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Original Article

Epidemiology and Clinical Peculiarities of Norovirus and Rotavirus Infection in Hospitalized Young Children with Acute Diarrhea in Taiwan, 2009

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BACKGROUND/PURPOSE: Acute diarrhea is one of the most common morbidities in pediatrics worldwide. We conducted a study to investigate the incidence of norovirus in young children hospitalized with acute diarrhea in Taiwan and its clinical peculiarity compared with rotavirus gastroenteritis.

METHODS: Between January and December, 2009, patients younger than 5 years and admitted to hospital with acute diarrhea were randomly selected; and their stool samples were collected and tested for presence of rotavirus and norovirus by enzyme immunoassay and reverse transcription-polymerase chain reaction, respectively. The clinical manifestations and laboratory findings of the enrolled patients were analyzed.

RESULTS: A total of 989 cases were enrolled with a mean age of 21.6 ± 13.7 months and a male proportion of 56.0%. Rotavirus and norovirus was detected in 20.2% and 14.6% of all patients, respectively. Genogroup II was the predominant strain of norovirus (80.6%). Children aged 6–36 months accounted for the majority of patients positive for rotavirus and norovirus (73.0% and 81.3%, respectively). The incidences of norovirus

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and rotavirus infection were higher during winter and early spring. Most patients with rotavirus and norovirus diarrhea experienced vomiting (74.9% *vs.* 74.8%, respectively) and fever (94.7% *vs.* 71.3%, respectively).

CONCLUSION: Most young diarrheal patients presenting with vomiting were likely to have norovirus or rotavirus infection. Patients with norovirus diarrhea experienced an absence of, or low-grade fever and longer duration of vomiting compared with those positive for rotavirus infection. A family history of current gastroenteritis may suggest the possibility of norovirus infection.

KEYWORDS: acute diarrhea, norovirus, rotavirus, Taiwan, young children

Introduction

Acute diarrhea is one of the most common morbidities among pediatric patients worldwide. Because of easy access to medical services, acute gastroenteritis seldom causes mortality but it remains a significant disease burden for young children and an economic burden in industrial countries. In a questionnaire-based study conducted in Taiwan, 55.78% of children younger than 5 years had experienced acute diarrhea, and the prevalence increased with age, ranging from 15.45% among infants less than 6 months of age to 82.22% among children aged 4–5 years.¹ In a study of economic burden, families spent on average US\$294 per month for a child admitted with rotavirus gastroenteritis, accounting for nearly 40% of the monthly salary of an unskilled or service worker.²

With the advancement of public health over the past two decades, viral agents have replaced bacteria as the leading cause of infectious diarrhea.³ As shown in a review about gastroenteritis in Taiwan, rotavirus is the leading cause (30.4–48.0%) of infectious gastroenteritis, followed by adenovirus (9.1–19.8%), norovirus (8.2–25.0%), astrovirus (2.7–2.9%) and enterovirus (<5.2%).⁴ According to the review on rotavirus and norovirus gastroenteritis published by the United States Centers for Disease Control and Prevention, rotavirus was estimated to cause 25 million clinic visits, 2 million hospitalizations and 352,000–592,000 deaths worldwide each year in children younger than 5 years.⁵ However, it was estimated that norovirus caused 900,000 clinic visits and 64,000 hospitalizations among children in developed countries and up to 200,000 deaths of children younger than 5 years in developing countries each year.⁶ In recent studies,^{3,7–9,14,15} norovirus was recognized as the major infectious agent attributed to outbreaks and sporadic cases of infectious gastroenteritis.

Rotavirus has received considerable attention because it causes more severe clinical symptoms compared with other enteric viruses. Rotavirus is usually identified among nonbacterial gastroenteritis cases by enzyme immunoassay at most hospitals. In contrast, testing for norovirus is not routinely carried out because its clinical symptoms are less severe and testing methods are inefficient. With the increasing popularity of rotavirus vaccines, the incidence of rotavirus infection in patients hospitalized with diarrhea is estimated to have decreased, and the relative importance of norovirus infection is gradually rising.

Previous studies indicate that acute gastroenteritis mainly affected children younger than 5 years of age.^{10,11} Therefore, we conducted a hospital-based (3 hospitals) study to investigate the incidence of norovirus among young children hospitalized with acute diarrhea in Taiwan and to compare its clinical peculiarity and severity of symptoms with rotavirus gastroenteritis.

Methods

From January to December, 2009, a prospective observational study was conducted in Taiwan; it included three medical centers located in the southern, northern and central regions of Taiwan. The hospitals were Chang-Gung Memorial Hospital, Kaohsiung Branch; Chang Gung Memorial Hospital, Linko Branch; and Changhua Christian Hospital. The protocol was approved by the local institution review boards of these three hospitals. Enrolled subjects were patients less than 5 years of age, admitted to hospital with acute diarrhea. Diarrhea was defined as the passage of liquid or looser-than-normal stools occurring three or more times daily. Patients with diarrhea for more than 14 days were excluded. After obtaining informed parental consent, stool specimens and demographic information (including age, sex

and members living together with diarrhea and/or vomiting within 1 week), clinical manifestations (including diarrhea, vomiting, fever and associated upper respiratory symptoms), and laboratory findings were collected and analyzed.

A fecal sample was collected within the first 48 hours after admission and stored at 4°C before testing. Each fecal sample was tested for the presence of rotavirus by enzyme immunoassay (Ridascreen; γ -biopharm, Germany).¹² The remaining stool specimen was kept frozen at -20°C in the hospital until delivered to the laboratory at the Centers for Disease Control of Taiwan for norovirus testing by reverse transcription-polymerase chain reaction (RT-PCR) using two sets of PCR primers: G1SKF (5'-CTG CCC GAA TTY GTA AAT GA-3') and G1SKR (5'-CCA ACC CAR CCA TTR TAC A-3') for GI norovirus, and G2SKF (5'-CNT GGG AGG GCG ATC GCA A-3') and G2SKR (5'-CCR CCN GCA TRH CCR TTR TAC AT-3') for GII norovirus.¹³

Statistical analysis

Data were analyzed using SAS version 9.1 (SAS Inc., Cary, NC, USA). The results shown are given as the mean value with standard deviation (SD) or proportion. As for the comparison of clinical manifestations and laboratory results among diarrheal patients, we categorized subjects into four subgroups according to the laboratory test results for rotavirus and norovirus. The percentages were compared using χ^2 tests of homogeneity for the four subgroups and a partitioning of the χ^2 method (Brunden, 1972) for specific pair-wise comparisons. Kruskal-Wallis one-way analysis of variance by ranks and a multiple-comparison procedure

were used for testing the difference of ordinal variables among the four subgroups. The one-way analysis of variance method with the least significant difference procedure was applied to compare the difference of continuous measurements among the four subgroups. Statistical significance was defined as a $p < 0.05$ for two-tailed analysis in comparing overall groups and the least significant difference procedure. For each pair-wise comparison, a $p < \alpha_1$ (at an appropriate threshold) was conducted under a partitioning of the χ^2 method ($\alpha_1 = 0.05/3$) or the Kruskal-Wallis multiple-comparison procedure ($\alpha_1 = 0.05/6$).

Results

A total of 989 subjects were enrolled in the study, with a mean age of 21.6 ± 13.7 months and a male proportion of 56.0% (554/989). Children aged 6–36 months were at the highest risk of hospitalization with acute diarrhea (77.4%, 765/989) (Table 1). Overall, the detection rate of rotavirus was 20.2% (200/989) and that of norovirus was 14.6% (144/989). Among these patients, 29 cases were tested positive for both rotavirus and norovirus. Among patients positive for norovirus, 116 (80.6%) were genogroup II and 28 (19.4%) were genogroup I. Of the patients that were rotavirus positive, the most common G genotype was G1 (68.7%), followed by G3 (12.8%), G2 (8.0%), and the most common P genotype was P[8] (84.7%), followed by P[4] (9.2%).

No significant difference in the affected sex was found between the rotavirus positive and norovirus positive patient groups. The mean age of patients positive for rotavirus

Table 1. Age distribution of all diarrheal cases, rotavirus positive cases and norovirus positive cases from January to December, 2009

Features	All AGE ($n=989$)	Rota (+) ($n=200$)	Noro (+) ($n=144$)
Age (mo)			
Mean \pm SD	21.6 \pm 13.7	25.0 \pm 14.6	21.3 \pm 13.5
Median	17.7	21.3	17.1
Range (mo)			
0–5	52 (5.3)	8 (4.0)	5 (3.5)
6–11	233 (23.6)	31 (15.5)	37 (25.7)
12–23	366 (37.0)	71 (35.5)	55 (38.2)
24–35	166 (16.8)	44 (22.0)	25 (17.4)
36–47	100 (10.1)	23 (11.5)	12 (8.3)
48–59	72 (7.3)	23 (11.5)	10 (6.9)

AGE=acute gastroenteritis; SD=standard deviation.

was older than that for norovirus (25.5 ± 14.6 months *vs.* 21.6 ± 13.7 months, $p < 0.01$). The cumulative age distribution for rotavirus positive cases was 55.0% ($n = 110$) for patients younger than 24 months and 77.0% ($n = 154$) in those younger than 36 months. For norovirus positive cases, 67.4% ($n = 97$) were younger than 24 months, and 84.7% ($n = 122$) were younger than 36 months. Compared with other groups of enteropathogens, the history of household members simultaneously suffering from diarrhea and/or vomiting within 1 week was more common among norovirus and rotavirus infection groups ($p < 0.0001$) (Table 2). The “other enteropathogens” group refers to those cases that were both rotavirus and norovirus negative.

The incidence of rotavirus infection was higher in the northern and central regions of Taiwan compared with the southern region. However, the detection rate of norovirus infection was higher in the southern region (Table 3). The seasonal distribution of norovirus gastroenteritis was similar to that of rotavirus gastroenteritis, with higher prevalence during the winter and early spring months (Figure). The prevalence of norovirus gastroenteritis was observed to peak in January, followed by a peak in rotavirus infections, which occurred in February.

Most patients with rotavirus or norovirus diarrhea experienced vomiting (74.9% *vs.* 74.8%, respectively), and the proportion was significantly higher than that of the other enteropathogens group (41.1%). Blood-tinged stools were rarely found in patients with either rotavirus or norovirus diarrhea compared with the other enteropathogens group. Fever was found more commonly in patients with rotavirus gastroenteritis than in those with norovirus gastroenteritis (94.7% *vs.* 71.3%) (Table 2). Concerning the severity of the clinical manifestations between norovirus and rotavirus gastroenteritis, more patients with norovirus infection experienced a longer duration of vomiting than those with rotavirus infection, but the frequency of vomiting was not found to be significantly different in this study. There was also no difference between the norovirus and rotavirus infected groups with respect to clinical manifestations, including the duration and frequency of diarrhea, duration of fever, and days of hospitalization. Of the patients that were rotavirus and norovirus positive, the severity of clinical symptoms was similar to those infected with rotavirus or norovirus alone (Table 2). The leukocyte counts and C-reactive protein level in norovirus positive patients

were not significantly different from the rotavirus positive cases. However, a greater number of patients infected with rotavirus were found elevated aspartate aminotransferase levels compared with norovirus infected individuals (30.4% *vs.* 15.7%), but this difference was not significant (Table 2).

Discussion

In this study, norovirus was detected in 14.6% and rotavirus in 20.2% of all fecal samples. These results indicate that norovirus is a major viral pathogen, secondary to rotavirus, in younger children hospitalized with acute diarrhea in Taiwan. In recent studies,^{3,7-9,14,15} the increase in the incidence of norovirus infection, from 17.3–29.0%, were comparable with our results. This may be because current testing methods are more sensitive; the incidence of norovirus detection nearly doubled when enzyme immunoassays were combined with the more sensitive RT-PCR, as previously proposed by Wu et al.⁷ Norovirus genogroup II was predominantly responsible for norovirus gastroenteritis worldwide as shown in most studies,^{7,8,13,14,16} and our findings are consistent with these results.

Rotavirus is the leading cause of acute gastroenteritis in children worldwide. The incidence of rotavirus gastroenteritis (25–30%) in recent reports^{7,8,10,12} was decreased compared with the results of earlier studies,^{3,15,17-20} with a range of 35–66%. The surveillance data reported by the Asian Rotavirus surveillance Network (ARSN) also confirm this trend.^{21,22} The most prevalent genotype was G1P [8] among rotavirus positive cases in our study, consistent with the report of ARSN.¹² In the present study, the overall detection rate of rotavirus (20.2%) was lower, and noticeably lower (12%) in the hospital from southern Taiwan. In fact, the detection rates of rotavirus for the two hospitals located in the northern and central regions of Taiwan (23.1% and 24.7%, respectively) in this study were close to the results from the Taiwan surveillance study (25%) of 2005–2007 and the results of other studies in recent years.¹² A total of 158 cases from three hospitals received an oral rotavirus vaccine, accounting for 16% of all cases in this study. The proportion of immunized children was approximately 20% of the eligible infants that received the vaccine in 2007.¹² No difference was found between the rates of rotavirus vaccination of enrolled patients at three

Table 2. Comparison of the clinical manifestations of diarrheal cases from rotavirus, norovirus, both rotavirus and norovirus, and enteropathogens other than rotavirus and norovirus infections

Features	Stool test for rotavirus and norovirus				p for overall groups ^a	p ^b for comparing Rota+, Noro- vs. Rota-, Noro+
	Rota+, Noro- (n=171)	Rota-, Noro+ (n=115)	Rota+, Noro+ (n=29)	Rota-, Noro- (n=674)		
Sex, male ^c	96 (56.1)	65 (56.5)	17 (58.6)	376 (55.8)	0.9909	0.9493
Age (mo)						
Mean±SD ^d	25.5±14.8	21.0±13.7	22.5±13.2	20.7±13.3	0.0007**	0.0066**
Median	22.0	16.0	19.0	17.0		
Household member with AGE history	63 (36.8)	52 (45.2)	15 (51.7)	99 (14.7)	<0.0001**	0.1574
Symptoms ^c						
Diarrhea alone	4 (2.3)	4 (3.5)	1 (3.5)	33 (4.9)	0.5061	0.5675
Associated vomiting	128 (74.9)	86 (74.8)	23 (79.3)	277 (41.1)	<0.0001**	0.9892
Associated fever	162 (94.7)	82 (71.3)	21 (72.4)	623 (92.4)	<0.0001**	<0.0001***
Bloody stool	27 (15.8)	24 (20.9)	3 (10.3)	292 (43.3)	<0.0001**	0.2720
Duration of symptoms						
Vomiting						
Duration (d), mean±SD ^e	1.6±1.6	2.2±2.4	3.2±5.7	1.0±1.9	<0.0001**	0.3015
> 2 d ^c	35 (20.5)	42 (36.5)	9 (31.0)	88 (13.1)	<0.0001**	0.0027***
Freq. ≥ 4 episodes/d ^c	87 (50.9)	54 (47.0)	17 (58.6)	71 (10.5)	<0.0001**	0.5163
Diarrhea						
Duration (d), mean±SD ^e	5.5±1.9	6.1±3.0	5.4±2.7	6.5±2.9	0.0004**	0.2981
> 5 d ^c	71 (41.5)	57 (49.6)	13 (44.8)	387 (57.4)	0.0014**	0.1805
Freq. ≥ 5 episodes/d ^c	134 (78.4)	86 (74.8)	23 (79.3)	560 (83.1)	0.1304	0.4818
Fever						
Duration (d), mean±SD ^e	3.0±2.2	2.9±3.0	3.0±3.4	4.4±2.8	<0.0001**	0.6010
> 2 d ^c	90 (52.6)	54 (47.0)	12 (41.4)	521 (77.3)	<0.0001**	0.3475
BT > 38.5°C ^c	123 (71.9)	53 (46.1)	14 (48.3)	556 (82.5)	<0.0001**	<0.0001***
Hospital stay (d)						
Duration (d), mean±SD ^e	4.7±1.8	5.1±2.6	5.6±3.1	5.1±2.4	0.5561	0.5155
> 5 d ^c	41 (24.0)	39 (33.9)	6 (20.7)	220 (32.6)	0.0823	0.0669
URI symptoms (+) ^c	105 (61.4)	63 (54.8)	19 (65.5)	354 (52.5)	0.1238	0.2656

(Contd)

Lab data on admission								
WBC (1,000/ μ L), mean \pm SD ^d	11.4 \pm 5.2	11.5 \pm 6.1	12.3 \pm 6.0	10.4 \pm 5.1	0.0177**	0.8802		
> 15 ^{cf}	33 (19.4)	17 (15.2)	6 (20.7)	101 (15.1)	0.4925	0.3633		
missing data	1 (0.6)	3 (2.6)	0 (0)	5 (0.7)	0.1537			
Platelet (1,000/ μ L), mean \pm SD ^d	304.6 \pm 90.9	332.4 \pm 122.0	355.6 \pm 83.7	273.5 \pm 102.6	<0.0001**	0.0266**		
missing data	1 (0.6)	3 (2.6)	0 (0)	5 (0.7)	0.1537			
CRP (mg/L), mean \pm SD ^d	21.0 \pm 40.0	17.1 \pm 28.1	14.8 \pm 20.0	58.9 \pm 66.8	<0.0001**	0.6178		
missing data	27 (15.8)	22 (19.1)	9 (31.0)	52 (7.7)	0.4630			
AST (U/L), mean \pm SD ^d	49.8 \pm 22.8	47.5 \pm 27.7	42.8 \pm 10.6	47.6 \pm 50.3	0.9718	0.7893		
missing data	115 (67.3)	64 (55.7)	20 (67.0)	378 (56.1)				

^aStatistically significant; $p < 0.05$ ** for the least significant difference procedure; ^b $p < \alpha$; *** (an appropriate threshold) for each pair-wise comparison between Rota+, Noro- vs. Rota-, Noro+, under a partitioning of the χ^2 method ($\alpha_1 = 0.05/3$) or Kruskal-Wallis multiple-comparison procedure ($\alpha_1 = 0.05/6$); ^c χ^2 test for the comparison of categorical data, and a partitioning of the χ^2 method (Brunden, 1972) for each pair-wise comparison; ^done-way analysis of variance with the least significant difference procedure for continuous data; ^eKruskal-Wallis one-way analysis of variance by ranks with a multiple-comparison procedure in ordinal data; ^fthe percentage was calculated by number of events divided by number of remaining samples after excluding number of missing. AGE=acute gastroenteritis; AST=aspartate aminotransferase; BT=body temperature; CRP=c-reactive protein; SD=standard deviation; URI=upper respiratory infection; WBC=white blood cell.

hospitals (Table 3). Several studies found a higher prevalence of rotavirus disease at colder temperatures, low relative humidity and in dry weather.²³⁻²⁶ This may be because families are more likely to stay indoors in cold weather, leading to an increase in contact transmission, with the dry conditions encouraging aerosol formation of virus-laden particles from a patient's feces. The regional differences of incidence could possibly be the result of shorter colder months (January and February) and higher relative humidity (77-81%) in the southern regions compared with the climate of northern and central Taiwan (colder weather during January and April, relative humidity of 68-74%). In contrast, the incidence of norovirus infection was slightly higher in the southern region compared with the northern and central regions of Taiwan.

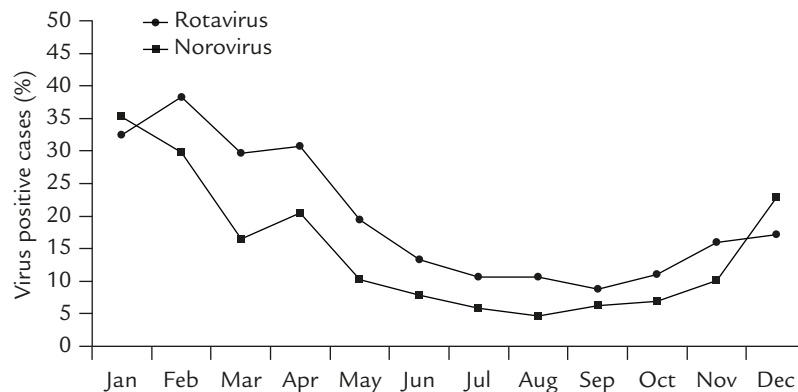
To the best of our knowledge, norovirus can be easily be transmitted via contaminated food or drinking water, leading to diarrheal outbreaks. We speculate that this difference is probably due to poor hygiene as a higher proportion of grandparents serve as primary caregivers in southern Taiwan, likely increasing the risk of norovirus transmission.

Rotavirus is the leading cause of gastroenteritis in infants and younger children, with the findings of most studies consistently demonstrating that rotavirus mainly affects younger children aged less than 5 years and the proportion of rotavirus infections among younger children was higher than that in the older age groups.^{3,7,15,27,28} The general belief is that norovirus is a major pathogen leading to diarrheal outbreaks and causes symptomatic infections in older children and adults. However, some studies^{12,14,15} demonstrated that norovirus also has an impact on children younger than 24 months, which is consistent with the finding of the current study. This study showed children hospitalized with rotavirus and norovirus infection were around the same age and, in the main, younger than 36 months. The proportion of rotavirus positives among different age groups was increased from 13.7% to 26.6% as the age increased, but the proportion of norovirus positives was maintained around 12.8-15.0% in each age group. Because the current study is focused on hospitalized patients with acute diarrhea and limited to subjects aged less than 5 years, this study indicates that rotavirus infection might possibly cause more intense diarrhea and/or vomiting than norovirus, leading to older children still requiring hospitalization. However, norovirus infection

Table 3. Comparison of epidemiology of diarrheal cases in three Taiwanese hospitals

	All (<i>n</i> =989)	Hospital			<i>p</i> ^a
		Chang Gung Linko (<i>n</i> =442)	ChangHua (<i>n</i> =255)	Chang Gung Kaohsiung (<i>n</i> =292)	
Sex, male ^b	554 (56.0)	251 (56.8)	141 (55.3)	162 (55.5)	0.9072
Age (mo)					
Mean ± SD ^c	21.6 ± 13.7	21.5 ± 14.0	21.7 ± 13.3	21.7 ± 13.5	0.9765
Median	17.8	17.4	18.0	18.0	
Distribution (mo) ^b					0.2142
0–5	51 (5.2)	31 (7.0)	9 (3.5)	11 (3.8)	
6–11	233 (23.6)	103 (23.3)	57 (22.4)	73 (25.0)	
12–23	366 (37.0)	156 (35.3)	104 (40.8)	106 (36.3)	
24–35	167 (16.9)	72 (16.3)	40 (15.7)	55 (18.8)	
36–47	100 (10.1)	51 (11.5)	28 (11.0)	21 (7.2)	
48–60	72 (7.3)	29 (6.6)	17 (6.7)	26 (8.9)	
Household member with AGE history (Vomiting or diarrhea) ^b	229 (23.2)	97 (22.0)	64 (25.1)	68 (23.3)	0.6353
Stool test					
Rotavirus ^b	200 (20.2)	102 (23.1)	63 (24.7)	35 (12.0)	0.0001 ^a
Norovirus ^b	144 (14.6)	56 (12.7)	36 (14.1)	52 (17.8)	0.1506
Oral rotavirus vaccine ^b				0.5885	
With vaccine	158 (16.0)	65 (14.7)	42 (16.5)	51 (17.5)	
Without vaccine	831 (84.0)	377 (85.3)	213 (83.5)	241 (82.5)	

^a*p* < 0.05 for the χ^2 test or ANOVA; ^b χ^2 test for comparison of categorical data; ^cOne-way analysis of variance (ANOVA) for continuous data. SD=standard deviation; AGE=acute gastroenteritis.

**Figure.** Monthly distribution of norovirus and rotavirus among hospitalized young children with acute diarrhea in Taiwan, 2009.

could indeed be more frequent in older children and adults but not severe enough to require hospitalization.

One review study demonstrated that norovirus gastroenteritis predominantly occurs in cold weather between

November and March in the northern hemisphere.²⁹ However, the prevalent season of norovirus infection was highly variable in different regions as shown in some studies.^{8,15,30} A study conducted in China showed that norovirus infection

peaked in autumn (August–November). It has been reported that norovirus is prevalent all year around in Hong Kong and during the warmer months in Indonesia. Some studies indicate that the prevalence of rotavirus infection is higher during cooler months in temperate zones.^{9,11,13,17–20,52,56–59} However, infection shows less distinct seasonality but has a peak during the dry months in tropical countries. This study demonstrates that the detection rates of rotavirus and norovirus were both higher during winter and early spring (December–April) in Taiwan but the peak incidence of norovirus occurred earlier than that of rotavirus.

As shown in many previous studies,^{7,15,32,33} rotavirus infection typically manifested as fever and vomiting, followed by profuse diarrhea. Norovirus infection results in a higher rate of vomiting in children but diarrhea in adults, and usually a shorter course of disease, around 1–3 days. Our findings show that patients with norovirus gastroenteritis presented with a low grade fever, or no fever at all, and a longer duration of vomiting compared with those with rotavirus gastroenteritis. We found the severity of diarrhea and days of hospitalization for patients positive for norovirus were not less than those infected with rotavirus. These findings differ from those of studies in northern Taiwan^{3,7} that demonstrated patients with rotavirus gastroenteritis had a longer course than those with norovirus diarrhea. An explicit finding of this study indicated a far higher proportion of diarrheal patients infected by either norovirus or rotavirus was associated with vomiting (74.8% and 74.9%, respectively) compared with the other enteropathogens group. Some studies in northern Taiwan^{3,7} demonstrated that higher levels of C-reactive protein along with variable leukocytosis were noted in patients with rotavirus diarrhea compared with those with norovirus diarrhea. However, no apparent difference in the laboratory findings was found between patients with rotavirus and norovirus diarrhea in our study.

Our study had several limitations. First, only patients suffering from acute diarrhea were enrolled, and this enrolled criteria possibly underestimated the true occurrence rate of enteropathogen infection if patients initially presented with vomiting and less intense diarrhea. The severity of gastroenteritis for hospitalized pediatric patients was roughly estimated by duration and frequency of vomiting and diarrhea, and no apparent difference was found between norovirus and rotavirus diarrheal cases. A more objective

dehydration scale should be introduced to assess the severity of gastroenteritis resulting from different infectious pathogens.

In conclusion, norovirus was one of the major infectious agents, secondary only to rotavirus, which caused hospitalization of children less than 5 years of age with acute diarrhea in Taiwan. The prevalent season for norovirus gastroenteritis was similar to that of rotavirus gastroenteritis, i.e. winter and the early spring months. We found it difficult to differentiate norovirus from rotavirus according to the laboratory findings and the clinical symptoms; however, norovirus infection came with a lower grade fever and longer duration of vomiting. A history of household members simultaneously suffering from gastroenteritis might hint at the possibility of norovirus infection.

References

1. Chang CW, Chen PY, Huang FL. Epidemiology of diarrhea among young children: a questionnaire-based study in Taiwan. *J Microbiol Immunol Infect* 2009;42:265–70.
2. Chen KT, Fana SF, Huang YF, Lee PI, Chen PY, Tang CW. Hospital-based study of the economic burden associated with rotavirus diarrhea in Taiwan. *Vaccine* 2007;25:4266–72.
3. Chen SM, Ni YH, Chen HL, Chang MH. Microbial etiology of acute gastroenteritis in hospitalized children in Taiwan. *J Formos Med Assoc* 2006;105:964–70.
4. Lu TM, Tsai HT, Cheng YW, Chin LW, Yang CC. Gastroenteroviruses infection in Taiwan. *The Open Infect Diss J* 2009;3:37–43.
5. Parashar UD, Hummelman EG, Bresee JS, Miller MA, Glass RI. Global illness and deaths caused by rotavirus disease in children. *Emerg Infect Dis* 2003;9:565–72.
6. Patel MM, Widdowson MA, Glass RI, Akazawa K, Jan Vinjé, Parashar UD. Systematic literature review of role of noroviruses in sporadic gastroenteritis. *Emerg Infect Dis* 2008;14:1224–31.
7. Wu TC, Liu HH, Chen YJ, Tang RB, Hwang BT, Yuan HC. Comparison of clinical features of childhood norovirus and rotavirus gastroenteritis in Taiwan. *J Chin Med Assoc* 2008;71:566–70.
8. Cheryl S.Y.Li, Paul K.S. Chan, and Julian W. Tang. Prevalence of diarrhea viruses in hospitalized Children in Hong Kong in 2008. *J Med Virol* 2009;81:1903–11.
9. Junquera CG, de Baranda CS, Mialdea OG, Serrano EB, Sánchez-Fauquier A. Prevalence and clinical characteristics of norovirus gastroenteritis among hospitalized children in Spain. *Pediatr Infect Dis J* 2009;28:604–7.
10. Chen SY, Chang YC, Lee YS, Chao HC, Tsao KC, Lin TY, et al. Molecular epidemiology and clinical manifestations of viral gastroenteritis in hospitalized pediatric patients in Northern Taiwan. *J Clin Microbiol* 2007;45:2054–7.

11. Lu CY, Lauderdale TL, Fang YH, Wang CY, Ho YH, Hung CL. Disease burden and related medical costs of rotavirus infections in Taiwan. *BMC Infectious Diseases* 2006;6:176.
12. Wu FT, Liang SY, Tsao KC, Huang CG, Lin CY, Lin JS, et al. Hospital-based surveillance and molecular epidemiology of rotavirus infection in Taiwan, 2005–2007. *Vaccine* 2009; 27S:F50–4.
13. Wu FT, Oka T, Katayama K, Wu HS, Donald Jiang DS, Miyamura T, et al. Genetic diversity of noroviruses in Taiwan between November 2004 and March 2005. *Arch Virol* 2006;151:1319–27.
14. Victoria M, Carvalho-Costa FA, Heinemann MB, Leite JP, Miagostovich M. Prevalence and molecular epidemiology of noroviruses in hospitalized children with acute gastroenteritis in Rio de Janeiro, Brazil, 2004. *Pediatr Infect Dis J* 2007;26:602–6.
15. Subekti D, Lesmana M, Tjaniadi P, Safari N, Frazier E, Simanjuntak C, et al. Incidence of Norwalk-like viruses, rotavirus and adenovirus infection in patients with acute gastroenteritis in Jakarta, Indonesia. *FEMS Immunol Med Microbiol* 2002;33:27–33.
16. O’Ryan ML, Lucero Y, Prado V, Santolaya ME, Rabello M, Solis Y, et al. Symptomatic and asymptomatic rotavirus and norovirus infections during infancy in a Chilean birth cohort. *Pediatr Infect Dis J* 2009;28:879–84.
17. Mamdoh M, Meqdam I, Ibrahim R, Thwiny. Prevalence of group A rotavirus, enteric adenovirus, norovirus and astrovirus infections among children with acute gastroenteritis in Al-Qassim, Saudi Arabia. *Pak J Med Sci* 2007;23:551–5.
18. Nguyen VM, Nguyen VT, Huynh PL, Dang DT, Nguyen TH, Phan VT, et al. Vietnam Rotavirus Surveillance Network. The epidemiology and disease burden of rotavirus in Vietnam: sentinel surveillance at 6 hospitals. *J Infect Dis* 2001;183:1707–12.
19. Bresee J, Fang ZY, Wang B, Nelson EA, Tam J, Soenarto Y, et al. Asian Rotavirus Surveillance Network. First report from the Asian Rotavirus Surveillance Network. *Emerg Infect Dis* 2004;10:988–95.
20. Karadag A, Acikgoz ZC, Avci Z, Catal F, Gocer S, Gamberzade S, et al. Childhood diarrhoea in Ankara, Turkey: epidemiological and clinical features of rotavirus-positive versus rotavirus-negative cases. *Scand J Infect Dis* 2005;37:269–75.
21. Nelson EA, Widdowson MA, Kilgore PE, Steele D, Parashar UD. A decade of the Asian Rotavirus Surveillance Network: achievements and future directions. *Vaccine* 2009;27(Suppl 5):F1–3.
22. Nelson EA, Bresee JS, Parashar UD, Widdowson MA, Glass RI; Asian Rotavirus Surveillance Network. Rotavirus epidemiology: the Asian Rotavirus Surveillance Network. *Vaccine* 2008;26:3192–6.
23. Brandt CD, Kim HW, Rodriguez WJ, Arrobio JO, Jeffries BC, Parrott RH. Rotavirus gastroenteritis and weather. *J Clin Microbiol* 1982;16:478–82.
24. Levy K, Hubbard AE, Eisenberg JN. Seasonality of rotavirus disease in the tropics: a systematic review and meta-analysis. *Int J Epidemiol* 2009;38:1487–96.
25. Atchison CJ, Tam CC, Hajat S, van Pelt W, Cowden JM, Lopman BA. Temperature-dependent transmission of rotavirus in Great Britain and The Netherlands. *Proc Biol Sci* 2010;277:933–42.
26. Morris OP, Edward AE. Influence of humidity on rotavirus prevalence among Nigerian infants and young children with gastroenteritis. *J Clin Microbiol* 1982;15:212–5.
27. Xu J, Yang Y, Sun J, Ding Y, Su L, Fang Z, Glass R. Molecular epidemiology of rotavirus infections among children hospitalized for acute gastroenteritis in Shanghai, China, 2001 through 2005. *J Clin Virol* 2009;44:58–61.
28. Chiu TF, Lee CN, Lee PI, Kao CL, Lin HC, Lu CY, et al. Rotavirus gastroenteritis in children: 5-year experience in a medical center. *J Microbiol Immunol Infect* 2000;33:181–6.
29. Mounts AW, Ando T, Koopmans M, Bresee JS, Noel J, Glass RI. Cold weather seasonality of gastroenteritis associated with Norwalk-like viruses. *J Infect Dis* 2000;181(Suppl 2):S284–7.
30. Xu J, Yang Y, Sun J, Ting Y. Molecular epidemiology of norovirus infection among children with acute gastroenteritis in Shanghai, China, 2001–2005. *J Clin Virol* 2009;81:1826–30.
31. Mast TC, Chen PY, Lu KC, Hsu CM, Lin HC, Liao WC, et al. Epidemiology and economic burden of rotavirus gastroenteritis in hospitals and paediatric clinics in Taiwan, 2005–2006. *Vaccine* 2010;28:3008–13.
32. Cheng AC, McDonald JR, Thielman NM. Infectious diarrhea in developed and developing countries. *J Clin Gastroenterol* 2005;39:757–73.
33. Narkeviciute I, Tamusauskaite I. Peculiarities of norovirus and rotavirus infections in hospitalised young children. *J Pediatr Gastroenterol Nutr* 2008;46:289–92.