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Impacts of the *Filoviridae* family

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Abstract

Over 40 filovirus disease outbreaks have been reported since the discovery of the first member of the *Filoviridae* family, and most of the outbreaks have occurred in Africa. In addition to deaths (primary impacts), there have also been health, social, economic, and political effects (secondary impacts) due to the outbreaks. Two large filovirus disease outbreaks have occurred in West and Central Africa in recent times, and direct and indirect repercussions resulting from the outbreaks underscores the need to strengthen the capacity of health services in disease hotspots.

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Introduction

History is littered with major infectious disease outbreaks that have caused significant woes to affected persons, nations, and the world as a whole. Although global efforts have been made to reduce the burden of infectious disease outbreaks, the frequency of the outbreaks have increased over the past few decades and has been attributed to human activities and climate change [1]. The risk of infectious diseases outbreaks is profound in low- and middle-income countries because of gaps in disease outbreak detection and response systems, such as timely detection of disease, availability of basic care, tracing of contacts, and quarantine and isolation procedures [2]. Disease outbreaks in these regions usually have long-lasting direct impacts, as well as secondary health, social, economic, and political impacts [3].

Filoviruses are capable of causing severe hemorrhagic fever outbreaks in humans with a case fatality of up to 90% depending on the virus [4]. Almost all filovirus disease outbreaks have originated or occurred in Africa, and the frequency of the outbreaks have been increasing since the first outbreak in 1967, with the origins, natural history, and ecology of the outbreaks being somewhat mysterious. Recent ecological and epidemiological evidence, however, implicate bats as one possible reservoir of filovirus [5]. Although filovirus disease outbreaks are of zoonotic origin and occur due to spillovers from wildlife reservoirs to humans, a persistent source of infection from an infected person (survivor of an earlier outbreak) can spark a new outbreak [6]. In this review, we elucidate mainly the impacts of the two largest filovirus disease outbreaks that have occurred in West and Central Africa by highlighting the direct and indirect consequences of the outbreaks and stress the need for strengthening capacity in disease hotspots. Figure 1 shows countries in Africa that have been most affected by filovirus disease outbreaks.

The *Filoviridae* family

Filoviruses are non-segmented negative-stranded RNA viruses belonging to the order *Mononegavirales*, and are genetically, morphologically, and biologically distinct from other members [7]. Currently, members of the *Filoviridae* family are classified into five genera, *Ebolavirus, Marburgvirus*, *Cuevavirus, Striavirus, and Thamnovirus*, with the proposal of a sixth genus, *Dianlovirus* [8]. While the *Ebolavirus* genus consists of six virus species *(Zaire ebolavirus, Sudan ebolavirus, Tai Forest ebolavirus, Reston ebolavirus, Bundibugyo ebolavirus*, and *Bombali ebolavirus)*, the *Cuevavirus, Striavirus, Thamnovirus*, and *Marburgvirus* genera each consist of one virus species, *Lloviu cuevavirus, Xĭlăng striavirus*, *Huangjião thamnovirus*, and *Marburg marburgvirus*, respectively.

There are six viruses within the *Ebolavirus* genus, Ebola virus (EBOV), Sudan virus, Tai Forest virus, Reston virus, Bundibugyo virus, and Bombali virus, two in the *Marburgvirus* genus, Marburg virus (MARV) and Ravn virus, and a single virus each in the *Cuevavirus, Striavirus*, and *Thamnovirus genus;*L. cuevavirus, Xĭlăng striavirus, and Huangjião thamnovirus, respectively [8,9]. Among the 12 filoviruses, six are known to cause disease in humans,

Figure 1

Map of Africa showing countries that are most affected by filovirus disease outbreaks. Highlighted in blue, are countries that have recorded at least 100 human cases.

with EBOV and MARV considered to be the most virulent members of the *Filoviridae* family. EBOV and MARV have caused several human and animal outbreaks across the world [10] and have been listed as high-priority pathogens by the World Health Organization because of the epidemic potential of the viruses [11].

Primary impacts of Filovirus disease outbreaks

Filovirus disease outbreaks have caused significant loss of human and animal lives. Since the discovery of the first member of the *Filoviridae* family (MARV) in 1967, tens of thousands of lives have been lost, including the decimation of some primate species (reviewed in the study by Languon and Quaye [10]). Filovirus outbreaks that resulted in 100 or more human cases are listed in Table 1.

The largest filovirus disease outbreak to date is the 2013–2016 Ebola virus disease (EVD) outbreak, which began in West Africa and later spread to other parts of the world. A total of 28,616 cases with 11,310 deaths were recorded over the two-and-a-half-year period that the outbreak occurred [12]. While the West African EVD epidemic was raging, a concomitant EVD outbreak was reported in the Équateur Province of the Democratic Republic of the Congo (DRC), which resulted in 49 deaths among a total of 69 recorded cases [13]. Three years after the West African EVD epidemic, an outbreak

Table 1

List of filovirus disease outbreaks with more than 100 recorded human cases.

Filovirus Subtype	Affected Country	Year (s)	Recorded human cases	Recorded deaths
SUDV	Sudan	1976 (June–November)	284	151
EBOV	DRC	1976 (September–October)	318	280
EBOV	DRC	1995	315	250
MARV (& RAVV)	DRC	1998–2000	153 (1)	128
SUDV	Uganda	2000–2001	425	224
EBOV	Gabon and Republic of Congo	2001–2002 (October–March)	124	97
EBOV	Republic of Congo	2002–2003 (December–April)	143	128
MARV	Angola	2004–2005	252	227
EBOV	DRC	2007	264	186
BDBV	Uganda	2007–2008 (December–January)	131	42
EBOV	Multiple countries	2013–2016 (December–March)	28, 616	11,310
EBOV	DRC	2018–2020 (August–June)	3,470	2,280

EBOV, Ebola virus; MARV, Marburg virus; RAVV, Ravn virus; SUDV, Sudan virus.
Table adapted from the study by Languon and Quaye [10].

of EVD was reported in the Bas Uélé District of the DRC, involving 8 reported cases and 4 deaths [14]. In May 2018, an outbreak of EVD was reported in the Bikoro health zone of Équateur Province, DRC [15]; the ninth EVD outbreak in the DRC since the discovery of EBOV in 1976. After 2 months of intensive control measures and vaccination, the ninth outbreak was declared to be over with a total of 54 cases, including 33 deaths [15].

In August 2018, the DRC Ministry of Health declared the tenth outbreak of EVD in the North Kivu Province [15]; an announcement that was made only a week after the ninth outbreak was declared to be over in the northwestern Équateur Province [16]. Despite the lessons learned from the 2013–2016 West African EVD, the outbreak in North Kivu and Ituri Provinces lasted for almost two years (August 2018 to June 2020) and resulted in 2,287 deaths out of 3,470 recorded cases [17]. The tenth episode is the second-largest EVD outbreak in recent history, the largest outbreak ever recorded in the East African Region. While the tenth EVD outbreak in the DRC was winding down, the eleventh outbreak was reported in the northwestern Équateur Province again, but genome sequences confirmed it has no association with the tenth outbreak in North Kivu [18]. The eleventh outbreak involved 13 health zones and was declared to be over in November 2020, after 130 cases, including 55 deaths, had been recorded [19]. In February 2021, the twelfth EVD outbreak in the DRC was declared in the North Kivu Province and has been linked to the 2018–2020 outbreak (the tenth outbreak) in North Kivu and Ituri Provinces [20]. A total of 12 cases including 6 deaths were recorded over the course of the outbreak, which was declared to be over on May 3, 2021 [21].

A week after the declaration of EVD outbreak in the DRC, the Ministry of Health in Guinea also declared an outbreak of EVD in Gouécké, a town in the N'zérékoré region. Although inconclusive, genomic sequences strongly suggest that the source of the outbreak is a survivor of the 2013–2016 West African EVD epidemic and not a spillover event [6]. The outbreak was declared to be over on June 19 2021, after a total of 23 cases including 12 deaths were recorded [22]. More than 10,800 people were vaccinated over the course of the outbreak.

A number of Marburg virus disease outbreaks have also been reported, with the most fatal ones occurring in DRC from 1998 to 2000 and in Angola from 2004 to 2005 [10]. In the DRC outbreak, a total of 153 cases were recorded, including 128 deaths, and for the outbreak in Angola, 227 deaths were recorded out of 252 total cases.

Secondary impacts of Filovirus disease outbreaks

Health impact

Filovirus disease outbreaks can have devasting health impacts, and outbreaks that explode into epidemics can indirectly increase morbidity and mortality due to other health conditions. Owing to fragile health systems, African countries in which filovirus disease outbreaks have occurred usually struggle to cope with regular health issues during the outbreaks, as funds (including donor funds), resources, and personnel for regular healthcare are either diverted or depleted [2,24]. For example, during the 2013–2016 EVD epidemic, the diversion of resources in affected regions resulted in increased deaths from regular health problems such as diarrhea, HIV/AIDS, and tuberculosis [24,25]. In Guinea, Liberia, and Sierra Leone, the lack of routine care for malaria, HIV/AIDS, and tuberculosis patients led to an estimated 10,600 additional deaths, with a 30% decrease in routine childhood vaccinations; the authors, however, cautioned about the difficulty in distinguishing between deaths attributable to an epidemic, and those that may

be merely coincidental [2]. In Sierra Leone, advances made in the health sector (child mortality, maternal mortality, HIV/AIDS, malaria) were reversed because of the closure of health facilities and the diversion of resources to combatting the EVD epidemic [26]. Restriction on travel and the enforcement of infection control measures deterred people from accessing health care facilities for regular health needs and thus adding on to the number of deaths. Although such restrictions were not imposed during the 2018–2020 EVD outbreak in North Kivu Province, DRC, insecurity coupled with poor roads, telecommunications, and health system infrastructure thwarted efforts to respond to the outbreak [27] and resulted in deaths from regular health problems [28].

The absence of robust public health systems in affected countries has been highlighted as a contributory factor to the devastating impact of filovirus disease outbreaks. The large number of deaths resulting from recent filovirus outbreaks have spurred the organization of local rapid response teams, along with the strengthening of laboratory and public health services in communities of affected countries [29–31]. A global rapid response funding was established by the World Health Organization in 2016 to respond to disease outbreaks [32,33] and has aided in tackling various disease outbreaks around the world, including the 2018 EVD outbreak in the DRC [34].

Social impact

The fear of infection, breakdown of trust, and changes in behavior affected social cohesion, as disease survivors and their families, health workers, and individuals who were directly involved in controlling the outbreaks experienced stigmatization resulting in social exclusion [35]. Some survivors of the 2013–2016 Ebola virus outbreak were evicted from rented houses and chased out of their communities [36,37]. In the USA, health care providers were shunned and stigmatized for working in a hospital where an EVD patient was being treated [38], and Africans in Hong Kong, the USA and Canada were shunned and socially excluded during the 2013–2016 Ebola virus crisis [2,39]. In addition, some colleges in the United States rejected the applications of African students because of fear of importing EVD cases into their home country [40].

Filovirus disease outbreaks had a negative effect on education, either because of school closures or the reluctance of parents to send their wards to school for fear of getting infected; as the outbreak raged on, months of schooling were lost, and some children found it difficult to re-enroll after the crisis [41,42]. Funds for educational purposes were diverted to outbreak responses and negatively affected investment in the education system. Owing to disease response measures during the 2013–2016 EVD epidemic in West Africa, education was interrupted in the three most affected countries, with a similar occurrence during the 2018 EVD outbreak in the DRC [35,41,43]. Across Guinea, Liberia, and Sierra Leone, an estimated 5 million children did not attend school during the 2013–2016 EVD outbreak due to school closures [44], followed by an increase in the rate of student dropout and child labor [45].

The diversion of resources that were intended for education to major filovirus disease outbreaks delayed investments that were needed for education [41]. In Liberia, UNICEF's Peacebuilding, Education and Advocacy programme, originally meant to reinforce the capacity of education to contribute to peacebuilding by reducing education inequality in rural communities, was reoriented to tackle the 2013–2016 EVD outbreak [41]. While it was a good decision at the time to divert funding for Peacebuilding, Education and Advocacy to fight the EVD outbreak, it impeded the work required to ensure that the education sector served as an engine of peace and sustainable development [41].

Economic impact

Response measures to stop the spread of infection during filovirus disease outbreaks included trade and travel restriction, which had significant economic impacts [39,46]. A reduction in the labor force due to sickness and/or mortality, coupled with fear of associating with others, negatively affected economic activities during the outbreaks [47]. The economies of countries/regions where filovirus disease outbreaks occurred suffered negatively in both the short and longer terms; travel restrictions, quarantines, bans on social gatherings, closure of borders and markets severely disrupted businesses and trade [48]. All sectors of the economies faced disruption during the severe filovirus outbreaks and led to shortages and hoarding of commodities, as well as increased pricing for stable goods, and stress on the finances of families, private firms, and governments [2,45].

The occurrence of the 2013–2016 EVD outbreak in West Africa coincided with land preparation, planting, and harvesting of farm produce, and thus negatively affected the agricultural sectors of Guinea, Liberia, and Sierra Leone, as labor and markets were lost [45]. Estimates in 2014 showed that rice production fell by 20%, coffee by half, cocoa by a third, and corn by a quarter in Guinea [49]. In Liberia, which is a largely agrarian society, labor mobilization for planting and harvest was hampered because of fear of infection [48] and resulted in a reduction in the size of rice plantations and yield [45,49,50]. The livelihoods of women were the most affected by bans and travel restrictions during the EVD crisis in Guinea, Liberia, and Sierra Leone, because

women dominate the agricultural sectors in these countries [49]. In Sierra Leone alone, the number of working traders reduced by 20% during the epidemic [51], and production of goods traded with neighboring countries, and which involved in-person cooperation, declined steeply in affected areas [24]. Lockdowns in the West Point quarter in Liberia restricted the movement of individuals who sold smoked fish to other parts of the city, thus destroying livelihoods and food supplies, and contributed to protests over mistrust of government [37]. During the 2013–2016 EVD epidemic, Kirigia et al. [52] calculated the non-health gross domestic product losses associated with EVD deaths to be $155,663,244 (international dollars); with Sierra Leone and Liberia bearing the highest losses. The monetary value of years of life lost (MVYLL) was estimated to be $17,761,539 (international dollars) for the recent 2018/2019 EVD outbreak in North Kivu Province, DRC; the second-largest EVD outbreak to date [53].

The tourism industry in the whole of West Africa was not spared during the 2013–2016 Ebola virus outbreak due to cessation of flights to and from affected and neighboring countries, and the issuance of travel warnings to tourists by countries which are sources of revenue to the tourism industry [49,54,55]. Hotels, airlines, restaurants, and guest houses were shut down in Sierra Leone, which led to a 50% drop in tourism from 2013 to 2014 [56] and an increase in unemployment across the country [54,56]. The outbreak led to a decline in foreign and domestic investment in the affected countries [24,49] as there was a rise in uncertainties, and the zeal of investors was dampened [24]. The number of business visitors arriving at Lungi International Airport in Sierra Leone from January to June 2014 declined by 46.9% compared to the same period in 2013 [49].

Political and security impacts

In Liberia, the 2013–2016 Ebola virus outbreak negatively affected the citizens' perceptions of the government and public workers and weakened the trust that Liberians had in their institutions [41,50]. Two years after the epidemic in West Africa, it was reported that religious communities and areas that were hard hit had lower levels of trust in the government, than pre-epidemic levels [57], and was attributed to the impact of behavioral sanctions on cultural practices of the inhabitants during the epidemic. The cancellation of presidential and legislative elections during the 2018–2020 in North Kivu Province EVD outbreak resulted in mistrust of the government, as the directive was interpreted by many as being disenfranchised rather than controlling the outbreak [57].

Conclusion and recommendations

The African continent has disproportionately been affected by filovirus disease outbreaks with gross primary and secondary impacts and, therefore, underscores the need for governments and stakeholders in Africa to work closely together to curb the increased occurrence of outbreaks in recent years. The adoption of a One Health approach in the surveillance, detection, prevention, and control of filovirus disease outbreaks in countries with an elevated risk of outbreak occurrence should be encouraged. In addition, the strengthening of the capacity of health services in countries that are hotspots of outbreaks would aid in early disease detection and management, which will help in mitigating future epidemics and/or pandemics.

Author contribution

Conceptualization: SL and OQ; Data curation: SL and OQ; Formal analysis: SL and OQ; Project administration: SL and OQ; Supervision: OQ; Validation: OQ; Writing - original draft: SL; Writing - review & editing: SL and OQ. Both authors approved the manuscript for publication.

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Conflict of interest statement

Nothing declared.

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