Title:

Spatio-Temporal Analysis of Ebola Virus Disease in Sierra Leone, May 2014-September 2015

Authors:

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Abstract

Background

The 2014-2015 Ebola virus disease (EVD) outbreak was unprecedented, affecting ten countries, with the greatest burden of cases and deaths occurring in Guinea, Sierra Leone, and Liberia. Over two years, Sierra Leone experienced 14,124 suspected and/or confirmed cases and 3,956 deaths. The timing and location of these cases, however, was not homogenous. We aim to measure the location and timing of EVD clustering using chiefdom-level data to shed light on the utility of geospatial tools in infectious disease surveillance.

Methodology/Principle Findings

A total of 8,358 confirmed EVD cases were documented from May 23, 2014 to September 13, 2015 by the Sierra Leonean Ministry of Health and Sanitation. Spatial scan statistics were used to describe the trajectory of EVD clusters over space and time. Areas of high and low clustering were detected using cases aggregated into one- and two-week periods. Four clusters of high transmission were identified, the first of which was detected on June 20, 2014, three months prior to the deployment of the United Nations Mission for Emergency Ebola Response. Three regions of low transmission clustering were detected, beginning in January 2015 and persisting until the epidemic's end on September 13, 2015.

Significance

The use of spatial scan statistics to identify clustering of EVD in Sierra Leone successfully described the timing and spread of the virus across the country. Disease surveillance that incorporates freely available geospatial tools to prospectively analyze routine data recorded by the health system can contribute to deploy early emergency responses, and therefore thwart the spread of infectious agents.

Introduction

Ebola virus disease (EVD) is a viral hemorrhagic fever classified by its high fatality rate and infectiousness. It is transmitted human-to-human through close contact with an infected individual's bodily fluids such as blood, vomit, and diarrhea. Additionally, close contact with an infected corpse immediately after death can lead to infection [1]. Therefore, healthcare workers, family members of infected individuals, and those who attend burial ceremonies are at high risk for EVD infection [1].

The first recorded EVD outbreaks occurred simultaneously in what is now the Democratic Republic of Congo and South Sudan in 1976 [2]. Since then, many outbreaks have been reported in equatorial Africa, including Democratic Republic of the Congo, Sudan, Uganda, Gabon, and Republic of the Congo, but have rarely surpassed several hundred cases [3]. Before 2014, the largest EVD outbreak was recorded in 2000-2001 in Uganda, with a total of 425 cases [3].

The most recent EVD outbreak, however, was different: a total of 28,652 cases and 11,325 deaths across ten countries (Liberia, Sierra Leone, Guinea, Nigeria, Senegal, Spain, United States, Mali, United Kingdom, and Italy) were recorded over a period of approximately two years. Transmission was highest in West Africa, a region that had never before experienced an EVD outbreak (3). The outbreak began in December 2013, when a 2-year-old boy died of an unknown illness in Meliandou, Guinea. Over the following days, several of his family and community members fell ill and succumbed to similar deaths. Within weeks, the disease spread across the country to Guinea's capital, Conakry. It was not until March 21, 2014, that the mysterious hemorrhagic fever was confirmed as EVD [4], and the World Health Organization (WHO) declared EVD a state of emergency only on August 8, 2014. The United Nations (UN) initiated its Mission for Emergency Ebola Response (UNMEER) on September 19, 2014 [5]. The Mission established itself in Guinea, Liberia, and Sierra Leone with the goal of providing logistics, personnel, and funding to stop the epidemic. Primary activities included case finding and management, ensuring proper burials, and social mobilization [6].

The first case in Sierra Leone was reported in May 2014, manifesting in a traditional healer who had traveled from Guinea. Over the following year and a half, cases and deaths caused by EVD in Sierra Leone and its neighboring countries grew at an unprecedented rate. In the latter half of 2014, through the efforts of both local governments and the international community, deaths caused by EVD in Sierra Leone leveled off, followed by cases throughout 2015 (Fig 1) [3].

Fig 1. Cumulative EVD suspected/confirmed cases and deaths in Sierra Leone, 2014-16. Information on cases and deaths was extracted from the Centers for Disease Control (CDC) [3].

Despite the international response, by the epidemic's end in December 2015, Sierra Leone had experienced 14,124 suspected and/or confirmed cases and 3,956 deaths [3]. This can be attributed to several obstacles and failures. First, the international community did not launch a sizeable response until three Westerners became infected, despite the number of cases proliferating in West Africa [7]. The absence of a prompt response to the outbreak contributed to its large caseload and high fatality rate [8]. In addition, a major barrier to implementing an adequate response was coordination, which was deficient in both planning and implementation, when central leadership was absent [9]. In fact, the establishment of UNMEER bypassed an already existing UN body responsible for emergency response, the Office for the Coordination of Humanitarian Affairs, obscuring the roles of foreign actors and contributing to confusion on the ground [10]. Once the response was launched, sending personnel, materials, and funding to West Africa occurred at a staggeringly slow pace [11]. Finally, Sierra Leone's weakened health system exacerbated the spread of EVD: prior to the outbreak, Sierra Leone had only 2 physicians for 100,000 individuals [12]. A reported 328 health workers, including nurses, physicians, and laboratory workers, became infected EVD in Sierra Leone [13]. Among those for whom the outcome is known, two-thirds of infected health workers died from the virus [13].

Although cases of EVD reached each of the fourteen districts of Sierra Leone, the spread of the virus did not occur uniformly across the country. Genetic analysis of viral mutations in confirmed cases of EVD across West Africa have characterized the diffusion of the virus across the region over space and time [14, 15, 16]. Heterogeneity in transmission dynamics over space and time has been described through modeling [17, 18]. Weighted-average linkage-clustering methods and Poisson regressions were applied to characterize groups of epidemic patterns (from sporadic to prolonged outbreaks), and to identify factors associated with disease spread (e.g., proximity to hospitals and roads) [19]. However, a comprehensive analysis of the spread of EVD over space and time in Sierra Leone, taking response efforts into consideration, has not been conducted.

In this paper we conduct a comprehensive spatio-temporal analysis of confirmed weekly EVD cases in Sierra Leone (recorded between May 2014 and September 2015) by chiefdom to shed light on the role that the timing of the UNMEER introduction might have had in the spread of the disease. Specifically, we address three issues. First, we characterize the pattern of EVD transmission in space and over time, identifying how clusters of high and low EVD cases evolved. Second, we assess if the launching of international support on the ground occurred before the disease had spread nationally. Third, we assess if the clustering pattern of high EVD transmission waned after September 18, 2014, when the UNMEER was initiated in the country.

Methods

Study area

Sierra Leone, located on the coast of West Africa bordering Guinea and Liberia, is divided into 14 districts; within those districts it is further divided into 149 chiefdoms [20]. With a population of roughly 6.4 million and a life expectancy of 49 years for men and 51 years for women [21], Sierra Leone is currently ranked in the 181st position in the Human Development Index, characterized by low life expectancy, inadequate educational attainment, and high levels of inequality [22]. The population is roughly 60% Muslim and 10% Christian [12]; both religions engage in burial practices that involve bathing the dead, which exacerbated the spread of EVD [23].

Data Sources

EVD data were provided by the Sierra Leone Ministry of Health and Sanitation (SLMHS) and compiled by Fang et al (2016). Specifically, we obtained individual records of 8,358 confirmed cases of EVD from May 23, 2014, to September 13, 2015, detailed by: date of onset of symptoms (day/month/year), date of confirmed case of EVD (day/month/year) and chiefdom of case (except for cases in the capital, Freetown, where the geographic unit is district), (S1 Table). In addition, we used 2014 population estimates by chiefdom based on the 2004 Sierra Leonean Population Census [24] and further interpolated by Fang et al (2016) using district population sizes in 2014 (S2 Table) [19, 25].

Spatio-temporal clusters

Space-time scan statistics [26] were used to assess the spatio-temporal clustering pattern of EVD in Sierra Leone. The statistic computes expected case counts considering a cylindrical scanning window, where the height of the cylinder represents time units and the base defines the spatial neighborhood area [26]. The null hypothesis posits that the case load of EVD is the same both inside and outside of the cylinder, proportional to population size. Our spatial unit of analysis was the chiefdom, and data were related to each chiefdom centroid. The size of the neighborhood window was limited to up to 25% of the population at risk, and the temporal window was set at 50% of the time span. Significance tests were based on the likelihood ratio, with p-values calculated by 999 Monte Carlo replications [26].

Space-time scan statistics were run to detect areas of both high and low clustering throughout the epidemic. We used count data of EVD cases for the entire time series (May 23, 2014 to September 13, 2015), considering two week aggregations and one week aggregations. One and two weeks both fall within the incubation period for EVD (2-21 days). One and two week periods also allow for a level of granularity that describes what occurred over 16 months but is more easily interpretable than clusters by day. Maps for Sierra Leone were obtained from the GADM database v2.8 [19]. Mapping and centroid calculation was done in ArcGIS v10.3.1 (Environmental Systems Research Institute, Redlands, CA). The space-time scan statistic was run in the freely available SaTScan™ software v9.4.2 [27].

Results

The spatio-temporal analysis indicated that significant clusters of EVD cases were observed, but the clustering pattern changed quite quickly. Considering a temporal aggregation of cases in two-week periods, four clusters of high transmission were observed over the 16-month study period (Fig 2 and Table 1). The earliest cluster was detectable on June 20, 2014 and lasted until September 12, 2014; it contained only one chiefdom, Nongowa, accounting for 331 cases of EVD (Relative Risk (RR)=24.46, $p<0.0001$). Since the first case of EVD confirmed in Sierra Leone was in Nongowa, this cluster likely reflects the epicenter of EVD transmission in the country. The second cluster of high transmission was much larger in spatial extent and persisted for a longer period of time. It occurred from August 29, 2014 to December 19, 2014, containing 21 chiefdoms (RR=8.88, $p<0.0001$). A third cluster was detected from October 24, 2014, to November 7, 2014, encompassing 46 chiefdoms. It was the largest in spatial extent, and had the highest relative risk (RR=25.68, $p<0.0001$); however, it had the lowest attack rate, implying that the overall level of expected EVD cases across Sierra Leone was lower during this time. The cluster that persisted longest was detected from September 12, 2014 to January 16, 2015. It contained Freetown, Sierra Leone's capital, and surrounding chiefdoms (RR=10.14, $p<0.0001$). No significant clusters of high transmission were detected after January 16, 2015, despite confirmed cases continuing to September 13, 2015. Considering a temporal aggregation of EVD cases in one-week periods resulted in a very similar clustering pattern (Fig 2 and Table 1), with four clusters of high transmission detected. The only notable difference was the spatial extent and timing of the easternmost cluster that spanned from December 17, 2014 to January 9, 2015. For the one-week analysis, this cluster included 11 chiefdoms and was detected for a period of 12 weeks, while the two-week period analysis detected a cluster of 46 chiefdoms for only 2 weeks.

Fig 2. Clusters of high EVD transmission in Sierra Leone, May 2014 to September 2015. Clusters were identified using the Scan statistic: (a) using a two-week temporal aggregation, and (b) using a one-week temporal aggregation.

Table 1. Significant clusters of high EVD cases in Sierra Leone, May 2014 to September 2015.

Dates	Number of weeks in cluster	Number of chiefdoms in cluster	Radius of cluster (km)	Expected number of EVD cases	Observed number of EVD cases	Cluster attack rate (cases/1000 people)	Relative Risk	p-value
Two-week temporal aggregation								
6/20/2014 to 9/12/2014	12	1	0	13.18	311	4.61	24.46	<0.0001
8/29/2014 to 12/19/2014	16	21	54.99	242.79	1,754	1.97	8.88	<0.0001
10/24/2014 to 11/7/2014	2	46	123.39	4.30	109	0.07	25.68	<0.0001
9/12/2014 to 1/16/2015	20	6	44.11	492.32	3,246	2.08	10.14	<0.0001
One-week temporal aggregation								
6/20/2014 to 9/12/2014	12	1	0	14.70	311	4.61	21.94	<0.0001
8/29/2014 to 12/26/2014	17	21	54.99	281.22	1,814	2.03	7.96	<0.0001
10/17/2014 to 1/9/2015	12	11	48.42	89.47	339	0.82	3.91	<0.0001
9/19/2014 to 1/23/2015	20	6	44.11	530.54	3,262	2.06	9.44	<0.0001

With regard to the occurrence of low transmission, three clusters were detected when an analysis was run in two-week periods (Fig 3 and Table 2). The first two clusters, both large in spatial extent, appeared on January 17, 2015, and persisted until the final case was recorded on September 13, 2015. The larger cluster encompassed most of northern Sierra Leone (RR=0.080, $p<0.0001$), and the smaller included the southeast (RR=0.00085, $p<0.0001$). A third area of low-transmission clustering was detected from March 14, 2015 to September 13, 2015. This area included Freetown and its surrounding chiefdoms (RR=0.13, $p<0.0001$). Similar results were found when considering one-week time aggregations, with the only detectable difference being the dates of the clusters and their respective relative risks and attack rates (Fig 3 and Table 2).

Fig 3. Clusters of low EVD transmission in Sierra Leone, May 2014 to September 2015.

Clusters were identified using the Scan statistic: (a) using a two-week temporal aggregation, and (b) using a one-week temporal aggregation.

Table 2. Significant clusters of low EVD cases in Sierra Leone, May 2014 to September 2015.

Dates	Number of weeks in cluster	Number of chiefdoms in cluster	Radius of cluster (km)	Expected number of EVD cases	Observed number of EVD cases	Cluster attack rate (cases/1000 people)	Relative Risk	p-value
Two-week temporal aggregation								
1/17/2015 to 9/13/2015	34	48	72.70	1035.56	1	0.00063	0.00085	<0.0001
1/17/2015 to 9/13/2015	34	50	164.61	1040.27	94	0.059	0.080	<0.0001
3/14/2015 to 9/13/2015	26	6	44.11	792.94	116	0.0070	0.013	<0.0001
One-week temporal aggregation								
1/10/2015 to 9/7/2015	34	48	72.70	1037.61	3	0.0019	0.0025	<0.0001
1/10/2015 to 9/7/2015	34	50	164.61	1042.33	106	0.067	0.090	<0.0001
3/28/2015 to 9/13/2015	24	6	44.11	711.81	101	0.064	0.013	<0.0001

Discussion

Sixteen months of daily data on confirmed EVD cases by chiefdom in Sierra Leone were compiled, amounting to 8,358 observations. Using the scan statistics, we were able to demonstrate that significant clustering of high and low transmission of EVD occurred in Sierra Leone. Clusters were confined to certain areas and time periods, with little variation when considering different time aggregations.

Areas of high clustering from May 23, 2014 and September 13, 2015, clearly demonstrate the progression of EVD transmission from the southeast, where the first cases appeared, moving across the country, and persisting in the capital. The earliest detectable cluster occurred during the week of June 20, 2014, with a very high relative risk and attack rate (RR=24.46, Attack Rate (AR)=4.61/1,000 population), confirming our hypothesis that clustering was present prior to the deployment of UNMEER in September 2014. A trend surface analysis found diffusion corridors in a similar vicinity but appearing earlier than these clusters, with one in the southeast beginning on May 18, 2014, one month prior to our findings, and another in the vicinity of the capital beginning on June 25, 2014, over two months prior [19]. This pattern was likely enhanced by the presence of super-spreaders, who were responsible for an estimated 61% of infections [28]. In addition, the timing of appearance of high EVD clusters is corroborated by the migration pattern of the virus in West Africa, as described by genomic sequence data analysis [29].

Our results also indicate that no space-time clusters of high EVD transmission were detected after January 16, 2015. However, Figure 1 demonstrates that the cases of EVD did not begin to level off in early 2015. Therefore, this result does not mean that the spread of EVD declined in January 2015, but most likely that transmission was widespread and uniformly high (at least for a period of time until it began to decrease).

The clustering pattern of low EVD transmission highlighted three issues. First, the average radius of low clusters in one-week aggregates (93.81 kilometers) was larger than the average radius of high clusters in one-week aggregates (36.88 kilometers). Low clusters also persisted longer: results from our analysis using two-week periods showed that high transmission clusters lasted an average of 10 weeks, while low clusters had an average duration of 31.3 weeks. Second, low clustering first appeared in January 2015, implying that UNMEER and other efforts to thwart the epidemic did not change the EVD clustering pattern until several months after implementation. Third, Freetown and its surrounding chiefdoms appear as both a high cluster (until January 2015) and a low cluster (from March 2015 until the end of the epidemic). Therefore, the capital and its vicinity went from being an area in Sierra Leone with the most intense transmission of EVD to an area with the least intense transmission of EVD (relative to the rest of the country).

Our findings suggest that geospatial methods have great potential to monitor disease transmission and to inform the mitigation of disease outbreak. We argue that a simple surveillance effort employing widely and freely available resources to monitor the spread of diseases spatially and temporally could have pointed to the gravity of the epidemic at its start (particularly indicating the areas most in need for emergency intervention). This could have contributed to trigger an earlier deployment of aid, and thus to curb the spread of the epidemic, reducing the burden on health facilities and human lives lost. For example, although data are unavailable prior to October 2014, there were only four Ebola treatment centers (ETCs) and no community care centers (CCCs) on October 20, 2014; these figures were 23 and 53, respectively, spread across the country at the response's height in January 2015 [19]. However, if we consider the epidemiological curve of the disease, public health responses must be launched prior to the peak of transmission for optimized impact [30].

Although reporting mechanisms were likely poor in Sierra Leone, case estimates were being updated daily by the Sierra Leonean Ministry of Health and Sanitation. Doctors Without Borders warned of the unique nature of this EVD outbreak in June 2014, two months before the WHO declared a state of emergency [29], but, coincidentally, exactly the time when the first significant high EVD cluster was detected in our analysis. Although infectious disease surveillance is typically performed temporally and not spatially [26], the spread of EVD is likely to be influenced by a multitude of factors, several of which are spatial in nature (e.g., urbanization, migration, environmental change, and seasonality) [30, 31]. Thus, we argue that the application of prospective spatial analyses (such as the scan statistic) to fine spatial resolution data (e.g., chiefdom), could have contributed to the early deployment of targeted interventions in areas with highest transmission, with the potential to curb the spread of the disease and thus the magnitude of the outbreak.

Improvements of data collection and surveillance, digital technologies, and data sharing could have drastic effects in reducing the burden of epidemics in the future [32]. Efforts are in place to develop and employ inexpensive, digitized reporting mechanisms that would enhance the ability to detect an outbreak and follow its trajectory. For example, Nigeria, which had a total of 19 EVD cases and 7 deaths, is seen as a success story [33]. Although this success can be attributed to many factors, the Nigerian response included the use of digital technologies for contact tracing and case identification such as Open Data Kit and ArcGIS, which contributed significantly to the prompt containment of EVD [33]. Other efforts to engage crowd-sourced data on infectious diseases, such as HealthMap, have great potential to facilitate the use of spatial tools for infectious disease surveillance [34, 35]. The African Union's newly launched Africa Centers for Disease Control and Prevention (Africa CDC) would be an ideal body to support and promote the use of these inexpensive yet beneficial tools [36].

While the urgency of the epidemic underscores the necessity for prompt responses, careful documentation of control strategies is paramount for future evaluation purposes. For example, progressive changes in clustering patterns could be analyzed in light of efforts deployed, thus providing lessons of what are the successful mechanisms that may have hindered the spread of the virus.

Our analysis has several limitations. First, we did not have information on EVD cases for Guinea and Liberia, the two other countries hardest hit by the epidemic. Since they share borders with Sierra Leone, it is possible that the timing and the spatial extent of the clusters detected in our analysis would be slightly different if data from neighboring countries were included. Yet, our analysis considers a scenario in which the local health system would leverage their own information to deploy responses, which is the most common situation. In addition, importation and exportation of EVD from Sierra Leone after the initial imported case from Guinea was rare, therefore this analysis reflects the spread of EVD from within the country [16]. Second, given that the chiefdom-level population counts were estimates based on 2004 census data, they do carry some uncertainty. Nevertheless, it is unlikely that dramatic population changes might have occurred in a 10-year interval, and changes that did occur were taken into account using interpolation with 2014 district-level population sizes [19]. Third, we did not have access to any other variables characterizing the cases of EVD, and therefore we could not control for any other factors that might have contributed to the observed spatial and temporal pattern of disease transmission in the country. In addition, we did not have information on local resources, such as the location of Ebola Treatment Centers (ETCs) – distance from an ETC could have affected the observed trajectory of transmission. However, for the purpose of deploying prompt responses to the outbreak, we argue that the prospective knowledge of the spatio-temporal pattern of transmission (as presented here) would suffice.

In conclusion, this retrospective analysis not only sheds light on the poor timing of UNMEER efforts (three months after the first detected area of high transmission clustering), but also implies that there is great potential for the use of freely available geospatial tools in the future. Simple and inexpensive analyses using information as it is collected could prevent the spread of infectious diseases, saving money and, above all, lives.

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