Paediatrica Indonesiana

VOLUME 45 March - April • 2005 NUMBER 3-4

Original Article

Clinical manifestations of rotavirus diarrhea in the outpatient clinic of Cipto Mangunkusumo Hospital, Jakarta

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ABSTRACT

Background Rotavirus is one of the most common cause of acute diarrhea among hospitalized and pediatric outpatients, especially those aged 6-24 months. Data of hospitalized children showed that rotavirus causes severe diarrhea, but data of outpatient children in Indonesia, especially at Cipto Mangunkusumo Hospital Jakarta, is limited.

Objective To characterize the clinical manifestations of rotavirus diarrhea in the pediatric outpatient clinic at Cipto Mangunkusumo Hospital Jakarta.

Methods This was a cross-sectional study, done in July 2003 – March 2004. Stool specimens were collected from patients aged 6-24 months with diarrhea and tested for rotavirus by ELISA.

Result Of the 98 children enrolled, 35 (35.7%) children excreted rotavirus. Rotavirus diarrhea was seen in 43.8% of children aged 6-11 months, of whom 37.0% of them were undernourished. Males were affected 1.4 times as much as females. The clinical manifestations were passage of diarrheic stools more than 10 times a day (58.3%), mild-moderate dehydration (55.8%), cough (51.9%), rhinorhea (46.0%), vomiting (44.8%), fever (41.1%), yellow stools (38.9%), and mucus in the stool (20.0%). The highest prevalence of rotavirus diarrhea was identified in the combination of diarrhea, fever, vomiting and cough/rhinorrhea (55.3%). Stool analysis revealed that the prevalence of rotavirus diarrhea among children with fat malabsorption, lactose malabsorption, and stool leukocyte of +2 were 50.0%, 46.7% and 33.9%, respectively.

Conclusion The prevalence of rotavirus diarrhea in the pediatric outpatient clinic of Cipto Mangunkusumo Hospital, Jakarta was 35.7%. The highest prevalence of rotavirus diarrhea was identified in the combination of diarrhea, fever, vomiting and cough/rhinorhea (55.3%) **[Paediatr Indones 2005;45:69-75].**

Keywords: *rotavirus, diarrhea, clinical manifestations, outpatients*

Cook *et al*[1] reported that rotavirus is the most common cause of acute diarrhea among outpatients and hospitalized children in 34 countries, causing 11-71% of diarrhea in children, with a median rate of 33%. Rotavirus was identified especially in children between 6 and 24 months of age.[2-12] Recent data of outpatients in several countries showed that prevalences of rotavirus varied between 15-34%.[4-7] Data of prevalence and morbidity of rotavirus diarrhea among outpatient settings in Indonesia, particularly at Cipto Mangunkusumo Hospital, Jakarta are very limited. Hegar's study of a new drug at Cipto Mangunkusumo Hospital (1999-2001) reported that the prevalence of rotavirus diarrhea was 61.1%;[13] while Setiyadi (2003) reported that the prevalence of rotavirus diarrhea among several primary health care centers in Bandung was 48.8%.[11]

Suharyono (1982) identified that 56.3% of children with rotavirus diarrhea suffered severe diseases.[8] In contrast, Hegar *et al* (1999-2001) found that all rotavirus diarrhea outpatients presented to the hospital with only mild diarrhea.[13] We predict that there

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have been changes in the clinical presentations of rotavirus diarrhea, which lead to high prevalence among outpatient settings.[13] On the other hand, it is quite costly to establish the diagnosis of rotavirus diarrhea; therefore, a further study on the clinical presentation of rotavirus diarrhea among outpatients is needed in order for patients to receive proper management and to prevent unnecessary use of antibiotics. The aim of this study is to characterize the clinical presentations of rotavirus diarrhea in the outpatient clinic of Cipto Mangunkusumo Hospital, Jakarta.

Methods

This was a cross-sectional study done at the outpatient clinic of Cipto Mangunkusumo Hospital from July 2003 to March 2004. Subjects included were children aged 6–24 months who suffered diarrhea for < 7 days. They were excluded if there was bloody diarrhea; if parents refused to join the study; or if they failed to have their stool specimens taken on the same day of their visits to the clinic. The study was approved by The Committee for Medical Research Ethics of the Faculty of Medicine, University of Indonesia, and informed consent was obtained from parents or caregivers of the children who served as subjects in this study. After informed consent was obtained, the parent or caregiver was interviewed to obtain detailed information regarding the symptoms of the child's illness. A stool specimen was collected at enrollment and stored at –20^{0}C until tested. Stool specimens were tested for rotavirus antigen using a commercial ELISA preparation (*RotaStick, Novamed*). Subjects were recruited by consecutive sampling, with a minimum of 96 subjects required for the study.

Diarrhea was defined as an episode of $\geq$ 3 stools in a 24-hour period judged by the caregiver to be looser than normal.[2,12,14-16] Fever was defined as an axillary temperature of > 37.2^{0}C.[17] Degree of dehydration was determined based on the WHO standard.[18] Nutritional status was determined by using body weight (BW) and body height (BH) based on growth charts of the NCHS (National Center of Health Statistic, Maryland, United States of America). Nutritional index was determined based on BW (without dehydration) to BH.[19] Body weight without dehydration was estimated; if there was mild-moderate dehydration, 5% of the measured body weight was added; if there was severe dehydration, 12.5% of the measured weight was added. Lactose malabsorption was determined by clinitest and fat malabsorption was determined by light microscopy.[20]

Data collected from completely filled forms were processed using computer program SPSS 12.0.

Results

Out of 158 children eligible for the study, only 98 (62%) were screened (**Figure 1**). Of these, 35 (35.7%) were rotavirus-positive.

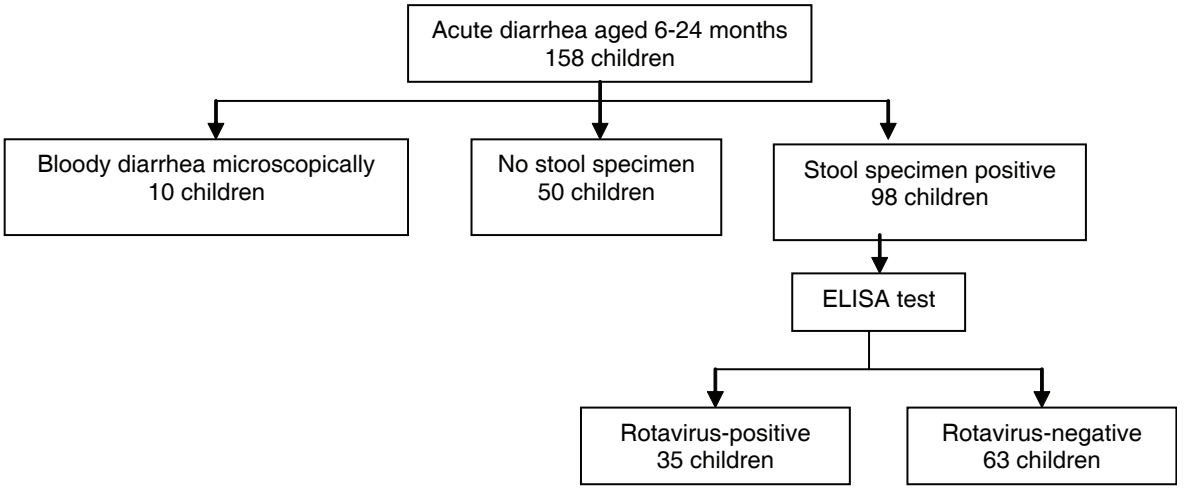

Figure 1. Enrollment and sample collection in the study

The characteristics (age, sex, and nutritional status) of subjects are shown in **Table 1**. The prevalence of rotavirus diarrhea between July 2003 and March 2004 in the pediatric outpatient clinic of Cipto Mangunkusumo Hospital ranged from 0-50% (mean of monthly prevalences 35.7%). Rotavirus diarrhea was present almost all year, except in November 2003. The wet season began in October 2003 and lasted until the end of study.

TABLE 1. CHARACTERISTICS OF SUBJECTS

Characteristics	Rotavirus-positive		Rotavirus-negative	
	No.	%	No.	%
Total	35	35.7	63	64.3
Age (months)				
6-11	21	43.8	27	56.2
12-24	14	28.0	36	72.0
Sex				
Male	26	39.4	40	60.6
Female	9	28.1	23	71.9
Nutritional status				
Well-nourished	15	34.1	29	65.9
Undernourished	20	37.0	34	63.0

The clinical manifestations of rotavirus diarrhea seen in our subjects can be seen in **Table 2**. Fever and vomiting were less frequent in rotavirus diarrhea than in non-rotavirus diarrhea (41.1% vs 58.9% and 44.8% vs 55.2%). Rotavirus was identified most frequently in yellow stools (38.9%), but if mucus was found in the stools, rotavirus was found only in 20.0%. The prevalence of rotavirus diarrhea became higher in subjects with frequency of diarrhea of more than 10 times a day (58.3%) and in those with mild-moderate dehydration (55.8%). Nineteen of all rotavirus diarrhea (54.3%) progressed to hospitalization due to mild-moderate dehydration. The indications for hospitalization were a decrease in intake and frequent diarrhea. Our study revealed that rotavirus diarrhea was accompanied by cough (51.9%), rhinorrhea (46.0%), stool leukocyte of +1 (30.6%), stool leucocyte of +2 (33.9%), lactose malabsorption (46.7%), and fat malabsorption (50.0%).

Table 3 shows the combination of clinical manifestations of rotavirus diarrhea. The highest prevalence of rotavirus diarrhea was identified in subjects with the combination of diarrhea, fever, vomiting and cough/rhinorrhea (55.3%) (**Table 3**).

Discussion

There were several limitations of our study. The number of patients who could not have their stools examined was almost 30%, since the laboratory had been closed before they sent the specimen. Another limitation was that we did not conduct the study at the peak season of rotavirus diarrhea, so the number of rotavirus cases was low. Nevertheless, we believe that our findings represent the population, since we obtained more subjects than the required minimum sample size.

Our study identified rotavirus in 35.7% of pediatric outpatients. This finding is similar to those of previous studies.[1,5,6] Ford-Jones *et al*[14] in Canada and Kelkar *et al*[7] in India found the prevalence to be 28% and 15%. Those studies were population-based, while ours was hospital-based. Our finding was lower than those of Setiyadi[11] and Hegar *et al*[13] (48.8% and

TABLE 2. CLINICAL PRESENTATIONS OF DIARRHEA AMONG OUTPATIENTS

Clinical presentations		Rotavirus	
		Positive (%)	Negative (%)
Fever	Yes	30 (41.1)	43 (58.9)
	No	5 (20.0)	20 (80.0)
Vomiting	Yes	30 (44.8)	37 (55.2)
	No	5 (16.1)	26 (83.9)
Color of stool			
• Yellow		28 (38.9)	44 (61.1)
• Yellow-green		6 (27.3)	16 (72.7)
• Green		1 (25.0)	3 (75.0)
Mucus on stool	Yes	6 (20.0)	24 (80.0)
	No	29 (42.7)	39 (57.3)
Frequency of diarrhea			
• 1 – 5 times/day		8 (21.1)	30 (78.9)
• 6 - 9 times/day		13 (36.1)	23 (63.9)
• ≥ 10 times/day		14 (58.3)	10 (41.7)
Cough	Yes	27 (51.9)	25 (48.1)
	No	8 (17.4)	38 (82.6)
Rhinorhea	Yes	23 (46.0)	27 (54.0)
	No	12 (25.0)	36 (75.0)
Degree of dehydration			
• No dehydration		11 (20.0)	44 (80.0)
• Mild-moderate		24 (55.8)	19 (44.2)
Leukocyte			
• + 1		15 (30.6)	34 (69.4)
• + 2		20 (33.9)	39 (66.1)
Lactose malabsorption	Yes	7 (46.7)	8 (53.3)
	No	28 (33.7)	55 (66.3)
Fat malabsorption	Yes	11 (50.0)	11 (50.0)
	No	24 (31.6)	52 (68.4)

TABLE 3. COMBINATION OF CLINICAL PRESENTATIONS OF DIARRHEA AMONG OUTPATIENTS

Combination of clinical presentation		Rotavirus	
		Positive (%)	Negative (%)
Diarrhea+cough/rhinorheae	Yes	27 (46.6)	31 (53.4)
	No	8 (25.0)	32 (75.0)
Diarrhea+vomiting+cough/rhinorheae	Yes	23 (52.3)	21 (47.7)
	No	12 (22.2)	42 (77.8)
Diarrhea+fever+cough/rhinorhea	Yes	24 (49.0)	25 (51.0)
	No	11 (22.5)	38 (77.5)
Diarrhea+fever+vomiting	Yes	27 (49.1)	28 (50.9)
	No	8 (17.4)	38 (82.6)
Diarrhea+fever+vomiting+cough/rhinorhea	Yes	21 (55.3)	17 (44.7)
	No	14 (23.3)	46 (76.7)

61.1%, respectively). This might be due to the fact that our study was conducted mostly during the wet season, while the others were conducted at the peak period of the disease (in the dry season). The prevalence of rotavirus diarrhea would have increased slightly if a full year's data had been examined. All of the studies show that rotavirus is the most common cause of acute diarrhea, compared to other microorganisms, which have a cumulative prevalence of 1-20%.[13,15,21]

In tropical countries like Indonesia, rotavirus is present year-round.[1,7,9,22] The absence of rotavirus cases in November 2003 is probably due to a true absence of the disease, or, more likely, it was present at a level that was lower than the limit of detection.[1]

We found that prevalence of rotavirus diarrhea was higher among the 6-11 month age group than in the 12-24 month age group (**Table 1**). This agreed with the findings of Fürhwirth *et al*[5] and Kelkar *et al*[7], but contrasted with those of Ford-Jones *et al*[4] and Setiyadi.[11] All these studies reveal that rotavirus diarrhea was common in children aged 6-24 months. Infants younger than six months are protected by transplacental antibody and breastfeeding, whereas 80-100% of older children are protected by antibody due to previous infection.[3,23-25]

Males were affected 1.4 times as much as females (**Table 1**), which was similar to results of previous studies,[4,5,11] but differed from those of Kelkar *et al*[7]. Until now, we have not been able to find any literature which explains the gender-specific difference in the prevalence of rotavirus diarrhea.

Table 1 shows that rotavirus diarrhea is more prevalent in undernourished than in well-nourished children. This is similar to the findings of Rialdi[10] in M. Jamil Hospital, Padang, who found that rotavirus was more prevalent in undernourished than well-nourished children (71.8% vs 34.5%). In contrast, Setiyadi[11] found rotavirus diarrhea to be more prevalent in the well-nourished than in the undernourished (53.0% vs 49.2%). Another study by Soenarto[12] did not find any statistically significant role of nutritional status in the incidence of rotavirus infection. In Soenarto's study, the risk for acquiring rotavirus infection was similar among different nutritional status.[12] Disease severity, prolonged clinical illness, delayed recovery, and mortality risks were increased among the undernourished, especially in malnourished children.[15,26] This could be attributed to the altered immune response and gastrointestinal tract function which lead to longer and more severe diarrhea, especially in the malnourished.[27]

Prevalence of fever and vomiting in this study was lower in rotavirus diarrhea than non-rotavirus diarrhea (**Table 2**). These findings were different from previous studies, which were conducted in the epidemic season. They showed that fever and vomiting occured more frequently with rotavirus diarrhea (70.6-75.0% and 57.1-63.3%, respectively).[11,13] Hegar *et al*[13] found that the prevalence of fever and vomiting were not significantly different between rotavirus diarrhea and non-rotavirus diarrhea.

Table 2 shows that the prevalence of rotavirus diarrhea increased up to 58.3% if diarrhea was with

a frequency of more than 10 times per day. In those with a frequency of diarrhea of more than 6 times per day, the prevalence of rotavirus infection was 45.0%. This finding was similar to those of Hegar *et al*[13], who found than among those with frequency of more than five times a day, 67.7% were rotavirus-positive. Rotavirus destroys villus tip cells in the small intestine, leading to osmotic diarrhea and frequent diarrhea. Frequent diarrhea in infants is the cause of dehydration and it necessitates patients to be hospitalized.[2,3,22,23,26,28] Dehydration still occurred although most subjects received oral rehydration therapy (75%). Our study revealed that rotavirus was more prevalent among those with mild-moderate dehydration than those without dehydration (55.8% vs 20.0%). Setiyadi[11] found similar results (67.9% vs 43.3%). The number of patients hospitalized in this study (54.3%)was similar to that in the study of Ford-Jones *et al* (60%).[4]

Our study revealed that the prevalence of rotavirus diarrhea among patients with cough and rhinorrhea were 51.9% and 46.0%, respectively (**Table 2**). Setiyadi[11] found that the prevalence of rotavirus diarrhea among patients with cough/rhinorrhea was 46.8%. Ariyani[21] reported that cough/rhinorrhea was common in rotavirus diarrhea (positive likelihood ratio 12.4). Several studies have noted that rotavirus infection may involve the respiratory tract; it is believed that rotavirus diarrhea spreads via airborne droplets.[1,29-31]

Previous studies usually found that stools in rotavirus diarrhea tend to be yellow to green.[2] The present study found that rotavirus was more prevalent in yellow stools. These data were obtained from anamnesis, which was very subjective. Rotavirus is less frequent in stools with mucus (20.0% vs 42.7%). Other studies concur that rotavirus stool does not contain blood, white cells, or mucus.[2,16,22,26,28] Our study showed that the prevalence of rotavirus diarrhea among those with stool leukocyte of +2 and +1 were 33.6% and 30.6%. Our findings were similar to Rialdi's[10], who found rotavirus in 35.3% of patient with stool leukocyte of +2. Stool leukocyte of +2 was probably due to mixed infection with other microorganisms, but it was difficult to prove since we did not perform stool culture.

Prevalence of rotavirus diarrhea among those with fat malabsorption was 50.0%. Fat malabsorption in diarrhea is due to increased transit time of the intestine.[32] Rotavirus was identified in 46.7% of patients with lactose malabsorption. Lactose malabsorption occurs when rotavirus destroys the villus cells and diminishes disaccharide enzyme production, leading to a decrease in disaccharide, especially lactose, absorption.[2,15,16,22,23,26] Lactose in the small intestine is fermented by bacteria and leads to acidic stool. The finding of lactose malabsorption with mild-moderate diarrhea (as in this study) is not an indication to change a child's diet,[33] since mucosal structural abnormalities are mild.[24] If diarrhea becomes more severe, then a lactose-free formula should be considered.[33]

Table 3 shows that rotavirus was much more prevalent in the combination of diarrhea, vomiting, and cough/rhinorrhea with (55.3%) or without (52.3%) fever. Due to the absence of peak rotavirus season, our findings were lower than those by Setiyadi[11] who found the above prevalence to be 70.6% and 57.6%, respectively. Suharyono[8] (1982) identified that 56.3% of children with rotavirus diarrhea suffered severe diseases. On the contrary, Hegar *et al* (1999-2001)[13], found that all rotavirus diarrhea patients presented to the hospital with only mild diarrhea.[13] Our study captured the presence of accompanying symptoms such as cough and rhinorrhea, which indicates that clinical presentations among outpatients have changed and have become milder than in the previous study.[8]

In conclusion, the prevalence of rotavirus diarrhea in the outpatient clinic of Cipto Mangunkusumo Hospital, Jakarta was 35.7%. The highest prevalence of rotavirus diarrhea was identified in the combination of diarrhea, fever, vomiting, and cough/rhinorrhea (55.3%). The clinical manifestations of rotavirus diarrhea seem to have changed to a milder course of disease.

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