Factors associated with acute diarrhoea in children in Dhahira, Oman: a hospital-based study

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مسببات الإسهال الحاد لدى الأطفال في الظهيرة، بسلطنة عُمان: دراسة في مستشفى

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الخلاصة: لتوضيح الجراثيم المسببة للإسهال لدى الأطفال في الظهيرة، أجرى الباحثون هذه الدراسة على 856 طفلاً ممن تقل أعمارهم عن 12 عاماً أدخِلوا إلى مستشفى إبري المرجعي الإقليمي بسبب إصابتهم بالإسهال في ما بين 2000 و2002. وقد كان متوسط العمر 2.4 عاماً (الانحراف المعياري 2.3) وكان معظمهم (92.9٪) ممن تقل أعمارهم عن 5 سنوات. وقد اكتُشفت المسببات الجرثومية في 15.2٪ من الحالات، وكان 10.6٪ منها ناجماً عن الشيغيلا و2.1٪ منها ناجماً عن السالمونيلا، وكان النمط المصلي الخنزيري sonnei هو أكثر الأنماط المصلية للشيغيلات شيوعاً، وترافقت العدوى بالسالمونيلات بمعدَّل يُعْتَدُّ به إحصائياً مع المغص، في حين ترافقت العدوى بالشيغيلات بالحمى والبراز المدمَّى وبالمغص. وقد وصفت المضادات الحيوية في 36.2٪ من الحالات وكانت المقاومة للمضادات الحيوية الشائعة منخفضة.

ABSTRACT To elucidate the bacterial etiology of childhood diarrhoea in Dhahira, 856 children < 12 years admitted for diarrhoea to Ibri Regional Referral Hospital from 2000 to 2002 were studied. The mean age was 2.4 (SD 2.3) years; the majority (92.9%) were < 5 years. Bacterial etiology was found in 15.2% of cases; 10.6% due to ***Shigella*** and 2.1% to ***Salmonella***. ***Sh. sonnei*** was the commonest ***Shigella*** serogroup isolated. ***Salmonella*** infection was significantly associated with cramps, while ***Shigella*** infection was associated with fever, bloody stools and cramps. Antibiotics were prescribed in 36.2% of cases and the resistance to the common antibiotics tested was low.

Facteurs associés à la diarrhée aiguë chez les enfants de la province de Dhahira (Oman) : étude en milieu hospitalier

RÉSUMÉ Afin d'élucider l'étiologie bactérienne de la diarrhée chez l'enfant dans la Dhahira, 856 enfants de moins de 12 ans admis pour diarrhée à l'hôpital de recours régional d'Ibri entre 2000 et 2002 ont fait l'objet d'une étude. L'âge moyen des enfants était de 2,4 ans (écart type 2,3) ; la majorité des enfants (92,9 %) avaient moins de 5 ans. L'étiologie bactérienne a été établie dans 15,2 % des cas ; 10,6 % étaient dus à ***Shigella*** et 2,1 % à ***Salmonella***. Parmi les sérogroupes de ***Shigella*** isolés, ***Sh. sonnei*** était le plus courant. L'infection à ***Salmonella*** était associée de façon significative à des crampes, alors que l'infection à ***Shigella*** était associée à de la fièvre, des selles sanglantes et des crampes. Des antibiotiques ont été prescrits dans 36,2 % des cas et la résistance aux antibiotiques courants testés était faible.

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Received: 24/10/05; accepted: 26/03/06

Introduction

Diarrhoea is one of the leading causes of mortality and morbidity in developing countries. Annually 1.5 billion diarrhoea episodes and 4 million deaths caused by this disease occur in children under 5 years of age [*1*]. Diarrhoea can be caused by wide range of bacteria (e.g. *Shigella* species, *Salmonella* species, *Escherichia coli* and *Vibrio cholerae)*, enteroparasites (e.g. *Giardia* species and *Entamoeba histolytica*) and viruses (rotavirus, adenovirus and Norwalk virus) [*1*].

There has been a marked decline in diarrhoea-related mortality as well as morbidity in Oman, ever since the introduction of the control of diarrhoeal diseases (CDD) programme in 1985. The CDD programme is now incorporated in the integrated management of childhood illnesses (IMCI) programme. The main aim of the CDD programme is to reduce the morbidity and mortality due to diarrhoea especially among children under 5 years. In Oman, the morbidity and mortality from diarrhoeal diseases decreased from 745 episodes/1000 children < 5 years and 12 deaths in 1991 to 314 episodes/1000 children < 5 years and zero deaths in 1999. The CDD programme as well as general socioeconomic development, improvement in environmental sanitation, safe water and health education have contributed to this decrease [*2*]. In Dhahira region the incidence of diarrhoeal diseases in the year 2000 was 265 episodes/1000 children < 5 years and there were no deaths reported with diarrhoea as the primary cause [*3*].

The annual incidence and the etiologic profile of diarrhoea in different populations may vary with several risk factors. In industrialized countries, rotavirus is the predominant cause, while bacterial causes are commonly found in children from developing countries [*4*]. Studies on the etiologic profile of diarrhoea cases are lacking in Oman and Dhahira region. To further reduce the incidence of diarrhoea among children, epidemiological information on cause-specific morbidity and mortality is necessary in order to devise appropriate intervention measures. Therefore, in the year 2000 diarrhoeal disease surveillance was established in sentinel sites (regional hospitals) in Oman including Dhahira region to study the morbidity pattern of all admitted cases of diarrhoea and to elucidate the bacterial enteropathogens responsible for diarrhoea among hospitalized children. This study was carried out as a part of this sentinel surveillance and analyses data obtained over 2 years of surveillance.

Methods

This was a prospective hospital-based study of all patients under the age of 12 years admitted for diarrhoea to the paediatric wards of Ibri Regional Referral Hospital, Dhahira from 1 November 2000 to 31 October 2002. Dhahira region has 207 015 inhabitants. Ibri Regional Referral Hospital is the only secondary hospital in Dhahira and serves 68.8% of the population of the region. Diarrhoea was defined as 3 or more watery or loose stools in a 24-hour period prior to the hospital admission.

The data about the patients and their illness were recorded during hospitalization on a proforma pretested in a pilot study. Personal details (name, age, sex, nationality and residence), clinical history, presenting symptoms and laboratory details were documented in the proforma by the attending staff of the paediatric department (doctor and nurse). A doctor and nurse were the focal points to collect the data and supervise the surveillance activities in

the hospital. The regional epidemiologist coordinated the implementation and data management of the surveillance. A regional workshop was conducted prior to the study to explain the study to the paediatric staff and to standardize the data collection and procedures.

Stool samples were collected in a wide-necked sterile container before antibiotic administration and bacterial culture was carried out using routine standard microbiology laboratory methods. The specimens were subjected to microscopic examination in saline and iodine preparation. Motility tests and Gram stained smears were done in cases where cholera was suspected. Faeces were cultured directly on MacConkey agar, salmonella–shigella agar (SSA) and thiosulfate citrate bile sucrose (TCBS) agar. After overnight incubation at 37 °C the plates were observed for *Salmonella* and *Shigella* colonies. At the same time, approximately 1–2 g of stool sample was inoculated in selenite F broth and incubated overnight. Next day, thin subcultures were done on MacConkey and SSA for suspected *Salmonella* and *Shigella* colonies.

Suspected cholera samples were inoculated on alkaline peptone water and incubated for 6–8 hours and then further inoculated onto TCBS selective media and incubated for 18–24 hours at 37 °C. The suspected colonies were subcultured in nutrient/blood agar and incubated overnight at 37 °C. Presumptive *Vibrio cholerae* identification was based on positive oxidase test and reading from the analytical profile index (API) 20 E system (bioMérieux, Marcy l'Etoile, France). Grouping was done by using polyvalent antiserum (MAST GROUP, United Kingdom) by slide agglutination method. All the cases positive for bacterial infection were sent to the Central Public Health Laboratory, Muscat for reconfirmation and serotyping.

Antibiotic sensitivity of all the positive cultures was done by disc diffusion (Kirby–Bauer) method using diagnostic sensitivity test agar. The following antibiotic discs were tested: ampicillin, cefotaxime, ceftriaxone, chloramphenicol, ciprofloxacin, nalidixic acid, tetracycline and trimethoprim/sulfamethoxazole. These are the antibiotics commonly prescribed for childhood diarrhoea according to hospital policy.

The level of dehydration was recorded by the paediatrician according to the child's presenting signs. Mild to moderate dehydration was recorded when the child had 2 of the following signs: restlessness and irritability, sunken eyes, thirst and eager drinking, and slow return of skin pinch. Severe dehydration was recorded when the child had 2 of the following signs: lethargy or unconsciousness, sunken eyes, inability to drink or drinking poorly, and very slow return of skin pinch [*5*]. Associated illness, such as malnutrition and acute respiratory illness, was also noted by the paediatrician. Prior antibiotic administration for the present episode was recorded by consulting the referral records and also by asking the mother.

The data were computed and analysed by using *SPSS*, version 9. Descriptive statistics were expressed as proportion, and mean and standard deviation (SD). Proportions were compared using the chi-squared test. Adjusted odds ratios (OR) with 95% confidence interval (CI) (regression analysis) were calculated to compare bacterial isolation and various characteristics of the episode. The dependent variable was bacterial positivity. Independent variables used in the regression analysis were age, sex, level of dehydration, number of stools per day, blood in stool, any associated illness and prior antibiotic administration. For statistical significance, a P-value < 0.05

was considered significant. Assuming 50% prevalence, the sample size required to obtain a representative sample with 95% CI and 5% margin of error was 400.

Results

A total of 880 diarrhoea cases were recorded in the pretested proforma during the study period. Complete data were available for 856 cases (97.2%) and these were included in the analysis. The majority of the children (830/856, 97.0%) were Omanis and 53% were male (male:female ratio = 1.1:1). The peak incidence of diarrhoea was during November–January in both study years. There were no deaths among the study subjects. The majority (92.9%) of the children were < 5 years of age and of these, 55% were under 1 year; the mean age was 2.4 (SD 2.3) years. The mean number of stools per day per child was 6.8 (SD 3.3). Table 1 shows the frequency of different characteristics of the diarrhoea episodes among the study subjects. The majority (97%) of the children had mild to moderate dehydration.

Table 1 **Distribution of various characteristics of diarrhoea among the study subjects**

Characteristics	No. of children (*n* = 856)	%
Onset of symptoms		
Acute	787	91.9
Chronic	69	8.1
Presenting symptoms[a]		
Watery stool	830	97.0
Vomiting	708	82.7
Fever	635	74.2
Blood and mucus	150	17.5
Abdominal cramps	239	27.9
Number of stools per day		
1–5	328	38.3
6–9	361	42.2
10–19	151	17.6
20–30	16	1.9
Associated illness	96	11.2
Respiratory illness (***n*** = 96)	70	72.9
Others[b] (***n*** = 96)	26	27.1
Antibiotics prescribed	310	36.2
Ampicillin (***n*** = 310)	208	67.1
Nalidixic acid (***n*** = 310)	94	30.3
Chloramphenicol (***n*** = 310)	8	2.6

[a]Numbers and percentages do sum to 856 and 100% as the patients could present with multiple symptoms.
[b]Protein–energy malnutrition, sickle-cell disease, glucose-6-phosphate dehydrogenase deficiency, impetigo and seizures.

The bacterial pathogens isolated are shown in Table 2. Overall, a potential pathogen was found in 15.2% of cases. *Shigella* species was the commonest bacterial pathogen, found in 10.6% of cultures, identified in 70.0% of cases where bacteria were isolated.

Prior antibiotics were given in 11.2% of cases and antibiotics were prescribed in 36.2% of the study patients upon admission. Only 3 antibiotics were prescribed in the treatment of diarrhoea in this study: ampicillin, nalidixic acid and chloramphenicol (Table 1); ampicillin was the most commonly prescribed antibiotic, prescribed in 67.1% of cases where antibiotics were given.

Approximately 10% of the *Salmonella* isolates were resistant to ampicillin and 7.1% were resistant to nalidixic acid and trimethoprim/sulfamethoxazole. With the *Shigella* isolates, 20% were resistant to ampicillin, nalidixic acid and trimethoprim/sulfamethoxazole. Both organisms were sensitive to cefotaxime, ceftriaxone, ciprofloxacin, chloramphenicol and tetracycline.

Bacterial infection was more commonly (although not statistically significantly) associated with age 3–5 years, being female, and having an associated illness. However, it was significantly associated with bloody stools (adjusted OR = 3.0; 95% CI: 1.6–5.7) (Table 3). *Salmonella* infection was sig-

Table 2 **Prevalence of bacterial pathogens among the study subjects**

Culture result	No. (*n* = 856)	%	95% CI
No bacteria isolated	726	84.8	82.2–87.0
Bacteria isolated	130	15.2	12.9–17.7
Shigella sonnei	73	8.5	6.8–10.6
Sh. flexneri	18	2.1	1.3–3.3
Salmonella[a]	18	2.1	1.3–3.3
Vibrio cholerae	2	0.2	–
Monganella	6	0.7	–
Enteropathogenic Escherichia coli	14	1.6	–

[a]***Salmonella serogroups were: B (4 cases), C (2), D (4), E (2). In 6 cases the serogroup was not evident.***
CI = confidence interval.

nificantly associated with cramps and *Shigella* infection with fever, bloody stools and cramps ($P < 0.05$).

Bloody diarrhoea was significantly associated with age > 5 years compared to age < 5 years ($\chi^2 = 15.7$, $P < 0.05$) but was not significantly associated with sex ($\chi^2 = 0.21$, $P = 0.3$) and number of stools per day ($\chi^2 = 3.3$, $P = 0.1$). *Salmonella* infection was commoner among children > 5 years compared to those < 5 years, however this difference was not significantly significant ($\chi^2 = 2.8$, $P = 0.09$). *Shigella* infection was significantly commoner in children > 5 years ($\chi^2 = 6.4$, $P = 0.01$).

Discussion

The prevalence of diarrhoea with a known etiology was 15.2%. The prevalence of bacterial infection in cases of diarrhoea among children in other countries varies between 5.3% and 54% [*6–10*]. Similar to other studies [*10,11*] *Shigell*a species was the commonest pathogen isolated in our study, but other studies reported *Salmonella* species was commoner [*8,9*]. In our sample, enteropathogenic *E. coli* was not frequently associated with diarrhoea; however, it is more important in the epidemiology of diarrhoea in other countries [*11,12*]. *Sh. sonnei* was the predominant serogroup followed by *Sh. flexneri* in our study, which is different from other studies where *Sh. flexneri* was the predominant species followed by *Sh. sonnei* [*10,13,14*].

Approximately 84% of the diarrhoea cases had no bacterial pathogen, suggestive of probable viral origin. Antibiotics were prescribed in 36.2% of cases in our study, which is high when the bacterial positivity was only 15.2%. Most cases of acute gastroenteritis in children are viral, self-limiting and need only supportive treatment. Appropriate fluid and electrolyte therapy, with close attention to nutrition, remains central to treatment. Antibacterial therapy serves as an adjunct to shorten the clinical course, eradicate causative organisms, reduce transmission and prevent invasive complications. Selection of antibacterials to use in acute bacterial gastroenteritis is based on clinical diagnosis of the likely pathogen prior to definitive laboratory results [*15*]. Given that *Shigella* and *Salmonella* species were the predominant organisms responsible for bacterial diarrhoea in our study, school health and diarrhoeal disease control programmes should focus on the prevention and control of these infections in Dhahira region. This can be done through health education regarding general personal hygiene, sanitation and safe water. Further studies are needed to investigate the viral causes of diarrhoea in Dhahira.

In our study bloody diarrhoea was significantly associated with age > 5 years compared to < 5 years and not significantly associated with sex and number of stools per day. Another report found bloody diarrhoea was significantly associated with different age groups ($P < 0.001$) and also sex ($P =$

Table 3 **Bacterial isolation according to characteristics of the patients with the diarrhoea episode**

Characteristic	Bacterial culture result				Adjusted odds ratio	95% CI
	Negative		Positive			
	No.	%	No.	%		
Age group (years)						
< 1	445	94.7	25	5.3	0.2	0.08–0.50
1–3	145	75.9	46	24.1	1.3	0.5–3.2
3–5	84	62.7	50	37.3	2.4	0.9–6.1
> 5[a]	47	77.0	14	23.0		
Sex						
Male	396	87.2	58	12.8	0.5	0.3–1.0
Female[a]	330	82.1	72	17.9		
Level of dehydration						
Mild to moderate	706	84.9	126	15.1	1.4	0.3–8.3
Severe[a]	20	83.3	4	16.7		
Number of stools/day						
1–5	278	84.8	50	15.2	0.7	0.3–1.6
6–9	311	86.1	50	13.9	0.7	0.3–1.6
10–30[a]	136	81.4	31	18.6		
Associated illness						
Yes	74	77.1	22	22.9	1.8	0.8–4.2
No[a]	652	85.8	108	14.2		
Prior antibiotics given						
No	650	85.5	110	14.5	0.4	0.2–1.1
Yes[a]	76	79.2	20	20.8		
Blood in stool						
Yes	98	65.3	52	34.7	3.0	1.6–5.7
No[a]	628	89.0	78	11.0		

[a]Reference group.
CI = confidence interval.

0.02) [*16*]. *Salmonella* infection was not significantly associated with age. However, *Shigella* infection was significantly higher in children older than 5 years compared with those younger than 5 years, which is similar to a study conducted in Brazil, where *Shigella* was the most frequent pathogen isolated from the stools of children between 5 and 15 years old [*11*]. On the other hand our results differ from those of other studies that reported *Shigella* was more commonly associated with younger age groups [*6,14*].

Cramps was significantly associated with *Salmonella* infection while fever, bloody stools, and cramps were associated with *Shigella* infection. This indicates there should be a strong suspicion of bacterial infection if these symptoms are present and that antibiotic treatment may be required. A study in Egypt also showed that blood in stools was significantly associated with *Shigella* infection [*14*].

Antibiotic resistance was low in our study, in contrast to a Yemen study where

more than two-thirds of the *Salmonella* isolates were resistant to nalidixic acid, chloramphenicol, co-trimoxazole, gentamicin and amoxicillin, while 42% were resistant to cefotaxime. Most of the *Shigella* isolates were susceptible to nalidixic acid and cefotaxime, and resistant to the other antibiotics [*12*]. Resistance in our study was probably low because of the controlled antibiotic use in the Ministry of Health in Oman. A surveillance system in the region would be useful to maintain this and monitor the situation in other countries.

Conclusion

This study suggests that *Shigella*, *Salmonella* and enteropathogenic *E. coli* are the most important bacterial pathogens among paediatric diarrhoea cases admitted to hospital in Dhahira region. These pathogens were also found in association with bloody diarrhoea. Diarrhoea in a child < 12 years associated with cramps, fever, and bloody stools strongly suggests bacterial infection. *Shigella*-associated diarrhoea remains relatively common in children in Dhahira and supports the need for additional control measures. While antibiotic resistance was relatively low, such resistance needs monitoring. Studies to determine the cost-effective algorithms for diarrhoea diagnosis and antibiotic treatment are warranted as are studies to determine the etiology of viral, unexplained diarrhoea which is clearly the commonest cause for diarrhoea.

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Planning for IMCI implementation at district level: a capacity-building workshop, Suez, Egypt, 16–19 February 2008

A workshop to build capacity of national IMCI coordinators and district staff in planning for IMCI implementation at district level was conducted in Suez, Egypt, from 16 to 19 February 2008. Technically and financially supported by the WHO Regional Office for the Eastern Mediterranean (EMRO) and conducted in Arabic, the 4-day workshop was an opportunity not only to introduce the newly developed WHO/EMRO *Regional guide on planning for IMCI implementation at district level* to national coordinators from 6 countries (Egypt, Jordan, Morocco, Sudan, Tunisia and Yemen), but also to use it at the same time with 49 staff of 6 districts and with the participation of high-level officials of their respective governorates in Egypt. The outcome of the workshop was one-year plans of action for IMCI implementation developed for each district, including human resources development, health systems support elements and community component.