Diarrhoea in north Karnataka: Rotavirus versus non-rotavirus

***Shankar Gouda V Patil[1], Bhavana Bhushan Lakhkar[2], S S Kalyanshettr[2]**

Sri Lanka Journal of Child Health, 2018; **47**: 204-209

Abstract

Background: As children with diarrhoea are often prescribed antibiotics, it was decided to study the causative organisms. Rotavirus is a major cause of diarrhoea and diarrhoea related mortality in most parts of India. Rotavirus vaccine is available but expensive. According to the World Health Organisation (WHO) the vaccine should be used in areas where diarrhoea related under five mortality is around 10%. The situation in north Karnataka is not known.

***Objectives*:** To find proportions of rotavirus and non-rotavirus diarrhoea in children of north Karnataka and study the key clinical features of rotavirus diarrhoea.

Study design and settings: Prospective observational study conducted in patients from the paediatric ward and outpatient department in a tertiary care hospital.

Method: Children 1 to 36 months old, presenting with acute diarrhoea from July 2014 to May 2016 and fulfilling selection criteria were included. Demographic and clinical details were noted. Stools were collected within 24 hours and subjected to routine and microscopic examination, test for presence of reducing substance, bacterial culture and Rapid ELISA test for rotavirus using antigen detection micro-well ELISA kit by Premere Rotaclone.

Results: A total of 168 children was recruited**.** Children positive for rotavirus ELISA were labelled as having rotavirus diarrhoea and comprised 52 (31%) of total, including 17 with mixed infection and 15% were bacterial culture positive. Most common age group affected was 7 to 18 months (79%). Male female ratio was same in rotavirus and non-rotavirus diarrhoea. The clinical features defining rotavirus diarrhoea were fever, vomiting, watery stools, respiratory symptoms and perianal excoriations. Moderate and severe dehydration were common. There was no mortality.

Conclusions*:* Around one third (31%) of diarrhoea cases were positive for rotavirus and 15% were of only bacterial aetiology. Key clinical features in rotavirus infection were fever, vomiting, watery stools, respiratory symptoms and perianal excoriations.

DOI: http://dx.doi.org/10.4038/sljch.v47i3.8539

(Key words: Viral diarrhoea, rotavirus vaccine, prevalence)

[1]*Professor and Head of Department of Paediatrics,* [2]*Professor, Paediatrics, Shri BM Patil Medical College, Vijayapur, India*

**Correspondence:* svpdr@yahoo.com

(Received on 26 July 2017: Accepted after revision on 18 August 2017)

The authors declare that there are no conflicts of interest

Personal funding was used for the project.

Introduction

The proportion of rotavirus as a cause of death among causes of diarrhoea in children ranges in different states of India from 7% in Vellore to 50% in Manipur[1]. According to the World Health Organisation (WHO), the under-five mortality has come down from 528,000 in 2000 to 215,000 in 2013 but 22% of global rotaviral deaths occurred in India[2]. The prevalence of rotavirus among all diarrhoeal causes has not been studied in Karnataka after 2002, to the best of our knowledge. Some anecdotal studies have reported 19.5% to 28% prevalence in south Karnataka[3,4]. Prevalence in North Karnataka has not been reported.

Objectives

To find the proportion of rotavirus and non-rotavirus diarrhoea in children of north Karnataka and to study the key clinical features of rotavirus diarrhoea.

Method

A prospective, observational study was conducted from July 2014 to May 2016 in the Department of Paediatrics, Shri BM Patil Medical College and Research Centre, Vijayapur Karnataka, India. Children between 1 to 36 months of age clinically diagnosed as acute diarrhoea[5], and whose parents' consent could be obtained, were included. As per sample size calculation based on rotavirus prevalence in India[6], 168 children were recruited from ward and outpatient department (OPD). Confidence interval at 7.5% margin of error was 95%. Children immunized with rotavirus vaccine, had immunodeficiency disease or where parents denied consent were excluded.

Ethical approval was obtained from institutional ethical committee of BLDE University Vijayapur.

Demographic information, feeding details, clinical presentation, complications, past significant history especially of diarrhoea, and anthropometry details were entered in a pre-validated, pretested proforma. Pre-validation and testing were done in 20 cases where proformas were filled and analysed for any deficiency of information. Then the format used in study was finalized. This finalized proforma was also validated by an external expert. Faecal samples were collected within 24 hours and were subjected to routine, microscopic examination, test for reducing substance, bacterial culture and rapid ELISA test for rotavirus using antigen detection micro-well ELISA kit by Premere Rotaclone. This kit qualitatively determines the rotavirus antigen in stool samples. As this kit was newly introduced in the hospital, around 200 investigations (Elisa Kit and stool culture) were made free for research. The sensitivity of this kit is 76.8% and specificity 100% when reverse transcriptase –PCR (RT-PCR) was used as the gold standard[7].

Diagnosis of rotavirus diarrhoea was made if rotavirus ELISA was positive. If bacterial culture and rotavirus ELISA were both positive it was labeled as mixed infection. If only bacterial culture was positive, it was considered as bacterial diarrhoea. Dehydration was assessed and classified as mild, moderate and severe[8].

Statistical analysis: All characteristics were summarized descriptively. For categorical data, number and percentage were used in data summaries. Chi-square (χ^2)/ Freeman-Halton Fisher exact test was employed to determine the significance of differences between groups for categorical data. If the p-value was <0.05, results were considered to be significant. Data were analysed using SPSS software version 23.0.

Results

A total of 168 patients were recruited. Patient characteristics are presented in Table 1.

A history of loose stools was present in 168 (100%) patients, vomiting in 137 (81%), fever in 164 (98%), perianal excoriation in 28 (17%) and cold and cough indicating upper respiratory infection in 47 (28%) patients. Dehydration was present in all (100%) patients and was moderate in 94 (56%) patients, severe in 35 (20.8%) and mild in 39 (23%) patients.

A total of 52 (31%) were rotavirus ELISA test positive. Of these 17 (10% of total) also had positive culture for bacteria and were categorized as mixed infection. Common associations were with *Escherichia coli* (12 cases), *Klebsiella* (4 cases) and *Proteus* (1 case). In 25 (15%) cases stool culture was positive only for bacteria, *Escherichia coli* and *Klebsiella* being more common.

Table 1: *Patient characteristics (n=168)*

Patient characteristic	Number (%)
Age (months)	
1 – 12	71 (42.1)
13-24	49 (28.9)
25 - 36	48 (28.5)
Sex	
Male	99 (58.9)
Female	69 (41.1)
Nutritional status	
Normal	111 (66.1)
Grade 1	36 (21.4)
Grade II	19 (11.3)
Grade III+IV	02 (01.2)
Feeding pattern	
Exclusive breastfeeding	32 (19.0)
Top feed only	08 (05.0)*
Supplementary feed	86 (51.0)
Family diet	42 (25.0)

* *Top fed children received other milk only*

Risk factors, clinical features, investigations and complications were compared in rotavirus and non-rotavirus diarrhoea (Table 2). The most common age group affected by rotavirus was 7 to 18 months. Rotavirus infection was uncommon below 7 months and above 24 months. The 17 cases with mixed infection also showed a similar distribution of age groups. In rotavirus negative diarrhoea, though the most affected age group was the same, children below 7 months and above 2 years were substantially affected. Sex ratio was not significantly different and there was no mortality in either group.

Mean duration of diarrhoea at the time of admission in rotavirus positive children was 2±1 days in children with mild dehydration and 3±1 days in children with moderate dehydration. There were only 8 children with grade II and III malnutrition in the rotavirus positive group, of whom 2 had mild and 6 had severe dehydration. There was no difference between malnourished children and normal children as far as dehydration is concerned (p>0.05) in rotavirus group.

Correlation of type of feeding and rotavirus positivity is shown in Figure 1. Minimum prevalence of rotavirus infection was in the exclusively breast fed group. Significant correlation was found between nutritional status and prevalence of rotavirus diarrhoea (Odds ratio =3.1 at 95% CI).

Table 2: ***Comparison of rotaviral and non-rotaviral diarrhoea***

Feature	Rotavirus positive (n=52)*	Rotavirus negative (n=116)	P value
Age groups (months)			
1-6	03 (06%)	18 (16%)	
7-12	25 (48%)	25 (22%)	
13-18	16 (31%)	32 (27%)	0.0025 (S)
19-24	06 (11%)	01 (0.9%)	
>24	02 (04%)	40 (34%)	
Sex (M:F)	1.3:1	1.4:1	0.827 (NS)
Clinical features			
Vomiting	48 (92%)	89 (77%)	0.016 (S)
Fever	52 (100%)	114 (98%)	0.95 (NS)
Upper respiratory infection	31 (60%)	16 (14%)	<0.05(S)
Perianal excoriation	22 (42%)	06 (05%)	<0.05(S)
Dehydration			
Mild	05 (09.6%)	34 (29%)	0.003(S)
Moderate	21 (40.0%)	73 (62%)	0.006(S)
Severe	26 (50.0%)	09 (08%)	0.000(S)
Stool sample			
Pus cells	17 (32%)**	30 (26%)	0.362 (NS)
Reducing substance present	05 (10%)	02 (04%)	0.018 (S)
Nutritional status			
Normal	25 (48%)	86(74%)	
Grade I	19 (36%)	17(15%)	0.006(S)
Grade II	07 (13%)	12(10%)	
Grade III	01 (02%)	01(0.9%)	

**17 cases had mixed infection*
***15 cases had mixed infections*
(S): Significant, (NS): Not significant

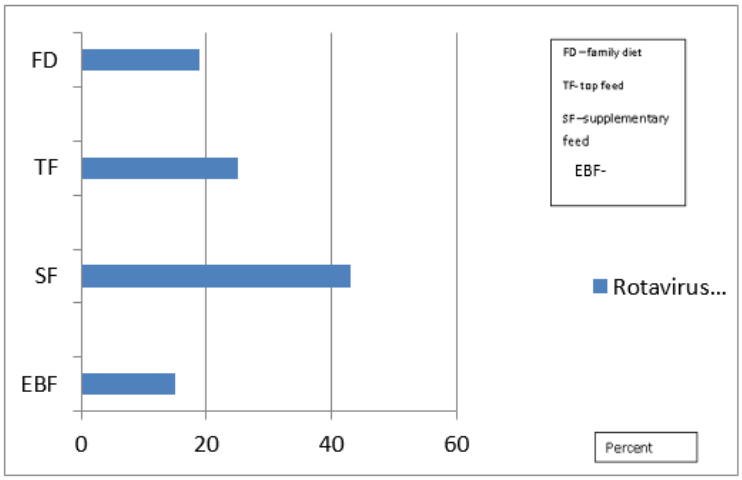

Figure 1: ***Correlation of type of feeding and rotavirus positivity***

Stool samples in rotavirus positive children showed pus cells in 17 samples (32%) of which 15 were mixed infections. Among the 25 bacterial culture positive children 18 (72%) and among the 91 bacterial culture negative children 12 (19%) showed pus cell in stools. In pure rotavirus infection only 2 samples showed pus cells. In the rotavirus group 10% (5 samples) and in non-rotavirus group 4% (5 samples) showed presence of reducing substance ($p<0.05$). Thus, presence of reducing substances is significantly more in rotavirus diarrhoea. Mean duration of diarrhoea in rotavirus

children with reducing substance was 4 ± 3 days, whereas in non-rotavirus diarrhoea it was 6 ± 3 days.

Discussion

WHO recommends inclusion of rotavirus vaccine in immunization programmes globally[9]. The present study gives some idea about the rotavirus burden in and around Vijayapur, north Karnataka, though community based studies are preferable. Community based studies are presently not available and data from the present study can be used keeping the limitations in mind. Moreover, prevalence of rotavirus diarrhoea in the community usually comes as low as most of these cases are in hospital due to severe dehydration[10]. Vijayapur has a mixed population from Karnataka and Maharashtra of around 2.2 million with mixed culture and religion, 76% hailing from rural areas. Though published data are not available, it is our observation from cases referred to this tertiary care hospital that most practitioners treat diarrhoeal episodes with antibiotics. The recognition of rotavirus aetiology clinically, might help in avoiding antibiotics.

Prevalence of rotavirus infections varies from country to country[10-12] and in different states of India[1]. Prevalence varies in outpatient and inpatients settings of any hospital and in the community. In admitted patients it varies from 20 to 40% whilst in outpatient and in the community, median proportions are 16% and 15% respectively[1]. Our sample was from a mixed population of outpatients and inpatients and 31% of all diarrhoeal cases were positive for rotavirus which is similar to the above observation[1]. Age prevalence of 7 to 18 months, which we observed, has been described by other Indian studies[13,14] and studies outside India[11,12], though an occasional study found more involvement below 6 months[11]. Most studies[10-13] including ours, found some male gender preponderance though this was statistically insignificant.

Fever was seen equally in both groups and this was also noted by others[15]. Contrary to popular belief, fever is not a significant feature of viral infections and is more common in non-rotavirus diarrhoea[12]. Vomiting was observed by us and by most authors[12,16]. Vomiting was probably responsible for the moderate and severe dehydration (60% patients), common in rotavirus illness making oral intake impossible. This was also observed by other authors[1,3,12,13,14,16]. Respiratory symptoms were observed in 60% of our patients. Alkali et al[17] and Surajuddin *et al*[13] in Nigeria found respiratory symptoms in only 3-9% and 8% patients respectively which may be due to difference in strains in different geographical areas. Perianal excoriation due to secondary transient lactose intolerance was seen significantly more in rotavirus positive diarrhoea in the present study and is also described classically[5].

As per 2008 estimates of global rotavirus linked mortality, 23% of all rotavirus deaths were in the Indian subcontinent[17] and the main cause reported was severe dehydration. Rotavirus immunization programme planned by the Government of India may substantially reduce morbidity, cost of treatment and loss of working days for parents[18].

Type of feeding was an important risk factor for rotavirus diarrhoea in the present study (Figure 1), children on supplementary feeding being at greatest risk followed by top fed children. Exclusive breast feeding offered some protection. Similar observations about breast feeding were made by other authors[19]. Nitiema *et al* did not find any significant difference between rotavirus or non-rotavirus infection in breast fed babies but 67% of rotavirus infected children were either non breastfed or on mixed feeding[21]. Many authors, similar to us, reported nutritional status as a risk factor for rotavirus diarrhoea[21,22]. In fact, Nitiema *et al* observed more severity of rotavirus and mixed infections diarrhoea in wasted children and increased duration in wasted and stunted children[21].

Present study showed that in rotavirus positive children, presence of pus cells was not significantly different from non-rotavirus cases, but most rotavirus positive children with pus cells in stools had mixed infections. If these children with mixed infections are removed from the group then presence of pus cells was significantly more in non-rotavirus group. Sangkapali *et al*[16] did not find any difference in stools of the two groups when tested for lactose intolerance. Present study showed significantly more children with reducing substance in stools in rotavirus diarrhoea (10% vs 4%).

Around 10% of patients in the study had mixed infections, the commonest combination being rotavirus and E Coli. Bhavani *et al* studied diarrhoeal diseases in the community and found 21% had mixed infections[23]. Most common association observed by them was rotavirus, E coli as well as Giardia. They also observed increased severity of diarrhoea during co-infection like present study[23]. Bilenko *et al* had contradictory findings where co-infection did not change the severity[24]. This difference in the observations may be due to different geographical locations, socioeconomic and nutritional status of patients and virulence of organisms of different strains. The hospital based nature of the study is one of the main limitations. A larger sample size also

would have been better. Most children with rotavirus diarrhoea needed hospital admission increasing cost of treatment. This indicates a definite need for the introduction of rotavirus vaccine to the immunization schedule in this area.

Conclusions

Around one third (31%) of all diarrhoea cases in our study were positive for rotavirus and 15% were of only bacterial aetiology. Key clinical features in rotavirus infection were fever, vomiting, watery stools, respiratory symptoms and perianal excoriations.

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