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Original Article

Prospective hospital-based surveillance to estimate the burden of rotavirus gastroenteritis in children less than five years in Bhubaneswar

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ABSTRACT

Background: Burden of severe rotavirus illness and deaths falls heavily upon children in the less developed countries of the world. Limited data on rotavirus disease burden and rotavirus strains is available in India. The study was done as a part of a multicentric trial to understand the temporal and regional strain diversity of rotavirus in Odisha.

Objectives: 1. To estimate the burden of gastroenteritis attributable to rotavirus among under five hospitalized children. 2. To grade the severity of the diarrhea and assess the epidemiologic correlates.

Methods: Study center was one of the 12 hospital sites in India selected for the hospital-based surveillance among children aged less than five years who presented to hospital with acute gastroenteritis and required hospitalization. Fecal sample was collected from every fifth child and sent for detection of rotavirus using commercial enzyme immunoassay. Strain testing was done at an accredited lab using reverse-transcription polymerase chain reaction. **Results:** 250 samples were collected of which 58 (23.2%) tested positive for rotavirus. Highest rate of hospitalization was seen in 12–23 months i.e. 41%, more in males and infection was highest in winter months. 59% of the positive infections were of G9 genotype.

Conclusion: The study reinforces the substantial health burden of rotavirus acute gastroenteritis hospitalization among Indian children.

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1. Introduction

The burden of severe rotavirus illness and deaths falls heavily upon children in the poorer countries of the world, with more

than 80% of rotavirus-related deaths estimated to occur in lower income countries of Asia, and sub-Saharan Africa.¹ India, with more than 1 billion people, 11% of whom are <5 years of age, has an especially large population at risk of clinically significant rotavirus GE.² Among Group A rotaviruses, 10

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G (VP7) and 10 P (VP4) types have been reported to cause infection in man, but clinically by far the most important have been serotypes G1–G4 and G9 and P[8] and P[4].³ Typical clinical signs of infection include fever, projectile vomiting, and profuse watery diarrhea, which may significantly dehydrate the infected child calling for hospital based management.

The current study is a part of a multicentric study done to present in detail a method for hospital-based surveillance of rotavirus gastroenteritis in children ≤ 59 months of age. The data collected in such studies should allow investigators to summarize local epidemiological and virological features of rotavirus and to develop estimates of disease burden in the populations under surveillance.

2. Aims & objectives

- ▶ To estimate the burden of gastroenteritis attributable to Rotavirus among under five hospitalized children.
- ▶ To grade the severity of the diarrhea and assess the regional epidemiological correlates.

3. Methodology

The same study was done at 12 centers in India among which the study center was among the eastern centers. The study was initiated after the Institutional Ethics Committee approval and also Human Research Protocol was duly abided under the scrutiny of the Ethics Committee. As decided by all centers children aged less than five years who presented to hospital with acute gastroenteritis and required hospitalization with rehydration for at least 6 h were enrolled successively. Fecal

sample (bulk stool, approximately 5 ml, preferably on the day of presentation to hospital) was collected from every fifth child under aseptic conditions in a sterile container after due informed consent from the guardian and maintained in deep freezer. In batches of 15, the collected samples were tested for rotavirus VP6 antigen using commercial enzyme immunoassay (Premier Rotaclone Qualitative EIA) at the microbiology lab.

Taking the study of one year passive surveillance study of 62,475 children <5 years of age in New Delhi, India, where incidence of rotavirus was found to be nearly 23%,⁴ the current statistically adequate sample for the study was found to be 250, where $Z = 3.96$; and the sample error was taken to be 5%. The study was conducted from April 2010 to August 2011. The diarrhea was also graded for severity using Vesikari scoring. Finally the genotype testing for stool samples testing positive with rotavirus done at the accredited lab of CMC Vellore using reverse-transcription polymerase chain reaction.

4. Results

During the study period 250 diarrheal samples (every fifth sample out of 1050 patients admitted in the hospital for diarrhea during the study period) were recruited in the study, out of which 58 (23.2%) were due to rotavirus (Table 1).

Also seen in Table 1 is that overall incidence of diarrhea was more after 6 months suddenly peaking to nearly 35% and the incidence of Rota positive diarrhea was highest in 12–23 months infants, nearly 41% ($p = 0.03$). The difference in the incidence of rotavirus diarrhea was much higher in males which was statistically significant in the study (65.5% vs 34.5%; $p = 0.000$).

As per the protocol all severe cases of diarrhea that needed hospitalization were included in the study frame, thus the

Table 1 – Epidemiological variations in rotavirus diarrhea in the study sample.

Age (months)	Diarrhea (n = 192)	%	Rota +ve (n = 58)	%, p Value
0–2	6	3.1	0	2.4
3–5	15	7.8	01	6.4
6–11	67	34.9	16	33.2
12–23	69	35.9	33	40.8
24–59	35	18.2	08	17.2; $p = 0.03$
Sex	Diarrhea (n = 192)	%	Rota +ve (n = 58)	%
Male	122	63.5	38	65.5
Female	70	36.5	20	34.5; $p = 0.000$
Vesikari score	Diarrhea (n = 192)	%	Rota +ve (n = 58)	%
13–16	20	11.4	4	6.9
17–19	170	88.6	53	91.4
20 and above	2	1.0	1	1.7; $p = 0.914$
Mother's education	Diarrhea (n = 192)	%	Rota +ve (n = 58)	%
Illiterate	38	19.8	14	24.1
Primary	79	41.1	17	29.3
Secondary	50	26.0	16	27.6
Graduate and above	25	13.0	11	19.0; $p = 0.765$
Working status of mother	Diarrhea (n = 192)	%	Rota +ve (n = 58)	%
Working	112	58.3	31	53.4
Not working	80	41.7	27	46.6; $p = 0.01$

Percentages in bold indicate the highest and second highest genotype in Rota virus as indicated in KIMS data.

Fig. 1 – Monthly variation of diarrheal incidence vs rota diarrhea.

Fig. 2 – Genotypes of rota in the study sample.

Vesikari scoring was >11 which is the criteria for moderate to severe diarrhea, the minimum being 13 and maximum being 20, mode being 18. Rota diarrhea for nearly 91% of the cases had a score between 17 and 19. The mother's education and working status was taken in the study as a proxy for the socio-economic condition of the family and incidence of rota diarrhea showed no significant association with mother's education but mild association was seen for working mothers where

the rota positive diarrhea was 53.4% as against non working women nearly 47% ($p = 0.01$).

The rotavirus diarrhea showed a definite peak in the post rainy and winter months. The diarrheal cases overall show a high incidence in the May and June months of the year, while for rest of the year we see almost uniform incidence; whereas the rota virus diarrhea in this cohort definitely shows a peak in November and December months and a second peak in spring season as depicted in Fig. 1.

In the data which can be representative of Odisha G9 genotype was predominant (59%) followed by G1 (21%) as depicted in Fig. 2. Table 2 shows the phenogenotypic breakup of all rota positive stool detected during the study.

5. Conclusions

The study shows a definite diarrheal burden attributable to rotavirus; nearly 23%. Incidence peaks after 6 months; max in this study 12–23 months of age. Incidence definitely higher in winter months. G9 genotype was detected highest in this part of eastern zone i.e. 59% (of which G9P4 was 52%) followed by G1 of which G1P8 was detected in 17% of the cases.

6. Discussion

Rotaviruses are the leading cause of severe, dehydrating diarrhea in children aged <59 months globally, with an estimated >25 million outpatient visits and >2 million hospitalizations attributable to rotavirus infections each year.⁵ It is estimated that by the age of five, nearly every child will have had an episode of rotavirus gastroenteritis, 1 in 5 will visit a clinic, 1 in 50 will be hospitalized, and approximately 1 in 205 will die.⁶ A one-year passive surveillance study of 62,475 children <5 years of age in New Delhi, India, identified 584 who had been hospitalized for diarrhea, 137 (23.5%) of whom had rotavirus

Table 2 – Genotyping detected in the rota positive stool.

Genotype of rota virus	Frequency (n = 58)	Percentage
G1P4P8	1	1.7
G1P4	2	3.4
G1P8	10	17.2
G2P4	1	1.7
G9P4P8	3	5.1
G9G1P4P6	2	3.4
G9P4	30	51.7
G9P6	1	1.7
G12P6	3	5.2
G12P8	5	8.6

Percentages in bold indicate the highest and second highest genotype in Rota virus as indicated in KIMS data.

identified in stool specimens. Ninety-eight percent (98%) of the hospitalized children were <2 years of age and 69% were <1 year of age.⁴ This matches with current study results of 23% incidence and more in the just above one year age group. This study findings also corroborates the two other major studies i.e. presenting test results for 15,476 stool samples from children hospitalized for gastroenteritis at various times from 1982 to 2004 in 22 Indian cities identified rotavirus in 6–45% (median 20.8%),⁷ while a WHO report covering a similar period cited 5 studies in India showing that 23–35% of children hospitalized with diarrhea tested positive for rotavirus.⁸ The incidence of rota diarrhea being higher after 6 months and maximum in 12–13 months may be attributed to increased environmental exposure through diet and varied care patterns in the family and decline in maternal protective antibodies. Being a surveillance data there were limitations of collecting detailed family data which could have given more information on the reasons for higher diarrheal incidence.

Testing by monoclonal antibodies or primers specific for G1–G4 and G9 of 1998 rotavirus-positive stool specimens collected from hospitalized children in various regions of India between 1990 and 2004 showed that approximately two-thirds of the specimens from these severe cases were types G1–G4: 26% G1, 23% G2, 6% G3, and 9% G4.⁷ In New Delhi study G9 was noted as 14%.⁴ In this study G9 strain clearly comes out as the predominant strain accounting for nearly 59% of rota infections followed by G1. Interestingly G3 & G4 genotypes were not detected at all. The children identified with rotavirus had not taken the vaccine and only 2 children in the whole cohort had been vaccinated though the information was not given reliably.

The study reiterates the need of vaccination against this disease which definitely has a presence in India. The genotypes too hint at region based strain diversity. In the nutshell regional diversity in the prevalence of different rotavirus genotypes, as well as temporal changes in genotype prevalence within a given region, mean it will be important to continue careful monitoring of these genotypes as rotavirus vaccine programs are implemented in India.

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Conflicts of interest

All authors have none to declare.

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