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PREVALENCE OF ROTAVIRAL DIARRHOEA IN HOSPITALIZED CHILDREN UNDER FIVE YEARS IN A TERTIARY CARE HOSPITAL OF EASTERN INDIA

Microbiology

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ABSTRACT

Introduction – Rotaviral diarrhoea is a leading cause of morbidity and mortality in fewer than five children in India and accounts for about one third of diarrhoeal deaths. India has estimated annual burden of 2.0-3.4 billion cases of diarrhoea attributable to rotavirus. Recent estimates have shown that about 872,000 hospitalizations and 78,500 deaths occur due to rotavirus infections annually in India. Availability of efficacious rotavirus vaccines has warranted extensive epidemiological studies on Rotavirus diarrhea.

Methodology – We conducted a pilot study in our Rajendra Institute of Medical Sciences which is a tertiary care hospital with the objective to estimate the prevalence of diarrhoea due to rotavirus among hospitalized children younger than 5 years of age. Classification of dehydration and management was done based on WHO guidelines for diarrhea management. The stool samples were collected as per exclusion and inclusion criteria and the test was carried out by ELISA kit by DRG Diagnostics, DRG Instruments GmbH, Germany. The test was performed as per the manufacturer's instructions.

Results – The total number of 140 (27.13%) patients were positive for Rota virus. The maximum percentage of Rota virus infection was observed in 2013 with 33% of infectivity. The maximum prevalence of Rota virus infection was seen in among children aged between 0 – 12 months, while the year 2013 has maximum number of Rota virus prevalence.

Discussion and Conclusion – The prevalence of rotavirus in neonates is high in India, ranging from 22% to 73%. In one study, rotavirus positivity rates varied greatly between different settings - diarrhea hospitalizations (20%), neonatal infections (35%), symptomatic and asymptomatic infections in the community (15.1% and 6.3% respectively). In our study, there was no statistically significant association of infection and time of the year. Our study had a few limitations. This was a hospital based study and hence the results are unlikely to be a true reflection of the disease burden in the community. Isolated rotavirus positivity in a given case of diarrhea may not necessarily rule out an alternative infection or co-infection.

KEYWORDS

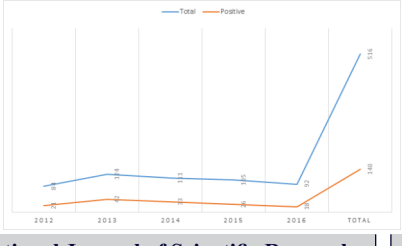
Rota virus, diarrhea, Eastern India, Prevalence

INTRODUCTION – Rotaviral diarrhoea is a leading cause of morbidity and mortality in fewer than five children in India and accounts for about one third of diarrhoeal deaths in fewer than five children. As per WHO (April 2016), globally 2, 15,000 children died due to rotaviral diarrhoea in the year 2013. India, Nigeria, Pakistan and Kango tops the list and account for 49% rotaviral diarrhoeal deaths in 2013. India contributes 22% of global rotaviral deaths. The burden of rotavirus gastroenteritis is highest in very young children and decreases rapidly thereafter. Rotaviral diarrhoea causes 4.4% and 3.2% of deaths worldwide in children below 1 year and between 1-4 years of age respectively [1]. India has estimated annual burden of 2.0-3.4 billion cases of diarrhoea attributable to rotavirus. Recent estimates have shown that about 872,000 hospitalizations and 78,500 deaths occur due to rotavirus infections annually in India [2]. Because of this disease burden, several vaccines against rotavirus have been developed or are in development, and they are expected to be introduced within the next few years [3]. Before the introduction of a vaccine, it is important to document both the disease burden and strain circulation, to establish a baseline against which the effect of the introduction of a vaccine can be measured. Advances in hygiene and sanitation have reduced the predominance of the other gut pathogens, while leaving rotavirus incidence almost unaffected. Rotavirus vaccines are being projected as a solution to this problem. Availability of efficacious rotavirus vaccines has warranted extensive epidemiological studies on rotavirus diarrhea. It was with this background that this study was carried out to add to the existing knowledge on the magnitude of the problem in a tertiary care hospital setting. There are limited data on rotavirus disease burden among children in Jharkhand and there is a need for data on prevalence of rotavirus diarrhea especially in our setting. So we conducted a pilot study in our VRDL, Department of Microbiology, Rajendra Institute of Medical Sciences which is a tertiary care hospital with the objective to estimate the prevalence of diarrhoea due to rotavirus among hospitalized children younger than 5 years of age.

MATERIALS AND METHOD –The study was conducted for 5 years from 2012 – 2016 at Department of Microbiology at ICMR, VRDL Rajendra Institute of Medical Sciences, Ranchi. The inclusion criteria consisted of all children less than five years with fever, acute diarrhea, vomiting. Acute diarrhea was considered as passage of loose watery stools or an increased frequency of stools. The exclusion criteria consisted of children with dysentery, diarrhea more than 14 days, or diarrhea developing after hospitalization due to any other cause. The stool samples were collected as per exclusion and inclusion criteria and the test was carried out by ELISA kit by DRG Diagnostics, DRG Instruments GmbH, Germany. The test was performed by as per the manufacturer's instructions. Warm all the reagents to room temperature before use and mix gently without causing foam. Dispense 75µl of HRP conjugate per well and add 75µl of positive 75µl of negative and 50µl of sample diluent and mix gently. Cover the wells and incubate them for 60 minute at room temperature. Wash each well with 300 µl of wash solution 5 times and tap dry to absorbent paper. Now dispense 75µl of substrate TMB buffer to each well and incubate for 10 minute in dark, add 75µl of stop solution and mix gently and read the absorbance within 30 minute at ≥620 nm. The Cut off is determined by OD negative control + 0.20. Positive value is calculated by ≥ cutoff while negative value is calculated by less than the cutoff value. The results are recorded for future reference.

RESULTS – A total of 516 children and infants stool samples were collected as per the inclusion and exclusion criteria defined above who were admitted to Rajendra Institute of Medical Science, Ranchi. The total number of 140 (27.13%) patients were positive for Rota virus. The maximum percentage of Rota virus infection was observed in 2013 with 33% of infectivity. The year wise detail is mentioned in Graph 1.

Graph I – Year wise infectivity of Rota virus infection.



The maximum prevalence of Rota virus infection was seen in among children aged between 0 – 12 months, while the year 2013 has maximum number of Rota virus prevalence. The prevalence of Rota virus infection was highest in 2015 among children between age group 13 – 24 months, with prevalence rate being 38% while the lowest prevalence was observed in 2016 among children aged between 37 -48 months and 49 – 60 months. The age wise distribution in different year is as depicted in Table 1.

Table – 1 Year wise prevalence of Rota virus infection among different age group

Age in months	2012		2013		2014		2015		2016		Total	
	Sample	Positive	Sample	Positive	Sample	Positive	Sample	Positive	Sample	Positive	Sample	Positive
0 – 12	38	12 (31.5%)	64	23 (35.9%)	49	13 (36%)	36	12 (33%)	44	9 (20.4%)	231	69 (29.8%)
13 – 24	18	4 (22.2%)	37	13 (35.1%)	25	8 (32%)	21	8 (38%)	28	5 (17.8%)	129	38 (29.4%)
25 – 36	11	3 (27.2%)	13	4 (30.7%)	16	6 (37.5%)	19	3 (15.7%)	11	4 (36.3%)	70	20 (28.5%)
37 – 48	10	2 (20%)	6	1 (16.6%)	12	4 (33%)	16	2 (12.5%)	6	0 (0%)	50	9 (18%)
49 – 60	7	0 (0%)	4	1 (25%)	9	2 (22%)	13	1 (7.6%)	3	0 (0%)	36	4 (11%)
Total	84	21 (25%)	124	42 (33.8%)	111	33 (29.7%)	105	26 (24.7%)	92	18 (19.5%)	516	140 (27.1%)

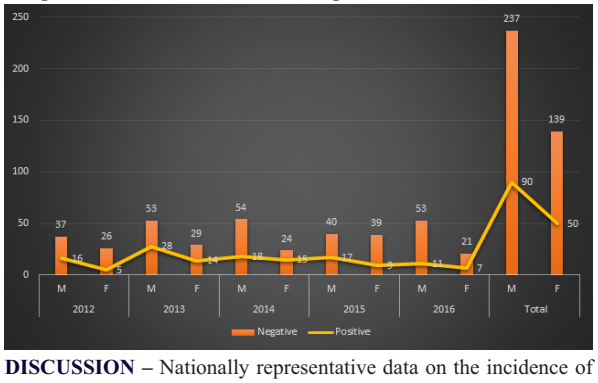
The clinical manifestation which were presented at the time of admission include fever, vomiting, dehydration and nutritional status. Classification of dehydration and management was done based on WHO guidelines for diarrhea management. The children in the study were treated with oral rehydration therapy or intravenous fluids depending on severity of dehydration. It has been observed that vomiting was most common cause in people having infection with rota virus followed by some dehydration as per WHO classification of dehydration management. Most of the children were normal than being malnourished. It is also observed that children who are above 37 months or older faced less severe symptoms of rota viral infection.

Table – Age wise distribution of the patients with clinical presentation

	Clinical Conditions of Symptomatic Patients							
Age in months	Positive	Fever	Vomiting	Dehydration			Nutritional status	
				No	Some	Severe	Normal	Malnourished
0 – 12	69	28 (40.5%)	58 (96.66%)	4 (5.79%)	58 (84.05%)	7 (10.14%)	46 (66.6%)	23 (33.3%)
13 – 24	38	16 (42.10%)	32 (84.2%)	16 (42.10%)	19 (50%)	3 (7.89%)	29 (76.3%	9 (23.6%)
25 – 36	20	8 (40%)	11 (55%)	11 (55%)	7 (35%)	2 (10%)	16 (80%)	4 (20%)
37 – 48	9	2 (22.2%)	5 (55%)	4 (44%)	5 (55%)	0 (0%)	7 (77.7%)	2 (22.2%)
49 – 60	4	1 (25%)	3 (75%)	2 (50%)	2 (50%)	0 (0%)	4 (100%)	0 (0%)

In 5 years a total of 90 males were positive out of 237 with a 37.9% positivity rate among males and a total of 50 males were positive out of 139 with a 35.9% positivity rate. The maximum number of male positivity being in year 2013, 2014 and 2016 with 7% of positivity. The maximum number of female positivity being in year 2015 5% of positivity. The graphical representation is as mentioned below.

Graph – Year wise distribution of the positive results



DISCUSSION – Nationally representative data on the incidence of severe rotavirus disease in India are lacking. However, a recent prospective birth cohort study in Vellore rigorously characterized the burden of rotavirus infection among children under 3 years of age [4]. The peak in this study was observed in 2013 and lowest was observed in 2016. The prevalence of rotavirus in neonates is high in India, ranging from 22% to 73% [5-9]. Neonatal infections are commonly asymptomatic, with 69-95% not showing overt signs of gastroenteritis [7-10]. The study by Sarvanana et al in Chennai showed an overall infection rate of 22.55% among children with acute diarrhea. The age group analysis of rotavirus positive children with acute diarrhoea manifested a significant increase in the infection rate among the age group of 7-12 months with 29.95%. Various studies depicted in Table shows the proportion of Rota Virus infection from 1992 – 2007.

TABLE I Proportion of Diarrhea Cases Due to Rotavirus

Study Location	*Proportion RV+*	*Total Diarrhea Cases*	*Age*	*Year*
Hospital Studies				
Pune[11]	28.2%	945	<5	1992-1996
Pune[12]	28.3%	628	<5	1993-1996
Chennai[13]	22.5%	745	<3	1995-1999
Vellore[14]	21.0%	602	<5	1995-1999
Kolkata[15]	34.7%	266	<4	1998-2000
Delhi[16]	23.5%	584	<5	2000-2001
Vellore[17]	27.4%	343	<5	2002-2003
Kolkata and Berhampur [18]	36.3%	545	<4	2003-2005
Lucknow[19]	19.2%	412	<3	2004-2008
Kolkata[20]	37.3%	668	<4	2005-2006
Delhi[21]	36.9%	862	<2	2005-2007
Nationwide[22]	39.2%	4243	<5	2005-2007
Manipur[23]	49.9%	489	<5	2005-2008
Summary	33.6%	11,332		
Community Studies				
Pune[12]	15.5%	489	<5	1993-1996
Vellore[16]	7.1%	351	<2	2002-2003

In one study, rotavirus positivity rates varied greatly between different settings - diarrhea hospitalizations (20%), neonatal infections (35%), symptomatic and asymptomatic infections in the community (15.1% and 6.3% respectively) and nosocomial enteric infections (22.5%).[23] In another study on prevalence of rotavirus diarrhea in two settings in the same geographical region, the occurrence of rotavirus diarrhea was more among hospitalized children as opposed to the out-patients.[24] A large number of studies conducted in India regarding rotavirus diarrhea have been hospital based and have shown positivity of upto 34%.[25,26,27]

In one study, rotavirus positivity rates varied greatly between different settings - diarrhea hospitalizations (20%), neonatal infections (35%), symptomatic and asymptomatic infections in the community (15.1% and 6.3% respectively) and nosocomial enteric infections (22.5%).[27]

In another study on prevalence of rotavirus diarrhea in two settings in the same geographical region, the occurrence of rotavirus diarrhea was more among hospitalized children as opposed to the out-patients. Our study also showed a higher proportion of rotavirus positive cases in in-patients (45.2%) as opposed to out-patients (15.25%). This increased prevalence amongst hospitalized children may be because of the higher admission rate with rotavirus diarrhea.[28] The association between seasonality and rotavirus diarrhea has not been clear with evidence both for and against it.[29] [30] In our study, there was no statistically significant association of infection and time of the year,

CONCLUSION – Our study had a few limitations. This was a hospital based study and hence the results are unlikely to be a true reflection of the disease burden in the community. Isolated rotavirus positivity in a given case of diarrhea may not necessarily rule out an alternative infection or co-infection.

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