Acute diarrhea with dehydration is an important health problem in children less than five years of age in developing countries. The Paediatric Department of Mayo Hospital in Lahore, Pakistan is the center for the Control of the Diarrheal Disease Program for the World Health Organization, where enteropathogens causing diarrhea in children have been previously investigated. Shigella is well known for its clinical severity in bacterial dysentery. Dysentery is characterized by blood, pus, and mucus in stools, which indicates coloectal inflammation. These types of symptoms are common to infections by Shigella, Campylobacter, Salmonella, amoeba, and Clostridium difficile. Shigella spp. are a major cause of acute dysentery in children. Most severe infections require treatment with antibiotics, which leads to over use and misuse of many of the drugs. Moreover, knowledge is insufficient in Pakistan regarding the development of resistant strains to antibiotics most frequently used for the treatment of shigellosis. The aim of the present study was to determine the frequency of Shigella in stools of hospitalized children with enterocolitis and the susceptibility of Shigella spp. to three antibiotics: ampicillin, cotrimoxazole and nalidixic acid, which are generally used for the treatment of bacillary dysentery. In addition, the frequency of Campylobacter and Salmonella was also determined.

Statistical analysis. The differences in proportions were tested by the chi-square test with one degree of freedom or Fisher’s exact test, where applicable. Significance levels were chosen at 0.05 level with a two-tailed test.

RESULTS

The isolation rate of Shigella, Campylobacter, and Salmonella in diarrheic children (< 6 years of age) passing blood and mucus in their stools was 31.6%. No child was...

OCCURRENCE AND SUSCEPTIBILITY TO ANTIBIOTICS OF SHIGELLA SPECIES IN STOOLS OF HOSPITALIZED CHILDREN WITH BLOODY DIARRHEA IN PAKISTAN

KAUSAR KHALIL, SHAUKAT R. KHAN, KHADIJA MAZHAR, BERTIL KAISER, AND GUN-BRITT LINDBLOM

Pathology Laboratory, Department of Paediatrics, King Edward Medical College, Lahore, Pakistan; Department of Clinical Bacteriology, Goteborg University, Goteborg, Sweden

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infected with more than one enteropathogen. The frequency of isolation of *Shigella* was high (19.1%) compared with *Campylobacter* (7.9%) and *Salmonella* (4.6%) (Table 1).

*Shigella* was significantly less (P < 0.001) frequently isolated in children less than one year of age (8 of 96) compared with older age groups (21 of 96). Within the age groups, *Campylobacter* was isolated only from the stools of children less than one year of age (12 of 96) and the overall isolation rate was significantly higher (P < 0.001) in this age group compared with *Salmonella* (3 of 96) but was not significantly different (P > 0.05) from the isolation rate of *Shigella* (8 of 96). The seven *Salmonella* isolates were evenly spread in the different age groups with a higher relative frequency in children more than one year of age (Table 1).

Regarding the species distribution of 29 *Shigella* strains, *S. flexneri* (41.5%) was more frequent than *S. dysenteriae* (34.5%), *S. boydii* (17.2%), and *S. sonnei* (6.8%) (Table 2). All *Shigella* were susceptible to nalidixic acid (100%), while only two *S. dysenteriae* (7.0%) were susceptible to cotrimoxazole and one *S. sonnei* (3.5%) was susceptible to ampicillin (Table 2).

**DISCUSSION**

Epidemics caused by *Shigella* were reported in 1968 from Central America and Mexico because of drug-resistant strains of *S. dysenteriae* (World Health Organization 1988, unpublished data) and later on in Asia and Africa (World Health Organization 1988, unpublished data). Since 1968, *S. dysenteriae* 1 epidemics have been recorded in Central America and Mexico (1969–1972), Bangladesh (1972–1978), the Maldives (1982), Burundi (1982–1985), Nepal (1984–1985), India (1984–1986), and Thailand (1985–1986) (World Health Organization 1988, unpublished data). The fury of the epidemics appears to have subsided in most of these areas, but sporadic cases continue to occur and there is no reason to believe that epidemics will not break out again (World Health Organization 1988, unpublished data).

In our study, *Shigella* spp. were a more commonly occurring enteric pathogen than *Campylobacter* spp. and *Salmonella* spp., which was similar to findings in other studies from Africa and Asia.1,7,9 *Shigella flexneri* was the most frequently identified species compared with *S. dysenteriae*, *S. boydii*, and *S. sonnei*. These results are comparable with results of other studies.11–13

<table>
<thead>
<tr>
<th>Age (months)</th>
<th>Shigella</th>
<th>Campylobacter</th>
<th>Salmonella</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–5</td>
<td>35</td>
<td>2</td>
<td>5.7</td>
<td>11.4</td>
</tr>
<tr>
<td>6–11</td>
<td>61</td>
<td>6</td>
<td>9.8</td>
<td>8</td>
</tr>
<tr>
<td>12–17</td>
<td>21</td>
<td>7</td>
<td>33.3</td>
<td>0</td>
</tr>
<tr>
<td>18–23</td>
<td>6</td>
<td>3</td>
<td>50.0</td>
<td>0</td>
</tr>
<tr>
<td>24–35</td>
<td>11</td>
<td>5</td>
<td>45.5</td>
<td>0</td>
</tr>
<tr>
<td>36–47</td>
<td>7</td>
<td>2</td>
<td>28.5</td>
<td>0</td>
</tr>
<tr>
<td>48–59</td>
<td>6</td>
<td>2</td>
<td>33.3</td>
<td>0</td>
</tr>
<tr>
<td>60–72</td>
<td>5</td>
<td>2</td>
<td>40.0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>152</td>
<td>29</td>
<td>19.1</td>
<td>12</td>
</tr>
</tbody>
</table>

The incidence of shigellosis in endemic areas usually peaks during the hot, humid, and rainy season.11,13 Our study included the months of June to September, which have the same climatic conditions, verifying the high incidence of *S. dysenteriae*. This was seen in epidemics in most of the other countries, although the seasonality was less pronounced in Africa.14 Transmission of *Shigella* most commonly occurs by direct person-to-person contact and through food, water, and fomites.15,16 Flies are considered to play an important role in the spread of *Shigella* and *Campylobacter* because of the low infective dose needed to cause diarrhea.17,18 A low infective dose explains why epidemics of shigellosis are hard to control. *Shigella* are excreted in stools in large numbers (107–109/g), but they die off quickly because stools are acidic. There is little information on the survival of *S. dysenteriae* 1 in different environments. *Shigella flexneri* and *S. sonnei* survive in soiled linen for 9–46 days, in water for up to six months, and in various foods for three weeks to six months, usually in decreasing numbers, although initial multiplication was found to occur in milk.17 They survive for longer periods at temperatures below 25°C.

*Shigella* was the most frequently found agent in children more than 12 months of age in our study. Disease caused by *S. dysenteriae* 1 in particular and that caused by other *Shigella* species has a wide spectrum and is more commonly severe in infants who are not breastfed and the malnourished.18–20 In Zaire and Tanzania, infants less than six months of age, particularly when breastfed, were generally spared from *Shigella* dysentery.9 The high degree of protection against severe shigellosis was evident in Bangladesh for breastfed children up to 35 months of age.21

*Campylobacter* was the most commonly identified pathogen in the stools of children less than one year of age in the present study, which was similar to the results of another study.22

In the present study, all *Shigella* strains isolated from children with bloody diarrhea were sensitive to nalidixic acid and rarely susceptible to ampicillin and cotrimoxazole, which is similar to the results of other results.13,23 In earlier studies of *S. dysenteriae* epidemics, strains were found to be resistant to common antimicrobials such as sulfonamides, tetracyclines, and chloramphenicol.23 In addition, resistance to ampicillin and trimethoprim-sulfamethoxazole was present, or appeared to varying degrees, sometimes quite rapidly, following wide use of these drugs.13,24 Resistance to nalidixic acid also appeared after it came into use.24 Resistance to a particular antibiotic might occasionally disappeared when its use was diminished.25

In Pakistan, laboratory support is not readily available and there is no information on the drug resistance pattern of re-
cent isolates for shigellosis. In view of the emergence of strains resistant to available antimicrobials, research aimed at developing new and safe antimicrobials for shigellosis is receiving high priority. Oral gentamicin and quinolone derivatives such as norfloxacin and ciprofloxacin are currently being evaluated.\textsuperscript{26} Norfloxacin is effective in adults with shigellosis but its use has not been approved for use in children, similar to other quinolones, and has been associated with adverse effects on cartilage and bone growth in animals. There is no suitable vaccine for the control of shigellosis and campylobacteriosis, despite many years of interest and research. Community outbreaks of shigellosis end when an appreciable percentage of high-risk hosts develop protective antibodies. If the safety and efficacy of \textit{Shigella} vaccines can be established, their use in high-risk groups may be effective in preventing and controlling morbidity and mortality due to severe diarrhea in children.\textsuperscript{27–29}

In heavily populated areas of Pakistan, similar to other developing countries, the ecosystem contains a high background level of fecal pollution\textsuperscript{30} associated with the transmission of enteric pathogens through water, food, humans, and animals. In the presence of these factors, gastroenteritis remains one of the major causes of disease in the paediatric population of Pakistan. There is increasing resistance of \textit{Shigella} to most of the antibiotics in use. Development and use of new drugs are expensive and have severe limitations in the third world. Simple prophylactic alternatives are therefore required, such as awareness of hygienic child care practices and early promotion of breast feeding.\textsuperscript{14, 30, 31}

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Authors’ addresses: Kausar Khalil, Shaukat R. Khan, and Khadija Mazhar, Department of Paediatrics, King Edward Medical College, Lahore, Pakistan. Bertil Kajser and Gun-Britt Lindblom, Department of Clinical Bacteriology, Goteborg University, Guldhedsgatan 10 A, S-413 46 Goteborg, Sweden.

Reprint requests: Bertil Kajser, Department of Clinical Bacteriology, Goteborg University, Guldhedsgatan 10 A, S-413 46 Goteborg, Sweden.

REFERENCES


