Shifting Prevalence of Major Diarrheal Pathogens in Patients Seeking Hospital Care during Floods in 1998, 2004, and 2007 in Dhaka, Bangladesh

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Abstract. Bangladesh experienced severe flooding and diarrheal epidemics in 2007. We compared flood data from 2007 with 2004 and 1998 for diarrheal patients attending the ICDDR,B hospital in Dhaka. In 2007, *Vibrio cholerae* O1 (33%), rotavirus (12%), and enterotoxigenic *Escherichia coli* (ETEC) (12%) were most prevalent. More severe dehydration was seen in 2007 compared with 2004 and 1998 (*P* < 0.001). In 2007, *V. cholerae* O1 Inaba (52%) and Ogawa (48%) were seen, whereas in 2004 and 1998 it was primarily Inaba and the Ogawa types, respectively (*P* < 0.001). In 2007, 51% of ETEC produced the heat labile toxin (LT) (*P* < 0.001 compared with 2004); 22% expressed the heat stable (ST) (*P* < 0.001), and 27% were ST/LT positive (*P* = 0.231). The CS7 colonization factor (CF) was the most prevalent in 2007 (20% compared with 6% in 2004; *P* = 0.05). Our findings demonstrate alterations in clinical features and phenotypic changes of major bacterial pathogens in the recent Bangladesh flood.

INTRODUCTION

Bangladesh is prone to severe flooding. Floods have occurred in the recent past, including those during the monsoons of 1998, 2004, and 2007. The frequency of floods has increased in recent years, and over 50% of Bangladesh can be inundated during severe floods, causing epidemics of infectious diseases, especially diarrheal disease.1 In addition to flood-related epidemics, Bangladesh faces seasonal diarrheal peaks resulting from an increased incidence of waterborne diseases, which are a cause of significant morbidity.2,3 Clinical features of diarrheal diseases seen at health facilities tend to be more severe during floods.4 In earlier studies, we have evaluated the characteristics of patients and etiologic agents during floods.4,5

*Vibrio cholerae* and enterotoxigenic *Escherichia coli* (ETEC) are the two most frequently isolated bacterial pathogens from patients presenting with diarrhea at the International Center for Diarrheal Disease Research, Bangladesh (ICDDR,B) hospital in Dhaka.4,5 *Vibrio cholerae* isolates are now predominantly of the El Tor biotype, serogroup O1, and include both Ogawa and Inaba serotypes.9 The ETEC is the most commonly isolated bacterial cause of diarrheal illness in children and can produce a heat-labile enterotoxin (LT), a heat-stable enterotoxin (ST), or both, and is able to produce over 25 different colonization factors (CFs) that are known to be important virulence factors.7 Both *V. cholerae* and ETEC cause seasonal, bi-annual peaks of diarrhea in patients seeking care at the ICDDR,B, with even greater peaks during flood-related epidemics.5

In the present study, we sought to better understand how flooding influences the epidemiology and microbiological etiology of diarrheal pathogens, with an emphasis on the two major bacterial pathogens, *V. cholerae* and ETEC. We analyzed data from the recent flood of 2007, which occurred between July and September 2007, when 60% of Bangladesh was inundated with water, and examined the epidemiology, clinical features, and the major pathogens isolated during this epidemic, with a specific emphasis on ETEC, to determine if phenotypic and antigenic shifts were taking place. We compared these data to those obtained during the floods of 2004 and 1998, and to corresponding non-flood periods in adjacent years.

MATERIALS AND METHODS

Study site. This study was performed at the diarrheal hospital of ICDDR,B, in Dhaka, Bangladesh. Dhaka is bordered by the Turag and Buriganga rivers. Data for this analysis was extrapolated from a 2% systematic surveillance system maintained at the ICDDR,B.5 In the surveillance system, every fiftieth patient attending the hospital is included in the database for demographic, socioeconomic, clinical, and microbiologic analyses. A physician documents the clinical condition, including dehydration status, and a stool or rectal swab sample is collected for microbiologic evaluation.9,10 All demographic, microbiologic, treatment, and outcome data are systematically recorded and entered into a database, which was used for the present study.

Microbiologic evaluation. As part of the surveillance system at the ICDDR,B hospital, stool and/or rectal swab specimens are routinely evaluated for enteric pathogens including *V. cholerae*, *Salmonella* spp., *Shigella* spp., *Campylobacter jejuni*, and rotavirus using standard techniques.10,11 Stool specimens were also screened for enteric parasites. Furthermore, specimens were tested for ETEC during the entire year of 1997, 1998, and 2007, and between July–August during the 2004 flood period.12 Other diarrheagenic *E. coli* were not routinely tested in the different study periods.

For microbiologic analyses, specimens were plated directly on taurocholate-tellurite-gelatin and MacConkey agar for culturing *V. cholerae* and *E. coli*, respectively.13,14 Specimens were also enriched in alkaline peptone water for 4 hours and then cultured; isolated *V. cholerae* were classified by sero-
group, biotype, and serotype. For detection of ETEC, six freshly lactose-fermenting E. coli colonies were isolated on overnight cultured MacConkey agar plates and tested for the presence of LT, ST. Detection of LT was carried out with a ganglioside GM1 enzyme-linked immunosorbent assay (ELISA) and ST was detected by an inhibition ELISA. Colonies that tested positive for either toxin were plated onto colonization factor antigen (CFA) agar with bile salts for identifying the CFs using a dot blot immunosassay technique with specific monoclonal antibodies. Rotavirus was identified by ELISA using standard methods.

**Definition of flood periods.** A flood period was defined from the earliest date that any of the rivers surrounding Dhaka exceeded the predetermined flood stage through the latest date that any of the river levels fell below the flood stage. The flood stage of individual rivers was defined by the Flood Forecasting Watch Center, Bangladesh. Using this data, there were four flood periods defined for analysis: July 25–October 13, 1998; July 20–August 21, 2004; September 16–October 24, 2004; and 20 July 08–September 30, 2007. The corresponding non-flood periods were defined as the matching dates in the year prior to each flood.

**Statistical methods.** Statistical analyses were performed using Statistical Package for Social Sciences (SPSS, Chicago, IL) version 12.0, GraphPad Prism version 4.0 (GraphPad Software, Inc., San Diego, CA), and EpiInfo version 3.4 (EpiInfo 2001, CDC). Differences in proportion of cases were assessed by Pearson’s χ² analysis. Associations were made by calculation of the odds ratio (OR) with 95% confidence intervals (CI). Statistical significance was defined as a two-tailed P value < 0.05.

**RESULTS**

**Patient visits during flood periods.** Comparison of data from floods in 1998, 2004, and 2007 showed that there were 50 flood days in 1998, 2004, and 2007 had 84 flood days. There were a total of 122,000 patients who visited the ICDDR,B in 2007, and 43,250 patients were seen during the flood period (Figure 1A). There were a total of 58,600 children < 5 years of age who visited the hospital in 2007 (median age 11 months), and 16,150 of those visited during the flood period (Figure 1C).

**Demographic and clinical characteristics of patients in flood versus non-flood periods.** Patient characteristics for those visiting the ICDDR,B during the flood and non-flood seasons are summarized in Table 1. The median age of patients seen at the ICDDR,B during the flood of 2007 was 16 years of age; this was greater, although not significant, than the median age in the corresponding non-flood period in 2006 (13 years; P = 0.07). The same age differences were seen for the floods in 2004 and 1998 compared with the corresponding non-flood periods. There were significantly more males than females that visited the hospital during both the flood and non-flood periods, and the proportion of males visiting the ICDDR,B increased even further during the flood of 2007 (Table 1). Patients had significantly higher rates of severe dehydration and more commonly required intravenous rehydration during all three flood periods as compared with non-flood periods (P < 0.001 for all comparisons; Table 1). Furthermore, there was a difference between the rates of severe dehydration between the individual flood years; patients in 2007 were significantly more dehydrated on admission than those in the 1998 and 2004 floods (P < 0.001; Table 1). The clinical features of diarrheal disease in patients during the flood years included less fever, more watery stools, and more severe dehydration than in the comparable non-flood periods (Table 1).

**Pathogens isolated during floods.** The most common pathogen isolated during each flood season was V. cholerae O1 (Figure 1B). The isolation rate of V. cholerae during the 2007 and 2004 floods were similar (both 33%), and this was lower than that during the 1998 flood (40%, P < 0.001) (Table 1). Even though more cholera cases visited the hospital in 2007 compared with 2006, there was no significant difference between the rates of V. cholerae O1 isolated in 2007 (33%) compared with the frequency of isolation during the corresponding non-flood year in 2006 (35%) (Table 1). However, in the 1998 flood, the isolation rate of V. cholerae O1 was significantly higher than that of the corresponding non-flood period in 1997 (40% versus 13%; P < 0.001), whereas the flood and non-flood matched periods of 2004 and 2003 showed a general trend of increasing cholera prevalence even during non-flood periods (Table 1).

During the recent flood period of 2007, V. cholerae O1 Ogawa was isolated from 48% of cholera patients, whereas V. cholerae O1 Inaba was isolated from 52%. This is markedly different from the floods of 1998, when V. cholerae O1 Ogawa was isolated from over 98% (P < 0.001 compared with 2007), and V. cholerae O1 Inaba was isolated from none of the cholera patients; the remaining 2% of isolates were V. cholerae O139. And during the 2004 floods, V. cholerae O1 Inaba (78%) was isolated most frequently (P < 0.001 compared with 2007). In the non-flood period in 2006, 89% of cholera cases were caused by V. cholerae O1 Inaba and 11% were the result of V. cholerae O1 Ogawa, suggesting that V. cholerae O1 Inaba has been increasing over the last decade independent of flood periods.

A second important bacterial pathogen isolated during the floods was ETEC, and was present in 9%, 18%, and 11% of the patients during the floods of 1998, 2004, and 2007, respectively (Table 1). For the non-flood comparison periods for ETEC, we only had data for 1997, which showed significantly more ETEC isolates compared with those of the floods in 1998 (23% versus 9%; P < 0.001).

The most common pathogen isolated from children < 5 years of age throughout 2007 was rotavirus (Figure 1C). Rotavirus was less prevalent in the recent 2007 flood period compared with 1998 (12% versus 16%, P < 0.001; Table 1). Furthermore, rotavirus was significantly less prevalent during all the flood periods (12–18%) compared with the corresponding non-flood periods (18–25%; P < 0.01; Table 1).

Other pathogens isolated during the diarrhea epidemics represented a minority of diarrhea cases and included Shigella spp., Salmonella spp., E. histolytica, G. lamblia, C. jejuni, and Cryptosporidium (Table 1). Although V. cholerae, ETEC, and rotavirus prevalence increased during the 2007 flood, the prevalence of Shigella spp. did not increase (Figure 1B and C). No pathogen was identified for 38–74% of the patients.

**Toxin types and colonization factors expressed by ETEC isolated in the 2007 flood compared with 2004.** A significantly higher percentage of LT-producing ETEC were isolated in the 2007 flood than in previous floods. Approximately 51% of ETEC isolates were LT producers and 27% were ST/ LT producers, whereas 22% expressed ST only (Table 2). This was
significantly different from the pattern seen in the 2004 flood period, when 67% of ETEC isolates were ST positive, 19% produced ST and LT (total 86% ST positive), and 14% were LT positive ETEC ($P < 0.001$). Overall, during the 2007 flood period, 78% of ETEC isolates expressed LT (as LT or ST/LT), which was significantly higher than the 33% isolated during the 2004 flood period ($P < 0.001$).

During the 2007 flood, 43% of ETEC strains tested positive for colonization factors (CFs) compared with 78% seen in the 2004 floods ($P < 0.001$; Table 2). The major CFs detected on ETEC during the 2007 flood were: CS7 (20%), CS6 (15%), CFA/I (12%), and CS14 (12%). During the 2004 flood, CFA/I was the most prevalent (25%), followed by CS5 + CS6 (20%), CS4 + CS6 (18%), CS6 (12%), and CS7 (6%). Comparing the two flood periods, CS7 expressing ETEC strains shifted from a low prevalence in 2004 to the most common CF identified in 2007 (Table 2). When we analyzed the overall prevalence of different CF phenotypes of ETEC for the entire 2007 period, we found: CS5 + CS6 (16%), CFA/I (14%), and CS7 (13%). Thus, the previously less prevalent CS7 phenotype was seen in higher frequency during the flood and non-flood periods in 2007. Comparable data for the non-flood period in 2004 were

![Figure 1](image-url)
Clinical characteristics and etiologies of diarrhea in patients during the flood (1998, 2004, and 2007) and corresponding non-flood periods in 2% hospital surveillance data

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>1998 N = 1049 (%)</th>
<th>2004 N = 885 (%)</th>
<th>2007 N = 885 (%)</th>
<th>1997 N = 395 (%)</th>
<th>2003 N = 377 (%)</th>
<th>2006 N = 493 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 2</td>
<td>360 (34)*</td>
<td>217 (32)*</td>
<td>236 (27)*</td>
<td>200 (51)</td>
<td>182 (48)</td>
<td>177 (36)</td>
</tr>
<tr>
<td>2 to 4</td>
<td>132 (13)*</td>
<td>76 (11)</td>
<td>80 (9)</td>
<td>30 (7)</td>
<td>37 (10)</td>
<td>32 (6)</td>
</tr>
<tr>
<td>5 to 14</td>
<td>140 (13)*</td>
<td>69 (10)</td>
<td>98 (11)</td>
<td>36 (9)</td>
<td>31 (8)</td>
<td>44 (9)</td>
</tr>
<tr>
<td>≥ 15</td>
<td>417 (40)*</td>
<td>322 (47)*</td>
<td>451 (52)</td>
<td>129 (33)</td>
<td>127 (34)</td>
<td>240 (49)</td>
</tr>
<tr>
<td>Male sex</td>
<td>593 (57)</td>
<td>363 (53)*</td>
<td>515 (60)</td>
<td>222 (56)</td>
<td>224 (59)</td>
<td>289 (59)</td>
</tr>
<tr>
<td>Fever (&gt; 37.8°C)</td>
<td>45 (4)</td>
<td>19 (3)</td>
<td>17 (2)</td>
<td>25 (6)</td>
<td>15 (4)</td>
<td>17 (4)</td>
</tr>
<tr>
<td>Watery stool</td>
<td>991 (94)</td>
<td>657 (96)</td>
<td>825 (95)</td>
<td>363 (92)</td>
<td>360 (96)</td>
<td>462 (94)</td>
</tr>
<tr>
<td>Vomiting &gt; 10 times prior to admission</td>
<td>103 (10)‡</td>
<td>79 (12)</td>
<td>113 (13)</td>
<td>22 (6)</td>
<td>33 (9)</td>
<td>49 (10)</td>
</tr>
<tr>
<td>Severe dehydration on presentation</td>
<td>318 (30)*</td>
<td>267 (39)*</td>
<td>414 (48)‡</td>
<td>41 (10)</td>
<td>79 (21)</td>
<td>193 (39)</td>
</tr>
<tr>
<td>Required intravenous rehydration</td>
<td>392 (37)*</td>
<td>312 (46)*</td>
<td>452 (52)‡</td>
<td>61 (15)</td>
<td>97 (26)</td>
<td>215 (44)</td>
</tr>
</tbody>
</table>

Pathogens

- Rotavirus: 168 (16)*, 122 (18)*, 100 (12)*, 89 (23), 96 (25), 88 (18)
- Vibrio cholerae O1§: 423 (40)*, 227 (33)*, 282 (33), 51 (13), 79 (21), 172 (35)
- ETEC: 97 (9)*, 63 (18)†, 95 (11), 92 (23), n/a, n/a
- Other pathogens§: 251 (24)*, 62 (9), 42 (5), 148 (38), 30 (8), 38 (8)
- No pathogen detected: 402 (38)*, 421 (61)*, 561 (65), 213 (54), 280 (74), 296 (60)

Comparing a flood year to a corresponding non-flood year:

Not available for analysis, although CS7 was not the most prevalent antigenic type in 2004.

The prevalence of CF positive ETECs based on the toxin phenotypes was also determined: 44% of LT-producing ETEC, 48% of ST-producing ETEC, and 38% of ST/LT-producing ETEC strains were positive for CFs for the entire period of 2007. The number of CF positive ETEC isolated in 2004 were significantly higher: 56%, 79%, and 92% for the LT, ST, and ST/LT producing types, respectively.

Clinical features of cholera and ETEC patients during the 2007 floods. We wanted to determine if there were any differences between disease presentations of patients with cholera or ETEC diarrhea during the most recent 2007 floods. There were more cholera patients (N = 282), and they were older (median age 20 years) than the 88 patients with ETEC diarrhea (median age 14.5 years) (Table 3). There was no significant gender difference between patients presenting with either pathogen. There were more patients infected with ETEC than with cholera that presented with fever (5% versus <1%; P = 0.003), and a significantly higher proportion of ETEC patients had a duration of diarrheal symptoms of over 4 days before presenting to the hospital (14% versus 4%; P < 0.001). There were no significant differences between the consistencies of stool, watery versus bloody diarrhea, from patients infected with the two pathogens. However, the consistency of stool for both cholera and ETEC patients was primarily watery (99% and 97%, respectively). Cholera patients had a significantly higher risk of diffuse vomiting of more...
Clinical characteristics of patients with enterotoxigenic *Escherichia coli* (ETEC) diarrhea compared with cholera during the floods of 2007 extrapolated from the 2% hospital surveillance data

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cholera*</th>
<th>ETEC†</th>
<th>Odds ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (years)</td>
<td>20</td>
<td>14.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 2</td>
<td>23 (8)</td>
<td>28 (32)</td>
<td>0.19 (0.10–0.37)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>2 to 4</td>
<td>25 (9)</td>
<td>9 (10)</td>
<td>0.85 (0.36–2.06)</td>
<td>0.699</td>
</tr>
<tr>
<td>5 to 14</td>
<td>46 (16)</td>
<td>7 (8)</td>
<td>2.26 (0.93–5.71)</td>
<td>0.051</td>
</tr>
<tr>
<td>≥ 15</td>
<td>188 (67)</td>
<td>44 (50)</td>
<td>2.00 (1.20–3.35)</td>
<td>0.005</td>
</tr>
<tr>
<td>Male sex</td>
<td>165 (59)</td>
<td>58 (66)</td>
<td>0.73 (0.43–1.24)</td>
<td>0.216</td>
</tr>
<tr>
<td>Fever (&gt; 37.8°C)</td>
<td>1 (&lt; 1)</td>
<td>4 (5)</td>
<td>0.07 (0.00–0.72)</td>
<td>0.003</td>
</tr>
<tr>
<td>Diarrhea for &gt; 4 days</td>
<td>13 (5)</td>
<td>12 (14)</td>
<td>0.31 (0.12–0.75)</td>
<td>0.003</td>
</tr>
<tr>
<td>Watery stool</td>
<td>280 (99)</td>
<td>85 (97)</td>
<td>4.94 (0.66–43.0)</td>
<td>0.056</td>
</tr>
<tr>
<td>Bloody stool</td>
<td>0 (0)</td>
<td>1 (1)</td>
<td>0.00 (0.00–4.51)</td>
<td>0.073</td>
</tr>
<tr>
<td>Vomiting &gt; 10 times prior to admission</td>
<td>54 (19)</td>
<td>8 (9)</td>
<td>2.37 (1.03–5.64)</td>
<td>0.027</td>
</tr>
<tr>
<td>Severe dehydration on presentation</td>
<td>212 (75)</td>
<td>35 (40)</td>
<td>4.59 (2.69–7.85)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Required intravenous rehydration</td>
<td>221 (76)</td>
<td>35 (40)</td>
<td>5.49 (3.19–9.47)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

*Cholera cases of culture confirmed *Vibrio cholerae* O1.
†88 ETEC cases were available for analysis from the hospital surveillance. Odds ratios (OR), confidence intervals (CI), and P values were derived from χ² comparing cholera to ETEC.

**DISCUSSION**

Our data from the 2007 floods show that *V. cholerae* O1 is still the most commonly identified pathogen causing diarrhea requiring hospitalization during flood-related diarrheal epidemics in Dhaka, Bangladesh. As expected, rotavirus was the major pathogen causing diarrheal disease in children < 5 years of age during the flood periods (Figure 1B). However, ETEC was a major cause of diarrhea not only in children (13%) but also adults (11%).

Another major observation from this study was that the severity of dehydration in hospitalized patients has been increasing over the last decade. Among the three flood periods, 2007 had the highest rate (48%) of patients who presented with severe dehydration (75% versus 40%; P < 0.001), and more frequently required intravenous rehydration (78% versus 40%; P < 0.001).

Transmission of water-borne pathogens increases during flood periods,19 and the patterns of prevalence of *V. cholerae* and ETEC appear to have shifted during the 2007 flood. In southeastern Bangladesh, a post-flood bacteriologic survey during the 1998 diarrheal epidemic found 25 (33%) *V. cholerae* O1 Ogawa and 14 (18%) *V. cholerae* O139 in 76 patients analyzed; they did not mention any *V. cholerae* O1 Inaba detected.20 At the ICDDR,B, the proportion of cholera cases resulting from the Ogawa serotype was 98% in 1998 and 24% in 2004.4 During the 2007 floods, *V. cholerae* O139 was not detected, and the rates of *V. cholerae* O1 Inaba and Ogawa were 52% and 48%, respectively. Comparing this to the corresponding non-flood period of 2006, it was evident that the high rate of *V. cholerae* O1 Inaba (89%) isolated had occurred independently of the flooding in the following year. An interesting observation was that rotavirus was more prevalent during the non-flood periods in the three time periods when analyses were carried out.

The ETEC is an important cause of flood-related diarrheal epidemics in the developing world.2 Historically, hospitals have not actively screened for ETEC during natural disasters; however, in addition to cholera, ETEC is a common cause of diarrhea in Bangladesh.21,22 In the 2004 flood, ETEC predominantly produced ST only.5 This trend has been reported previously over the last decade in Bangladesh; ST-producing ETEC have been most commonly isolated, ranging from 48–66%, whereas LT-producing ETEC have ranged from 15–27%.7,23–25 Isolates from the recent flood in 2007, however,
demonstrate that ETEC strains have shifted from ST-producers to significantly more LT-producing strains (Table 2). Countries in Latin America, such as Mexico, Peru, and Argentina, have shown a high prevalence of LT-producing ETEC also: 41%, 56%, and 53%, respectively. The CFs are fimbrial or fibrillar proteins on ETEC that aid colonization of the small bowel, allowing expression of LT and/or ST in close proximity to the intestinal epithelium, with production of diarrhea. Of the 25 CFs, studies from different regions have shown that CFA/I, CS1, CS2, CS3, CS5, and CS6 are most frequently isolated. These CFs are commonly seen in association with ST-producing ETEC. The LT is more immunogenic than ST, is antigenically similar to cholera toxin, and there is immunologic cross-protection to cholera toxin. Because the majority of CFs expressed on clinical isolates are from ST or ST/LT-expressing strains, protection from ST-ETEC might be elicited through inducing responses to the generally immunogenic CFs. The ETEC vaccines tested in the past or that are being produced currently are based on the immunogenic properties of CFs. Our data from the 2007 flood show that changes in current vaccine strategies may be necessary to make them more effective, to reflect the shift from CF-positive ST-producing ETEC to the increasingly prevalent CF-negative LT-producing ETEC. On the basis of this information, addition of LT and CS7 to vaccine strategies appears to be important, as the CS7 antigen has gradually increased in prevalence (Table 2). CS7 is particularly expressed by LT-producing ETEC, suggesting that a new vaccine formulation with LT and important CFs, such as CS7, CS6, and CFA/I, may be more appropriate to ensure broad coverage of varying ETEC strains.

This study has certain limitations that should be considered. Our analysis was conducted using a hospital surveillance system on a 2% patient sampling. The ETEC data prior to 2007 is incomplete, and our analysis used data collected in a previous sample of patients for the 2004 period. However, these limitations should not alter the results or conclusions of our study.

Our data demonstrate the shifting microbiology among common pathogens responsible for flood-related diarrhea epidemics in Bangladesh. Surveillance of the changing etiologic agents, as well as the rapid shifts in antigenic types of flood-related pathogens, is important for successful public health interventions, using both vaccines and antimicrobial therapy, to prevent and control diarrhea related morbidity and mortality.

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