



Changing Epidemiology of West Africa Ebola Outbreaks 1994-2014

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Authors' contributions

This work was carried out in collaboration between both authors. Author JBK designed the study, wrote the protocol and the first draft of the manuscript. Author MK managed the literature searches and reviewing. Both authors read and approved the final manuscript.

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ABSTRACT

The severity, epidemic duration and general epidemiology of viral epidemic depends on determinants such as viral strain, ecological, environmental and socioeconomic factors. The West Africa Ebola outbreaks in Guinea, Sierra Leone and Liberia in 2014 and in Ivory Coast, Liberia and Gabon in 1994 were reviewed and compared because of their similarity in terms of their geographic location, proximity to each other, pre-outbreak Preparedness status, mortality, epidemic duration, as well as access to international health aid by the affected countries. Data for this study were obtained from the health ministries of Sierra Leone, Guinea, Gabon and Liberia, the United States Center for Disease Control and Prevention (CDC), the World Health Organisation (WHO) published data on Ebola virus disease outbreaks in Guinea, Liberia, Gabon, and Sierra Leone. Sierra Leone recorded its first confirmed Ebola outbreak in 27th May 2014. Both Guinea and Liberia recorded confirmed Ebola outbreaks in March 2014. The 2014 Ebola outbreak in West Africa has a long epidemic duration compared to the 1994 and 1996 outbreaks in Ivory

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Coast and Gabon respectively partly because of the misdiagnosis of earlier cases and the poor containment measures of the 2014 Ebola outbreak.

Keywords: Ebola; infection; mortality; hemorrhagic; outbreak, containment.

1. INTRODUCTION

The first outbreak of Ebola occurred in 1976 in the Democratic Republic of the Congo and Sudan; more than 600 cases were reported and 15 documented observations were made [1]. Almost all Ebola outbreaks are African in origin except for the Ebola-Reston outbreak in United States [2]. The natural reservoir of Ebola virus still remains unknown, but primates native to Africa are generally regarded as the prime suspects [3]. Primary contact for Ebola is usually initiated through blood contact with an infected primates but secondary infection which account for majority of Ebola cases during outbreak occurs from person to person transmission through contact with contaminated body fluids [3].

The incubation period for Ebola Hemorrhagic Fever (EHF) disease in humans is 4–10 days [3]. Signs and symptoms usually involve fever, headache, weakness, and other flulike symptoms that generally lead to rapid health deterioration. The most severe cases of Ebola Viral Disease (EVD) involves internal bleeding and the appearance of small reddish rashes over the body. Deaths from EVD cases occur 6–9 days after the onset of symptoms and is usually due to shock syndrome following the dysfunction of the vascular system and internal body tissues injury [4].

Ebola has a high case fatality rate of 90% in some cases [2]. The infectious agent is an RNA virus belonging to the *Filoviridae* family. According to the Center for Disease Control and Prevention (CDC) five subtypes exist; Ebola-Zaire, Ebola-Sudan, Tai Forest Virus (TAFV), Ebola-Bundibugyo and Ebola-Reston [2]. Ebola-Zaire, Ebola-Sudan, (TAFV) and Ebola-Bundibugyo are known to affect humans. Ebola-Reston affects non-human primates [4].

The EVD outbreaks in Democratic Republic of Congo and Uganda in 2010 were caused by Ebola-Zaire and Ebola-Sudan strains respectively. Ebola-Zaire strain is the most virulent and contagious with a case fatality rate ranging from 44%-90% [5].

2. REVIEWS

We reviewed documented cases of the 2014 West Africa Ebola Disease (EVD-2014) outbreak in Sierra Leone, Guinea and Liberia, and the 1994 Ebola outbreaks (EVD-1994) in Ivory Coast, Gabon and Liberia and the 1994 Ebola outbreaks (EVD-1996) in Gabon in terms of mortality, outbreak duration, viral strain, transmission pattern, outbreak containment measures, and clinical presentations. Most human clinical studies of EVD cases are done retrospectively considering the virulence of the infection. Only one human Ebola case has been rigorously studied [6].

Data for this study were obtained from the health ministries in Sierra Leone, Guinea, Gabon and Liberia, the United States Center for Disease Control (CDC). We also reviewed World Health Organisation (WHO) published data on the 2014 and 1994 EVD outbreaks in Guinea, Sierra Leone, Liberia, Gabon and Ivory Coast, medical correspondences of Medicine Sans Frontier (MSF) relating to previous Ebola outbreaks, and scientific publication on the 2014 EVD outbreak by Jean Mérieux-Inserm BSL-4 Laboratory, Lyon and the Institut Pasteur based in Paris in France.

We used February 2014-June 2014 as our review period for the EVD 2014 outbreak though the epidemic was still ongoing during the time of publication. The first suspected case for EVD-2014 outbreak was a 2-year-old boy who died in Meliandou, Gueckedou prefecture in Guinea on December 2013 [7]. This case was not indexed although the deceased had all the signs and symptoms of Ebola prior to his death. We also reviewed the medical history of 15 EVD-2014 patients from Guinea, one EVD-1994 patient from Ivory Coast and Liberia, and 15 patients from Gabon. Gabon though not in West Africa was included for reviewed in this study because it is the nearest country to West Africa to have experienced ebola outbreak. Gabon has so many sociocultural characteristics including language and ethnic groups similar to the West African countries (See Fig. 1) that have experienced Ebola outbreak.



Fig. 1. Countries in West Africa affected by the 2014 Ebola outbreak
 Source: Center for disease control and prevention, USA

The initial diagnosis of patients for EVD-2014 was done by researchers in France attached to Jean Mérieux-Inserm BSL-4 Laboratory, Institute Pasteur and clinicians working at the Metabiota Laboratory in Sierra Leone. Viral strain identification of EVD-2014 was by full-length genome sequencing and phylogenetic analysis [8].

The clinical presentations reviewed in this study include but not restricted to gum bleeding, petechia, hematemesis, melena. Other nonspecific clinical presentations but consistent symptoms such as high fever, myalgia, headache, and nausea were also reviewed. Abdominal pain and diarrhea which are often regarded as the predictive signs for EVD were also noted.

We also use clinical and demographic data for 15 EVD-2014 patients from Guinea whose laboratory test results were published as part of a preliminary scientific findings during the investigation of EVD-2014 [8]. No informed consent from patients whose clinical and demographic data were reviewed was sought by the principal investigators since their work was performed as part of a global public health response to contain the outbreak of EVD-2014 [8].

2.1 Guinea

Guinea is the epicenter for the EVD-2014 outbreak and was the first country in the region to have initially reported confirmed cases of EVD-2014 in four southeastern districts: Guekedou, Macenta, Nzerekore, and Kissidougou on the 25th March 2014. On the 26th March 2014 initial virological investigations identified the pathogen responsible for EVD-2014 to be of a clade of the Ebola Zaire previously identified in the Democratic Republic of Congo and in Gabon [8]. Prior undocumented reports from Guinea had earlier linked an earlier death of a young boy from an undiagnosed disease with signs and symptoms similar to the Ebola in December 2013 [7].

The cumulative morbidity and mortality for the West Africa EVD outbreak for Guinea for the period March 2014-June 2014 was 390 and 270 respectively [9]. Part of Guinea's Ebola response include the activation of its national health emergency committees and creation of an Ebola surveillance and response team to carry out disease surveillance, case tracking and monitoring, as well as response needs assessments. Guinea's Ebola outbreak response initiative also involves the deployment of the European mobile laboratory consortium capable of performing molecular viral diagnosis of pathogens in risk group 3 and 4 categories.

2.2 Sierra Leone

Sierra Leone reported its first confirmed EVD outbreak on 27th May 2014 with morbidity and mortality of sixteen and five respectively [9]. Prior to the Ebola outbreak Sierra Leone's state of preparedness for an EVD outbreak was non-existing. EVD-2014 was the country's first experience. The country's EVD response involves the formation of an Ebola technical task force with the objectives of surveillance, case identification, EVD case tracking and monitoring. The EVD-2014 cumulative morbidity and mortality for Sierra Leone for the period March 2014-June 2014 were 158 and 58 respectively [9]. The epicenter for the 2014 West Africa EVD outbreak in Sierra Leone is Kailahun District which is close to the epicenter of the outbreak in neighbouring Guinea.

2.3 Liberia

Only 1 documented Ebola case involving a warrior chief was reported in Liberia in 1994 although there were reports of at least 40 Ebola fatalities during that year [10]. The 1994 Ebola outbreak in Liberia occurred in the mining forest area of Piblo but largely went unnoticed because of the civil war in Liberia at the time. Piblo is home to a wide variety of wild life including chimpanzees, monkeys and bats in Liberia. No additional Ebola case was discovered in Liberia after the 1994 episode following epidemiological surveillance till 2014. What had kept the infection at bay requires further studies.

The second episode (EVD-2014) of Ebola outbreak in Liberia was indexed on the 31st March 2014 with 2 confirmed morbidities and no mortality [9]. Most of the EVD cases came from Lofa and Montserrado counties. Lofa County lies in the northeast of Liberia close to the EVD outbreak epicenters in Sierra Leone and Guinea. Montserrado County where the capital Monrovia is located lies in the south and several hundred kilometers away from the border of Sierra Leone and Guinea but very close to Piblo-the epicenter of the first EVD outbreak in Liberia. The cumulative confirmed EVD morbidity and mortality in Liberia for the period March 2014-June 2014 were 51 and 34 respectively [9].

2.4 Ivory Coast

A 34-year-old female Swiss ethnologist; one of the three scientists performing the necropsy on

the chimpanzee found on November 16, 1994, contracted Ebola, presumably from the necropsy she was doing at the Tai National Park, in Ivory Coast [11]. Although she had no wounds or punctures at the time and used household latex gloves to perform the necropsy, she is believed to have contracted the infection probably as a result of coming in contact with the chimpanzee blood either by the projection of droplets onto the face, particularly mucous membranes, or on the hand. This is among one of few reported human documented case of the infection associated with naturally infected nonhuman primates in Africa [6]. There is only one detailed seminal study of human Ebola infection involving human in the past [6]. The Swiss patient was confirmed positive for Ebola following the detection of serum antibodies IgM and IgG in her blood. Her clinical presentation were fever, nausea, diarrhea, hematuria [11]. Although early PCR analysis of viral isolates for most of them negative for the infection, the finding was however consistent with the convalescent stage of EVD. During EVD convalescence viral isolates are rarely present [8]. She received a rigorous treatment of fluid and electrolyte replacement therapy. Despite the lack of strict containment measures, no secondary transmission occurred as a result of her infection. The lack of secondary transmission even though strict containment measures were not taken supports the theory that Ebola is not airborne but requires direct contact with the patient or the patient's bodily secretions/fluids. On day 15 of her hospitalization, she was discharged from the hospital. She did not fully recover until 6 weeks after her infection.

2.5 Gabon

Gabon though not in West Africa was included in this study because it is the nearest country to West Africa to have experienced ebola outbreak. Gabon has so many sociocultural and demographical characteristics that are similar to those West African that have experienced EVD outbreak in the past. Gabon has been struck twice by an Ebola outbreak; first in 1994 and in 1996. The first Ebola outbreak in Gabon occurred in November 1994 in two gold-mining settlements of Mekouka and Andock [12]. By December 1994 the outbreak had spread to Kinkebe. The epicenters for the first Ebola outbreak in Gabon were remote pristine rain forest. Blood samples from patients were obtained from the Makokou referral hospital in the prefecture of Minkebe. The main clinical

symptoms for this first Ebola outbreak in Gabon were fever, abdominal pain, black diarrhoea, and conjunctival injection. Four out of the first batch of eight blood samples sent to Pasteur Institute in France for diagnosis detected a high titre of Ebola IgM. No viral isolation tests were done because of the low volume of blood samples. Among the batch of 33 persons presenting Ebola symptoms in December 1994, two men (34 and 28 yrs) had additional symptom of haemorrhagic fever. Twenty-seven percent (9/33) had Ebola specific IgM in their sera [12]. A nucleocapsid gene sequencing of the Ebola Gabon 1994 strain revealed it to be closely related to Ebola Zaire isolated in 1976 [12]. The impact of the 1994 outbreak increased active surveillance of unusual diseases in the Makokou region and may have been responsible for the drop in the number of Ebola outbreak in Gabon.

There were two Ebola outbreaks in Gabon in 1996. Thirty-seven Ebola cases were recorded in February 1996 in the village of Mayibout in the Ogooue-Ivindo prefecture had a case fatality rate of 57% (21/37) [13]. The second Ebola outbreak in 1996 which occurred between July to December in Booue but later reached Johannesburg via the Gabonese town of Makokou had 52 cases and a CFR of 77% (40/52) [14]. The sequencing of the PCR amplified genes of sera samples obtained from patients of the Ebola outbreak during the second outbreak are nearly identical to the viral strain responsible for the 1994 Ebola outbreak in Gabon [12].

3. DISCUSSION

The most important clinical features of the EVD-2014 infection were fever, severe diarrhea, and vomiting. Twenty-seven percent (4/15) of the EVD-2014 cases reviewed were hemorrhagic. The case fatality rate of EVD-2014 in Guinea was determined as 86% [9].

Most EVD-2014 patients showed similar clinical features including progressive loss of memory, fatigue, hyperpyrexia, vomiting, diarrhoea, and haemorrhaging that were cardinal to that of EVD 1994. However, EVD-2014 exhibited acute and high virulence compared to EVD-1994 which could be attributed to differences in viral strain. EVD-2014 is caused by a clade of Ebola-Zaire which is more pathogenic than (TAFV) that was responsible for the EVD 1994 outbreak in Ivory Coast [10]. The viral strain responsible for EVD 2014 is also more pathogenic than Ebola Zaire

that was responsible for the 1994 and 1996 EVD outbreak in Gabon [12].

There are many determinants that influence the severity, duration and socioeconomic impact of viral epidemic. We compared EVD-2014 outbreak to the Ebola episodes in 1994 in Ivory Coast, Gabon and Liberia in terms of ecological settings, epidemic duration, epidemic preparedness, response and containment, and the severity of the outbreak. The factors that enforce such comparison includes but not restricted to geographical proximity, pre outbreak medical aid access, climatic, socioeconomic and ecological settings.

The various epicenters (Gueckedou Prefecture in Guinea, Kailahun District in Sierra Leone and Lofa County in Liberia) for the EVD-2014 outbreaks and those of the 1994-EVD outbreaks in Gabon, Ivory Coast and Liberia are identical in many respect including their demography and the means by which residents obtain their livelihood. Gueckedou Prefecture in Guinea lies few kilometres from Kailahun District in Sierra Leone and Lofa County in Liberia; and all three regions have identical ethnic groups as a result of inter-marriages. These epicenters are surrounded by dense tropical rain forest which is home to many primates including chimpanzees, monkeys, gorillas and bats. Residents in these regions thrive mainly on subsistence farming and wildlife hunting. Ebola is a zoonotic infection predominantly found in bats and primates. From this investigation it emerged that EVD outbreaks in West Africa commences around November which is characterised by lesser rains, commencement of farming activities and game hunting. While EVD-1994 episode in Ivory Coast was accidental in origin, our hypothesis is that EVD-2014 was sparked by human activities such as wildlife hunting, mining, deforestation from mining. However, the emergence of a clade of Ebola Zaire in West Africa requires further scientific investigation.

The various epicenters in the EVD-2014 outbreak like the previous outbreak in 1994 were surrounded once by pristine forest landscape that has now evolved into a mosaic of human settlements bring wild animals closer to humans. This change in human habitation has also forced animal hosts for many zoonotic infections to seek for new habitats amongst human population. A large proportion of the forests in Sierra Leone, Liberia and Guinea have been sold off to mining international conglomerate for mining and

agricultural purposes. Guekedou-south east of Guinea where EVD-2014 was first reported has iron ore reserve which implies high seasonal human movement in search of employment. Human mobility enables Ebola to manifest itself in new environs since such movement brings man in close proximity to wild animals who serves as zoonotic host for the pathogen.

The situation is not different from the rapid and ongoing investment in mineral mining in Sierra Leone and Liberia. Sierra Leone GDP grew by 20% in 2013 as a result of upsurge in mining investment by British iron ore companies [15].

The role of previous conflict in establishing the outbreak 2014 EVD is also important within this context. Survivors of the rebel wars in Liberia and Sierra Leone in the late 1990's who refused to be reunited with the greater national population in their respective countries could be found inhabiting the forest regions around the epicenters in Guinea, Sierra Leone and Liberia. This inhabitation of humans in large number within formerly uninhabited ecological terrains has important implications for disease transmission due to the increased cross-border interactions in these regions. When people moved in large numbers they tend to serve as disease carriers. According to a UNEP post-war Sierra Leone report most people in the country have become increasingly reliant on forest animals for food, and wood from trees for fuel and building materials [16].

Climate change which is also product of large human population migration could have played a role in the emergence and prolongation of EVD-2014 compared.

When people relocate to a new environment en-masse their human activities will create a shift in the normal ecological parameters of their new found locality over a given period of time through activities like farm land overgrazing and deforestation. A 2013 International Food Policy Research Institute report states that West African countries are now feeling the effects of climate change as is evident in more unusual weather patterns such as land slide, flooding changing rainfall pattern, thunderstorms and seasonal droughts [17]. These climatic abnormalities coupled with the aggregation of large human population in one locality create an atmosphere that brings man in direct contact with wild animals such as bats and chimpanzees which are zoonotic to Ebola. These shift in weather

pattern where hardly noticeable during the 1994 Ebola outbreaks and may be responsible for the prolongation and severity of EVD-2014.

The various epicenters of the EVD-2014; Guekedou, Lofa County, and Kailahun District all lacked sufficient preparedness to handle viral epidemic prior to the 2014 outbreak. The situation was the same for the 1994 and 1995 EVD episodes in Ivory Coast and Liberia respectively. Also, all countries in West Africa that were affected by EVD-2014 had similar access to international health donor agencies like the World Health Organisation, Centre for Disease Control, USA and Medicine Sans Frontier MSF.

EVD-2014 varies from EVD-1994 in terms of severity and epidemic duration. This could be accounted for by the viral strain, the level of containment practices, healthcare response to the epidemic, immunological response of the infecteds, or a combination of these factors. During EVD-1994 episodes in Ivory Coast and Liberia, prompt extra precautionary containment measures were taken to prevent spread of the infection from the index cases. These containment methods include but not restricted to vigorous early contact tracing of contact persons close to the indexed cases. People who had direct face-to-face contact with an individual diagnosed positive for ebola or his bodily fluid two days before the onset of the illness or during the cause of the illness are described as contact persons. Contact persons serologically tested for Ebola during the EVD-1994 episodes' contact tracing included family members of indexed Ebola patients, laboratory technicians who handled both Ebola patients and infected chimpanzees' organs, as well as aircraft crew members who transported Ebola patients and serum for further diagnosis and treatment. Transmission of EHF requires prolong physical contact with a patient who come in contact with blood or secretions [18]. During the early EVD-1994 episodes, mandatory universal precautions and barrier nursing methods were implemented thereby reducing the number of EHF cross-infection compared to the high prevalence of cross-infection that occur during EVD-2014.

There was poor containment practice during the early course of EVD-2014. The first suspected EVD-2014 morbidity and subsequent mortality was a two-year old who died in Meliandou, Guéckédou prefecture in Guinea on December 6, 2013 [7]. The indexed case of EVD-2014 was

registered on the 25th March 2014 in Guéckédou, Guinea. This 3-month lapse between the first suspected Ebola case and the indexed case coupled with insufficient containment procedures could have been responsible for the long duration of EVD 2014 compared to that of EVD-1994 episodes. The long period to register the index case considering the time the first suspected case was observed may have contributed to the spread and the inability of containment methods to quickly bring the EVD 2014 under control. The long period taken for the index case to be recorded during the EVD-2014 outbreak could be attributed to the remoteness of the epicenters and the low state of preparedness to handle viral epidemic of such nature within these countries where EVD-2014 occurred. The epicenters of Guéckédou Prefecture, Kailahun District and Lofa County in Guinea, Sierra Leone and Liberia respectively are remote subterranean communities with little or no presence of organised central government system. The main referral hospitals in these regions are often poorly monitored and are usually ill-equipped hence outbreak of epidemics of such nature are rarely reported promptly.

The large proportion of persons affected by EVD-2014 could also be attributed to poor containment method. EVD epidemics were a large proportion of the cases are primary infecteds i.e. people who became infected by coming in direct contact with EVD-infected primates has long epidemic duration and is more severe compared to those in which cross or secondary infections outweighs primary infections humans. EVD infection acquired directly from its zoonotic source has high viral load compared to EVD cross-infection.

EVD-2014 outbreak has long outbreak duration and was severe because high number of those affected by EVD-2014 were primary infected who came in contact with zoonotic sources at the various epicenters. The increased number of primary infected EVD patients in 2014 could have been possible because of the large presence of human inhabitation coupled with the high human trafficking at the various epicenters in each country prior to the outbreak. Large number of people became infected with EVD in 2014 by coming in direct contact with EHF infected primates such as apes, chimpanzee and bats or their products. This infection pattern was made possible due to the presence of large settlement of people within each regions where the epicenters are located. The various

epicenters for EVD-2014 in Guinea, Liberia and Sierra Leone are at close proximity and there has been a massive influx of people in these regions following the end of the civil war in Sierra Leone and Liberia in 1999. The various epicenters are similar ethnically and demographically and share identical geographical features.

A large proportion of persons affected by EVD-2014 do so because of poor containment method. During EVD-2014 outbreak large number of healthcare givers were affected when they became unknowingly infected with EHF when treating Ebola patients. Most of these healthcare workers also became infected with EHF because of the lack of or use of inappropriate logistics such as personal protective equipment (PPE) when caring for an Ebola infected patient. It is thus evident that in EVD epidemic, the infection is greatly spread and becomes difficult to contain because of the large number of secondary or cross-infections.

The long duration of EVD-2014 compared to EVD-1994 can also be attributed to the lack of proper early diagnosis or misdiagnosis of tropical infections in Africa. Because EVD initially presents malaria-like syndromes most healthcare workers in remote Africa regions where Ebola emerges often misdiagnose the infection thereby causing the delay in having a proper early containment policy and hence an outbreak. EVD 1994 outbreak had a shorter duration because of prompt and correct diagnosis of the early cases.

4. CONCLUSION

The mode of EVD transmission plays an important role in determining its duration. From this review it is clear that EVD-2014 was very severe, has a longer duration and poor containment procedure compared to EVD-1994 and EVD-1996. It also appears that EVD-2014 was more severe than the other previous EVD outbreaks because it involves a different clade of Ebola-Zaire strain.

This review once again illustrate the role of climate change in the transmission and emergence of diseases in communities where they never existed or where they once do. Human activates such as aggressive mineral extraction, en-masse human movement and deforestation may have led to the emergence of Ebola in West Africa a decade after it was first reported.

5. RECOMMENDATION

This review emphasises the need for regular upgrading of clinical diagnostic kit for the diagnosis of new and existing tropical diseases in Africa. There are several non-malarial cases common to West Africa including bacterial (i.e., typhoid fever, typhus, leptospirosis) or viral infections which could easily be passed off as malaria infection or its complications. This study stresses that for effective future EVD containment, negative malaria blood culture cases that have been unsuccessfully treated with antibiotic treatment should be considered arboviral or hemorrhagic fever infection in origin. Considering the large number of tropical human pathogenic arboviruses and the growing number of clinical diagnostic tests required for their diagnosis in resource-poor countries including those in West Africa, it will be most appropriate if such infections can be categorised on the their geographical origin and clinical signs.

CONSENT

Not applicable.

ETHICAL APPROVAL

Not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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