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Clinical and Epidemiologic Features of Severe Viral Gastroenteritis in Children: A 3-Year Surveillance, Multicentered Study in Taiwan With Partial Rotavirus Immunization

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Abstract: The global epidemiological landscape of childhood acute gastroenteritis (AGE) is changing after the introduction of 2 effective rotavirus vaccines in 2006. A comprehensive evaluation for viral etiology of childhood AGE in Taiwan, where rotavirus vaccination was provided by the private sector since 2006, is lacking.

From 2009 to 2011, children younger than 5 years of age with AGE who were hospitalized at 3 sentinel hospitals were enrolled in this surveillance study. Stool specimens were tested for rotavirus, norovirus, enteric adenovirus, and astrovirus. The epidemiologic and clinical information was collected by questionnaire-based interviews and chart reviews.

Viral agents were detected in 1055 (37.5%) of 2810 subjects, with rotavirus (21.2%) being the leading cause of disease, followed by norovirus (14.9%), enteric adenovirus (3.74%), astrovirus (2.10%), and a mixture of at least 2 of 4 above-mentioned viruses (4.06%). The majority (56%) of the viral AGE occurred in children <2 years of age. Rotavirus and norovirus were detected more frequently in cool seasons ($P < 0.0001$ for both), whereas no seasonal variation was observed for adenovirus and astrovirus. Adult households with diarrhea and a Vesikari score >10 were independent factors respectively associated with an increased risk of norovirus (adjusted odds ratio [aOR] 9.034, $P = 0.0003$) and rotavirus (aOR, 3.284, $P < 0.0001$) infections. Rotavirus immunization and female gender were protective factors against rotavirus (aOR, 0.198, $P < 0.0001$) and astrovirus (aOR, 0.382, $P = 0.0299$) infections, respectively.

Rotavirus and norovirus are the 2 most important viral agents of childhood AGE in Taiwan with partial rotavirus immunization. In addition, different enteric viruses are associated with distinct epidemiologic and clinical features.

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Abbreviations: AGE = acute gastroenteritis, Taiwan CDC = Centers for Disease Control, Taiwan, PCR = polymerase chain reaction.

INTRODUCTION

Acute gastroenteritis (AGE) is a very common pediatric illness and remains a significant cause of childhood morbidity and mortality worldwide.[1,2] Children younger than 5 years of age are most vulnerable to severe AGE. In 2010, it is estimated that 2.7 diarrhea episodes per child, yearly, occurred in children aged 0 to 4 years, and acute diarrhea accounted for 700,000 pediatric deaths in 2011 worldwide.[2] Since 2006, the disease burden of AGE and rotavirus-associated AGE has been significantly reduced following the implementation of a rotavirus immunization program in the United States.[3] Norovirus has now became the leading cause of medically attended AGE in US children.[4] The changing epidemiology of pediatric diarrhea has also been impacted by the frequent emergence of new variants of enteric viruses and their associated global AGE epidemics.[5,6]

Before the introduction of rotavirus vaccines in 2006, rotavirus was the leading cause of severe diarrhea in Taiwanese children.[7] Similar to the conditions in the United States and other countries, with the increasing use of immunizations against rotavirus, it appeared that the incidence of severe rotavirus AGE in children was decreasing in Taiwan.[8] However, complete information regarding enteric viral agents and epidemiologic features of severe pediatric AGE is lacking[9], and comprehensive investigation on a national scale and across multiple seasons has not yet been performed since the introduction of the rotavirus vaccine. To monitor the epidemiologic changes in pediatric AGE in the postvaccine era, we conducted a 3-year sentinel surveillance study to investigate the viral etiologies and their associated epidemiological and clinical features in severe childhood AGE.

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METHODS

Study Design

This was a multicenter, prospective surveillance study evaluating the epidemiology of acute diarrhea due to various viral and bacterial etiologies in Taiwanese children. The study was conducted in 3 sentinel hospitals from January 1, 2009 to December 31, 2011. Children were eligible for the surveillance study if they met all of the following criteria: hospitalized in 1 of the 3 hospitals; aged 2 to 60 months; and presented with diarrhea without any known underlying disease. Diarrhea was defined as the occurrence of 3 or greater episodes of unformed stool within a period of 24 hours of acute illness. Active surveillance of acute diarrhea was conducted by monitoring the reception log of stool samples subjected to microbiology tests in the clinical microbiology laboratory in each of the 3 hospitals. Those who met the inclusion criteria, and for whom a written informed consent was obtained from the parents or guardians, were enrolled in the study. The surveillance study was approved by the institutional review boards of the National Health Research Institute of Taiwan and each of the 3 study sites.

Demographics and Anthropometric Characteristics of the Subjects

A standardized questionnaire-based interview of the parents or primary caregivers of the enrolled subjects was performed to collect demographic and anthropometric information (Table 1). Information on the clinical features of the diarrhea illness was obtained by chart review. The severity of AGE was defined according to the Vesikari clinical severity scoring system.[10] Briefly, the system contains 7 scoring parameters including maximum number and duration of diarrhea, maximum number and duration of vomiting, body temperature, degree of dehydration, and treatment. Each of the 7 parameters is broken into thirds according to an equally divided severity distribution (bottom third = 1, middle third = 2, top third = 3). A sum of the scores of less than 7, 7 to 10, and greater than 10 was considered as mild, moderate, and severe, respectively. The demographic and clinical data were digitized and organized in a computer core laboratory before statistical analysis. The data of air temperature of each month during the period of study were obtained from the Central Weather Bureau in Taiwan.

Stool Collection and Microbiological Tests

Stool samples were collected from subject patient during the period of hospitalization. All of the stool specimens were screened for rotavirus VP6 antigen using an enzyme immunoassay kit (RIDASCREEN Rotavirus, R-Biopharm AG, Darmstadt, Germany) at each study site. All specimens were then sent to the reference laboratory at the Centers for Disease Control, Taiwan (Taiwan CDC) for confirmatory testing of rotavirus and further detection of norovirus, enteric adenovirus, astrovirus by well-established polymerase chain reaction (PCR) methods as described elsewhere.[11–15] For identification of enteric bacteria, the culture methods were used in both the clinical microbiology laboratory at each sentinel sites and the reference laboratory of Taiwan CDC. All stool samples were frozen and stored at −80°C until the time of assay.

Statistical Analysis

The descriptive statistics were performed using an SAS 9.3 for windows (SAS Institute, Inc., Cary, NC). Comparison of categorical variables between 4 viral agents was performed with a χ^2 test or with the Fisher exact test where appropriate, whereas differences among the numerical variables were analyzed by an 1-way ANOVA test. Multinomial logistic regression analysis was applied to explore factors associated with infection of rotavirus, norovirus, and astrovirus using adenovirus as referent. The trends in the proportions of specific viral agents in 5 defined age groups were tested by the Mantel–Haenszel χ^2 method. Statistical significance was defined as a P-value of <0.05.

RESULTS

Epidemiology of Viral Gastroenteritis in Taiwanese Children, 2009 to 2011

From January 2009 to December 2011, a total of 2810 children aged 2 to 60 months (mean age, 22.1 ± 13.9 months) with acute diarrhea were enrolled in this surveillance cohort. Of these included children, 42.9% were female. The age and gender distributions were not significantly different for the subjects across the different study sites ($P = 0.7521$ and 0.2501, respectively) and different years of enrollment ($P = 0.3561$ and 0.1950, respectively). Viral agents were detected in 1055 (37.5%) subjects, with rotavirus (21.2%) representing the leading cause of disease, followed by norovirus (14.9%), adenovirus (3.74%), astrovirus (2.10%), and mixed viruses (4.06%). Infections with bacterial pathogens including *Salmonella* spp. and *Campylobacter* spp. were identified in 27.4% and 2.25% of subjects, respectively. The detailed distribution of viral etiologies among subjects from distinct study sites from different years is displayed in Table 2. The prevalence of rotavirus infection differed across the 3 study sites (range, 18.8–23.8%, $P = 0.0408$) but did not change significantly according to year of enrollment ($P = 0.8137$). The prevalence of norovirus was relatively consistent among the 3 study sites ($P = 0.2077$) but varied significantly across study years (range, 11.9–17.8%, $P = 0.0026$). Adenovirus and astrovirus were identified at low frequencies, and each infection accounted for less than 5% of diarrhea cases within any single site or any year of study. The case distributions across sites and years of study were not significantly different for either virus (Table 2).

Age-Specific Distribution of Viral Etiologies in Pediatric Diarrhea

The majority of pediatric diarrhea cases requiring hospitalization occurred in children younger than 2 years of age in this cohort and accounted for 56.0% (591/1055) of subjects with viral gastroenteritis, 51.0% (304/596) of subjects with rotavirus gastroenteritis, and 64.1% (264/412) of subjects with norovirus gastroenteritis. The increased proportion of viral to all-cause gastroenteritis when age advanced was highly significant for rotavirus (P for trend < 0.0001). These proportions did not change significantly in distinct age groups for norovirus ($P = 0.1269$) and adenovirus ($P = 0.8856$). Additionally, there was no obvious trend of proportion changes for astrovirus with increasing age (P for trend $= 0.1107$) (Table 3).

Temporal Distribution of Enteric Viruses and Correlation With Air Temperature

Viral gastroenteritis occurred more frequently in cool seasons (November to April) when the average air temperature was below 25°C compared to the warm seasons (May to October) when the average temperature was above 25°C (52.4% vs. 23.6%, $P < 0.0001$). This increased incidence of

TABLE 1. Univariate Analysis of Epidemiological Factors and Clinical Features in Pediatric Diarrhea of Distinct Viral Origin

Factor	Rotavirus, N = 498	Norovirus, N = 320	Adenovirus, N = 80	Astrovirus, N = 43	*P*-Value
Demographics					
Female gender (%)	43.5	40.3	41.3	20.9	0.0376
Age in months (mean ± SD)	26.9 ± 15.3	21.8 ± 13.0	22.5 ± 13.7	27.1 ± 15.2	<0.0001
Race/ethnicity					0.9684
Han Taiwanese (%)	91.0	91.0	91.3	88.4	
Offspring of foreign parents (%)	7.04	6.88	7.69	6.98	
Aborigines (%)	2.01	2.19	2.50	4.65	
Rotavirus immunization					
Any dose of RotaTeq (%)	0.60	9.69	5.0	14.0	<0.0001
Any dose of Rotarix (%)	4.02	12.5	18.8	14.0	<0.0001
Any dose of either vaccine (%)	4.62	22.2	23.8	27.9	<0.0001
Year, season, and site of disease occurrence					
2009/2010/2011 (%)	33.6/35.2/31.2	34.4/43.8/21.9	32.5/41.3/26.3	27.9/30.2/41.9	0.0254
Cool season, Nov-Apr (%)	67.6	71.6	55.0	51.2	0.0043
Site I/II/III (%)	40.0/30.3/29.7	38.4/24.1/37.5	41.3/21.3/37.5	51.2/16.3/32.6	0.0737
Household condition					
Number of members (mean ± SD)	4.7 ± 2.2	4.6 ± 2.0	4.7 ± 2.1	5.0 ± 3.1	0.7473
Acute diarrhea episodes in					
Any household member (%)	40.2	47.5	23.8	41.9	0.0014
Parents or grandparents (%)	12.3	26.9	3.75	16.3	<0.0001
Siblings (%)	30.5	29.1	20.0	39.5	0.1203
Animal contact					
Dogs (%)	17.7	15.3	15.0	6.98	0.2879
Cats (%)	2.21	3.44	5.00	4.65	0.4228
Clinical features					
Appearance of URI symptoms* (%)	65.6	56.3	63.8	62.8	0.0620
Total fever duration (days, mean ± SD)	3.2 ± 2.2	2.8 ± 2.8	3.4 ± 3.0	3.6 ± 3.8	0.0299
Max. body temp. (°C, mean ± SD)	39.2 ± 0.7	39.1 ± 0.9	39.4 ± 0.8	39.1 ± 0.6	0.0413
Total vomiting duration (days, mean ± SD)	1.7 ± 1.5	1.7 ± 1.9	1.6 ± 2.0	1.1 ± 1.7	0.1788
Max. vomiting episodes/24 hours (mean ± SD)	4.8 ± 3.3	4.5 ± 4.0	2.9 ± 2.7	2.7 ± 2.5	<0.0001
Total diarrhea duration (days, mean ± SD)	5.1 ± 2.0	5.6 ± 2.6	6.9 ± 3.4	5.7 ± 2.5	0.0019
Max. diarrhea episodes/24 hours (mean ± SD)	7.7 ± 4.1	7.3 ± 4.4	6.9 ± 3.4	7.2 ± 3.5	0.2344
Vesikari score >10 (%)	57.0	32.8	27.9	26.3	<0.0001
Hospital stay (days, mean ± SD)	4.5 ± 2.1	4.7 ± 2.3	5.0 ± 2.6	4.5 ± 1.9	0.2625
Laboratory data (mean ± SD)					
White blood cell counts	10,961 ± 6144	11,150 ± 5543	12,343 ± 5011	10,359 ± 3894	0.1996
CRP (mg/L)	14.1 ± 30.6	18.2 ± 35.1	23.5 ± 39.6	17.5 ± 30.3	0.1119
Bacterial coinfection† (%)	6.22	13.1	13.8	11.6	0.0045

CRP = C-reactive protein, Max = maximal, SD = standard deviation, URI = upper respiratory tract infection.
* URI symptoms indicated cough and rhinorrhea.
† *Salmonella* spp. or *Campylobacter* spp. infections.

viral gastroenteritis occurring more frequently in cool seasons was significant for rotavirus (29.8% vs. 13.2%, $P < 0.0001$) and norovirus (22.7% vs. 7.8%, $P < 0.0001$) but not for adenovirus (4.41% vs. 3.31%, $P = 0.0735$, Fisher exact test) or astrovirus (2.42% vs. 1.80, $P = 0.2883$, Fisher exact test) (Figure 1).

Etiology-Specific Features for Distinct Viral Gastroenteritis

Among 1055 subjects with confirmed viral infections, 468 (44.4%) had a Vesikari score >10 indicating severe gastroenteritis. The mean hospital stay was 4.65 ± 2.26 days (range, 1–22 days), and the mean duration for fever, vomiting, and diarrhea was 3.12 ± 2.59, 1.68 ± 1.71, and 5.40 ± 2.31 days, respectively. The epidemiological and clinical features of subjects infected with the 4 distinct viral agents are displayed in Table 1. The 4 groups of subjects differed significantly in demographics and immunization history against rotavirus. The subjects also differed according to the rates of household members with acute diarrhea, with the highest incidence (47.5%) for norovirus infection. The appearance of symptoms of upper respiratory tract infection was very common and occurred in 56.3% to 65.6% of the subjects with viral gastroenteritis. Coinfection with bacteria was less frequently identified in rotavirus infections (6.22%, $P = 0.0045$). Nevertheless, rotavirus was associated with the greatest disease severity, as indicated by a higher incidence of subjects with a Vesikari score >10 in rotavirus infections (57.0%) compared to infections with the other 3 viruses (range, 26.3–32.8%, $P < 0.0001$).

Multinomial logistic regression analysis identified different panels of factors associated with distinct types of viral gastroenteritis (Table 4). In particular, immunization against

TABLE 2. Distribution of Viral Etiologies of Acute Pediatric Diarrhea in Three Medical Centers in Taiwan From 2009 to 2011

			Study Site, %				Study Year, %			
Organism	Tested Samples, No.	Positive Samples, No. (%)	Site I, N = 1087	Site II, N = 772	Site III, N = 951	*P*-Value	2009, N = 1003	2010, N = 953	2011, N = 854	*P*-Value
Any virus	2810	1055 (37.5)	38.6	37.2	36.7	0.6701	36.0	42.0	34.4	0.0019
Rotavirus	2809	596 (21.2)	21.4	23.8	18.8	0.0408	20.6	21.8	21.2	0.8137
Norovirus	2766	412 (14.9)	14.8	13.3	16.3	0.2077	14.6	17.8	11.9	0.0026
Adenovirus	2810	105 (3.74)	3.86	3.11	4.10	0.5468*	3.49	4.62	3.04	0.1954*
Astrovirus	2766	58 (2.10)	2.72	1.84	1.60	0.1974*	1.90	2.10	2.34	0.7814*
Mixed viruses†	2810	114 (4.06)	3.86	4.53	3.89	0.7311*	4.59	4.09	3.40	0.4384*
Mixed virus/bacteria‡	2810	83 (2.95)	3.13	4.15	1.79	0.0127*	3.09	3.57	2.11	0.1681*

* Fisher exact test comparing the yearly incidences of indicated virus during 2009 and 2011.

† Coinfections with 2 viral agents were identified in 112 cases, including rotavirus and norovirus in 75 cases, rotavirus and adenovirus in 11 cases, rotavirus and astrovirus in 10 cases, norovirus and adenovirus in 13 cases, norovirus and astrovirus in 2 cases, and adenovirus and astrovirus in 1 case. Coinfections with 3 viral agents (norovirus, rotavirus, and astrovirus) were identified in 2 cases.

‡ The bacterial agents were identified as *Salmonella* spp. and/or *Campylobacter* spp. Other potential bacterial pathogens of enterocolitis (ie, *Escherichia coli* and *Staphylococcus aureus*) were not included for analysis.

rotavirus was associated with a decreased incidence of rotavirus infection (adjusted odds ratio [aOR] 0.198, $P < 0.0001$), whereas a Vesikari score >10 increased the risk of rotavirus infections (aOR, 3.284, $P < 0.0001$). In addition, parents or grandparents with diarrhea was associated with 9-fold increased risk of norovirus infection (aOR, 9.034, $P = 0.0003$). The cold season was a significant factor predicting norovirus infection (aOR, 1.914, $P = 0.0173$), whereas female gender was a protective factor against astrovirus infection (aOR, 0.382, $P = 0.0299$).

DISCUSSION

Results from the present study indicate that rotavirus remained the leading cause of viral gastroenteritis requiring hospitalization in Taiwanese children from 2009 to 2011. Rotavirus vaccines, including Rotarix (GlaxoSmithKline Biologicals, Rixensart, Belgium) and RotaTeq (Merck and Co., Inc., West Point, PA), were introduced into Taiwan as a self-paid vaccine during late 2006. The uptake rate of full-dose vaccine (2 doses for Rotarix and 3 doses for RotaTeq) was estimated to be 19.4% for each annual birth cohort from 2009 to 2011 (merged data from Merck and Co. and GlaxoSmithKline, Taiwan branch). This estimate was generally consistent with the data in the present study showing that 21.6% (609/2810) of all subjects reportedly received at least 1 dose of rotavirus vaccine. Under partial immunization, we demonstrated that 21.2% of the pediatric diarrhea cases requiring hospitalization remained related to rotavirus infections. Nevertheless, this rate was largely reduced compared to data in the prevaccine era. From 2001 to 2006, the rates were at least 2-fold higher, ranging from 43% and 46%, respectively, in 2 large-scale hospital-based studies with similar design and similar age groups (<5 years old).[16,17] Results from the Asian Rotavirus Surveillance Network disclosed an even higher rate of 49% (range, 43–53%) in Taiwan from 2001 to 2002.[7] Taken together, these data suggest a marked reduction of rotavirus-associated hospitalizations in Taiwan when approximately 20% of the vulnerable population was immunized.

The present study provides comprehensive information on the epidemiologic and clinical features associated with each of

TABLE 3. Age-Specific Etiologies of Pediatric Diarrhea Requiring Hospitalization in Taiwan, 2009–2011

	Age in months, No (%)						
Organisms	2–12, N = 782	13–24, N = 1014	25–36, N = 513	37–48, N = 293	49–60, N = 208	*P*-Value	P_{TREND}†
Any virus	228 (29.2)	363 (35.8)	221 (43.1)	137 (46.8)	106 (51.0)	<0.0001	<0.0001
Rotavirus	113 (14.5)	191 (18.8)	123 (24.0)	98 (33.5)	71 (34.1)	<0.0001	<0.0001
Norovirus	97 (12.7)	167 (16.7)	80 (15.8)	37 (12.7)	31 (15.1)	0.1269	0.6323
Adenovirus	29 (3.71)	39 (3.85)	18 (3.51)	9 (3.07)	10 (4.81)	0.8856*	0.8786
Astrovirus	18 (2.35)	9 (0.90)	16 (3.17)	9 (3.09)	6 (2.93)	0.0064*	0.1107
Mixed viruses	28 (3.58)	42 (4.14)	16 (3.12)	16 (5.46)	12 (5.77)	0.3050*	0.1545
Mixed virus and bacteria	19 (2.43)	33 (3.25)	25 (4.87)	7 (2.39)	8 (3.85)	0.1565*	0.2427

* Fisher exact test.

† *P*-value for trend. The significance between prevalence trend and age was determined with the Cochran–Mantel–Haenszel method.

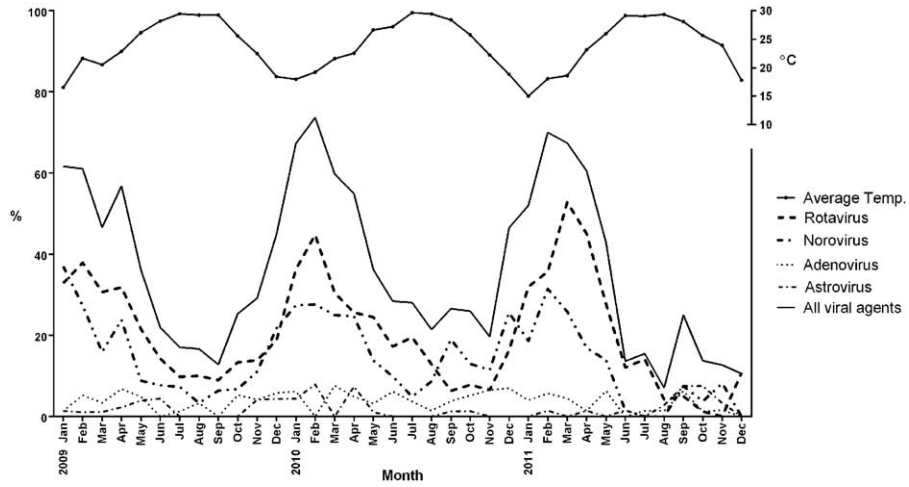

FIGURE 1. The average air temperatures and monthly distributions of viral etiologies in Taiwanese children with AGE requiring hospitalization from 2009 to 2011.

the 4 most common enteric viruses in children. The simultaneous evaluation of the viruses generated different panels of etiology-specific features, which are relevant in studies of viral behavior and useful in clinical practice. For instance, immunization with any dose of rotavirus vaccine substantially diminished the probability of rotavirus infection by approximately 80%. In contrast, a Vesikari score >10 was strongly suggestive of rotavirus infection. Subjects with a greater severity of rotavirus infection, compared to those with other enteric viral infections designated by the measurement of Vesikari scores, has been demonstrated elsewhere.[18,19] Parents or grandparents with acute diarrhea was a significant factor predicting norovirus infection. The household diarrhea history was of marginal significance for rotavirus and astrovirus infection. The observation was consistent with the previous findings that norovirus was capable of causing severe disease in subjects, irrespective of age, whereas symptomatic infections of rotavirus and enteric adenovirus generally occurred in children younger than 5 years of age.[1,20]

Norovirus is the most common agent responsible for foodborne gastroenteritis outbreaks worldwide.[21,22] It was intriguing to learn that the annual incidence of norovirus infections fluctuated from year to year across the 3 years of the study. This observation occurred in contrast to rotavirus, for which the year-to-year rate was relatively stable (Table 2). It has been well documented that new variants of norovirus emerge frequently and that global pandemics usually occur every few years.[5] The epidemic outbreaks associated with emerging variants can have a substantial impact on the local epidemiology of norovirus diseases. Indeed, the emerging pandemic strains in the past decade, including ''Hunter'' virus, the ''2006a and 2006b'' strains, and the ''Sydney'' strain of GII.4 norovirus, which were, respectively, identified in 2004, 2006, and 2012, also caused outbreaks in Taiwan in the indicated years.[8,23] Another new epidemic strain, GII.4 2010, was associated with an outbreak of severe norovirus infections in Taiwanese children in 2010.[8] This new variant also likely affected the temporal distributions of norovirus in the study years and may have been

TABLE 4. Etiology-Specific Factors of Acute Viral Gastroenteritis Requiring Hospitalization in Taiwanese Children, Identified by Comparing the Factors Between the Indicated Virus, and Adenovirus Using Multinomial Logistic Regression Analysis

Factors	Rotavirus aOR (95% aCI)	*P*-Value	Norovirus aOR (95% aCI)	*P*-Value	Astrovirus aOR (95% aCI)	*P*-Value
Female gender	1.065 (0.647–1.753)	0.8052	0.989 (0.593–1.650)	0.9661	0.382 (0.160–0.910)	0.0299
Age in month	1.008 (0.990–1.027)	0.3676	0.993 (0.974–1.012)	0.4522	1.024 (0.997–1.053)	0.0829
Rotavirus immunization	0.198 (0.098–0.400)	<0.0001	0.923 (0.493–1.728)	0.8024	1.357 (0.541–3.406)	0.5156
Disease occurring in						
Cool season	1.273 (0.761–2.129)	0.3578	1.914 (1.121–3.265)	0.0173	0.766 (0.351–1.672)	0.5040
2009 (vs. 2011)	0.761 (0.400–1.447)	0.4051	1.324 (0.679–2.582)	0.4095	0.635 (0.244–1.650)	0.3510
2010 (vs. 2011)	0.675 (0.366–1.245)	0.2085	1.188 (0.630–2.241)	0.5938	0.469 (0.188–1.169)	0.1042
Parents or grandparents with diarrhea	3.468 (1.047–11.492)	0.0419	9.034 (2.761–29.557)	0.0003	4.695 (1.131–19.496)	0.0332
Vesikari score >10	3.284 (1.911–5.644)	<0.0001	1.299 (0.738–2.285)	0.3643	1.003 (0.429–2.344)	0.9952
Bacterial coinfection	0.562 (0.252–1.250)	0.1575	1.280 (0.594–2.761)	0.5286	0.609 (0.172–2.155)	0.4421

aCI = adjusted confidence interval, aOR = adjusted odds ratio.

responsible for the increased number of cases in 2010 in the present study.

Astrovirus infection was reported in a range of 2% to 16% of children hospitalized for diarrhea worldwide,[24–26] and a hospital-based survey in northern Taiwan in 1998 to 1999 disclosed that 2.9% of childhood diarrhea was caused by astrovirus.[27] In the present study, astrovirus infection accounted for a similar low rate of AGE cases (2.1%). The data indicated that astrovirus was of relatively low virulence and played a limited role in severe diarrhea in Taiwanese children. Interestingly, approximately 80% of subjects with astrovirus infection were male. The particular vulnerability of male children to severe astrovirus infections was also observed in the above-mentioned survey in northern Taiwan, in which male gender accounted for 75% (9/12) of astrovirus-infected subjects.[27] Further investigation may be required to explore the biologic role of gender in astrovirus infection. Alternatively, the gender factor may be merely a confounding factor, given that potential host factors including cleanliness or other personal hygiene behaviors were not collected for analysis.

Although diarrhea can be seen in ''respiratory'' types of adenovirus infections (ie, types 3 and 7), adenoviral gastroenteritis is mainly caused by the enteric fastidious species types 40 and 41, which were reported in 5% to 15% of cases of acute pediatric diarrhea.[28–30] We observed a slightly lower incidence of 3.74% in the present study. Adenovirus shared similar patterns of temporal distributions with astrovirus. In particular, these infections occurred throughout the year during the period of study without the significant seasonal variation seen in cases of rotavirus and norovirus infection.

Among the study subjects, an increasing proportion of rotavirus etiology was noted as their age advanced (Table 3). However, this factor of age for rotavirus etiology was not statistically significant after adjusted by multinomial logistic regression analysis (Table 4). In addition, these data should be interpreted with caution and should not be interpreted as the older children with an increased risk of severe rotavirus infection. Rather, this finding suggests that rotavirus be a more virulent agent than the other 3 viruses, capable of causing severe disease even in the older age group. Young children, particularly those less than 2 years of age, remained the population with the largest disease burden of severe rotavirus gastroenteritis in Taiwan.

In conclusion, this sentinel surveillance study provides a landscape view of the epidemiology of severe viral gastroenteritis in Taiwanese children from 2009 to 2011. Rotavirus remained the leading cause of severe viral gastroenteritis and was associated with the greatest disease severity among subjects with enteric viral infections. However, a marked reduction in rotavirus-associated hospitalization was observed when the population was partially immunized. Norovirus infection was characterized by a substantial fluctuation in yearly incidence, and simultaneous occurrence of diarrhea in adult households. Enteric adenovirus and astrovirus were infrequent enteropathogens in severe childhood AGE. The identified epidemiologic and clinical features associated with each enteric virus are relevant for studies concerning viral behavior and should be useful for healthcare workers dealing with pediatric diarrhea.

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