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Severity of rotavirus gastroenteritis in an Indian population: Report from a 3 year surveillance study



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ABSTRACT

This study investigated the severity of rotavirus gastroenteritis (RVGE) in hospitalized children less than 60 months of age and compared severity in the first five months of life to severity in children 6 to 23 months of age. Results from a 3 year surveillance study show an early peak of rotavirus disease, with 117 (31%) RVGE hospitalizations in children <6 months old. Higher incidence of severe dehydration, acidemia and acidosis at admission and prolonged hospitalization ≥ 7 days were seen in infants 0–5 months of age. The findings support the need for consideration of timely immunization or an accelerated immunization schedule with a birth dose to protect this vulnerable age.

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1. Introduction

Rotavirus is the leading cause of diarrhea related hospitalization among infants and young children worldwide. Annually in India, rotavirus diarrhea causes nearly 100,000 deaths and over half a million hospitalizations in children less than 5 years [1,2].

Severe dehydration, leading to acute shock with electrolyte imbalance is believed to be the major cause of death in rotavirus gastroenteritis (RVGE) [3–5]. A low serum bicarbonate or venous pH has been reported to be the best predictor of dehydration correlating strongly with worsening clinical dehydration, greater diarrhea severity and younger age [6]. The amount of bicarbonate lost in stool depends on the volume of diarrhea and the bicarbonate concentration of the stool which tends to increase with more severe diarrhea [7]. Studies have reported that in acute episodes of RVGE as compared to non-rotavirus diarrhea, there is a higher incidence of complications from severe dehydration and acid-base and electrolyte imbalances [8,9].

Vaccination is considered one of the most effective public health strategies to prevent rotavirus infection and reduce disease burden [10]. Data on the age-specific burden of RVGE and frequency of complications would better identify vulnerable age groups to target for rotavirus vaccination and guide research on rotavirus vaccines. The purpose of this study was to assess the age distribution of children

with RVGE admitted to an urban pediatric unit and to evaluate the incidence of complications from severe dehydration, acid–base and electrolyte abnormalities in RVGE at admission.

2. Materials and methods

2.1. Setting

The study was conducted at St. Stephens' Hospital Delhi (SSH), India: a 595 bedded multi-specialty tertiary care hospital with approximately 3000 deliveries taking place annually. The pediatric department has 40 beds, an intensive care unit with 6 beds and a neonatal intensive care unit. Patients are admitted from the city and nearby villages, and referred from general practitioners, clinics and various hospitals in Delhi. Most patients are of middle and lower income groups.

2.2. Study design and definitions

During a 3-year period from December 2005 through November 2008, children less than 59 months of age hospitalized in the ward or pediatric intensive care unit with acute gastroenteritis (AGE) (>3 loose or watery stools in a 24 h period) were included in the study after written informed consent was obtained. The history, severity of dehydration and treatment were recorded in patients' hospital records. Electrolytes and blood gas analysis were done as clinically indicated by the admitting physician. Treatment for dehydration,

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electrolyte and fluid imbalance was based on WHO and department protocols [11].

2.3. Laboratory methods

Stool samples were collected within 48 h of admission and tested for rotavirus by an enzyme immunoassay (Dako IDEIA Rota, Ely, UK). Serum electrolytes were analyzed in a Roche Hitachi 917. The acid-base status was established by blood gas analysis done in a Radiometer ABL 555 blood gas analyzer. All machines are calibrated once daily, according to the standards provided by the manufacturer.

2.4. Data collection

Data was obtained from hospital charts on demographic details, severity of dehydration, serum electrolytes and blood gas analysis entered at admission. Three rotavirus positive and six rotavirus negative cases were excluded as age was not entered in the patient records.

2.4.1. Severe dehydration

The clinical definition of a case of severe dehydration at admission was diarrhea that required re-hydration therapy equivalent to WHO plan C (intravenous re-hydration therapy of 100 mL/kg over 3 or 6 h depending on age) [11].

2.4.2. Definitions of serum electrolyte and acid-base abnormalities

Severe acidemia was defined as $\text{pH} \leq 7.2$; severe acidosis was defined as bicarbonate ≤ 8 mEq/L; moderate acidosis as bicarbonate 9–12 mEq/L; hypokalemia was defined as serum potassium < 3.5 mEq/L; hypernatremia as sodium level ≥ 150 mEq/L; severe hypernatremia $\text{Na} > 160$ mEq/L; hyponatremia as sodium level < 130 mEq/L [7,12–14].

2.4.3. Prolonged hospitalization with RVGE

Prolonged hospitalization was defined as children with rotavirus gastroenteritis requiring admission for ≥ 7 days.

2.5. Statistical methods

Analysis was done using SPSS v.11 software. Percentages, proportions and rates were computed and the statistical significance of the differences tested using the Chi-square test and Fisher's exact test.

3. Results

Over the 3-year period, of 1208 children hospitalized with gastroenteritis, 974 (80.6%) had a stool specimen collected. All results are only for children who tested rotavirus positive.

3.1. Age of children hospitalized due to RVGE

Over the 3 years of the study, 39% (379/974) of these children hospitalized with gastroenteritis from whom stool samples were collected tested positive for rotavirus. The age distribution of children hospitalized for RVGE from December 2005 to December 2008 is presented in Fig. 1. December 2008 was included, because the samples from December 2007 was lost during transport. Of the rotavirus hospitalizations, 31% occurred during the first 5 months of life, 49% by 8 months of age, and 64% by 11 months, 89% by 23 months. Approximately 11% were 2–5 years of age.

Rotavirus accounted for 33% of all hospitalizations for gastroenteritis among children in the 0–2 month age group, 46% of those

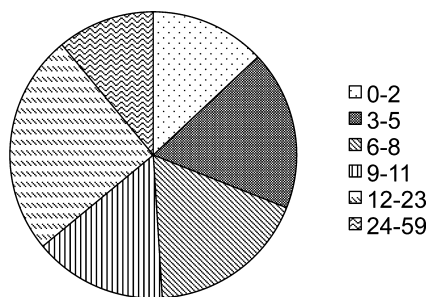


Fig. 1. Age in months of children less than 60 months hospitalized with rotavirus gastroenteritis at St. Stephen's Hospital, Delhi between December 2005 and December 2008.

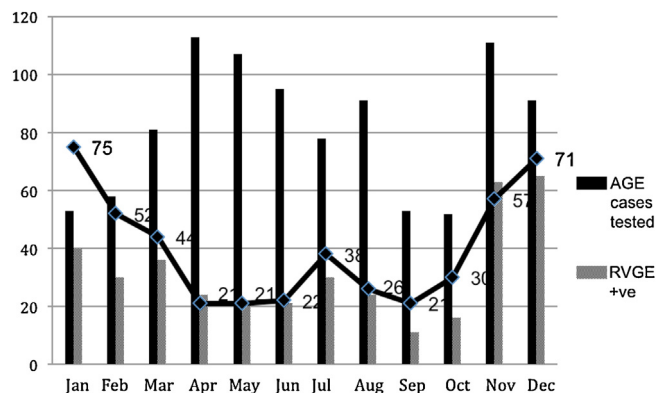


Fig. 2. Seasonal distribution of cases admitted with acute gastroenteritis (AGE) and positive for rotavirus (RVGE) over 3 years of surveillance at St. Stephen's Hospital, Delhi. The line indicates the percentage of cases positive for rotavirus by month.

3–5 months and about 27% of all hospitalizations for gastroenteritis among children 2–5 years of age.

3.2. Seasonality of RVGE

Delhi has a temperate climate. There was a winter peak during January and December with $> 70\%$ of hospitalizations for gastroenteritis being associated with rotavirus (Fig. 2).

3.3. Complications at first evaluation of RVGE

The mean Vesikari score was 13 (inter-quartile range 11–16) indicating that the children had severe RVGE. The study found severe dehydration in 59 (15.6%) children and acidosis with bicarbonate ≤ 12 mEq/L in 70 (18.4%) children, this included 39 (10%) with severe acidosis with bicarbonate ≤ 8 mEq/L. We found acidemia with a pH of ≤ 7.2 in 44 (11.6%) children; hypernatremia $\text{Na} \geq 150$ mEq/L in 44 (11.6%) children; hyponatremia $\text{Na} < 130$ mEq/L in 9 (2.4%) children; hypokalemia ($\text{K} < 3.5$ mEq/L) in 43 (11.3%) children and 16 (4.2%) had $\text{K} \leq 2.9$ mEq/L.

Seizures during hospitalization occurred in 27 children, with 8/27 with hypocalcaemic seizures due to rickets based on reports of low calcium and raised alkaline phosphatase or raised parathormone. Two children with seizures were hypernatremic and one was hyponatremic. One child had cerebral palsy which could have pre-disposed to seizures.

The median duration of hospitalization was 3 days (inter-quartile range, IQR, 2–4), and 35 cases (9.2%) had hospitalization for ≥ 7 days.

Table 1

Comparison of complications in children between 0–5 months and 6–23 months hospitalized with rotavirus gastroenteritis.

		Age group (months)		P-value
		0–5 Months, 117 cases n (%)	6–23 Months, 222 cases n (%)	
Severe dehydration		30(25.6)	25(11.3)	0.006
Acidosis	HCO ₃ ≤8 mEq/L	24(20.5)	14(6.3)	0.001
	HCO ₃ 9–12 mEq/L	16(13.7)	14(6.3)	0.022
pH	≤7.2	29(24.8)	14(6.3)	0.001
Hypernatremia	Na ≥150 mEq/L	19(16.2)	25(11.3)	0.254
Hyponatremia	Na <130 mEq/L	3(2.6)	6(2.7)	0.749
Hypokalemia	K <3.5 mEq/L	13(11.1)	23(10.3)	0.92
Prolonged hospitalization	≥7 Days	22(18.8)	11(5.0)	0.001
Seizure		14(11.9)	9(4.05)	0.011

3.4. Complications in different age groups of children with RVGE

The number and proportion of children with complications from RVGE in the age groups 0–5 and 6–23 months are shown in Table 1. At admission the study found increased incidence of complications of severe dehydration ($P=0.006$), severe acidemia $\text{pH} \leq 7.2$ ($P=0.001$) and severe acidosis $\text{HCO}_3 \leq 8$ mEq/L ($P=0.001$), in 0–5 months compared with 6–23 months age group. A significantly higher number in the age group 0–5 months required admission ≥ 7 days as compared with those in 6–23 months age category ($P=0.01$), although data for other causes for prolonged hospitalization were not examined. The proportion of seizures was not significantly different in 0–5 months versus 6–23 months. A large proportion, 19/44 cases, of hypernatremia ($\text{Na} \geq 150$ mEq/L) occurred in the 0–5 month children, though this was not statistically significant.

4. Discussion

The findings in this study differ from a study in Europe where the severity of all diarrheas including rotavirus diarrhea in early infancy was less than that in older children [15]. The findings in this study population show an early peak of rotavirus disease with increased disease severity in early infancy and rotavirus detected in 39% (379/974) of children hospitalized with gastroenteritis. A total of 117 (31%) cases of RVGE hospitalizations occurred among children <6 months old, including 13% of all cases which were hospitalized at <3 months of age, and 18% hospitalized between 3 and 5 months of age.

We found greater dehydration and metabolic dysfunction in younger children and a significantly higher number in age group 0–5 months required prolonged hospitalization (admission ≥ 7 days) as compared with those in 6–23 month age category ($P < 0.0001$). A Swedish study [5] reported high incidence of hypernatremia in RVGE and in this study ten of eleven cases of severe hypernatremia (>160 mEq/L) occurred in infancy. Although rotavirus is known to cause seizures [16], this could have been associated with other causes, some of which, such as rickets, were found in this study.

In this study only 11% (40/379) of all hospitalized children were between 24 months and 59 months of age, and had very few complications. Black et al found that children who are small because of young age and/or malnutrition lost a greater proportion of their total body fluid volume during diarrhea and may be expected to have a higher frequency of dehydration and death if untreated [17].

The methodological limitations of our analysis must be acknowledged. In our study, the age distribution of community acquired cases may be skewed towards the younger age group relative to overall distribution in the community because infants may be more compromised by gastroenteritis than older children and/or parents may be more likely to seek medical attention for younger than for older children. The pediatric department of the

hospital is a referral centre with an intensive care unit, where a significant proportion of hospitalized children are cases referred by smaller clinics, hospitals and by general practitioners when children cannot be managed in less advanced facilities. Additionally, nutritional information was not collected or analysed, and it is likely that malnutrition could have contributed to the higher rates of complications in the younger children.

Rotavirus vaccines have been shown to decrease severity of rotavirus gastroenteritis in all settings where they have been evaluated, and hence present an attractive option for decreasing the burden of disease. However, the finding in this study of early age of hospitalization with complicated disease supports the need to consider an accelerated immunization schedule. Advancing the age of administration of the first dose of rotavirus vaccine to birth (from the current schedule where the first dose is given from 6 to 12 weeks of age) will provide several weeks of protection for this vulnerable age group before the next dose is due, especially as vaccination schedules are often delayed in poorer countries [18]. Researchers in Ghana evaluating a similar schedule found the vaccine safe and efficacious [19].

The early onset and severity of disease noted in this study demonstrates the need for healthcare facilities with equipment and trained manpower to manage critically ill children with gastroenteritis as well as the need to adopt preventive strategies including control strategies for diarrhea, appropriate treatment and vaccination.

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Conflict of Interest statement

None reported.

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