Plesiomonas shigelloides infection in Hong Kong: retrospective study of 167 laboratory-confirmed cases

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Objective. To study the epidemiological, clinical, and microbiological features of *Plesiomonas shigelloides* infection in Hong Kong.
Design. Retrospective study.
Setting. Infectious Disease Unit of a district hospital, Hong Kong.
Patients. Patients with laboratory-confirmed cases of *Plesiomonas shigelloides* infection between 1 January 1995 and 31 December 1998.
Main outcome measures. Epidemiological and clinical data, antibiotic sensitivity, and clinical outcome.
Results. There was an increasing trend in the number of isolates of *Plesiomonas shigelloides* obtained and the prevalence of the bacterium. A total of 197 isolates were obtained from 188 patients, and most isolates (172; 87.3%) were obtained during the summer. Clinical and epidemiological data were available for 167 patients (85 males, 82 females). Patient age ranged from 1 month to 95 years; the mean and median ages of the patients older than 15 years were 51.0 and 40.5 years, respectively (n=132). Only 35 (21.0%) of the 167 patients had a history of travel outside Hong Kong, whereas 21 (12.6%) had a history of consuming seafood or uncooked food; 39 (23.4%) had underlying medical conditions. Most patients (165; 98.8%) had symptoms of *Plesiomonas shigelloides* infection. Nine (5.4%) patients had had chronic diarrhoea for more than 2 weeks; watery and bloody diarrhoea was discharged by 122 (73.1%) and 42 (25.1%) of the patients, respectively. All 197 *Plesiomonas shigelloides* isolates were sensitive to ofloxacin, or levofloxacin and ceftriaxone. Resistance or partial resistance was recorded for ampicillin (72%), tetracycline (67%), co-trimoxazole (12%), and chloramphenicol (5%). The majority of patients (142/167; 85.0%) had self-limiting cases of infection, but 25 patients were given antibiotics for more severe symptoms at the time of presentation; there were two deaths.
Conclusions. The occurrence of *Plesiomonas shigelloides* infection in Hong Kong is increasing, although most of the cases are self-limiting.

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Key words: Diarrhea/microbiology; Gastroenteritis; Gram-negative bacterial infections; Plesiomonas/drug effects

Introduction

Plesiomonas shigelloides is a facultatively anaerobic, flagellated, Gram-negative rod from the family Vibrionaceae. The bacterium was first isolated in 1947.[1] It is ubiquitous and can be isolated from soil, water, and cold- and warm-blooded animals. It is not considered to be an indigenous organism of the human gastro-intestinal tract, and it has been implicated as an aetiological agent in sporadic cases and outbreaks of diarrhoea in various parts of the world.[2,3] This study aimed to provide a local perspective to disease caused by *P shigelloides*.

Methods

Patients who submitted stool specimens to the microbiology laboratory of the Princess Margaret Hospital (PMH) between 1 January 1995 and 31 December 1998 were enrolled in the study, if the culture test yielded *P shigelloides*. Sources of specimens included the Accident and Emergency Department of the PMH, all in-patients, and patients from other institutions who were referred to the Infectious Disease Team of the PMH for acute dysentery syndrome. Stool culture

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tests that yielded *P shigelloides* as the sole organism or one of the organisms present were retrieved from the computer database of the microbiology laboratory of the PMH.

Clinical and epidemiological details were collected by reviewing patient records. The following information was collected: time of stool collection, age, sex, presence of diarrhoea, nature of stool (presence of blood or mucus), abdominal pain, vomiting, fever, tenesmus, duration of symptoms before the patient sought medical attention (acute symptoms, <2 weeks; chronic symptoms, >2 weeks), total duration of illness, concomitant infection with enteric pathogens other than *P shigelloides*, presence of faecal leukocytes and red cells, and endoscopic findings if available. Other information that was retrieved included history of underlying disease, drugs recently used, recent travel out of Hong Kong, and consumption of seafood or uncooked food within 1 week of the onset of illness. The culture and sensitivity patterns of the isolates were provided by the microbiology laboratory. Outcome measures used were antibiotics given, duration of illness, duration of hospital stay, mortality rate, and long-term morbidity rate.

The microbiology laboratory used the same stool culture system during the study period. Stool specimens were cultured on xylose-lysine-deoxycholate agar, deoxycholate-citrate agar, Monsur agar, thiosulphate-citrate–bile salts sucrose, and *Campylobacter*-selective agar to detect *Salmonella, Shigella, Vibrio,* and *Campylobacter* species. *Plesiomonas* species grow well on deoxycholate-citrate agar and Monsur agar, on which the organism appears as small colonies with a transparent periphery and a dark centre. *Plesiomonas* species are oxidase-positive, indole-producing, and non-halophilic. They are further differentiated from *Vibrio* and *Aeromonas* species as containing arginine dihydrolase, lysine, and ornithine decarboxylase. All the isolates were confirmed by the API20NE bacterial identification system (BioMérieux, Hazelwood, United States).

Results

During the 4-year study period, a total of 197 specimens that were positive for *P shigelloides* were isolated from 188 patients (Table 1). *Plesiomonas shigelloides* accounted for 5.9% of bacterial stool isolates seen during the study period. Except for the year of 1996,

Table 1. Prevalence of *P shigelloides* isolates cultured by the microbiology laboratory of the Princess Margaret Hospital, 1995 to 1998

Year	No. of isolates	No. of patients with complete records	Prevalence among bacterial isolates (%)
1995	28	21	4.4
1996	12	9	1.4
1997	53	47	5.8
1998	104	90	7.9
Total	197	167	5.9

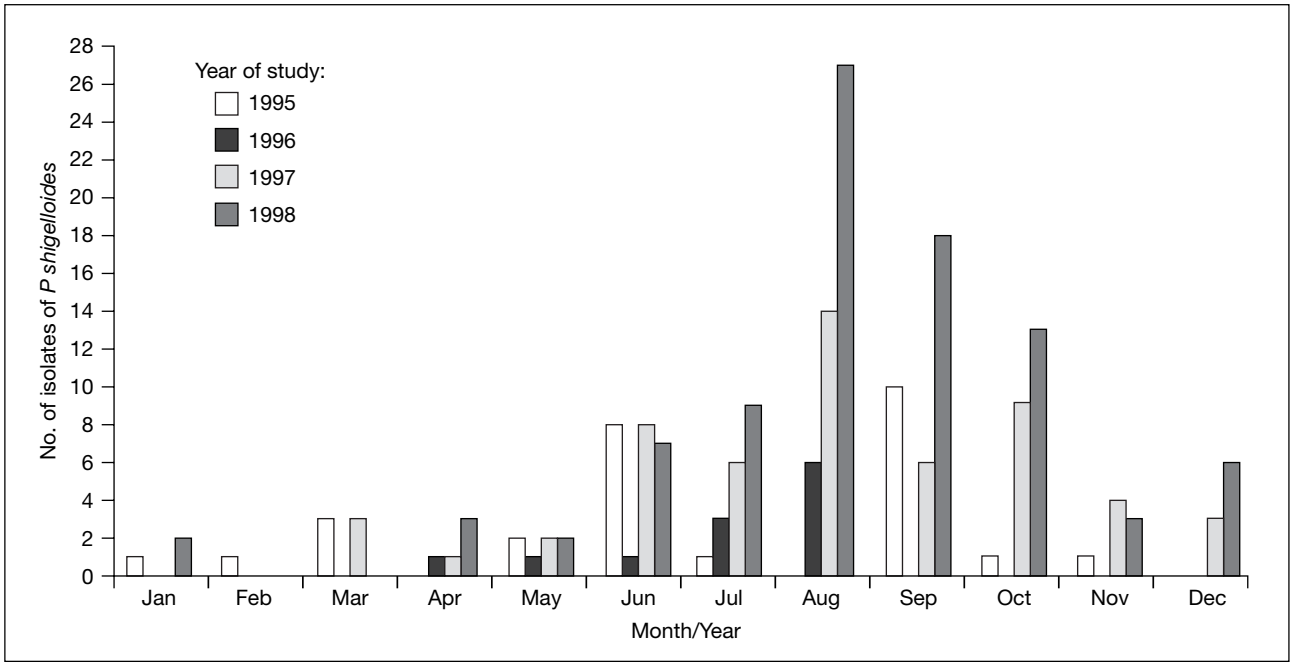

Fig. Monthly variation of the frequency of *P shigelloides* isolates cultured by the microbiology laboratory of the Princess Margaret Hospital, 1995 to 1998

the number of cases isolated and prevalence of *P shigelloides* among bacterial isolates in the hospital showed an increasing trend. The total number of isolates in 1998 accounted for more than half of the total number of isolates in the 4-year period. Most infections (172/197; 87.3%) occurred in the summer months, from June to October (Fig).

Clinical and epidemiological data were available for 167 of the 188 patients. There were 85 males and 82 females, whose ages ranged from 1 month to 95 years. The mean and median ages for patients older than 15 years were 51.0 and 40.5 years, respectively (n=132). Twenty-nine (17.4%) patients were younger than 1 year. Thirty-five (21.0%) patients reported a history of travel outside Hong Kong within 2 weeks of the date of onset of their symptoms. Travel locations included mainland China, South-East Asia, and Macau. Twenty-one (12.6%) patients had a history of consuming seafood or uncooked food within the week preceding their illness. Twelve (7.2%) patients reported that relatives or friends who shared the same meal also had diarrhoea. The largest food-poisoning outbreak caused by *P shigelloides* occurred in 1998 and affected eight people who had dined in a local restaurant.

Thirty-nine (23.4%) patients had significant underlying medical conditions. Twelve patients had diabetes mellitus, four had end-stage renal failure, and four had renal impairment. Underlying bowel diseases were found in six patients, four of whom had carcinoma of the colon, for which colostomy had been performed; one of the six patients had diverticulosis, one had Crohn's disease, and one had gastro-intestinal lymphoma. Five patients had liver cirrhosis (three with alcoholic liver cirrhosis, one with viral hepatitis B–related cirrhosis, and two viral hepatitis C–related cirrhosis). One patient had non-Hodgkin's lymphoma and was receiving chemotherapy. Five patients were receiving corticosteroid treatment at the time of stool collection. One patient was 5 days post-partum and one patient was 4 months pregnant.

All but two patients (165; 98.8%) had symptoms of *P shigelloides* infection, which included diarrhoea. Diarrhoea was defined as the discharge of three or more loose stools in a 24-hour period. Fifty-three (31.7%) patients were treated and discharged at the Accident and Emergency Department of the PMH. The duration of diarrhoea before medical attention was sought ranged from 1 day to 2 months. The median duration of acute diarrhoea (defined as diarrhoea lasting less than 14 days) for the hospitalised patients was 2.2 days. Nine (5.4%) patients had had chronic diarrhoea (ie for more than 14 days), which lasted from 2 weeks to 2 months. Of these nine patients, three had *P shigelloides* isolated from their stool samples on more than one occasion and three had an underlying bowel disease.

Table 2. Symptoms and signs of *P shigelloides* infection

Symptoms	Patients, n=167 No. (%)
Watery diarrhoea	122 (73.1)
Bloody diarrhoea	42 (25.1)
Visible mucus in stool	47 (28.1)
Fever	85 (50.9)
Vomiting	63 (37.7)
Abdominal pain	120 (71.9)
Signs	
Abdominal tenderness	
central	50 (29.9)
epigastric	23 (13.8)
right lower quadrant	5 (3.0)
Subtotal	77 (46.1)
Peritonism	2 (1.1)

The median frequency of diarrhoea discharge at the time of presentation was 5.1 times a day (range, three to 30 times a day on the first day of the onset of symptoms). The symptoms and signs of infection are shown in Table 2. Watery diarrhoea was the most common symptom, being present in nearly three quarters of the cases. Fever was common but usually subsided, because diarrhoea resolved in 1 to 3 days in most cases. About one quarter of the patients discharged bloody stools. This group of patients was usually admitted to the Infectious Disease Unit at the PMH as having cases of suspected dysentery. Abdominal pain and tenderness of varying degrees were present in approximately 72% and 46% of patients, respectively. Peritonism (a condition of shock simulating peritonitis but without inflammation of the peritoneum) was detected in two patients who were initially admitted to the surgical ward as having cases of suspected peritonitis. The site of abdominal pain was variable; central, generalised, and epigastric locations were common. Abdominal tenderness was usually noted in the corresponding site of abdominal pain. Twenty-two (13.2%) of the 167 patients had fever and bloody diarrhoea, which are both markers of more severe disease.

Nine of the 60 patients who had blood withdrawn for analysis were shown to have hypokalaemia. An increased serum urea level was found in five patients, excluding those who had known renal impairment. Higher than normal peripheral neutrophil counts were found in 26 of the 55 patients for whom blood count results were available. Six cases had an absolute neutrophil count in the range of 15 to 21 x 10^9 /L. Colonoscopy was performed for five patients because

of prolonged symptoms. The results were normal for four patients and a villous adenoma was detected in one patient. In three of the four normal cases, histological examination showed the presence of lymphocytic infiltration.

All 197 *P shigelloides* isolates were sensitive to ofloxacin, or levofloxacin and ceftriaxone. Resistance or partial resistance was recorded for ampicillin (72%), tetracycline (67%), co-trimoxazole (12%), and chloramphenicol (5%). Concurrent infection with other organisms was reported in 27 (16%) patients. The organisms isolated included *Salmonella* species (11 isolates), *Campylobacter jejuni* (three isolates), *Shigella sonnei* and *Shigella flexneri* (three isolates each), *Vibrio parahaemolyticus* (two isolates), and *Clostridium difficile* (one isolate). *Clonorchis* and *Strongyloides* infections were shown in three patients and one patient, respectively. Rotavirus infection was present in one patient. There was no positive blood culture for *P shigelloides* during the study period.

The median duration of stay for hospitalised patients was 4.6 days. The majority of patients (142/167; 85.0%) had self-limiting cases of infection. Antibiotics were administered to 25 of the in-patients because of more severe symptoms at presentation. They were usually given one of the quinolone group of antibiotics, and their symptoms had usually subsided on completion of the treatment. The median duration of hospital stay for patients given antibiotics was 5.0 days, possibly due to their more severe symptoms at presentation. Two patients died of symptoms related to *P shigelloides* infection. One patient who died was an 82-year-old man with alcoholic liver cirrhosis. He had had moderately severe diarrhoea with mucus for 2 days, was dehydrated on admission, and was shown to have hypokalaemia. He died 3 days after hospital admission. The second death was that of a 68-year-old man with diabetes mellitus and end-stage renal disease, which required continuous ambulatory peritoneal dialysis. He had had watery diarrhoea for 1 day, and turbid peritoneal fluid was isolated on the day of hospital admission. His condition was treated as a case of bacterial peritonitis, and intraperitoneal antibiotics were given. Culture of the patient's peritoneal fluid grew *Pseudomonas aeruginosa* and that of the stool grew *P shigelloides*. He died of persistent peritonitis and multi-organ failure.

Discussion

Plesiomonas shigelloides has been implicated as an aetiological agent in sporadic cases and outbreaks of diarrhoea in various parts of the world.[2-4] In an ecological study from Tokyo, *P shigelloides* was isolated from river water, sludge from wet river-beds, freshwater fish, and dogs and cats.[5] There have been reports of outbreaks attributed to contaminated water in Japan,[3] consumption of freshwater fish in Zaire,[6] and contaminated raw oysters and shellfish in the United States.[2,4] There has also been a report of a gastroenteritis outbreak in Amsterdam in the summer of 1990 among freshwater bathers.[7]

In this study, there was an increase in the number of isolates during the summer months (Fig), although no media were ever used to enhance the recovery of the organism during the study period. This seasonal variation has also been seen in Japan,[5] Europe,[8] and Bangladesh,[9] and there were also seasonal variations in the numbers of organisms detectable in surface water samples.[9] In some developing countries such as Bangladesh, *P shigelloides* has been isolated throughout the year from surface water samples and in every sample collected.[9] The organism favours warm environments for growth and does not grow at temperatures below 8ºC.[8]

In a case-control study from the United States in the 1980s, foreign travel (usually to Mexico) and the consumption of raw shellfish (usually oysters) were shown to be two factors that were strongly associated with infection with *P shigelloides*.[4] The bacterium is implicated as one of the aetiological agents causing travellers' diarrhoea in developed countries.[4,10-14] This study, however, shows that in Hong Kong, the number of cases of locally acquired diarrhoea caused by *P shigelloides* greatly exceeds that of cases in which there is a reported history of recent foreign travel. The fact that the majority of the patients in this study did not have a history of travel implies that the organism is rather ubiquitous locally.

Plesiomonas shigelloides has been isolated from <0.1% of asymptomatic individuals.[5] In this study, the majority of patients who had *P shigelloides* isolated from their stool samples had diarrhoea. A Japanese study showed that only three of 38 454 subjects studied harboured the organism as normal intestinal flora.[5] Furthermore, a carriage rate of as high as 5.5% has been reported in a survey from Thailand.[11] The most likely explanation is a higher prevalence of *P shigelloides*-associated diarrhoea in Thailand.

Plesiomonas shigelloides has been implicated as being an enteric pathogen in various clinical and epidemiological studies.[4,12-14] However, an understanding

of the mechanism of pathogenesis of the organism has been elusive, and previous in vitro studies of *P shigelloides* pathogenesis have been inconclusive.[13]

The most common manifestation of infection with *P shigelloides* is watery diarrhoea.[12] In otherwise healthy individuals, the diarrhoea is usually mild and self-limiting. The diarrhoea, however, may cause a cholera-like illness, with numerous bowel movements (up to 30) occurring during the peak of the illness.[9] Various studies have reported on the invasive nature of the infection.[4,13,14] Features that indicate acute colitis, which include severe abdominal cramps, and mucoid and bloody stool, occur in a substantial number of patients.[14] There have also been reports of sigmoidoscopic findings of multiple punctate lesions in the distal bowel[4] or inflamed, friable mucosa.[15] Biopsies have occasionally shown features consistent with colitis in such cases. In all, the organism is known to cause either secretory or invasive diarrhoea.[13,14] The incubation period is short, and usually less than 48 hours.[4] Most patients recover spontaneously within 4 weeks of the onset of symptoms, but up to 32% may remain chronically symptomatic.[14]

Plesiomonas shigelloides has occasionally caused extra-intestinal diseases in both immunocompromised and immunocompetent patients. Such infections include septicaemia, meningitis in neonates, cellulitis, septic arthritis, endophthalmitis, and acute cholecystitis.[13,14,16] The majority of bacteraemic cases that have been reported so far involve immunocompromised states either because of prematurity or because of an underlying disease (Hodgkin's disease, sickle cell disease, Felty's syndrome, or alcoholic liver disease).[16,17] Ten of the 12 patients reported to have bacteraemia died, despite the use of antibiotics.[18-21] In contrast, there has also been a report of the isolation of *P shigelloides* from the blood of a previously healthy 15-year-old girl who presented with mild gastro-enteritis and who recovered after receiving minimal drug treatment.[18]

The risk of extra-intestinal disease and severe disease is higher in people with underlying diseases.[13] One of the patients in this study presented with moderately severe diarrhoea; *P shigelloides* was the sole isolate and the patient died 3 days later. In this case, the patient had alcoholic liver cirrhosis. Other factors, such as electrolyte imbalance, may also be a concurrent contributing cause of death. The other patient who died in this study had end-stage renal failure presenting with diarrhoea. His peritoneal dialysis fluid grew *Pseudomonas* species and he had an increased white blood cell count. In this case, the immediate cause of death was not likely to be due to *P shigelloides* infection, although the organism was isolated from the patient's stool.

Immunocompromised individuals are prone to infection by *P shigelloides*.[13] Approximately 70% of patients who present with plesiomonal diarrhoea have either an underlying disease such as cancer or cirrhosis, or an identifiable risk factor such as foreign travel or the consumption of seafood or uncooked food.[13] Patients with underlying carcinoma of the bowel have been reported to be susceptible to infection with *P shigelloides*.[22] A substantial number of patients in this study (39/167; 23.4%) had underlying medical illnesses that are known to affect the host's immune competence. One patient with colonic T-cell lymphoma had repeated infections of the *P shigelloides* within a 1-month period. He was only mildly symptomatic with respect to bowel disturbance.

Antibiotic therapy is not usually necessary to manage infection with *P shigelloides*, because of the self-limiting nature of the illness in the majority of patients.[16,23] Nevertheless, the infection responds well to antibiotic therapy, which leads to a shorter illness compared with that in untreated patients.[4,14] Patients with severe and protracted symptoms, extra-intestinal infection, or a serious underlying disease may benefit from receiving antibiotic therapy. Twenty-five patients in this study were prescribed antibiotics empirically, because of their severe symptoms. It is not known if the duration of symptoms can be shortened by the use of antibiotics, and randomised controlled studies are needed in this area. In vitro experience has shown the organism to be susceptible to quinolones, chloramphenicol, tetracycline, co-trimoxazole, aminoglycosides, imipenem, and selected cephalosporins (ceftazidime, cefotaxime, and ceftriaxone).[13,24] Most isolates produce β-lactamases and are usually resistant to ampicillin.[25]

In conclusion, this study has shown that *P shigelloides* is a ubiquitous enteric pathogen in Hong Kong and the number of cases of infection each year has increased since 1996. Health care workers should be more aware of the organism's increasing occurrence and its pathogenic role, especially in immunocompromised hosts. Specific antibiotic therapy is not needed for the majority of patients.

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