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Original Article

Campylobacter enteritis in children in northern Taiwan — a 7-year experience

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Background and Purpose: *Campylobacter* infection is recognized as a major cause of acute enteritis in humans. The clinical characteristics may vary in different countries. This study investigated the clinical manifestations of pediatric *Campylobacter* enteritis in a medical center in northern Taiwan.

Methods: This was a retrospective review of *Campylobacter* enteritis infections at National Taiwan University Hospital, Taipei, Taiwan, from January 2000 to December 2006. All children who tested positive for *Campylobacter*, isolated from stool samples, were included in the study. Data collected and evaluated included the species of *Campylobacter*, age, gender, underlying disease, travel history, clinical manifestations and laboratory data.

Results: A total of 104 patients had enteric campylobacteriosis. *Campylobacter coli* was grown from 24 patients (23.1%), while *Campylobacter jejuni* was found in 80 patients (76.9%). More than half of the infections (60.6%) occurred in children less than 5 years old. The male-to-female ratio was 2.46:1. Fifteen patients had underlying diseases (14.4%), such as hematologic malignancy, solid organ transplantation and liver cirrhosis. Watery diarrhea (93.2%), abdominal pain (92.0%), fever (81.2%), and vomiting (46.1%) were the most common clinical manifestations. Three episodes of campylobacteriosis appeared to be imported from Southeast Asia and 3 were acquired nosocomially. One patient, who did not have any underlying disease, developed *Campylobacter* bacteremia. No Guillain-Barré syndrome was noted in our patients and none of our patients died due to campylobacteriosis. While both diseases had similar clinical manifestations, infections caused by *C. coli* seemed to be more severe than those caused by *C. jejuni*, as evidenced by a higher incidence of decreased activity and pus cells in the stool in patients infected with *C. coli*.

Conclusion: Even in patients with bacteremia or underlying disease, enteric campylobacteriosis usually runs a benign course regardless of treatment with antimicrobial agents in children in northern Taiwan.

Key words: *Campylobacter*; Child; Enteritis; Retrospective studies; Signs and symptoms

Introduction

Campylobacter organisms are mobile, non-spore-forming, Gram-negative rods [1]. Originally isolated from aborted sheep fetus in 1909, *Campylobacter* spp. are among the most common pathogens in humans and are commensals in birds, swine and cattle [2]. A leading bacterial cause of gastroenteritis in both developed and developing countries [3-5], *Campylobacter* may be responsible for 5% to 14% of diarrhea worldwide [6]. Clinical manifestations of campylobacteriosis include fever, abdominal pain, diarrhea and vomiting. Occasionally, *Campylobacter* infections can lead to reactive arthritis, acute appendicitis and Guillain-Barré syndrome. Guillain-Barré syndrome is thought to occur in 1 out of 1000 cases of *Campylobacter jejuni* infections [7,8]. The age and gender distribution of *Campylobacter* infections are different in developed and developing countries [6,9]. In this study, we analyzed childhood *Campylobacter*-associated enteritis in a medical center in northern Taiwan.

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Methods

This was a retrospective review of *Campylobacter* enteritis infections at the National Taiwan University Hospital (NTUH), Taipei, Taiwan, from January 2000 to December 2006. Only patients below 18 years of age were included. Data collected included the species of *Campylobacter*, age, gender, underlying disease, travel history and clinical manifestations.

Campylobacter isolation

Campylobacter agar contained 10% sheep blood and the antimicrobials amphotericin B, cephalothin, polymyxin B, trimethoprim and vancomycin. Inoculated plates were kept at 42°C in an atmosphere of approximately 5% to 10% oxygen and approximately 5% to 12% carbon dioxide. Plates showing positive oxidase activity were examined at 24 to 48 h by Gram stain. If curved, S-shaped or spiral Gram-negative bacteria were noted by Gram stain, hippurate hydrolysis was performed to differentiate between *Campylobacter coli* (negative reaction) and *C. jejuni* (positive reaction). Differentiation between *C. coli* and *Campylobacter lari* using tests to determine the susceptibility to nalidixic acid was not done, due to high drug resistance of *C. coli* to nalidixic acid in Taiwan.

Statistical analysis

Differences between groups were analyzed by Mann-Whitney *U* test, Pearson's chi-squared test, or Fisher's exact test, when appropriate. Statistical Package for the Social Sciences (SPSS) for Windows (Version 13.0; SPSS, Chicago, IL, USA) software was used. All tests of significance were 2-tailed, and a p value of 0.05 or less was considered statistically significant.

Results

We identified 104 patients with enteric campylobacteriosis. Among these patients, *C. coli* was identified in 24 patients (23.1%) and *C. jejuni* in 80 patients (76.9%). *C. jejuni* was the predominant species associated with *Campylobacter* enteritis ($p<0.001$). There was no seasonal preponderance in our study. During the 7-year period, 28.8% of enteric campylobacteriosis occurred in spring, 21.2% in summer, 29.8% in autumn, and 20.2% in winter. The seasonal peak varied in each year.

Campylobacter infection was most frequent in young children (Fig. 1). More than half (60.6%) of the infections occurred before the age of 5 years, with no significant difference between the incidence of *C. coli* and *C. jejuni* (62.5% vs 60.0%, $p=0.419$).

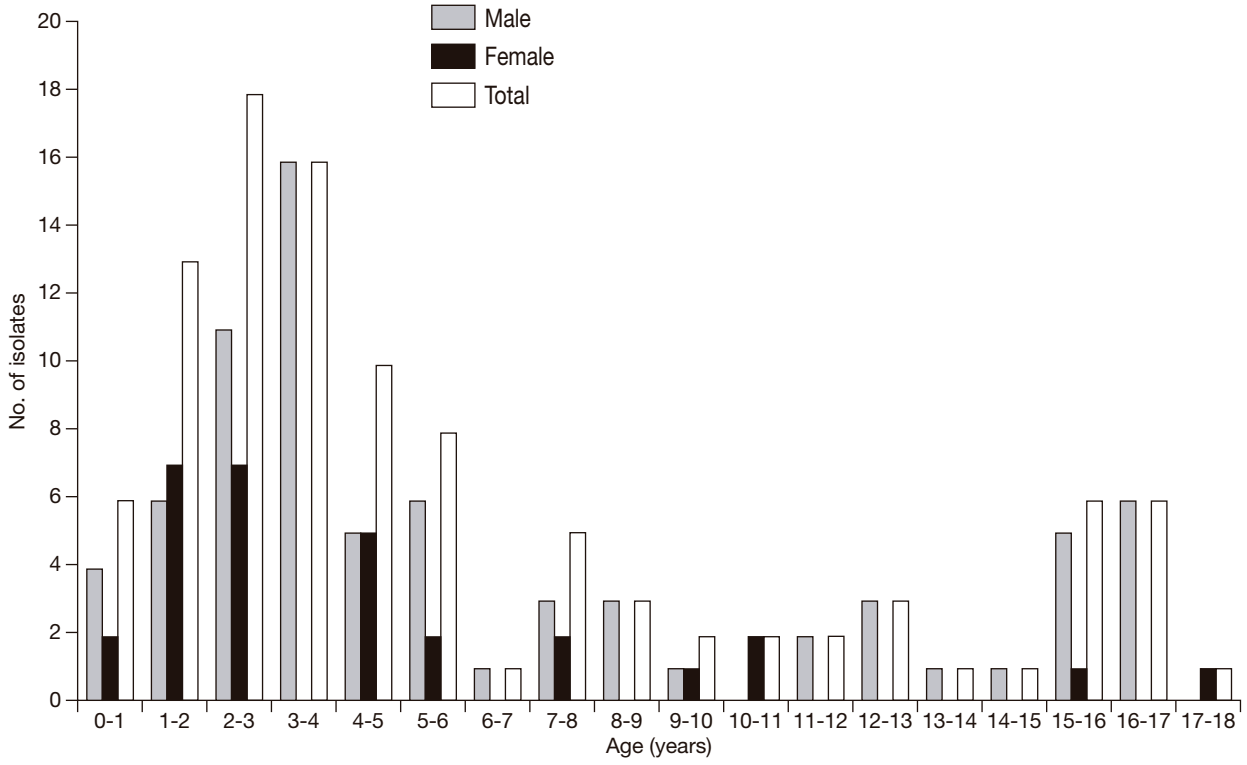

Fig. 1. Frequency of *Campylobacter* isolates by age and gender.

Table 1. Clinical characteristics and laboratory data of pediatric patients with *Campylobacter coli* and *Campylobacter jejuni* enteritis

Variable	No. of isolates/total (%)			*p*
	All isolates	*C. coli*	*C. jejuni*	
Age (years; mean)	5.46	5.08	5.58	0.689[c]
Gender (male/female)	74/30 (2.46:1)	19/5 (3.8:1)	55/25 (2.2:1)	0.323[c]
Underlying disease	15/104 (14.4)	2/24 (8.3)	13/80 (16.3)	0.511[c]
Fever	82/101 (81.2)	20/24 (83.3)	62/77 (80.5)	1[c]
Vomiting	35/76 (46.1)	10/21 (47.6)	25/55 (45.5)	0.866[c]
Abdominal pain	69/75 (92.0)	18/19 (94.7)	51/56 (91.1)	1[c]
Diarrhea	96/103 (93.2)	23/24 (95.8)	73/79 (92.4)	1[c]
Frequency of diarrhea (mean) [range]	5.60 (0-20)	5.02 (0-15)	5.81 (0-20)	0.813[d]
Decreased activity	51/85 (60.0)	16/19 (84.2)	35/66 (53.0)	0.015[c]
Decreased appetite	55/84 (65.5)	16/19 (84.2)	39/65 (60.0)	0.051[c]
Dehydration	54/90 (60.0)	14/21 (66.7)	40/69 (58.0)	0.476[c]
Hospitalization	41/104 (39.4)	10/24 (41.7)	31/80 (38.8)	0.798[c]
Hospital days (mean)[a]	4.64	4.56	4.67	0.911[c]
Antibiotic use[b]	29/104 (27.9)	10/24 (41.7)	19/80 (23.8)	0.086[c]
Laboratory data				
Stool occult blood	48/74 (64.9)	12/16 (75.0)	36/58 (62.1)	0.337[c]
Stool pus cell	37/67 (55.2)	11/13 (84.6)	26/54 (48.1)	0.018[c]
White blood cell (cells/μL; mean) [range]	9289 (300-24,470)	8809 (3880-19,340)	9420 (300-24,470)	0.407[d]
Band form (%; mean) [range]	2.8 (0-46)	5.0 (0-37)	2.1 (0-46)	0.200[d]
Seg (%; mean) [range]	60.3 (8-92)	57.2 (24-88)	61.3 (8-92)	0.464[d]
Lym (%; mean) [range]	25.5 (4-92)	25.9 (8-52)	25.4 (4-92)	0.641[d]
CRP (mg/dL; mean) [range]	5.14 (0.45-17)	4.56 (0.5-14)	5.34 (0.45-17)	0.600[d]

Abbreviations: Seg = segmented neutrophils; Lym = lymphocytes; CRP = C-reactive protein

[a]Excluding patients with underlying disease.

[b]For *Campylobacter* with or without concomitant infection, before or after culture result.

[c]Pearson's chi-squared test or Fisher's exact test.

[d]Mann-Whitney *U* test.

Table 1 summarizes patients' clinical and laboratory data. The male-to-female ratio was 3.8:1 and 2.2:1, for *C. coli* and *C. jejuni* infections, respectively. The overall male-to-female ratio in 104 patients was 2.46:1. Fifteen patients had underlying disease (14.4%), including hematological malignancy in 8 patients, solid organ transplantation in 3, liver cirrhosis in 1 and congenital heart disease in 3 patients.

Watery diarrhea (93.2%), abdominal pain (92.0%), fever (81.2%) and vomiting (46.1%) were the most common clinical manifestations in enteric campylobacteriosis, and there was no difference in clinical manifestations between *C. coli* and *C. jejuni*. The frequency of diarrhea in children infected with *Campylobacter* (5.60 stool passages per day overall) was similar in those younger than 2 years (5.31 times/day) and older than 2 years (5.66 times/day). Dehydration developed in 60% of children. The only significant difference between *C. coli* and *C. jejuni* infection was the greater incidence of decreased activity in *C. coli* infection (84.2% vs 53.0%, p=0.015). Children less than 2 years old with *Campylobacter* infection stayed longer in the hospital (mean, 5.6 vs 4.6 days), but the difference was not statistically significant (p=0.33).

Positive occult blood and pus cells were noted in 64.9% and 55.2% of stool samples, respectively. *C. coli* and *C. jejuni* produced similar rates of occult blood in stool samples, but pus cells in stool were more frequent in infections caused by *C. coli* than *C. jejuni* (84.6% vs 48.1%, p=0.018). Mean white blood cell count was 9289 cells/μL (range, 300-24,470 cells/μL); 60.3% were segmented neutrophils and 25.5% were lymphocytes. The mean level of C-reactive protein was 5.14 mg/dL. No differences in hematological findings were observed between *C. coli* and *C. jejuni*.

Two children without underlying disease were infected with *Campylobacter* and rotavirus. One child with acute lymphocytic leukemia was infected with *Campylobacter* and *Salmonella*. In 2 patients

admitted for *Escherichia coli* septic shock, *Campylobacter* was isolated from the stool at the same time; one was a 17-year-old boy with liver cirrhosis and the other was a 12-year-old boy with acute lymphocytic leukemia. Three episodes of campylobacteriosis appeared to be imported from Southeast Asia, namely from Hong Kong, Thailand and Bali. Three patients had nosocomial campylobacteriosis, 1 patient had no underlying disease, and the others had hematological malignancy. A 4-year-old boy without underlying disease had *C. jejuni* bacteremia and was discharged from the hospital on day 4 without antibiotics. Antimicrobials were used in 29 patients (27.9%) who had campylobacteriosis only or had other infections. Antibiotics were prescribed to a greater proportion of patients with *C. coli* enteritis than *C. jejuni* enteritis (41.7% vs 23.8%, p=0.086). There was no case of Guillain-Barré syndrome in our patients and none died due to campylobacteriosis.

Discussion

Studies of diarrheal diseases in developed and developing countries have shown that *Campylobacter* spp. are a common bacterial cause of gastrointestinal illnesses. The incidence of human campylobacteriosis is increasing worldwide [9-16]. In developing countries, *Campylobacter* is most commonly isolated from children younger than 2 years of age [17,18]; adults have higher levels of antibody against *Campylobacter* and less *Campylobacter* infection [19]. This has led to the suggestion that repeated challenges with *Campylobacter* induce antibody responses, which protect adults from disease. In contrast, both adults and children in developed countries are susceptible to *Campylobacter* infection [6,20-25]. In this study in patients less than 18 years old, 18.3% of the *Campylobacter* infections occurred in patients under 2 years of age; however, only 9.1% of *Campylobacter* infections occurred below the age of 2 in all age groups at NTUH. Campylobacteriosis was not limited to young children in northern Taiwan. Hence, the epidemiology of *Campylobacter* infection in Taiwan was similar to what has been observed in developed countries. One previous study in Taiwan (Chang Gung Children's Hospital) showed that 85% of patients were less than 5 years old [26], while in this study 60.6% of patients were less than 5 years of age. The difference may be due to hygiene improvements during these years. In addition, there were fewer numbers of stool examinations for *Campylobacter* in our hospital than at Chang Gung Children's Hospital.

Campylobacter is frequently isolated together with other enteric pathogens in patients with diarrhea in developing countries [27,28]. In contrast, polymicrobial infections involving *Campylobacter* are less prevalent in developed nations [4,5]. Other coinfecting pathogens reported include *Salmonella* spp., *E. coli*, *Shigella* spp., *Clostridium* spp., *Giardia lamblia*, and rotavirus. We also identified 2 coinfections of *Campylobacter* with rotavirus and 1 episode of *Campylobacter* with *Salmonella*. Compared with Singapore [29], where the rate of coinfection with *Campylobacter* and other enteric pathogens was about 15%, the rate of polymicrobial infections involving *Campylobacter* was much less (2.89%) in northern Taiwan.

The distribution of *C. jejuni* and *C. coli* varies in different countries [4-6,26-35]. In northern Taiwan, *C. jejuni* (76.9%) was the major species, followed by *C. coli* (23.1%). This relative proportion of *C. jejuni* to *C. coli* was similar to those of other countries in Southeast Asia, such as Thailand (80% vs 20%), India (82.3% vs 16.1%), Singapore (89% vs 11%), and central Taiwan (81% vs 19%) [34-37], but different from data reported for the Central African Republic (45.3% vs 55.5%) and South Africa (96.9% vs 3.1%) [31,32].

Usually, infection with *Campylobacter* spp. results in an acute, self-limited gastrointestinal illness characterized by diarrhea, fever and abdominal cramps. We found that watery diarrhea (93.2%), abdominal pain (92.0%), fever (81.2%) and vomiting (46.1%) were the most common clinical manifestations of *Campylobacter* enteritis. Clinically, *Campylobacter* infection is indistinguishable from other bacterial enterocolitis. In Singaporean children with *Campylobacter* infection, the symptoms observed were fever and diarrhea in 50%, vomiting in 28%, and abdominal pain in 8% [29]. In Taiwanese children with *Campylobacter* infection, these symptoms were observed more frequently. Hence, it seemed that the clinical manifestation of *Campylobacter* infection was more severe in Taiwan. However, this was a retrospective study and sampling bias must be kept in mind. We traced the numbers of stool antigen tests for rotavirus and stool culture for *Campylobacter* in children during 2000 to 2006 at NTUH. The numbers of stool antigen tests for rotavirus were 1.5- to 2.5-fold higher than the numbers of stool cultures for *Campylobacter*. We believe that

physicians tend to order more tests for rotavirus when dealing with children with mild gastroenteritis, leading to underdiagnosis of *Campylobacter* enteritis in mild gastroenteritis cases.

In order to combat *Campylobacter* infection in Taiwan, it would be helpful to track and identify the source of human infection. A more detailed survey, particularly with regard to recent contact with animals and consumption of water and animal food products, would be helpful in defining risk factors of infection and possible transmission routes.

In conclusion, this study indicates that *Campylobacter* is a major enteric pathogen in northern Taiwan, especially in children younger than 5 years. Watery diarrhea, abdominal pain, fever, and vomiting were the most common clinical manifestations. *C. jejuni* (76.9%) was responsible for most of the campylobacteriosis in this study. Infection caused by *C. coli* seemed to be more severe than that caused by *C. jejuni*, as evidenced by the greater occurrence of decreased activity and pus cells in the stool. Furthermore, physicians tended to prescribe antibiotics for *C. coli* infections more frequently than for *C. jejuni* infections. However, even in patients with bacteremia or underlying disease, enteric campylobacteriosis usually runs a benign course with or without antimicrobial agents in children.

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