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Original Article

Scoring system to distinguish between rotavirus and non-rotavirus diarrhea in children

Atika Akbari[1], Hasri Salwan[1], Achirul Bakri[1], Erial Bahar[2]

Abstract

Background Distinguishing rotavirus from non-rotavirus diarrhea is helpful for managing the illness. However, definitively diagnosing rotavirus diarrhea from serology is difficult and expensive.

Objectives To distinguish between the clinical manifestations of rotavirus and non-rotavirus diarrhea, and to assess the accuracy of using such clinical manifestations to predict the type of diarrhea in children.

Methods A cross-sectional study was performed from April to October 2015 in all children less than 5 years of age who presented with acute diarrhea at the Pediatric Outpatient Clinic of the Department of Child Health and Emergency Department, Dr. Mohammad Hoesin and Bari Hospitals, Palembang, South Sumatera. Clinical manifestations were collected from history and physical examinations; stool specimens were examined by immunochromatography. Clinical parameters were analyzed by multivariate analysis, and scores given to each significant parameter. The accuracy of the scoring system based in these parameters was analyzed by means of receiver-operating characteristic (ROC) area under the curve (AUC).

Results Of 184 children, 92 had rotavirus and 92 had non-rotavirus diarrhea. Multivariate analysis showed 3 clinical parameters commonly seen in the rotavirus diarrhea cases: male sex (OR 2.718; 95%CI 1.373 to 5.382), cough (OR 3.500; 95%CI 1.788 to 6.582), and yellow-greenish stool (OR 4.009; 95%CI 2.061 to 7.797). A scoring system was constructed based on the parameters: male (score of 1), cough (score of 2), and yellow-greenish stool (score of 3). From ROC analysis, the AUC was 0.755. Using a cut-off score of $\geq$ 3, the sensitivity was 81.5%, specificity 51.1%, and PPV 62.5%.

Conclusion Cough, yellow-greenish stool, and male are significant parameters for differentiating rotavirus from non-rotavirus diarrhea. A scoring system from these parameters is sensitive for predicting rotavirus *vs.* non-rotavirus diarrhea in children less than five years of age. **[Paediatr Indones. 2016;56:338-42. doi: 10.14238/pi56.4.2016.338-42]**.

Keywords: *rotavirus diarrhea; non-rotavirus diarrhea; scoring system; immunochromatography; stool specimens*

Rotavirus diarrhea is the leading cause of acute diarrhea in Indonesia, affecting 60% of hospitalized children.[1] Studies on the prevalence of rotavirus diarrhea in Indonesia, especially in Palembang, have been limited. A previous study found that the prevalence of rotavirus diarrhea was 55% at Mohammad Hoesin Hospital in 2002.[2] Another study in 2006 showed that prevalence of rotavirus diarrhea was 64%, while the prevalence at Dr. Cipto Mangunkusumo Hospital in Jakarta was 67%.[3]

From the Department of Child Health[1] and Health and Medicine Research Unit[2], Sriwijaya University Medical School/Dr. Mohammad Hoesin Hospital, Palembang, South Sumatera, Indonesia.

Reprint requests to: Atika Akbari, Department of Child Health, Sriwijaya University Medical School/Dr. Mohammad Hoesin Hospital, Jl. Jenderal Sudirman Km. 3,5, Palembang 30126, South Sumatera, Indonesia; E-mail: atika.akbari@yahoo.com.

Managing rotavirus diarrhea is different from managing non-rotavirus diarrhea. Rotavirus diarrhea requires only supportive treatment, with appropriate fluid and electrolyte therapy, as well as close attention to nutrition remaining central to therapy. Non-rotavirus diarrhea should usually be treated with antibacterials, while antibacterials are only used in severe, unresponsive infections with enterohemorrhagic *E. coli* (EHEC), Yersinia, *Vibrio cholera*, *Clostridium difficile*, Aeromonas, and some strains of Salmonella, Shigella, and Campylobacter. For rotavirus diarrhea, antibacterials are not useful due to the viral etiology of the disease. In fact, antibiotics should be avoided in rotavirus diarrhea cases, because they may disrupt the intestinal flora and expose the patient to complications, such as antibiotic-associated diarrhea. Hence, worsening the initial problem. Moreover, a major concern is the emergence of antibiotic-resistant bacterial strains due to the widespread use of antibacterial agents.[4]

Rotavirus diarrhea can be confirmed by serological examination, an expensive and lengthy process. Clinical manifestations potentially offer an easier and more practical way of predicting rotavirus diarrhea. As such, we aimed to identify differences in rotavirus and non-rotavirus diarrhea and develop a scoring system to distinguish between the two types of diarrhea in children under the age of five years.

Methods

A cross-sectional study was conducted in the Pediatric Outpatient and Emergency Departments of Dr. Mohammad Hoesin and Bari Hospitals, Palembang from April to October 2015. Subjects were recruited by consecutive sampling. Inclusion criteria were acute diarrhea patients between the ages of 28 days and <5 years. Patients with meningitis or encephalitis were excluded. This study was approved by the Committee for Medical Research Ethics of Sriwijaya University, Faculty of Medicine.

Patient history of illness was collected from parents or caregivers, and physical examinations were done by the doctor in charge. Subjects' general characteristics (age, gender, nutritional status, maternal employment, maternal education, medical history in the 3 months prior, and history of rotavirus vaccination) and clinical manifestations (diaper rash, temperature, frequency of diarrhea, level of dehydration, cough, rhinorrhea, and stool characteristics such as consistency, color, mucus, blood, and pus) were documented by the doctor in charge. Stool specimens were collected at enrollment and tested by immunochromatography (*VIKIA-ROTA Adeno*®), with 100% sensitivity and 100% specificity.

Acute diarrhea was defined as an episode of ≥ 3 stools in a 24–hour period, as judged by the caregiver to be looser than normal, within a period of less than 14 days. Fever was defined as an axillary temperature of > 37.2^{0}C. Degree of dehydration was determined based on the WHO standard. Nutritional status was determined by using body weight and body height, based on the 2006 WHO growth chart. Cough was defined as frequency of cough >10 times in a day.

Differences between rotavirus and non-rotavirus diarrhea were analyzed by Chi-square and Fischer's exact tests. The effect of clinical manifestations to predict rotavirus diarhhea was analyzed using logistic regression test, with clinical manifestations as independent variables and rotavirus or nonrotavirus diarrhea as the dependent variable. A scoring system was constructed by giving values to each clinical parameter, based on the logistic regression results, followed by validation analysis for each scoring system. All statistical analyses were done with *SPSS version 19* software.

Results

Of 184 children with acute diarrhea who met the inclusion criteria, 92 (50%) were rotavirus-positive. Most patients were in the age group of 1-11 months (56%) and had good nutritional status (73.9%). Male to female ratio was 1.5:1. Characteristics of subjects are presented in **Table 1**.

Clinical manifestations of rotavirus and non-rotavirus diarrhea are shown in **Table 2**. There were more males in the rotavirus group compared to the non-rotavirus group (56.9% *vs.* 43.1%, respectively). The majority of children with rotavirus had good clinical appearance (53.5%) (data not shown), cough (65.9%), and good nutritional status (72.8%) (data not shown). Fever and rhinorrhea were less frequently noted in rotavirus cases than in non-rotavirus

Table 1. Baseline characteristics of patients

Characteristics	(N=184)	
Age, n (%)		
1 mo-11 mo	103	(56)
12 mo-23 mo	50	(27.2)
24 mo-35 mo	11	(6)
36 mo-60 mo	20	(10.9)
Gender, n (%)		
Male	109	(59.2)
Female	75	(40.8)
Nutritional status, n (%)		
Well-nourished	136	(73.9)
Undernourished	48	(26.1)
History of illness in the 3 months prior, n (%)		
Diarrhea	51	(27.7)
Acute respiratory infection	67	(36.4)
Measles	13	(7.1)
Varicella	5	(2.7)
History of rotavirus vaccinations, n (%)	0	(0.0)

diarrhea cases (47.4% *vs.* 44.7%, respectively) (data not shown). The prevalence of rotavirus diarrhea was higher in subjects with frequency of diarrhea < 10 times per day (52%) (data not shown), vomiting (54.8%), and yellow-greenish stool (64.2%). We found that rotavirus diarrhea was accompanied by diaper rash (42.3%) (data not shown), watery stool (50.0%) (data not shown), mucus in stool (56.7%), bloody stool (25.0%), and dehydration (49.7%) (data not shown).

There were no statistically significant differences between rotavirus and non-rotavirus patients in terms of general appearance, rhinorrhea, frequency of diarrhea, fever, diaper rash, stool consistency, bloody stool, pus in stool, and dehydration. However, there were significantly more males, cough, vomiting, and yellow-greenish stool in the rotavirus-positive subjects than in the rotavirus-negative subjects ($P<0.05$) (**Table 2**).

Logistic regression analysis revealed that 3 clinical parameters were risk factors for rotavirus diarrhea: male sex (OR 2.718; 95%CI 1.373 to 5.382), cough (OR 3.500; 95%CI 1.788 to 6.582), and yellow-greenish stool (OR 4.009; 95%CI 2.061 to 7.797) (**Table 3**).

Based on those findings, we constructed three scoring systems using the clinical manifestations to

Table 2. Characteristics of clinical manifestations of acute diarrhea in children less than five years old (n=184)

Characteristics	Rotavirus positive (N = 92)	Rotavirus negative (N = 92)	P value	OR (95%CI)
Gender, n (%)				
Male	62 (67.4)	47 (51.1)	0.024	1.979 (1.089 to 3.597)
Female	30 (32.6)	45 (48.9)		
Cough, n (%)				
Yes	54 (58.7)	28 (30.4)	0.000	(0.769 to 5.965)
No	38 (41.3)	64 (69.6)		
Vomiting, n (%)				
Yes	74 (80.4)	61 (66.3)	0.03	(0.066 to 4.093)
No	18 (19.6)	31 (33.7)		
Stool color, n (%)				
Yellow-greenish	68 (73.9)	38 (41.3)	0.000	(0.158 to 2.301)
Yellow-brownish	24 (26.1)	54 (58.7)		
Mucus in stool, n (%)				
Yes	51 (55.4)	39 (43.3)	0.077	(0.944 to 3.029)
No	41 (44.6)	53 (56.4)		

Table 3. Multivariate analysis of clinical manifestations to predict rotavirus diarrhea in children less than five years old

	Coefficient	S.E.	Wald	Df	P value	OR	95%CI
Male gender	1.000	0.349	8.229	1	0.004	2.718	1.373 to 5.382
Cough	1.253	0.343	13.362	1	0.000	3.500	1.788 to 6.852
Yellow-greenish stool	1.388	0.339	16.734	1	0.000	4.009	2.061 to 7.797
Constant	-1.952	0.399	23.947	1	0.000	0.142	

SE= standard error, Df= degree of freedom

predict a rotavirus diarrhea diagnosis. In the first version, a score of 1 was given for a risk factor and a score of 0 for not being a risk factor. The best cut-off point was ≥7 obtained from ROC analysis. In the second version, using odd ratios adjusted from multivariate analysis, we assigned a score of 3 for yellow-greenish stool, a score of 2 for cough, and a score of 1 for male gender (called multivariate A). The third version of the scoring system consisted of 2 parameters: a score of 3 for yellow-greenish stool and a score of 2 for cough (multivariate B). All 3 scoring systems were tested for accuracy using receiver operating curve (ROC) analysis. The ROC analyses revealed that the best AUC was 0.755 (95%CI 0.685 to 0.825) in the multivariate A scoring system (**Figure 1**). The best cut-off point (≥3) was in the multivariate A scoring system, with sensitivity 81.5%, specificity 51.1%, positive predictive value 62.5%, negative predictive value 73.4%, likelihood ratio positive 1.6, likelihood ratio negative 0.6, and accuracy 69.0% (**Table 4**).

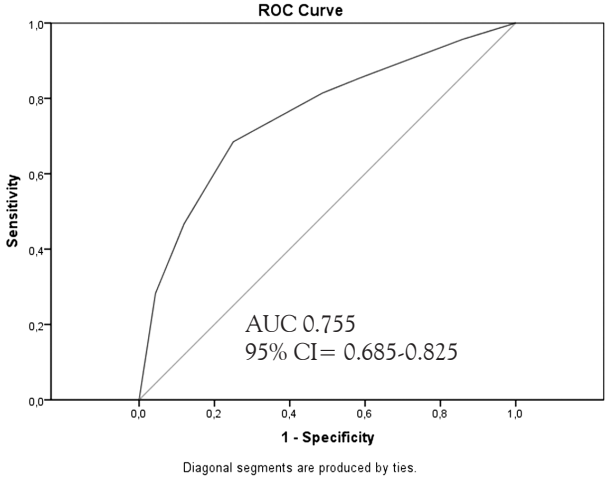

Figure 1. Receiver operating curve (ROC) of multivariate A scoring system.

Discussion

Some clinical manifestations were significantly different between rotavirus and nonrotavirus diarrhea. Multivariate analysis revealed that the parameters of male sex (OR 2.718; 95%CI 1.373 to 5.382), cough (OR 3.500; 95%CI 1.788 to 6.582), and yellow-greenish stool (OR 4.009; 95%CI 2.061 to 7.797) were the significant risk factors for rotavirus diarrhea. Wahyuni performed a multivariate analysis with the following variables: vomiting, fever, dehydration, mucus in stool, and liquid stool and showed that the risk factors for rotavirus diarrhea were dehydration (OR 2.949; 95%CI 1.746 to 4.949) and vomiting (OR 2.645; 95%CI 1.567 to 4.463). The fundamental difference in that study and our study was our use of primary data and immunochromatography as the diagnostic method, while Wahyuni used secondary data and PCR methods.[5]

Of the 92 subjects with rotavirus diarrhea, there were 62 males and 30 females with a male: female ratio of 2:1. Similarly, Soenarto *et al*. found that the prevalence of rotavirus diarrhea was higher in males (61%) than in females (39%).[1] Another study also found that rotavirus diarrhea was 1.4 times more common in males than females.[6] In contrast, Kelkar *et al*. found that there was no statistically significant difference in the incidence of rotavirus diarrhea in male and female children (62.9% vs. 60%, respectively).[7] To date, there is no explanation of how gender affects the prevalence of rotavirus diarrhea.

The prevalence of cough in patients with rotavirus diarrhea in our study was 58,7%. Tjitrasari *et al*. reported the prevalences of cough and colds in patients with acute rotavirus diarrhea to be 51.9% and 46.0%, respectively.[6] Some studies have suggested that rotavirus infection may involve the

Table 4. Validity test using cut-off points from each scoring system.

	Sen	Spec	PPV	NPV	LLH+	LLH-	Accuracy	COP	Total score
Total score	73.9	50.0	59.6	50.0	1.5	0.7	62.0	≥ 7	14
Multivariate A	81.5	51.1	62.5	73.4	1.6	0.6	69.0	≥ 3	6
Multivariate B	85.8	40.2	58.9	74.0	2.2	0.5	63.0	≥ 2	5

Sen=sensitivity, spec=specificity, PPV=positive predictive value; NPV=negative predictive value; LLH+= positive likelihood ratio; LLH-= negative likelihood ratio; COP=cut-off point

respiratory tract, hence, rotavirus may be spread through airborne droplets. Respiratory symptoms have been reported in 20-40% of patients with acute rotavirus diarrhea.[8]

Yellow-greenish stool color was more common in patients with rotavirus diarrhea than those with non-rotavirus diarrhea (73.9% *vs.* 41.3% , respectively). In contrast, Tjitrasari *et al*. reported that the majority of patients with rotavirus diarrhea had yellow-brownish stool.[6]

Based on odd ratios from multivariate analysis, a score was given to each clinical parameter: male gender, cough, and yellow-greenish stool. Three scoring system models were constructed and validation tests performed. The ROC analyses on all scores indicated that clinical parameters had good diagnostic value, because curve away from the line of 50% and close to the line 100%. The best AUC was found in the multivariate A scoring system, with a value of 0.755. Designed for daily use, the multivariate A scoring system consisted of three clinical parameters [gender (female: score 0, male: score 1), cough (no: score 0, yes: score 2), and stool color (yellow-brownish: score 0, yellow-greenish: score 3)], with a cut-off point of $\geq$3 and a maximum score of 6. Wahyuni reported diagnostic test results on each of the clinical symptoms of dehydration, vomiting, and fever, which suggested that dehydration had a sensitivity of 76% and a specificity of 58%, while vomiting had a sensitivity of 70% and a specificity of 63%.[5]

The multivariate A scoring system is a very simple and practical method for clinical practice that may help general physicians or pediatricians in predicting rotavirus diarrhea. By identifying male gender, cough, and yellow-greenish stool in child under five years old, 62.5% can predicted to have rotavirus diarrhea, and sensitivity 81.5% is good to perform screening test for rotavirus diarrhea in daily practice. Further study should involve examining more specific clinical manifestations for predicting acute rotavirus diarrhea *vs.* non-rotavirus diarrhea, such as frequency of vomiting and if vomiting occurred before or after diarrhea onset. This scoring system needs further prospective revalidation and reliability testing.

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Conflict of interest

None declared.

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