Comparison of acute bloody and watery diarrhea: a case control study

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The clinical and laboratory findings of 290 cases of bloody diarrhea who presented to the department of Diarrhea Training and Treatment between June 1998 and May 2002 were investigated, and compared to those of two consecutive cases who had watery diarrhea. The bloody diarrhea group had higher mean age, higher frequencies of diarrhea, lower frequencies of vomiting, and shorter durations of diarrhea at the time of admission as compared to the watery diarrhea group. The number of cases using antibiotics before the onset of diarrheal attacks was higher in the bloody diarrhea group, and sulbactam-ampicillin had been used more frequently in this group. The presence of dehydration was similar in the two groups, but the occurrence of moderate to severe dehydration was significantly less in the bloody diarrhea group. Salmonella was the most common enteropathogen in the bloody diarrhea group; however, isolation of shigella was similar in both groups. In the bloody diarrhea group, one had convulsion, one rectal prolapse, and one intussusception. The rates of hospitalization and antibiotic use were higher in the bloody diarrhea group. The use of antibiotics should be evaluated in cases with bloody diarrhea. Further studies are necessary to detect changes in the pathogens responsible for bloody diarrhea in developing and developed countries.

Key words: bloody diarrhea, watery diarrhea.

About 10% of diarrhea episodes in children under five years of age have blood visible in the stool, and these account for about 15% of diarrhea-associated deaths in this age group worldwide. Compared to watery diarrhea, bloody diarrhea generally lasts longer, is associated with more complications, is more likely to adversely affect a child's growth, and has a higher fatality rate[1]. Dysentery is characterized by the passage of watery stools containing blood and mucus, abdominal cramps, rectal burning, fever, and occasionally toxicity[2]. Watery diarrhea causes high incidences of vomiting, often before the onset of diarrhea, and relatively infrequent stools of large volume[3], whereas bloody diarrhea causes frequent stools of small volume[2]. Dehydration and vomiting are more common in watery diarrhea than in bloody diarrhea[1]. There are only a few studies comparing the clinical and laboratory features of bloody and watery diarrhea cases worldwide. To the best of our knowledge, there has been no such study conducted in Turkey. In the present study, the clinical and laboratory findings of children with bloody diarrhea were compared to those of children with watery diarrhea who presented to Hacettepe University İhsan Doğramacı Children's Hospital, Ankara, Turkey.

Material and Methods

This study included all cases with bloody diarrhea, from Central Anatolia, who admitted to Hacettepe University İhsan Doğramacı Children's Hospital, Department of Diarrheal Disease Training and Treatment, between June 1998 and May 2002. All cases were managed according to World Health Organization (WHO) criteria[1]. For every case of bloody diarrhea included in the bloody diarrhea group (BD group), two consecutive cases of watery diarrhea were added to the watery diarrhea group (WD group).

Diarrhea was defined as the passage of three or more loose stools during the 24-hour (h) period preceding hospital presentation[1]. Bloody diarrhea was defined as any diarrheal episode in which loose or watery stools contained gross blood[1].

In this retrospective case-control study, the histories of the patients, clinical and laboratory data were obtained from hospital files. The following information, when available, was recorded: age in months, gender, duration of illness before presentation, stool frequency, history of fever, vomiting, abdominal pain, presence of mucus in stool, seizures during the illness, antibiotic use before diarrheal episode, and antibiotic use for the treatment of diarrhea. Additionally, body weight at presentation and the presence of dehydration and coexisting disease were recorded. Laboratory information included stool examination for the presence of leukocytes and parasites, stool culture, Clostridium difficile toxin assay, complete blood count, blood pH, serum HCO_3^-, serum electrolyte, blood urea nitrogen (BUN), and creatinine and uric acid levels.

The nutritional status of the patients was evaluated using the National Charts of Health Statistics (NCHS) growth charts[4]. Leukocytosis was defined as a leukocyte value above 95 percentile according to age[5]. Hyponatremia was defined as serum sodium levels <130 mEq/L, hypernatremia as serum sodium levels >150 mEq/L, and hypopotassemia as serum potassium level <3 mEq/L[1].

All the stool samples were cultured on Salmonella-Shigella (SS) agar, eosin-methylene blue (EMB), and selenite F agar. Stool samples were not studied for viral agent.

All analyses were conducted using SPSS statistical software package (version 6.0 for Windows, SPPS Inc, Chicago, IL, USA). Student t-test or x^2 was used for statistical comparison when appropriate.

Results

Clinical Findings

Two hundred ninety children with BD group and 580 children with WD group were enrolled in the study. Table I shows the clinical characteristics of the patients in both groups. Patients with bloody diarrhea were older (Table I). Watery diarrhea was more common among children younger than 2 years of age (349/580, 60% of cases), whereas bloody diarrhea was more common among 2-10 year olds (158/290, 55% of cases). The male/female ratio was similar in both groups. There were fewer patients with low weight for age (<5th percentile for NCHS growth charts) in the BD group than in the WD group (4% and 9%, respectively; p=0.030) (Table I).

At presentation, patients in the BD group had shorter diarrheal duration, higher frequency of stool output, and less vomiting than the patients in the WD group. The presence of fever was similar in both groups. More patients in the BD

Table I. Clinical Features of Children in the Bloody Diarrhea and Watery Diarrhea Groups Upon Presentation

	Bloody diarrhea		Watery diarrhea		
	n/N	%	n/N	%	p
Male sex	159/290	55	328/580	57	0.664
Mean age (months)*	59.3±47.7		36.7±59.9		<0.001
Age <24 months	85/290	29	349/580	60	<0.001
Weight for age <5p	11/251	4	47/541	9	0.030
Duration of diarrhea (day)*	2.6±2.4		3.1±2.7		0.003
Frequency of stool (per day)*	12.1±11.2	(n:255)	6.9±4.9	(n:523)	0.001
Vomiting	85/290	29	321/580	55	0.001
Mucus in stool	149/165	90	150/309	49	0.001
History of fever	142/290	49	280/580	48	0.886
Abdominal pain requiring further evaluation	20/290	7	20/580	4	0.022
Dehydration	47/290	16	103/580	18	0.567
Mild	8/47	17	7/103	7	0.050
Moderate to severe	39/47	83	96/103	93	0.050

*mean±SD.

group required pediatric surgical consultation due to presence of abdominal pain (7% and 4%, respectively; p=0.022, Table I).

More children in the WD group had coexisting disease [WD group: 215/580 (37%); BD group: 75/290 (26%), p=0.001], and upper respiratory tract infection (URTI) was the most common, which appeared with similar frequency in both groups [BD group: 66/290 (23%); WD group: 160/580 (28%), p=0.125]. The other common coexisting diseases were lower respiratory tract infection [BD group: 3/290 (1%); WD group: 28/580 (5%), p=0.004] and urinary tract infection [BD group: 6/290 (2%); WD group: 24/580 (4%), p=0.115].

There was no difference in the age distribution of dehydrated patients in both groups (Table I). Moderate to severe dehydration was seen more frequently in the WD group. Overall, dehydration was more common among the children aged 0-2 years in the WD group [80/349 (23%) in <24 months age group; 23/231 (10%) in ≥24 months age group, p<0.001], but no difference was found in the BD group according to age groups [17/85 (20%) in <24 months age group; 30/205 (15%) in ≥24 months age group, p=0.170].

More patients had a history of antibiotic use before the onset of diarrhea in the BD group [BD group: 58/290 (20%); WD group: 82/580 (14%), p=0.027] (Table II). Sulbactam-ampicillin (SAM) was the most commonly used antibiotic before the onset of diarrhea in both groups, although SAM was used more frequently among the BD group patients before onset (Table II).

Laboratory Findings

The patients in the BD group had a higher mean hemoglobin level and leukocyte count, and leukocytosis was more common in the BD group than in the WD group (Table III). The BD group had a higher mean blood pH and serum HCO_3^- level. There was no significant difference between the two groups in the number of patients having blood pH <7.3. The ratio of patients with serum HCO_3^- level <15 mmol/L was lower in the BD group. The BD group also had lower mean serum BUN and uric acid levels. The mean serum creatinine and electrolyte values were similar in both groups. One patient in the BD group and one in the WD group had hyponatremia, one patient in the BD group and two in the WD group had hypernatremia, and one patient in the BD group had hypopotassemia (Table III).

The number of cases with five or more leukocytes in microscopic stool examination and positive stool cultures was higher in the BD than WD group [63/138 (38%); 18/166 (11%) respectively, p<0.001]. The number of patients with positive stool culture result was higher in the BD than WD group (Table IV). The isolation rate of salmonella and campylobacter species were higher in the BD group, while that of shigella was similar in the two groups. Salmonella species were the most frequently isolated enteropathogen in the BD group, whereas shigella species were the most frequently isolated enteropathogen in the WD group. *Shigella sonnei* was the predominant type among the shigella species; *Shigella boydii* and *Shigella dysenteriae* were not isolated from any

Table II. Antibiotic Use Before the Onset of Diarrhea

	Bloody diarrhea		Watery diarrhea			
Antimicrobial agent	n	%	n	%	Odds ratio (95% CI)	p
Penicillin	52	18	50	9	2.316 (1.526-3.515)	<0.001
SAM[α]	47	16	34	6	3.106 (1.948-4.952)	<0.001
Other than penicillin	6	2	32	6	0.164 (0.067-0.398)	0.013
Total antibiotic usage	58	20	82	14	1.518 (1.048-2.199)	0.027

CI: Confidence interval. SAM: Sulbactam-ampicillin.

Table III. Hematologic and Biochemical Parameters in the Bloody Diarrhea and Watery Diarrhea Groups During Presentation

	Bloody diarrhea		Watery diarrhea		
	n	mean±SD	n	mean±SD	p
Hemoglobin (g/dl)	129	12.2±1.7	276	11.4±1.5	<0.001
Hematocrit (%)	118	36.0±4.7	258	33.6±4.3	<0.001
WBC (x10^9/L)	127	12.3±4.7	274	11.0±4.5	0.009
Leukocytosis	30/127	(24%)	37/274	(14%)	0.012
Platelet (x10^9/L)	112	404±474	252	353±203	0.152
MCV (fl)	101	77.9±7.3	240	74.4±9.0	<0.001
RDW (%)	80	13.4±1.9	202	14.6±2.9	<0.001
pH	60	7.35±0.07	124	7.32±0.07	0.009
HCO_3^- (mmol/L)	59	20.0±3.0	124	17.2±4.1	<0.001
pH <7.3	15/60	(25%)	49/124	(40%)	0.069
HCO_3^- <15	3/59	(5%)	37/124	(29%)	<0.001
Sodium (mEq/L)	65	138±5	133	137±4	0.541
Potassium (mEq/L)	64	4.3±0.6	132	4.2±0.7	0.392
Chloride (mEq/L)	61	104±13	123	107±6	0.082
BUN (mg/dl)	27	9.2±4.5	57	13.6±9.6	0.005
Creatinine (mg/dl)	29	0.57±0.27	52	0.54±0.29	0.656
Uric acid (mg/dl)	24	4.6±2.5	49	6.2±3.2	0.022

WBC: White blood cell count. MCV: Mean corpuscular volume. RDW: Red cell distribution width. BUN: Blood urea nitrogen.

Table IV. Results of Stool Culture and Microscopic Examination of Stool in the Bloody Diarrhea and Watery Diarrhea Groups

	Bloody diarrhea (n:194)		Watery diarrhea (n:338)		
Microorganism	n	%	N	%	p
Salmonella species	15	8	9	3	0.007
Salmonella group D	11	6	4	1	
Salmonella group B	3	2	2	0.6	
Salmonella group C1	1	0.5	1	0.3	
Salmonella paratyphi			1	0.3	
Unknown			1	0.3	
Shigella species	8	4	14	4	0.991
S. sonnei	8	4	12	3	
S. flexneri			1	0.3	
Unknown			1	0.3	
Campylobacter	4	2	1	0.3	0.042
Positive stool culture	27	14	27	8	0.029

of the patients in either group, and *Shigella flexneri* was isolated from only one patient in the BD group (Table IV).

Giardia was found in two patients in each group, and none of the patients had amebiasis. *C. difficile* assay was performed in 14 patients in the BD group and the test results were negative.

Outcomes

There was no mortality among the patients in either group. In the BD group, one patient had invagination, one had perforation, and one had rectal prolapsus. The rate of hospitalization and antibiotic treatment was higher in the BD group (Table V). Trimethoprim-sulfamethoxazole (TMP/SMX) was the most commonly used antibiotic in both groups [BD group: 84/290 (29%); WD group: 7/580 (1%)]. Ciprofloxacin and metronidazole were the other most commonly used antibiotics [BD group: 49/290 (17%), 27/290 (7%); WD group: 4/580 (1%), 2/580 (0.3%), respectively]. Intravenous fluid therapy was administered to more of the patients in the BD group compared to the WD group, but the difference was not significant.

Table V. Treatment and Hospitalization in the Bloody Diarrhea and Watery Diarrhea Groups

	Bloody diarrhea		Watery diarrhea		
	n	%	n	%	p
ORT treatment	15	5	84	15	<0.001
Intravenous fluid treatment	24	8	31	5	0.093
Hospitalization	17	6	12	2	0.005
Antibiotic treatment	161	56	19	3	<0.001

ORT: Oral rehydration therapy.

The number of patients who required oral rehydration treatment (ORT) treatment was lower in the BD group; however, when age was taken into consideration, it was similar among children aged 0-2 years in both groups. None of the patients over the age of 2 years received ORT in the BD group, while five patients over 2 years of age required ORT in the WD group.

Discussion

Watery diarrhea was more common among children aged 0-2 years, whereas bloody diarrhea was more common among children aged 2-10 years, and the mean age was higher in the BD group. Similarly, it was shown that the peak prevalence of watery diarrhea occurs between the ages of 6 and 11 months, while the peak prevalence of bloody diarrhea occurs in children 18-23 months of age[6].

In the present study, the mean duration of diarrhea upon presentation was shorter in the BD group. This can be explained by parents' perceptions of bloody diarrhea as a more severe disease than watery diarrhea. There was a similar report from Bangladesh showing that children with bloody diarrhea were taken to hospital sooner after the onset of diarrhea than children with watery diarrhea[7].

The patients in the BD group of the present study had a higher frequency of diarrhea and less vomiting than those in the WD group. Large bowel involvement, which causes bloody diarrhea, produces frequent and small volume stools, whereas small bowel involvement, most commonly caused by rotavirus, produces a high incidence of vomiting, often before the onset of diarrhea, and large volume, watery, and relatively infrequent stools[2].

We found that the number of patients with fever was similar in the BD and WD groups. Fever in a child with diarrhea might be due to other coexisting infections (e.g. pneumonia or otitis media) or dehydration[1]. The BD group had more patients with abdominal pain and more patients that were consulted with pediatric surgery. Abdominal pain is more common in patients with bacterial diarrhea, which can cause bloody diarrhea, than in those having diarrhea caused by viral agents[2].

Antibiotic-associated diarrhea is a common complication of antibiotic therapy, occurring in 5 to 39% of patients receiving antibiotics[8]. In our study, the number of patients receiving antibiotics before the onset of diarrhea was higher in the BD group. Although the number of patients who received antibiotics was high, all of the *C. difficile* toxin assays were negative. Possible explanations for this are that *C. difficile* is the cause of only 10-25% of all antibiotic-associated diarrhea, the sensitivity of *C. difficile* toxin assay is 70-80%, and microorganisms other than *C. difficile* (e.g. *Staphylococcus aureus, Clostridium perfringens*) can also cause antibiotic associated diarrhea[8-10]. Moreover, antibiotics can have direct toxic and allergic effects on mucosa, and some of them can change intestinal motility and disturb the metabolic function of intestinal flora[8]. Antibiotic-associated diarrhea can occur in association with any antibiotic; however, it is most commonly associated with penicillin, ampicillin, clindamycin, and cephalosporin[11]. Although SAM was the most common antibiotic given in both groups prior to the onset of diarrhea, the number of patients receiving SAM was higher in the BD group. To the best of our knowledge, the present study is the first to report that SAM use was higher in a cohort of BD patients compared to a cohort of WD patients.

Although the number of patients with dehydration was similar in both groups, the frequency of moderate to severe dehydration was more common in the WD group. Since 80% of fluid absorption occurs in the small bowel, a pathologic process that predominantly affects the small

bowel, such as watery diarrhea, will predispose patients to more rapid dehydration[3]. In young infants, the intestinal mucosa tends to be more permeable to water[3]. As the child matures, the permeability of the mucosa diminishes. Therefore, in young infants, the impact of increased luminal osmolality due to the diarrheal process can result in greater net fluid and electrolyte loss than in older children with a similar process[3]. In our study, dehydration most commonly developed in patients under two years of age in the WD group, but no difference was found in the BD group according to age groups.

In the present study, the frequency of patients having URTI was similar in both groups. It has been reported that symptoms of URTI frequently accompany diarrhea[12].

The mean leukocyte count was higher in the BD group, as was the number of patients with leukocytosis. The hemoglobin, hematocrit, and corpuscular hemoglobin mean values were higher and the red cell distribution weight values were lower in the BD group. This may be related to presence of younger children in the WD group.

The mean blood pH and serum HCO_3^- levels and the number of patients with serum HCO_3^- levels <15 were lower in the WD group. This may have been due to the higher number of moderate to severely dehydrated cases in the WD group. Although electrolyte loss is known to be more common in cases of watery diarrhea than in bloody diarrhea[1], in the present study, the mean electrolyte levels and the number of patients with electrolyte imbalance were similar in both groups.

The higher frequency of fecal leukocytes in the BD group of our study might have been caused by the invasion of the intestinal epithelium by the pathogen, which usually results in an acute inflammatory response, even in the early stages of dysentery[13]. Although in the present study, the isolation rate of all pathogens was higher in the BD group than in the WD group, this rate was lower than what has been reported in other studies. A child with bloody diarrhea has a 50% chance of having a bacterial infection, while only one in three children with bacterial diarrhea will have bloody stools[3].

Even though it was shown that the isolation rate of shigella was higher in BD group than in the WD group in numerous reports from other developing countries[6,14,15], the present study found similar rates between the BD and WD groups. This might have been because of the particular shigella species seen in our patients. *S. sonnei* was the most common of the shigella species observed in this study, which is in concordance with previous reports from Turkey[16,17]. It is known that *S. sonnei* and *S. boydii* usually cause febrile, self-limiting watery diarrhea[18]. Salmonella was the most commonly isolated pathogen in the BD group. Higher rates of isolation of *S. sonnei* and of non-typhoidal salmonella species are trends that have been associated with socioeconomic development and improved sanitation in Europe, North America, and Israel[19,20]. A report from Israel found that since 1975 there has been an overall decrease in the isolation of shigella species, especially of *S. flexneri*, in cases of clinical dysentery in Israel, most probably the result of a concomitant increase in Salmonella spp[20]. On the other hand, it was reported that recent use of antimicrobials is significantly associated with salmonella infection[21]. In addition, antibiotic usage for bloody diarrhea before presentation to a hospital might inhibit pathogen isolation. In our study, the frequency of antibiotic use before the onset of diarrhea was high. Unfortunately, an association between antibiotic use and salmonella gastroenteritis could not be analyzed because of the limited number of cases in the present study.

In the present study, the isolation rate of campylobacter was higher in the BD group. Patients infected with campylobacter more frequently develop bloody diarrhea in developed countries, whereas they more frequently develop watery diarrhea in developing countries[22]. Amoebiasis is an unusual cause of bloody diarrhea in young children, usually causing less than 3% of episodes[1]. A Turkish study reported that *Entamoeba histolytica* was detected in 1.3% of patients with diarrhea[23]. In 93 stool examinations performed for *E. histolytica* conducted during the present study, all test results were negative.

The fatality rate of bloody diarrhea ranges from 1% to 13% when the appropriate treatment is not given[24,25]. This rate is 0.27% for watery diarrhea[26]. In our study, there was no mortality in either group. The convulsion rate is 10-45% in patients with shigellosis[27]. In our

study, only one patient in the BD group had convulsion. It was reported that the rate of hemolytic uremic syndrome is 11% in dysentery caused by shigella species[25]. In our study, none of the patients developed hemolytic uremic syndrome. Dysentery patients rarely develop intestinal complications, including rectal prolapsus, toxic megacolon, intestinal perforation, and invagination[19]. A report from Zimbabwe showed that among the hospitalized children with dysentery, 5% of them had rectal prolapsus and 6% had ileus[28]. In the present study, in the BD group, one patient developed rectal prolapsus, one had invagination, and another had perforation. Both the lack of mortality and the low complication rate observed in the present study may have been due to appropriate case-management based on WHO guidelines. Additionally, the shigella subtypes that were isolated in the BD group were not those associated with high mortality and complication rates.

The number of patients who were given antibiotics was higher in the BD group than in the WD group. Intravenous fluid treatment was more commonly administered to patients in the BD group. When a critically ill patient shows signs of toxicity, and the gut wall has been compromised to a significant extent, intravenous fluids should be administered, even when dehydration is not severe[2]. ORT use was more common in the WD group because there were slightly more patients in this group with moderate to severe dehydration. In addition, the number of patients who had metabolic acidosis was higher in the WD group.

The patients in the BD group were hospitalized at a higher rate than those in the WD group. It is suggested that because bloody diarrhea is a more severe disease than watery diarrhea[1], more patients required hospitalization in the BD group. A report from Thailand showed that the hospitalization rate is 9.5% in patients with dysentery[29]. In our study, 6% of the patients in the BD group were hospitalized. The low complication and hospitalization rate found in this study may be related to the low shigella isolation rate, which was lower than in other developing countries, in which the ratio of shigella in bloody diarrhea ranged between 22%-52%[14,15]. In addition, *S. sonnei*, which causes clinically mild disease, was the most common serotype, and neither *S. dysenteriae* nor *S. flexneri* was isolated in the BD group. Type I *S. dysenteriae* is the shigella species associated with the most severe disease and the highest fatality rates. The majority of deaths from shigellosis worldwide result from endemic disease, especially those caused by *S. flexneri*[1].

In conclusion, upon presentation, the mean age was higher, the duration of diarrhea was shorter, and the frequency of stool output, rate of vomiting, and use of antibiotics and SAM before the onset of diarrhea were higher in the BD group. The numbers of patients with leukocytosis and abdominal pain requiring pediatric surgery consultation were also higher in the BD group. More patients had positive stool cultures in the BD group and salmonella was the most common diarrheal agent isolated. There was no difference between the shigella isolation rates between the two groups, and the only shigella species isolated in both groups was *S. sonnei*, with the exception of *S. flexneri*, which was isolated in one patient in the WD group. In our study there was no death and the complication rate was lower than what has been reported from other developing countries. The numbers of patients who required hospitalization and antibiotic use were higher in the BD group.

REFERENCES

1. Division of Diarrhoeal and Acute Respiratory Disease Control. The Treatment of Diarrhoea – A Manual for Physicians and Other Senior Health Workers. Geneva, Switzerland: World Health Organization; 1995. WHO/CDR/95.3.
2. Guerrero R. Acute invasive diarrhea in the pediatric patient. Scand J Gastroenterol 1989; 169 (Suppl): 24-27.
3. DeWitt TG. Acute diarrhea in children. Pediatr Rev 1989; 11: 6-13.
4. Hamill PV, Drizd TA, Johnson CL, Reed RB, Roche AF, Moore WM. Physical growth: National Center for Health Statistics percentiles. Am J Clin Nutr 1979; 32: 607-629.
5. Nicholson JF, Pesce MA. Laboratory testing and reference values in infants and children. In: Behrman RE, Kliegman RM, Arvin AM (eds). Nelson Textbook of Pediatrics. Philadelphia: WB Saunders Company; 1996: 2031-2034.
6. Henry FJ. Epidemiologic importance of dysentery in communities. Rev Infect Dis 1991; 13 (Suppl): 238-244.
7. Ahmed F, Clemens JD, Rao MR, Ansaruzzaman M, Haque E. Epidemiology of shigellosis among children exposed to cases of Shigella dysentery: a multivariate assessment. Am J Trop Med Hyg 1997; 56: 258-264.

8. Bergogne-Berezin E. Treatment and prevention of antibiotic associated diarrhea. Intern J Antimicrob Agent 2000; 16: 521-526.
9. Bartlett JG. Antibiotic associated diarrhea. N Engl J Med 2002; 346: 334-339.
10. Yassin SF, Young-Fadok TM, Zein NN, Pardi DS. Clostridium difficile-associated diarrhea and colitis. Mayo Clin Proc 2001; 76: 725-730.
11. Surawicz CM, McFarland LV. Pseudomembranous colitis: causes and cures. Digestion 1999; 60: 91-100.
12. Mangia AH, Duarte AN, Duarte R, Silva LA, Bravo VL, Leal MC. Aetiology of acute diarrhoea in hospitalized children in Rio de Janeiro City, Brazil. J Trop Pediatr 1993; 39: 365-367.
13. Gilman RH. General considerations in the management of typhoid fever and dysentery. Scand J Gastroenterol 1989; 169 (Suppl): 11-18.
14. Prado V, Lagos R, Nataro JP, et al. Population-based study of the incidence of Shigella diarrhea and causative serotypes in Santiago, Chile. Pediatr Infect Dis J 1999; 18: 500-505.
15. Dutta P, Mitra U, Saha DR, Niyogi SK, Manna B, Bhattacharya SK. Mucoid presentation of acute enterocolitis in children: hospital based case-control study. Acta Paediatr 1999; 88: 822-826.
16. Ceyhan M, Akan O, Kanra G, Ecevit Z, Seçmeer G, Berkman E. Changing patterns of the prevalence of different Shigella species and their antibiotic susceptibilities in Ankara, Turkey. J Diarrhoeal Dis Res 1996; 14: 187-189.
17. Yurdakok K, Sahin N, Ozmert E, Berkman E. Shigella gastroenteritis: clinical and epidemiological aspects, and antibiotic susceptibility. Acta Paediatr Jpn 1997; 39: 681-684.
18. Ebrahim GJ. Shigellosis. J Trop Pediatr 1991; 27: 98-99.
19. Lopez EL, Prado-Jimenez V, O'Ryan-Gallardo M, Contrini MM. Shigella and Shiga toxin-producing Escherichia coli causing bloody diarrhea in Latin America. Infect Dis Clin North Am 2000; 14: 41-65.
20. Finkelstein Y, Moran O, Avitzur Y, et al. Clinical dysentery in hospitalized children. Infection 2002; 30: 132-135.
21. Borgnolo G, Barbone F, Scornavacca G, Franco D, Vinci A, Iuculano F. Case-control study of Salmonella gastrointestinal infection in Italian children. Acta Paediatr 1996; 85: 804-808.
22. Uysal G, Dogru U, Aysev D, Karabiber N. Campylobacter jejuni gastroenteritis in Turkish children. Infection 1997; 25: 159-162.
23. Doganci L, Tanyuksel M, Gun H. Overdiagnosis of intestinal amoebosis in Turkey. Lancet 1997; 350: 670.
24. Ries AA, Wells JG, Olivola D, et al. Epidemic Shigella dysenteriae type 1 in Burundi: panresistance and implications for prevention. J Infect Dis 1994; 169: 1035-1041.
25. Chopra M, Wilkinson D, Stirling S. Epidemic shigella dysentery in children in northern KwaZulu-Natal. S Afr Med J 1997; 87: 48-51.
26. Bhandari N, Bhan MK, Sazawal S. Mortality associated with acute watery diarrhea, dysentery and persistent diarrhea in rural North India. Acta Paediatr 1992; 81 (Suppl): 3-6.
27. Kavaliotis J, Karyda S, Konstantoula T, Kansouzidou A, Tsagaropoulou H. Shigellosis of childhood in northern Greece: epidemiological, clinical and laboratory data of hospitalized patients during the period 1971-96. Scand J Infect Dis 2000; 32: 207-211.
28. Nathoo KJ, Porteous JE, Siziya S, Wellington M, Mason E. Predictors of mortality in children hospitalized with dysentery in Harare, Zimbabwe. Cent Afr J Med 1998; 44: 272-276.
29. Taylor DN, Echeverria P, Pal T, et al. The role of Shigella spp., enteroinvasive Escherichia coli, and other enteropathogens as causes of childhood dysentery in Thailand. J Infect Dis 1986; 153: 1132-1138.