Avoidance of Antibiotic Administration to Campylobacter Enterocolitis Mimicking Severe Salmonellosis by Clinical and Laboratory Features

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Summary

Background: To compare the clinical and laboratory features of non-typhoid Salmonella (NTS) and *Campylobacter jejuni* enterocolitis in children and formulate a risk scoring system (with receiver-operating characteristic curve) to facilitate early decision making and avoid antibiotic overuse in *C. jejuni* enterocolitis.

Methods: Between January 2008 and December 2011, children (age <18 years) diagnosed as having *C. jejuni* enterocolitis and NTS enterocolitis in Kaohsiung Chang Gung Memorial Hospital were retrospectively enrolled. Clinical features and laboratory data were collected for analysis and a risk calculation score is created for the identification of Campylobacter infections.

Results: A total of 309 cases of *C. jejuni* enterocolitis and 496 cases of NTS enterocolitis were enrolled. Compared with Salmonella group clinically, the Campylobacter group had older age (81.06 ± 50.65 vs. 32.70 ± 34.88 months, $p <; 0.001$), more abdominal pain (69.26% vs. 37.5%, $p <; 0.001$) and more watery diarrhea (79.94% vs. 20.77%, $p <; 0.001$). In laboratory data, the Campylobacter group had higher level of white blood cell count ($11\,208 \pm 4380$ vs. 9095 ± 3598 cell/mm^3, $p <; 0.001$).

Conclusion: Four criteria including age (≥5 years), leukocytosis (≥10 000 cell/mm^3), abdominal pain and watery diarrhea were identified as good predictors of Campylobacter enterocolitis. When three criteria were fulfilled, Campylobacter enterocolitis was highly suspected and antibiotic could be withheld even when C-reactive protein is high and before stool culture results are known. When four criteria were fulfilled, antibiotic usage was absolutely unnecessary.

Key words: antibiotic, bacterial enterocolitis, Campylobacter, ROC curve, Salmonella.

Introduction

Non-typhoid Salmonella (NTS) and *Campylobacter jejuni* are the two most common pathogens of bacterial enterocolitis in children [1–3]. There has been a marked increase in the incidence of *C. jejuni* infections worldwide in recent years [4]. Both NTS and *C. jejuni* enterocolitis are generally self-limited and resolve without specific antibiotic treatment [5, 6]. In contrast to the benign course and few complications of *C. jejuni* enterocolitis, toxic megacolon, bacteremia and other forms of extraintestinal infection are serious complications of NTS that may not be suspected in the setting of a mild primary infection. Factors affecting the incidence of bacteremia include Salmonella serotype and host factors. Host risk

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factors for NTS bacteremia include extremes of age and chronic or immunosuppressing conditions, including malignancy and rheumatologic disease [7].

Clinically in Taiwan, the third-generation cephalosporin antibiotic ceftriaxone (Roche, Basel, Switzerland) is commonly used in severe NTS enterocolitis [with high C-reactive protein (CRP), bandemia and prolonged high fever] [8], but antibiotics are unnecessary for *C. jejuni* enterocolitis even with high CRP. However, lack of rapid diagnostic methods for enteric pathogens requires making a decision on antibiotic use as soon as the patient is admitted. Thus, it is practical to differentiate between the two pathogens to avoid antibiotic overuse in cases of *C. jejuni* enterocolitis.

Patients and Methods

This study, approved by the ethics committee of Chang Gung Memorial Hospital (IRB 100-2566B), retrospectively, reviewed medical records on patients less than 18 years of age who were admitted owing to *C. jejuni* enterocolitis or NTS enterocolitis. Patients accompanied with underlying hematologic disease, immune-compromised disease or other infection were excluded. Over a period of 10 years (2002–11), a trend of increasing incidence of *C. jejuni* enterocolitis in older children was noted with a mean age above 70 months old in the recent 4 years 2008–11. Thus, cases of *C. jejuni* enterocolitis and NTS enterocolitis in children (age < 18 years) between January 2008 and December 2011 in Kaohsiung Chang Gung Memorial Hospital were enrolled. The two groups were categorized according to stool culture with clinical and laboratory features being analyzed and compared. Clinical parameters included age, onset of gastrointestinal symptoms before admission, fever duration, clinical course, hospital stay, abdominal pain, watery (loose) stool and antibiotic therapy. Laboratory features included complete blood count, CRP, stool occult blood and stool pus cell.

Definitions

Campylobacter jejuni/NTS enterocolitis was defined as a decrease in consistency (i.e., soft or liquid) and an increase in frequency of bowel movements to ≥3 stools per day with stool cultures positive for *C. jejuni* or NTS. Clinical course was defined as the total duration of symptoms of enterocolitis such as diarrhea, abdominal pain. Pain assessments of abdomen were carried out during hospitalization using Neonatal Infant Pain Scale (NIPS) for neonates and infants, The Faces Legs Activity Cry Consolability Scale (FLACC) for children (<3 years) who were unable to communicate their pain and Wong-Baker FACES Pain Rating Scale (W-B PRS) for children ≥3 years. Abdominal pain was defined as scores of NIPS ≥5, FLACC ≥6 or W-B PRS ≥6. Watery (loose) stool was defined as any stool reported by the parent or guardian containing no blood tinged or mucus material. Fever was defined as ≥38°C as measured by thermometer in the ear. Antibiotic therapy was defined as antibiotic use for at least 3 days after admission. The decision to administer antibiotic treatment was at the discretion of the attending physician, with no input from the authors. The criteria for admission and discharge were customary. Patients were admitted if they presented with fever and diarrhea with any symptoms/signs of dehydration or bloody stool. Patients were discharged when afebrile for >24 hours and when the symptoms/signs of dehydration had resolved.

Statistical analysis

Each categorical variable's association with type of disease was assessed by χ^2 test and odds ratio with 95% confidence interval. Student's t test is used to compare continuous variables. All tests for significance were two-tailed and a p value < 0.01 was considered statistically significant. Four variables with statistical significance were used as criteria for Campylobacter enterocolitis. Receiver-operating characteristic (ROC) analysis was performed on these criteria to assess the ability to discriminate *C. jejuni* enterocolitis from NTS enterocolitis. A risk score was formulated using these four criteria and was validated on a prospectively collected data from 100 new patients, each with 50 *C. jejuni* enterocolitis and 50 NTS enterocolitis in 2012. All the analyses were implemented on SPSS 17.0 (Chicago, IL, US).

Results

A total of 309 cases of *C. jejuni* enterocolitis and 496 cases of NTS enterocolitis in children (age < 18 years) between January 2008 and December 2011 in Kaohsiung Chang Gung Memorial Hospital were enrolled. A trend of increasing incidence of *C. jejuni* enterocolitis in older children was noted with a mean age above 70 months old in the recent 4 years 2008–11 (Fig. 1A). The percentage of age 12–60 months was decreasing year by year, and the percentage of age above 60 months was increasing year by year (Fig. 1B).

Among children with *C. jejuni* enterocolitis, there were no significant differences in the clinical features except abdominal pain between the old (≥5 years old) and young (<5 years old) children (Table 1). In laboratory data, older children (≥60 months old) with *C. jejuni* enterocolitis were more segment predominant (76.09 ± 12.32 vs. $62.02 \pm 14.55\%$, $p < 0.001$) with a higher level of CRP (80.68 ± 63.21 vs. 49.65 ± 46.18 mg/L, $p = 0.005$) (Table 1).

Compared with the NTS group clinically, the Campylobacter group was older (81.06 ± 50.65 vs. 32.70 ± 34.88 months, $p < 0.001$), had more

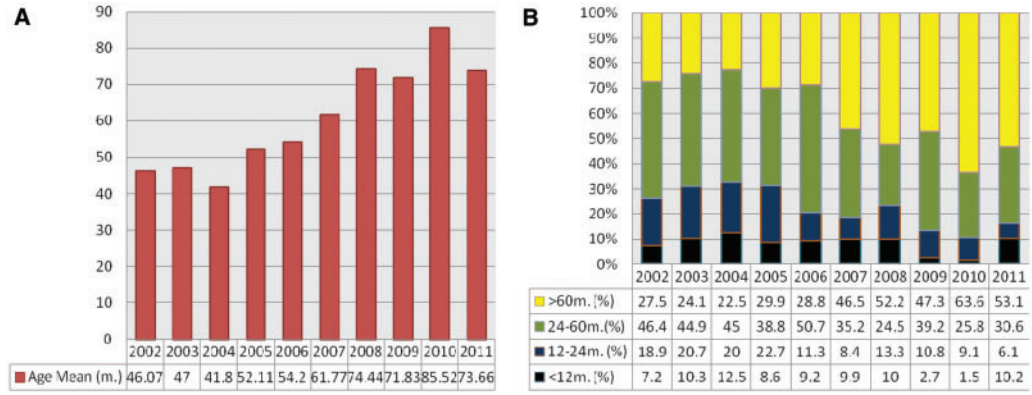

FIG. 1. (A) Mean age and (B) percentage of age of Campylobacter enterocolitis 2002–11. A trend of increasing incidence of *C. jejuni* enterocolitis in older children was noted with a mean age above 70 months old in the recent 4 years 2008–11. The percentage of age 12–60 months was decreasing year by year and the percentage of age above 60 months was increasing year by year.

TABLE 1
Clinical features and laboratory data of Campylobacter group, age ≧ 60 m/o vs <60 m/o

Clinical features/ Laboratory data	Campylobacter ≧ 60 m/o (n = 184)	Campylobacter < 60 m/o (n = 125)	Odds ratio (95% CI)	*p* value
Clinical features				
Age (m/o)	113.96 ± 38.05	31.96 ± 15.64	–	<0.001
Onset before admission (days)	2.78 ± 1.31	2.56 ± 1.36	–	0.384
Fever duration (days)	3.09 ± 1.55	3.39 ± 2.45	–	0.42
Clinical course (days)	5.79 ± 2.50	5.43 ± 1.53	–	0.386
Hospital stay (days)	4.01 ± 2.11	3.85 ± 1.63	–	0.653
Male gender (%)	108 (58.70%)	71 (56.80%)	1.10 (0.52–2.34)	0.807
Abdominal pain	157 (85.33%)	57 (45.6%)	0.145 (0.06–0.35)	<0.001
Watery stool	143 (77.72%)	103 (87.20%)	0.744 (0.287–1.931)	0.54
Laboratory data				
WBC (cell /mm^3)	11500 ± 4198	10624 ± 4703	–	0.30
Segment (%)	76.09 ± 12.32	62.02 ± 14.55	–	<0.001
Lymphocyte (%)	15.93 ± 10.81	26.92 ± 12.38	–	<0.001
Hb (g/dL)	12.92 ± 1.43	12.23 ± 1.25	–	0.009
Platelet (×10^3/mm^3)	229.63 ± 78.17	263.22 ± 64.24	–	0.017
CRP (mg/L)	80.68 ± 63.21	49.65 ± 46.18	–	0.005
Stool OB	1.33 ± 1.11	0.91 ± 0.92		0.04
Stool pus cell	0.62 ± 0.92	0.33 ± 0.75		0.86

CI, Confidence Interval; WBC, white blood cell count; Hb, hemoglobin; CRP, C-reactive protein.

abdominal pain (69.26% vs. 37.5%, $p < 0.001$) and more watery diarrhea (79.94% vs. 20.77%, $p < 0.001$) (Table 2). In addition, the Campylobacter group had shorter fever duration (3.17 ± 1.92 vs. 3.93 ± 2.27 days, $p = 0.01$), shorter clinical course (5.62 ± 2.15 vs. 6.81 ± 2.53 days, $p < 0.001$) and shorter hospital stay (3.91 ± 1.90 vs. 5.03 ± 2.15 days, $p < 0.001$) (Table 2).

In laboratory data, the Campylobacter group had higher level of white blood cell count (11 208 ± 4380 vs. 9095 ± 3598 cell/mm^3, $p < 0.001$) and was more segment predominant (70.48 ± 14.91 vs. 60.15 ± 15.26%, $p < 0.001$). However, bandemia and CRP levels were not statistically significant between the two groups (Table 2).

Four criteria including age ≥ 5 years, leukocytosis ≥ 10 000 cell/mm^3, abdominal pain and watery diarrhea were used to predict Campylobacter enterocolitis, and a ROC curve was analyzed (1 criteria: sensitivity = 0.973, specificity = 0.323; 2 criteria: sensitivity = 0.850, specificity = 0.719; 3 criteria: sensitivity = 0.611, specificity = 0.917; 4 criteria: sensitivity = 0.212, specificity = 0.99) (Fig. 2). The four criteria developed were validated on a prospectively collected data from 100 new patients, each with 50 *C. jejuni* enterocolitis and 50 NTS

TABLE 2
Clinical features and laboratory data of Campylobacter vs. Salmonella groups

Clinical features/ Laboratory data	Campylobacter group (n = 309)	Salmonella group (n = 496)	Odds ratio (95% CI)	*p* value
Clinical features				
Age(m/o)	81.06 ± 50.65	32.70 ± 34.88	–	<0.001
Onset before admission (days)	2.70 ± 1.33	2.72 ± 1.75	–	0.928
Fever duration (days)	3.17 ± 1.92	3.93 ± 2.27	–	0.01
Clinical course (days)	5.62 ± 2.15	6.81 ± 2.53	–	<0.001
Hospital stay (days)	3.91 ± 1.90	5.03 ± 2.15	–	<0.001
Male gender (%)	182 (58.90%)	283 (57.06%)	1.04 (0.61–1.80)	0.877
Abdominal pain	214 (69.26%)	186 (37.5%)	3.73 (2.09–6.64)	<0.001
Watery stool	247 (79.94%)	103 (20.77%)	15.2 (7.71–29.97)	<0.001
Antibiotic use	174 (56.31%)	212 (42.74%)	0.58 (0.33–1.01)	0.53
Laboratory data				
WBC (cell /mm^3)	11208 ± 4380	9095 ± 3598	–	<0.001
Segment (%)	70.48 ± 14.91	60.15 ± 15.26	–	<0.001
Cases with bandemia	25 (8.09%)	83 (16.73%)	0.45 (0.19–1.06)	0.63
Lymphocyte (%)	20.22 ± 12.59	29.91 ± 13.63	–	<0.001
Hb (g/dL)	12.64 ± 1.40	12.04 ± 1.049	–	0.001
Platelet ($\times 10^3$/mm^3)	243.58 ± 74.64	253.61 ± 88.47	–	0.375
CRP (mg/L)	67.69 ± 58.80	65.29 ± 64.77	–	0.779
Stool occult blood	1.16 ± 1.06	0.69 ± 0.82		0.001
Stool pus cell	0.50 ± 0.86	0.49 ± 0.84		0.928

CI, Confidence Interval; WBC, white blood cell count; Hb, hemoglobin; CRP, C-reactive protein.

enterocolitis in 2012. The overall discriminating ability of these criteria on the new data set as determined by the area under the ROC was 82.2% (95% CI, 0.74–0.904) similar to 85.5% (95% CI, 0.804–0.906) in the original data set (Fig. 2).

Discussion

A trend of increasing incidence of Campylobacter enterocolitis in older children

In this study, the first clinical feature that differentiated between *C. jejuni* and NTS enterocolitis was age. The Campylobacter group had older age (≥5 years), which is in contrary to previous published studies. Worldwide studies, including those from Taiwan, showed a bimodal age distribution, with the first peak occurring in children less than 5 years of age and a second peak at 15–29 years of age [9–12]. Our study showed a trend of increasing incidence of Campylobacter enterocolitis among older (≥5 y/o) children in recent years. Human Campylobacter cases in England and Wales reported to the Health Protection Agency's local and national surveillance also showed that there has been a marked decline in Campylobacter infection in children less than 4 years from 2000 onward [13].

The reasons for these age distributions remain unknown, but two key factors, immunity and environmental exposure, were reported to influence the age-specific rate of *C. jejuni* infection [14, 15].

The peak isolation rate in neonates and infants is attributed in part to susceptibility (immunity) on first exposure and to reporting bias, i.e., infants with diarrhea are more likely to be brought to medical care and more likely to have stool cultures done than older children or adults. But no reporting bias occurred in our study because both stool cultures, including Salmonella and Campylobacter, were undertaken in all of them.

The presence of Campylobacter-specific secretory IgA, serum IgA and oligosaccharides in breast milk correlates with protection against diarrhea [15–19]. Breast-feeding was promoted in the past 10 years in Taiwan, which may account for the low incidence rate of *C. jejuni* enterocolitis in young infants in our study.

In a case-control study in the Hunter region of New South Wales, Australia [20], 354 cases and 593 controls were recruited to investigate meat, other food and environmental exposures as potential risk factors for domestically acquired Campylobacter illness. They observed that eating restaurant-prepared red meat and swimming were significantly associated with Campylobacter illness in the older group (≥5 y/o) only. These findings demonstrate increasing risk factors in older children for campylobacteriosis.

The importance of differentiation between NTS and Campylobacter enterocolitis

Bacterial infection was suspected when high level of CRP [21] and leukocytosis with neutrophilia [22]

	Original			Validation		
	sensitivity	specificity	1-specificity	sensitivity	specificity	1-specificity
1 criteria	0.973	0.323	0.677	0.960	0.32	0.68
2 criteria	0.850	0.719	0.281	0.74	0.8	0.2
3 criteria	0.611	0.917	0.083	0.42	0.96	0.04
4 criteria	0.212	0.99	0.01	0.18	0.98	0.02
AUC	0.855			0.822		
95% CI	0.804-0.906			0.74-0.904		
P value	<0.001			<0.001		

AUC, Area Under the Curve; CI, Confidence Interval

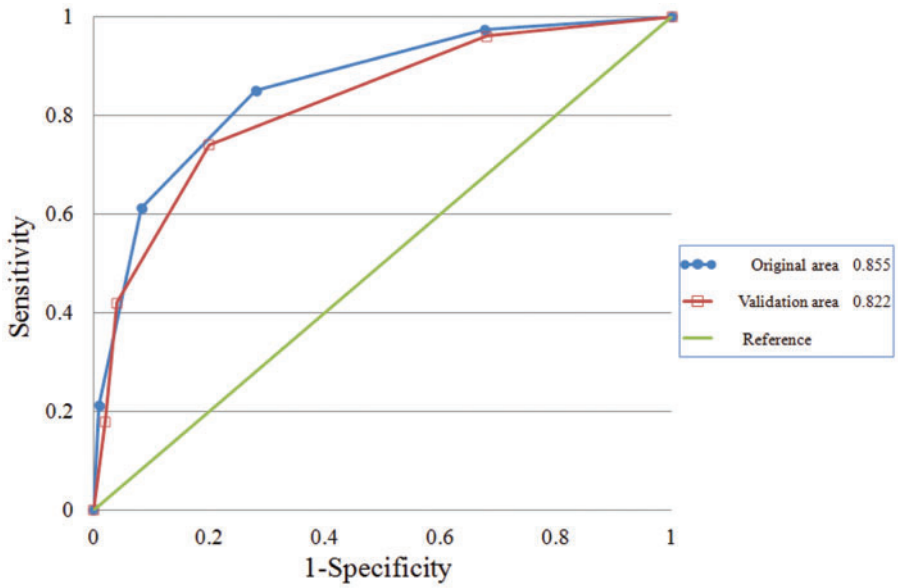

FIG. 2. ROC curve of original and validation data set. Four criteria including age ≥5 years, leukocytosis ≥10 000 cell/mm^3, abdominal pain and watery diarrhea were used to predict Campylobacter enterocolitis and an ROC curve was analyzed. The four criteria developed were validated on a prospectively collected data from 100 new patients, each with 50 *C. jejuni* enterocolitis and 50 NTS enterocolitis in 2012. The overall discriminating ability of these criteria on the new data set as determined by the area under the ROC was 82.2% (95% CI, 0.74–0.904) similar to 85.5% (95% CI, 0.804–0.906) in the original data set.

were found. The typical features of bacterial enterocolitis were mucoid and blood-tinged [23] diarrhea. NTS and *C. jejuni* are the two most common pathogens of bacterial enterocolitis in children [1–3]. However, studies on differences between the two bacterial enterocolitis were rarely reported. In this study, we found that *C. jejuni* enterocolitis had more abdominal pain, more watery diarrhea, shorter fever duration, shorter clinical course, shorter hospital stay and more leukocytosis with more segment predominant. However, bandemia and CRP were not statistically significant to differentiate between the two bacterial enterocolitis. It suggests that *C. jejuni* enterocolitis had a more benign clinical course even with more leukocytosis and more segment predominant than NTS enterocolitis. It adds to the difficulty of differentiating these two pathogens by leukocytosis, bandemia and high CRP.

In this study, compared with NTS enterocolitis, *C. jejuni* enterocolitis had more abdominal pain (69.26% vs. 37.5%, $p < 0.001$), of which 12.66% were severe cramping pain or even localized to the right lower quadrant of the abdomen (pseudoappendicitis), prompting further image study such as sonography or computed tomography. Severe abdominal pain before onset of diarrhea can mimic

acute appendicitis. In some cases, diarrhea is absent (this is most frequently observed among children aged 6–15 years). The pain is caused by acute ileocecitis. On clinical examination, tenderness may be observed but rebound tenderness and guarding are usually absent [24, 25].

Antibiotics are not generally recommended for the treatment of isolated uncomplicated Salmonella enterocolitis [26] because they may suppress normal intestinal flora and prolong both the excretion of Salmonella and the remote risk for creating the chronic carrier state (usually in adults) [27]. However, age >1 year, CRP > 200 mg/l were the significant factors associated with intestinal perforation in toxic megacolon complicating NTS enterocolitis [28]. Therefore, antibiotic treatment should be considered in a subset of severely ill immunocompetent individuals on an individualized basis [29]. Additionally, Huang, *et al*. [8] sought to develop a severity score to derive an objective guideline for antibiotic use in non-typhoid salmonellosis when the severity score is more than 3 (high CRP, bandemia, prolonged fever). In another recent study [30], patients with longer febrile duration and higher CRP levels (CRP $\geq$ 100 mg/l) may be considered as having 'severe NTS enteritis' and these patients appear to benefit clinically from antibiotic treatment. To suppress the load of Salmonella in the intestinal tract and to simultaneously prevent the possible induction of antibiotic resistance, a short course (3–5 days) of an adequate antibiotic such as ceftriaxone is suggested in the treatment of severe NTS gastroenteritis. It is mandatory to differentiate between NTS and *C. jejuni* enterocolitis to prevent antibiotic overuse because, in our study, both cases could have high CRP and bandemia.

With a similar sensitivity and specificity of the same criteria and area under the curve in ROC curves of the original and validation groups, the four criteria were good and steady predictors of Campylobacter enterocolitis. When more than three criteria were fulfilled, the specificity was more than 91% and Campylobacter enterocolitis was highly suspected. With these criteria, the following benefit could be encountered: lessening excess antibiotic use, avoiding unnecessary and prolonged hospitalization and evading needless appendectomy and expensive image study.

Conclusion

Four criteria of age ($\geq$5 years), leukocytosis ($\geq$10 000 cell/mm^3), abdominal pain and watery diarrhea were good predictors of Campylobacter enterocolitis. When three criteria were fulfilled, Campylobacter enterocolitis was highly suspected and antibiotic could be withheld even when CRP was high and before stool culture results were known. When four criteria were fulfilled, antibiotic usage was absolutely unnecessary.

References

1. Vital Signs Incidence and trends of infection with pathogens transmitted commonly through food—foodborne diseases active surveillance network, 10 U.S. Sites, 1996-2010. MMWR Morb Mortal Wkly Rep 2011;60:749–55.
2. Slutsker L, Ries AA, Greene KD, *et al*. *Escherichia coli* o157:H7 diarrhea in the United States: Clinical and epidemiologic features. Ann Intern Med 1997;126: 505–13.
3. Preliminary foodnet data on the incidence of infection with pathogens transmitted commonly through food—10 states, united states, 2005. MMWR Morb Mortal Wkly Rep 2006;55:392–5.
4. Coker AO, Isokpehi RD, Thomas BN, *et al*. Human campylobacteriosis in developing countries. Emerg Infect Dis 2002;8:237–44.
5. Onwuezobe IA, Oshun PO, Odigwe CC. Antimicrobials for treating symptomatic non-typhoidal salmonella infection. Cochrane Database Syst Rev 2012;11: CD001167.
6. Ternhag A, Asikainen T, Giesecke J, *et al*. A meta-analysis on the effects of antibiotic treatment on duration of symptoms caused by infection with campylobacter species. Clin Infect Dis 2007;44:696–700.
7. Gordon MA. *Salmonella* infections in immunocompromised adults. J Infect 2008;56:413–22.
8. Huang IF, Wagener MM, Hsieh KS, *et al*. Nontyphoid salmonellosis in taiwan children: clinical manifestations, outcome and antibiotic resistance. J Pediatr Gastroenterol Nutr 2004;38:518–23.
9. van Pelt W, de Wit MA, Wannet WJ, *et al*. Laboratory surveillance of bacterial gastroenteric pathogens in the Netherlands, 1991-2001. Epidemiol Infect 2003;130: 431–41.
10. Yang JR, Wu HS, Chiang CS, *et al*. Pediatric campylobacteriosis in northern taiwan from 2003 to 2005. BMC Infect Dis 2008;8:151.
11. Wang SC, Chang LY, Hsueh PR, *et al*. Campylobacter enteritis in children in northern taiwan—a 7-year experience. J Microbiol Immunol Infect 2008;41: 408–13.
12. Lin CW, Yin PL, Cheng KS. Incidence and clinical manifestations of campylobacter enteritis in central Taiwan. Zhonghua Yi Xue Za Zhi (Taipei) 1998;61: 339–45.
13. Nichols GL, Richardson JF, Sheppard SK, *et al*. Campylobacter epidemiology: a descriptive study reviewing 1 million cases in England and Wales between 1989 and 2011. BMJ Open 2012;2:pii: e001179.
14. Havelaar AH, van Pelt W, Ang CW, *et al*. Immunity to campylobacter: its role in risk assessment and epidemiology. Crit Rev Microbiol 2009;35:1–22.
15. Janssen R, Krogfelt KA, Cawthraw SA, *et al*. Host-pathogen interactions in campylobacter infections: the host perspective. Clin Microbiol Rev 2008;21:505–18.
16. Morrow AL, Ruiz-Palacios GM, Altaye M, *et al*. Human milk oligosaccharides are associated with protection against diarrhea in breast-fed infants. J Pediatr 2004;145:297–303.
17. Renom G, Kirimat M, Georges AJ, *et al*. High levels of anti-campylobacter-flagellin iga antibodies in breast milk. Res Microbiol 1992;143:93–8.
18. Ruiz-Palacios GM, Calva JJ, Pickering LK, *et al*. Protection of breast-fed infants against campylobacter

diarrhea by antibodies in human milk. J Pediatr 1990; 116:707–13.
19. Torres O, Cruz JR. Protection against campylobacter diarrhea: Role of milk iga antibodies against bacterial surface antigens. Acta Paediatr 1993; 82:835–8.
20. Unicomb LE, Dalton CB, Gilbert GL, *et al*. Age-specific risk factors for sporadic campylobacter infection in regional Australia. Foodborne Pathog Dis 2008;5:79–85.
21. Simon L, Gauvin F, Amre DK, *et al*. Serum procalcitonin and C-reactive protein levels as markers of bacterial infection: a systematic review and meta-analysis. Clin Infect Dis 2004;39:206–17.
22. Al-Gwaiz LA, Babay HH. The diagnostic value of absolute neutrophil count, band count and morphologic changes of neutrophils in predicting bacterial infections. Med Princ Pract 2007;16:344–7.
23. Talan D, Moran GJ, Newdow M, *et al*. Etiology of bloody diarrhea among patients presenting to united states emergency departments: prevalence of *Escherichia coli* o157:H7 and other enteropathogens. Clin Infect Dis 2001;32:573–80.
24. Puylaert JB, Vermeijden RJ, van der Werf SD, *et al*. Incidence and sonographic diagnosis of bacterial ileocaecitis masquerading as appendicitis. Lancet 1989;2:84–6.
25. van Spreeuwel JP, Lindeman J, Bax R, *et al*. Campylobacter-associated appendicitis: prevalence and clinicopathologic features. Pathol Annu 1987; 22(Pt 1):55–65.
26. Chiu CH, Lin TY, Ou JT. A clinical trial comparing oral azithromycin, cefixime and no antibiotics in the treatment of acute uncomplicated salmonella enteritis in children. J Paediatr Child Health 1999;35:372–4.
27. Aserkoff B, Bennett JV. Effect of antibiotic therapy in acute salmonellosis on the fecal excretion of salmonellae. N Engl J Med 1969;281:636–40.
28. Chao HC, Chiu CH, Kong MS, *et al*. Factors associated with intestinal perforation in children's non-typhi salmonella toxic megacolon. Pediatr Infect Dis J 2000;19:1158–62.
29. Wistrom J, Jertborn M, Ekwall E, *et al*. Empiric treatment of acute diarrheal disease with norfloxacin. A randomized, placebo-controlled study. Swedish study group. Ann Intern Med 1992;117:202–8.
30. Tsai MH, Huang YC, Lin TY, *et al*. Reappraisal of parenteral antimicrobial therapy for nontyphoidal *Salmonella Enteric* infection in children. Clin Microbiol Infect 2011;17:300–5.