children under 5 years of age and adults over 18 years of age. A total of 21.7% of children were found to be positive for rotavirus infection. Similar findings were reported by Saluja T et al., [13], which found a positivity rate of 21.6%, compared to the 21.7% found in present study. Some studies by Jain S et al., have reported a higher burden (40%) of rotavirus diarrhoea in children in Northern India, which was significantly higher than the findings in present study [14]. This difference may be attributed to the phased introduction of the oral rotavirus vaccine in Punjab since 2019, which has led to a decreased burden due to increased vaccination coverage. Seven out of 70 (10%) adult patients were found to be positive for rotavirus antigen in present study. The possible reason could be transmission from children to adults or immunocompromised states. Although the disease is confined in paediatric population, adults are also not spared from its impact.

Male preponderance was observed in present study, with 25 (78%) of rotavirus-positive patients being males while around 7 (21.8%) were females. This finding was consistent with other studies and may be due to the fact that the majority of enrolled individuals were male [15]. Present study showed the maximum positivity of rotavirus infection in the first two years of life, which was in concurrence with previous studies in this region [16-18]. Rotavirus antibodies are typically developed by two years of age, which helps explain the observed decreased incidence of rotavirus infection in later childhood. Sixteen (64%) of the rotavirus-infected children needed hospitalisation (p-value=0.02), and 9 (36%) were treated as outpatients. In contrast, among adults, only 3 (42.9%) patients were admitted, while 4 (57.1%) were treated as outpatients. Additionally, adult patients exhibited mild dehydration compared to moderate dehydration in rotavirus-positive children, highlighting that adults tend to experience relatively milder disease compared to children [7]. This is because of better mucosal immunity and previous exposure to the virus, leading to the formation of antibodies in adult patients. Rural areas, due to a lack of sanitation, poor drinking water sources, and unhygienic practices, were found to be more affected in present study. Since the virus is transmitted via the faecal-oral route, raising awareness about drinking water sources and sanitation is essential.

Breastfed infants were found to be less susceptible to rotavirus infections than those who were top-fed or bottle-fed. This may be because of increased opportunity for the spread of infection among bottle-fed infants [19]. The odds ratio for breastfeeding was 21.71, and the statistically significant p-value in present study suggests that non breastfed infants have a higher likelihood of developing rotavirus diarrhoea compared to breastfed infants. It was observed that most mothers of the affected children were not literate (as defined by the Census of India under the Ministry of Home Affairs, Government of India) and were unaware of proper breastfeeding practices. It can be stated that the literacy status of the mother plays an important role in the transmission of rotavirus infection in children and newborns. Rotavirus diarrhoea was found to be more common during the winter season in present study. Present study findings correlate well with other studies conducted in India

in the past [20]. This is due to the fact that rotavirus survives more effectively in cooler months, and it has been hypothesised that the spread of rotavirus occurs more in low humidity and with infrequent rainfall during winter months, combined with the drying of soils.

In present study, 7 (28%) of rotavirus-positive children were vaccinated, while 18 (72%) were not vaccinated. Those who had received the vaccine experienced a milder course of the disease, highlighting the importance of the rotavirus vaccine and its efficacy.

A significant increase in rotavirus vaccine coverage has been observed since the introduction of Rotavac®, an indigenous, live oral vaccine (Bharat Biotech, India). The Rotavac® vaccine was introduced in 2016 as part of India's universal immunisation programme and was implemented in the state of Punjab in July 2019.

The strength of this study lies in its contribution to understanding the burden of disease in rural areas of Punjab, which may be helpful in implementing vaccine strategies in the state.

Limitation(s)

A limitation of this study was that genotyping of the circulating strains was not performed, which could provide insight into any changes in the current strains of the rotavirus.

CONCLUSION(S)

The present study concludes that the burden of rotavirus diarrhoea is still prevalent, and vaccination strategies need to be intensified further. In this study, rotavirus diarrhoea was found to be more prevalent in children from rural areas who were non breastfed and non vaccinated. Rotavirus is a vaccine-preventable disease and its spread can be controlled by good hygiene practices, awareness of proper breastfeeding practices and an emphasis on safe sources of drinking water. Raising awareness about the vaccine and its implementation can hugely impact the economic burden of the disease, as well as reduce the severity and mortality caused by this virus.

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