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Prevalence and clinical manifestations of rotavirus diarrhea in children of rural area of Thailand

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ABSTRACT

Introduction/ Background: Rotavirus diarrhoea is a leading cause of child death. It is a major concern in emerging nations. Many studies and analysis were executed for genetic assessment of rotavirus, however, very few studies from Thailand focused on clinical manifestation.

Aim: To estimate the prevalence and clinical manifestations of rotavirus diarrhoea among children of Ongkaluck district, Nakorn Nayok rural area of Thailand.

Method: Children aged ≤ 7 with acute diarrhoea as presenting symptom during January 2008 to October 2008 were enrolled in the study. Demographic data, clinical manifestation, vital parameters, laboratory investigation of blood, urine and stool were examined. Clinical signs of dehydration were graded as per WHO scale. Stool examination for rotavirus was tested with immunochromatography assay.

Results: By executing statistical analysis, results were observed among 56 enrolled children 37 % (n=21) had been diagnosed as rotavirus positive. Rotavirus positive children had moderate to severe dehydration (42.9 % vs 11 %, p-value = 0.01), vomiting as presenting symptom (92.2 % vs 68.8 %, p-value = 0.02) and absence of fever (38.1 % vs 68.6 %, p-value= 0.03) compared to non-rotavirus group respectively. The odds ratio of being rotavirus diarrhoea was increased 10.8 fold (95% CI 1.2 to 97.4; p-value = 0.03) provided children had vomiting. Rotavirus positive children were prone to develop hypokalemia (p-value= 0.04), acidosis (p-value < 0.001), loss of bicarbonate (p-value < 0.001) and higher blood urea nitrogen (p-value = 0.02) than non-rotavirus group. Children with rotavirus diarrhoea had neutrophilia and less WBC in stool sample compared to Non-rotavirus acute diarrhoea group.

Conclusion: Children admitted to the hospital, with moderate dehydration, absence of fever and vomiting as presenting symptoms are more prone to have rotavirus infection.

Keywords: Rotavirus, Acute diarrhoea, Dehydration, Hypokalemia, Children, Thailand

Introduction

World Health Organization (WHO) is very concern regarding child morbidity and mortality. Among leading causes of death, diarrhoea is the second most common cause for child death [1]. The Inter-Agency Child Mortality Estimation Group (IACMEG) of WHO estimates that in 2009, 8.1 million children under five died; with four most common causes viz. pneumonia, diarrhoea, malaria and neonatal conditions [1]. In emerging nation like Thailand, childhood acute diarrhoea has shown increasing trend (one million cases annually have been

reported in 2007) [2], though significant development in sanitation and water coverage.

Common aetiological factor for acute diarrhoea is virus. Rotavirus is well-known causative agent in developing nations [3] of severe gastroenteritis in young children which led to death [4]. As per Centres for Disease Control (CDC) review, rotavirus was found to have caused 39% of all diarrhoea hospitalizations and 611,000 deaths annually [3]. By the age of five, nearly every child in the world has been infected with rotavirus at least once [5]. Acute onset of dehydration is a classical manifestation of rotavirus diarrhoea. Acute diarrhoea is having propensity to demonstrate fatal course. This starts with gastroenteritis and having classical symptom of severe acute diarrhoea. Nowadays researchers focus on either treatment or phylogenetic analysis of rotavirus infection in child. There was lesser study which concerns regarding clinical and investigational manifestation of rotavirus diarrhoea. Previous study revealed that rotavirus and non-rotavirus diarrhoea had similar characteristics too [5]. However, there were few published studies about rotavirus in Asian children.

In the process of effective child survival through better aetiological identification approach, present study is directed to have insight regarding prevalence of rotavirus infection in Thailand and clinical presentation.

Materials and Methods

Study populations

This was a cross-sectional analysis carried out Nakorn Nayok area of Thailand. Study was executed on children aged ≤ 7 years who admitted to paediatric unit of Sriakharinwirot University Hospital, Nakorn Nayok with the diagnosis of acute diarrhoea between January 2008 and October 2008. Children belonged to Ongkaluck district, Nakorn Nayok, which is the rural area of Thailand. Decision of admission to the hospital and general management during admission were made by physicians.

Inclusion criteria were children aged ≤ 7 years, children who passed abnormal watery and/or mucous stool ≥ 3 times within previous 24 hours and duration of diarrhoea < 72 hours. Exclusion criteria were children who had evidence of systemic infection or neurological disturbances or history of convulsions, chronic medical conditions e.g. immunodeficiency chronic gastrointestinal conditions or presented with signs of severe dehydration according to composite score [6] and children who received any treatment with probiotics or any medications interfering with intestinal motility for the present illness. Children and parents of children who met the eligibility criteria were asked for enrolment in the study. Thorough informed consent was obtained from children's parents and assent was obtained from child. The present study was approved by the Institutional Ethics Committee of Faculty of Medicine of the Srinakharinwirot University.

Process execution

After enrolment in study, demographic characteristics and clinical history were obtained. Weight to the nearest 100 gram and height to the nearest milimeter were measured with accuracy. Clinical signs of dehydration were accessed by using clinical findings at the admission and were graded in to 3 scales according to composite score [6]. Patients who had no signs or symptoms were graded as normal or mild dehydration. Patients were graded as moderate dehydration if they had any signs or symptoms of thirsty, restless or irritable behaviour, decrease skin elasticity, or

sunken eyeball. Patients were graded as severe dehydration if they presented with shock or diminished consciousness or lack of urine output or had cool, moist extremities, or a rapid and feeble pulse, or low/ undetectable blood pressure and pale skin. The end of diarrhoea episode was defined as the time of the first of the 2 consecutive semi-formed stools or the last stool subsequent by 12 hours without stool.

Laboratory analysis and detection of rotavirus

Blood samples were collected and measured for serum sodium, potassium, chloride, bicarbonate, blood urea nitrogen (BUN), creatinine and complete blood counts (CBC). Acidosis was determined by serum electrolytes only. A routine urinary analysis and stool sample were analysed at admission by central laboratory unit. Stool examination for rotavirus was tested with immunochromatography assay (Rota-strip, Coris Bioconcept, Belgium). Utilized diagnostic Rota-strip has sensitivity 100%, specificity 98.1%, positive predictive value 100%, negative predictive value 98.2% and accuracy 99.1% [7].

Statistical analysis

The normal distribution of data was analysed by Kolmogorov-Sminov test. Normally distributed data were descriptively presented as mean and standard deviation (SD). Non-normally distributed data were descriptively presented as median and inter-quartile range (IQR). Pearson chi-square or Fisher exact test were used to compare proportions between the groups. Student's t-test and Mann-Whitney U test were used to compare the continuous data of the normal and non-normal distributed data, respectively. Binary logistic regression was used for risk prediction of having rotavirus diarrhoea when the significant symptoms were present. Statistical analysis was performed with SPSS 11.0 software package. Population was calculated based on alpha error of 5 % with predicted power of study 90%. Statistical significance was considered on the basis of p-value <0.05.

Results

Among 67 consented children for present study, only 56 were enrolled in the study. Remaining 11 were not examined for stool of rotavirus and excluded. Among 56, Twenty-one (37.5%) children who admitted with diarrhea had positive stool test for rotavirus. As mentioned in Table 1, boys were higher in proportion in both the groups 68.6 % in Rotavirus group and 52.4 % in Non-rotavirus. Median age of onset in both the groups was around 1 year. Weight and height of enrolled children were almost similar in both the group.

Clinical Manifestation of children was presented in table 2. Rotavirus diarrhoea children had significant higher rate of vomiting as presenting symptom while hospital admission (92.2%) than non-rotavirus group (68.6%). Lower prevalence rate of fever (p-value = 0.03) and higher rate of significant dehydration (p-value = 0.01) were observed in rotavirus group compared to non-rotavirus diarrhea group. Duration of diarrhea was observed similar in both groups. There was slightly high frequency of stools observed in rotavirus group (8) than non-rotavirus ones (5), with no statistical significance.

Investigational parameter was observed as per the table 3. In rotavirus diarrhea group, children demonstrated lower level of serum

potassium, and showed trend to have hypokalemia (p-value = 0.04) compared to other group. Rotavirus positive children also had lower level of bicarbonate (n= 52.4 %) and higher incidences of acidosis and blood urea nitrogen than rotavirus negative groups (n= 8.6 %). On hematological parameter, children of rotavirus group showed higher incidence of neutrophilia than compared group (p-value= 0.02) and lower incidence of the present of WBC in stool examination, which was higher in non-rotavirus diarrhea group (71.4 %, p-value = 0.01). Sodium loss was almost similar in both the group.

For risk determination and significance estimation, odds ratio and significance test of Wald was used (Table 4). The odds ratio of being rotavirus diarrhoea was increased by a factor of 10.8 (95% CI 1.2 to 97.4; p-value = 0.03) provided children had vomiting. The odds ratio of being rotavirus diarrhoea was decreased by a factor of 0.25 (95% CI 0.07 to 0.83; p-value = 0.02) if children had fever (body temperature > 37.8^{o}C).

There were no significant differences in management and outcomes of treatment between children infected with rotavirus or non rotavirus diarrhoea, described in table 5.

Antibiotics used were ceftriaxone (14), norfloxacin (3), midecamycin acetate (1) and amoxicillin (1). Probiotics were *Lactobacillus acidophilus* (minimum of 10^{9}/ capsule) and *Bifidobacterium bifidum* (minimum of 10^{9}/ capsule) (Infloran®, Berna, Switzerland).

Discussion

Present study provides insight regarding acute diarrhoea in Thai children and prevalence of rotavirus diarrhoea in them. Among admitted 56 children 21 were diagnosed with rotavirus positive stool test, which comprised 37.5 %. This says common pathogen for acute diarrhoea in rural area of Thailand is still rotavirus, which infects almost one third child population. Though there is no statistical significance (p value = 0.14), median age at the time of diagnosis was 16 months in rotavirus group which was slightly higher than non-rotavirus group (11 months). Both groups had median age falling under infants. Boys were having more predominance to get diarrhoea (n=35) than girls. The contributing factor might be rural area as having more male child in census [8].

Taking clinical manifestations in account, rotavirus diarrhoea group had moderate to severe dehydration than non-rotavirus group. This could be reasoned as rotavirus leads to mal-absorption, which hampers fluid absorption and aggravates dehydration [9]. Rotavirus throws endotoxins into gut wall, this leads to activation of Enteric Nervous System (ENS). Affected ENS by endotoxins significantly influences gut motility and propels them into both ways of gastrointestinal [10]. Hence, rotavirus group developed moderate to severe diarrhoea, with vomiting as predominant or presenting feature. Vomiting was present in 92.2 % cases of rotavirus diarrhoea rather than non-rotavirus group of diarrhoea (68.6 %). This toxin propels motility more in aboral direction [11] and hence frequency of stools in 24 hours was higher in rotavirus group of children (8) compared to non-rotavirus group (5). Fever was absent in rotavirus group of children in present study, which was contradictory to the established literature. Previous studies depicted that fever was one of the classical symptom of rotavirus diarrhoea [12]. This was not the case in presented study, as rotavirus group had 38 % of children only with fever compared to non-rotavirus group (68%). Absence of fever in rotavirus group is novel and significant finding of this study. This might have implication on management of

rotavirus infection than non-rotavirus ones. Duration of diarrhoea was similar in both the groups, without statistical significance.

Rotavirus diarrhoea group of children were having higher potassium loss. It could be because of moderate dehydration, led to electrolyte imbalance [13]. As non-rotavirus group had mild diarrhoea, chances of electrolytes loss were obviously lower. In addition to potassium, bicarbonate ions were lost more in rotavirus group of children, which ultimately developed acidosis [13]. Infection to gut cells lead to lesser fluid absorption could be a possible explanation for developed acidosis. Moderate dehydration led to higher nitrogen in blood in form of urea [14]; which was depicted in rotavirus group. Rotavirus infection like other infection also attacks on defence system of host. Study of result too in line with previous study, as patients having neutrophilia and less presence of WBC in stool were more in rotavirus group [5]. Physicians had focused treatment on symptomatic relief only; hence there were no significant changes in management of diarrhoea in both the groups. Common treatment protocol was followed including symptomatic treatment with antibiotics [15]. Using antibiotics, though universally accepted, it is not the right choice. This could be a fallacy to use antibiotics in viral conditions. Despite this fact, it has been used widely with the justification to prevent secondary infection [16]. To tap up the loss of gut flora, *Lactobacillus acidophilus* and *Bifidobacterium bifidum* were used. Standard guideline for treating acute diarrhoea [17] mentions that non-therapeutic approach with oral rehydration solution and symptomatic support should be primary treatment. For persistent diarrhoea, antibiotics should be used after culture and sensitivity testing. For rotavirus diarrhoea, same approach is to be used for manegment. Availability of rotavirus vaccine is the only differeing management than non-rotavirus diarrhoea for prevention [17].

Risk determination through odds ratio said having rotavirus diarrhoea was 10 times higher in preponderance if patient had vomiting and absence of fever. Regression logistic also showed significance with the combination of vomiting and absence of fever with rotavirus diarrhoea.

Conclusion

Rotavirus diarrhoea, being one of the most common causes of child death, needs identification of clinical manifestation and prevalence. Present study has established the direction regarding risk factors of presented symptoms. In rural area of Thailand, children are infected more with rotavirus infection and presented as acute diarrhoea. Moderate dehydration, absence of fever and vomiting are predisposing signs of rotavirus diarrhoea in children.

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Conflict of interest: The authors have no conflict of interest to report.

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Table 1: Demographic data of 56 children

	Non-Rotavirus diarrhoea (N = 35)	Rotavirus diarrhoea (N = 21)	p-value
Age* (months)	11.0 (10.0)	16.0 (23.5)	0.14
Boy; n (%)	24 (68.6)	11 (52.4)	0.18
Weight* (kg)	9.1 (5.0)	10.0 (4.5)	0.61
Length/ height* (cm)	73.0 (25.0)	83.0 (29.5)	0.11

*Results are presented as median (interquartile range)

Table 2: Clinical Manifestation observed in enrolled children

	Non-Rotavirus diarrhoea (N = 35)	Rotavirus diarrhoea (N = 21)	p-value
Hydration status; n (%)			
• Mild or no dehydration	31 (88.6)	12 (57.1)	0.01
• Moderate dehydration	4 (11.4)	9 (42.9)	0.01
Numbers of stools in previous 24 hours*	5 (3)	8 (6)	0.22
Duration of diarrhoea* (hours)	24 (60)	24 (60)	0.77
Presence of vomiting; n (%)	24 (68.6)	20 (92.2)	0.02
Fever; n (%)	24 (68.6)	8 (38.1)	0.03

*Results are presented as median (interquartile range)

Table 3: Investigational results observed

	Non-Rotavirus diarrhoea (N = 35)	Rotavirus diarrhoea (N = 21)	p-value
Sodium (mmol/L); mean (SD)	134.6 (3.0)	134.8 (2.4)	0.86
Hyponatremia (sodium <135 mmol/L); n (%)	17 (48.6)	9 (42.9)	0.78
Potassium (mmol/L); mean (SD)	4.2 (0.6)	3.9 (0.5)	0.04
Hypokalemia (potassium <3.5 mmol/L); n (%)	4 (11.4)	5 (23.8)	0.27
Bicarbonate (mmol/L); mean (SD)	19.1 (3.3)	15.5 (3.6)	<0.001
Chloride (mmol/L); mean (SD)	99.3 (2.9)	100.5 (3.6)	0.18
Acidosis (bicarbonate <15 mmol/L); n (%)	3 (8.6)	11 (52.4)	<0.001
Urea nitrogen (mmol/L)	3.8 (1.6)	5.1 (2.4)	0.02

Creatinine* (μmol/L)	44.2 (8.8)	44.2 (17.6)	0.92
Urine specific gravity*	1.015 (0.010)	1.015 (0.010)	0.30
Haemoglobin (g/L); mean (SD)	117.3 (11.9)	121.7 (12.6)	0.19
White blood cell count* ($x10^9$/L)	10,600 (5,100)	13,000 (6,500)	0.23
% neutrophil*	48.9 (32.0)	69.7 (34.8)	0.02
% lymphocyte*	43.8 (30.0)	20.7 (38.6)	0.04
Presence WBC in stool; n (%)	25 (71.4)	7 (33.3)	0.01
Presence of RBC in stool; n (%)	7 (20.0)	2 (9.5)	0.46

*Results are presented as median (interquartile range)

Table 4: Odds ratio of being rotavirus diarrhoea by the variables of vomiting and fever

Symptom	B	S.E.	Wald	df	Sig.	Exp(B)	95.0% C.I.for EXP(B)	
							Lower	Upper
Vomiting	2.381	1.122	4.508	1	.034	10.818	1.201	97.451
Fever (BT>37.8)	-1.408	.622	5.114	1	.024	.245	.072	.829
Constant	-1.779	1.080	2.715	1	.099	.169		

Table 5: Treatment and outcomes

	Non-Rotavirus diarrhoea (N = 35)	Rotavirus diarrhoea (N = 21)	p-value
Duration of diarrhoea during admission (hours)	40.5 (35.5)	39 (45.5)	0.78
Diarrhoea < 24 hours; n (%)	11 (28.6)	8 (38.1)	0.72
24-48 hours	13 (37.1)	6 (28.6)	
> 48 hours	12 (34.3)	7 (33.3)	
Number of stool during admission	9 (11.5)	6 (9.0)	0.23
Total fluid therapy (ml/kg/hr)	5.1 (3.0)	5.9 (3.1)	0.62
Antibiotics used; n (%)	14 (40.0)	5 (23.8)	0.26
Probiotics used; n (%)	21 (60.0)	16 (76.2)	0.26