DIARRHEA AMONG CHILDREN ADMITTED TO A PRIVATE TERTIARY-CARE HOSPITAL, BANGKOK, THAILAND: A CASE SERIES

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Abstract. We report here a case series of pediatric diarrhea cases admitted to a private tertiary-care hospital in Bangkok, Thailand. Retrospective data were collected from computerized medical records of 2,001 children with diarrhea (80.9% Thai), ages birth to 14 years, admitted to our facility during 2000-2005. The most common symptom leading to admission was vomiting (34.6%), while the most common sign was dehydration (63.6%). The largest proportion was comprised of toddlers (45.4%), followed by infants (24.2%). Of the total 2,564 admissions, 1,874 (73.1%) stool samples were collected and examined for red blood cells (RBC) and white blood cells (WBC); 57.1% and 70.6% were negative for RBC and WBC, respectively. Of the 1,878 blood specimens collected for electrolytes, 21.6% show acidosis. Of 1,793 stool specimens collected, the majority revealed normal flora (72.9%). Enteropathogenic *Escherichia coli* (EPEC) were seen in 10.8%. *Campylobacter jejuni* was found in only 2.9% of specimens, while of 1,065 specimens tested for rotavirus antigen, 23.9% were positive. In addition to bacterial cultures and their anti-microbial sensitivities, factors associated with rotavirus infection, *C. jejuni*, and metabolic acidosis, were also explored in this study. Rotavirus infections were more likely to be associated with children older than toddlers (3-14 years old), being admitted within the first day of the symptoms,those who were more acidotic, and was more common in the first 3 months of each year. Our data were little different from community-acquired infections reported among the general population.

INTRODUCTION

Diarrheal diseases constitute a critical, global, public-health problem, being a major cause of illness and death among infants and young children in developing countries. The incidence of diarrhea in Thailand has increased markedly in recent years, where about one million cases annually have been reported in recent years (Center of Epidemiological Information, 2007) despite significant improvements in water and sanitation coverage. Of those reported, nearly half were children (Center of Epidemiological Information, 2007). Although there have been several reports on diarrhea of different etiologies and populations in Thailand (Pancharoen *et al,* 2004; Jiraphongsa *et al,* 2005; Lee *et al,* 2005; Prohmmo *et al,* 2006) there has been no report from the private sector, where the healthcare-seeking characteristics of patients may differ from the general Thai population. We sought to document children diagnosed with diarrhea admitted to our hospital's in-patient facility during 2000-2005, and to describe the clinical features. Because severe diarrhea and metabolic acidosis are correlated, we explored factors associated with metabolic acidosis in this dataset. We also explored factors asso-

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ciated with rotavirus and *Campylobacter jejuni* infections.

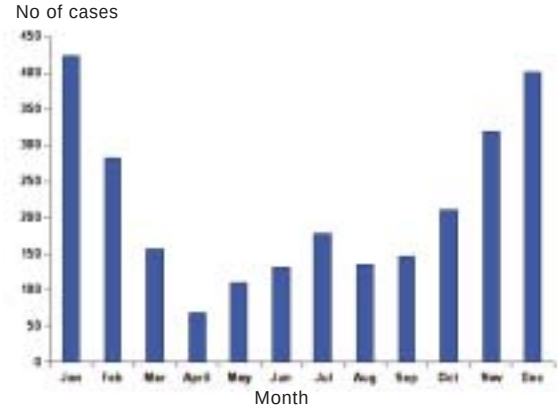
MATERIALS AND METHODS

Bumrungrad International Hospital is a private tertiary-care hospital in Bangkok, Thailand. It has 554 acute care beds and serves over a million patients annually; over 40% of its patients are non-Thais. This retrospective study used data abstracted by authorized persons using computerized hospital records (Hospital 2000 Software, Global Care Solutions-Asia Pacific, Bangkok, Thailand). Inclusion criteria were: the medical records of all children ages birth to14 years who attended our facility during 2000-2005, and whose diarrhea was categorized by the International Classification of Diseases, 10th revision (ICD-10). Medical records of patients diagnosed with other enteric diseases not compatible with severe diarrhea were excluded. Study variables included demographics, symptoms, signs, laboratory investigations, imaging, therapy, and clinical outcomes. We defined metabolic acidosis in children as having a serum bicarbonate of 15 mmol/l or lower. Rotavirus antigen was determined by the Rotalex® test (Orion Diagnostica, Espoo, Finland). The study was approved by the Bumrungrad International Hospital Institutional Review Board. Data were analyzed using Stata/SE 9.2 for Windows (StataCorp LP, College Station, TX, USA). Descriptive statistics were used for analysis and statistical significance was set at $\alpha = 0.05$. Unconditional binary logistic regression (Hosmer and Lemeshow, 2000) was used to analyze factors associating with metabolic acidosis and rotavirus infection.

RESULTS

General description

From January 2000 to December 2005, 2,001 children were diagnosed with diarrhea needing admission to our in-patient facility, totaling 2,564 admissions (median number of admissions: 1; range 1-9). Of these children, 44.9% were females. The patients' mean age (±SD) was 2.6 ± 2.4 (range: 3 days-13.7 years). The largest proportion was comprised of toddlers (1-3 years old, 45.4%), followed by infants (birth to one year old, 24.2%), and others (30.4%). The median time for symptoms before admission was 1 day (range: $^1/_2$ day to 15 days), and 65.1% came within one day of experiencing symptoms. Most of the cases were admitted between November and February (Poisson mean = 42.7/month, 95% confidence interval 39.1-46.6/month, Fig 1). The majority of these patients (80.9%) were Thai nationals, 5.0% were Japanese, 2.7% were Americans, and 11.4% were others. The median length of stay was 2 days (range 1-15 days).



Poisson means = 42.7/month, 95% confidence intervals 39.1-46.6/month

Fig 1–Total monthly admissions of diarrheal cases Bumrungrad International Hospital, 2000-2005.

About one-third (34.6%) had vomiting as their chief complaint, 33.5% had loose stool, 23.9% had fever (body temperature ≥ 37.8ºC), and 4.1% had other complaints. Among those with fever, the mean temperature (±SD) was 38.5 ± 0.6ºC (range: 37.8-41.0ºC). The most common sign leading to admission was

dehydration (63.6%), followed by various other signs.

Of the 2,564 admissions, 1,874 (73.1%) stool samples were examined for red blood cells; 57.1% were negative, 33.7% had 1-5 red blood cells/high power field (RBC/HPF), and the remainder (9.2%) had higher counts. Stool examination for white blood cells (WBC) was negative in 70.6%, 25.0% had 1-5 WBC/HPF, and the rest (4.4%) had higher counts. Stool occult blood was negative in 45.8% of cases, 27.1% had trace results, 3.5% had 4+ test results, and the remainder (23.6%) had in-between positive results.

On complete blood count (n = 2,454) and electrolytes (n = 1,878), 53.8% had a white-blood-cell count > 10 x $10^3/\mu l$, 22.4% had a serum sodium < 135 mmol/l, 1.0% had a serum sodium > 145 mmol/l; 3.5% had a serum potassium < 3.5 mmol/l, and 21.6% had a serum bicarbonate of 15 mmol/l or lower.

Of the admissions, 11 (1.7%) were associated with surgical conditions, such as intussusception. Of the total 2,564 admissions, 2,529 (98.6%) were discharged with improvement, those who did not improve were those who underwent surgical procedures, such as appendectomy or endoscopy.

Bacterial cultures and sensitivities

One thousand seven hundred and ninety-three stool specimens were collected for bacterial culture, of which 1,497 (83.5%) were positive for oragnisms. The majority grew out normal flora (72.9%), 10.8% grew out enteropathogenic *Escherichia coli* (EPEC), *Salmonella* spp (group B) was found in 5.3%, *Salmonella* spp (group C) was found in 4.2%, *Campylobacter jejuni* in 2.9%, *Salmonella* spp (group D) in 1.1%, and others which included a small number of *Vibrio parahaemolyticus* and *Shigella* spp (Table 1). One thousand sixty-five stool specimens were tested for rotavirus antigen, of which 23.9% were positive. Of 579 blood samples sent for hemoculture, nearly all (97.9%) were negative; the tiny number that were positive (12 samples) had a variety of different bacteria.

Table 2 shows the proportions of sensitivities to commonly used antimicrobials for the bacterial organisms (EPEC, *Salmonella* spp groups B, C, D, and *C. jejuni*). All (except *C. jejuni*) had *in vitro* sensitivity to amikacin. More than 83% of EPEC were sensitive to ceftriaxone, cipro-floxacin, or gentamicin; while 90.8% were resistant to the extended-spectrum β-lactamases (ESBL).

Table 1
Bacterial stool cultures in admitted pediatric diarrheal patients, Bumrungrad International Hospital, Bangkok, Thailand.

Species	Frequency (%)
Normal flora	1,091 (72.9)
Enteropathogenic *Escherichia coli* (EPEC) only	161 (10.8)
Salmonella spp (group B) only	79 (5.3)
Salmonella spp (group C) only	63 (4.2)
Campylobacter jejuni only	43 (2.9)
Salmonella spp (group D) only	16 (1.1)
Others and/or their combinations[a]	44 (2.8)
	1,497 (100.0)

[a]Including specimens positive for *Vibrio parahaemolyticus* (6), *Shigella sonnei* (6), and one each for *Shigella boydii*, *Shigella dysenteriae*, and *Shigella flexneri*.

Table 2
Culture and sensitivity results of commonly grown bacteria, admitted pediatric diarrheal patients, Bumrungrad International Hospital, Bangkok, Thailand.

Antimicrobial	No. of samples	Sensitive	Intermediate response	Resistant
a) Enteropathogenic *Escherichia coli* (EPEC)				
Amikacin	191	100.0	0.0	0.0
Amoxicillin/clavulanate	191	58.1	67.1	21.5
Ceftriaxone	191	87.4	2.3	11.5
Ciprofloxacin	191	83.2	1.2	16.2
Gentamicin	190	83.2	1.2	16.3
Trimethoprim	191	52.4	0.0	47.6
ESBL[a]	153	9.2	0.0	90.8
b) *Salmonella* spp group B				
Amikacin	93	100.0	0.0	0.0
Amoxicillin/clavulanate	93	59.1	33.8	19.4
Ceftriaxone	92	98.9	0.0	1.1
Ciprofloxacin	93	98.9	0.0	1.1
Gentamicin	93	64.5	9.3	29.0
Trimethoprim	93	72.0	0.0	28.0
c) *Salmonella* spp group C				
Amikacin	73	100.0	0.0	0.0
Amoxicillin/clavulanate	73	80.8	7.4	11.0
Ceftriaxone	73	98.6	1.0	0.0
Ciprofloxacin	73	100.0	0.0	0.0
Gentamicin	73	78.1	14.1	6.8
Trimethoprim	73	91.8	0.0	8.2
d) *Salmonella* spp group D				
Amikacin	19	100.0	0.0	0.0
Amoxicillin/clavulanate	19	68.4	10.5	21.1
Ceftriaxone	19	100.0	0.0	0.0
Ciprofloxacin	19	100.0	0.0	0.0
Gentamicin	19	79.0	21.0	0.0
Trimethoprim	19	52.6	0.0	47.4
e) *Campylobacter jejuni*				
Amoxicillin/clavulanate	43	97.7	0.0	2.3
Ceftriaxone	19	31.6	57.9	10.5
Ciprofloxacin	43	7.0	9.3	83.7
Erythromycin	38	97.4	2.6	0.0
Gentamicin	43	97.7	0.0	2.3
Trimethoprim	43	2.3	0.0	97.7

[a]Extended spectrum β-lactamases

Most of the *Salmonella* spp group B specimens were sensitive (98.9%) to ceftriaxone and ciprofloxacin; similar patterns were observed for *Salmonella* spp group C. Most *Salmonella* spp group B were sensitive to ceftriaxone and ciprofloxacin. Most *C. jejuni* were sensitive to amoxicillin/clavulanate, erythromycin, and gentamicin (> 97%).

Table 3
Means (± SD) comparisons of selected variables between diarrheal patients who tested rotavirus-positive.

Variable	Rotavirus test results		p-value
	Positive	Negative	
Age (year, *n*)	2.6 ± 1.9 (254)	2.2 ± 1.8 (811)	<0.001[a]
White blood cells (10 x $10^3/\mu l$)	1.129 ± 0.413 (241)	1.113 ± 0.472 (787)	0.961[b]
Serum sodium (mmol/l)	137.3 ± 3.5 (211)	136.7 ± 3.6 (637)	0.044[a]
Serum potassium (mmol/l)	4.3 ± 0.46 (211)	4.3 ± 0.49 (637)	0.559[a]
Serum bicarbonate (mmol/l)	17.1 ± 3.4 (212)	17.8 ± 3.5 (640)	0.013[a]
Length of stay (days)	2.9 ± 1.3 (254)	2.7 ± 1.7 (811)	0.097[b]

[a]*t*-test with equal variances
[b]*t*-test with unequal variances

Table 4
Multiple logistic regression analysis of factors associated with rotavirus infection[a].

Variables	Adjusted odds ratio (OR)	95% confidence interval (95% CI)	p-value
Sex			
Female	1.0[b]		
Male	0.8	0.6-1.2	0.26
Age			
Others	1.0[b]		
Infant and toddler	0.5	0.4-0.7	< 0.001
Time prior to admission			
≤ 1 day	1.0[b]		
1 -3 days	0.7	0.5-1.1	0.135
> 3 days	0.5	0.3-0.9	0.042
Acidosis			
No	1.0[b]		
Yes	1.6	1.1-2.3	0.009
Year's quarter			
First	1.0[b]		
Second	0.2	0.1-0.5	< 0.001
Third	0.1	0.05-0.4	< 0.001
Fourth	0.3	0.2-0.4	< 0.001

[a]Hosmer and Lemeshow goodness of fit p = 0.272
[b]Referent

Exploration of factors associated with either rotavirus or *C. jejuni* infections

Our series found 254/1,065 children (23.9%) tested positive for rotavirus antigen. Of these, 26.0% of females (114/438) and 22.3% of males (140/627) tested positive but the difference was not significantly different (χ^2-test p-value = 0.163). Of those without

Table 5
Multiple logistic regression analysis of factors associated with *C. jejuni* infection[a].

Variables	Adjusted odds ratio (OR)	95% confidence interval (95% CI)	p-value
Sex			
Female	1.0[b]		
Male	1.1	0.5-2.2	0.84
Age			
Others	1.0[b]		
Toddler and older (3-14 years old)	3.3	1.2-8.7	0.02
Stool white blood cells			
Negative	1.0[b]		
1-5/HPF	3.7	1.1-12.2	0.03
> 5/HPF	13.1	3.7-46.0	< 0.01
Stool red blood cells			
Negative	1.0[b]		
1-5/HPF	2.8	1.1-6.8	0.03
> 5/HPF	5.0	1.7-15.4	< 0.01

[a]Hosmer and Lemeshow goodness-of-fit p = 0.703
[b]Referent

fever, 24.0% tested positive for rotavirus, and for those with fever, 23.4% were positive for rotavirus (χ^2-test p-value = 0.842). Those with rotavirus infection were more likely to be brought for admission within one day of onset of symptoms (χ^2-test p-value = 0.001). Children with rotavirus-positive stools were on average six months older (p < 0.001), had slightly higher serum sodium levels (0.6 mmol/l, p = 0.044) and lower serum bicarbonate (0.7 mmol/l, p = 0.013) levels than those with negative stools. There were no significantly differences in white-blood-cell counts, serum potassium levels or lengths of hospital stay when those with and without rotavirus infection were compared (p > 0.09 for each variable, Table 3). Of those who tested rotavirus positive, 26.2% had red blood cells in their stools, and 44.9% had white blood cells in their stools. Logistic regression analysis showed that those with rotavirus infection were two times less likely to be toddlers or infants (odds ratio-OR, 0.5), were admitted within the first day of illness, were 1.6 times more likely to be acidotic, and were more likely to be admitted more frequently during the first 3 months of the year (Table 4).

For *C. jejuni* infection, infected patients were more likely to have higher red- and white-cell counts in their stools, and toddlers and older children were more likely to be at risk for admission with this infection (Table 5).

The factors associated with metabolic acidosis were explored using multiple logistic regression analysis; the results are shown in Table 6. Infants and toddlers were about 1.8 times more likely to have metabolic acidosis than children of other ages. Two organisms were associated with metabolic acidosis, those with salmonella infection were about 2.1 times (1/0.47) less likely to have acidosis, and those with rotavirus antigen were at about 1.6 times more likely. Those who came to the hospital within the first three days of this illness were about 1.8 times more likely to have metabolic acidosis than those who came later.

Table 6
Multiple logistic regression analysis of factors associated with metabolic acidosis[a].

Variables	Adjusted odds ratio (OR)	95% confidence interval (95% CI)	p-value
Age			
Others	1.0[b]		
Infant and toddler	1.8	1.2-2.9	0.01
Presence of any salmonella infection			
No	1.0[b]		
Yes	0.5	0.3-0.9	0.03
Presence of rotavirus antigen			
No	1.0[b]		
Yes	1.6	1.1-2.5	0.03
Time prior to admission (days)			
< 1 day	1.0[b]		
1-3 days	1.8	1.2-2.6	0.01
> 3 days	1.7	0.9-3.1	0.09

[a]Hosmer and Lemeshow goodness-of-fit p = 0.487
[b]Referent

DISCUSSION

This study provides information regarding pediatric diarrhea patients at a private tertiary-care hospital in Bangkok. The most common pathogen isolated, EPEC, had an incidence similar to that found in both developed and developing countries (Ahmetagic *et al*, 2003; Diniz-Santos *et al,* 2005; Klein *et al,* 2006; Vernacchio *et al,* 2006; Vu *et al,* 2006). This reflects the fact that EPEC remains a leading cause of bacterial diarrhea in developing countries, although its frequency is decreasing in industrialized countries (Nataro and Kaper, 1998). Rotavirus antigen was observed with an incidence differing from some studies (Ahmetagic *et al*, 2003; Diniz-Santos *et al,* 2005; Klein *et al,* 2006; Vernacchio *et al,* 2006; Vu *et al,* 2006). Our rotavirus-infected patients were more likely to be older than toddlers, more likely to be acidotic, and more likely to be admitted on the first day of symptoms reflecting a greater severity in those cases. An explanation for the differences in degree of severity may be the variations in the infecting serotypes (Mota-Hernández *et al* 2003), which were not collected in our study. The seasonal variation was similar to that observed in nearby countries, *ie*, the cool and dry seasons (Moe *et al* 2005; Nguyen *et al,* 2007). The presence of rotavirus as a factor associated with acidosis may lead to a more systematic surveillance of the organism in the hospital (Vaccine Assessment and Monitoring Team, 2002). Another important fact is that rotavirus was not ordered in all patients. Physicians may have been more likely to order stool for rotavirus in sicker patients and therefore will find rotavirus more often in sicker patients making it appear that rotavirus is associated with more pathology. This could be corrected for only by ordering stool for rotavirus in all patients which is not practical. It is important to note that the data presented here were obtained during the period when rotavirus vaccine, probably the most effective preventive method to date after good hygiene and sanitation, was not yet licensed for use in Thailand.

Our study also documents the antimicrobial sensitivity of various pathogens detected from stool cultures; the results are mostly comparable with patterns observed in other regions (Gales *et al,* 2002; Streit *et al,* 2006). It is, however, important to note that these findings may not generally reflect the patterns in the population, due to the tertiary-care referral setting.

Our laboratory facilities detected *C. jejuni* in at least 2.9% of stool samples. Although common manifestations of patients with laboratory-confirmed infections with *C. jejuni* (a small subset of all cases) included diarrhea, fever, and abdominal cramping (Altekruse *et al*, 1999), multivariate analysis showed a high correlation with increased red and white blood cells in the stools, and were more likely to be toddlers or older children. This finding is consistent with a report in the United States. (Blaser *et al,* 1983).

Although diarrhea can lead to mortality, especially among young children, fortunately there were no mortalities in this series. This is perhaps because most of our patients were admitted very early in the course of illness (median time of symptoms = 1 day).

In summary, this report describes a case series of pediatric patients with diarrhea hospitalized at a private tertiary-care setting in Bangkok. The data were little different from community-acquired infections among the general population (Ahmetagic *et al*, 2003; Diniz-Santos *et al*, 2005; Klein *et al*, 2006; Vernacchio *et al*, 2006; Vu *et al*, 2006). This may serve as a baseline for future studies of this important public health problem.

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