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Rotavirus gastroenteritis in children: 5-year experience in a medical center

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Rotavirus infection is the leading cause of childhood gastroenteritis. We retrospectively reviewed cases of rotavirus gastroenteritis at National Taiwan University Hospital from January 1993 to December 1997. During the study period there were 429 patients with rotavirus infection with ages ranging from 1 day to 16 years with a median of 13 months. The male-to-female ratio was 1.2:1. Infection occurred before the age of 2 years old in 76% of patients. The seasonal peak occurred in the late winter and early spring during 1993 to 1996, but the case number increased in late spring and summer in 1997. The G serotype of the rotavirus was identified in 302 patients (70%). Vomiting and dehydration developed more frequently following infection with G1 rotaviruses, while an increased frequency of seizures was noted following G2 infection; the differences were not statistically significant. One patient had two episodes of infection; the first one was caused by G1 rotavirus, and the strain causing the second infection could not be typed. In conclusion, the results suggest that there is a strong seasonal variation in the incidence and characteristics of rotavirus infection in Taipei area. The infections caused by G1 and G2 rotaviruses were clinically indistinguishable.

Key words: Epidemiology, gastroenteritis, rotavirus, serotype

Rotavirus was first described in 1973. It was discovered by electron microscopic examination of duodenal and fecal specimens from children with diarrhea in Melbourne [1]. Rotavirus is now known to be a major cause of gastroenteritis in children less than 3 years old [2]. There are three different groups of rotaviruses, group A, B, and C, which cause diseases in humans. The most common group causing outbreaks is group A rotavirus. Outer capsid proteins, VP4 and VP7, determine rotavirus serotypes and serotyping based on VP7 (G serotype) is the most commonly used technique. At least nine G serotypes can infect humans, but most human infections are caused by G1 to G4 [3,4]. The majority of rotavirus infections are asymptomatic or result in gastroenteritis episodes that are self-limited and last for about a week [5]. Analyses of clinical manifestations have been derived mostly from hospitalized children, and most commonly include fever, vomiting, diarrhea, and dehydration. Some cases also had respiratory tract symptoms [6]. A small proportion of rotavirus infections can be severe and need to be treated in the hospital. It has been estimated that worldwide rotavirus accounts for 30% to 50% of all hospitalizations due to childhood gastroenteritis [7]. One early study in Taipei showed that 43% of admissions due to childhood gastroenteritis were caused by rotavirus [8]. Development of a rotavirus vaccine has been pursued for decades, and the first commercially available rotavirus vaccine was approved for general use in 1998.

The epidemiology of rotavirus infection is heavily influenced by the local climate. Although rotavirus has been identified as the major pathogen associated with "winter" gastroenteritis, the seasonal peak may vary with different climates [7,9]. The purpose of this study was to examine rotavirus epidemiology during the 5-year period from 1993 to 1997, and to determine the clinical features associated with the different serotypes of this infection.

Patients and Methods

We retrospectively reviewed the chart records of all children with rotavirus gastroenteritis treated at National Taiwan University Hospital from January 1993 to December 1997. The parameters observed and examined included age, sex, symptoms and signs, stool

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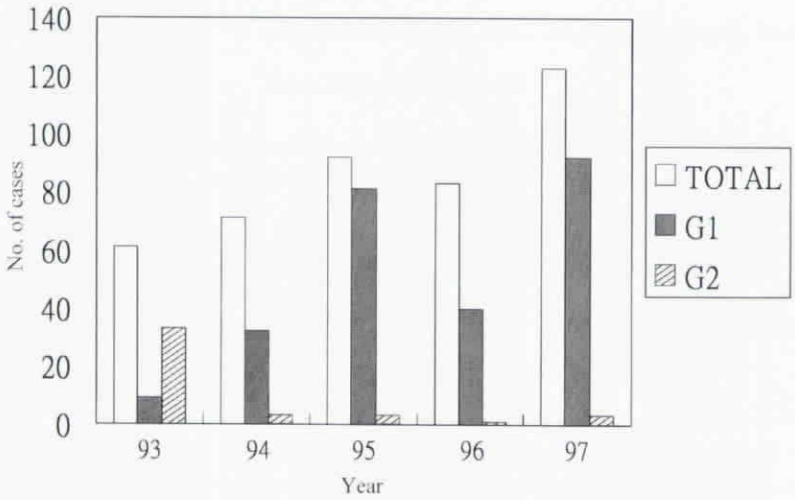

Fig. 1. Yearly distribution of cases of rotavirus gastroenteritis during 1993-1997.

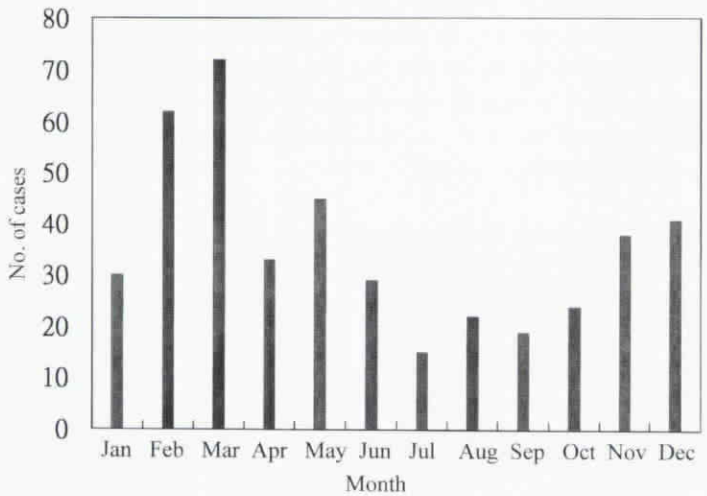

Fig. 2. Monthly distribution of cases of rotavirus gastroenteritis during 1993 and 1997.

characteristics, and presence of other intestinal pathogens. Symptoms and signs included vomiting, diarrhea, fever, dehydration, and seizure or change of consciousness. Fever was defined as a rectal temperature greater than 38 °C. A diarrhea episode was defined as the passage of unformed stool with at least twice the usual daily frequency for a child during a 24 h period. Nosocomial infection was defined as symptoms and signs occurring 72 h after admission. The antigen in fecal specimens was detected by monoclonal antibody incorporated enzyme-linked immunosorbent assay (ELISA; Rotaclone, Meridian Diagnostic, Cincinnati, OH, USA).

The stools that were rotavirus positive by ELISA were further analyzed for VP7 (G) serotypes [10]. Rotavirus RNA was extracted from stool samples and treated with CF 11 cellulose powder (Whatman Chemical Separation Ltd, England) to remove inhibitors

Table 1. Clinical symptoms and signs of rotavirus gastroenteritis (n = 429)

Symptom/sign	No. of cases (%)
Diarrhea	427 (99.3)
Fever	293 (68.1)
Vomiting	290 (67.4)
Dehydration	115 (26.7)
Stool with mucus	36 (8.4)
Afebrile seizure	17 (4.1)
Febrile seizure	16 (3.7)
Stool with blood	14 (3.3)

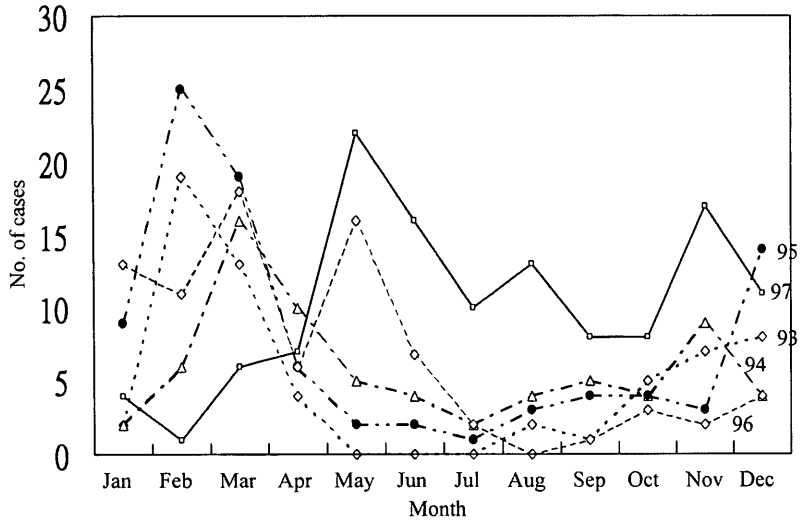

Fig. 3. Monthly distribution of cases of rotavirus gastroenteritis by year from 1993 to 1997.

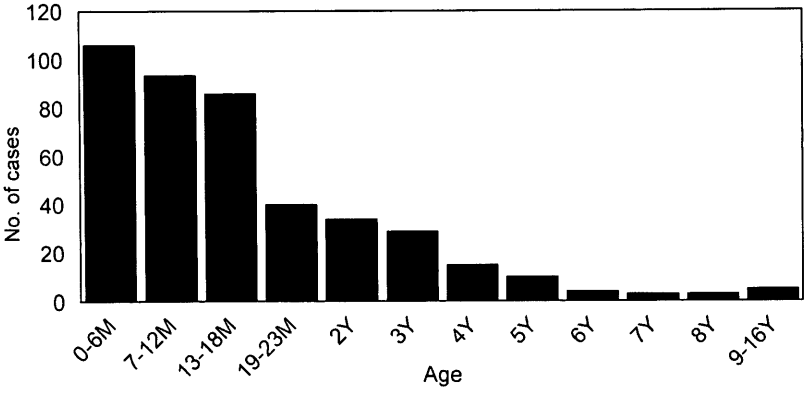

Fig. 4. Age distribution of cases of rotavirus gastroenteritis.

in stools [11]. Reverse transcription-polymerase chain reaction (RT-PCR) was performed with serotype-specific primers [11,12].

Some of the fecal specimens were also cultured for bacteria including *Salmonella, Shigella*, and *Campylobacter jejuni*.

The statistical method used to compare proportions between groups was Chi-square test with Yates' correction.

Results

A total of 429 patients aged between 1 day and 16 years with a median age of 13 months were treated during the study period. One patient experienced two episodes of infection separated by 6 months. Nosocomial infection occurred in 66 patients (15.3%). The clinical manifestations are listed in Table 1. The most common symptoms were diarrhea, vomiting, and fever. Dehydration was noted in 26.7% of patients.

The distribution of cases of rotavirus gastroenteritis in each year is shown in Fig. 1. The monthly distributions of rotavirus infection from 1993 to 1997 are shown in Fig. 2 and 3. The seasonal peak occurred in late winter and early spring during the period from 1993 to 1996, but the number of cases increased in late spring and summer in 1997. The virus was detected in children as young as 1 day and as old as 16 years of age, but 76% of all cases occurred before the age of 2 years old. The age distribution of patients with rotavirus infection is illustrated in Table 2 and Fig. 4.

G serotypes could be determined in 302 strains (70%). The distribution of serotypes G1 and G2 did

Table 2. Age distribution of patients with rotavirus serotype G1 and G2 infections

Age (month)	Serotype		No. of cases (%)
	G1 (%)[a]	G2 (%)[b]	
0-6	58 (23)	7 (16)	106 (25)
7-12	49 (19)	14 (32)	94 (22)
13-24	80 (32)	11 (26)	126 (29)
>24	67 (26)	11 (26)	103 (24)
Total	254 (100)	43 (100)	429 (100)

[a]G1 = serotype G1 based on rotavirus outer capsid protein
[b]G2 = serotype G2

not differ significantly among different age strata (Table 2). Serotype G1 was prevalent throughout the study period except in 1993 but by G2 rotavirus was more prevalent thereafter. G3 serotype was identified in three cases in 1997, and two cases had mixed infections (G1 + G2 in one case, and G1 + G3 in the other). The clinical manifestations were similar in both serotypes (Table 3). Eight patients had positive stool cultures for *Salmonella*. It was difficult to differentiate whether these patients had coinfection or were chronic carriers of rotavirus or *Salmonella* from the available clinical data. All patients recovered smoothly following proper supplement of fluid either orally or parenterally.

Discussion

Rotavirus is a well-known pathogen which is a common cause of acute watery diarrhea in young children. Our results showed that 76% of the infected children were less than 2 years old. This finding is consistent with most seroprevalence studies throughout the world showing that all children have been infected with rotavirus by the age of 3 years [13]. Rotavirus infections in this study mainly resulted in watery diarrhea and two-thirds of the infections were associated with vomiting and fever. Dehydration is the most common condition associated with rotavirus gastroenteritis leading to grave morbidity and mortality in developed and developing countries. While one-fourth of the infected children in the present study were dehydrated, none of these patients died after appropriate treatment. Although pus and/or blood in the stool is considered to be characteristic of bacterial enterocolitis, rotavirus infection is also capable of inducing similar stool changes [6,14]. This observation is supported by our findings that 3.3% and 8.4% of subjects had blood or mucus in stool, respectively.

Thirty-three children (7.6%) were noted to have seizure attack concomitant with their diarrhea symptoms. Sixteen patients had fever at the time of the seizure episode. Eleven of these patients were aged between 6 months and 5 years, and their convulsions were generalized tonic-clonic. Based on the available clinical information in these 11 cases it was difficult to determine whether these were purely febrile convulsions or whether rotavirus played a more specific role in their onset. Another four patients had focal seizure, and one patient was 8 years old at the time of the episode which was much older than the other patients. Most patients with either febrile or afebrile seizure recovered smoothly during the follow-up period. A previous study found that the incidence of convulsion in children with rotavirus infection in Taipei country during 1988 to 1989 was 6.4% [15]. Although a previous study using an animal model suggested that enterotoxin or direct viral invasion may be the cause of seizure [16], the exact pathogenesis is still not clear.

The nosocomial infection rate of rotavirus was 15.3% in our study. Rotavirus is a frequent cause of

Table 3. Clinical symptoms and signs of patients with rotavirus serotype G1 and G2 infections

Symptom/sign	Serotype		*P*
	G1 (%)	G2 (%)	
Diarrhea	252 (99)	42 (98)	0.91
Vomiting	186 (73)	26 (60)	0.13
Fever	181 (71)	30 (70)	0.99
Dehydration	76 (30)	8 (19)	0.18
Afebrile seizure	11 (4)	0	0.34
Febrile seizure	7 (3)	6 (14)	0.004

nosocomial infection in young children and neonates. Some studies showed that 20% to 43% of rotavirus infections occurred in the hospital setting [17,18]. This high rate of spread is due to the ability of this pathogen to survive for long periods on hard surfaces, human hands, in potable water, and its stability between a wide range of pH environments from pH 3 to 10. Rotavirus also resists commonly used disinfectants and hygienic hand-wash agents. Early detection and proper isolation is vital to control nosocomial spreading of the infection. Good handwashing practices with proper disinfectants are also important to prevent nosocomial transmission [19,20].

There are differences in the seasonal variation in the prevalence of rotavirus gastroenteritis in different geographic areas. In temperate regions, most of the rotavirus infections occur in winter [21]. In contrast, rotavirus infections occur year round in tropical areas [22]. Cook *et al* analyzed reports on childhood diarrhea published during the period of 1974 to 1988 and found that the incidence peaked in winter primarily in the United States and in the autumn or spring in other parts of the world. The peak in the incidence of rotavirus infection in Taiwan has been reported to be between November and December [7], or January to March in a recent study [15]. In this study, we found that rotavirus infections most commonly occurred around late winter and early spring from 1993 to 1996, but the seasonal peak shifted to late spring and summer in 1997. More specific explanation of the seasonal variation of rotavirus infection and its causes in Taiwan is needed.

In this study we identified the G serotypes of rotavirus in 302 patients; of these, 254 (59% of the total) were G1 and 43 (10% of the total) were G2. Serotype G1 was the most prevalent serotype from 1994 to 1997, and serotype G2 was the major serotype in1993. The change in the prevalence of G1 serotype between 1993 and 1994 could have been related to the development of serotype specific antibodies following each epidemic season. No apparent association between the proportions of serotype G1 and G2 and children's age was found. Similar results were found in Africa and Venezuela [23,24]. Though vomiting and diarrhea were observed more frequently in G1 infections and seizure was more common in G2 infections, these differences did not reach statistical significance in this study. In addition there were no significant differences in the occurrence of fever and dehydration among patients with these two serotypes, although some studies showed that dehydration was more common in children infected with G2 than G1 [24,25].

One boy in this series was infected at the age of 1 year and 3 months, and developed a subsequent infection 6 months later. The first infection was caused by serotype G1 but the second episode was nontypable. Most symptomatic reinfections in previous series were caused by different serotypes, but infection with the same serotype did occur [24-26]. The severity of the second infection with different serotypes also varied in these studies.

In conclusion, infections caused by serotypes G1 and G2 were clinically indistinguishable in this series. A shift in the prevalence of rotavirus infection to the warmer season was noted in this long-term study but further data on current seasonal variation is needed.

References

1. Bishop RF, Davidson GP, Holmes IH, Ruck BJ. Virus particles in epithelial cells of duodenal mucosa from children with acute nonbacterial gastroenteritis. Lancet 1973;2:1281-3.
2. Urasawa S, Urasawa T, Taniguchi K, Chiba S. Serotype determination of human rotavirus isolates and antibody prevalence of pediatric population in Hokkaido, Japan. Arch Virol 1984;81:1-12.
3. Hoshino Y, Kapikian AZ. Rotavirus antigens. Curr Top Microbiol Immunol 1994;185:179-227.
4. Kapikian AZ, Chanock RM: Rotaviruses. In: Fields BN, Knipe DM, Chanock RM, Hirsch MS, Melnick JL, Monath TP, Roizman B, eds. Virology. Vol 2. 2nd ed. New York: Raven Press, 1990:1353-404.
5. Zheng BJ, Lo SKF, Tam JSL, Lo M, Yeung CY, Ng MH. Prospective study of community-acquired rotavirus infection. J Clin Microbiol 1989;27:2083-90.
6. Rodriguez WJ, Kim HW, Arrobio JO, Brandt CD, Chanock RM, Kapikian AZ, Wyatt RG, Parrott RH. Clinical features of acute gastroenteritis associated with human reovirus-like agent in infants and young children. J Pediatr 1977;91:188-93.
7. Birch CJ, Lewis FA, Kennett ML, Homola M, Pritchard H, Gust ID. A study of the prevalence of rotavirus infection in children with gastroenteritis admitted to an infectious disease hospital. J Med Virol 1977;1:69-77.
8. Lin CL, Huang FY, Chou SC, Lee HC. Clinical observation of rotavirus gastroenteritis in children. Acta Paed Sin 1984;25: 407-11.
9. Kapikian AZ, Kim HW, Wyatt RG, Cline WL, Arrobio JO, Brandt CD, Rodriguez WJ, Sack DA, Chanock RM, Parrott RH. Human reovirus-like agent as the major pathogen associated with "winter" gastroenteritis in hospitalized infants and young children. N Engl J Med 1976;294:965-72.
10. Lee CN, Kao CL, Ning HC, Fuh HL, Lee CY. Identification of VP7 serotypes of human rotaviruses by enzyme-linked immunosorbent assay and reverse transcription- polymerase chain reaction. Acta Paed Sin 1997;38:454-62.
11. Wilde J, Eiden J, Yolken R. Removal of inhibitory substances from human fecal specimen for detection of group A rotaviruses by reverse transcriptase and polymerase chain reactions. J Clin Microbiol 1990;28:1300-7.
12. Gouvea V, Glass RI, Woods P, Taniguchi K, Clark HF, Forrester B, Fang ZY. Polymerase chain reaction amplification and typing of rotavirus nucleic acid from stool specimens. J Clin Microbiol 1990;28:276-82.

13. Yolken R, Wyatt R, Zissis G. Epidemiology of human rotavirus types 1 and 2 as studied by enzyme-linked immunosorbent assay. N Engl J Med 1978;299:1156-61.
14. Steinhoff MC. Rotavirus: the first five years. J Pediatr 1980; 96:611-22.
15. Chen HJ, Chen BS, Wang SF, Lai MH. Rotavirus gastroenteritis in children, a clinical study of 125 patients in Hsin-Tien area. Acta Paed Sin 1991;32:73-8.
16. Delem A, Berge E, Brucher JM. The neurovirulence of human and animal rotaviruses in Cercopithecus monkeys. J Bio Stand 1985;13:107-14.
17. Lam BCC, Tam J, Ng MH, Yeung CY. Nosocomial gastroenteritis in paediatric patients. J Hospital Infection 1989; 14:351-5.
18. Steele AD, Mnisi YN, William MM, Bos P, Aspinall S. Electrophoretic typing of nosocomial rotavirus infection in a general paediatric unit showing the continual introduction of community strains. J Med Virol 1993;40:126-32.
19. Ansari S, Springthorpe V, Sattar S. Survival and vehicular spread of human rotavirus: possible relation to seasonality of outbreaks. Rev Infect Dis 1992;13:448-61.
20. Keswick B, Pickering L, Dupont H, Woodward W. Survival and detection of rotaviruses on environmental surfaces in day care centers. Appl Environ Microbiol 1983;46:813-6.
21. Brandt CD, Kim HW, Yolken RH, Kapikian AZ, Arrobio JO, Rodriguez WJ, Wyatt RG, Chaonck RM, Parrott RH. Comparative epidemiology of two rotavirus serotypes and other viral agents associated with pediatric gastroenteritis. Am J Epidemiol1979;110:243-54.
22. Stoll BJ, Glass RI, Huq MI, Khan MU, Holt JE, Banu H. Surveillance of patients attending a diarrheal disease hospital in Bangladesh. BMJ 1982;285:1185-8.
23. White L, Garcia D, Boher Y, Blanco M, Perez M, Romer H, Flores J, Perez-Schael I. Temporal distribution of human rotavirus serotypes 1, 2, 3, and 4 in Venezuelan children with gastroenteritis during 1979-1989. J Med Virol 1991;34:79-84.
24. Yolken RH, Wyatt RG, Zissis G, Brandt CD, Rodriguez WJ, Kim HW, Parrott RH, Urrutia JJ, Mats L, Greenberg HB, Kapikian AZ, Chanock RM. Epidemiology of human rotavirus types 1 and 2 as studied by enzyme-linked immunosorbent assay. N Engl J Med 1978;299:1156-61.
25. Bern C, Unicomb L, Gentsch JR, Banul N, Yunus M, Sack BR, Glass GI. Rotavirus diarrhea in Bangladeshi children: correlation of disease severity with serotypes. J Clin Microbiol 1992;30:3234-8.
26. Ilmamura Y, Hamada N, Nagai T, Shingu M. Detection and typing of human rotavirus in reference to repeated acute gastroenteritis in infants. Microbiol Immunol 1994;38:673-6.