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Original Article

Epidemiology, clinical features, and microbiology of patients with diarrhea in community clinics in Taiwan

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Abstract *Objective:* To investigate the clinical features and microbiology of patients with diarrheal diseases in Taiwan.
Methods: From March 2014 to October 2014, patients with diarrheal diseases referred from the community clinics were enrolled into our prospective study. Demographics and clinical features of the participants were acquired. Stool samples were examined by the Luminex Gastrointestinal Pathogen Panel assay. Data were analyzed by SAS version 9.4.
Results: A total of 545 patients were enrolled into this study. Male and adults accounted for 52.3% and 82.6% of patients, respectively. The median age was 36 years. Enteropathogen(s) was identified in 43.3% of patients and 8.5% of them had more than one agent in their stool samples. Viruses, especially norovirus GI/GII, were the predominant agents of gastroenteritis. Moreover, *Campylobacter* species was the most common bacterial agent. Bloody stool was frequently reported in patients with bacterial diarrhea ($P = 0.002$); contrarily, watery stool was significantly associated with viral diarrhea ($P < 0.0001$). Regional variation and seasonality of microbiological distribution were also observed.
Conclusion: In Taiwan, viruses were the predominant pathogens among patients with diarrheal diseases who visited community clinics. The therapeutic strategies for diarrheal patients should be based on the epidemiological and clinical characteristics.

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Introduction

Diarrheal disease remains an important medical conundrum and causes significant morbidity and mortality.[1–4] In the past decades, the distribution of enteropathogens among diarrheal patients has been reported by various studies.[2,5–13] However, most of these studies have focused on a selected population of patients who had presented to general practitioners or visited/admitted to hospital-based medical care[2,5–9]; only few reports describe general practice (GP)-based investigations of diarrheal diseases among all patients visiting community clinics.[10–13] Similarly, in Taiwan, most if not all studies concerning diarrheal diseases have focused on a specific pathogen, particular patient population, or patients with severe disease,[14–16] and no GP-based study could be found in the literature.

Conventional laboratory diagnosis of infectious diarrhea is currently based on the combined use of different tests, such as culture, microscopy, antigen detection, and real-time PCR assays. In addition to variable sensitivity and specificity, these identification methods are often laborious, time-consuming, and sometimes require skilled technicians.[17,18] In recent years, the Luminex Gastrointestinal Pathogen Panel (xTAG® GPP), one of the multiplex molecular assays, is increasingly used in clinical practice to identify common enteropathogens among patients with diarrheal diseases.[3,4,19] This test has a short turnaround time (4–5 h) and can detect 15 common enteropathogens and toxins causing infectious diarrhea in a single stool sample.[3,17]

In 2013, we conducted a pilot study using xTAG® GPP to investigate enteropathogens among diarrheal patients who visited community clinics at Taichung county. A total of 250 stool samples were collected and enteropathogens were detected in 17 of these samples (10 *Salmonella* species, 5 *Campylobacter* species, and 2 *Cryptosporidium* species). According to these preliminary data, we conducted the current study to investigate the epidemiology, clinical manifestations, and microbiology of gastroenteritis among patients of all ages who visited community clinics in Taiwan.

Materials and methods

Patients, settings, and definitions

From March 2014 through October 2014, we invited community clinics (1 clinic/200,000 population) from 4 different counties in Taiwan, including Hualien (eastern), Tainan (southern), Taichung (western), and New Taipei City (northern), to participate in our prospective study. All patients presented with an episode of diarrhea reported by the responsible clinics were enrolled. A questionnaire was given to the participants to record their basic demographics, co-morbidities, and associated symptoms at the time of stool specimen collection. Diarrhea was defined as a passage of three or more loose or liquid stools per day. The type of diarrhea was categorized as acute if $<$2 weeks, persistent if 2–4 weeks, and chronic if $>$4 weeks in duration.[20] Mixed infection was defined if more than one pathogen were identified from a stool sample. Medical history of using antibiotics, steroids, or herbs before the diarrheal episode was included in the questionnaire. A question about diarrheal illness among family members, friends, or co-workers (cluster history) was also inquired. Patients who took long-term stool softener, were treated with chemotherapeutic agents, had a history of pathological changes in their intestines (especially inflammatory bowel diseases), or were recruited into another clinical trial in recent one month were excluded from the current study. According to the testing results of stool specimen, patients were divided into two groups, group 1 (negative test result) and group 2 (positive result). This study was approved by the Institutional Review Board of China Medical University Hospital (CMUH104-REC2-009). Informed written consent was obtained from all participants or their guardians in accordance with the Declaration of Helsinki.

Specimen collection and identification of enteropathogens

The stool sample was initially collected in a sterile container, maintained in Cary–Blair transport medium (Becton Dickinson, Franklin Lakes, NJ, USA), and submitted to the central laboratory (Ruei Fu Shih Medical Lab., Taichung, Taiwan) within one day for enteropathogen analysis. Before nucleic acid extraction, each stool sample was pretreated and processed by the following steps: 100 μl stool sample, 1 ml NucliSENS easyMAG Lysis Buffer (bioMérieux, Lyon, France®) and 10 μl xTAG® MS2 were added into a Bertin SK38 Soil Grinding Lysis Bead Tubes, then vortex 5 min and incubated the tube at room temperature for 10–15 min. After centrifuging 2 min at 14000 rpm, 200 μl supernatant was removed for nucleic acid extraction. The DNA/RNA extraction of each sample was performed by QIAamp MinElute Virus Spin Kit (QIAGEN, Valencia, CA®).

Extracted and purified nucleic acid of each sample was underwent multiplex amplification by xTAG® GPP. Each PCR tube contained 10 μl extracted nucleic acid, 15 μl master mix, 2.5 μl xTAG® RNase-free water, 7.5 μl xTAG® OneStep Buffer, 2.5 μl xTAG® GPP Primer Mix, 0.5 μl xTAG® BSA (10 mg/mL), and 2.0 μl xTAG® OneStep Enzyme Mix. The multiplex amplification was carried out for 20 min followed by 38 cycles of 30 s at 95 °C for denaturation, 30 s at 58 °C for annealing, and 30 s at 72 °C for extension, and 2 min at 72 °C for the final extension.

Thereafter, each PCR product was added with 75 μl of xTAG® 0.22 SAPE which was diluted by xTAG® Reporter Buffer (contains 0.15 M NaCl). Then 5 μl final product was added with 20 μl xTAG® GPP Bead Mix for bead hybridization (3 min at 60 °C and 45 min at 45 °C). The data acquired by the Luminex® 100/200™ System (Austin, TX, USA) were analyzed by the xTAG Data Analysis Software (TDAS).

Statistics

Continuous variables were presented as the mean ± standard deviation or median (interquartile rang, IQR), and categorical variables were reported as a number and percentage. Bivariate statistical methods were used to explore data features. Multiple logistic regression analysis was done to evaluate the odds ratios (ORs) and their

corresponding 95% confidence intervals (CIs). Statistical significance was set at P value < 0.05. Two-sided test was used. All analyses were performed with SAS version 9.4 (SAS Institute Inc, Cary, NC).

Results

Demographics and clinical features of patients with diarrhea

A total of 48 clinics (Taichung [15], New Taipei City [15], Tainan [15], and Hualien [3]) were invited to participate in our study. During the study period, a total of 548 patients were enrolled and same number of stool specimens (one from each patient) was submitted to the central laboratory for microbiological analysis. Three patients were excluded for the reasons of leakage of stool specimen during transportation and inadequate sample amount for further analysis. Finally, 545 patients and their stool samples were collected and analyzed. Table 1 summarizes the clinical features of patients. The median age of patients was 36 years (range, 19 days to 92 years) and 52.3% of whom were male. Adults (≥18 years) accounted for 82.6% of patients. Hypertension was the most common co-morbidity, followed by diabetes mellitus. Regarding the types of diarrhea, 528 patients (97.8%) had acute diarrhea, 7 cases (1.3%) with persistent diarrhea, and 5 cases (0.9%) with chronic diarrhea. The median frequency of diarrhea before visiting clinics was 5 times per day (range, 3 to 36 times). Nearly one-third of patients had fever (29.7%) and 17.7% of patients had preceding respiratory symptoms. Watery stool (64.2%) was the most common stool characteristic, followed by loose stool (45.3%). Sixteen patients (2.9%) had a history of antibiotic use before the diarrheal episode. A cluster history and a possible food-related event were reported in 16.8% and 25.3% of patients, respectively. The median duration of diarrhea was 2 days. None of the participants required hospitalization.

Table 1 Clinical features of patients with diarrhea.

Parameter	Total (n = 545)	Group 1 patients (n = 309, 56.7%)	Group 2 patients (n = 236, 43.3%)	P value
Age [years; median (IQR[a])]	36 (23–55)	38 (26–56)	34 (20.5–54)	**0.013**
Sex (male)	285 (52.3)	164 (53.1)	121 (51.3)	0.676
Adult (>18)	450 (82.6)	263 (85.1)	187 (79.2)	0.073
County				0.114
Taichung	229 (42)	127 (41.1)	102 (43.2)	
New Taipei City	145 (26.6)	74 (24)	71 (30.1)	
Tainan	155 (28.4)	96 (31.1)	59 (25)	
Hualien	16 (2.9)	12 (3.9)	4 (1.7)	
Co-morbidity				
Diabetes mellitus	39 (7.2)	30 (9.7)	9 (3.8)	**0.008**
Hypertension	76 (13.9)	51 (16.5)	25 (10.6)	**0.048**
Heart disease	11 (2)	7 (2.3)	4 (1.7)	0.764
Malignancy	3 (0.6)	2 (0.7)	1 (0.4)	1.000
Symptoms and stool feature				
Fever	161 (29.7)	65 (21.1)	96 (40.9)	**<0.0001**
Respiratory symptoms[b]	96 (17.7)	62 (20.3)	34 (14.4)	0.077
Watery stool	350 (64.2)	179 (57.9)	171 (72.5)	**0.001**
Loose stool	247 (45.3)	147 (47.6)	100 (42.4)	0.227
Semi-formed	58 (10.6)	43 (13.9)	15 (6.4)	**0.005**
Bloody stool	11 (2)	3 (1)	8 (3.4)	0.064
Type of diarrhea				0.899
<2 weeks	528 (97.8)	297 (97.4)	231 (98.3)	
2–4 weeks	7 (1.3)	5 (1.6)	2 (0.9)	
>4 weeks	5 (0.9)	3 (1)	2 (0.9)	
Drug use history				
Antibiotics	16 (2.9)	10 (3.2)	6 (2.5)	0.634
Chinese herbs	16 (2.9)	9 (2.9)	7 (3)	0.971
Steroids	2 (0.4)	2 (0.7)	0 (0)	0.508
Diarrhea history in people around (cluster)	91 (16.8)	39 (12.8)	52 (22.1)	**0.004**
Food-related	138 (25.3)	84 (27.2)	54 (22.9)	0.252
Frequency of diarrhea [times; median (IQR)]	5 (3–6)	4 (3–6)	5 (4–7)	**0.003**
Duration of diarrhea [days; median (IQR)]	2 (1–3)	2 (1–3)	2 (1–3)	**0.001**

[a] IQR-interquartile rang.
[b] Including cough, sneezing, rhinorrhea, and sore throat.
Statistical significances are represented in bold.

Comparison of clinical features between patients with and without enteropathogen infections

As shown in Table 1, enteropathogens were detected in 236 cases (group 2 patients) with an overall positive rate 43.3%. The rest cases (group 1 patients, 56.7%) had no identifiable pathogens in their stool samples. The median age of group 2 patients was younger than that of group 1 patients (34 years vs. 38 years, P = 0.013). No differences were found between these two patient groups with regard to sex, the proportion of adults, origin of county, history of drug use, and food-related event. A significantly higher proportion of the group 1 patients had a history of diabetes mellitus (9.7% vs. 3.8%, P = 0.008) or hypertension (16.5% vs. 10.6%, P = 0.048). The median frequency (P = 0.003) and duration (P = 0.001) of diarrhea were significantly different between these two patient groups. A cluster history of diarrhea was reported more frequently by the group 2 patients (12.8% vs. 22.1%, P = 0.004). A significantly higher proportion of the group 2 patients had fever (21.1% vs. 40.9%, P < 0.0001) and watery stool (57.9% vs. 72.5%, P < 0.0001). Contrarily, semi-formed stool was reported more frequently by the group 1 patients (13.9% vs. 6.4%, P = 0.005).

Next, we stratified patients into adults and children and the analytic results are summarized in Supplementary Table 1 (ST1). Regarding adult patients, cases with positive xTAG® GPP tests (group 2) were younger (40 years vs. 44 years, P = 0.045), had a higher frequency (P = 0.005) and shorter duration of diarrhea (P < 0.0001) than those with negative test results (group 1). A cluster history of diarrhea was reported more frequently by the group 2 adult patients (11.9% vs. 18.8%, P = 0.043). Fever (P < 0.0001) and watery stool (P = 0.002) were again noted more frequently in group 2 adult patients. Distinct from adult patients, the group 2 children had an older median age (2.8 years vs. 6 years, P = 0.018). However, no difference was observed between the group 1 and group 2 children with regard to the symptoms, pattern of diarrhea, frequency and duration of diarrhea, and cluster history. With multivariate analysis, fever and watery stool were the two parameters to predict a positive xTAG® GPP result in adults, and their corresponding ORs (95% CIs) were 2.05 (1.28–3.29, P = 0.003) and 1.71 (1.06–2.76, P = 0.028), respectively. On the other hand, fever and age were the parameters for children to predict a positive xTAG® GPP result, and their ORs (95% CIs) were 3.61 (1.3–10.04, P = 0.014) and 1.15 (1.02–1.28, P = 0.019), respectively.

Comparison of clinical features between adults and children with enteropathogen infections

We then analyzed the clinical features of patients with positive xTAG® GPP results. As shown in Table 2, no difference in sex distribution was observed between adults and children (P = 0.117). A higher proportion of children had a history of antibiotic use before the diarrheal episode (8.2% vs. 1.1%, P = 0.018; ST1) and longer duration of diarrhea (median, 3 days vs. 2 days, P < 0.0001; ST1). Fever (57.1% vs. 36.6%, P = 0.009), loose stool (55.1% vs. 39.0%, P = 0.043), bloody stool (14.3% vs. 0.5%, P < 0.0001), and a cluster history (34.7% vs. 18.8%, P = 0.017) were reported more frequently in children. However, more adult patients had a food-related event (8.2% vs. 26.7%, P = 0.006).

Microbiological distribution of infectious gastroenteritis and associated clinical features

Two hundred and fifty-seven pathogens, including 135 viruses, 117 bacteria and 5 parasites, were identified by using xTAG® GPP assay (Fig. 1). Norovirus GI/GII (33.9%) was the most common pathogens, followed by rotavirus A (17.9%) and *Campylobacter* species (16.7%). Single viral, bacterial, or parasitical infection was recorded in 116 patients, 99 patients, and 1 patient, respectively. Among these single-agent induced gastroenteritis (Table 2), viral infections were more likely associated with watery diarrhea (83.2% vs. 58.8%, P < 0.0001) and a history of cluster (27.1% vs. 15.7%, P = 0.041); however, loose (32.8% vs. 53.9%, P = 0.002) or

Table 2 The clinical relationship among sex, symptom, stool feature, cluster history, and food with age, pathogens, or type of infection.

Parameter	Age (%)[a]			Pathogen (%)			Type of infection (%)		
	Children (n = 49)	Adults (n = 187)	P value	Viruses[b] (n = 119)	Bacteria[b] (n = 102)	P value	Single (n = 216)	Mixed (n = 20)	P value
Sex (male)	30 (61.2)	91 (48.7)	0.117	62 (52.1)	53 (52)	0.983	110 (50.9)	11 (55)	0.727
Fever	28 (57.1)	68 (36.6)	**0.009**	47 (39.8)	43 (42.2)	0.726	88 (40.9)	8 (40)	0.936
Respiratory symptom[c]	8 (16.3)	26 (13.9)	0.667	22 (18.5)	12 (11.8)	0.167	33 (15.3)	1 (5)	0.323
Watery stool	33 (67.4)	138 (73.8)	0.368	99 (83.2)	60 (58.8)	**<0.0001**	155 (71.8)	16 (80)	0.430
Loose stool	27 (55.1)	73 (39)	**0.043**	39 (32.8)	55 (53.9)	**0.002**	90 (41.7)	10 (50)	0.471
Bloody stool	7 (14.3)	1 (0.5)	**<0.0001**	0 (0)	8 (7.8)	**0.002**	6 (2.8)	2 (10)	0.140
Cluster history	17 (34.7)	35 (18.8)	**0.017**	32 (27.1)	16 (15.7)	**0.041**	46 (21.4)	6 (30)	0.400
Food-related	4 (8.2)	50 (26.7)	**0.006**	27 (22.7)	22 (21.6)	0.842	49 (22.7)	5 (25)	0.785

[a] Patients with positive xTAG® GPP test.
[b] Only cases with pure viral or bacterial infections were analyzed.
[c] Including cough, sneezing, rhinorrhea, and sore throat.
Statistical significances are represented in bold.

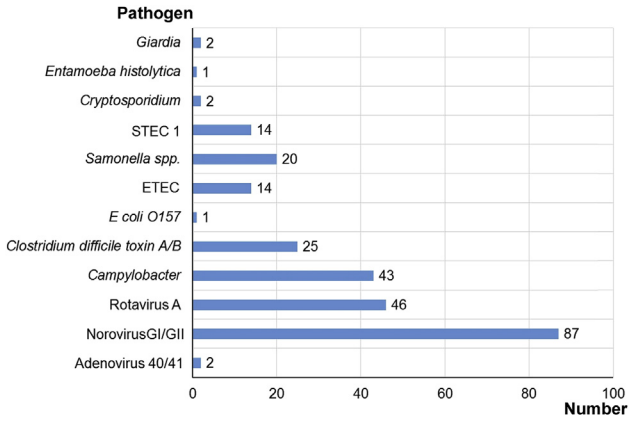

Figure 1. Cases of various enteropathogens detected in patients with infectious gastroenteritis. *E. coli*: *Escherichia coli*; ETEC: Enterotoxigenic *E. coli*; spp.: species; STEC: Shiga-like toxin producing *E. coli*.

bloody (0% vs. 7.8%, P = 0.002) stool was more likely observed in patients with bacterial infections. Twenty patients (8.5%) had mixed infection and their associated enteropathogens are listed in ST2. Norovirus GI/GII (60%) and *Escherichia coli* (40%) were the two most common isolates in patients with mixed infection. Only one patient had triple infection. There was no difference in stool characteristics, symptoms, cluster history, and food-related events between patients with single-agent infection and mixed infection (Table 2).

As shown in Fig. 2A, the distribution of enteropathogens differed significantly among different counties (P = 0.020). Viruses were recovered more frequently in patients from Taichung (60/107. 56.1%) and New Taipei City (46/75, 61.3%). On the other hand, bacteria were more commonly found in patients living in Tainan (43/70, 61.4%) and Hualien (3/5, 60.0%). With the exception of Hualien, norovirus was the most common agent causing infectious gastroenteritis, followed by *Campylobacter* spp. or rotavirus. For both adults and children, there was no sex difference in the distribution of enteropathogens (P = 0.968). However, a major difference in the distribution of pathogens was observed between adults and children (Fig. 2B, P = 0.005). Viruses (114/199, 57.3%) were the leading cause of infectious gastroenteritis in adults, and norovirus (78/199, 39.2%) was the most common isolate, followed by rotavirus (35/199, 17.6%). On the other hand, bacteria (37/58, 63.8%) accounted for a significant proportion of pathogens in children, and *Clostridium difficile* (12/58, 20.7%) was the most common isolate. Most of the *C. difficile* isolates (11/12, 91.7%) were found in patients ≤5 years.

Either for adults or children, a significant difference in the seasonal distribution of enteropathogens was observed

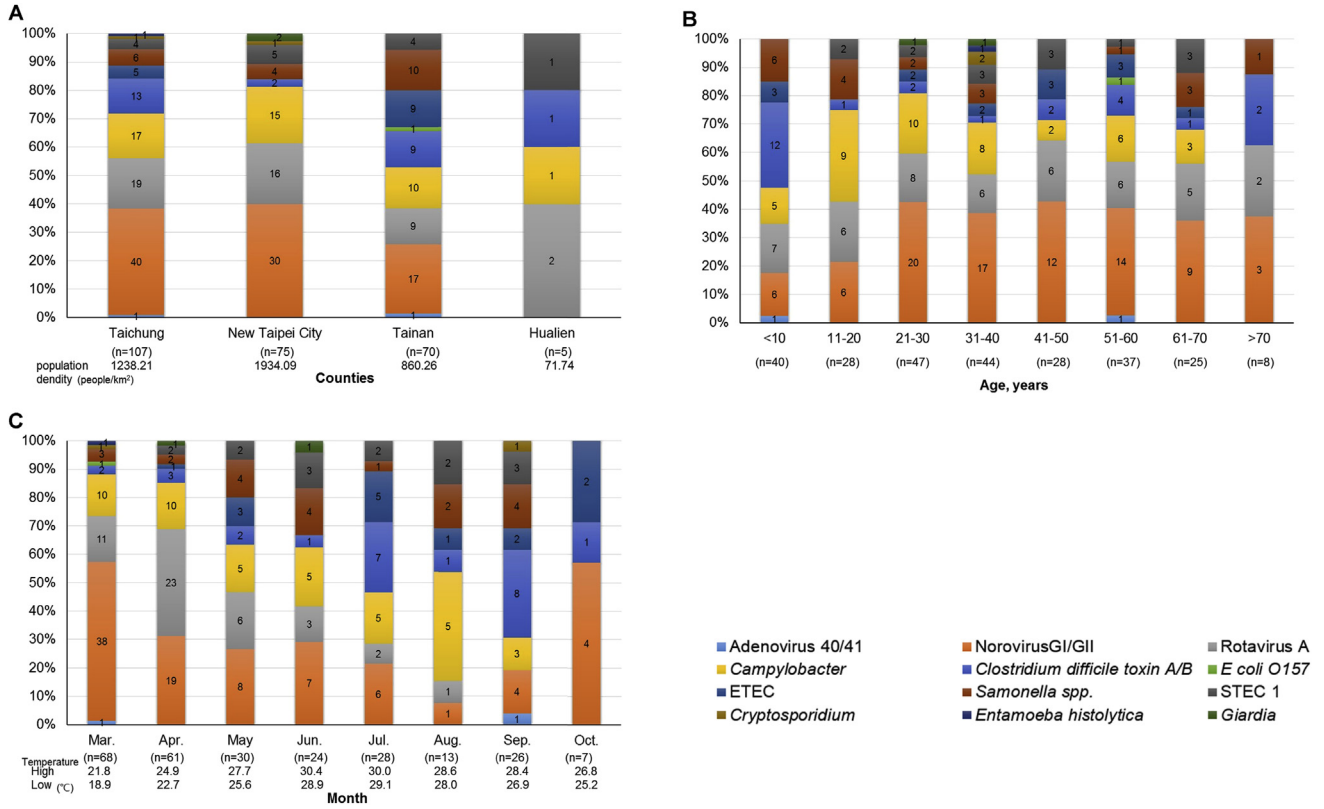

Figure 2. The distribution of enteropathogens in various conditions. [A] Counties, including the population density (person/km^2) of each county (data from Department of Statistics, Ministry of the Interior, Taiwan). [B] Different age groups. [C] Months, including average high and low temperatures (°C) of each month (data from Central Weather Bureau, Ministry of Transportation and Communications, Taiwan). *E. coli*: *Escherichia coli*; ETEC: Enterotoxigenic *E. coli*; spp.: species; STEC: Shiga-like toxin producing *E. coli*.

during the study period (P = 0.001 to < 0.0001). During the colder months in Taiwan (March, April, and October), norovirus (31.1%–55.9%) and rotavirus (16.2%–37.7%) accounted for the majority of enteropathogens (Fig. 2C). With an increment in climate temperature (from May to September), the number of isolated viruses decreased sharply. However, the number of bacteria remained stable through March to September (Fig. 3). Collectively, during the colder months, viruses were the main etiologies responsible for infectious gastroenteritis; as weather became warmer, bacteria replaced viruses to be the major pathogens of gastroenteritis.

Discussion

Depending on the laboratory methods used, the geographical location and the population of patients studied, enteropathogens were detected in 23%–81% of patients with diarrheal diseases.[2,5–14,21] Among these heterogeneous studies, a higher prevalence rate (56%–81%) was observed in those patients who visited or admitted to hospital-based service.[2,5–8,14] Contrarily, a lower prevalence rate (23%–46%) was reported in GP-based studies conducted in the developed countries.[10–13] Similar prevalence rate (43.3%) was also observed in our GP-based study. In addition to the reasons described above, disease severity is another possible explanation for the different prevalence rates of enteropathogens between GP-based and hospital service-based studies. Patients with infectious diarrhea, especially caused by bacteria, are more likely accompanied with systemic symptoms and will search for hospital-based medical service more frequently than those with non-infectious diarrhea.[8,11,13] Therefore, such behavioral preference in seeking medical aid may influence the prevalence rate of enteropathogens in patients with diarrheal diseases in different studies.

Similar to the observation made by several authors,[5,6,10] a cluster history of diarrheal disease was reported more frequently by patients with positive xTAG® GPP results, especially among patients less than 18 years (34.7%). In a study conducted by Leder and colleagues, they found that

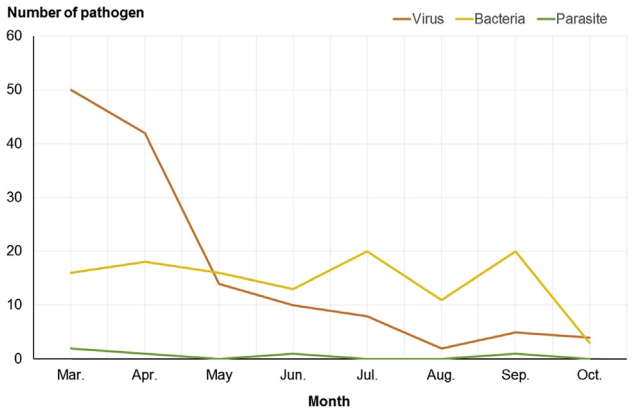

Figure 3. The number of enteropathogens detected in various months. With the increment of climate temperature, in comparison with bacteria and parasites, the number of viruses decreases sharply.

clustering of gastrointestinal symptoms within household occurred commonly.[22] In Taiwan, most individuals less than 18 years live with their family. Taken such regional culture and the results of Leder's study together, it is not surprising that clustering of diarrheal disease occurs more frequently in patients younger than 18 years (P = 0.017). Similar to the study conducted by Leder et al.,[22] viruses (69%) were the most common agents in patients with a cluster history. Food consumption is another important medical history in assessing patients with diarrheal diseases.[23] In the present study, especially among the adult patients (26.7%), a possible food-related event was reported before the onset of diarrhea. Viruses were again the most common isolates (32/54) and most of them were noroviruses (72%). Food-borne outbreak of norovirus infection has been repeatedly reported in the literature.[24,25] Although 20% of patients with possible food-borne diseases also had a cluster history, no outbreak was officially reported during the study period.

Clinical symptoms of infectious diarrhea are non-specific and not related to the type of infection. However, in both GP- and hospital service-based studies, fever, bloody stool, and abdominal cramping pain were commonly reported in patients with bacterial infections[6,8,11,13]; however, viral pathogens were associated with vomiting.[8,11,13] Similarly, bloody stool was reported more frequently by our patients with bacterial infection (P = 0.002); contrarily, watery stool was significantly associated with viral infection (P < 0.0001). Such difference in the stool characteristics between viral and bacterial infections might be partly explained by the mechanisms of diarrhea involved in various types of infections.[20]

Consistent with the results of other GP-based studies,[10–12] norovirus was the most common enteropathogen in the present study. In the cases of viral infection, particularly for norovirus and rotavirus, young children and elderly >60 years were the main patient groups affected.[10,11,13] In our study, however, most of the norovirus cases (72%) and 57% of the rotavirus cases were distributed between the age of 20 years and 60 years. Such discrepancy in the distribution of viral infections between our data and others may be partially explained by the dissimilar proportion of patient age groups and different laboratory methodologies used.[10,11,13] Higher proportion of our patients (63.9%) was aged 20–60 years. Similar to the results reported by de Wit et al.,[13] *Campylobacter* species was the predominant bacterial agent in our patients with diarrheal diseases. This pathogen is always recognized as one of the 3 leading bacterial pathogens in the GP-based studies.[11–13] Toxigenic *C. difficile* was identified in 21% of our patients with bacterial infection and nearly half of them (48%) occurred in children. It is well-known that *C. difficile* colonization is a common phenomenon in children <3 years and current recommendations advise against testing of *C. difficile* in infants and children <2 years of age.[26] Therefore, the use of xTAG® GPP test in these patients should be seriously re-evaluated. In the GP-based studies,[11–13] mixed infection was reported in 2.3%–5.6% patients with diarrheal disease. However, a higher rate (8.5%) was reported in our patients and this may be explained by the different laboratory methods used.[17] As described by other authors,[10,11] further research is needed to elucidate the clinical significance and contribution of each pathogen to mixed infection.

Similar to earlier studies,[7,11,12,15] seasonality of microbiological distribution was observed in our study. Viral infections, particularly norovirus, were the predominant agents in the colder months; contrarily, bacterial infections occurred all year round. Moreover, the degree of urbanization or sanitization seemed to affect the distribution of enteropathogens. For example, bacteria were more frequently identified in those counties with lower population density.

Inevitably, this study has some limitations. First, the xTAG® GPP assay only detects 15 enteropathogens. However, these agents represent the most common and important pathogens causing gastroenteritis. Second, a recent contact history with the healthcare system was not included in the questionnaire; the possibility of healthcare-associated diarrhea could not be totally excluded. Third, for patients with a cluster history or food-related events, we only inquired symptoms in people around the patients or possible implicated foods. No microbiological testing was performed to confirm the causative agents in foods or connected persons. Fourth, confined to the regulations of the funding organization, we did not recruit patients during the wintertime (December to February); nevertheless, present data still provided valuable information about the epidemiology and microbiology of diarrheal patients in Taiwan. Finally, no control cases were included in this study and the colonization rate of various enteropathogens among non-diarrheal individuals is unknown.

In conclusion, our study showed that viruses were the predominant enteropathogens among patients who visited community clinics for diarrheal diseases in Taiwan. Additionally, we observed that the clinical features of patients in different age groups or with various agents were different. Regional difference and seasonality of microbiological distribution were the other featured findings in this study. Overall, this study provided valuable information about the clinical features and microbiology of patients with diarrheal diseases to the general practitioners in Taiwan.

Author contributions

CYC designed the study, analyzed data, and wrote the manuscript; LNL wrote the manuscript and analyzed data; CMH wrote the manuscript; CHC and MWH collected and collated data; JHW designed the study.

Potential conflicts of interest

All authors declare no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jmii.2017.05.003.