CLINICAL AND LABORATORY CHARACTERISTICS OF ROTAVIRUS – ASSOCIATED DIARRHOEA

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SUMMARY

A prospective clinical study comparing 74 cases of rotavirus-associated diarrhoea and 100 cases of non-rotavirus-associated diarrhoea revealed a higher incidence of vomiting to be the only significant difference in the former. Bloody stools were seen in about 5–10%, fever in about two-thirds and respiratory symptoms in a quarter of cases regardless of aetiology. The overwhelming majority had mild dehydration of the isonatremic type. Hypokalemia was noted in a quarter of the cases in both groups.

INTRODUCTION

Diarrhoeal diseases are still a major cause of mortality and morbidity in children, particularly in developing countries. In West Malaysia, in 1980, "gastroenteritis" accounted for 4.27% of admissions to Government hospitals for all ages, being the third common cause of admission. In the same year, diarrhoeal diseases and enteritis accounted for 6.5% of all deaths in the zero to four year age group of children.[1]

Previous studies on the clinical features of HRV diarrhoea have revealed many common characteristics.[2,3] However, some conflicting observations on certain features such as the nature of stools, vomiting and upper respiratory tract involvement have also been noted.[3,4] Maiya and Kumar did not find any clinical difference between HRV positive and HRV negative cases.[5,6] Hieber noted a higher proportion of fever.[2] Rodriguez in Washington, Ryder in Bangladesh and Quak in Singapore have reported a higher incidence of vomiting.[3,7,8]

From these reports, it appears that the clinical features of HRV diarrhoea is not unequivocal and may have some regional variations. This paper reports the results of a prospective study comparing the clinical characteristics of HRV positive and HRV negative diarrhoea in Malaysian children.

We have earlier reported the incidence of rotavirus-associated diarrhoea in Malaysian children to be 46.3% based on a study of 587 cases.[9]

MATERIAL AND METHODS

Children admitted to the Gastroenteritis Ward (Ward 3, UKM), General Hospital, Kuala Lumpur, with diarrhoea of less than two weeks' duration between November 1981 and November 1982, were enlisted in the study. These admission were on every alternate day. The admissions on the other days went to the Government unit which was not enlisted in the study. Cases where adequate clinical or laboratory data were not obtainable were dropped from the study.

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A detailed history and physical examination findings were recorded in specially prepared standard forms. Dehydration was assessed clinically as mild (< 5%), moderate (5–10%) or severe (> 10%) according to standard paediatric criteria. The following investigations were carried out on admission: haemoglobin, total white and differential count (TWDC), blood urea, serum sodium, serum potassium, stool culture for bacterial pathogens, and stool test for rotavirus. Other tests including stool for ova or cyst were done selectively.

The Rotazyme Rotavirus Diagnostic Kit (Abbott Laboratories N. Chicago, Illinois) was used to detect rotavirus antigen in stools using the ELISA technique (enzyme-linked immunoassay). This technique utilizes the "Sandwich" principle or solid phase immunoassay technique to detect rotavirus antigen in stools. Plastic beads coated with guinea pig antibody provided the solid phase. A 200μl sample of each supernatant prepared from the stool was tested for the presence of antigen by the standard method. After incubation, the beads were washed thoroughly with jets of water as an additional precaution to remove nonspecific antigens. Assay results were read by the naked eye utilizing the colour chart provided. The readings ranged from 0 to ++++. A reading of (+) was taken as positive for rotavirus. Ten specimens each positive for rotavirus to different degrees (0 to ++++) by ELISA were examined under the Electron Microscope (EM).

Rotavirus was detected in all specimens (2+) and above. No viruses were seen in the weak (1+) or from any of the ten specimens negative for rotavirus by ELISA (Table I).

TABLE I

COMPARISON OF THE SENSITIVITY OF ELISA AND EM IN THE DETECTION OF ROTAVIRUS IN STOOLS

Degree of Positive Rotavirus by ELISA	Proportion of Rotavirus cases positive by EM*
4+	10/10
3+	10/10
2+	10/10
1+	0/10
0	0/10

*Stool specimens clarified and concentrated by ultra-centrifugation were negatively stained with 2% phosphotungstic acid.

We used the ELISA test in our study because we found it to be a simpler and more sensitive test than electron microscopy. We have tried to minimise the chances of false positive results by thoroughly washing the plastic beads with water jets after incubation with the stool specimen.

RESULTS

One hundred-and-seventy-four patients, aged between one month to six years, were studied. The proportion of children in a particular age group were: less than 1 month – 4.1%; one month to one year – 64.7%; one to two years – 18.6%; two to six years – 12.7%. The results are tabulated in Tables II, III and IV.

The most significant clinical characteristic in the HRV–positive (HRV+) group is the incidence of vomiting which was found in a much higher proportion in the HRV+ group (Table II). However there was no difference in the number of vomiting episodes per day between the groups. The majority (70%) had less than four vomiting episodes per day (Table III).

TABLE II

CLINICAL FINDINGS OF HRV+ AND HRV– DIARRHOEAL PATIENTS

Clinical characteristics	% with each clinical characteristic	
	HRV+ group (n = 74)	HRV– group (n = 100)
Vomiting	75+	45+ *
Stools:		
Watery	87	78
Semi-loose	13	12
Mucoid	21	27
Bloody:	10	15
– with bacteria pathogen	2.5	4
– with parasites	2.5	2
– without bacterial or parasite pathogens	5.0	9
Dehydration:		
mild (<5%)	89	88
moderate (5–10%)	11	11
severe (>10%)	0	1
Fever (37.3°C):	69	66
to 38°C	44	45
>38°C	56	55
Lethargy	12	15
Cough	14	18
Upper respiratory tract infection:	22	25
tonsillitis	5	2
rhinitis	5	2
pharyngitis	3	11
otitis media	1	2
Lower respiratory tract infection	3	4

* X^2 test – significant difference $p < 0.005$.

TABLE III
FREQUENCY AND DURATION OF DIARRHOEA AND VOMITING

Clinical Features	HRV status	Frequency/duration						
		mean	1–2	3–4	5–6	7–8	9–10	10
Duration of diarrhoea (day*)	+	5.1	11†	41	25	11	7	5
	–	6.8	3	38	24	13	9	13
Diarrhoeal episode/day**	+	6.9	4	21	32	14	23	6
	–	6.5	2	29	32	14	12	11
Vomiting episode/day**	+	3.5	44	29	17	4	0	6
	–	3.2	44	28	20	4	2	2

† % of total cases
* total number of days with diarrhoea before and after admission.
** on admission

TABLE IV
LABORATORY INVESTIGATIONS

	% with each laboratory characteristic	
	HRV+ (n = 74)	HRV– (n = 100)
Total white and differential cell count (TWDC): mm^3		
5,000 – 10,000	84	81
>10,000	7	9
<5,000	7	10
Urea (7 mmol/l)	15	6
Sodium:		
130 – 150 mmol/l	90	80
<130 mmol/l	6	19
>150 mmol/l	4	1
Potassium:		
3.5 – 5.5 mmol/l	68	70
<3.5 mmol/l	28	27
>5.5 mmol/l	4	3
Bacterial pathogens in stool:	8	18
Enteropathogenic *E. coli*	4	6
Shigella	3	5
Salmonella	1	7

The mean duration of diarrhoea (from onset at home to termination in hospital) was 5.1 days for the HRV+ group, and 6.8 days for HRV– group. About two-thirds of the cases in both groups had diarrhoea between three to six days and one-third more than six days. The mean frequency of diarrhoeal episodes was 6.5 per day in the HRV+ and 6.9 per day in HRV– groups. About 50% had between three to six episodes with the remainder having more than six episodes per day.

The majority of the patients had watery stools in both HRV+ (87%) and HRV– (78%) groups. Semi-loose stools were noted in about 12% of both groups. There was a small proportion of patients with bloody diarrhoea in both groups (10% and 15%). In both groups of bloody diarrhoea, *Shigella* and *Salmonella* species were the sole bacterial causes while *Trichuris trichura* was the major parasitic cause, apart from a solitary case due to *Entamoeba histolytica.* Frank bloody stools were the characteristic of diarrhoea caused by *Shigella* species, *Entamoeba histolytica* and *Trichuris trichura,* while the rest of the diarrhoeas had blood streaking of stools only.

The proportion with fever was the same in both groups (about two-thirds). Half of them had high grade fever (> 38°C) and the remaining half low grade fever.

Almost 90% of the cases in both groups had mild dehydration. The remaining 10% had moderate dehydration. Only 1% of the HRV– group and none in the HRV+ group had severe dehydration.

Cough was seen in about 15% of cases in both groups. Clinical evidence of URTI was observed in one quarter of the patients in both groups. Lower respiratory tract involvement was seen in 3–4% of both groups. About 12 – 15% of the cases were noted to be lethargic on admission.

Laboratory investigations revealed that the majority of the cases had isonatremic dehydration (90% HRV+ and 80% HRV–). Hyponatremic dehydration was second with the proportion being 6% in the HRV+ and 19% in the HRV– groups respectively. The incidence of hypernatremic dehydration was much smaller (5% and 1% respectively).

Hypokalemia was seen in about one quarter of the cases in both groups and the proportions were similar (28% HRV+ and 27% HRV–) A smaller percentage had hyperkalemia (HRV+ 3% and HRV– 4%).

The majority of the cases had a normal TWDC in both groups. Elevated blood urea was seen in 15% of the HRV+ and 6% of the HRV– groups respectively.

Bacterial enteropathogens were found in 12% of all cases; in 8% of the HRV+ group and in 18% of the HRV– group. In about 45% of cases, no organisms were isolated.

DISCUSSION

A higher incidence of vomiting was the only significant clinical difference in the children with HRV– associated diarrhoea. This observation is supported by other studies done in temperate and tropical climates.[3,7,8] However, we did not notice any difference in the frequency of vomiting in the two groups as reported by some workers.[2,3] The mean duration of HRV-associated diarrhoea was lower in our children (five days as compared to eight and nine days in Hiebers group) but compares similarly to others.[7,10] Stool frequency in both groups was the same. The vast majority had watery diarrhoea, a typical feature of HRV– associated diarrhoea noted by previous workers.[3,4,11] While blood was seen in 10% of the HRV+ positive cases, in half of them no associated bacterial pathogens were detected. Iynkaran *et. al.,* reported a 2.8% incidence of bloody diarrhoea associated with viral aetiology. Clemens et. al., in a randomised surveillance study from Bangladesh reported bloody and non-watery diarrhoea as a different manifestation of the expanding clinical spectrum of Rotavirus diarrhoea.[13] However, in the above studies and ours, *Campylobacter jejuni* as a possible cause of the bloody diarrhoea was not excluded.[12,13]

There was no case of severe dehydration with the HRV- associated diarrhoea. This is in agreement with some studies but in variance with others where it accounted for 20–40% of the cases.[14,15] The paucity of severe dehydration may be due mainly to the shorter duration of diarrhoea, where being the major city hospital, urban patients tend to seek treatment early unlike the rural population. However the blood urea was twice as high in the HRV+ group which is in agreement with the findings of other studies.[2,3] The majority in both groups had isonatremic dehydration, followed by hyponatremic dehydration and in less than 4% was hypernatremic dehydration noted. In Rodriguez series, hypernatremic dehydration was second and no hyponatremic cases were noted. The relative proportions in the osmolarity of the dehydration appears to have regional variations though isonatremia appears to be the commonest.[14,15] Hypokalemia seen in a quarter of our patients, occasionally caused gut ileus and muscle weakness. Maiya[5] found hypokalemia in 20% of the total cases regardless of aetiology while Iyngkaran[12] reported in 12% of cases with viral aetiology.

Evidence of respiratory tract infection was found in about a quarter of our cases. However, there was no difference in the incidence between the two groups. The incidence of upper respiratory tract involvement associated with rotavirus has been reported to vary widely.[3,4,6,10] Though there was no virological or serological evidence for HRV infection of the respiratory tract in the above studies, Santosham has reported isolating HRV virus from the respiratory tract in children with pneumonia.[16] It is possible that the true incidence of the respiratory tract involvement may be underestimated because of the possible omission of relatively mild respiratory symptoms in a predominantly gastrointestinal illness or vice versa.

CONCLUSION

In this study of comparing clinical characteristics of rotavirus and non-rotavirus associated diarrhoea, a higher incidence of vomiting was the only significant clinical symptom seen in the former.

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REFERENCES

1 Annual Report 1980. Health Status. Ministry of Health, Malaysia, 1982; 3 : 13–14.

2 Hieber JP, Shelton S, Nelson JD, Leon J, Mohs E. Comparison of human rotavirus disease in tropical and temperate settings. *Am J Dis Child* 1978; 132 : 853–858.

3 Rodriguez WJ, Kim HW, Arrobio JO, *et. al.* Clinical features of acute gastroenteritis associated with human reovirus-like agent in infants and young children. *J Pediatr* 1977; 91 : 188–193.

4 Lewis HM, Parry JV, Devies HA, *et. al.* A year's experience of the rotavirus syndrome and its associa-

tion with respiratory illness. *Arch of Disease of Childhood* 1979; 54 : 339–346.

5 Maiya PP, Pereira SN, Nathan M, Bhat P, Albert, M J, Bakar S J. Aetiology of acute gastroenteritis in infancy and early childhood in Southern India. *Arch Dis Child* 1977; 52: 482–485.

6 Kumar A, Washington WJ, Mariapurram J. Clinical features and laboratory diagnosis of rotavirus associated gastroenteritis in infants and children. *Journal of Diarrhoeal Disease Research* 1984; 2 (3) : 142–146.

7 Ryder RW, Sack DA, Kapikean AZ, *et. al.* Enterotoxigenic *Escherichia coli* and reovirus-like agent in rural Bangladesh. *Lancet* 1976; i : 659–662.

8 Quak SH, Wong HB. Rotavirus gastroenteritis in Singapore children. *The Journal of the Singapore Paed Soc* 1983; 25 : 52–54.

9 Yap KL, Dahlan Sabil, Paranjothy M. A hospital-based study of rotavirus in children with acute gastroenteritis. *J of Tropical Pediatrics* 1984; 30 : 131–135.

10 Spence L, Singer O, Kibsey P, Fanvel M. Rotavirus infection in children with diarrhoea admitted to a general hospital in Metro, Toronto. *Canadian Journal of Public Health* 1985; 76 : 17–20.

11 Rotchanakul Louisiri S, Wasi, Satrasook, Surakhaka M, Thongcharoen P. Rotavirus in paediatric diarrhoea at Siriraj Hospital, Bangkok, Thailand. *Southeast Asian J Trop Med Pub Health* 1984; 15; 3 : 348–351.

12 Iyngkaran N, Abidin Z, Lam SK, Puthucheary SD. Acute gastroenteritis in Malaysian children: aetiological and therapeutic considerations. *Med J Malaysia* 1980; 30 : 403–408.

13 Clemens JD, Ahmed M, Butler T, Greenough W, Sack D, Stanton B. Rotavirus diarrhoea: an expanding clinical spectrum. *J of Tropical Medicine and Hygiene* 1983; 83 : 117–122.

14 Shepherd RW, Truslow S, Walker Smith JA *et. al.* Infantile gastroenteritis: a clinical study of reovirus-like agent infection. *Lancet* 1975; ii : 1082–1083.

15 Tallet S, Mackenzie C, Middleton P, Karzues B, Hamilton R. Clinical, laboratory and epidemiologic features of viral gastroenteritis in infants and children. *Paediatrics* 1977; 60 : 217–222.

16 Santosham M, Yolken RH, Quiroz E, *et. al.* Detection of rotavirus in respiratory secretion of children with pneumonia. *Journal of Paediatrics* 1983; 103 : 583–585.