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Linköping University Post Print

N.B.: When citing this work, cite the original article.

Original Publication:
Copyright: WB Saunders http://www.elsevier.com/
Postprint available at: Linköping University Electronic Press http://urn.kb.se/resolve?urn=urn:nbn:se:liu:diva-120614
Twenty-one days of isolation: A prospective observational cohort study of an Ebola-exposed hot zone community in Liberia

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Received 9 May 2015
Available online 14 May 2015

Summary Background: As West Africa continues to suffer from a deadly Ebola epidemic, the national health sectors struggle to minimize the damages and stop the spread of disease. Methods: A cohort of inhabitants of a small village and an Ebola hot zone in Sinoe County of Liberia was followed on a day-by-day basis to search for new cases and to minimize the spread of Ebola to the other community members or to other regions. Technical, clinical, and humanistic aspects of the response are discussed in this report. Results: Of the 22 confirmed Ebola cases in Sinoe County since the beginning of outbreak (June 16, 2014), 7 cases were inhabitants of Polay Town, a small village 5.5 miles east of Greenville, the Sinoe County capital. After the last wave of outbreak at the beginning of December, enhanced response activity provided essential coordination and mobilized the resources to stop the epidemic. Despite unprotected contacts in crowded houses, no new cases were detected among the contact families, or in the surrounding houses or communities.
Introduction

The Zaire strain of the Ebola virus (EBOV), a highly virulent pathogen from the family Filoviridae, is currently responsible for one of the worst Ebola outbreaks in West Africa. This is the 25th outbreak since the discovery of this disease in 1976 when 318 cases of acute viral hemorrhagic fever occurred in northern Zaire. The index case in this outbreak had onset of symptoms on 1st September 1976, five days after receiving an injection of chloroquine for presumptive malaria at the outpatient clinic at Yambuku hospital. The disease was secondary spread to the people who had contact with the patients.

A contact person to EBOV is one who has had exposure to the blood and body fluids of persons with Ebola but has not yet exhibited signs and symptoms of the disease. Among contacts, one is considered infected and contagious once the body temperature reaches 38°C warranting isolation. If the presence of virus is verified by PCR analysis of blood or oral swabs the case is considered as confirmed. If there is no body temperature increase during the incubation period (2–21 days), the contact person can be declared “free of Ebola” on the 22nd day. Exposure that was most predictive of risk for secondary transmission was direct physical contact with an ill family member either at home in the early phase of illness or during the hospitalization. The viral load level of EBOV varied during the course of infection. Survivors of EBOV had persistent serum neutralizing activity and IgG immunoreactivity against the viral protein GP1,6,49 12 years after infection, and this protein stimulated high levels of cytokine expression after whole-blood stimulation.

The current Ebola outbreak originated in Southeast Guinea, bordering Liberia and Sierra Leone. It began in December 2013, but was not initially recognized by healthcare workers. Liberia’s capital, Monrovia in Montserrado County, has been severely affected by Ebola viral disease (EVD).

Vaccines to prevent EBOV are not yet available. The response has involved an immediate rapid scaling up of currently available non-pharmaceutical intervention strategies, intended to minimize the occurrence of new EVD cases and death and to maximize the effectiveness of EVD treatment centers (ETU). The WHO issued a call for infection control professionals to work in affected countries. In August 2014, the WHO concluded that the use of unproven medical treatments was ethical in the circumstances of the Ebola outbreak. A national mobilization effort was initiated at the county level.

A longitudinal study is a research study that involves observations of the same items over long periods of time. The longitudinal studies track the same people, and therefore the differences observed in those people are less likely to be the result of genetic or cultural differences. Because many longitudinal studies are observational, it means that it cannot be strongly manipulated.

In the course of deadly epidemic and due to limited resources all efforts are focused on inhibiting the disease and treating the patients. Therefore the majority of studies are performed retrospectively based on available reports and by other scientists than the people who had conducted the response. Important information might therefore be missing. This report is a prospective day-to-day observation of a community in which all of the cases and contacts from a secondary outbreak were inhabited. The report documents the course of the outbreak, response activities, and outcomes in this EBOV-exposed community in Sinoe County.

Settings and methods

Sinoe County

Sinoe County (5°20′N 8°40′W), located in the Southeastern region of Liberia (Fig. 1), is a rural area of 10,137 km² with a population of 116,715. The climate is moist equatorial, and the region’s main economic activities include agriculture, fishing, wood industry, and small-scale mining. The capital of Sinoe County is Greenville, which lies on a lagoon near the Sinoe River and the Atlantic Ocean. Greenville is located about 150 miles southeast of Monrovia, and the two cities are connected by a road that takes 8 h to travel and is almost impassable during rainy weather. Roads and footpaths in the city are severely eroded. Most homes lack domestic water or sewage systems, and get electricity from private gasoline generators. Most families keep goats, sheep, chickens, and other domestic animals. Many species of wild birds are common, and hundreds of bats fly through the city during the day and late in the evening.

The County Director of Health Services in Greenville heads the Sinoe County health system. Sinoe County has 17 administrative districts, and is divided into 10 health districts and 306 communities. The county is served by a single hospital (F.J. Grante Hospital) and 33 clinics, which employ 2 medical doctors, 18 physician assistants, and 67 nurses. The hospital has capacity of 100 beds. However, only the emergency and obstetrics wards were in use during the epidemic.

At the start of the epidemic in Sinoe County, an Ebola treatment unit (ETU) tent with four beds was temporarily set up in the backyard of the hospital. As of September, 2014, this ETU served as an isolation and treatment unit for suspected and confirmed cases of Ebola in the county (Fig. 2). A station where the medical staff changed to personal protective equipment (PPE) was located in a corridor connected to the surgical department, with a
door that opened to the backyard and five stairs leading to the yard. The medical staff walked approximately 25 m through the open yard to enter a tent of $5 \times 4$ m$^2$ in which EBOV patients were isolated and treated. No physical barriers separated the red zone from other parts of the hospital area. The medical staff used the same door to exit to the yard, where they were sprayed with 0.5% chlorine, removed their PPE, and washed their hands in a bucket containing 0.05% chlorine outside the tent before walking back to enter the hospital. Patients who had the strength could sit or walk in the area outside the tent. No latrines or domestic water supply were available for the ETU. Electricity was supplied during the late evening and night.

EBOV diagnosis was performed by semi-quantitative RT-PCR. Specimens from suspected EBOV patients were safely collected by a laboratory technician and were sent by motorcycle to Monrovia. Results were obtained within 48 h during the week.

Polay Town

Polay Town is a village located by the Dugbe River, 5.5 miles east of Greenville. Traveling between Greenville and Polay Town takes approximately 2 h by car. Polay Town has 342 inhabitants, of which 101 are children under the age of 10. The town includes 44 houses located 18–20 m from each other, and mostly built of mud, wattle, and bamboo tree, with thatched or corrugated iron roofs. The town also includes an assembly hall where the community members gather, and a school that was closed at the time of observation. Cassava, maize, and other staples are grown on many small subsistence plots.

Data sources and methods

Surveillance records include Ebola treatment unit (ETU) reports as well as our own observations during response activities. The national task force for the Sinoe County Ebola outbreak authorized data collection and publication. No additional ethical approval was necessary, since we used data routinely collected in an emergency situation. Patients, relatives, and healthcare workers were informed that the report would be published and that their privacy would be respected. The Ministry of Health granted permission to publish the data.

Results


A total of 22 confirmed cases (including 12 female patients) and 5 Ebola transmission clusters were identified and followed in Sinoe County. The most common general symptoms at admission were intensive fatigue, fever, and appetite loss. No cases showed signs of non-vaginal bleeding. The case fatality rate (CFR) for hospitalized EVD cases was 47.3% (22% for males and 78% for females). None of the medical staff working at the ETU in Sinoe County became infected with EVD.

Onset of secondary outbreak in Polay Town (Fig. 1)

The index case was a 21-year-old woman who became sick in Niplikpo, Jloh (Grand Kru). She was in contact with her 3-year-old relative who then became sick and was cared for by his father who took him home to Polay Town. The child’s 51-year-old grandmother brought the boy to the ETU where EBOV was confirmed. He died on November 13, 2014. The grandmother returned to Polay Town and then disappeared. On November 29, 2014, the grandmother was reported dead in a house in the middle of Polay Town near the community assembly hall. The burial team arranged a safe burial. The EBOV test was positive.

On December 8, 2014, the 39-year-old father of the child, his 29-year-old pregnant wife, and an 8-year-old daughter...
who had taken care of the grandmother became sick. Within one day after debut of fever, they were transferred to the ETU where EBOV was confirmed in all three cases. The wife breastfed her symptom-free 1-year-old son, until the child was separated from the mother and cared for by a 40-year-old female survivor at the empty pediatric ward at the hospital. The community had concealed a related 17-year-old woman. She developed fever and diarrhea and was admitted to the ETU on December 11th where EBOV was confirmed. Her 13-year-old sister disappeared. At this point, national and international resources were mobilized to intensify the response to the outbreak.

Outbreak response cooperation

The Sinoe Ebola Task Force (SETF)—chaired by the Superintendent and co-chaired by the County Health Officer—coordinated the overall EVD response in the county. The SETF met twice a week, and included all stakeholders in the county, including traditional leaders, youth and women groups, and partner organizations. An Incident Management Team (IMT) was headed by the Sinoe County Health Team, and included partner organizations working in the county EVD response. The IMT had daily meetings (Monday—Friday) to discuss the latest news about activities and international support. Meeting reports were documented digitally and mailed to the attending groups.

Response

The number of cases exceeded the capacity of the hospital ETU. The rapid spread of disease among the family members in Polay Town motivated an accelerated response to achieve the following goals: 1) secure an isolation center with capacity for EVD cases and a safe environment for the medical staff, 2) overcome the fear, panic, and mistrust in the community, 3) identify and quarantine contacts within the community, 4) enact professional triage and differentiate between cases of Ebola and other diseases, 5) facilitate communication and immediate transfer of suspected cases to the ETU, 6) create a mobile diagnostic facility in Greenville, and 7) observe and document the course of the epidemic on a daily basis.

During the week of December 12–20, 2014, a temporary ETU (Fig. 3) was established at the football field in Greenville, using tents with a total capacity of 10 patients. This project was supported by partners and technical consultation with Medecins Sans Frontieres (MSF). A mobile diagnostic facility was established, which started analyzing samples on December 23, 2014. An ambulance was prepared to transfer suspected EBOV cases to the ETU.

A team of six contact tracers and two contact tracing supervisors was deployed to the area to conduct daily contact tracing, temperature monitoring, and active case searches. The teams contacted the village chief, and enlisted support for house-to-house surveillance. The entire community was divided into four blocks to facilitate daily active case searches. The name of each family head, and the name, sex, age, and presence/absence of each family member in Polay Town were recorded daily. Two members of the contact tracing team were assigned to each block. A supervision and monitoring team from Greenville, comprising the County Health Team and other partners, visited the town daily to monitor the work of the contact tracers and to continuously engage the community residents. A physician monitored the team with frequent field visits and administrative reviews (Fig. 4).
Food was regularly provided to all contacts and to the rest of the community throughout the duration of the follow-up. Meetings were regularly held with the community to communicate information about the EVD status and deaths of patients isolated from the community, as well as to reintegrate survivors who recovered and contacts who completed 21 days of follow-up. The psychosocial team provided regular psychosocial services to the bereaved families and the entire community. Ongoing house-to-house awareness activities and social mobilization activities were conducted to reduce stigmatization and sensitize the community. Soaps, chlorine, and buckets were distributed to all households, and the use of chlorine solutions was monitored throughout the community.

Events

The one-year-old child developed fever on December 16, 2014. His EBOV test was negative and his temperature decreased to normal after anti-malaria treatment. The child was kept at the hospital near the mother. The 8-year-old daughter and the 17-year-old relative died at the ETU. The 39-year-old male patient and his wife were transferred to the new temporary ETU on December 20, 2014.

A 60-year-old grandmother, who had taken care of the 17-year-old relative while she was hidden, developed depression and refused to eat for one week. She fainted on December 22, 2014. She had no fever or other symptoms, but was extremely weak. The psychosocial team had several sessions counseling her. On December 25, she developed fever and diarrhea and the ambulance was sent directly to her place, but she strictly refused to be transferred to the ETU. The next day, she became worse with vomiting and frequent diarrhea, and local authorities and family members successfully convinced her to go to the ETU. Blood testing revealed a high EBOV viremia. She died on December 29, 2014. On the same day, her son, daughter-in-law, and the one-year-old grandson returned home to Polay Town.

Figure 3  The temporary ETU at the football field.

Figure 4  The contact child with ulcer on the foot is being treated by the uncle under supervision of Medical staff.
A total of 41 contacts were identified in three households. Twenty contacts were released on January 3, 2015. In 21 cases, the isolation period was prolonged to January 16, 2015. During the last five days of isolation, the ambulance was in the nearby village of Karqueckpo. No other cases of EBOV were observed in the contact family or surrounding households. All contacts were released on January 17, 2015. No other new confirmed cases from Sinoe County were isolated at the ETU (Table 1).

Case management

The chief medical doctor at the hospital was the physician in charge of the ETU at the F.J Grante hospital, as well as the temporary ETU at the football field in Greenville. The hospital staff wore PPE when caring for suspected or confirmed cases, in accordance with WHO guidelines. Therapy included oral rehydration/intravenous fluid therapy, analgesics, oral/intravenous antibiotics, and blood transfusion from survivors. Among the confirmed cases in Polay Town, five patients were admitted to the ETU. Two patients survived. The 39-year-old man recovered from symptoms within a few days and helped the other members of his family at the ETU. His pregnant 29-year-old wife experienced vaginal bleeding that resulted in miscarriage after admission. She suffered from diarrhea and extreme weakness. The pH of loose feces was in the normal range (5–6), excluding a bowel translocation and septicemia. She received intravenous fluid therapy and blood

<table>
<thead>
<tr>
<th>Date</th>
<th>Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dec. 9, 2014</td>
<td>Three suspected EVD cases and a child were transferred to the ETU at F.G. Grante Hospital.</td>
</tr>
<tr>
<td>Dec. 11, 2014</td>
<td>Three cases were confirmed as EBOV. A hidden 17-year-old relative was transferred to the ETU.</td>
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<tr>
<td>Dec. 13, 2014</td>
<td>Active case tracing was initiated in Polay Town together with partners. The community was divided into 4 blocks.</td>
</tr>
<tr>
<td>Dec. 15, 2014</td>
<td>The 8-year-old patient died in the ETU. She suffered from fatigue, vomiting, and diarrhea. The contact family members were informed at Polay Town.</td>
</tr>
<tr>
<td>Dec. 16, 2014</td>
<td>The one-year-child developed fever, and a blood test was performed.</td>
</tr>
<tr>
<td>Dec. 17, 2014</td>
<td>The EBOV test in the one-year-old child was negative. The temperature normalized after malaria treatment. The pregnant EVD patient experienced miscarriage, vaginal bleeding, and constant diarrhea.</td>
</tr>
<tr>
<td>Dec. 18, 2014</td>
<td>Blood transfusion was performed on the woman at the ETU.</td>
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<tr>
<td>Dec. 19, 2014</td>
<td>The 17-year-old EVD patient died after a short period of acute abdominal pain. The family members and community were contacted.</td>
</tr>
<tr>
<td>Dec. 20, 2014</td>
<td>Two patients were transferred to the ETU at a football field. Information was provided to the community and a meeting was held.</td>
</tr>
<tr>
<td>Dec. 22, 2014</td>
<td>A 60-year-old grandmother in the contact family fainted. She had no fever. An ambulance was sent to her home and triage begun.</td>
</tr>
<tr>
<td>Dec. 23, 2014</td>
<td>Contact family members were examined for symptom, including follow-up of ulcers in children. A mobile laboratory and the US navy were in function in Greenville.</td>
</tr>
<tr>
<td>Dec. 24, 2014</td>
<td>Two patients at the ETU recovered. Blood tests were analyzed for EBOV, and the results were negative. A meeting with the community was held.</td>
</tr>
<tr>
<td>Dec. 26, 2014</td>
<td>The 60-year-old grandmother developed symptoms and after meeting with her opposition, she was transferred to the ETU. She was highly positive for EBOV.</td>
</tr>
<tr>
<td>Dec. 27, 2014</td>
<td>A meeting was held with the contact family for psychological support, and evaluation of reactions and follow-up of the other treatments.</td>
</tr>
<tr>
<td>Dec. 28, 2014</td>
<td>Sanitization of the grandmother’s house and body wastes were monitored. Information was provided to the community about survivors.</td>
</tr>
<tr>
<td>Dec. 29, 2014</td>
<td>The ETU personnel’s strike over delayed payments was resolved. The patients (now survivors) and their child—followed by several partners and supplied with a discharge packet—returned to Polay Town. The 60-year-old grandmother died at the ETU. A meeting with the community was held and support provided to the family.</td>
</tr>
<tr>
<td>Dec. 30, 2014</td>
<td>A meeting was held with the contact families, and psychosocial support provided to the family members.</td>
</tr>
<tr>
<td>Jan. 2, 2015</td>
<td>A meeting was held with the community, including a discussion about mistrust of the contact tracers.</td>
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<tr>
<td>Jan. 3, 2015</td>
<td>Twenty contact persons were released from quarantine. A meeting was held with the community together with the released contacts.</td>
</tr>
<tr>
<td>Jan. 5, 2015</td>
<td>A visit to the new Community Care Centre under construction at Karqueckpo.</td>
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<tr>
<td>Jan. 8, 2015</td>
<td>One contact who had left the community to visit a relative in a nearby village was delivered back to Polay Town.</td>
</tr>
<tr>
<td>Jan. 12, 2015</td>
<td>The ambulance was located at Karqueckpo to provide a rapid response to contacts during the last days.</td>
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<tr>
<td>Jan. 17, 2015</td>
<td>All partners traveled to Polay Town to assist with re integrating the last 21 contacts who were completing their 21-day monitoring process. No EVD cases had been found at the ETU since Dec. 29, 2014.</td>
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transplant and recovered. Deceased patients with EVD were buried at the EVD cemetery in Greenville using barrier nursing conditions.

Discussion

In the present work, we followed an EBOV-exposed community on a day-to-day basis and prospectively observed the course of the epidemic and the outcomes. The disease had spread rapidly among five family members who had taken care of patients. However, the organized and regular response activity limited further transmission.\textsuperscript{18,22}

The Ebola virus belongs to the Filoviridae family, and occurs as the Zaire, Sudan, Reston, and Co\’Ate d’Ivoire subtypes.\textsuperscript{1,23} The viral envelope glycoprotein (GP) plays a role in EBOV pathophysiology.\textsuperscript{10} Although not thoroughly studied, EBOV is quite susceptible to detergents and other antiseptics. We observed how the adults cared for the infected 60-year-old grandmother, touched her, gave her food, and supported her when she had diarrhea and probably had a high virus load in her blood at least one day before she was transferred to the ETU.\textsuperscript{24} On several occasions, this family was observed to practice frequent washing and disinfection of hands after touching surfaces.

Additionally, several children suffered from infected open ulcers on their feet and played near the infected 60-year-old woman. Regarding to the role of humoral immunity in the survival of EVD cases, active immunization after exposure to inactivated virus in the environment or an asymptomatic infection in contacts might play a role in limiting further transmission. It has also been reported that young children were not as frequently infected as adults in EBOV epidemics.\textsuperscript{25}

Humans can be infected with Ebola virus without developing symptoms. These asymptomatic individuals produced specific IgM and IgG, starting 2–3 weeks after initial exposure to infected body materials. EBOV RNA was detectable in the white blood cells of these subjects for up to 3 weeks after their initial exposure. However EBOV PCR results in blood were negative and these individuals could not transmit the disease.\textsuperscript{26–29} Convalescent whole blood containing neutralizing immunoglobulins has been used for Ebola treatment.\textsuperscript{30,31}

The response activity in Polay Town met with serious challenges, including rumor circulation, mistrust, and fear in the community. Two patients were hidden and the actual number of contacts was not disclosed. Without regular provision of information to the public, there are bound to be deleterious rumors. Implementation relied heavily on open, frank, and frequent discussion of the epidemic in the local language at community meetings; and on being available and prepared for questions and sharing valuable occasions with the community members.

Lessons learned

Working in a wide-spreading and deadly epidemic presents a valuable opportunity for medical staff and scientists to see how the difference between death and survival hinges on strict biological regulations. Investigation and recognition of the characteristics of pathogens in an environment, and disseminating this knowledge to health workers and community members in an organized and cooperative manner is enormously important in overcoming challenges, stopping the course of an epidemic, and saving human resources.

Conflicts of interest

There is no conflict of interest.

Acknowledgements

We sincerely acknowledge the contributions from all the organizations, institutions, professionals, health care workers, and political and civic leaders as well as the support from the international and local communities whose efforts contained this epidemic. We are especially grateful to Professor Hans Rosling for the valuable support and to Simson Wiah, Oliver Jah, Benjamin Karmo and Lelebor Gornor-pewu.

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