

# The Epidemiology and Burden of Childhood Rotavirus Infection in a Tertiary Hospital in Sabah, Malaysia

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## SUMMARY

We aimed to determine the epidemiology and burden of rotavirus (RV) gastroenteritis (GE) in children requiring hospital care in an urban setting in Sabah, Malaysia. A prospective study of all patients younger than 12 years of age admitted with acute GE to Queen Elizabeth Hospital, Sabah, over a six-month period (October 2005 to March 2006) was conducted. During the study period, a total of 167 children with acute GE who had stool samples examined for RV were studied. RV accounted for 16% of all diarrhoeal cases, and 1.7% of all admissions to the children's wards during the study period. There was no difference in severity of GE between RV and non-RV groups. RV infection is a common cause of childhood GE requiring hospital care in Sabah.

## KEY WORDS:

Childhood rotavirus infection, Sabah

## INTRODUCTION

Diarrhoeal disease is a major cause of morbidity and mortality in children the world over<sup>1</sup>. World Health Organization (WHO) estimates that each year approximately 18% of all deaths in children younger than five years of age could be attributable to diarrhoeal disease<sup>1</sup>. An estimated 40% of all diarrhoeal disease is caused by rotavirus (RV)<sup>2</sup>. Each year, RV causes approximately 111 million episodes of gastroenteritis (GE) requiring only home care, 25 million clinic visits, 2 million hospitalizations, and 444,000 deaths in children younger than 5 years of age<sup>3</sup>.

The development of a RV vaccine provides the potential to improve the morbidity and mortality of RVGE. Many studies have been performed to determine the burden of RVGE and the potential cost-effectiveness of RV vaccines<sup>4,6</sup>. In Malaysia, gastrointestinal infection was the second most common indication of hospital admission to government hospitals<sup>7</sup>. RV is the most common cause of childhood GE<sup>7-10</sup>. Hospital-based studies have shown that RV accounts for 24 - 35% of admissions for childhood GE in Malaysia<sup>8, 11</sup>. The cost of providing inpatient care for childhood rotavirus GE in Malaysia was estimated to be US\$1.8 million annually<sup>6</sup>.

To date, there has been no study documenting the epidemiology or burden of RVGE in Sabah, East Malaysia. A prospective study was carried out at the paediatric department of a tertiary referral hospital in Sabah to

determine the epidemiology, morbidity and burden to hospital resources in patients younger than 12 years of age with RVGE who required in-patient care.

## MATERIALS AND METHODS

This was a six-month prospective, observational study conducted from 1st October 2005 to 31st March 2006, at the children's wards of Queen Elizabeth Hospital, which is the major tertiary referral hospital in the state of Sabah. All children up to 12 years of age with acute GE on admission were enrolled in the study. Acute GE was defined as the presence of loose stools of three or more episodes during a 24-hour period lasting less than 10 days' duration. Children undergoing chemotherapy, who were immunosuppressed and newborn infants aged one month and below, were excluded. In addition, children with duration of diarrhea lasting more than 10 days prior to admission were excluded as well.

Clinical features of patients were recorded using standardized data sheets. Junior medical staffs (medical officers and house officers) were trained to interview the parents during admission. The following data were collected: duration of diarrhoea before admission, presence of vomiting and fever, blood in the stool, anthropometric data and severity of dehydration on admission as noted by clinical examination were recorded. Failure to thrive was defined as the weight below the 3rd centile when compared with age- and sex-appropriate WHO growth charts<sup>11</sup>.

Severity of dehydration was classified according to WHO criteria<sup>12</sup>. Severe dehydration was defined as having at least two of the following features: lethargic or unconscious, sunken eyes, not able to drink/drinks poorly, skin pinch goes back very slowly (> 2 sec). Some dehydration was defined as having at least two of the following: restlessness and irritability, sunken eyes, drinks eagerly, thirstily when offered fluids, and skin pinch goes back slowly. No dehydration as having not enough features to classify according to the above criteria<sup>12</sup>.

Stool samples were collected routinely for all patients on admission and tested for RV using Rota-Strip®, which is an immunochromatographic test for RV (CORIS BioConcept, Gembloux, Belgium). The test has a sensitivity of 97.3% and a specificity of 97.7% for the detection of RV in stool as compared to an ELISA test<sup>14</sup>.

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Student's t-test was used for continuous data with normal distribution. Chi-square test and Fisher's Exact test was used for categorical data. A p-value of < 0.05 was taken as significant.

## RESULTS

### *Incidence of rotavirus gastroenteritis*

During the study period, a total of 182 patients aged 12 years or younger with acute GE were admitted to the children's wards of Queen Elizabeth Hospital, Kota Kinabalu. Of these, 15 patients had no stools samples collected for RV, the main reason being cessation of diarrhoea on admission. Stool samples of the remaining 167 (91% of 182) patients were examined for RV, and was positive in 27 (16%) of stools examined.

During the same period, a total of 1546 children aged younger than 12 years old were admitted to the paediatric wards of Queen Elizabeth Hospital, Kota Kinabalu for medical care. Thus paediatric GE accounted for 11.7% of all admissions during the study period while RV GE accounted for 1.7% of the total admissions.

### *Demographics*

Table I shows the demographic features of the patients studied. RVGE was more common in children younger than two years of age with 66% of RVGE occurred in this age group. There was a slight female preponderance with the male to female ratio being 1:1.2.

Bajau ethnic group as well as non-citizens formed the two largest ethnic groups of patients with acute GE, reflecting the ethnic distribution of the population utilizing the services provided by Queen Elizabeth Hospital, Sabah.

### *Clinical features and complications*

Generally there was no statistically significant difference between the RV status in the stool and the clinical features (fever, vomiting, presence of bloody stools, presence of failure to thrive) of patients admitted with acute GE Table II. Most patients (n=121, 72%) presented within the first three days of the onset of illness. Two-third (68%) of children with RVGE had moderate to severe dehydration upon admission. Generally, all patients with RVGE had diarrhoea which resolved within six days of the onset of illness. No deaths due to acute GE was observed in this present study. Other complications such as lactose-intolerance and cow's milk protein allergy were not looked at as it was not within the scope of the study.

A sub-analysis of RV-positive patients according to age group (below two years of age vs. above two years of age) was performed. There was no statistically significant difference in the clinical features for patients aged two years and below as compared to those who were older than two years of age (Table III).

## DISCUSSION

The development of RV vaccines has spurred the interest of study on the burden of RV infection in Malaysia. Hsu *et al* estimated that in Malaysia, 1 in 61 children will be

hospitalized for RV disease and that 1 in 37 children will seek treatment as an outpatient annually<sup>15</sup>. Lee *et al* estimated that each year, the financial burden of providing in-patient for RVGE in Malaysian children was US\$1.8 millions<sup>6</sup>.

Our study confirmed that RV is an important aetiological agent causing acute GE in children who required hospital care in Kota Kinabalu. This is similar to other studies from Malaysia<sup>6, 8-11, 15</sup>. Lee *et al* showed that rotavirus is the most important cause of severe diarrhoea in children in Malaysia<sup>8, 11</sup>.

In addition, our study also revealed that acute GE caused RV is an important cause of hospital admission, and hence hospital resource utilization. During the study period, acute and RVGE accounted for 11.7% and 1.7% of all paediatric admissions to the children's wards of Queen Elizabeth Hospital, respectively. The corresponding figures noted by Lee *et al* were 8.2% and 1.2%, respectively<sup>11</sup>.

A 12-month study in 2002 revealed that RV was responsible for about 30% of all admissions for childhood GE in University Malaya Medical Centre, Kuala Lumpur and Hospital Sultanah Aminah (HSA), Johor Bahru, respectively<sup>7</sup>. These figures are much higher than the 16.2% we observed during our six month study. One explanation for this discrepancy is the fact that the study done by Lee *et al* included the period of January 2002 to March 2002, during which time there was a period of hyperendemic RVGE in those two urban centres<sup>8</sup>. An earlier study done in University Malaya Medical Centre, Kuala Lumpur from 1996 to 1999 had shown that rotavirus accounted for 24% of all acute GE admissions<sup>11</sup>.

Another possible explanation is the seasonal variation of RV infection. Year long studies have shown that rotavirus infection generally peaks during the rainy season in Malaysia<sup>8, 11</sup>. As the study period of the present study covered only a period of six months, this seasonal variation may have accounted for the lower incidence noted.

As no stool samples for other enteropathogens were studied in the present study, it is conceivable that there might have been an outbreak of GE caused by other viral or bacterial

Table I: Demographics of study group (n=167)

Ethnic Group	N (%)
Bajau	44 (26.3)
Kadazan	26 (15.6)
Dusun	8 (4.8)
Murut	1 (0.6)
Brunei	2 (1.2)
Chinese	11 (6.6)
Malay	5 (3.0)
Others	37 (22.2)
Non-local	33 (19.8)
<b>Gender</b>	
Male	95 (56.9)
Female	72 (43.1)
<b>Age (months)</b>	
0 – 24	111 (66.5)
25 – 60	34 (20.4)
>60	22 (13.2)

**Table II: Comparison between of rotavirus-positive and negative childhood acute gastroenteritis admitted to the children's ward, Queen Elizabeth Hospital, Sabah**

		Rotavirus Positive	Negative	p
Total		27 (16.2%)	140 (83.8%)	
Gender	Female	14 (51.9%)	58 (41.4%)	0.317
	Male	13 (48.1%)	82 (58.6%)	
Age group (months)	0-24	18 (66.7%)	93 (66.4%)	0.924
	25-60	6 (22.2%)	28 (20.0%)	
	> 60	3 (11.1%)	19 (13.6%)	
Other siblings with diarrhoea	Yes	0 (0.0%)	16 (11.4%)	0.077
	No	27 (100.0%)	124 (88.6%)	
Presence of failure to thrive	Yes	8 (29.6%)	48 (34.3%)	0.639
	No	19 (70.4%)	92 (65.7%)	
Documented fever during hospital stay	Yes	21 (77.8%)	92 (65.7%)	0.220
	No	6 (22.2%)	48 (34.3%)	
Vomiting	Yes	24 (88.9%)	99 (70.7%)	0.057
	No	3 (11.1%)	41 (29.3%)	
Presence of blood in stool	Yes	3 (11.1%)	17 (12.1%)	1.000
	No	24 (88.9%)	123 (87.9%)	
Degree of dehydration on admission	None / Mild	7 (25.9%)	45 (32.1%)	0.099
	Some	19 (70.4%)	71 (50.7%)	
	Severe	1 (4.0%)	24 (17.1%)	
Duration of diarrhoea prior to admission (days)	1 to 3	19 (70.4%)	102 (72.9%)	0.102
	4 to 6	8 (29.6%)	24 (17.1%)	
	>7	0 (0.0%)	14 (10.0%)	
Total number of days of diarrhoea (prior and during admission)	1-3 days	20 (74.1%)	86 (61.4%)	0.133
	4-6 days	7 (25.9%)	36 (25.7%)	
	>7days	0 (0.0%)	18 (12.9%)	
Total days of admission	1-2 days	9 (33.3%)	43 (30.9%)	0.096
	3-4 days	9 (33.3%)	31 (22.3%)	
	5-6 days	7 (25.9%)	24 (17.3%)	
	>7 days	2 (7.4%)	41 (29.5%)	

**Table III: Comparison of clinical features in Rotavirus positive patients according to age group**

		Age < /= 2 Years n (%)	> 2 Years n (%)	p
Total		19 (61.3%)	12 (38.7%)	
Gender	Female	9 (47.4%)	8 (66.7%)	0.461
	Male	10 (52.6%)	4 (33.3%)	
Documented fever during hospital stay	Yes	15 (78.9%)	7 (58.3%)	0.253
	No	4 (21.1%)	5 (41.7%)	
Vomiting	Yes	16 (84.2%)	10 (83.3%)	1.000
	No	3 (15.8%)	2 (16.7%)	
Presence of blood in stool	Yes	3 (15.8%)	0 (0.0%)	0.265
	No	16 (84.2%)	12 (100.0%)	
Degree of dehydration on admission	None / Mild	6 (31.6%)	4 (33.3%)	0.722
	Some	12 (63.2%)	8 (66.7%)	
	Severe	1 (5.2%)	0 (0.0%)	

pathogen during the six-month period of the study. This could account for the low RV positivity.

A recent study by Albano *et al* noted that GE was more severe in RVGE than in RV negative children<sup>16</sup>. However we did not find any significant difference between RV and non-RV groups. This may be due to the relatively small number involved in the present study.

The most significant limitation to this study was the relatively short duration of study period, i.e. six months only. The fact that RV shows a seasonal variation may account for underestimation or overestimation of the burden of disease.

Another limitation is that we did not test for the presence of other organisms causing GE. Although RV is still a cause of GE in a significant number of children, we are unable to comment on whether it is the most common cause. Other bacterial, viral and parasital causes of GE were not performed for the present study.

This study also did not include children presenting with GE who did not require admission. This group of children may have different enteropathogens compared with those requiring admission.

The observed difference in the results as compared to previous data could be the difference in the methods

employed in RV detection. In addition the inclusion/exclusion criteria of sampled patients varied in different studies.

In conclusion, in this preliminary study, for the first time it is demonstrated that RV is an important cause of childhood GE requiring hospital care in Sabah, being responsible for 16.2% of all community-acquired childhood GE. This finding is similar to other studies from Malaysia.

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