

Prevalence of Rotavirus Diarrhea among Hospitalized Under-five Children

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Objectives: To estimate the prevalence of rotavirus diarrhea among hospitalized children less than 5 years of age in Kerala State and to determine the circulating strains of rotavirus in Kerala.

Design: Multicenter, cross-sectional study.

Setting: Eight representative hospitals in Kunnathunadu Thaluk, Ernakulam district, Kerala.

Participants: Children in the age group under 5 years

Methods: Hospitalized children admitted with acute diarrhea were examined and standardized case report form was used to collect demographic, clinical and health outcome. Stool specimens were collected and ELISA testing was done. ELISA rotavirus positive samples were tested by reverse transcription

PCR for G and P typing (CMC Vellore).

Results: Among the 1827 children, 648 (35.9%) were positive for rotavirus by the Rotaclone ELISA test. The prevalence of rotavirus diarrhea in infants less than 6 months of age was 24.7%; 6- 11 months 31.9%; 12- 23 months 41.9%; 24- 35 months 46.9%; and 33.3% in 36- 59 months. Rotavirus infections were most common during the dry months from January through May. G1P[8] (49.7%) was the most common strain identified followed by G9P[8] (26.4%), G2P[4] (5.5%), G9P[4] (2.6%) and G12P[6] (1.3%).

Conclusions: The prevalence of rotavirus diarrhea among hospitalized children less than 5 years is high in Ernakulam district, Kerala State.

Keywords: Kerala, Rotavirus diarrhea, Rotavirus infections.

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Rotavirus is a leading cause of severe acute gastroenteritis requiring hospitalization among infants and young children worldwide [1]. Data on rotavirus disease burden are needed across India to support credible, evidence-based decisions regarding any intervention. There is a lack of nationally representative data on the incidence of severe rotavirus disease in India [2]. Previous studies in the Indian Rotavirus Strain Surveillance Network have confirmed that rotavirus accounts for 39% of acute diarrheal hospitalizations [3]. There is a need for additional research and public health surveillance to ensure that adequate information about rotavirus is obtained from diverse populations in India.

There are limited data on rotavirus disease burden among children in Kerala. We conducted a systematic study of rotavirus diarrhea among children in Ernakulam district, Kerala with the objectives to estimate the prevalence of diarrhea due to rotavirus among hospitalized children younger than 5 years of age and also to describe the circulating strains of rotavirus in this population.

METHODS

This was a multicenter study conducted in 8 hospitals in Kunnathunadu Thaluk, Ernakulam district, Kerala. In 2001 national census, Kunnathunadu had 47,743 children less than 5 years of age. For this study the Malankara Orthodox Syrian Church Medical College (MOSC), a tertiary care referral hospital, was the base hospital and 2 government and 5 private hospitals were selected.

All children aged <5 years who presented to a study hospital with acute watery diarrhea and required hospitalization were enrolled after informed consent was obtained from the parent or guardian. The study was conducted over a period of 24 months between February 1, 2009 and January 31, 2011.

A case of diarrhea was defined as increased stool frequency compared with the usual pattern occurring in a child less than 5 years old for whom parents sought care for treatment of diarrhea. The indications for hospitalization were (i) severe dehydration requiring intravenous hydration, (ii) malnourished children with dehydration, (iii) toxic appearance, changing mental status or seizure, (iv) fever >38.5°C for infants <6 months

or >39°C for 6- 36 months, (v) high output diarrhea (>10 large volume stool/day), (vi) persistent vomiting or diminished or no oral intake, (vii) suboptimal or no response to ORT or further deterioration, (viii) inability of the caregiver to administer ORS, (ix) suspected surgical cause, and (x) history of premature birth, chronic medical conditions or concurrent illness [4,5].

Hospitalized children less than 5 years of age admitted with acute diarrhea were examined by trained medical staff. The subject's parent or guardian was interviewed concerning date of onset of diarrhea and on vomiting and fever. Information was collected on the duration of diarrhea, maximum number of stools passed per day, duration and frequency of vomiting, degree of fever, presence and severity of dehydration, and treatment. The severity of dehydration was assessed according to the WHO Integrated Management of Childhood Illness Model Handbook guidelines and was categorized into severe, some or no dehydration [5]. Data concerning primary method of feeding and duration of exclusive breast feeding were collected.

A standardized case report form based on the WHO generic protocol [6] was used to collect demographic, clinical and health outcome data.

Stool collection and laboratory analysis: Stool specimens were collected from hospitalized patients and stored in the refrigerator at 4°C and later transported to the base hospital in icebox and stored at -20°C in the testing laboratory. ELISA testing (RotaClone, Meridian diagnostics, Cincinnati,OH) was done twice weekly for detection of rotavirus antigen. The enzyme-linked immunosorbent assay was highly sensitive (100%) and specific (97%) for rotavirus antigen. ELISA Rotavirus-positive samples were analyzed by reverse transcription-polymerase chain reaction for G and P typing at Christian Medical College, by previously reported methods [7].

Data management and statistical analysis: Data were entered on a weekly basis into database management software, which was created for the surveillance system and was based on an MS Visual FoxPro platform. Analysis was performed using SAS software. Tests of proportion were applied. A *P* value <0.05 was considered to be statistically significant.

The protocol was reviewed and approved by the local independent ethics committee/ institutional review board for each participating centre.

RESULTS

1827 children with diarrhea were admitted to study health facilities and had a stool specimen collected for rotavirus

testing during the study period. There were 20 children just above five years of age; they were excluded from final analysis (*n*=1807). Of the 1807 stool specimens tested, 648 (35.8%) were positive for rotavirus by the RotaClone ELISA test (**Table I**). The mean (SD) age of children was 17.9 (13.8) months; male 17.2 (13.7) vs. female 18.8 (13.9).

Fig. 1 shows the cumulative age distribution of rotavirus cases. There was no mortality in the study population. Rotavirus infections were seen throughout the year and were most common during the hot dry months from January through May (**Fig. 2**). Of the 648 samples that were ELISA rotavirus positive, genotyping (**Table II**) was done for 450 (81.6%) randomly selected samples. The majority (49.7%) of rotavirus strains typed were G1P[8] strains. An additional 12 (2.6%) samples were untypable.

DISCUSSION

This is the first systematic study to assess the prevalence of rotavirus diarrhea among children younger than 5 years of age in Kerala. In this study, rotavirus was detected in 35.9% of diarrhea-related hospital admissions among children less than 5 years of age in Ernakulam district, Kerala.

TABLE I ROTAVIRUS RESULTS OF CHILDREN WITH DIARRHEA, KERALA, INDIA, JANUARY 2009 TO JANUARY 2011

	<i>RV-Positive (n= 648)</i>
<i>Age group (mo)</i>	
<6 (<i>n</i> =235)	58 (24.7%)
6-11 (<i>n</i> =568)	181 (31.9%)
12-23 (<i>n</i> =535)	233 (41.9%)
24-35 (<i>n</i> =194)	91 (46.9%)
36-59 (<i>n</i> =255)	85 (33.3%)
<i>Fever group (°C)*</i>	
≤ 37.5 (<i>n</i> =935)	307 (32.8%)
37.6 -38.6 (<i>n</i> =690)	256 (37.1%)
≥ 38.7 (<i>n</i> =182)	85 (46.7%)
<i>Length of stay (days)*</i>	
≤ 2 (<i>n</i> =858)	300 (34.9%)
3- 6 (<i>n</i> =779)	267 (34.3%)
≥ 7 (<i>n</i> =170)	81 (47.6%)
<i>Dehydration#</i>	
None (<i>n</i> =1292)	416 (32.2%)
Some (<i>n</i> =503)	228 (45.3%)
Severe (<i>n</i> =9)	4 (44.4%)

**P*<0.01; #*P*<0.001.

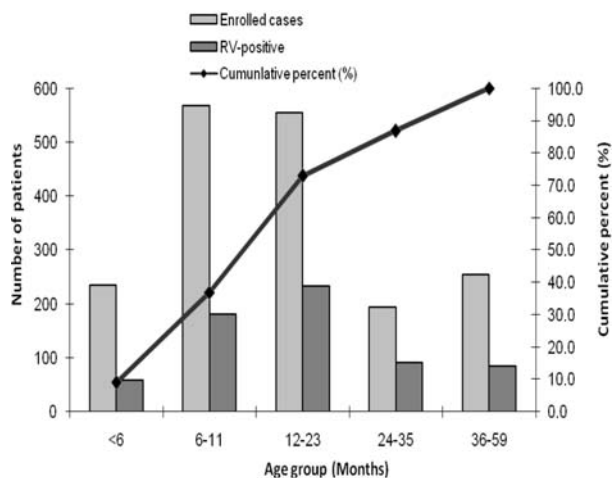


FIG. 1 Age distribution of children with diarrhea, Kerala, India, February 2009 to January 2011.

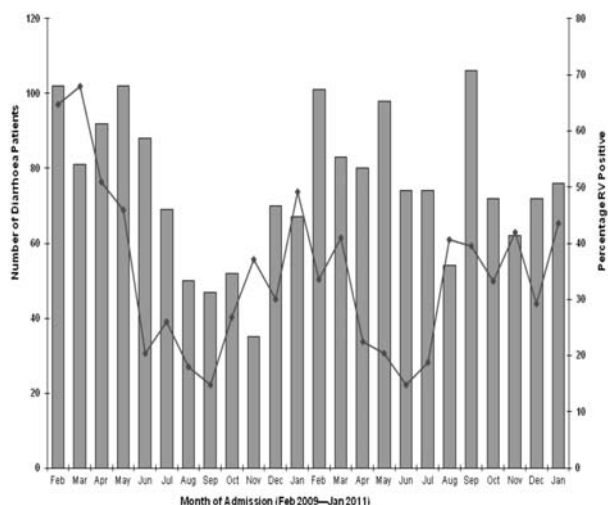


FIG. 2 Monthly distribution of rotavirus-positive patients, Kerala, India, February 2009 – January 2011 (n=1807).

A review of studies performed in India during 1990-2005 had estimated that rotavirus disease accounted for 20.8% of all diarrhea-related hospital admissions [7]. The Indian Rotavirus Strain Surveillance Network carried out a multi-centric study in seven different regions of India and reported that rotavirus was detected in stools of 39% children aged <5 years [3]. Inclusion of children at hospitals caring for lower acuity diarrheal episodes or less severe disease may account for a lower percentage of rotavirus positive cases among the total number of

enrolled patients in our study compared with previous studies [3,8-15].

TABLE II DISTRIBUTION OF G AND P TYPES AMONG A RANDOMLY SELECTED SUBSET (N=450) OF ROTAVIRUS POSITIVE SAMPLES

Genotype (n=450)	Number
G1 P[8]	224 (49.7%)
G9 P[8]	119 (26.4%)
G2 P[4]	25 (5.5%)
G9 P[4]	12 (2.6%)
G12 P[6]	6 (1.3%)
G1 P[6]	4 (0.8%)
G12 P[8]	4 (0.8%)
G1 P[4]	1 (0.2%)
G1 P[Untypable]	2 (0.4%)
G9 P[Untypable]	11 (2.4%)
Partially typed	6 (1.3%)
Mixed infections	24 (5.3%)
Both G and P untypable	12 (2.6%)

The prevalence of rotavirus diarrhea in infants aged <6 months was 24.7%, with high prevalence in children aged 6 months to 11 months and 12-23 months (31.9% and 41.9%, respectively). These data are important because they demonstrate that the vast majority of cases could be prevented by an effective rotavirus vaccine given to children along with their primary immunization series. But for a setting in a developing country, this is somewhat lower than expected since ~80% to 85% of all rotavirus cases in children under 5 years occurred by 18 months of age in hospital-based studies [16]. These observations may indicate that the epidemiology of rotavirus in Kerala may differ from other parts of India, because general living conditions and socio-economic status are better in Kerala.

A marked seasonality was not seen in our study and rotavirus infections peaked from January through May and were less common during the monsoon season months of June through September. Rotavirus is markedly seasonal in Northern temperate locations but was less seasonal in Southern locations with a tropical climate [3,10,17,18]. It has been observed that with minimal seasonality, rotaviruses circulate at a relatively higher level all year round, resulting in children being exposed at an early age and experiencing severe illness [14].

This is the first study in Kerala to provide information on both rotavirus G and P types. The results of G and P typing shows that the G1P[8] strain is the most common contributing half the number of cases. This finding is also

WHAT IS ALREADY KNOWN?

- Rotavirus is the leading cause of severe diarrhea in Indian children less than 5 years.

WHAT THIS STUDY ADDS?

- High prevalence of rotaviral diarrhea in Ernakulam, Kerala state, accounting for 35.9% of diarrhea-related hospitalizations among children less than 5 years of age.

consistent with the results from national rotavirus surveillance in India showing that the G1P[8] strain was among the two most common strains from December 2005 to November 2007. However, there were differences in that the G9P[8] strain is the second most common strain found in the Kerala field site and 5.5% of strains were G2P[4], while overall in the national Indian surveillance network the G2P[4] and G9 P[8] strains accounted for 25.7% and 8.5%, respectively of all rotavirus strains [3]. A recent study from Vellore reported that the most common types were G1P[8] (in 15.9% of infections), G2P[4] (in 13.6%), G10P[11] (in 8.7%), G9P[8] (in 7.2%), G1P[4] (in 4.4%), G10P[4] (in 1.7%), G9P[4] (in 1.5%), G12P[6] (in 1.1%), and G1P[6] (in 0.6%) [19]. The proportion of untypable strains may suggest the potential for emergence of new rotavirus strains in Kerala.

The strengths of this study include the use of the WHO generic protocol and laboratory confirmation of rotavirus diarrhea in a single reference laboratory including genotyping of rotavirus strains. Potential limitations are the small study population and the lack of ability to extrapolate disease burden to milder disease because this was a hospital-based study.

In conclusion, this study highlights that rotavirus diarrhea accounts for a large proportion of diarrheal disease in hospitalized children less than 5 years in Ernakulam district in Kerala.

Contributors: MAM: conceived and designed the study and revised the manuscript for important intellectual content. He will act as guarantor of the study; AP: collected data and drafted the paper; MKC, GK and SC: did final revision of manuscript. GK conducted the laboratory tests, and interpreted them; PK: analysed the data and helped in manuscript writing. The final manuscript was approved by all authors.

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