TRANSMISSION OF EPIDEMIC *VIBRIO CHOLERAE* O1 IN RURAL WESTERN KENYA ASSOCIATED WITH DRINKING WATER FROM LAKE VICTORIA: AN ENVIRONMENTAL RESERVOIR FOR CHOLERA?

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Abstract. Sub-Saharan Africa has the highest reported cholera incidence and mortality rates in the world. In 1997, a cholera epidemic occurred in western Kenya. Between June 1997 and March 1998, 14,275 cholera admissions to hospitals in Nyanza Province in western Kenya were reported. There were 547 deaths (case fatality rate = 4%). Of 31 Vibrio cholerae O1 isolates tested, all but one were sensitive to tetracycline. We performed a case-control study among 61 cholera patients and age-, sex-, and clinic-matched controls. Multivariate analysis showed that risk factors for cholera were drinking water from Lake Victoria or from a stream, sharing food with a person with watery diarrhea, and attending funeral feasts. Compared with other diarrheal pathogens, cholera was more common among persons living in a village bordering Lake Victoria. Cholera has become an important public health concern in western Kenya, and may become an endemic pathogen in the region.

Since 1817, Vibrio cholerae O1 has emerged from the Indian subcontinent in seven pandemics of acute diarrheal disease, the most recent beginning in 1961 and continuing to the present day in Asia, Africa, the Middle East, and South and Central America. In many areas cholera has become an endemic disease.

The burden of cholera is highest in sub-Saharan Africa. In 1996, Africa reported the largest number of cholera cases in the world, with 108,535 cases, more than three times the number in the rest of the world combined. In addition, 6,216 deaths were reported, representing a case fatality rate of 5.7% and accounting for 93% of all reported cholera deaths worldwide. Cholera is essentially a disease of poor sanitation, and epidemics in Africa have been linked to consumption of food and water from unsafe sources, e.g., drinking or bathing in lakes, drinking river water, eating at large funeral feasts, and eating cold leftover foods. Western Kenya has had several discrete waves of cholera during the seventh pandemic, in 1971–1972, 1980–1984, 1992–1993, and most recently, beginning in 1997.

The current outbreak in Kenya began in June 1997 when cholera was first reported in Nyanza Province near the Tanzanian border, along Lake Victoria. The disease crept slowly up the coast of Lake Victoria until October, when it reached more densely populated areas and accelerated both inland and along the lake. In mid-October, the epidemic reached Kisumu, the third largest city in Kenya with a population of more than 300,000. By early November, cholera had spread northwest of Kisumu into Siaya District, including the 200km² Asembo region where ongoing diarrheal disease surveillance was being conducted through a collaboration between the Kenya Medical Research Institute (KEMRI) and the Centers for Disease Control and Prevention (CDC) (Figure 1). The first case of cholera in the Siaya District was detected by this surveillance system on October 22, 1997, and a specific cholera surveillance form, linked to a casecontrol study, was distributed within one week to clinics in Asembo.

Here we describe the cholera outbreak in western Kenya,

highlighting the risk factors for transmission in Asembo identified by the results of a clinic-based case-control study, and discuss the potential for cholera to become endemic in this region. Ongoing diarrheal surveillance in Asembo enabled us to study this epidemic in detail at the local level over several months, to use accurate denominator data to assess the burden of cholera in Asembo, and to monitor the development of antimicrobial resistance.

METHODS

The policies of CDC and KEMRI with regard to human subjects during outbreak situations were adhered to in this investigation. Informed consent was obtained from participants using a standardized form read in Dho Luo, and no personal identifiers were maintained. Cholera surveillance in Nyanza Province was performed by the Kenya Ministry of Health, using inpatient hospital admission data from the 10 districts in the Province. In each district, several hospitals were established to handle cholera patients, and all patients with suspected cholera were referred to these facilities for treatment. Thus, the inpatient surveillance for the Province was conducted through a weekly census of patients admitted to these facilities with a clinical diagnosis of cholera, based on the World Health Organization (WHO) definition.⁵ As proposed by WHO, in epidemic settings, for surveillance purposes, watery diarrhea in patients five years of age and older is considered cholera.5

In Asembo, cholera surveillance was conducted by CDC/KEMRI staff at seven health facilities, five of the 13 health facilities within the region and two in neighboring regions frequented by Asembo residents. Five of the sites were ambulatory clinics and two were hospitals. Asembo is a rural region bordering Lake Victoria, with a population of approximately 53,000 persons living in 76 villages; its residents are primarily subsistence farmers and lishermen.

For surveillance in Asembo, all patients more than five 5 years of age presenting after October 22, 1997 with a history of watery diarrhea for any duration of time were considered

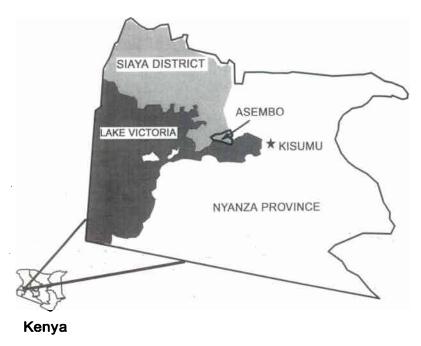


FIGURE 1. Map of Nyanza Province in western Kenya.

to meet the WHO clinical case definition for cholera.⁵ Population and demographic data from Asembo were gathered in the context of ongoing KEMRI/CDC malaria research in the region.

We performed a case-control study at the seven sites in Asembo, enrolling all patients identified through surveillance and matching controls by age, sex, and clinic to each case. When possible, two controls were matched to each case-patient, but a single matched control was accepted if a second suitable control could not be identified. Controls were selected from patients attending the same clinic within two days of presentation by the case-patient and were excluded if they described any diarrheal episode (> 3 loose stools per 24 hr) in the preceding 30 days. Questionnaires were administered to gather clinical data for case-patients, and information about demographics, and food and water consumption, and handling practices of case-patients and controls in the five days preceding their clinic visit.

Laboratory surveillance for diarrheal pathogens, including V. cholerae O1 and other vibrios, was conducted at three of the health facilities (two clinics and one mission hospital). Whole stools or rectal swabs were obtained from patients with diarrhea, and all specimens (including a swab of each whole stool specimen) were immediately placed in Carv-Blair transport medium, and were kept either in a refrigerator or on ice for same-day transport to the CDC/KEMRI Microbiology Laboratory in Kisian, near Kisumu. All specimens arrived at the laboratory within 6 hr of collection and were plated on thiosulfate-citrate-bile salts agar the same day. Isolates of V. cholerae O1 were identified by using serogroup O1 and O139 antisera and biochemical tests. Representative isolates were biotyped and tested at CDC by the polymerase chain reaction for cholera toxin subunit A gene sequences. 6.7 Vibrio cholerae isolates were tested in Kisian and confirmed at CDC by the disk diffusion method for susceptibility to the following antimicrobials: ampicillin, amoxicillin-clavulanic acid, ceftriaxone, chloramphenicol, ciprofloxacin, gentamicin, nalidixic acid, streptomycin, sulfisoxazole, tetracycline, and trimethoprim-sufamethoxazole. Since interpretive criteria for amoxicillin-clavulanic acid, ceftriaxone, ciprofloxacin, gentamicin, nalidixic acid, and streptomycin have not been established for *V. cholerae*, criteria standardized for the *Enterobacteriaceae* were used for interpretation of zone sizes for these agents.

A geographic analysis was performed on the cohort of patients whose stool specimens yielded bacterial pathogens between October 22, 1997 and February 28, 1998. Patients with cholera were compared with those with any other laboratory-confirmed bacterial pathogen to determine if a difference existed in their villages of residence.

Data were analyzed using Epi-Info 6.02 computer software (CDC, Atlanta, GA) and SAS version 6.12.9 For univariate analysis, matched odds ratios and their 95% confidence intervals (CIs) were calculated for water and food exposure data among case-patients and controls. For multivariate analysis, we used conditional logistic regression modeling and calculated adjusted odds ratios and their 95% CIs. No interactions were significant among independent variables. Attributable risks and their 95% CIs were calculated for independent variables. For the geographic analysis, among all patients whose stool specimens yielded bacterial pathogens, risk ratios (RRs) were calculated for the likelihood of living in a village bordering Lake Victoria; 95% CIs intervals were used for RRs.

RESULTS

From June 1, 1997, through March 13, 1998, 14,275 cholera admissions to hospitals in Nyanza Province were reported to the Kenyan Ministry of Health (Figure 2) from 49 hospitals in six of the 10 districts in the Province. There were 547 cholera-related deaths reported, giving a case-fa-

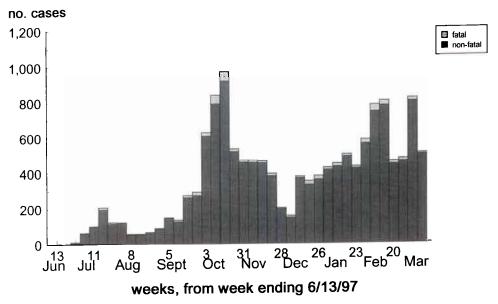


FIGURE 2. Hospital admissions for cholera, by week of admission and patient outcome, Nyanza Province, Kenya, June 1997-March 1998.

tality rate of 4%. In Siaya District, 1,268 cholera admissions and 50 deaths were reported, also giving a case-fatality rate of 4% (Kenya Ministry of Health, 1998, unpublished data). The population of the affected districts in Nyanza Province was approximately 3,027,000 persons, giving an attack rate of 0.5%. The population of Slaya District was approximately 772,000, giving an attack rate of 0.2% for the District.

Between October 28, 1997, and March 1, 1998, at the seven surveillance sites around Asembo, 103 patients were identified who met the clinical definition of cholera. One (1%) patient presented in October, 47 (46%) patients presented in November, 14 (14%) in December, 15 (15%) in January, and 26 (25%) in February following the temporal distribution for the province as a whole (Figure 2). Four deaths (4%) were reported among these patients. The median age was 24.5 years (range = 5-85 years) and 66 (64%) patients were female. Fifty-seven (55%) patients resided in villages within Asembo.

Of these 103 patients, 53 (51%) were identified at the three clinics where specimens were also collected; of these, 46 (87%) provided a specimen; 31 (67%) of these specimens

TABLE 1

Percent of Vibrio cholerae O1 isolates susceptible to antimicrobial agents (n = 31), Asembo region, Kenya, October 1997–March 1998

Antimicrobial agent	% susceptible	
Trimethoprim-sulfamethoxazole	0	
Sulfisoxazole	0	
Streptomycin	0	
Nalidixic acid	0	
Chloramphenicol	3	
Tetracycline	97	
Kanamycin	97	
Cirntamicin:	97	
Ampicillin	100	
Amoxicillin-clavulonic acid	100	
Ciprofloxacin	100	
Ceftriaxone	100	

yielded *V. cholerae* O1. All isolates were biotype El Tor, and 30 (97%) were serotype Ogawa; one was serotype Inaba. All isolates contained cholera toxin subunit A gene sequences. Most isolates were either fully or partially resistant to trimethoprim-sulfamethoxazole, sulfisoxazole, streptomycin, nalidixic acid, and chloramphenicol, and susceptible to tetracycline, kanamycin, gentamicin, ampicillin, amoxicillinclavalonic acid, ciprofloxacin, and ceftriaxone (Table 1). One strain, isolated in February 1998, was resistant to tetracycline.

Laboratory-confirmed patients and other patients had similar symptom profiles, and the results are reported together. Eighty-nine (87%) experienced abdominal cramps, 85 (83%) had vomiting, and 59 (58%) reported fever; 77 (75%) had signs of dehydration, with either extreme thirst, dry mucous membranes, or poor skin turgor on presentation.

Of the 103 patients identified at the surveillance sites, 61 (59%) were matched to either one (9) or two (52) control patients, for a total of 113 controls. Although in univariate analysis multiple factors were associated with increased risk or protection from cholera, in multivariate analysis, only drinking water from Lake Victoria or a stream, sharing meals with someone with watery diarrhea, and attending funeral feasts were independent risk factors for illness (Table 2). Within this model, the attributable risk for drinking from Lake Victoria was 27% (95% CI = 19%, 37%), for drinking from a stream 17% (95% CI = 10%, 26%), for attending a funeral feast 36% (95% CI = 26%, 45%), and for sharing a meal with a person with watery diarrhea 20% (95% CI = 12%, 30%).

A separate geographic analysis of all patients with diarrhea who provided specimens between October .22 and March 1 at the three designated clinics for laboratory-based cholera surveillance revealed that patients from whom V. cholerae O1 was isolated were more likely to live in a village bordering Lake Victoria than were those with other identified pathogens (Shigella spp., Campylobacter spp., Salmonella spp.) (Figure 3). Among 27 patients from whom V.

TABLE 2

Risk factors associated with cholera in the Asembo region of Nyanza Province in western Kenya, October 1997–February 1998*

Behavior† (in the previous 5 days)	Cases with exposure reported/total (%)	Controls with exposure reported/total (%)	Univariate analysis MOR (95% CI)	Multivariate analysis AOR (95% CI)
Drinking water from Lake Victoria	33/102 (32)	9/113 (8)	5.6 (2.0, 15.8)	6.5 (1.6, 25.5)
Drinking water from a stream	19/103 (18)	4/113 (4)	7.6 (1.8, 77.9)	10.8 (1.7, 70.1)
Drinking water from a borehole	22/102 (22)	35/113 (31)	0.3 (0.1, 0.8)	
Drinking rain water	50/103 (49)	73/113 (65)	0.4 (0.2, 0.8)	
Attending a funeral feast	51/103 (50)	23/113 (20)	4.4 (2.0, 9.9)	3.6 (1.3, 10.3)
Eating food at a funeral or gathering	40/95 (42)	16/109 (15)	3.9 (1.6, 10.1)	
Eating food at home compound	82/96 (85)	109/113 (97)	0.1 (0.0, 0.4)	
Eating raw fruits or vegetables	41/96 (43)	30/113 (27)	2.3 (1.1, 4.6)	
Eating washed fruits or vegetables	44/96 (46)	86/113 (76)	0.2 (0.1, 0.6)	
Sharing food with a person with watery diarrhea	19/84 (23)	2/109 (2)	5.3 (1.2, 24.2)	7.8 (1.3, 49.0)
Sharing a latrine with a person with watery diarrhea	21/78 (27)	6/88 (7)	5.1 (1.4, 19.0)	

^{*} MOR = matched odds ratio; AOR = adjusted odds ratio.

cholerae O1 was isolated and whose village of residence within Asembo was known, 15 (56%) lived in a village bordering Lake Victoria, compared with eight (23%) of 35 patients whose stools yielded any other bacterial pathogen during this time period (RR = 2.1, 95% CI = 1.2, 3.7). Overall, only 16% of the population in Asembo lived in villages bordering the lake (CDC/KEMRI, 1997, unpublished data).

DISCUSSION

After a four-year absence, epidemic cholera returned to western Kenya in the second half of 1997. The overall case fatality rate of 4% for Nyanza Province was high, although slightly lower than the 5.7% rate reported for Africa during 1996. However, the 4% rate was likely an underestimate since it accounted only for patients who were admitted to and died in the designated cholera hospitals. This high mortality rate occurred despite efforts by the Kenyan Ministry of Health and other non-governmental organizations (most

notably Medecins Sans Frontieres) to identify and rehydrate all suspected cholera patients promptly with oral rehydration solution (ORS) or intravenous fluids, to ban funeral feasts, and to educate the public regarding safe food and water sources. In addition, the Ministry of Health attempted to provide prophylactic antibiotics, primarily tetracycline, to all close household contacts of patients. As of May 1998, this practice was being reconsidered because of its unclear effectiveness in reducing secondary transmission, the belief among those treated that they had acquired long-term protection from cholera, and concern by the Ministry of Health that tetracycline resistance would emerge. With the Latin American experience used as a model, 12 mortality rates during a cholera epidemic ideally should be kept below 1%.

In Asembo, ongoing diarrheal surveillance provided an opportunity to carefully monitor cholera emergence and risk factors for transmission. Educational efforts were also begun in Asembo early in the epidemic, including provision of rehydration guidelines to all clinic staff and village health

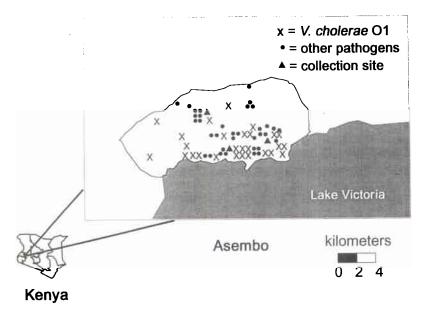


FIGURE 3. Patients with culture-confined cholera in Asembo compared with those infected with other bacterial pathogens, by village of residence, October 1997–February 1998 (n = 27 cholera, 35 other pathogens).

[†] Behaviors are not mutually exclusive.

workers, promotion of the use of boiled water or water treated with lemons, ¹³ and distribution of information pamphlets translated into the local language. The overall effect of these efforts was difficult to assess, and the 4% mortality rate among the 103 patients identified through our surveillance did not differ from the reported rate for Siaya District or the Province as a whole.

In the setting of a cholera epidemic, WHO recommends using a clinical case definition of watery diarrhea for persons five years of age or older. The fact that 67% of such patients in our study who provided specimens had stools yielding *V. cholerae* O1 validates the use of this definition. The antimicrobial susceptibility patterns we observed were similar to those seen in recent East African cholera epidemics³ (CDC, 1998 unpublished data).

The finding of a tetracycline-resistant isolate is worrisome. Resistance to tetracycline is plasmid-mediated, and this resistance plasmid is maintained in the setting of heavy antibiotic use. 14,15 Cholera isolates from western Kenya in the 1980s became resistant to tetracycline following intensive use of this agent for both treatment and prophylaxis. 15 Because tetracycline is the currently recommended antimicrobial agent to treat cholera in western Kenya, careful monitoring for further resistance is warranted. The finding of a tetracycline-resistant isolate lends further support for discontinuing chemoprophylaxis of contacts of cholera patients in this region.

Among the risk factors for cholera identified in this study, drinking water from Lake Victoria is of particular interest. The epidemic most affected those districts of Nyanza Province near Lake Victoria (Figure 1). In addition, in Asembo, culture-confirmed cholera was more common among residents of villages bordering Lake Victoria, compared with other diarrheal pathogens, a finding that supports the risk associated with drinking water from the lake as an important source of infection. In previous cholera outbreaks in Africa, consumption of lake water was identified as a source of infections. However, it may not be feasible to encourage use of other water sources; unfortunately, Lake Victoria provides the only convenient source of water for many villages in the region, especially during the driest months of the year. This highlights the need for effective decontamination of drinking water.16

Another independent risk for cholera transmission was sharing meals with persons with watery diarrhea during the previous five days. Sharing meals was likely a risk for cholera either because of contamination of food or water, or as a marker for some common exposure among those who shared meals, which was not identified by our study.

Attending funeral feasts was also found to be a risk factor for cholera in multivariate analysis. Eating food at a funeral has been shown to be a risk factor for cholera in previous studies, and during this epidemic the Ministry of Health attempted to ban funeral feasts; unfortunately, this campaign had limited success, especially in rural regions such as Asembo. In Asembo. 25% of the households report funeral attendance by someone in the home during any given month, and most attendees are women (CDC/KEMRI, unpublished data). Thus, funeral attendance may in part explain why 64% of suspected cholera patients in our study were female. Our

study lends further support to the policy of restricting or postponing funeral feasts during cholera epidemics.

There are early indications that cholera may become established as an endemic or recurrent pathogen in western Kenya, as it has in parts of South America since first appearing in 1991.¹⁷ The prolonged bimodal course of the epidemic suggests the possible establishment of at least a transient environmental reservoir for cholera in the region. The decrease in cases during the period between November 28 and January 28 coincided with a nationwide nurses' strike that reduced hospital admissions; additional cases that occurred during that period may have gone unrecorded. Our case-control study in Asembo was also affected by the nurses' strike, and enrollment was lowest in December and January, when some of the surveillance sites either closed or operated with reduced hours. In addition, this period corresponded to high rainfall in western Kenya, which may have decreased the incidence of cholera by providing alternate sources of drinking water in the region.

The pattern of spread along the shore of Lake Victoria, and the risk associated with drinking water from the lake are also worrisome in light of the infestation of water hyacinth (Eichornia crassipes) in this region of the lake during in 1997 and 1998. The unchecked growth of water hyacinth, a non-native plant introduced into the lake, has emerged as an important environmental concern; it has closed ports and disrupted fishing routes throughout the province, and it may create an improved environment for the growth and survival of V. cholerae in a contaminated body of water. A 1981 study in Bangladesh demonstrated that five days after experimental inoculation of a water pool, there was a 300-fold greater concentration of V. cholerae on water hyacinth than in surrounding water.18 The investigators suggested that enhanced survival of V. cholerae associated with water hyacinth may play a role in maintaining environmental sources of toxigenic cholera strains in endemic-disease regions during interepidemic periods.18 Although the effect of water hyacinth on the cholera epidemic in western Kenya is difficult to determine, this 1981 study, the pattern of spread along the lake shore, and the documented risk associated with drinking lake water suggest that further research into the possible role of the water hyacinth in maintaining an environmental reservoir for V. cholerae O1 is warranted.

Endemic cholera is a highly preventable disease, requiring only proper sanitation and safe drinking water to greatly reduce its transmission within a community. In the developed world, safe municipal reservoirs and treatment facilities defeated cholera before the discovery of antibiotics and ORS. These lessons from the pre-antibiotic era should not be forgotten; in addition to the promotion of ORS as the mainstay of treating clinical cases of cholera, public health efforts should focus on bringing safe, reliable drinking water to regions such as Asembo. Point-of-use chlorination programs and safe water storage containers are an inexpensive approach^{19,20} that can be rapidly implemented. More permanent measures are the construction of water- and sewage-treatment facilities. Until such measures are taken, cholera and other diseases of poor sanitation will persist, and the human costs will exceed the price of prevention.

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