Cholera Outbreak Investigation in the Central African Republic
October – November 2011

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Background

Cholera is a diarrheic disease caused by vibrio cholera and is characterized by a sudden onset of profuse and painless watery stools. It is caused by an enterotoxin that affects the small intestine. The disease manifests through nausea and profuse vomiting in the early course of illness. When it is not treated, it can lead to rapid dehydration, acidosis, circulatory collapse, hypoglycemia in children, and renal failure. In most cases, infection is asymptomatic or causes mild diarrhea, especially with organisms of the El Tor biotype; asymptomatic carriers can transmit the infection. In severely dehydrated cases, death may occur within a few hours, and the case-fatality rate may exceed 50%. With proper and timely rehydration, the death rate can be less than 1% (1).

The Central African Republic (CAR) is not immune to this disease. The country recorded 77 cases and 35 deaths of cholera in 1997 in the sub-prefecture of Ngaoundaye, which is located on the border with Chad. The mortality rate in 1997 was 45.5%. In 1999, the country recorded 35 cases and 7 deaths along the Oubangui River with a mortality rate of 20% (2).

On September 21st, 2011, health facilities of the Ministry of Health in the Central African Republic (CAR) reported unusual cases of watery diarrhea from Sékia moté village. On September 23rd, the son of the chief of village fell sick and died. The chief reported this tragedy to the governor of the district on the same day it occurred, who later notified the Ministry of Health immediately (the same day). Since the notification of the first cholera case from Sékia moté village, the outbreak has spread to five villages in the prefecture of Lobaye, 7 villages in Ombella Mpoko district and six arrondissements (sub-divisions) in the city of Bangui. A suspected cholera case was defined as any person of any age presenting with acute watery

diarrhea. On September 25th 2011, a stool sample was collected for laboratory testing from a transferred patient admitted at the community hospital in Bangui by the two laboratory residents from the Central African Field Epidemiology and Laboratory training Program (CAFELTP). Within 3 days the National Laboratory in Bangui isolated *vibrio cholera* serogroup 131 from that stool specimen assisted by a laboratory expert, from the NCIRD/GID/Strengthening Immunization Systems Branch, Global Immunization Division, Centers for Disease Control and Prevention (CDC), and staff from Bangui National Laboratory . On September 30th, the Minister of Health officially declared a cholera outbreak in CAR.

The Minister of Health (MOH) put in place a rapid response team that included CAFELTP residents, MOH staff, staff from MSF, WHO, UNICEF, and others. The team came up with a series of prevention and control measures to stop the propagation of the outbreak: 1) enhancing cholera surveillance and treatment capacity at existing health facilities; 2) establishing cholera treatment centers in the city of Bangui and the affected villages ; 3) providing health education on general hygiene, improvement of sanitation, food preparation, funerals and burial practices; 4) advising affected people to use oral rehydration solution immediately and seek health care at the onset of watery diarrhea; 5) providing chlorine to treat drinking water. As of October 23rd, the rapid response team reported a total of 172 people who suffered from acute watery diarrhea and 16 cholera deaths. This investigation was conducted to identify risk factors associated with this outbreak, to assess the level of preparedness in the affected districts and to control the outbreak.

Methods

A. Epidemiologic Investigation

The CAFELTP resident advisors received an invitation to assist the Ministry of Health in Central African Republic in the investigation and control of the cholera outbreak. The CAFELTP residents were already part of the rapid response team that was working in the affected sites. One of the epidemiology residents was responsible for collecting and reporting data on the cholera

outbreak. The 2 lab residents were responsible for collecting and analyzing samples. The resident advisors (RAs) arrived in Bangui on Saturday October 22nd 2011, the 42nd epidemiological week (October 17 - 23, 2011). Upon arrival, the RAs were briefed by the CAFELTP residents and staff from the MOH on the situation on the ground and the evolution of the cholera. The CAFELTP residents and the RAs developed a protocol and data collection instruments. Drinking untreated water and lack of sanitation infrastructure, attending a cholera case funeral were hypothesized to be the main risk factors. Questionnaires were pre-tested at the Cholera Treatment Center in Bangui and Bimbo district. In-country procedures before going to the field were also followed (eg. submission of terms of reference, mission orders). During that time, several cholera awareness campaigns were taking place in various areas of the country including community education sessions and use of mobile Information Education Communication (IEC) materials that were displayed on cars, posters, radio, television and mobile phone prevention messages. The director of disease control conducted training sessions to health personnel in the affected districts on management of cholera in the clinics/hospitals and in the community. A review of the weekly notification records kept jointly by the World Health Organization (WHO) Bangui office and MOH identified 172 persons with diagnoses of suspected cholera, with a national case fatality rate of 9.3% for the period of September 20th to October 26th in the CAR. Information on the number of people infected with cholera was obtained from the WHO Bangui office, the health centers in the affected villages and cholera treatment centers coordinated by Medecins Sans Frontiers (MSF). The investigators used this information to perform a descriptive analysis of the cholera outbreak. A checklist was used to assess the level of epidemic preparedness and response in each district. An environmental investigation was carried out to assess the general hygiene in the affected areas. Water and stool samples were taken to the laboratory to be tested for vibrio cholerae.

B. Case-Control Study

CAFELTP trainees, along with the resident advisors conducted a retrospective frequency matched case-control study in Mbaiki district specifically in Zinga and Mongo villages from October 24 thru November 5, 2011. These two villages in this district were chosen because they were the most affected by cholera. Due to security issues, we were unable to expand the study to other affected sites. A questionnaire was developed that included demographic characteristics, symptoms, potential exposures (e.g., related to food, water, personal hygiene, and sanitation), funeral gatherings and knowledge of cholera prevention. Case-patients were identified through the register from the health centers. After identifying a case, investigators were accompanied to their residences by a member of the community or health personnel. Once a case was included in the study, the control was selected from the same community. Cases and controls were matched by age, sex and neighborhood. For the purposes of the study, a case was defined as illness in a person living in Zinga or Mongo villages aged two years or more who presented at the health center with acute watery diarrhea (with or without vomiting) since September 15, 2011. A control was any person who lived in one of the two villages who did not present any of the above mentioned symptoms in the three months prior to the beginning of the outbreak. Among those households with more than one case-patient, only the first ill person was enrolled in the study. Interviewers traveled to each case-patient's place of residence and matched each case-patient to one community control by age (within 5 years), sex, and neighborhood. Selected control residences were chosen randomly. Sample size was set to 37 cases and 37 controls in order to identify an odds ratio of 4.5 (for a risk factor on which intervention would have a significant impact), assuming 40% prevalence of exposure among controls, with an alpha risk of 5% and 80% power (3). Case patients and control subjects were asked for their age, gender, place of residence, and selected risk factors. Since we could only get 35 cases in the community, we increased the number of controls to 39 to keep the sample size at 74. Both bivariate (chi-square)

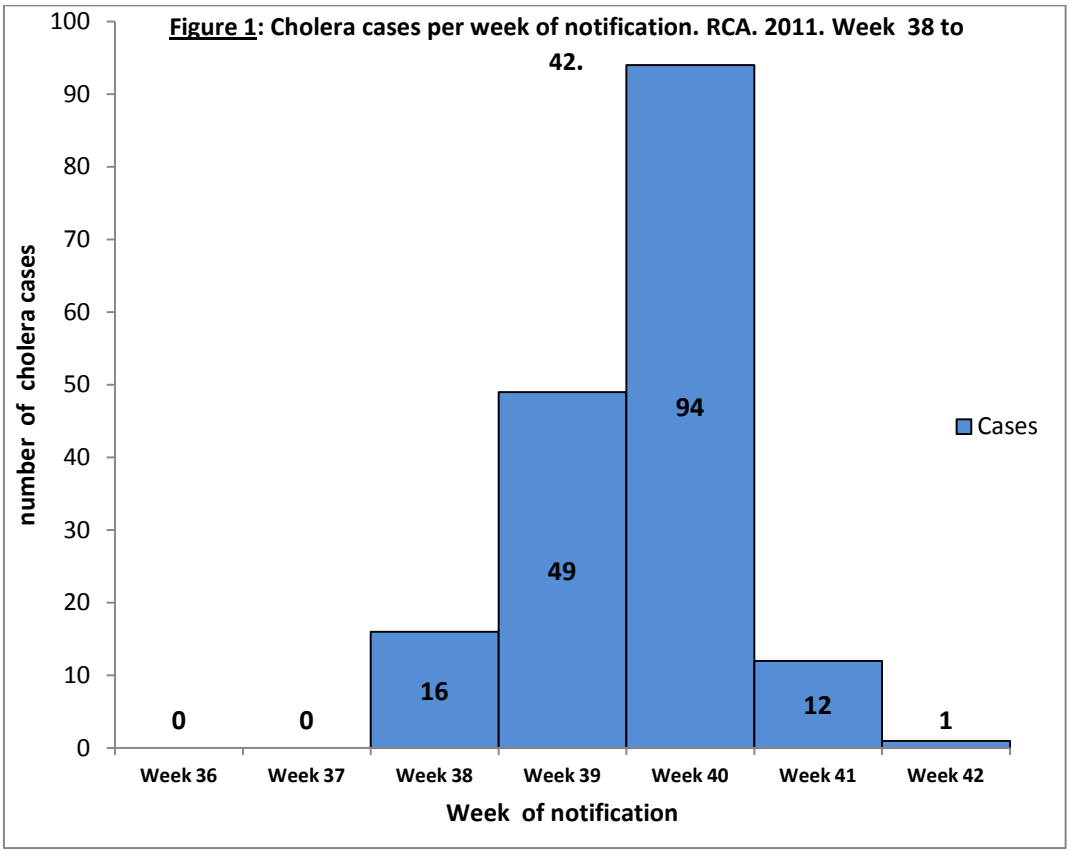
and multivariable analyses were performed. Stool results were obtained from the reports of the analysis done at the Institute Pasteur and the National laboratory of Public Health in Bangui.

Results

A. Descriptive epidemiology

1. Distribution of cholera cases and deaths per week

Cholera cases were notified from week 38, the number increased exponentially from week 39 to reach a peak in week 40 (October 3-9, 2011) before dropping sharply in week 41. Only one case was notified in week 42 (October 17 – 23). Figure 1 below summarizes the number of cholera cases per week of notification.



Distribution of cholera cases and deaths per district of origin

Only two regions (Region 1 and Region 7 (city of Bangui)) out of 7 regions were affected by the outbreak. Most notified cases were from Region 1, 159 (92.5%) out of 172. The prefecture (sub-

division) of Lobaye notified 126 (79%) out of 159 cases from this region. Mongo village was the most affected with 67(54%) cases out of 126, followed by Sédalé village 27(21%) cases, Ngbango 19(15%)cases, Sekia mote 17(13,5%) cases, Zinga 10 (8%) cases and Bimbo 7(6%)cases. The other villages had reported either 0 or less than 5 cases each for this period. Out of 8 arrondissements in Bangui, only six arrondissements in Bangui notified cholera cases. The most affected area in Bangui was the second arrondissement with 7 cases, followed by the eighth arrondissement with 2 cases. The other arrondissement notified one case each with the exception of the first and the fifth arrondissements. The two prefectures reported 8 deaths from each districts. The Case Fatality Rate (CFR) was 6.3% in Lobaye and 24.2% in Ombella Mpoko. The national CFR was 9%. Figure 2 below shows the affected villages.

Figure 2. Villages affected by the cholera outbreak in the Central African Republic in Sept. 2011

Distribution of cholera cases by gender

Women were more affected by the outbreak than men. Out of 172 notified cases, 90(52.5%) were women and 82(47,7%) were men.

Distribution of cholera cases by age group

The most affected age group was the under five age group (22%) followed by 5-9 age group (13%) and the 25-29 age group (13%) . The least affected age group was 35-39 and comprised 3% of all notified cases. Table 1. Below summarizes the distribution of cholera cases by age group.

Table 1. Distribution of cholera cases per age group

Age groups	Number of cases	Percentage
<5 yrs	37	22%
5-9	22	13,3%
10-14	16	9.7%
15-19	17	10.3%
20-24	14	8.5%
25-29	22	13.3%
30-34	9	5.5%
35-39	5	3.0%
40-44	8	4.8%
45-49	9	5.5%
50 +yrs	13	7.9%
Total	**172**	**100%**

Epidemic preparedness and response

None of the districts that we visited had an epidemic preparedness plan or an epidemic preparedness committee in place prior to the outbreak. The protective materials and IV fluids were provided after the occurrence of the outbreak. Although Mbaiki health district had a functional radio system for communication, the health centers in Mongo and Zinga villages did not have means of communication. They had to travel almost 35 Km by foot or bicycle to communicate with the health district. There was no epidemic management funds available in the country prior to the occurrence of the epidemic. Disinfectants were available at all health districts that we visited. The ministry of health distributed chlorine for water treatment in the two villages. Cholera treatment centers were erected at Bangui community hospital, Bimbo and Zinga health centers. They were still functional at the time of the visit and each had at least one patient with cholera. The public health surveillance system is run by one person in Zinga and Mongo village. The system was not evaluated prior to the occurrence of the epidemic.

Environmental Investigation

Most houses were built along the Oubangui River. The distance between those houses and the river was less than 20 meters. The general hygiene in the villages was poor. There were stagnant water and mud almost everywhere. Children were playing and walking in the mud with bare feet and at times not fully dressed. The use of pit latrine was common but most of these latrines were poorly maintained. The Oubangui River is used as a source of drinking water and for swimming, defecation and fishing.

B. Laboratory Results.

We only obtained the results for 7 stool samples that tested positive for *vibrio cholerae* sero-group 131. The rapid control team did not keep the results for stool samples that tested negative for vibrio cholerae. Samples of water were collected by the 2 CAFELTP laboratory residents (1st

Cohort) to analyze for possible contamination with vibrio cholerae sero-group 131. Results of the water samples revealed only the presence of Shigella and E.coli.

C. Analytic epidemiology

The mean age of both case-patients and controls was 23 years (range: 2 - 65 years for cases and 3 - 67 for controls); 2% of case-patients and 1% of controls were aged <5 years. Other symptoms included vomiting, fever, and leg cramps. Half of the case-patients presented with severe dehydration (self reporting). Treatment consisted of oral fluids, tetracycline, doxycycline, and intravenous fluids and varied among case-patients. All the case-patients received oral fluids.

The unadjusted matched analysis (Table 2) indicated that persons who ate cold cassava leaves (one of the step foods in the region. Odds ratio (OR) = 3.07; 95% Confidence Interval (C.I) = [1.155; 8.163]; P = 0.020) were at greater odds of having cholera. The association was statistically significant at $P < 0.05$. Drinking water from the Oubangui river (OR=1.16, 95% C.I = [0.415 ; 3.239] P= 0.983); drinking water sold on the street (OR = 0.25, 95% C.I= [0.027 ; 2.421] P= 0.422); eating hot cassava leaves (OR= 0.57, 95%CI= [0.090 ; 3.669] P= 0.900); and attending funerals from September 2011 (OR= 0.56, 95% C.I= [0.192 ; 1.643] P= 0.627) were not associated with having cholera. No significant associations were observed between cholera and the hygiene related factors like washing hands after using the toilet 0.85 [0.295 ; 2.493] P=0.395, Washing hands before eating (OR=1.05,[0.318 ; 3.512] P=0.466). The risk factors are summarized in Table 2.

Table 2. Risk factors for Cholera in Mbaiki District

Risk factors	Odds ratio	95% Confidence interval	P values
Drinking water from the Oubangui river	1.16	[0.415 ; 3.239]	0.983
Drinking water sold on the street	0.25	[0.027 ; 2.421]	0.422
Eating cold cassava leaves	3.07	[1.155 ; 8.163]	0.020
Eating hot cassava leaves	0.57	[0.090 ; 3.669]	0.900
Attending funerals from September 2011	0.56	[0.192 ; 1.643]	0.627
Washing hands after using the toilet	0.85	[0.295 ; 2.493]	0.395
Eating outside	0.66	[0.259 ; 1.713]	0.206
Eating dried meats	0.45	[0.184 ; 1.208]	0.062
Eating fresh meats	0.41	[0.143 ; 1.228]	0.060
Eating hot smoked fish	0.83	[0.328 ; 2.111]	0.354
Eating cold smoked fish	0.89	[0.360 ; 2.235]	0.410
Washing hands before eating	1.05	[0.318 ; 3.512]	0.466

Discussion

The outbreak caused several deaths in the district. The highest case fatality rates recorded in this outbreak was 24.2% in Ombella mpoko, which was much higher than the national rate of 9%. Interventions by the ministry of health assisted by different partners in putting in place cholera treatment centers in affected villages yielded useful results. The cholera outbreak in Mbaiki district, Central African Republic in which more than 170 cases and 16 deaths were reported was

associated to food borne risk factors. The case-control study identified a significant association between eating cold cassava leaves and cholera. Epidemiological evidence from Zambia showed that contaminated food was a major vehicle of transmission of cholera during an outbreak (4). An asymptomatic but infected person could inoculate Vibrio cholerae into cooked food after preparation. While the source of contamination of the cassava leaves may vary and could not be determined by this study, previous studies have shown that food can be contaminated through soiled kitchen ware, where Vibrio cholerae can persist for 1 – 2 days (5). Another finding in this study is the lack of significant associations between cholera and water-related risk factors. Direct waterborne transmission played an insignificant role in these villages. In other previous studies, consumption of water sold on the street was associated with cholera during previous outbreaks in Latin America (6) (7) (8). This study also provides the epidemiological information that rules out the association between drinking untreated water, lack of sanitation and attending cholera cases funerals in the district and cholera. Houses in both villages are located a short distance from the river. It is a potential risk for waterborne diseases especially in case of floods. Although it was not evidenced in this study, consumption of untreated water has proven to be a risk factor for cholera in many previous studies. The use of untreated water from the Oubangui river as a source of drinking water should be discouraged. The delay in the analysis of stool sample needs to be avoided, because it can lead to the delay in the confirmation of the outbreak and the implementation of control measures. In this case, the delay was due to the fact that the case occurred out of the city of Bangui. The Bangui National Laboratory did not have transport media to collect stool specimens from cases occurring outside the capital city. It is critical to have the necessary materials at hand during an outbreak. The availability of an epidemic preparedness plan and committee in the districts leads to timely and effective management of the outbreak. The management of the public health surveillance system by only one person in the district may not work efficiently for the detection of the majority of public health threats.

Conclusion and recommendations:

The cholera outbreak in the Central Africa is still ongoing; however the current situation is much less severe than three weeks ago. The case-control study identified a significant association between eating cold cassava leaves and cholera. The outbreak affected only region1 and region 7. The most affected people were under 10 year-old children and women living in villages located along the Oubangui river. The lack of laboratory transport media at the National Laboratory delayed the confirmation of the outbreak. The implementation of the prevention control measures like establishment of cholera treatment centers, health education on general hygiene and good food and funeral practices, treatment of drinking water and others proved to be effective. We recommend that:

- The districts continue with health education and social mobilization on eating habits, personal and community hygiene, sanitation and burial practices.
- Districts strengthen the public health surveillance system
- Districts promote the use of eating hot food.
- The Ministry of Health supports each health district in developing a functional epidemic preparedness and response committee and a clearly defined epidemic preparedness and control plan as soon as possible.
- The Ministry of Health and the Ministry in charge of water ensures that the population has access to potable water.
- Laboratories acquire basic laboratory materials to avoid delay in confirmation of outbreaks. Efforts should be made to collaborate with the local Institute Pasteur before, during, and after the epidemic.
- The districts should strengthen their surveillance system to be able to detect outbreaks and notify others in a timely manner.

Constraints and limitations.

This study was conducted during a particularly busy period. The resident advisors could not be with the residents at the investigation site for the full duration of the investigation due to delay with in-country procedures. Hence, all administrative documents were obtained 3 days after arrival in Bangui. The study had other limitations. Controls were not tested for serological evidence of recent cholera infection. Because some cholera patients may remain asymptomatic for the duration of the infection, controls might have been misclassified despite the fact that they did not have diarrhea during the epidemic. This kind of misclassification would lead to findings towards the null hypothesis. Finally, we could not accurately establish the difference in the economic status between patients and their controls in this study. It is possible that subtle differences may have existed between the two categories despite neighborhood-matching.

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Ms Marceline Djeintote (Lab) is interviewing a case in Zinga Village.

Dr Joachim Tembeti (EPI) – Right, and Mr Augustin Balekouzou (Lab) – Left, interviewed a father who had cholera.

Dr Alain Penguele (EPI) interviewed a young lady who had cholera

Investigation team (Resident Advisors, Residents, and a Surveillance Officer).

This is latrine used in Zinga district, around this hole is human stool.

Members of the investigation team crossing the Lobaye river.

This picture showcases the distance between the Oubangui River and the houses.

Members of the investigation team in Zinga village.

Mud outside a house in Zinga village.

Cholera Treatment Center in Zinga village.

Mud outside a house in Zinga village.