Original Article

Epidemiological and Clinical Profile of Rotavirus Gastroenteritis among Children Younger than 5 Years of Age

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ABSTRACT

Background: Acute gastroenteritis is on one of the leading causes of morbidity and mortality in children below 5 years of age. Among the various pathogens, rotavirus (RV) is responsible for 25–50% of all diarrheal hospitalizations. **Objective:** The objective of the study was to assess epidemiological and clinical features of RV among children younger than 5 years of age hospitalized with acute gastroenteritis and to compare it with RV negative diarrhea. **Materials and Methods:** A prospective descriptive hospital-based study was carried out among 162 children with acute gastroenteritis in a tertiary care teaching hospital from April 2017 to March 2018. Epidemiological profile, clinical features, and laboratory findings were recorded and compared between RV diarrhea (n=53) with non-RV (NRV) diarrhea (n=109) cases. **Results:** Mean age of patients was comparable between groups (RV-19.52±11.3 months; NRV-18.0±14 (p=0.47). Peak RV infection was observed during winters (66.03%) and NRV diarrhea occurred predominantly during summer months (38.53%). Comparison of clinical features of acute gastroenteritis between groups showed higher incidence of vomiting (p=0.006), diarrhea (p=0.049), and severity based on the Vesikari score (p=0.003) in RV group. Severe dehydration was observed in 5.6–7.3% in RV and NRV group, respectively (p=0.635). Around 26.41% incidence of dyselectrolytemia was seen in RV group. **Conclusion:** Studying the epidemiology and clinical profile of RV diarrhea will not only help in management of diarrhea, but will also provide useful information for indigenous vaccine development in India.

Key words: Acute gastroenteritis, Epidemiology, Rotavirus

Diarrheal diseases are the third most causes of mortality due to infectious diseases worldwide, accounting for 2 million deaths per year. In the developing countries, acute diarrhea is on one of the leading causes of morbidity and mortality in children below 5 years of age [1], with an estimated incidence of 1.4 billion acute diarrheal episodes per year [2]. Among other pathogens, rotavirus (RV) causes 25–50% of all diarrheal hospitalizations in both developing and developed countries and 23 million outpatient visits annually [3]. Of the 611,000 (454,000–705,000) RV gastroenteritis deaths occurring annually among children under 5 years of age worldwide, over 80% occur in developing countries in Africa and South Asia, with over 20% of these deaths are estimated to occur in India alone [4]. Studies conducted in India from 2001 to 2010 showed an increasing trend of RV isolation from 23.5% to 39.2% among hospitalized children with diarrhea [5-7].

The RNA virus is transmitted primarily through feco-oral contamination through person-to-person contact or contact with RV contaminated items such as respiratory secretions. Clinical manifestations include, vomiting, fever, diarrhea, and abdominal pain which occur after 24–72 h of incubation period and may last for as long as 3 weeks [8]. Management of RV gastroenteritis focuses on treating the effects of dehydration using supportive intravenous (IV) rehydration or oral rehydration [6]. RV vaccines are also being projected as a solution to this problem to prevent severe disease in children. Studying the epidemiology and clinical profile of RV diarrhea will not only help pediatricians and healthcare workers in treatment, prognostication, prevention, and anticipation of early complications but will also provide useful information for indigenous vaccine development in India. In view of the increased incidence of RV infection in India, the present study was carried out with an objective to assess epidemiological and clinical features of RV among children younger than 5 years of age hospitalized with acute gastroenteritis and to compare the epidemiological profile and severity between RV positive versus RV negative diarrhea.

MATERIALS AND METHODS

A prospective descriptive hospital-based study was carried out among 162 children between 2 months and 5 years of age with

Access this article online	
Received - 31 November 2020 Initial Review - 31 December 2020 Accepted - 15 January 2021	Quick Response code
DOI: 10.32677/IJCH.2021.v08.i01.009	

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acute gastroenteritis in a tertiary care teaching hospital from April 2017 to March 2018. Children with a primary diagnosis other than acute gastroenteritis, children with dysentery on presentation, children with diarrhea of >10 days duration, and those who developed diarrhea after hospitalization were excluded from the study. Ethical committee approval was obtained before initiation of the study. Parents of children were briefed about the nature of infection and the usefulness of the study and consent was taken. On admission, a detailed relevant history of acute gastroenteritis was obtained from the parent/guardian. Patient demographics including age, gender, demographic data, and socioeconomic status as per modified Kuppuswamy scale, the feeding practices, duration and severity of diarrhea, were oral rehydration therapy started at home, anthropometric parameters were recorded. Furthermore, history of receipt of RV vaccine including the number of doses, dates of administration, and type of the RV vaccine was noted.

Diarrhea was defined as passage of 3 or more unformed stools in children and dehydration was assessed according to World Health Organization (WHO) IMNCI dehydration criteria. The 20-point Vesikari scale assigns points according to duration and intensity of diarrhea, vomiting, body temperature, behavioral symptoms, and the treatment given. Based on this, severity of disease was graded as mild, score ≤6; moderate, score 7–10; and severe, score ≥11. Vital signs and maximum number of stools and vomiting were recorded on admission and child was started on treatment. Three stool samples were collected in a sterile screw cap plastic containers simultaneously (~5 ml) of whole stool from each possible case during the acute illness as early as possible, preferably within 24 h of hospitalization. Two samples were sent to the hospital for routine examination and stool culture. 3rd Stool sample was transported on ice to the laboratory of National Institute of Virology, Pune, for detection of RV antigen by enzyme-linked immunosorbent assay (ELISA) test using commercially available kit (Premier Rotaclone, Meridian Bioscience, Inc. USA).

The children were monitored for new signs of dehydration and were followed up till discharge taking into consideration the episodes of diarrhea, vomiting, total IV fluid, and oral rehydration solution (ORS) (ml/kg body weight) taken in a day along with maximum temperature recorded in a day. Treatment given to the child namely zinc supplementation, antibiotics, and probiotics were recorded along with exact duration of hospital stay. Data obtained were entered and analyzed in Microsoft excel. Data were summarized using descriptive statistics, quantitative data were reported as mean, and median and categorical variables were reported as percentage. The proportion of RV gastroenteritis among all the hospital admissions for acute gastroenteritis was calculated with the exact binomial 95% confidence interval. $p<0.05$ was considered significant.

RESULTS

A total of 2587 children were admitted in the pediatric unit from May 2017 to April 2018, out of which 200 children presented with acute gastroenteritis. After excluding 38 children with dysentery, a total of 162 children were enrolled for the study whose samples underwent RV detection by ELISA. The end point analysis was done on all 151 patients. Out of the total patients, 5 children took leave against medical advice, 4 children succumbed due to sepsis, and other causes. There were no deaths in the RV positive children. Rest 142 children were discharged after resolution of diarrhea.

In our study, out of total of 162 with acute gastroenteritis, 53 (32.72%) children were enterovirus positive and 109 were RV negative. Mean age of patients with RV infection was 19.52±11.3 months and non-RV (NRV) infection was 18.0±14 months (p=0.47). Most of the patients (41.51%) with RV infection belonged to the age group of 13–34 months, whereas NRV infection (33.94%) was common in the 6–12 month age group. Epidemiological characteristics of both groups are summarized in Table 1. Peak RV infection was observed during November to February (66.03%), while lowest rate was observed during the months of April-July (15.2%). On the other hand, NRV diarrhea occurred predominantly during summer months from April to July accounting for 38.53% of total hospitalization.

Clinical features of the hospitalized children are summarized in Table 2. Vomiting was the most common presenting symptom reported in both groups (p=0.006). The mean duration of diarrhea in both the groups were comparable; however, RV group had higher number of diarrhea episodes each day as compared to NRV group (p=0.049). Mean duration of hospital stay and degree of dehydration were similar in both the groups (p=0.6). There was no significant association between disease severity score with degree of dehydration (p=0.073) and with age (p=0.93) as shown in Table 3.

No significant difference was found in the laboratory investigation between both groups as shown in Table 4. Association of age with electrolytic imbalance in RV patients was analyzed

Table 1: Epidemiology of study population

Variable	RV (n=53) (%)	NRV (n=109) (%)	p-value
Age (months)			
Mean±SD	19.52±11.3	18.0±14	0.47
<6 months	5 (9.43)	16 (14.6)	0.258
6–12 months	12 (22.64)	37 (33.94)	
13–24 months	22 (41.51)	33 (30.28)	
>25 months	14 (26.42)	23 (21.10)	
Gender			
Male	30 (56.6)	60 (55.1)	0.868
Female	23 (43.4)	49 (44.9%)	
Socioeconomic status			
Lower	3 (5.7)	8 (7.3%)	0.876
Upper lower	8 (15.1)	19 (17.4%)	
Lower middle	25 (47.1)	41 (37.6%)	
Upper middle	14 (26.4)	33 (30.2)	
Upper	3 (5.7)	7 (7.3)	
Kuppuswamy score	14.64±5.03	15.54±5.26	

RV: Rotavirus; NRV: Non-rotavirus

Table 2: Clinical features of children admitted with diarrhea

Variable	RV (n=53) (%)	NRV (n=109) (%)	p-value
Presenting features			
Fever	22 (41.5)	51 (46.7)	0.452
Vomiting	35 (66.04)	44 (52.2)	0.006
Diarrhea	18 (33.9)	57 (40.3)	
High grade fever (>38c)	7 (13.2)	20 (18.3)	0.381
Duration of vomiting (d)	2.08±1.2	1.64 ±1.38	0.058
Vomiting Episodes/day	2.7±1.6	2.2±1.7	0.098
Duration of diarrhea (d)	2±1.1	2.2±1.3	0.324
Diarrhea Episodes/day	7.4±2.06	6.6±2.8	0.049
Hospital stay (d)	2.55±1.20	2.57±1.60	0.924
Degree of dehydration			
No	25 (47.1)	58 (53.2)	0.635
Some	25 (47.1)	43 (39.4)	
Severe	3 (5.6)	8 (7.3)	
Mode of rehydration			
IV fluids	46 (86.7)	83 (76.1)	0.114
ORS	7 (13.2)	26 (23.8)	
Severity (Vesikari score)			
N/A	3 (5.7)	8 (7.3)	0.003
Moderate	8 (15.1)	43 (39.4)	
Severe	42 (79.2)	58 (53.2)	
Weight/height			
Normal	32 (60.3)	56 (51.3)	0.561
MAM	15 (28.3)	38 (34.8)	
SAM	6 (11.3)	15 (13.7)	

RV: Rotavirus; NRV: Non-rotavirus; ORS: Oral rehydration solution; IV: Intravenous

Table 3: Assessment of severity with age and WHO dehydration scores

RV	Vesikari score		p-value
	Moderate	Severe	
Degree of dehydration			
No	7	17	0.073
Severe	0	3	
Some	1	22	
Total	8	42	
Age			
<12 months	3	13	0.93
>12 months	5	29	
Total	8	42	

RV: Rotavirus

and significant association was found only with hypernatremia (p=0.028), (Table 5). The mean duration of hospital stay, vomiting, diarrhea (duration and episodes) disease severity by degree of dehydration, and Vesikari score were comparable in children with co-infections and children with isolated RV diarrhea; however, there were not statistically significant (p>0.05) (Table 6).

DISCUSSION

In India, acute viral diarrhea is the second most common cause of mortality in children under 5 years of age and RV infection contributes to 25–50% of all hospitalizations due to diarrhea [5]. The prevalence of rotaviral diarrhea in our study was 32.72% among the children with acute gastroenteritis which is in accordance with study by Bahl *et al*. [6] (23.5%) and Kahn *et al*. [9] (34%). These results indicate that every third child requiring hospitalization due to diarrhea is probably infected with RV. Epidemiological profile of RV diarrhea like any other disease is multifactorial. Although RV infection is seen throughout the world, the severity of diarrhea and early dehydration is more common in developing countries due to lack of healthcare services and immunization pitfalls coupled with poor socioeconomic status of the dwelling population which makes it a major health hazard in such circumstances.

The mean age of presentation of RV diarrhea was 19.5±11.3 months. Previous studies have indicated that around 10–25% hospitalizations due to RV infection occur before 6 months of age and by 18–24 months the incidence increases by 79.53–87% [7,10-13]. In our study, almost 23.81% of RV diarrheal hospitalization occurred before 6 months of age and around 88.3% hospitalizations occurred before 2 years of age. Although maternal antibodies are thought to be protective in children below 6 months of age, higher prevalence of RV diarrhea in children <6 months clearly indicates that these antibodies may not last long and weans very rapidly. Early immunization of these vulnerable children as per Indian academy of pediatrics schedule may help prevent majority of these cases.

Rotaviral diarrhea being an infective pathology would affect both the genders equally but various studies conducted globally and in India showed slight male preponderance to RV diarrhea [13-17]. Similarly we observed slight male predominance in our study. Previous studies have demonstrated a

Table 4: Laboratory investigations

Variable Mean (SD) or n (%)	RV (n=48) (%)	NRV (n=95) (%)	p-value
Hemoglobin (g/dl)	12.2±1.32	10.3±1.5	0.663
Total Leucocyte count (/mm^3)	11765±3602.2	11442.1±4951.3	0.665
Serum sodium (Meql/dl)	137.3±7.93	135±6.75	0.085
Hyponatremia (Na <130 meq/dl)	2(4.1)	13 (13.68)	0.091
Hypernatremia (Na >145 meq/dl)	5 (10.4)	5 (5.26)	0.254
Serum Potassium	4.40±0.69	4.63±0.4	0.314
Hypokalemia (<3.5meq/dl)	5 (10.4)	6 (6.3)	0.508
Hyperkalemia (>5.5 meq/dl)	2 (4.1)	8 (8.4)	0.496
Stool culture positivity n (%)	12 (22.6)	44 (40.3)	0.05

RV: Rotavirus; NRV: Non-rotavirus

Table 5: Association of dyselectrolytemia with age

Electrolytes	<12 months (n=15) (%)	>12 months (n=33) (%)	p-value
Hyponatremia	0 (0)	2 (6.06)	0.999
Hypernatremia	4 (26.67)	1 (3.03)	0.028
Hypokalemia	2 (13.33)	3 (9.09)	0.642
Hyperkalemia	0 (0)	2 (6.06)	0.999

Table 6: Clinical features and severity in RVD and co-infections

Variable	RV (+) Co(+) n=12	RV(+) Co(-) n=37	p-value
Duration of vomiting (d)	2.04±1.27	2.08±1.28	0.925
Vomiting Episodes/day	2.74±1.64	2.68±1.65	0.998
Duration of diarrhea (d)	1.9±1.10	2.0±1.12	0.788
Diarrhea episodes/day	7.3±2.05	7.4±1.97	0.880
Hospital stay (d)	2±1	2±1	0.999
Degree of dehydration			
No	4	19	0.550
Some	7	16	
Severe	1	2	
Vesikari score	12.13±1.75	12.13±1.69	0.999
Moderate	2	6	
Severe	10	31	

RV: Rotavirus

distinct seasonality in trends of rotaviral diarrhea with most cases (59–72%) occurring during winters [10-13,18]. Similarly, we observed 66.03% RV diarrhea cases from November to February. Socioeconomic status is inversely related to severity of diarrhea due to lack of education, poor sanitation, contamination, and overcrowding [19]. In our study, most children (47.2%) belonged to lower middle class according to modified Kuppuswamy scale 2016.

Although RV and NRV diarrhea in children are different in etiology and epidemiology, the clinical presentation and constellation of symptoms are overlapping with slight differences between the two groups [9,10,13]. In our study, on comparison between the epidemiology of RV diarrhea and NRV diarrhea, no significant difference was observed with respect to age, sex, and socioeconomic class. This suggests that improvement in socioeconomic conditions, sanitation may have only a limited impact on prevention of rotaviral diarrhea and hence, other strategies for prevention like vaccination may be the way forward in reducing the burden of diarrheal diseases in children which remains a major contributor of under-5-mortality in children.

Comparison of clinical features of acute gastroenteritis between groups showed higher incidence of vomiting, diarrhea, Vesikari score, and severity of disease in RV group, which is in accordance with the previous reported literature [10,13-16]. Vomiting was the most common presenting symptom reported in both groups (p=0.006). Mean duration of vomiting and number of episodes of vomiting were slightly higher in the RV group as compared to NRV negative group (p>0.05). Similarly, higher incidence of vomiting has been reported previously [20] which may be attributed to delayed gastric emptying because of RV infection. Since vomiting make oral rehydration difficult, leading to early dehydration and increase in severity of the disease.

Studies conducted worldwide report mean duration of diarrhea to be between 2.19 and 3.3 days, while purge rate in RV positive children were variably high ranging from 9.8 to 13.13 episodes each day [16,21,22]. In our study, mean duration of diarrhea in both the groups was comparable; however, the RV group had higher number of diarrhea episodes each day (7.4±2.06 vs. 6.6±2.8), (p=0.049). Incidence of diarrhea in our study was less as compared to previous studies in India who reported dehydration in 56.9% children with 15.6% being severely dehydrated [10,16,23]. Antiemetic with or without IV fluids may help prevent dehydration in children with vomiting.

Vesikari score have been used previously to assess the disease severity [9,10,16,23]. A study by Kahn *et al*. [9] have inferred that clinical severity in RV diarrhea is higher with nearly 2.8%, 56.5%, and 38.7% of the children having very severe, severe, and moderate disease severity, respectively. In our study, Vesikari scores in both the groups were similar (p=0.93). Disease severity was higher in RV group (79.2%) as compared to NRV group (53.2%) (p=0.003). However, there was no association between disease severity with age and degree of dehydration. Although, the application of Vesikari severity scoring in clinical practice is of less importance as compared to end point analysis of vaccine trial efficacy studies, it predicts the severity of disease which is beneficial to plan and implement cost effective strategies for prevention.

Complications of RV diarrhea ranges from severe dehydration, electrolytes disturbances to aseptic meningitis, acute myositis, hepatitis, hemophagocytic lymphohistiocytosis, and polio like paralysis but their relationship with RV infection remains unclear. The overall incidence of dyselectrolytemia was low in RV group (26.41%) and was comparable to a study by Mathew *et al*., [10] (21.7%). Although, the overall incidence of hypernatremic dehydration was slightly higher in the RV group as compared to NRV group; none of these electrolyte imbalances increased morbidity, severity, or resulted in prolonged hospitalization. In our study, age was significantly associated with hypernatremia (p=0.028), while Mathew *et al*. [10] did not find an association between age and dyselectrolytemia. Nearly 86.7% of children in the RV diarrhea required IV fluid replacement as compared to 76.1% of children in NRV diarrhea which indirectly indicates the higher degree of dehydration and disease severity in children in the RV group in our study.

The presence of co-infections in children with RV diarrhea ranges from 4 to 9.9% [14]. On examination of stool samples, we observed co-infections in 22.6% of RV diarrhea. Most common bacterial isolate was *Escherichia coli* (18.9%) followed by extended-spectrum beta-lactamase *E. coli* (1.9%). Since most of these infections are due to feco-oral transmission, co-infection is more likely seen in children with poor socioeconomic background where overcrowding, sanitation, and hygiene practices remained poor. The symptoms, degree of dehydration, and severity were

similar in children with or without co-infections. On the contrary, Nyugen *et al*. [14] found differences in clinical profile of children with co-infections; however, the disease severity remained comparable between both groups. Management approach remains same in patients with or without co-infection, except in some bacterial diarrhea where antibiotics may be considered.

Our study has some limitations as it was a hospital-based study and was conducted for a short duration; therefore, the results may not be the actual representation of the prevalence of RV infection in the community. G and P typing of RV positive children was not possible because of logistic issues, also virus isolation was not done in NRV group which could be a possible cause of diarrhea.

CONCLUSION

RV diarrhea causes substantial mortality and morbidity in young children in India with the greatest burden among children <2 years of age, robust vaccination may prevent severe disease and hospitalization in the under 5 age group. The present study demonstrated that RV accounts for approximately one third of acute diarrhea among children presenting to hospital below 5 years of age with 88.3% hospitalizations occurred by 2 years of age.

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Funding: None; Conflicts of Interest: None Stated.

How to cite this article: Rana R, Dahiphale R, Kalrao V. Epidemiological and Clinical Profile of Rotavirus Gastroenteritis among Children Younger than 5 Years of Age. Indian J Child Health. 2021; 8(1):46-50.