Prevalence, clinical profile, and laboratory features of hospitalized under-five children with rotavirus-induced diarrhea

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ABSTRACT

Background: Rotavirus is considered as an important causative agent for pediatric diarrhea. Despite recent studies, data available on the prevalence of diarrhea due to rotavirus, among under-five children, are scarce. **Objective:** The objective of this study is to estimate the prevalence, clinical profile, and laboratory features among hospitalized under-five children with rotavirus-induced diarrhea. **Materials and Methods:** A total of 145 under-five children with diarrhea were included in the study. The sociodemographic characteristics, clinical profile, and laboratory investigations of all the children were recorded. Stool samples collected were tested for rotavirus antigen using enzyme immunoassay. **Results:** Of 145 stool samples processed, rotavirus antigen was positive in 33.10% of cases, and male-to-female ratio was 1.1:1. The majority (62.76%) of the children with diarrhea were aged ≤12 months. Rotavirus infection was significantly associated with socioeconomic status of the parents (p=0.023), maternal education (p=0.028), fever (p=0.029), vomiting (p=0.001), restlessness (p=0.001), perianal excoriation (p=0.045), bottle feeding (p=0.014), hypernatremia (p<0.001), and presence of reducing substances (p 0.001). **Conclusion:** Rotavirus-induced diarrhea was diagnosed in one-third of the study children. Maternal education, symptoms of fever, vomiting, presence of reducing substances, and age ≤12 months were found to be predisposing factors for rotavirus infection in under-five children. However, periodic review on rotavirus and other co-pathogenic infections are required to validate the current findings.

Key words: *Diarrhea, Enzyme immunoassay, Pediatric, Rotavirus infection*

Diarrheal disease, a third leading cause of childhood morbidity and mortality, accounts for about 1.5 million deaths globally every year with an increased prevalence in the developing countries [1-3]. In India, it accounts for about 13% deaths every year in under-five children [4-6]. Bacteria, virus, and parasites are known to cause diarrhea in young children; notable viral agents are rotavirus, astrovirus, adenovirus, and Norwalk-like viruses [7]. Among these, human rotavirus has been attributed as a leading cause of severe diarrhea among young children [4]. In India, rotavirus is responsible for 39% of childhood diarrheal hospitalizations and about 1.13 lakh deaths yearly in under-five children [8].

It has been postulated that children with the rotavirus infection have a wide variation in clinical presentation [9]. Rotavirus infection typically instigates with sudden onset of fever, diarrhea, and vomiting [10]. Although fever is common, it remains underreported. A concurrent upper respiratory tract infection has also been documented in few earlier reports [9]. The incubation period of the disease was reported to be 1–3 days [10]. Enzyme immunoassay (EIA) and latex agglutination are the laboratory investigations available for the identification of rotavirus infection [10].

In India, especially in Karnataka, low socioeconomic status, inappropriate feeding, and child-rearing practices along with malnutrition contribute to high morbidity and mortality in diarrheal disease caused by rotavirus infection. However, there is a lack of documentation in our population in this regard. Information about rotavirus infection in correlation with clinical symptoms and epidemiological factors is important for pediatricians and health-care workers. Such information will not only help to improve the diagnosis and treatment of diarrhea in children but also provide useful information for vaccination in future. Hence, the present study was undertaken with an aim to estimate the prevalence, clinical profile, and laboratory features among hospitalized under-five children with rotavirus-induced diarrhea.

MATERIALS AND METHODS

This cross-sectional study was conducted at the department of pediatrics of a tertiary care teaching institute of Karnataka from June 2014 to August 2015. The ethical clearance was obtained from the Institutional Ethical and Research Committee. Parents or legal guardians of the children were briefed about the nature of the study in their local language, and a written informed consent was obtained.

Inclusion criteria consisted of all children admitted with acute diarrhea of <5 days' duration. Children above 5 years of

age, children with bloody and chronic diarrhea, and children who acquired diarrhea during hospitalization for treatment of other diseases were excluded from the study.

The sample size was calculated using the following formula, n=4*pq/d²

Where n=total sample size, p=prevalence of diarrhea cases in pediatric admissions (36), q=100–p (100–36=64), d=standard error (8%), and n=144. Based on the past 14 months admission rate in our hospital, with requisite inclusion and exclusion criteria, the final sample size of 145 children, aged 0–5 years, was taken in the study.

Sample collection and processing were done in the following manner. The child was placed either on a rubber sheet or a diaper. In case of diaper usage, it was reversed, and the non-absorbent surface was placed against the skin. Stool from the diaper or the sheet was scooped with a spatula and transferred into stool collection container. If the stool was watery, it was directly transferred from the plastic sheet into the stool container. These stool samples were sent for the detection of rotavirus by EIA using Premier Rotaclone kit. The detection was done as part of National Hospital Based Rotavirus Surveillance Network of Indian Council of Medical Research. Adequate samples collected were stored in the refrigerator between 2 and 8°C, until use. A second stool sample was collected within 24–48 h to avoid nosocomial infection (before the administration of antibiotics) and was subjected to laboratory examinations, such as stool routine, microscopy, reducing substances, stool culture, and sensitivity.

Sociodemographic data including age, gender, socioeconomic status (categorized according to modified B.G. Prasad's classification) [11], and maternal education were collected. Clinical profile including vomiting, feeding pattern, history of associated illness (perianal excoriation, fever, thirst, and restlessness), and hydration status was examined. Laboratory investigations comprising total leukocyte count, neutrophilia, serum electrolytes (hypernatremia, hyponatremia, and hypokalemia), hemoglobin levels, reducing substances, macroscopic (consistency, color, and smell), and microscopic stool examinations (presence of starch, fat globules, and pus cells) of all the children were recorded on a pre-designed and pre-tested pro forma.

Statistical Analysis

The data obtained were coded and entered into Microsoft Excel spreadsheet. Data were analyzed using the Statistical Package for the Social Sciences (SPSS) software version 22.0 (SPSS, IBM Inc., New York). Categorical data were expressed as rates, ratios, and percentage. Continuous data were expressed as mean±standard deviation. Chi-square test and Fisher's exact test were used to find an association between two variables. p≤0.05 was considered statistically significant.

RESULTS

During the study period, a total of 290 cases were admitted with diarrhea, of which 145 fulfilling the inclusion criteria were

selected. Most of the children were aged below 12 months with slight male child preponderance (54.48%). All the children in the study were vaccinated with routine free vaccines supplied by the government. Among the 145 samples processed for EIA, rotavirus antigen was positive in 48 (33.10 %) cases. Rotavirus infection was significantly associated with the socioeconomic status of the parents (p = 0.023) and maternal education (p=0.028) (Table 1).

Among the clinical parameters, vomiting (p=0.001), restlessness (p=0.001), fever (p=0.029), perianal excoriation (p=0.045), and bottle feeding (p=0.014) were associated statistically significant with rotavirus infection. However, other variables including breastfeeding, top feeding, associated-illness, thirst, and hydration status showed no significant association with rotavirus-induced diarrhea (p>0.05; Table 2).

Laboratory investigations including the presence of reducing substances and hypernatremia (p<0.001) were significantly associated with rotavirus infection, whereas other variables such as total leukocyte count, neutrophilia, and hemoglobin levels were not significantly associated with rotavirus-induced diarrhea (p>0.05; Table 2). Among the 48 rotavirus-positive cases, the most common bacterial organism (31.25%) isolated was *Escherichia coli*. Microscopic examination revealed pus cells and normal cells in 33.33% and 29.17% of the children with rotavirus infection, respectively. The hospital stays of the children also was not associated significantly with rotavirus infection.

DISCUSSION

In this new millennium, emerging new infections and diseases are instigating a global health concern. Gastrointestinal tract infections such as diarrheal disease and respiratory infections (pneumonia) are the leading causes of mortality in young

Table 1: Association of demographic characteristics of children with rotavirus infection

Variables	Rotavirus infection		p
	Present, n=48 (%)	Absent, n=97 (%)	
Gender			
Male	28 (58.33)	51 (52.58)	0.512
Age-wise distribution (months)			
12 or less	35 (72.92)	56 (57.73)	0.279
12 or more	13 (27.08)	41 (42.26)	
Socioeconomic status			
Class I	1 (2.08)	0	0.023*
Class II	2 (4.17)	0	
Class III	5 (10.42)	19 (19.59)	
Class IV	20 (41.67)	53 (54.64)	
Class V	20 (41.67)	25 (25.77)	
Mother's education			
Illiterate	7 (14.58)	2 (2.06)	0.028*
Literate	41 (85.42)	95 (97.93)	

*Statistically significant

Table 2: Association of clinical and laboratory characteristics with rotavirus infection

Parameter	Rotavirus infection		p value
	Present, n=48 (%)	Absent, n=97 (%)	
Incidence of vomiting, n=84	37 (77.08)	47 (48.45)	0.001*
Electrolyte imbalance, n=28	13 (27.08)	15 (15.46)	0.095
Hypernatremia, n=11	10 (20.83)	1 (1.03)	<0.001
Hyponatremia, n=2	1 (2.08)	1 (1.03)	0.609
Hypokalemia, n=3	2 (4.17)	1 (1.03)	0.211
Exclusive breast feeding, n=137	44 (91.67)	93 (95.88)	0.249
Bottle feeding, n=9	8 (16.67)	1 (1.03)	0.014*
Top feeding, n=4	3 (6.25)	1 (1.03)	0.106
Weaning after 6 months, n=119	42 (87.50)	77 (79.38)	0.230
Reducing substances, n=11	9 (18.75)	2 (2.06)	< 0.001*
History of associated illness, n=122	44 (91.67)	78 (80.41)	0.081
Perianal excoriation, n=29	14 (29.17)	15 (15.46)	0.045*
Fever, n=111	42 (87.50)	69 (71.13)	0.029*
Thirst, n=76	27 (56.25)	49 (50.51)	0.800
Restlessness, n=119	32 (66.67)	87 (89.69)	0.001*
Dehydration status, n=30	13 (27.08)	17 (17.52)	0.265
Low hemoglobin levels (<11) (g %), n=103	37 (77.08)	66 (68.04)	0.259
Abnormal TLC (cells/cumm), n=75	24 (27.08)	51 (52.57)	0.937
Abnormal neutrophils (%), n=125	43 (89.58)	82 (84.53)	0.116
Hospital stay (>7 days), n=83	30 (62.50)	53 (54.64)	0.553

*Statistically significant. TLC: Total leucocyte count (cells/cumm)

children [12]. Although there are various prevalence studies in India regarding rotavirus-induced diarrhea, there is a paucity of data from this part of the country [13]. Therefore, the present study was undertaken to estimate the prevalence, clinical profile, and laboratory features among hospitalized children under 5 years of age with rotavirus-induced diarrhea.

The prevalence of rotavirus infection observed in the present study (33.10 %) was within the reported range (30–50 %), however, slightly low compared to a very recent study by Mathew *et al.*, wherein authors reported rotavirus infestation in 35.9% of diarrhea-related hospital admissions among under-five children [7,14]. The age distribution is comparable to other studies in different regions. The highest prevalence of the rate of infection

was reported under 12 months of age [10,15]. In the present study, males were marginally more susceptible to rotavirus infection than females. Although there was no significant association, this difference of susceptibility of male children could be attributed to a higher likelihood of them being brought for medical care [16]. Similarly, Mathew *et al.* reported seven positive cases among 23 male children, and three positive cases among 12 female children [14].

Social deprivation such as poor maternal education influences the prevalence of rotavirus infection in children [17]. Similarly, in our study, educational status of the mother was associated with rotavirus-induced diarrhea. Studies conducted by Paul *et al.* and Nakawesi *et al.* also reported that maternal education was an important determinant in the risk assessment of both rotavirus infection and diarrhea [18,19]. Furthermore, socioeconomic status of the mothers in our study was also associated with rotavirus-induced diarrhea. A study by Shetty *et al.* reported a higher prevalence of rotavirus-induced diarrhea in children with low family income than with high family income [20]. Similar studies conducted in different parts of the world also stated that lower socioeconomic status influences the prevalence of rotavirus infection among younger children [15,21].

Breastfeeding provides numerous benefits to the child. It significantly protects the child against various infections. The breast milk contains high levels of anti-rotavirus secretory IgA and other rotavirus-specific antibodies, which protect the infants against rotavirus-induced diarrhea. Various studies conducted and also documented the protective efficacy of exclusive breastfeeding against rotavirus positivity within young children [10,22]. In this study, children acquired rotavirus infection in spite of exclusive breastfeeding, although it was not statistically significant. This might be due to improper maintenance of personal hygiene and poor knowledge and practice of environmental sanitation [3]. On the contrary, children with bottle feeding were significantly associated with rotavirus infection.

Among the various pathogens causing diarrhea, rotavirus is considered to be associated with the triad of fever, vomiting, and dehydration [10]. All these symptoms may occur alone or in combination with others, resulting in the hospitalization of children for further treatment. Similarly, in our study, increased thirst, fever, vomiting, and perianal excoriation were the most common clinical symptoms in both children with and without rotavirus infection. Furthermore, our study reported a significant association between rotavirus infection and symptoms of fever, vomiting, and perianal excoriation.

Among the complications of electrolyte imbalance, hypernatremia was associated significantly with rotavirus infection. However, there is a lack of literature to support this finding. As hypernatremia was reported in most of the children, the correction of sodium levels can be done by administering oral rehydration solutions to prevent adverse effects of hypernatremia, such as convulsions or cerebral edema [23]. The reducing substances in rotavirus-infected stool were more compared to non-infected stools, and a significant association was found between

reducing substances and rotavirus infection. These findings could not be compared with other studies due to unavailability of data in the literature.

More than half of the study population had a hospital stay of more than 7 days in our study. However, the duration of hospital stay was not associated with rotavirus infection. In contrast, various studies reported an average of 5–6 days of hospital stay in both rotavirus-positive and negative cases [24,25]. However, there was no mortality among the admitted diarrhea cases, including the rotavirus-positive cases.

The small sample size, shorter duration of the study, and lack of ability to extrapolate disease burden to milder diseases were the few potential limitations of our study. A periodic review of infections with rotavirus and other copathogens are required to validate the current findings. Rotavirus vaccination in the national immunization program might decrease the disease burden among young children.

CONCLUSION

The prevalence of rotavirus-induced diarrhea in the study area was high, as nearly one-third of the study population was found to be infected. The significant predisposing factors were socioeconomic status, maternal education, and bottle feeding. Rotavirus infection was associated with symptoms of fever, vomiting, perianal excoriation, hypernatremia, and the presence of reducing substances on stool examination.

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