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Severity and treatment level of acute gastroentritis with rotavirus in children under 5 years in Indonesia

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ABSTRACT

Rotavirus diarrhea causing gastroenteritis in children under five years is an important issue that urgently needs to be addressed globally. Delay in management of rotavirus diarrhea can be fatal. Diagnostic tool for detecting rotavirus is, therefore, needed. However, until now the gold standard diagnostic tools are expensive, often not available and affordable in health care settings. The aim of the study was to compare the Vesikari clinical severity score of rotavirus-positive with rotavirus-negative in hospitalized children with acute gastroenteritis. Furthermore, the difference of the level of treatment between rotavirus-positive with rotavirus-negative was also evaluated. This was a cross sectional study that using secondary data from medical records of five general teaching hospital in Indonesia. Subjects were children aged <5 years with acute watery diarrhea admitted to the hospital. Statistical analysis used was chi square test, U-Mann Whitney, and Kruskal Wallis. The results showed that the patient with rotavirus positive have higher dehydration (80.2%) compared to rotavirus negative (70%). The severity level of clinical feature was higher in diarrhea due to rotavirus positive than non rotavirus (11.47± 2.89 vs 10.41 ± 2.70; p<0.000). The level of treatment was higher in rotavirus positive. The majority had treatment plan C (47.7%) higher than plan B and A (45.6% and 30.9%; p<0.050). This was opposite with patient with rotavirus negative that majority had treatment in plan A (69.1%) higher than plan B and C (54.4% and 52.3%) (p<0.001). In conclusion, the severity of gastroentrities in children under 5 years using vesikari score are higher in diarrhea due to rotavirus positive than non rotavirus. The treatment level plan C is higher than plan B and A in diarrhea due to rotavirus. This is opposite with non rotavirus majority have treatment in plan A higher than plan B and C.

ABSTRAK

Diare rotavirus yang menyebabkan gastroenteritis pada anak usia di bawah lima tahun merupakan masalah penting yang sangat perlu ditangani terutama di negara berkembang. Keterlambatan penanganan diare rotavirus dapat berakibat fatal secara klinis. Oleh karena itu, suatu alat diagnostik untuk mendeteksi rotavirus sangat diperlukan. Namun, hingga saat ini standar emas alat diagnostik tersebut masih mahal dan sering tidak terjangkau dipusat pelayanan kesehatan. Penelitian ini bertujuan untuk membandingkan skor tingkat keparahan klinik Vesikari pada anak gastroenteritis dengan rotavirus-positif dan rotavirus negatif yang di rawat di rumah sakit. Selanjutnya perbedaan tingkat pengobatan antara

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rotavirus-positif dan rotavirus-negatif juga akan dikaji. Penelitian ini merupakan penelitian potong lintang menggunakan data sekunder dari rekam medis di lima rumah sakit pendidikan di Indonesia. Subjek penelitian adalah anak usia < 5 tahun dengan diare akut yang masuk rumah sakit. Analisis statistik yang digunakan adalah uji chi square, U-Mann Whitney, dan Kruskal Wallis. Hasil penelitian menunjukkan bahwa pasien dengan rotavirus positif sebagian besar mengalami tingkat dehidrasi lebih tinggi (80.2%) daripada pasien dengan rotavirus negatif (70%). Tingkat keparahan klinis diare lebih tinggi pada rotavirus positif dari pada non rotavirus (11,47 ± 2,89 vs 10,41 ± 2,70; p<0,000). Pengobatan penderita yang terinfeksi rotavirus positif sebagian besar menggunakan perlakuan plan C (47,7%) lebih tinggi dari pada plan B dan A (45,6% dan 30,9%). Hal ini berbeda penderita yang terinfeksi rotavirus negatif yang mayoritas menggunakan plan A (69,1%) lebih tinggi dari plan B dan C (54,4% dan 52,3%; p <0,001). Dapat disimpulkan, tingkat keparahan gastroentrities pada anak usia <5 tahun menggunakan skor vesikari lebih tinggi pada diare akibat rotavirus positif daripada non rotavirus. Tingkat perlakuan dengan plan C lebih tinggi dari plan B dan A pada diare karena rotavirus. Hal ini berlawanan dengan mayoritas non rotavirus yang menggunakan plan A lebih tinggi dari plan B dan C.

Keywords: rotavirus - acute gastroentrities - treatment level - vesikari score - children

INTRODUCTION

Acute gastroenteritis is an inflammation of the stomach and intestines *caused by* viral or non viral infections leading to diarrhoea, vomiting and abdominal discomfort. Non viral acute gastroenteritis can be caused by bacteria, protozoa and helminths, whereas viral acute gastroenteritis can be caused by rotavirus, enteric adenovirus, calciviruses, astroviruses and enteroviruses.[1,2] Acute gastroenteritis remains a major cause of morbidity and mortality in children worldwide, accounting for 124 million clinic visits, 9 million hospitalizations, and 1.34 million deaths annually in children under 5 years old with more than 98% of these deaths occurring in the developing countries.[3-5]

Among causes of viral acute gastroenteritis in children, rotavirus is the most common cause with the most severe clinical manifestations and rapidly progressive lethal dehydration especially in infants and young children.[5-7] It causes approximately 111 million cases requiring only home care, 25 million clinic visits, 2 million hospitalizations, and 352,000–592,000 deaths in children under 5 years old.[8] Rotavirus gastroenteritis is transmitted primarily via fecal-oral contamination through person-to-person contact or contact with rotavirus contaminated items such as respiratory secretions. In developing countries 75% of children are infected prior to 12 months of age and attack rates peak at 6 months of age, but in developed countries, the first episode usually does not occur between 2 and 5 years of age. Once infection has occurred there is an approximate 24 to 72 hour incubation period followed by between 3 and 8 days of vomiting and diarrhea that may be accompanied by fever and abdominal pain and may last for as long as 3 weeks.[9]

The severity of clinical features of acute gastroenteritis is associated with its etiology. It was reported that patients with rotavirus-positive gastroenteritis have a higher incidence of vomiting compared to patients with rotavirus-negative gastroenteritis lead to the higher need for intravenous rehydration therapy and the duration of hospitalization.[10,11] However, the confirmation of viral etiology has not been applied in the clinical practice due to the limitations of laboratory facilities,

time-consuming and economical raisons. To overcome the limitations, the clinical severity scoring systems in viral gastroenteritis has been proposed as clinical predictors.[12,13] The Vesikari clinical severity scoring system is currently considered the best predictor tool for identifying the severity of acute gastroenteritis. In this study, we reported the Vesikari clinical severity score rotavirus-positive gastroenteritis compared to rotavirus-negative gastroenteritis in hospitalized children in Indonesia.

The severity of clinical features of acute gastroenteritis will determine the treatment level. World Health Organization (WHO) recommended the level of treatment for acute gastroenteritis based on its severity of dehydration i.e. treatment plan A, B and C. In this study, we also reported the level of treatment for diarrheal rotavirus-positive gastroenteritis compared to that rotavirus-negative gastroenteritis.

MATERIALS AND METHODS

Subjects

This was observational study with a cross sectional design using secondary data from Rotavirus Surveillance Study conducted by Soenarto *et al.*[14] from the Pediatric Research Office, Department of Pediatric, Dr. Sardjito General Hospital/Faculty of Medicine, Universitas Gadjah Mada, Yogyakarta from year 13 in five academic hospital in Indonesia i.e. Dr. Hasan Sadikin General Hospital, Bandung, West Java, Mataram General Hospital, West Nusa Tenggara, Dr. Sardjito General, Hospital, Yogyakarta, Sanglah General Hospital, Denpasar, Bali and Kulon Progo District Hospital, Kulon Progo, Yogyakarta. All children under 5 years old who experienced acute diarrhea and fulfil the inclusion and exclusion criteria were involved in this study. The inclusion criteria were all the children aged < 5 years with acute watary diarrhea who visited the 5 hospitals. The exclusion criteria were the stool sample was not enough to do the experiment in laboratory testing, incomplete variable on data or the parents and children did not agree to participate in the study.

Protocol of study

Subjects who fulfil the inclusion and exclusion were grouped into diarrheal rotavirus-positive gastroenteritis and rota-virus-negative gastroenteritis based on the laboratory viral examination results. A standardized clinical data of all subjects included the date of admission, age and sex of the patient, nutritional status, duration and frequency of diarrhea, duration and number of vomiting, previous treatment, status of dehydration, symptoms of illness were then collected. Nutritional status was determined based on ratio between weight and height according to WHO criteria i.e. malnutrition if weight and height ratio ≤ -2 SD; under nutrition if weight and height ratio -2 SD; well nutrition if weight and height ratio >2 SD. Acute diarrhea was defined as ≥ 3 loose stools within 24 h and for a duration of < 2 weeks. The clinical data were then used to calculate Vesikari clinical severity score as presented in TABLE 1.

TABLE 1. Vesikari clinical severity scoring system[13]

Parameter	1	2	3
Diarrhea			
Duration of diarrhea (day)	1-4	5	≥6
Maximum frequency per day	1-3	4-5	≥6
Vomiting			
Duration of vomiting (day)	1	2	≥3
Maximum number per day	1	2-4	≥5
Maximum body temperature (°C)	37.1-38.4	38.5-38.9	≥39
Degree of dehydration (%)	No	1-5	≥6
Treatment	Rehydration	Hospitalization	No
Severity rating scales	<7 (mild)	7-10 (moderate)	≥11 (severe)

Level of treatment was measured based on the WHO 2013 criteria that divided into 3 plans i.e. plan A for non dehydration, plan B for some dehydration and plan C for severe dehydration. The study has been approved by the Medical and Health Research Ethics Committee, Faculty of Medicine, Universitas Gadjah Mada, Yogyakarta.

Statistical analysis

Data were analysed using statistical SPSS version 19.0. Chi-square, multivariate and U-Mann Whitney and Kruskal Wallis analysis were performed to determine the significance of difference observed between two different groups of patients. Statistical significance assigned to p value of <0.05.

RESULTS

In period of 12 months from January to December 2013, 592 data of acute diarrhea patients from the computerized data base of the 5 academic hospital were gathered and selected. As much as 586 (99%) data were available for analysis and only 6 data were excluded due to not available of rotavirus examination data of the stools. Among 586 data analysed, 242 data were rotavirus-positive and 344 data were rotavirus-negative acute gastroenteritis. Characteristics and clinical symptoms of the patients are presented in TABLE 2. This study showed an association between rotavirus-positive gastroenteritis and nutritional status, number of vomiting and degree of dehydration ($p<0.05$). In contrast, no an association between rotavirus-positive gastroenteritis and age, sex, duration of diarrhea, frequency of diarrhea, duration of vomiting, treatment and temperature was observed ($p>0.05$).

TABLE 2. Characteristic and clinical symptoms of acute gastroenteritis in children under 5 years old in 5 hospitals in Indonesia

Characteristic	Total n=586	Rotavirus (+) n=242 (41.3%)	Rotavirus (-) n=344 (58.7%)	p
Age (median in month)	378.5	370.0	383.0	0.975
Sex of patient (n/%)				
Male	362(61.8)	147(25.1)	215(36.7)	0.667
Female	224 (38.2)	95(16.2)	129(22.0)	
Nutritional status (n/%)				
Malnutrition	34 (5.8)	7(1.2)	27(4.6)	
Undernourished	120 (20.5)	43(7.3)	77(13.1)	0.010
Well nourished	432 (73.7)	195(32.8)	240(41.0)	
Duration of diarrhea (n/%)				
1-4	486 (82.9)	205(35.0)	281(48.0)	
5	42 (7.2)	18(3.1)	24(4.1)	0.379
≥ 6	58 (9.9)	19(3.2)	39 (6.7)	
Maximum frequency of diarrhea (n/%)				
1-3	38 (6.5)	9(1.6)	29(4.9)	
4-5	200 (34.1)	84(14.3)	116(19.8)	0.073
≥6	348(59.4)	149(25.4)	199(34.0)	
Duration of vomiting (n/%)				
1	175 (29.9)	77(31.8)	98(28.5)	
2	105 (17.9)	49 (20.2)	56(16.3)	0.368
≥ 3	92(15.7)	50(20.7)	42(12.1)	
Maximum number of vomiting (n/%)				
1	17 (2.9)	6(2.5)	11(3.2)	
2-4	187 (31.9)	73(30.1)	114(33.1)	0.001
≥5	168 (28.7)	97(40.1)	71(20.6)	
Treatment (n/%)				
Rehydration	41 (7.0)	17(2.9)	24(4.1)	0.982
Hospitalized	545 (93.0)	225(38.4)	320(54.6)	
Temperature (n/%)				
<37.1	269 (45.9)	99 (16.9)	170 (29.0)	
37.1-38.4	245 (41.8)	114(19.5)	131(22.3)	0.143
38.5-38.9	44 (7.5)	19(3.2)	25(4.3)	
≥39	28 (4.8)	10(1.7)	18(3.1)	
Degree of dehydration (n/%)				
Not dehydration	151 (25.8)	48(8.2)	103(17.6)	
1-5%	390 (66.6)	171(29.2)	219 (37.4)	0.015
≥6%	45 (7.6)	23(3.9)	22(3.7)	

A multivariate analysis showed that nutritional status, number of vomiting and degree of dehydration could be considered as strong predictor factors for rotavirus-positive gastroenteritis ($p<0.05$) as presented in TABLE 3. Furthermore, the Vesikari score and clinical severity level of rotavirus-positive acute gastroenteritis was significantly higher than that of rotavirus-negative acute gastroenteritis ($p<0.05$) as presented in TABLE 4.

TABLE 3. Multivariate analysis of characteristic and clinical symptoms of acute gastroentritis in children under 5 years old in 5 hospitals in Indonesia

Variables	Coefficient regression	OR	p
Nutritional status	0.46	1.58	0.041
Number of vomiting	0.59	1.82	0.001
Degree of dehydration	0.51	1.67	0.011

TABLE 4. Vesikari score and severity level of acute gastroentritis between rotavirus-positive and rotavirus-negative in children under 5 years in 5 hospitals in Indonesia

Vesikari score	Rotavirus (+) n = 242	Rotavirus (-) n = 586	p	Multivariate (OR; p)
Score (mean ± SD)	11.47± 2.89	10.41±2.70	0.000	(1.14; 0.000)
Severity level (n/%)				
Mild<7	13 (5.4)	28 (8.1)		
Moderate 7-10	67 (27.7)	133 (38.7)	0.004	
Severe ≥11	162 (66.9)	183 (53.2)		

TABLE 5 shows the differance of the treatment level between rotavirus-positive and rotavirus-negative acute gastroenteritis. The children with rotavirus-positive acute gastroenteritis had higher treatment level compared with those rotavirus-negative ($p<0.05$). The children with rotavirus-positive majority had treatment plan C higher than plan B and A, whereas the children with rotavirus-negative majority had treatment plan A higher than plan B and C ($p<0.05$).

TABLE 5. Treatment level of acute gastroentritis in children under 5 years in 5 hospitals in Indonesia

Treatment level	Rotavirus (+)	Rotavirus (-)	p	Multivariate (OR; p)
Mean rank	376.61	277.24	0.001	(1.59; 0.002)
Plan A (n/%)	55 (30.9)	123 (69.1)	0.003	
Plan B (n/%)	166 (45.6)	198 (54.4)		
Plan C (n/%)	21 (47.7)	23 (52.3)		

DISCUSSION

Acute gastroenteritis in children remains a major health problem in both developing and developed countries.[8,9,15] Although the diseases is usually self-limited, it can cause severe clinical manifestations that need hospitalization especially in infants and young children. This study showed that rotavirus-positive gastroenteritis was more prevalent in male children than in female children in this study indicating that male children was more susceptible to rotavirus infection than female children. This result is in agreement with previous studies that reported boys are twice more suffered from rotavirus infection than girls and are more likely to be hospitalized.[16] Junaid *et al.*[17] reported that male children excrete rotavirus at a significant higher rate than female children in Nigeria with the ratio 1.8:1. Shim *et al*.[18] also reported that the number of rotavirus infected male was higher the number of rotavirus infected female in Korea.

Significantly association between rota-virus-positive gastroenteritis and nutritional status, number of vomiting and degree of dehydration was observed in this study ($p<0.05$). The children with rotavirus-positive gastroenteritis had low nutritional status compared to those with rotavirus-negative gastroenteritis. The association between nutritional status and susceptibility to rotavirus infection remains not well understood. Some studies provide evidences for the different association between nutritional status and rotavirus infection. Nitiema *et al.*[19] also reported that acute malnutrition is significantly associated with more severe symptoms in rotavirus-induced diarrhea and undernourished children also exhibits a prolonged duration of diarrheal episodes. In contrast, Mpabalwanit *et al.*[20] reported that rotavirus infection is more common in the hospitalized children with normal nutritional status than in those with malnutrition in Zambia. Furthermore, Das *et al.*[21] reported that rotavirus infection among overweight and obese children is higher compared to those well-nourished and malnourished children attending at Dhaka Hospital, Bangladesh. A recent longitudinal study in Bangladesh reported that healthy growth and development over the first 3 years of life are positively associated with a risk of symptomatic rotavirus infection.[22]

The identification of the etiology acute gastroenteritis is very useful to help determine appropriate therapy. Unfortunately, clinicians often have difficulties to distinguish between viral or non viral causes of acute gastroenteritis. Stool culture examination has been considered as a standard diagnostic to identify the etiology. However, it is time-consuming, expensive and not applicable. The clinical severity scoring systems has been applied as clinical predictors to determine clinical conditions of patients with acute gastroenteritis. The Vesikari clinical severity scoring system is the severity scale that was originally developed to evaluate the effectiveness and efficacy of rotavirus vaccines.[16] Recently, the system is used for predicting the viral or non viral pathogens in acute gastroenteritis.

This study showed that the Vesikari clinical severity score of rotavirus-positive acute gastroenteritis (11.47 ± 2.89) was significantly higher than that of rotavirus-negative (10.41 ± 2.70) ($p<0.05$) indicating severe symptoms were observed in children with rotavirus-positive. The Vesikari clinical severity score was supported with the clinical symptoms of patients where the children with rotavirus-positive gastroenteritis suffered more often vomiting (71.9% vs. 56.9%) and dehydration (80.2% vs. 70%) compared to

those with rotavirus-negative. This results showed that there is association between the Vesikari clinical severity score and clinical severity symptoms of the rotavirus infections indicating it could be used as diagnostic tool for predicting the rotavirus infection in acute gastroenteritis in children. However, the cut-off point values to achieve an acceptable overall diagnostic to distinguish between retrovirus and non retrovirus in acute gastroenteritis should be further optimized.

Vomoting and dehydration appeared to be more common in children with rotavirus-positive gastroenteritis in this study. This result is in agreement with previous studies reported by some authors.[16,17] These symptoms could determine the different of treatment level. Results of this study showed that the children with rotavirus-positive had treatment plan C higher than plan B and A, whereas the children with rotavirus-negative had treatment plan A higher than plan B and C. It was indicated that children with rotavirus-positive was more effective to be treated with treatment plan C, whereas children with negative-rotavirus was still effective to be treated with treatment plan A (at home) and plan B (treat some dehydration with oral rehydration salts/ORS).

Some diagnostic tools for the confirmation of rotavirus infection in children with gastroenteritis have been used routinely in diagnostic laboratories include enzyme linked immunosorbent assay (ELISA), latex agglutination assay (LA), polyacrylamide gel electrophoresis (PAGE), electron microscopy (EM) and real-time reverse transcription-polymerase chain reaction (RT-PCR).[23-26] However, these diagnostic tools are not always applicable in hospitals with limited laboratory facilities. Moreover, some of these diagnostic tools are expensive and time consuming. In regard of these conditions, the Vesikari clinical severity score system could be alternative diagnostic tool. The Vesikari clinical severity score system as a noninvasive test is recommended for children to avoid painful procedures such as venipuncture or invasive endoscopy. The Vesikari clinical severity score system could be useful to standardize assessment and to guide decision making among clinicians with differing levels of training by scoring the symptoms patients, because it can be calculated using clinical findings by trainees and experienced staff alike.

CONCLUSION

In conclusion, the Vesikari clinical severity score of rotavirus-positive acute gastroenteritis is significantly higher than that of rotavirus-negative. The children with rotavirus-positive majority receive treatment level plan C higher than plan B and A, whereas the children with rotavirus-negative majority recieve treatment plan A higher than plan B and C. It is demonstrated that the Vesikari clinical severity score can be used as a diagnostic tool for rotavirus acute gastroenteritis.

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