JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Original Article

Prevalence and factors associated with different pathogens of acute diarrhea in adults in Beijing, China

Lei Jia[1], Changying Lin[1], Zhiyong Gao[1], Mei Qu[1], Junyong Yang[2], Jingyi Sun[3], He Chen[4], Quanyi Wang[1]

[1] *Institute for Infectious Disease and Endemic Disease Control, Beijing Center for Disease Prevention and Control, Beijing, China*
[2] *Institute for Infectious Disease and Endemic Disease Control, Fengtai District Center for Disease Prevention and Control, Beijing, China*
[3] *Institute for Infectious Disease and Endemic Disease Control, Xicheng District Center for Disease Prevention and Control, Beijing, China*
[4] *Institute for Infectious Disease and Endemic Disease Control, Daxing District Center for Disease Prevention and Control, Beijing, China*

Abstract

Introduction: Only a small proportion of patients with diarrhea are diagnosed with laboratory tests in China, and most are diagnosed based on clinical symptoms. Therefore, understanding the prevalence of different diarrheal pathogens and their specific symptoms is important.
Methodology: Data from a prospective study in Beijing of acute diarrhea and the related pathogens were used to study the association between different pathogen groups and the infected patients' characteristics. A total of 355 patients with acute diarrhea, clinically diagnosed with infectious or noninfectious diarrhea by general practitioners (GPs), were recruited from three districts.
Results: Different species of diarrheal pathogens were detected in 133 (37.5%) patients. The most prevalent pathogen was calicivirus (42.9%), followed by rotavirus (30.1%), *Vibrio parahaemolyticus* (13.5%), and *Salmonella* spp. (10.5%). The detection rates in patients diagnosed with infectious or noninfectious diarrhea by GPs did not differ significantly ($\chi^2 = 0.026$, $p = 0.873$). Abdominal pain correlated negatively with viral pathogens, whereas nausea, living in the suburbs, and winter infection correlated positively with viral infection. Abdominal pain and leukocytosis were positively associated with bacterial infections, whereas winter infection correlated negatively with them.
Conclusion: In this study, we found that the detection rates in patients diagnosed with infectious or noninfectious diarrhea by GPs was the same. We also revealed the improper prescription of antibiotics by GPs based simply on clinical diagnoses. A further analysis of diagnostic accuracy and methods is required to assist GPs in improving their diagnoses when insufficient laboratory tests are available and budgets are limited.

Key words: acute diarrhea; virus; bacteria; characteristic; China.

J Infect Dev Ctries 2016; 10(11):1200-1207. doi:10.3855/jidc.6831

(Received 03 March 2015 – Accepted 10 November 2015)

Introduction

Diarrheal diseases are an important public health issue. Although the mortality associated with diarrheal diseases has decreased progressively throughout the world, the morbidity of the disease has increased slightly in recent years [1,2]. There are two main types of diarrhea: infectious and noninfectious. Infectious diarrhea is usually a symptom of gastrointestinal infection caused by a variety of bacteria, viruses, and parasites. Noninfectious diarrhea is caused by many factors, including appendicitis, hypoimmunity, and renal transplantation [3-5].

It is very important to classify cases of diarrhea correctly because the diagnosis affects both the treatment and the prevention and control measures. Because many diagnoses of infectious diarrhea are made by general practitioners (GPs) rather than by laboratories in China, understanding the pathogenic spectrum and the differences in the clinical symptoms caused by these pathogens is extremely important.

In past decades, limited laboratory capacity and lack of funding have restricted the etiological testing of acute diarrhea in China. Moreover, parasites, bacteria, or viruses have been studied separately, with no description of the complete spectrum of diarrheal pathogens [6-9]. In 2012, we established hospital-based sentinel sites in three districts of Beijing to monitor adult patients (≥ 18 years of age) with acute diarrhea attending as outpatients and to test them for both viruses and bacteria. The infection rates of parasites were too low (2.9% in 2002 and 0% in 2006–2010 [6,7]) to be included in our study. The objectives of the study were to obtain information about the distribution of diarrheal pathogens and to evaluate the association between individual pathogens and symptoms. These results should provide valuable diagnostic information for GPs in the clinical context.

Methodology

Surveillance sites and population

Seven sentinel hospitals affiliated with three different districts of different geographic and socio-economic situations in Beijing, China, were investigated in 2012. The average number of recruited patients with diarrhea attending the outpatient departments every month exceeded 10 patients per district. The outpatients were investigated and sampled on Tuesdays in the first and third weeks of every month, and five outpatients were enrolled per week.

Case definition and enrollment of patients

Adults (≥ 18 years of age) were considered eligible for enrollment if they presented in one of the seven surveillance hospitals with symptoms of diarrhea. A case of diarrhea was defined as the passage of three or more stools in 1 day that appeared loose, watery, bloody, or contained mucus. The exclusion criteria were the systemic use of antibiotics after diarrhea, and persistent diarrhea, which was defined as diarrhea lasting for more than 14 days before presentation at the hospital.

All subjects were informed about the study by the doctors and agreed to participate and provide stool samples. The clinical and epidemiological information for each patient was recorded with the electronic gastrointestinal clinic surveillance and reporting system in Beijing, and included the following information: age, sex, residence, clinical symptoms (fever, vomiting, abdominal pain, nausea, frequency of diarrhea), laboratory test results, and epidemiological history (such as the consumption of suspicious food). Based on their epidemiological history and clinical symptoms, all the patients were diagnosed with infectious or noninfectious diarrhea by the GPs, with no laboratory confirmation. The patients clinically diagnosed as infectious could be given antibiotics after sample collection.

A stool sample was collected from each patient on the day of presentation, and was analyzed within 24 hours by the laboratory of the district Center for Disease Prevention and Control (CDC). The isolated strains and their preliminary biochemical and serological results were sent to the laboratory of the Beijing CDC for confirmatory tests.

Bacterial detection

Bacterial pathogens were isolated from the fecal samples with standard microbiological and biochemical tests, and included *Shigella* spp. [10], *Salmonella* spp., diarrheagenic *Escherichia coli* (DEC), and *Vibrio parahaemolyticus* [11]. Briefly, a loop of fecal sample was first streaked onto plates of MacConkey agar, sorbitol-MacConkey agar, xylose lysine deoxycholate agar, and *Salmonella–Shigella* agar (Becton Dickinson Co., Sparks, USA). A swab of fecal sample was also used to inoculate peptone water containing 3% NaCl, and was cultured for 6 hours at 37°C for *Vibrio* spp. A loop of supernatant was then streaked on a plate of CHROMagar Vibrio Agar (CHROMagar Co., Paris, France).

After culture at 37°C for 24 hours, suspicious colonies from the plates described above were picked from the plates to test the isolated strains with Gram staining, oxidase and catalase tests, and biochemical identification with the VITEK-2 Compact (BioMerièux, Lyon, France). All the isolated bacterial strains were serotyped with the slide agglutination test using commercially available antisera (antiserum for *Salmonella* was purchased from SSI Diagnostica, Hillerod, Denmark; antisera for *Shigella* and *Vibrio* were from Denka Seiken, Tokyo, Japan; antisera for *E. coli* were from Tianrun, Ningbo, China and SSI Diagnostica, Hillerod, Denmark).

Salmonella, *Shigella*, DEC, and *V. parahaemolyticus* strains that were isolated and confirmed with various methods in the laboratory were used as the quality control in every step of the identification process.

Viral detection

The fecal samples were also used to detect viral pathogens, including rotavirus and human calicivirus. A small amount of sample was added to an Eppendorf tube with 10 volumes of sterile saline to prepare a 10% (v/v) stool suspension. Rotaviruses were identified with an enzyme-linked immunoassay kit for group A rotaviruses (ProSpecT Rotavirus Microplate Assay, Oxoid, Basingstoke, UK), according to the manufacturer's instructions.

Human caliciviruses were detected with reverse-transcription polymerase chain reaction (RT-PCR) using the 289/290 primers, which target the polymerase gene region [12]. Viral RNA was extracted from 140 μL of the stool suspensions described above using the

QIAamp Viral RNA Mini Kit (Qiagen, Hilden, Germany), according to the manufacturer's instructions. The RNA was eluted in 50 µL of RNase-free distilled water and stored at -80°C. A one-step RT-PCR (OneStep RT-PCR Kit; Qiagen, Hilden, Germany) was performed at 42°C for 1 hour and 95°C for 15 minutes, followed by 40 cycles of 94°C for 60 seconds, 58°C for 80 seconds, and 72°C for 60 seconds, with a final extension at 72°C for 7 minutes. The amplified PCR products were visualized with electrophoresis on the QIAxcel System (Qiagen, Hilden, Germany).

Statistical methods

Pearson's χ^2 test was used to test the association between the viruses or bacteria and patient-related factors such as age, month of onset, and clinical diagnosis. A logistic regression analysis was used to examine the association between each pathogen and abdominal pain, nausea, vomiting, season, minimum number of stools per day, and leukocytosis. All variables were added step-wise to the model, with an entry level of 0.05 and a removal level of 0.1. For each selected variable, the estimated effect is presented as an adjusted odds ratio and a 95% confidence interval. All statistical analyses were performed with SPSS version 16.0 (SPSS Inc., Chicago, USA). Statistical significance was set at $p < 0.05$.

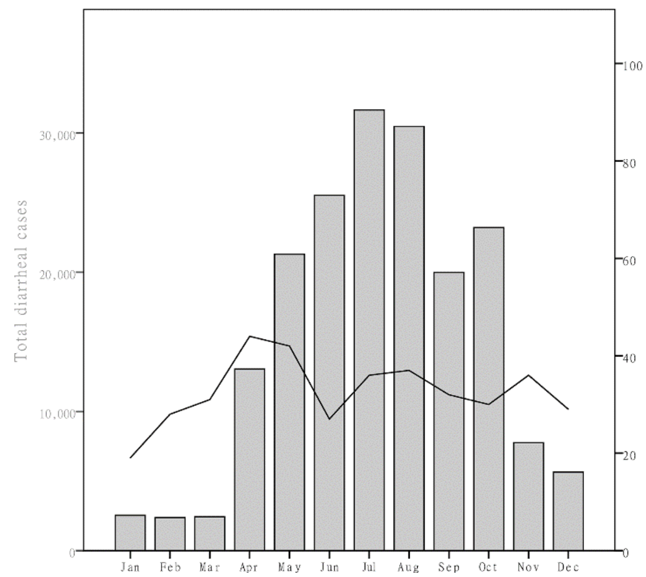
Ethics statement

The study was approved by the ethics committee of the Beijing Center for Disease Prevention and Control.

Results

In total, 355 (2.3%) patients were recruited from 15,122 outpatients with diarrhea who attended the seven sentinel hospitals in 2012, and all these patients had mild diarrhea. The average monthly enrollment was 13–40 patients (Figure 1). Of the 355 subjects enrolled, 169 (47.6%) were women. The median age was 35.0 years (range: 18.2–89.0 years). Of the 355 enrolled patients in whom the average frequency of diarrhea was five times per day in the acute phase, 234 subjects (234/355; 65.9%) presented with loose stools and 121 subjects (121/355; 34.1%) presented with watery stools. Abdominal pain was the predominant clinical symptom in 200 subjects (200/355; 56.3%), and most pain (146/200; 73.0%) was peri-umbilicus pain.

Figure 1. Monthly distribution of admitted and enrolled patients.



In total, 140 pathogens were detected in 133 patients (37.5%). In the positive samples, a single pathogen was observed in 126 cases, and mixed infections were detected in 7 cases. The prevalence of different microorganisms is shown in Table 1. The rates for viral (single pathogen), bacterial (single pathogen), and mixed infections were 24.5%, 11.0%, and 2.0%, respectively. The most frequently detected pathogens in these diarrheal patients in Beijing were calicivirus, rotavirus, *V. parahaemolyticus*, and *Salmonella* spp.

The predominant serotype of *V. parahaemolyticus* detected was O3:K6 (12/18; 66.7%), followed by

Table 1. Distribution of different microorganisms detected in diarrheal patients (n = 355).

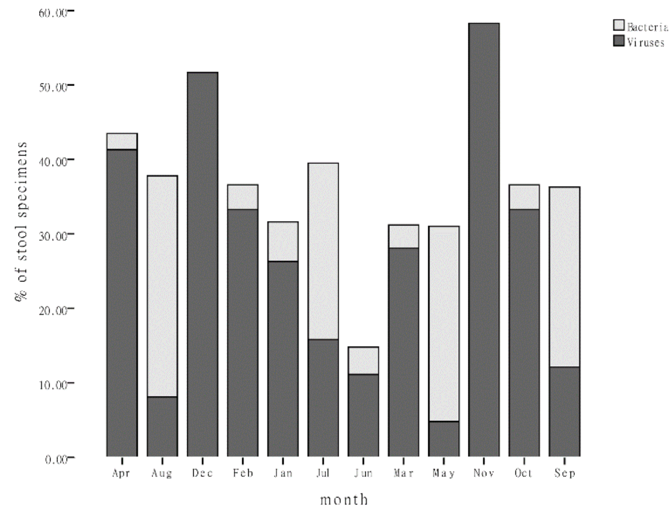
Microorganisms		No. detected	Positive rate (%)
Single infection	Calicivirus	50	14.1
	Rotavirus	37	10.4
	V. parahaemolyticus	17	4.8
	Salmonella spp.	14	3.9
	Shigella spp.	5	1.4
	Diarrheagenic *E. coli*	3	0.8
Mixed infection	Calicivirus/rotavirus	3	0.8
	V. parahaemolyticus/ Calicivirus	1	0.3
	Shigella spp./ Calicivirus	1	0.3
	Diarrheagenic *E. coli*/ Calicivirus	2	0.6
Total		**133**	**37.5**

O4:K8 (3/18; 16.7%). Of the 14 *Salmonella* spp. isolates, 5 (35.7%) were *S. agona*, 5 (35.7%) were *S. enteritidis*, 2 (14.3%) were *S. senftenberg*, and 2 (14.3%) were *S. typhimurium*. The most prevalent *Shigella* spp. was *Shigella sonnei* (3 strains; 50.0%) and *Shigella flexneri* (3 strains; 50.0%). No *Shigella dysenteriae* or *Shigella boydii* was detected. The two most prevalent DECs were enteropathogenic *E. coli* (3 cases; 60.0%) and enterotoxigenic *E. coli* (2 cases; 40.0%). No enterohemorrhagic *E. coli* was detected. Mixed calicivirus and rotavirus infections were detected in 4 samples.

The subjects were divided into three age groups: 18–40, 41–60, and > 60 years. Calicivirus, rotavirus, and *Salmonella* spp. were detected in every age group. There was no significant difference in the viral or bacterial detection rates among the three age groups ($\chi^2 = 4.529$, $p = 0.339$; Table 2).

In 2012, bacterial pathogens were more frequently detected from May to September, whereas viral pathogens predominated in the other months (Figure 2). According to the climatography [13], spring occurs in April–May in Beijing, summer in June–August, autumn in September–October, and winter in November–March of the following year. The detection rates for viruses and bacteria differed significantly among the different seasons ($\chi^2 = 3\ 9.365$, $p < 0.05$). The viral infection rate was high in winter, whereas bacterial infections were more common in summer (Table 3).

Figure 2. Monthly distribution of pathogen groups.



Among the 355 diarrheal patients, 123 (33.5%) were clinically diagnosed as having infectious diarrhea and the others (66.5%) were considered to have noninfectious diarrhea, such as indigestion and gastrointestinal dysfunction. The GPs selected treatment based on the clinical manifestations. Patients diagnosed with infectious diarrhea had the highest rate of antibiotic therapy, which was significantly different from that of patients with other diagnoses ($\chi^2 = 82.482$, $p < 0.05$), although 21.9% of patients diagnosed with diarrhea of unknown origin were also administered antibiotics (Table 4).

Table 2. Microorganisms detected in diarrheal patients in different age groups.

Microorganisms	No. of patients (%) who tested positive, including patients with mixed infections			
	18–40 years (n = 211)	**41–60 years (n = 101)**	**> 60 years (n = 43)**	**All (n = 355)**
Calicivirus	31 (14.7)	21 (20.8)	5 (11.6)	57 (16.1)
Rotavirus	22 (10.4)	13 (12.9)	5 (11.6)	40 (11.3)
V. parahaemolyticus	13 (6.2)	5 (5.0)	0 (0)	18 (5.1)
Salmonella spp.	8 (3.8)	2 (2.0)	4 (9.3)	14 (3.9)
Shigella spp.	5 (2.4)	1 (1.0)	0 (0)	6 (1.7)
Diarrheagenic *E. coli*	4 (1.9)	1 (1.0)	0 (0)	5 (1.4)
Total	**83 (39.3)**	**43 (42.6)**	**14 (32.6)**	**140 (39.4)**

Table 3. Seasonal distribution of pathogen groups.

Season	No. of patients (%), including mixed infection			All
	Viral pathogens (%)	**Bacterial pathogens (%)**	**No pathogens (%)**	
Spring	16 (19.8)	12 (14.8)	53 (65.4)	81
Summer	10 (10.8)	21 (22.6)	63 (67.7)	93
Autumn	13 (23.2)	7 (12.5)	37 (66.1)	56
Winter	55 (44.0)	3 (2.4)	69 (55.2)	125
Total	**94 (26.5)**	**43 (12.1)**	**222 (62.5)**	**355**

Table 4. Antibiotic therapies administered to patients with acute diarrhea.

Clinical diagnosis	Without antibiotic therapies (%)	With Antibiotic therapies (%)	All
Infectious diarrhea	50 (40.7)	73 (59.3)	123
Gastrointestinal dysfunction	44 (100.0)	0 (0)	44
Indigestion	27 (96.4)	1 (3.6)	28
Diarrhea of unknown origin	125 (78.1)	35 (21.9)	160
Total	**246 (69.3)**	**109 (30.7)**	**355**

Table 5. Pathogen distribution in patients with different diagnoses.

Clinical diagnosis	Detection result (including mixed infection)			All
	Virus (%)	Bacteria (%)	Negative (%)	
Infectious diarrhea	22 (17.9)	25 (20.3)	78 (63.4)	123
Gastrointestinal dysfunction	10 (22.7)	4 (9.1)	30 (68.2)	44
Hypopepsia	8 (28.6)	2 (7.1)	18 (64.3)	28
Diarrhea of unknown origin	54 (33.8)	12 (7.5)	96 (60.0)	160
Total	**94 (26.5)**	**43 (12.1)**	**222 (62.5)**	**355**

Table 6. Antibiotic therapies in patients with different laboratory results.

Laboratory results	Without antibiotic therapies (%)	Withantibiotic therapies (%)	All
Virus	66 (73.3)	24 (26.7)	90
Bacteria	22 (56.4)	17 (43.6)	39
Mixed infection	3 (75.0)	1 (25.0)	4
Negative	155 (69.8)	67 (30.2)	222
Total	**246 (69.3)**	**109 (30.7)**	**355**

Table 7. Multivariate logistic regression of the association between illness characteristics and pathogen groups.

Illness characteristics	Number of patients with illness characteristics and odds ratios (OR) with 95% confidence intervals (CI) for pathogens						No pathogen
	Viral pathogens		Bacterial pathogens		Any pathogen		
	No.	OR (95% CI)	No.	OR (95% CI)	No.	OR (95% CI)	No.
Abdominal pain	44	0.49 (0.29–0.82)	34	2.60 (1.15–5.86)	76	—	279
Nausea	69	2.38 (1.37–4.12)	30	—	95	2.16 (1.36–3.43)	260
Suburb	73	1.72 (1.97–3.05)	31	—	101	—	254
Season							
Summer	11	—	21	—	31	—	324
Spring	16	1.81 (0.77–4.25)	12	0.77 (0.34–1.76)	28	1.18 (0.62–2.25)	327
Winter	58	7.05 (3.35–14.85)	3	0.12 (0.03–0.41)	59	2.00 (1.12–3.53)	296
Autumn	13	2.76 (1.12–6.84)	7	0.48 (0.18–1.28)	19	1.13 (0.55–2.33)	336
Diarrhea frequency ≥ 6/day	48	—	25	1.95 (0.98–3.90)	70	1.67 (1.07–2.61)	318
Vomiting	32	—	21	—	51	—	304
Leukocytosis	34	—	110	2.80 (1.37–5.73)	61	—	294

The detection rates for different pathogens in the infectious and noninfectious diarrhea groups diagnosed by GPs did not differ significantly ($\chi^2 = 0.026$, $p = 0.873$). Bacterial infection was more common in those patients diagnosed with infectious diarrhea, whereas viral infection was more frequent in those diagnosed with noninfectious diarrhea, including those diagnosed with gastrointestinal dysfunction, hypopepsia, or suspected diarrhea ($\chi^2 = 17.830$, $p < 0.05$; Table 5). Based on the laboratory test results, the sensitivity of clinically diagnosed infectious diarrhea by GPs was only 33.8%. Mixed infections were excluded from the analysis because of the limited number of cases. Table 6 shows that the rates of antibiotic therapy administered to patients with different laboratory results (*i.e.*, viral infection, bacterial infection, or none) did not differ significantly ($\chi^2 = 3.757$, $p = 0.153$).

A multivariate logistic regression analysis of the association between the illness characteristics and the pathogen groups detected was performed for the 355 patients with a simple infection (viral or bacterial pathogen detected) or no detectable infection (Table 7). Abdominal pain, nausea, living in a suburb, and autumn or winter infection were associated with viral pathogens. Abdominal pain correlated negatively with viral infection, whereas the other factors correlated positively. Bacterial pathogens were positively associated with abdominal pain and leukocytosis, but negatively with winter infection. All pathogens correlated positively with nausea, winter infection, and a minimum of six stools per day. There were tendencies for positive associations between viral pathogens and spring infections, between bacterial pathogens and a minimum of six stools per day in the acute phase, and between any pathogen and a minimum of six stools per day.

Discussion

We established seven sentinel hospitals affiliated with three different districts, representing different types of areas in Beijing: urban areas, suburbs, and remote suburbs. The seven sentinel hospitals in this study received 15,122 diarrheal patients in 2012, which constituted 8.1% of all the reported cases of diarrhea (185,961 cases) in Beijing in that year. The results of the electronic gastrointestinal clinical surveillance and reporting system showed that 180,000–190,000 cases of diarrhea occur each year in Beijing, of which about 35% are clinically diagnosed as infectious diarrhea. In China, GPs make clinical diagnoses of infectious diarrhea without laboratory results that identify the bacterium, virus, or parasite involved; therefore, it is extremely important that the GPs understand the pathogenic constitution of infectious diarrhea and the characteristic symptoms of different pathogenic groups. The equipment and funding for pathogen sampling and detection are limited in Beijing, so the constitution of the acute diarrhea observed in this city remains unclear, and the etiology of acute diarrhea is usually attributed to enteropathogenic bacteria and childhood diarrhea [14,15].

At least one enteric pathogen was detected in 133 (37.5%) of the 355 stool specimens examined in this study. This proportion is consistent with the findings in several other countries [16-18]. The rates of viral (single pathogen), bacterial (single pathogen), and mixed infections were 24.5%, 11.0%, and 2.0%, respectively. Viruses were the leading cause of diarrhea in all age groups, which agrees with the finding of Karsten *et al.* [18]. Although the detection rate of viruses in patients with diarrhea varies widely in different areas of China, ranging from 14.7% to 94.1%, the most common viruses detected are rotavirus and calicivirus [8,9,19]. In our study, the rate of calicivirus infection (16.1%) was higher than that of rotavirus infection (11.3%), which is similar to the results for Tianjin, a municipality close to Beijing [8]. The rates and serotype spectra of *V. parahaemolyticus*, *Salmonella* spp., and DEC were similar to those of previous studies in Beijing, whereas the rate of *Shigella* spp. detected dropped from 5.95% to 1.7% [14]. Previous data showed that the rate of *Shigella* spp. detection varied greatly in these years, from 11.2% to 2.0%, and that *Shigella sonnei* had been the predominant species in Beijing since 2006–2007 [20,21]. However, *S. sonnei* is predominant in children and adolescents [21] and our study subjects were adults (over 18 years of age), so the number of cases of *S. sonnei* infection was similar to that of *Shigella flexneri*, rather than being the predominant strain. The limited number of *Shigella* spp. isolated may be related to the age of the study population.

Because China is a developing country, not all diarrheal patients can be diagnosed through laboratory testing in China. GPs often divide diarrheal patients into infectious and noninfectious cases based on their clinical symptoms and the results of routine stool tests. They then select the antibiotics prescribed based on this clinical diagnosis. This study shows that GPs may not always identify infectious diarrhea correctly. If we use laboratory results as the golden standard, the diagnostic sensitivity of infectious diarrhea was only 33.8%. In general, GPs more accurately diagnosed infectious diarrhea caused by bacteria, but there was no significant difference in antibiotic treatments prescribed to patients with different laboratory results. This undoubtedly leads to the irrational use of antibiotics, at least to some extent. Further study of the diagnostic accuracy and the antibiotic therapies offered in Beijing is required because the number of cases examined in the present study was limited.

Our analysis of the association between patient-related factors and different pathogen groups (viral, bacterial, or mixed infections) confirms some of the findings of Dutch and Nordic studies [22,23]. Nausea, living in a suburb, and autumn or winter infection correlated positively with viral pathogens, whereas abdominal pain was negatively associated with viral pathogens. Bacterial pathogens were positively associated with abdominal pain and leukocytosis, but correlated negatively with winter infection. All pathogens correlated positively with nausea, winter infection, and a minimum of six stools per day. There were also tendencies towards positive associations between viral pathogens and spring infection, bacterial pathogens and a minimum of six stools per day, and any pathogen and a minimum of six stools per day. Our study found no association between fever, travel, or vomiting and intestinal infection because few of the patients reported these factors. Nausea, place of residence, leukocytosis, and abdominal pain correlated differently with viral and bacterial infections. Many studies have reported that viral pathogens are more likely to be transmitted by person-to-person contact [22-24]. Although very few cases were reported to be transmitted by other patients in this study, we found that living in a suburb of Beijing was associated with viral infection. Living in a suburb of Beijing implies a crowed environment, with many opportunities to contact individuals with diarrhea.

This study had some limitations. First, other potential enteric pathogens, such as parasites, adenoviruses, astroviruses, and *Clostridium difficile*, were not included in the detection panel, which might have reduced the detection rates. Second, the detection methods used may have affected the detection rates, especially for bacteria. Third, the information about the patients in the clinics was subject to selection bias. Fourth, this study did not include patients who experienced only nausea and/or vomiting, so the results do not reflect the pathogenic constitution of all patients with gastrointestinal illness. Moreover, the study only lasted for one year, which was insufficient to completely describe the etiological constitution and the trends in the development of diarrhea. Further study is required in this field.

Conclusions

At least one enteric pathogen was detected in 37.5% of adult (≥ 18 years of age) patients with diarrhea in Beijing in 2012, and the rate of viral infection was higher than the rate of bacterial infection. The detection rate for pathogens in the stool specimens from patients diagnosed with infectious diarrhea by GPs was only 36.6%, which did not differ significantly from that (37.9%) in patients diagnosed as noninfectious. Because GPs' decisions regarding treatment are mainly based on these clinical diagnoses, inaccurate diagnoses will lead to the irrational use of antibiotics. We observed associations between the different types of infection and specific symptoms, such as abdominal pain, leukocytosis, nausea, living in a suburb, and a minimum of six stools per day. Information about these features may improve the decisions of GPs regarding microbiological testing and treatment.

Acknowledgements

We thank the staff of the seven sentinel hospitals and the three district CDCs (Xicheng CDC, Fengtai CDC, and Daxing CDC) who were responsible for recruiting patients, collecting and processing samples, and collecting epidemiological information during the execution of this study. This work was supported by grants from the National Key Program for Infectious Disease of China (2012ZX10004215-003-001), the Beijing Municipal High-level Technical Training Plan (2013-3-099), and the Beijing Natural Science Foundation (7132045).

References

1. Bern C, Martines J, de Zoysa I, Glass RI (1992) The magnitude of the global problem of diarrhoeal disease: a ten-year update. Bull World Health Organ 70: 705-714.
2. Guerrant RL, Kosek M, Moore S, Lorntz B, Brantley R, Lima AA (2002) Magnitude and impact of diarrheal diseases. Arch Med Res 33: 351-355.
3. Enav BI, Mogilner J, Jaffe M, Shaoul R (2002) Acute appendicitis presenting as secretory diarrhea. J Pediatr Surg 37: 928-929.
4. Krones E, Hogenauer C (2012) Diarrhea in the immunocompromised patient. Gastroenterol Clin North Am 41: 677-701.
5. Zhao YJ, Wen JQ, Cheng K , Ming YZ, She XG, Liu H, Liu L, Ye QF, Ding BN. (2013) Late, severe, noninfectious diarrhea after renal transplantation: high-risk factors, therapy, and prognosis. Transplant Proc 45: 2226-2232.
6. He ZY, Gan YD, Wang XM, Wang QY, Li XY (2013) Analysis on the epidemiological situation of soil-transmitted nematode infections in Beijing municipality, 2006-2010. Int J Med Parasit Dis 40: 1-3.
7. Jia L, Wang XM, Ma XY, Tang YW, Wu J, He X, Gao GH, Han QY, Peng T, Yu HZ, Wang HY (2006) The current

prevalence of intestinal parasites in Beijing. Chin J Parasitol Parasit Dis 24: 313-314.
8. Tian H, Lei Y, Liu Y, Zhang Y, Li JM (2011) Pathogenic analysis on viral diarrhea in Tianjin. J Environ Health 28: 605-608.
9. Yan Y, Guo J, Tian KC, Jiang WJ, Li SJ, Wang Y, Wang DM (2013) Analysis on the pathogeny of viral diarrhea in summer and fall of 2010 in Guiyang districts. Mod Prevent Med. 40: 1201-1208.
10. National Health and Family Planning Commission of the People's Republic of China (2008) Diagnostic criteria for bacillary and amoebic dysentery [Article in Chinese]. Available: http://www.moh.gov.cn/zwgkzt/s9491/200802/39040/files/9c939b0b5de04a14be37e02421adc661.pdf. Accessed 16 October 2015.
11. National Health and Family Planning Commission of the People's Republic of China (2008) Diagnostic criteria for infectious diarrhea [Article in Chinese]. Available: http://www.moh.gov.cn/zwgkzt/s9491/200704/38817/files/4c71b9f101344f12801c94255383219f.pdf. Accessed 16 October 2015.
12. Borges AM, Teixeira JM, Costa PS, Giugliano LG, Fiaccadori FS, Franco Rde C, Brito WM, Leite JP, Cardoso Dd (2006) Detection of calicivirus from fecal samples from children with acute gastroenteritis in the West Central region of Brazil. Mem Inst Oswaldo Cruz 101: 721-724.
13. Climate Reference Room of Beijing Meteorological Bureau (1987) Climatography of Beijing. Beijing: Beijing Press. 24 p.
14. Qu M, Deng Y, Zhang X, Liu G, Huang Y, Lin C, Li J, Yan H, Li X, Jia L, Kan B, Huang F, Wang Q (2006) Etiology of acute diarrhea due to enteropathogenic bacteria in Beijing, China. J Infect 65: 214-222.
15. Kain KC, Barteluk RL, Kelly MT, He X, de Hua G, Ge YA, Proctor EM, Byrne S, Stiver HG (1991) Etiology of childhood diarrhea in Beijing, China. J Clin Microbiol 29: 90-95.
16. de Wit MA, Koopmans MP, Kortbeek LM, van Leeuwen NJ, Bartelds AI, van Duynhoven YT (2001) Gastroenteritis in sentinel general practices, The Netherlands. Emerg Infect Dis 7: 82-91.
17. Sinclair MI, Hellard ME, Wolfe R, Mitakakis TZ, Leder K, Fairley CK (2005) Pathogens causing community gastroenteritis in Australia. J Gastroenterol Hepatol 20: 1685-1690.
18. Karsten C, Baumgarte S, Friedrich AW, von Eiff C, Becker K, Wosniok W, Ammon A, Bockemühl J, Karch H, Huppertz HI (2009) Incidence and risk factors for community-acquired acute gastroenteritis in north-west Germany in 2004. Eur J Clin Microbiol Infect Dis 28: 935-943.
19. Wang WR, Xu HR, Xu SH, Chang CY (2013) Analysis on surveillance of viral diarrhea, Jinan city, 2011. Prev Med Trib 19: 441-445.
20. Wu XN, Jia L, Liu GR, Dou XF, Li XT, Li XY, Wang QY (2011) Analysis of the epidemiological characteristics of dysentery-like cases from 2004 to 2009 in Beijing. Chin J Dis Control Prev 15: 872-875.
21. Mao Y, Cui E, Bao C, Liu Z, Chen S, Zhang J, Wang H, Zhang C, Zou J, Klena JD, Zhu B, Qu F, Wang Z (2013) Changing trends and serotype distribution of *Shigella* species in Beijing from 1994 to 2010. Gut Pathog 5: 21.
22. de Wit MA, Koopmans MP, Kortbeek LM, van Leeuwen NJ, Vinje J, van Duynhoven YT (2001) Etiology of gastroenteritis in sentinel general practices in the netherlands. Clin Infect Dis 33: 280-288.
23. Hilmarsdottir I, Baldvinsdottir GE, Harethardottir H, Briem H, Sigurethsson SI (2012) Enteropathogens in acute diarrhea: a general practice-based study in a Nordic country. Eur J Clin Microbiol Infect Dis 31: 1501-1509.
24. Temu A, Kamugisha E, Mwizamholya DL, Hokororo A, Seni J, Mshana SE (2012) Prevalence and factors associated with Group A rotavirus infection among children with acute diarrhea in Mwanza, Tanzania. J Infect Dev Ctries 6: 508-515. doi:10.3855/jidc.1816.

Corresponding author
Quanyi Wang, MD, Professor and Director
Institute for Infectious Disease and Endemic Disease Control
Beijing Center for Disease Prevention and Control
He Pingli Middle Street, No.16, 100013, Beijing China
Phone: (86) 10 6440 7109
Fax: (86) 10 6440 7109;
Email: lailajia@126.com

Conflict of interests: No conflict of interests is declared.