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EPIDEMIOLOGY OF HUMAN EBOLA VIRUS DISEASE OUTBREAK IN SUB-SAHARAN AFRICA

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ABSTRACT

Ebola virus disease (EVD) is a zoonotic disease that has afflicted people for the past forty years, particularly in sub-Saharan Africa (SSA), where case fatality rates can reach over 90%. As of September 2015, a record 11,306 people had died from the latest EVD in West Africa, out of 28,200 cases reported from 10 countries. First, the profile of the EVD epidemic in SSA needs to be given. Second, an analysis of the distribution and location of EVD epidemics in SSA will be conducted. Again, to determine what causes EVD to spread during significant outbreaks. A comprehensive analysis of studies on the Ebola virus in sub-Saharan Africa. Nine databases were the focus of the search: Academic Search Complete, AJOL, Google Scholar, PubMed, Medline, Health Source, CINAHL Complete, BioMed Central, EBSCOhost (Discovery), and AJOL. Additionally, the reference lists of pertinent works were searched. As the geographical niche of EVD spreads from east to west of SSA, the review emphasized the rising frequency of EVD outbreaks, mobility, and death, with border regions being high-risk locations. Furthermore, urbanization, human mobility, and population increase have all had an impact on the spread of EVD in recent years. In order to prevent future Ebola outbreaks, the evolving patterns of EVD spread necessitate comprehensive preparedness, which comes from knowledgeable individuals, communities, regions, nations, and the international community at large. To prepare stakeholders for any eventuality, this study also recommends additional research in the areas of advancement in the clinical care of EVD in SSA.

KEYWORDS: *Epidemiology of Outbreak, Epidemic, Ebola Disease, Haemorrhagic Fever, Sudan, Gabon, Uganda, West Africa, Congo*

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INTRODUCTION

Ebola outbreaks, also known as Ebola virus disease (EVD) epidemics, are complex public health issues that require a thorough examination of their socio-anthropological aspects. The more popular term for Ebola is Ebola haemorrhagic fever. It continues to be a persistent public health issue in sub-Saharan Africa (Muzembo et al., 2022). This zoonotic disease, which was initially discovered approximately forty years ago, kills up to 90% of people (Lokko & Lokko, 2016). The first recorded cases of EVD in Sub-Saharan Africa (SSA) occurred in 1976 during two concurrent outbreaks in the Democratic Republic of the Congo (DRC)'s Yambuku and Sudan (Nzara). The latter took place in a community close to the Ebola River, which takes its name from the disease (Cenciarelli et al., 2015; Hayman et al., 2015; Mirazimi, 2015).

Cueva virus, Marburgvirus, and Ebolavirus are the three genera that make up the Filoviridae family, which contains the Ebola virus.

The Ebolavirus can be classified into five distinct species which are the Zaire Ebolavirus (EBOV), Sudan Ebolavirus (SUDV), Bundibugyo Ebolavirus (BDBV), Tai Forest Ebolavirus (TAFV) and Reston Ebolavirus (RDV) (Baştuğ et al., 2015). The Zaire Ebolavirus is the most lethal; the Reston Ebolavirus is not known to cause human disease; and only one human case of Tai Forest Ebolavirus has been reported in one human case (Van Kerkhove et al., 2015). Close contact with the body fluids of an infected animal host introduced the Ebola virus into the human population (Roddy, 2014). Symptoms of EVD range from, initial fever and fatigue before descending into headaches, vomiting, violent diarrhoea, then multiple organ failure and massive internal bleeding (Tambo et al., 2014). Currently, there are no proven cures, vaccines or even specific treatments available to prevent this infection, so supportive care for severely ill patients focuses on alleviating the symptoms. (Amandu, et al., 2015; Getz et al., 2015; Zhang et al., 2014). EVD typically starts in remote areas and spreads through hospitals, healthcare centers, or communities; several infections often occur before diagnosis.

Although research has implicated fruit bats of multiple species as natural reservoirs, scientists are not certain and the search for a possible reservoir is ongoing (Leroy et al., 2009; Roddy, 2014). However, Sub-Saharan Africa increasingly worried about the disease's public health burden because the sub-region continually battled this fatal disease with frequent outbreaks. As of September 2015, the 2014 West Africa Ebola outbreak alone has claimed 11 306 deaths out of 28 200 cases reported from 10 countries (CDC, 2015; Lokko & Lokko, 2016), making the 2014 West Africa outbreak several times larger than all previous outbreaks combined (Alexander et al., 2015; WHO, 2015;). Those numbers may be drastically underestimating the true case burden. In late August 2014, the World Health Organization (WHO) estimates the true prevalence to be two to four times higher than the reported figures. Given this, in August 2014 WHO declared the West African outbreak as a Public Health Emergency of International Concern, which needs to be tackled from all fronts (WHO, 2015). This, according to Piot (2015) calls for more research on EVD to appreciate the burden of the disease in SSA going forward to help fight the disease when it emerges again. However, researchers have done much work on the clinical presentation and management of the disease (Bah et al., 2015; Rubin et al., 2014; Goeijenbi et al., 2014; Lado et al., 2015; Liddell et al., 2015; Lyon et al., 2014; MacNeil et al., 2010; Piot et al., 1978; Ther et al., 2015; Clark et al., 2012; Dallatomasina et al., 2015; Gulland, 2014; Hunt et al., 2015; Mupapa et al.,1999; Ndambi et al., 2000; Yan et al., 2015). Much work on EVD control and prevention has also been carried out (Danasekaran et al., 2014; Hewlett et al., 2003; Jezek, 2001; Lamunu et al., 2004; Roca et al., 2015; Tramèr, 2014). Again, Althaus (2014); Chowell et al., (2004); Chowell et al., (2015); and Legrand et al., (2007) have developed a mathematical model of EVD transmission in SSA. However, not much work has been done on the factors associated with the spread of EVD in recent times. Hence, this paper outlines the EVD epidemic profile, the location and the spread of the various outbreaks in SSA and identifies the factors associated with the spread of EVD in major outbreaks.

This review highlights the gaps in knowledge of the spread of human EVD in SSA and factors associated with the spread in major outbreaks to identify high-risk areas and thereby help various stakeholders draw a preparedness plan for EVD prevention and control.

METHODS

Search Strategy and Study Selection

We retrieved articles from nine electronic databases: EBSCOhost (Discovery), Academic Search Complete, AJOL, Google Scholar, PubMed, Medline, Health Source, CINAHL Complete and BioMed Central. An additional search of reference lists of relevant papers was conducted. Search terms included were: "Epidemiology of outbreak (epidemic)", "Ebola disease (haemorrhagic fever)", "Sudan", "Gabon", "Uganda", "West Africa", "Congo". We restricted the search to the period of 1976 to September 2024. A total number of twenty (20) articles were reviewed. Articles included descriptive studies, Ebola reports, conference proceedings and articles published in peer-reviewed journals looking at the EVD epidemic profile, the location of the various outbreaks and factors associated with the spread of EVD in SSA. The literature search yielded 22,738 articles (Figure 1). 22,635 articles out of 22,738 were disqualified because they had nothing to do with human beings, Africa or sub-Saharan Africa, the Ebola virus, or duplication. After screening the remaining 103 articles by title and abstract, 71 were disqualified because they lacked full texts and were unrelated to important terms. Twelve articles were eliminated because they were not written in English after 32 items were evaluated for eligibility. Ultimately, this review contained 20 papers

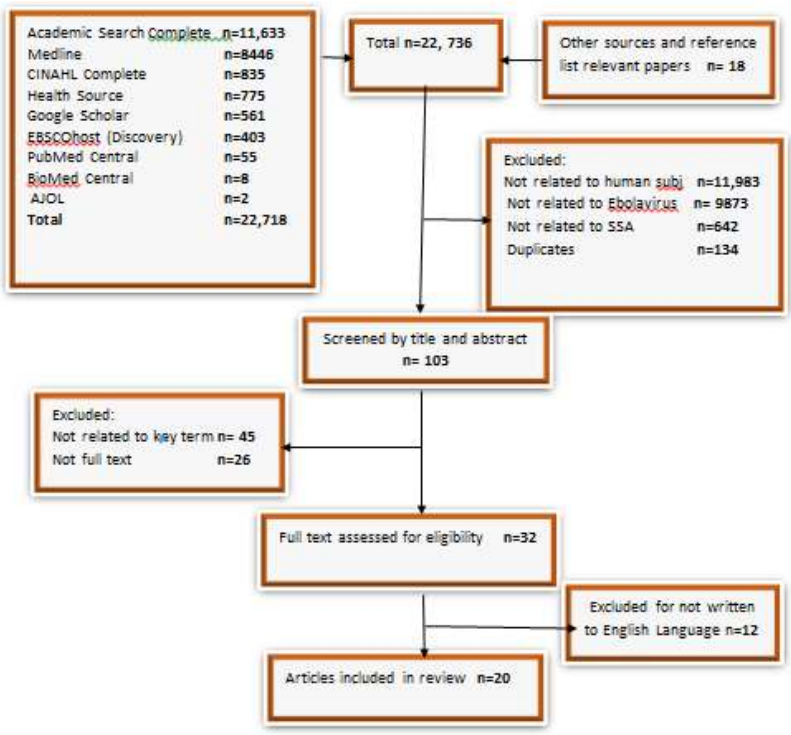

Figure 1: Flow Diagram of Systematic Review Process.

Description of Studies

Overall, 20 studies were included in the systematic review (Figure 1). The studies from West Africa (n=2). Studies from other West African countries were Cote d'Ivoire (n=1), Liberia (n =1), and Guinea (n=1). Studies from Central Africa include the Republic of Congo (n=1), the Demographic Republic of Congo (n=6) and Gabon (n=2). Studies from East Africa include Uganda (n=3) and South Sudan (n=3) (Appendix A). Studies were mainly descriptive of the various outbreaks. Fifteen (15) of the studies took place in the rural setting while five (5) occurred in urban settings.

Discussion

The virus types that caused the EVD in the literature reviewed were Zaire Ebolavirus (n=16), Sudan Ebolavirus (n= 7), Bundibugyo Ebolavirus (n=2) and Tai Forest Ebolavirus (n=1). One paper reviewed all the outbreaks in the Democratic Republic of Congo (DRC) and two papers on Gabon with one of the papers also describing the South African case. Three papers each reviewed all the outbreaks in Sudan and Uganda. Two in West Africa, one each in Liberia, Guinea, and Cote d'Ivoire. Six papers described all the seven outbreaks in DRC. Three articles included in the literature review were WHO documents. The review is organized into three sections based on the aim of the paper. The first section looks at the Ebola epidemic profile in SSA. The second section briefly describes the location and spread of the various EVD outbreaks. This is followed by the third section which discusses factors associated with the distribution of the spread of EVD in SSA.

Major Ebola Epidemic Profile in SSA from 1976 to 2024

In this section, the paper outlines the various major Ebola outbreaks in East Africa, Central Africa, Southern Africa and West Africa.

Ebola Outbreaks in East Africa

Several literatures have examined EVD in East Africa and have recorded eight (8) EVD epidemics, all occurring in South Sudan and Uganda. Sudan recorded three epidemics in 1976, 1979 and 2004, all were caused by Sudan Ebolavirus (SUDV). According to WHO (1978), East Africa recorded the first documented EVD in SSA in June 1976, in the border villages of Nzara and Maridi located in the Western Equatorial State, which borders CAR and DRC. The index case was an employee of a cotton factory in Nzara. However, the source of the infection was unknown. The resultant epidemic spread to other towns affecting family members and healthcare workers, recording 284 cases and 151 deaths with a fatality rate of 53% (WHO, 1978). Baron et al., (1983) indicated that Sudan was again hit by EVD in 1979 in the border villages of Nzara and Yambio in the same State of the first outbreak, with the index case again being an employee of the same cotton factory recorded in the previous outbreak. In all, 34 cases, 22 deaths and a mortality rate of 65% were recorded (Baron, et al.,1983). Again, the WHO (2005) report on Sudan recorded another outbreak in 2004. Two healthcare workers (HCWs) and five households were impacted by the EVD outbreak that occurred in Yambio. A total of 17 cases, 7 fatalities and a 41% case fatality rate (CFR) were noted (WHO, 2005).

Five (5) EVD epidemics have been documented in Uganda, all occurring in 2000, 2007, 2011, 2012 and 2012-2013, respectively. Except for the 2007 epidemic which was caused by BDBV, all the rest were caused by SUDV. In research by Lamunu et al. (2004) in Uganda recorded its first EVD outbreak where SUDV caused an outbreak in Gulu in the Northern Acholi Region which borders Sudan and Uganda. This outbreak spread to the cities of Mbarara and Masindi, with a total of 425 cases and 224 deaths with a CFR of 53% (Lamunu et al., 2004). Okware et al. (2015), 2007 documented the new Bundibugyo Ebolavirus species which was identified in a 26-year-old pregnant woman from Kabango, a border village of Kasitu in Bundibugyo district in the Bunyoro Region, which shares a boundary with DRC. She was hospitalized but died after delivering a preterm infant. Later, the neonate, sister, mother, and 2 nieces of the index patient also died. In total, 116 cases, 39 deaths and a CFR of 34% were recorded (Okware et al., 2015). Further, Shoemaker et al.,(2012) recorded an isolated case caused by SUDV in 2011 with a CFR of 100%. The Index case is a 12-year-old girl from Nakisamata village in Luwero District in the Central Region, which shares a boundary with Tanzania. The source of infection was however unknown but several species of bats in the village were identified (Shoemaker et al., 2012). Again, (Okware et al., 2015) documented Uganda's fourth EVD outbreak in July 2012 occurring in the Kibaale district of the

Western Region, with a 16-year-old female from Kikaara who was working in the forest, fell sick and died later at the hospital. Nine relatives who participated at the funeral died including a mother, sisters and a priest as well as a HCW. The outbreak which was contained in six weeks recorded 24 cases, 16 deaths and a CFR of 67% (Okware et al., 2015).

Furthermore, Okware et al., (2015) provided an account of the next Ebola outbreak in Uganda which started in October 2012 in the same Luwero district. The index case was a 30-year-old motorcycle taxi rider. He was admitted but died and was buried by relatives 70 miles away in Jinja. Two weeks later his wife, mother and a sister all died. The brother of the index case had fled but was quickly apprehended and isolated. The Jinja contact too developed fever, but was identified early and isolated. The epidemic which was contained in 6 weeks recorded 6 cases, and 4 deaths with fatalities of 67% (Okware et al., 2015).

Ebola Outbreaks in Central Africa

Several researchers indicate that Central Africa has recorded fifteen EVD epidemics occurring in Gabon, the Democratic Republic of Congo (DRC) and the Republic of Congo (ROC). Gabon, DRC and ROC have experienced four, seven and four EVD outbreaks respectively. All fourteen outbreaks were caused by the EBOV, except for the 2012 DRC epidemic which was caused by BDBV(Alexander et al., 2015; Heymann et al.,1980; Khan et al., 1999; Kratz et al., 2015; Leroy et al., 2009; Nkoghe et al., 2011; WHO, 1978).

According to WHO (1978), the Democratic Republic of Congo (DRC) recorded its first Ebola outbreak in September 1976. This outbreak occurred in the rural town of Yambuku and its surrounding areas in the Equateur Region. This is close to the Sudanese border where Sudan's first case was recorded in Nazra. Infections spread in major health centres across DRC. A total of 318 cases, 280 deaths and a CFR of 88% were recorded (WHO, 1978). Heymann et al (1980) discovered that EVD made its second appearance in 1977, infecting a 9-year-old girl living in Tandala, a DRC town close to the border with Central Africa Republic (CAR) and Yambuku. Investigations undertaken revealed that two previous clinical infections with the Ebola virus had occurred in 1972 and that about 7% of the residents had immunofluorescent antibodies to the virus. No other clues to the still-mysterious natural reservoir of the Ebola virus were uncovered (Heymann et al., 1980).

The DRC 1995 outbreak was investigated by Khan, et al., (1999) who reported that 315 cases, 250 deaths and 81% were recorded with the index case, a 42-year-old male charcoal maker in the forest of Mwembe resident of Kikwit. Infection spread to HCWs, family members, community members and villages (Khan et al., 1999). Leroy et al. (2009) reported that in 2007, yet another outbreak hit DRC which was caused by EBOV in Mweka and Luebo of Occidental Kasai. A total of 69 cases and a mortality of 71% were recorded with an index case likely to be a 55-year-old woman who lived in Ndongo (Leroy et al., 2009). They further documented another outbreak from 2008-2009 in Inkanamongo village in the vicinity of Boende in Equateur province. In all 32 cases, 14 deaths, and a CFR of 43.8% was recorded and the index case was believed to be an 18-year-old girl who had died from post-abortion haemorrhage. However, the source of the infection remains unknown (Leroy et al., 2009).

Kratz et al., (2015) pointed out that the 6th DRC- EVD outbreak occurred in 2012 with 36 cases and 54.8% mortality in Isiro, the capital of Haut-Uele District, Province Orientale. Both the index case and the source of infection were not known. (Kratz et al., 2015). In a descriptive study, both Alexander, Sanderson, Marathe, Lewis, Rivers, et al. (2015) and Maganga et al. (2014) gave an account of the 2014 Boende in, DRC Ebola outbreak. The index case was a pregnant woman who handled bushmeat and subsequent infections in the community stemmed from contact with the

woman's body during the funeral rituals (Maganga et al., 2014). In all a total of 67 cases, 49 deaths and a CFR of 74% occurred.

Georges et al. (1999) and WHO (2003) explored secondary data and indicated that Gabon had four successive EVD outbreaks in 1994, 1996, 1997 and 2001-2002. The Gabon- Makouka 1994 outbreak involved gold-diggers in the Mekouka, Andock and Minkebe Forest of the Ogooue Ivindo province, a border region to ROC, who had killed a sick gorilla for food. The illness was initially confused with yellow fever and so initial mortality was high. This led to some of the victims leaving the mines for the nearest hospital, located in Makokou, where they infected other patients in neighbouring villages. In total, 52 cases with 60% mortality were recorded.

Again, (Georges et al., 1999) recorded in 1996, the second outbreak in Gabon which hit the villages of Mayibout I and II, located near Mekouka in Ogooue Ivindo province, the site of the first outbreak. The index cases were 18 children in Mayibout II village who had helped to carry and butcher a chimpanzee carcass found in the forest. They in turn transmitted the disease to neighbouring villages such as Mayibout I. In total, this outbreak affected 37 people with a mortality rate of 57% (Georges et al., 1999).

They further noted that the third outbreak occurred in the Booue of Ogooue Ivindo province in 1997 with the index case being a hunter. According to them, several carcasses of chimpanzees were found in the surrounding forest at the same time. A second hunter died with similar symptoms, while one of his friends fell ill later and was taken to Booue Hospital. This patient left the hospital for a village close to Booue, where he received traditional treatment, infecting the traditional healer, his assistant, and other patients and in turn transmitted the disease to inhabitants of several towns and villages in Gabon including the capital Libreville. In all, 60 cases with a CFR of 74% were recorded. This outbreak caused an isolated case in South Africa (Georges et al., 1999). In 2001-2002, Ogooue Ivindo province was again affected by a fourth epidemic causing 65 cases with 82% mortality with the index case coming into contact with either a gorilla, monkey or chimpanzee (WHO, 2003).

In the studies of Nkoghe et al (2011), the Republic of the Congo was struck by four successive Ebola outbreaks, 2001-2002, 2002-2003, 2003 and 2005. In 2001-2002, two independent index cases were infected with EVD while poaching gorilla carcasses in the villages of Olloba and Entsiami in Mbomo and Kelle Districts of Cuvette Ouest Region. In all, 57 cases, 42 deaths with CFR of 73.7% were recorded (Nkoghe, et al., 2011). They further noted that in 2002-2003, EVD re-emerged affecting 143 individuals in Mbomo and Kelle of the same Cuvette Quest Region and 128 deaths were recorded. Three independent index cases were identified regarding hunting episodes and contact with gorillas (Nkoghe et al., 2011).

Furthermore, Nkoghe et al. (2011) recorded in 2003, the third EVD outbreak in ROC which occurred at Mbandza village in Mbomo District of Cuvette Ouest Region, a border region to Gabon. In all 35 cases, 29 deaths with a CFR of 82.9% was recorded. The index cases were infected after handling and consuming the carcass of a great white nose monkey. Outbreak was short, limited in size and lasted 5 weeks (Nkoghe et al., 2011). In 2005 another EVD erupted in the ROC town of Etoumbi in the Cuvette Quest County with two index cases who were infected while poaching. A total of 12 cases, 10 deaths and a CFR of 83% was noted. The outbreak was also short, limited in size and lasted 5 weeks (Nkoghe et al., 2011).

Ebola Outbreaks in Southern Africa

Georges and his team studied "Ebola Haemorrhagic Fever Outbreak in Gabon" and noted that the 1997 EDV in South Africa was caused by a sick Gabonese physician who travelled to Johannesburg for medical treatment. There, he infected a nurse who died a few days later but he survived (Georges et al., 1999).

Ebola Outbreaks in West Africa

Formenty et al (1999) pointed out that in 1994 EVD appeared in Cote d'Ivoire which led to the discovery of a new species of Ebola virus, Tai Forest Ebolavirus (TAFV). This minor outbreak occurred in the Tai National Park located at the border of Region des Montagnes of Cote d'Ivoire and Liberia. The index case and the only case was an ethologist who was infected whilst performing an autopsy on a dead chimpanzee. She was subsequently treated outside the country (Formenty et al., 1999).

In the study of Oleribe et al., (2015) and Alexander et al., (2015), in 2014 EVD hit the sub region with the index case being a two-year-old in a border town of Guéckédou in Nzerekore, a region bordering Sierra Leone and Liberia. The outbreak spread mainly through major capitals including the capitals of Guinea, Liberia, Nigeria and Sierra Leone. As of September 2015, WHO has reported 28,200 cases and 11,306 deaths (CDC, 2015). According to Oleribe et al., (2015), the first case, which was imported to Nigeria was through a commercial airline and within days the disease spread to Lagos Port Harcourt, Abuja, Ibadan and Ille. The majority of the affected people were HCWs. The outbreak yielded 20 cases with 8 deaths. Senegal had one case being a student from Guinea Conakry who travelled to Senegal. Due to interventions put in place, the case was confirmed early and treated (Oleribe et al., 2015). Both Mali and Sierra Leone reported cases which were imported from Guinea with Mali reporting 4 cases with 75% mortality and Sierra Leone reporting 5,586 cases and 21.45% mortality (Oleribe et al., 2015).

Indeed several studies indicate that four Ebola subtypes (SUDV, EBOV, BDBV and TAFV) have caused all the EVD outbreaks in SSA (Baştuğ & Bodur, 2015; CDC, 2015; Dhama et al., 2015; Heymann et al., 1980). The studies show that out of the 26 outbreaks, EBOV accounted for 16 of the outbreaks with SUDV and BDBV accounting for 7 and 2 outbreaks respectively (table 1). The highest mortality rate of 47%–89% was seen with the EBOV, followed by the SUDV which accounted for CFR of 36%–65%. The BDBV has caused only two outbreaks to date, with a mortality rate of 25%-36%. As of September 2015, EBOV, which caused the outbreak in West Africa has recorded 11306 mortality out of 28200 cases reported from 10 countries (CDC, 2015). By contrast, all SUDV outbreaks reported to date have occurred either in Sudan or in neighbouring Uganda (Baron et al., 1983; Okware et al., 2015; WHO, 1978a, 2005) and only one isolated human case of TAFV from which the patient recovered (Formenty et al., 1999; Le Guenno et al., 1995).

Although outbreaks have been reported since 1976, there was an absence of reported outbreaks in humans for 15 years between 1979 and 1994 and the frequency of outbreaks increased substantially in post 2000 (Kuhn et al., 2008). Additionally, which reservoir species are responsible for maintaining Ebola transmission between outbreaks is not well understood (Peterson et al., 2004), but over the last decade, significant progress has been made in narrowing down the list of likely hosts (Leroy et al., 2011; 2009). Nonetheless, over recent years, significant research has been undertaken in investigating the role bats have to play in the transmission cycle of Ebola viruses (Olival et al., 2014). This research has implicated bats as the possible reservoir of the ebolavirus which is transmitted to non-humans and humans. However, in a recent development, several authors indicate that activities such as cooking or widespread practice of bushmeat and bat hunting, associated with the preparation of meat in forests, as well as any bush activities in SSA can expose humans to

acquiring EVD from animals (Alexander et al., 2015; Gonzalez et al., 2005; Kamins et al., 2011; Nkoghe et al., 2011; Okware et al., 2015; Shoemaker et al., 2012).

Table 1: Summary of EVD Outbreak Parameters in SSA

Sub Region	Location/Year	Cases (CFR)	Transmission Route	Source of Infection	Virus Types	Zone
East Africa	Sudan 1976 Nzara/Maridi	248 (53%)	Animal to human	Unknown	SUDV	Forest (Rural)
	Sudan 1979 Nzara/Yambio	34 (65%)	Animal to human	Unknown	SUDV	Forest (Rural)
	Sudan 2004 Yambio	17 (41%)	Animal to human	Monkey	SUDV	Forest (Rural)
	Uganda 2000-2001 Gulu	425 (53%)	Animal to Human	Unknown	SUDV	Forest (Rural)
	Uganda 2007 Bundibugyo	116 (34%)	Animal to human	Unknown	BDBV	Forest (Rural)
	Uganda 2011 Luwero	1 (100%)	Animal to human	Unknown	SUDV	Forest (Rural)
	Uganda 2012 Kibaale	24 (67%)	Animal to human	Unknown	SUDV	Forest (Rural)
	Uganda 2012-2013 Luwero	6 (67%)	Animal to human	Unknown	SUDV	Forest (Rural)
Central Africa	DRC 1976 Yambuku	318 (88%)	Animal to human	Unknown	EBOV	Forest (Rural)
	DRC 1977 Tandala	1 (100%)	Animal to human	Unknown	EBOV	Forest (Rural)
	DRC 1995 Kikwit	315 (81%)	Animal to human	Unknown	EBOV	Urban
	DRC 2007 Occidental Kasai	246 (71%)	Animal to human	Possibly bat	EBOV	Forest (Rural)
	DRC 2008 Boende	32 (43.8%)	Animal to human	Unknown	EBOV	Forest (Rural)
	DRC 2012 Isiro	36 (54.8%)	Animal to human	Unknown	BDBV	Forest (Rural)
	DRC 2014 Boende	67 (74%)	Animal to human	Possibly Fruit bat	EBOV	Forest (Rural)
	ROC 2001-2002 Cuvette Quest	57 (73.7%)	Animal to human	Gorilla	EBOV	Forest (Rural)
	ROC 2002-2003 Cuvette Quest	143 (89.5%)	Animal to human	Possibly Gorilla and chimpanzee	EBOV	Forest (Rural)
	ROC 2003 Cuvette Quest	35 (82.9%)	Animal to human	White-nose Monkey	EBOV	Forest (Rural)
	ROC 2005 Cuvette Quest	12 (83%)	Animal to human	Elephant	EBOV	Forest (Rural)
	Gabon1995-96 Makouba (Ivindo)	52 (60%)	Animal to human	Possibly Chimpanzee	EBOV	Forest (Rural)
	Gabon 1996 Mayibout (Ivindo)	24 (70.8%)	Animal to human	Chimpanzee	EBOV	Forest (Rural)
	Gabon 1996-1997 Booue (Ivindo)	60 (74%)	Animal to human	Chimpanzee	EBOV	Forest (Rural)
	Gabon 2001-2002 Mekambo (Ivindo)	65 (84.6%)	Animal to human	Possibly Chimpanzee	EBOV	Forest (Rural)

Table 1: Contd.,

Sub Region	Location/Year	Cases (CFR)	Transmission Route	Source of Infection	Virus Type	Zone
Southern Africa	South Africa Johannesburg 1997	2 (50%)	Human to human	Human	EBOV	Urban
West Africa	Cote D'Ivoire 1994 Tai Forest	1 (0%)	Animal to human	Chimpanzee	TAFV	Rural
	Guinea 2014 (Gueckedou)		Animal to human	Fruit bat	EBOV	Forest (Rural)
	Liberia 2014 Foya	6,878 (40.88%)	Human to human	Imported from Guinea	EBOV	Urban
	Sierra Leone 2014	5,586 (21.45%)	Humana to human	Imported from Guinea	EBOV	Urban
	Nigeria 2014 Lagos	20 (40%)	Human to human	Imported from Liberia	EBOV	Urban
	Mali 2014	4 (75%)	Human to human	Imported from Guinea	EBOV	Urban
	Senegal 2014 Dakar	1 (0%)	Human to human	Imported from Guinea	EBOV	Urban

Source: (Alexander et al., 2015; Baron et al., 1983; Formenty et al., 1999; Gatherer, 2014; Georges et al., 1999; Heymann et al., 1980; Khan et al., 1999; Kratz et al., 2015; Lamunu et al., 2004; Leroy et al., 2009; Maganga et al., 2014; Nkoghe et al., 2011; Okware et al., 2015; Oleribe et al., 2015; Shoemaker et al., 2012; WHO, 1978a, 1978b, 2003, 2005).

Location and Spread of EVD in SSA

Given the observation made in literature, EVD has mainly been centred in the remote, rural forest zones of Sudan and DRC (Pigott et al., 2014). However, in 1994 a non-fatal case of EVD appeared in the rural Tai forest of Cote d'Ivoire (Formenty et al., 1999). Since then, the incidence of EVD has increased but is limited to the rural forest zone of East and Central Africa (Groseth et al., 2007; Pigott et al., 2014). Nevertheless, Khan et al., (1999) reported that in 1995 the first EVD outbreak to occur in an urban area took place in Kikwit, DRC. Although the infection was claimed to have occurred in a rural area (Khan et al., 1999). In another development, Georges et al. (1999) who reported on the outbreaks in Gabon noted that the first imported EVD in SSA was from Gabon to an urban hospital in Johannesburg, South Africa (Georges et al., 1999). However, this resulted in just one case in a HCW at the hospital. In their study of the 2013 West Africa outbreak Oleribe et al., (2015), also noted that EVD appeared in Gueckedou, Guinea, a small village bordering Sierra Leone and Liberia. They equally observed the widespread importation of EVD to the capitals of Guinea, Sierra Leone, Liberia, Nigeria, Senegal and Mali (Oleribe et al., 2015). In most of the affected countries, the disease has circulated in a few areas within the same country. For instance, all four outbreaks in ROC happened in rural areas of the Cuvette Quest Region (Nkoghe et al., 2011). Sudan's outbreaks took place in the villages of Nzara, Maridi and Yambio (Baron et al., 1983; WHO, 1978, 2005). Also, two each of the outbreaks in DRC and Gabon took place in occidental Kasai province and Booue respectively (Georges et al., 1999; Kratz et al., 2015; Leroy et al., 2009). However, the recent West Africa outbreak started in Guinea and spread to other West African countries and beyond (Oleribe et al., 2015).

The source of infection in the primary human case has been a mystery, as in most of the studies the source was not identified at all (Sudan 1976, 1979; Uganda 2000, 2007, 2011, 2012, 2012-2013; and DRC 1976, 1977, 2008, 2011, 2012). Also, the sources of the index cases of infection were not identified and were casually linked to exposure to animals found dead in the forest of outbreak sites (DRC 1995, 1997; ROC 2001-2002, 2002-2003; and Gabon 1994, 2001-2002). In contrast, only a few outbreaks were linked to the source of infection which were mainly chimpanzees, gorillas, monkeys, elephants and bats (Cote d' Ivoire 1994; Gabon 1996; Sudan 2004; ROC 2003, 2005; and West Africa (Guinea) 2014).

This review highlights the fact that the geographic range of EVD is expanding from the east to the west of SSA. However, all outbreaks were within the tropical rainforest zone. Peterson et al., (2004) indicate that more than 50% of African evergreen forests are predicted to be within the niche of Ebola. Since its discovery in 1976, the 26 EVD outbreaks in Africa have all occurred within 10°north and south of the equator except the South Africa imported episode (Groseth et al., 2007). In the past spread of cases over longer distances is often associated with treatment-seeking that draws people from rural villages that typify the index case locations to big urban centres with central medical facilities (Georges et al., 1999; WHO, 1978). While this mostly involves domestic land travel as documented in the first Sudan outbreak where patients left Nzara for Khartoum (WHO, 1978a). In some instances, international importation by air travel has been documented in the Gabon case to South Africa case (Georges et al., 1999). However, in recent times the spread of the disease to other countries has been associated with both medical and other factors. For instance, the index case in Senegal was a Senegalese student who attended university in Guinea and imported the disease to Senegal on one of his vacations (Oleribe et al., 2015). Also, the disease was imported to Nigeria by a Liberian who was attending a conference (Oleribe et al., 2015).

Interestingly, except for the 2000, 2011 and 2013 outbreaks in Uganda, all reported indigenous EVD outbreaks seem to be associated with the region near borders. For instance, border towns like Yambio (Sudan), Olloba and Entsiami (ROC), Gueckedou (Guinea) and Foya Liberia have all played major roles in the spread of EVD in SSA (Alexander et al., 2015; Baron et al., 1983; Bausch et al., 2014; Nkoghe et al., 2011). In a well-documented study, Pourrut et al., (2005) noted that between 1976 and 2005 not less than seven (7) outbreaks started from border regions of SSA. However, this review suggests that the majority of EVD outbreaks in SSA occurred in border regions. All the South Sudan outbreaks all cases occurred in border regions of the country.

ROC outbreaks in the border region of Cuvette Quest and all Gabon outbreaks in the border region of Ogooue Ivindo province. Also, all 7 of the DRC EVD outbreaks occurred in border regions. Four in the northern border provinces of Equateur and Orientale and three in the southern border provinces of Bandundu and Kasai Occidental (Heymann et al., 1980; Khan et al., 1999; Rosello et al., 2015; Maganga et al., 2014; Rosello et al., 2015; WHO, 1978) in as well as Cote d'Ivoire outbreak have been documented to have occurred in border regions (Baron et al., 1983; Formenty et al., 1999; Georges et al., 1999; Heymann, 1980; Nkoghe et al., 2011; WHO, 1978a, 1978). This suggests that out of the total 25 documented indigenous outbreak EVD outbreaks in SSA, all occurred in border regions with 15 outbreaks occurring in towns close to borders. East African towns of Nzara, Maridi, Yambio and Bundibugyo have all experienced EVD outbreaks. The same can be said of the Central African towns of Yambuku, Tandala, Mbomo, Etoumbi, Mayibout, Mekambo and Makouba. Again, the West African towns of Foya, Tai Forest and Gueckedou have all had their share of the EVD epidemic. These findings bring to light the high risk of areas near borders in EVD outbreaks in SSA. This calls for further research into the reasons why border regions play a major role in Ebola outbreaks in SSA.

Factors Associated with the Distribution (Spread) of EVD in SSA

Research identified various factors that have fuelled the EVD epidemic in recent times (Pigott et al, 2014). The major factors are population growth, civil unrest, human mobility and urbanization (Alexander et al., 2015). Also, poor health care system, lack of logistics like PPEs and misdiagnoses of disease are associated with the spread of EVD in SSA (Osungbade & Oni, 2014). More so, exploitation of the forest, unhealthy cultural practices, bushmeat consumption, poor infrastructure and poverty have affected the spread of the disease (Alexander et al., 2015; Georges et al., 1999; Khan et al., 1999; Lamunu et al., 2004; Okware et al., 2015; Onyango et al., 2007; Wamala et al., 2010; WHO, 1978).

Before the 2014 West Africa EVD outbreak, the spread of the disease was influenced to a large extent by political, medical, economic and social factors. However, the recent outbreak in West Africa has highlighted the interplay between demographic processes and other factors in EVD (Alexander et al., 2015; Bausch et al., 2014; Gatherer, 2014). The unusual nature of the spread of the West African EVD outbreak indicates that the previous pattern for Ebola outbreaks in SSA is shifting (Briand et al., 2014). Many researchers indicate that this changing pattern in the spread of EVD in SSA was largely influenced by considerable changes in demographic patterns throughout the sub-region in the last four decades (Alexander et al., 2015; Cenciarelli et al., 2015; Bausch et al., 2014; Gatherer, 2014; Pigott et al., 2014). Over the last 40 years, the nexus between the demographic patterns and diseases in SSA has been complex (Pigott et al., 2014). Unfortunately, many researchers like Leroy et al (2011) did not envisage that these demographic patterns could impact the spread of EVD to cause a significant public health threat to West Africa. Rather Leroy et al (2011), argued that Ebola would never become a significant public health threat in Africa (Leroy et al., 2011). This suggests that the threat of EVD was underestimated back then. The threat of Ebola was manifested in the recent outbreak when West Africa struggled to contain EVD (Green, 2014). This exposed the weaknesses in the health system in West Africa (Bausch et al., 2014) which made WHO declare the EVD outbreak in West Africa a Public Health Emergency of International Concern (WHO, 2015).

The influence of population growth on the spread of EVD in recent times cannot be underestimated. In the past, EVD has centred in the remote forest regions of SSA, with relatively smaller populations. However, in recent years population growth in SSA has been dramatic, with population densities (people/km2) increasing by 223%, 178% and 275% in Guinea, Sierra Leone and Liberia respectively from 1960 to 2012 (Alexander et al., 2015: 12). Since the discovery of EVD, the total population living in those countries predicted to be within the EVD-prone area has nearly tripled from 230 million to 639 million in 2012 (Pigott et al., 2014).

Several studies suggest that the human population living within the EVD niche is larger, more mobile and better internationally connected than when the virus was first observed in 1976 (Alexander et al., 2015; Pigott et al., 2014). As a result, the West Africa EVD outbreaks spread through six countries in the sub-region. In West Africa, for example, human movement is a particular characteristic of the region (Awumbila et al., 2014), with migration rates exceeding movement in the rest of the world by more than 7-fold (Alexander et al., 2015). An estimated 11% of West African people live outside their country of birth, with between 30%–40% of people residing outside their district or village of birth (Maconachie et al., 2007). In Liberia, for example, 54% of the population over the age of 14 are identified as being internally displaced (Alexander et al., 2015). Large-scale population movements in the region, both within and between countries, have been driven by decades of conflict and the search for improved socioeconomic conditions and opportunities. As such, present-day population mobility in West Africa has been an important contributing factor to the volatile nature of the West African Ebola outbreak (Garcia et al., 2014).

The argument is supportive of the fact that the proportion of the population which is now urbanized has increased substantially across SSA and more significantly in Guinea (248%), Sierra Leone (130%) and Liberia (163%) from 1960 to 2013 (Alexander et al., 2015). Pigott et al. (2014) reaffirm the fact that the proportion of the population in these countries living in an urban setting has changed substantially over the past four decades. Rural-to-urban migration and growth in the affected countries have significantly increased the proportion of people living in urban environments, where EVD outbreaks have focused in West Africa. As a result, when spillover events do occur, the likelihood of continued spread amongst the human population is greater, particularly in areas with poor healthcare infrastructure. This will have a significant strain on healthcare systems that are already poorly provisioned (Briand et al., 2014).

Efforts to contain any EVD outbreak will require mobilization of many resources including medical personnel, educators, logistics, food, water, provision of modern health care and other essential needs. However, several studies point out that, the health system which is key in controlling EVD outbreaks in SSA countries is improvised and unable to provide quality health care. This is partly so because according to Bausch et al (2014), most of the SSA countries are living below the poverty line. They added that most of the countries are ranked low on the poverty scale by the United Nations Development Programme-Human Development Index. For example, EVD-affected countries such as Guinea, Liberia and Sierra Leone are ranked 178, 174 and 177 respectively out of 187 countries on the poverty scale. Moreover, most of the EVD affected countries have sustained various degrees of civil unrest over the last two decades (McPake et al., 2015). These factors, coupled with a lack of basic health infrastructure, shortages of HCW, inadequate hospital logistics and poor hospital sanitation among other things have undermined the health systems in SSA (Alexander et al., 2015).

According to Khan et al (1999), the DRC Kikwit 1995 outbreak recorded high mortality because of an inefficient health system. A similar observation was made by (Baron et al., 1983) in Sudan in 1979 and Lamunu et al (2004) in Uganda 2001-2002. In contrast, Senegal and Nigeria whose healthcare systems were also poor were able to control the epidemic in its early stages (Oleribe et al., 2015). In EVD outbreaks Health workers have been disproportionately affected because of the tremendous demands of patient care and due to the difficulty of implementing control measures to prevent the infection (Dhama et al., 2015). Even worse, an unprecedented number of health personnel risked their lives and died during EVD outbreaks in SSA (Liu et al., 2015; Mbonye et al., 2014). This has created fear and panic moments among health workers across SSA (Nyarko et al., 2015) and has led to the closure of hospitals, the refusal of HCWs to go to work, because of fear of dying in past outbreaks as seen in the outbreak in Kikwit, DRC in 1995 (Khan et al., 1999). Even for a country that is yet to experience an EVD outbreak like Ghana, Nyarko et al (2015) noted signs of fear and panic among health workers in line with their duty.

Increasing human encroachment and certain cultural practices sometimes linked with poverty, such as bushmeat hunting, result in increasing exposure of humans to animals which may harbour diseases including EVD (Wolfe, 2005). The changing pattern in the spread of EVD in SSA underscores the need for community, national and international preparedness against Ebola by constituting rapid response teams. This involves trained human resources from veterinary, medical and wildlife health streams. Strengthening diagnostic testing facilities, boosting EVD research and increasing public awareness (WHO, 2014). To prevent EVD, strong and comprehensive national preparedness is a prerequisite that involves screening passengers coming from Ebola-affected countries and creating awareness regarding the facts about Ebola. Only informed and empowered communities can complement public health efforts to fight Ebola (Lamunu et al., 2004). In Nigeria, massive mobilization, the excellent role of local skilled manpower, awareness creation, sensitization of the populace to the dangers, signs and symptoms of EVD, and acceptable practices within and outside the health institutions stopped the spread of EVD easily (Oleribe et al., 2015) Equally, Senegal's preparedness approach was seen to be effective to the extent that, there was only one case which did not end in fatality. These approaches include contact tracing, health educational activity, state-of-the-art laboratories, rapid response teams, ambulance service and mobile phones for easy communication. (Oleribe et al., 2015).

In Ghana, EVD preparedness is mainly centred on capacity building which focuses on health education and awareness creation, training and setting up of Ebola Treatment Centres (ETCs). Further, the Government of Ghana facilitated the establishment of the United Nations (UN) Ebola response mission in Africa (United Nations Mission for Ebola Emergency Response) to be headquartered in Ghana (Oleribe et al., 2015).

CONCLUSION

Finally, this research has brought to the fore the factors associated with major EVD outbreaks in sub-Saharan Africa. EVD outbreaks increased from 1976 to 2014 with high morbidity and mortality however, there were isolated reported cases of EVD in DR Congo from 2015 to date. The spread of EVD is within and across several urban centres in different countries with the geographical niche expanding from the east to the west with border regions being the starting point for most of the outbreaks. Furthermore, social, political, economic, medical, cultural and agricultural factors seem to be associated with the spread of EVD with demographic factors (population growth, human mobility and urbanization) being the underpinning factors influencing the 2014 West Africa outbreak, which is the longest and the biggest EVD outbreak so far. The changing patterns in the spread of EVD call for holistic preparedness which comes from well-informed individuals, communities, regions, countries and the international community as a whole to combat Ebola outbreaks in the future. This paper also suggests further research into why border regions of SSA are high-risk areas of EVD to equip stakeholders in border regions to draw EVD preparedness plans targeted at their locations for any eventuality.

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