ORIGINAL ARTICLE

Ebola Virus Disease Outbreaks - A Systematic Review

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ABSTRACT

Background: The expansion of the Ebola virus has created illnesses that are deadly to both animals and people. This spread has been driven by the rise of urbanization, the invasion of wooded regions, and the intimate connection with wildlife creatures. To this day, the Ebola virus illness, also known as EVD, has been responsible for the deaths of a significant number of people, with the continent of Africa reporting the highest incidence of the disease.

Aim: In order to investigate the Ebola outbreaks, as well as morbidity and fatality rates among EVD patients, a systematic review was carried out.

Method: Using MeSH keywords like Ebola outbreaks, Ebola virus disease, Ebola disease, and Ebola Epidemic, we searched Google Scholar, Science Direct, and PubMed for articles on EVD epidemics published between 1976 and 2022.

Results: Gabon, Guinea, the Republic of the Congo, and Zaire/Democratic Republic of the Congo have all been epicenters for at least 17 EVD epidemics since EBOV was first discovered in 1976. Although case statistics may vary significantly from source to source, as of this writing, there have been an estimated 34,442 EBOV infections in humans, with 4100 (11.9%) fatalities.

Conclusion: Multiple EVD pandemics have emerged, mostly in Africa. Although the exact point of genesis of the Ebola virus remains unknown, we do know that direct contact with infected animals may potentially convey the illness to humans.

Keywords: Ebola, Ebola Virus Disease, Ebola outbreaks, EVD, Ebola epidemic

INTRODUCTION

Symptoms of Ebola virus disease (EVD) include fever and malaise that come on suddenly, as well as myalgia, headache, vomiting, and diarrhea. Hemorrhagic manifestations occur in 30%-50% of people with EVD². Shock and mortality result from multiorgan malfunction, including damage to the liver, the kidneys, and the central nervous system in the most severe cases. Both the Sudan Ebolavirus and the Zaire Ebolavirus were identified in 1976, at the same time. The Sudan Ebolavirus was found in the Sudan, which is now known as the Democratic Republic of the Congo (DRC). The Zaire Ebolavirus was found in Zaire, which is now known as the DRC³. The Ebola virus, which belongs to the species Zaire ebolavirus, is responsible for the bulk of the over 20 Ebola virus disease outbreaks that have taken place in Central Africa since 1976. Additionally, the Ebola virus has the highest rate of case fatalities (up to 90%)¹.

Fruit bats may be part of the wildlife reservoir, although that hasn't been confirmed⁴. The virus is transmitted from person to person by contact with bodily fluids such as blood, urine, sweat, semen, and breast milk and is originally introduced to humans through contact with infected animals. The gestation period is from 2 to 21 days. The virus may be spread not just when a patient is contagious because of a high body temperature but also later in the course of the illness and even after death if mourners come into touch with the corpse. Furthermore, As late as 61 days after the sickness started, the virus was discovered in sperm samples.

Blood tests for Ebola virus RNA or antibodies are the gold standard for diagnosis³. The Kenema Government Hospital Viral Hemorrhagic Fever Laboratory in Sierra Leone, the Liberia Institute of Biomedical Research in Liberia, and the Institute Pasteur in Guinea are all doing testing related to this epidemic. There is currently no therapy for Ebola that has been proven to be both safe and effective. Clinical care includes vigorous monitoring of fluid and electrolyte balance, oral and intravenous feeding, and the use of drugs to reduce temperature and GI discomfort and ease pain, anxiety, and agitation^{2,3}. Care for patients also involves identifying and treating secondary illnesses, such as malaria and typhoid².

Controlling an EVD outbreak requires four main steps: 1) To stop the spread of the virus, it is important to detect infections as soon as possible and isolate patients from the general population; 2) Monitor all known contacts of an ill or deceased individual daily for the entire 21-day incubation period; 3) researching and documenting previous and current viral transmission networks; 4)

registering deaths and following proper burial procedures; and 5) instances reported every day^{2, 5, 6}. Due to the fact that transmission in the context of medical care has contributed during previous outbreaks, educating healthcare professionals on appropriate infection-control practices is crucial to protecting them and their patients^{2,7}.

METHODOLOGY

We searched for articles on EVD epidemics using MeSH keywords, including "Ebola," "Ebola virus disease," "Outbreak," and "Epidemic" in Google Scholar, Science Direct, and PubMed. From 1976 to 2022, every piece in print was read. UpToDate, the US Food and Drug Administration, the World Health Organization, and the CDC were all scoured for the most recent studies. Substantial research and review papers' citation networks were also taken into account. Only articles that fit the review's criteria were chosen.

RESULTS

Outbreaks of Ebola Virus Disease: Zaire (today the Democratic Republic of the Congo) was the site of the world's first confirmed case of Ebola virus disease in 1976. Virological and epidemiological evidence suggests that the Ebola virus predates any known outbreaks. However, urbanization, the invasion of forested areas, and close contact with wildlife species have all contributed to the rapid spread of the Ebola virus, causing devastating sickness in both animals and people. Although the Ebola virus's natural reservoir host has not been identified, scientists have long suspected that African fruit bats play a role in the virus's propagation and may even be the virus's reservoir host. Even though bats in Sierra Leone harbored the Ebola virus that was most recently isolated (the Bombali virus), researchers are still looking for proof that bats play a significant role in the disease's transmission³⁸⁻⁴⁰.

Table 1: The cases and outbreaks of Ebola virus disease by year.

Country (year)	Case-fatality rate (%)	Number of
	, , ,	cases
COD (then Zaire) (1976) ⁸	280 (88.1%)	318
Sudan (1976) ⁹	284 (53%)	284
COD (then Zaire) (1977) ¹⁰	1 (100.0%)	1
Sudan ¹¹	22 (65%)	34
Gabon (1994–1995) ¹²	31 (61%)	51
COD (then Zaire) (1995) ¹³	254 (81%)	315
Russiaa (1996)14	1 (100.0%)	1

South Africa ¹⁵	1 (50%)	2
Gabon (1996) ¹⁶	21 (67.7%)	31
Gabon (1996) ¹⁷	45 (75%)	60
Uganda (200) ¹⁸	224 (53%)	425
Republic of the Congo (2001) ¹⁹	44 (75%)	59
Gabon ²⁰	53 (81%)	65
Republic of the Congo (2003) ²¹	29 (83%)	35
Republic of the Congo (2003) ²²	128 (89%)	143
Russia (2004) ²³	1 (100.0%)	1
Sudan (2004) ²⁴	7 (41%)	17
Uganda (2007) ²⁵	42 (32%)	131
Democratic Republic of the Congo (2007) ²⁶	187 (71%)	264
Democratic Republic of the Congo (2008) ²⁷	15 (47%)	32
Uganda (2011) ²⁸	1 (100%)	1
Uganda (2012) ²⁹	3 (50%)	6
COG (2014) ³⁰	49 (71%)	69
Guinea, Liberia, Sierra Leone (2014) ³¹	11,308 (39%)	28,610
Italy (2014) ³²	0	1
Mali (2014) ³³	6 (75%)	8
Nigeria (2014) ³³	8 (40%)	20
Senegal (2014) ³³	0	1
Spain (2014) ³⁴	0	1
United Kingdom (2014) ²⁹	0	1
United States (2014)33	1 (25%)	4
DR Congo (2018 – 2020) ³⁵	2287 (66%)	3470
DR Congo (2021) ³⁶	9 (81.8%)	11
Uganda (2022) ³⁷	55 (33.5%)	164

In 1976, the first instances of disease caused by the Ebola virus were recorded in a village located along the Ebola River in DRC and South Sudan, which was then known as Zaire. The Zaire ebolavirus and the Sudan ebolavirus are two related but genetically separate viruses that produced these two epidemics. With 318 confirmed cases and 218 fatalities, the DRC outbreak is one of the worst in recorded history. Only 38 people have been verified to have survived the outbreak by serological testing. Transmission occurred mostly via direct patient-to-nurse contact and the reuse of contaminated needles and syringes in healthcare facilities. There were 284 confirmed cases of the epidemic in South Sudan, with 151 of those cases resulting in fatalities (a mortality rate of 53%). Workers in a cotton mill, where 37 percent of workers in the fabric room were sick, are generally considered to be the source of the outbreak, which moved to hospitals mostly through close personal contact among healthcare professionals38,40,41

An estimated 315 cases were documented in Kikwit in 1995, with 254 fatalities (representing 81% of all cases) and their origin traced back to a charcoal producer in the wooded regions around the city. Uganda reported 425 confirmed cases in 2000, with 224 deaths. The Gulu area was the first hit, but it quickly spread to Masindi and Mbarara. From 2001-2005, the Democratic Republic of the Congo reported 319 confirmed cases of Zaire ebolavirus, including 271 fatalities. Mbomo and Kéllé districts in the western Cuvette Ouest Department of the Republic of the Congo were among those hit by the epidemic, which occurred across the border from Gabon 39,40.

In 2007, Uganda and DRC reported 395 cases of Bundibugyo ebolavirus and 229 cases of Zaire ebolavirus, respectively, with 229 deaths. The new Bundibugyo ebolavirus strain has now been identified. However, as compared to other Ebola virus strains, Bundibugyo ebolavirus epidemics had a lower fatality rate. The 2014 West African Ebola pandemic was the greatest ever recorded outbreak of the virus. On March 23, 2014, authorities in rural south-eastern Guinea reported the onset of the disease. Then neighboring countries like Liberia and Sierra Leone started reporting instances. The lacklustre monitoring and shaky public health infrastructure made it hard to track down the instances. Additionally, the state of the epidemic is exacerbated by inadequate infection control and overburdened medical services. The WHO designated the outbreak in August 2014 as a PHEIC. The WHO, the CDC, the Ministries of Health of the affected countries, and other national and international partners worked together to announce an end to the epidemic in June of 2016⁴⁰.

In Mbandaka, Equateur Province, DRC, the authorities declared the 9th pandemic of Ebola virus infection on May 8, 2018, with 38 confirmed and 16 probable cases recorded. There were 54 recorded occurrences, 33 of which resulted in deaths and 21 in recoveries. On July 28, 2018, 42 days after the first case was reported, the final known patient tested negative, thereby ending the outbreak³⁸.

The regions of North Kivu, South Kivu, and Ituri in the Democratic Republic of the Congo had their eleventh pandemic on August 1, 2018. There were a total of 3317 confirmed cases and 153 cases that were deemed probable out of the total number of cases reported. Overall, there were 2287 people who lost their lives, while 1171 people survived. Since April 27, 2020, there have been no newly reported cases of Ebola Virus Disease (EVD) in North Kivu, South Kivu, or Ituri; hence, the epidemic came to an end on June 25, 2020³⁹.

The Équateur province's Wangata health zone had an Ebola virus illness epidemic on June 1, 2020, according to the government of the DRC. This would be the eleventh such outbreak since 1976, when the virus was first detected. Six cases of Ebola have been found in Wangata so far; four have died and two are now receiving medical attention⁴².

An estimated 3463 cases of EVD has been reported as of June 2, 2020 (3,317 verified cases and 146 suspected cases), with 2280 deaths (for an overall case-fatality ratio of 66%) and 1171 complete recoveries. There were 57% females, 29% younger than 18-year-olds, and 5% healthcare professionals among the total confirmed and probable cases. On the other hand, the World Health Organization said on June 9 of this year that the eleventh epidemic is unrelated to the tenth outbreak that occurred in the provinces of North Kivu, South Kivu, and Ituri, and that it is also separate from the ninth outbreak that was circulating in the province of Équateur in 2018. As of June 21st, 2020, a total of 3470 EVD cases have been documented (3,317 confirmed cases and 153 suspected cases), resulting in 2287 fatalities and 1171 recoveries^{42,43}.

The second greatest Ebola epidemic in history was reported on June 25th, 2020, and it happened in a war zone. Over 303,000 individuals were vaccinated with a recombinant vesicular stomatitis virus-Zaire Ebola virus (rVSV-ZEBOV) developed by the Government and Ministry of Health (MoH) of the DRC with help from the World Health Organization and partners⁴².

Nearly doubling in size since the 11th DRC was declared on June 1st, 2020 in Equateur Province, the western DRC Ebola epidemic surpassed 100 cases on August 21st, 2020. Forty-three persons have died, and 96 of the 100 cases recorded have been verified. Due to the fact that the illness moved from east to west and north to south across a span of around 300 km, the region that straddled the Equator made it exceedingly difficult to maintain control of the epidemic. On September 1, 2020, little than three months after it was announced that the eleventh outbreak had occurred in Equateur Province, the Democratic Republic of the Congo (DRC) stated that the number of patients had increased and that the disease had moved to other regions. As a whole 110 cases have been recorded, with 104 of them being confirmed and 6 being considered probable. There have been a total of 110 reported cases, with 47 fatalities (a fatality ratio of 43%) throughout 36 health areas and 11 health zones, and 24 confirmed cases 42-44.

The Equateur Province EVD epidemic was officially declared over by the DRC Ministry of Health on November 18th, 2020. The statement was made on October 6, 2020, 42 days after the second round of testing on the last verified case in the Makanza Health Zone in Equateur Province came back negative. This was done in compliance with World Health Organization protocols⁴².

In 1976, the second such EVD epidemic in the DRC was discovered in Equateur Province. During this outbreak, there were two different Ebola Zaire viruses going around. In 2018, an epidemic of Ebola spread across Equateur Province, where four people were sick. The other cases were infected with a new Ebola Zaire virus that came out in 2020. From June 2020 through

November 2020, a total of 130 cases of EVD were recorded, 119 of which were confirmed and 11 of which were suspected. Out of all the proven and likely cases, 45% were women, and 23% were children. Fifty-five people lost their lives, or 42% of the total number of reported cases; 29% (34/119) of those who contracted Ebola died outside of treatment facilities; 75% of those who were infected with EVD survived. Even though more than 26,000 touch cases of EVD were reported in Equateur Province during the outbreak, the disease can still spread from person to person^{42,45}.

Compared to the tenth epidemic, the fatality rate in Equateur province has decreased to 43%. The patients in the eleventh epidemic may have benefited from the advancement and development of vaccinations and curative therapy thanks to scientific advancements. More than 40 thousand persons were vaccinated against rVSV-ZEBOV during the 11th epidemic, according to the World Health Organisation⁴⁴. Table 1 displays the annual incidence and fatality rates.

CONCLUSION

Several epidemics of EVD have occurred, most often in Africa. To this day, we still don't know for sure where the Ebola virus originated, but we do know that infected animals may spread the disease to others via direct contact.

REFERENCES

- World Health Organization. Ebola viral disease: fact sheet. Geneva, Switzerland: Available Health Organization; 2014. at http://www. Wolfd reality Organization, 2017. Admission of the Wolfd Medicine Medicine Medicine Medicine Sans Frontières. Filovirus haemorrhagic fever guideline. Barcelona,
- 2 Spain: Médecins Sans Frontières; 2008:39-48.
- Formenty P. Ebola-Marburg viral diseases. In: Control of communicable diseases manual. Heymann DL, ed. Washington, DC: American Public Health Association; 3
- Leroy EM, Kumulungui B, Pourrut X, et al. Fruit bats as reservoirs of Ebola virus. 4 Nature 2005;438:575-6.
- 5 Rollin P, Roth C. Lassa fever. In: Control of communicable diseases manual. Heymann DL, ed. Washington, DC: American Public Health Association; 2008:335-7
- 6 Nkoghe D. Formenty P. Leroy EM, et al. Multiple Ebola virus haemorrhagic fever outbreaks in Gabon, from October 2001 to April 2002 [French]. Bull Soc Pathol Exot 2005:98:224-9.
- Pattyn SR, ed. Ebola virus haemorrhagic fever. Amsterdam, The Netherlands:
- World Health Organization. Ebola haemorrhagic fever in Zaire, 1976. Report of an International Commission. Bulletin of the World Health Organization. 8 1978;56(2):271-293.
- World Health Organization. Ebola haemorrhagic fever in Sudan, 1976. Report of 9 a WHO/International Study Team . Bulletin of the World Health Organization. 1978:56(2):247-270.
- Heymann DL, Weisfeld JS, Webb PA, et al. Ebola hemorrhagic fever: Tandala, 10 Zaire, 1977–1978. Journal of Infectious Diseases. 1980;142(3):372–376.
 Baron RC, McCormick JB, and Zubeir OA. Ebola virus disease in southern
- 11 Sudan: hospital dissemination and intrafamilial spread. Bulletin of the World Health Organization. 1983;61(6):997–1003 Milleliri JM, Tévi-Benissan C, Baize S, et al Les épidémies de fièvre 12
- hémorragique due au virus Ebola au Gabon (1994–2002): Aspects épidémiologiques et réflexions sur les mesures de contrôle. Bull Soc Pathol Exot, 2004, 97, 3, 199–205.
- Khan AS, Tshioko FK, Heymann DL, et al. The Reemergence of Ebola Hemorrhagic Fever, Democratic Republic of the Congo, 1995. Journal of Infectious Diseases. 1999;179:S76–S86. 13
- 14 Borisevich IV, Markin VA, Firsova IV, et al. Hemorrhagic (Marburg, Ebola, Lassa, and Bolivian) fevers: epidemiology, clinical pictures, and treatment. Voprosy Virusologii—Problems of Virology (Moscow). 2006;51(5):8-16 [Russian].
- 15 World Health Organization. Ebola haemorrhagic fever—South Africa. Weekly Epidemiological Record. 1996;71(47):359.
- Georges AJ, Leroy EM, Renaud AA, et al. Ebola hemorrhagic fever outbreaks in Gabon, 1994–1997: epidemiologic and health control issues. Journal of 16 Infectious Diseases. 1999;179:S65-75.
- 17 Okware SI, Omaswa FG, Zaramba S, et al. An outbreak of Ebola in Uganda. Tropical Medicine and International Health. 2002;7(12):1068–1075.
- World Health Organization. Outbreak(s) of Ebola haemorrhagic fever, Congo and Gabon, October 2001–July 2003. Weekly Epidemiological Report. 18 2003;78(26):223-225.

- 19 World Health Organization. Outbreak(s) of Ebola haemorrhagic fever, Congo and Gabon, October 2001-July 2003 . Weekly Epidemiological 2003;78(26):223-225.
- 20 World Health Organization, Ebola haemorrhagic fever in the Republic of the Congo—Update 6. Weekly Epidemiological Record. 6 January 2004.
 - Formenty P, Libama F, Epelboin A, et al. Outbreak of Ebola hemorrhagic fever in the Republic of the Congo, 2003: a new strategy? Médecine Tropicale (Marseille). 2003;63(3):291-295.
- Akinfeveya LA, Aksyonova OI, Vasilvevich IV, et al. A case of Ebola hemorrhagic 22 fever. Infektsionnye Bolezni (Moscow). 2005;3(1):85–88 [Russian].
- 23 World Health Organization. Outbreak of Ebola haemorrhagic fever in Yambio, Sudan, April-June 2000 . Weekly Epidemiological 2005;80(43):370–375.
- MacNeil A, Farnon EC, Morgan OW, et al. Filovirus Outbreak Detection and Surveillance: Lessons from Bundibugyo. Journal of Infectious Diseases. 24 2011;204:S761-S767.
- 25 World Health Organization, Ebola virus haemorrhagic fever, Democratic Republic of the Congo—Update. Weekly Epidemiological Record. 2007;82(40):345–346
- 26 World Health Organization. End of the Ebola Outbreak in the Democratic Republic of the Congo. Global Alert and Response. 17 February 2009.
- Shoemaker T, MacNeil A, Balinandi S, et al. Reemerging Sudan Ebola Virus 27
- Disease in Uganda, 2011. Emerging Infectious Diseases. 2012;18(9):1480–1483. Albarino CG, Shoemaker T, Khristova ML, et al. Genomic analysis of filoviruses 28 associated with four viral hemorrhagic fever outbreaks in Uganda and the Democratic Republic of the Congo in 2012. Virology. 2013;442(2):97–100.
- Maganga GD, Kapetshi J., Berthet N, et al. Ebola virus disease in the Democratic 29 Republic of Congo. New England Journal of Medicine. 2014; 371: 2083-91.
- Bell BP, Damon IK, Jernigan DB et al. Overview, Control Strategies, and Lessons Learned in the CDC Response to the 2014–2016 Ebola Epidemic. Morbidity and Mortality Weekly Report. 2016;65(3):4–11. 30
- World Health Organization. Ebola Virus Disease—Italy. Disease Outbreak News. 31 13 May 2015.
- Bell BP, Damon IK, Jernigan DB et al. Overview, Control Strategies, and Lessons Learned in the CDC Response to the 2014–2016 Ebola Epidemic. Morbidity and Mortality Weekly Report. 2016;65(3):4–11. 32
- 33 Word Health Organization. Ebola Virus Disease—Spain. 4 October 2014
- World Health Organization. Ebola Virus Disease—United Kingdom. Disease Outbreak News. 30 December 2014.
- Guetiya Wadoum RE, Sevalie S, Minutolo A, Clarke A, Russo G, Colizzi V, Mattei M, Montesano C. The 2018-2020 Ebola Outbreak in the Democratic Republic of Congo: A Better Response Had Been Achieved Through Inter-State Coordination in Africa. Risk Manag Healthc Policy. 2021 Dec 10;14:4923-4930. doi: 10.2147/RMHP.S327616. PMID: 34916862; PMCID: PMC8672027.
- World Health Organization. Ebola virus disease Democratic Republic of the Congo. 2021
- World Health Organization. Ebola outbreak 2022 Uganda. 2022 37
- World Health Organization. New Ebola outbreak detected in northwest Democratic Republic of the Congo; WHO surge team supporting the response. Available on: (https://www.who.int/news/item/01-06-2020-new-ebolaoutbreak-detected-in-northwest-democratic-republic-of-the-congo-who-surgeteam-supporting-the-response) (accessed on 16 January 2021).
- World Health Organization. Ebola Virus Disease Democratic Republic of Congo: External Situation Report 94 / 2019. WHO. Available on: (https://www.who.int/ publications-detail-redirect/10665-332654) (accessed on 16 January 2021).
- Centers for Disease Control and Prevention. History of Ebola Virus Disease (EVD). Available on: (https://www.cdc.gov/vhf/ebola/history/chronology.html) (accessed on 16 January 2021).
- Kamorudeen RT, Adedokun KA, Olarinmoye AO. Ebola outbreak in West Africa, 2014 - 2016: epidemic timeline, differential diagnoses, determining factors, and lessons for future response. J Infect Public Health 2020;13(7):956-62. https:// doi.org/10.1016/j.jiph.2020.03.014. Epub 2020 May 29. PMID: 32475805. World Health Organization. Ebola virus disease – Democratic Republic of the
- 42 Congo. WHO. Available on: (https://www.who.int/csr/don/04-June-2020-eboladrc/en/) (accessed on 16 January 2021). Gupta S, Gupta N, Yadav P, Patil D. Ebola virus outbreak preparedness plan for
- 43 developing nations: lessons learnt from affected countries. J Infect Public Health 2021;14(3):293–305. https://doi.org/10.1016/j.jiph.2020.12.030 Médecins Sans Frontières (MSF) International. DRC's Ebola outbreak crisis
- 44 update. Available on: (https://www.msf.org/drc-ebola-outbreak-crisis-update) (accessed on 16 January 2021).
- World Health Organization. Ebola virus disease Democratic Republic of the Congo. WHO. Available on: (https://www.who.int/csr/don/18-november-2020-ebola-drc/en/#:~:text=On%2018%20November%202020%2C%20the,EVD)
- (accessed on 16 January 2021].
 Farid G, Warraich NF, Iftikhar S. Digital information security management policy in academic libraries: A systematic review (2010–2022). Journal of Information 46 Science. 2023:01655515231160026.
- Khalid A, Malik GF, Mahmood K. Sustainable development challenges in libraries: A systematic literature review (2000–2020). The Journal of academic 47 librarianship. 2021 May 1;47(3):102347.