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Review article

Brief review on ebola virus disease and one health approach

Hassan Abdi Hussein

College of Veterinary Medicine, Department of One Health Tropical Infectious Disease, Jigjiga University, P.O. Box: 1020, Jigjiga, Ethiopia

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ABSTRACT

Ebola virus disease (EVD) is a severe and highly fatal zoonotic disease caused by viruses in the family *Filoviridae* and genus *Ebolavirus*. The disease first appeared in Zaire near the Ebola River in 1976, now in the Democratic Republic of the Congo. Since then, several outbreaks have been reported in different parts of the world, mainly in Africa, leading to the identification of six distinct viral strains that cause disease in humans and other primates. Bats are assumed to be the main reservoir hosts of the virus, and the initial incidence of human epidemics invariably follows exposure to infected forest animals through contact or consumption of bush meat and body fluids of forest animals harboring the disease. Human-to-human transmission occurs when contaminated body fluids, utensils, and equipment come in contact with broken or abraded skin and mucous membranes. EVD is characterized by sudden onset of 'flu-like' symptoms (fever, myalgia, chills), vomiting and diarrhea, then disease rapidly evolves into a severe state with a rapid clinical decline which may lead potential hemorrhagic complications and multiple organ failure. Effective EVD prevention, detection, and response necessitate strong coordination across the animal, human, and environmental health sectors, as well as well-defined roles and responsibilities evidencing the significance of one health approach; the natural history, epidemiology, pathogenesis, and diagnostic procedures of the Ebola virus, as well as prevention and control efforts in light of one health approach, are discussed in this article.

1. Introduction

Ebola virus is recognized as an emerging and re-emerging zoonotic disease that causes acute hemorrhagic fever in humans and has a high case fatality rate [1]. The virus infects humans who come into direct contact with sick animals or people, and most Ebola virus disease(EVD) outbreaks are caused by person-to-person transmission. Several thousand people died because of a recent EVD outbreak in West Africa [2]. The main outbreaks have been documented in humans, primarily in central Africa [3] (see Table 1).

The Ebola virus was initially identified in 1976 during two unrelated epidemics in southern Sudan and northern Zaire, the Democratic Republic of Congo. The virus was named Ebola virus after the Ebola river. Following laboratory characterization of the viruses recovered during these outbreaks, it was discovered that the viruses from the two outbreaks belonged to the *Zaire ebolavirus* and *Sudan ebolavirus* strains and were antigenically, biochemically, and virologically distinct [5]. A major outbreak of *Ebolavirus* disease in

Abbreviations: BDBV, Bundibugyo Ebolavirus; BSL, Biosafety Containment Level; CDC, Centre for Disease Control; DRC, Democratic Republic of Congo; EHF, Ebola Hemorrhagic fever; ELISA, Enzyme Linked Immuno-sorbent Assay; EVD, Ebola Virus Disease; FDA, Federal Drug Authority; GP, Glycoprotein; Kb, Kilo base; MHC, Major Histocompatibility Complex; MODS, Multiple Organ Dysfunction Syndrome; NAT, Nucleic Acid Testing; NP, Nucleoprotein; OH, One Health; RESTV, Reston Ebola Virus; RNA, Ribonucleic Acid; RT-PCR, Reverse Transcriptase–Polymerase Chain Reaction; SUDV, Sudan Ebolavirus; TAFV, Tai Forest Ebolavirus; USA, United States America; VP, Viral Protein; WHO, World Health Organization.

E-mail address: hassan.abdi@jju.edu.et.

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Western African countries in 2014 spread quickly to several other countries, culminating in an alarming situation worldwide [6].

The Ebola virus belongs to the family Filoviridae along with the genus *Marburgvirus*. This family is a member of the order Mononegavirales, which also includes members of Bornaviridae, Paramyxoviridae, and Rhabdoviridae [7]. Currently, the genus Ebola virus includes six distinct strains: *Zaire ebolavirus* (*EBOV*), *Sudan ebolavirus* (*SUDV*), *Tai forest ebolavirus* (*TAFV*), *Bundibugyo ebolavirus* (*BDBV*), *Bombali ebolavirus* (*BOMV*), and *Reston ebolavirus* (*RESTV*) [8,9]. Among these, *EBOV* causes Ebola Hemorrhagic Fever (EHF), which has the highest death rate in humans (57%–90%), followed by *SUDV* (41%–65%), and *Bundibugyo ebolavirus* (40%). *Tai Forest ebolavirus* has only been linked to one nonfatal human infection, whereas *Reston ebolavirus* causes asymptomatic infections in humans [10,11].

Ebola spreads through direct contact with the blood or bodily fluids of a person with a disease [12]. EVD begins with flu-like symptoms, stomach pain, diarrhea, and/or vomiting, followed by unexplained bleeding or characteristic hemorrhages caused by damaged blood vessels, eventually leading to high mortality [13]. The current nature of global trade and tourism has increased the chances of Ebola virus spreading to other continents, causing massive outbreaks. The recent epidemics should serve as a wake-up call to the world, ensuring that everyone is well prepared for the next pandemic if one occurs [14]. One Health Approach is a multidisciplinary approach that promotes collaboration between various sectors, including public, animal, and environmental health, to address the complex health concerns that the world is facing [15]. Ebola virus are believed to have originated in fruit bats. For instance, the 2007 Ebola virus disease outbreak in Luebo, DRC, originated from the consumption of a freshly killed bat [16]. Similarly, the 2014 outbreak of Ebola virus disease in West Africa started with a single zoonotic spillover event from fruit bats to a 2-year-old boy in Guinea [17]. Hence, preventing and controlling EVD require a multifaceted approach that includes surveillance, early detection, rapid response, and effective communication. One Health Approach recognizes that many diseases that affect humans originate in animals and that improving animal health can have a positive impact on human health [17]. The adoption of the One Health approach has

Table:1
a chronological list of the major outbreaks of Ebola virus disease in humans.

Year	Location	Strain	Confirmed cases	Death
1976	DRC	*Zaire Ebolavirus*	318	280
1976	Sudan	*Sudan Ebolavirus*	284	151
1976	UK	*Zaire Ebolavirus*	1	0
1977	DRC	*Zaire Ebolavirus*	1	1
1979	Sudan	*Sudan Ebolavirus*	34	22
1989	Philippines	*Reston Ebolavirus*	3	0
1989	USA	*Reston Ebolavirus*	4	0
1994	Gabon	*Zaire Ebolavirus*	51	31
1994	Cote D'Ivoire	*Taï Forest virus*	1	0
1995	DRC	*Zaire Ebolavirus*	315	254
1996	Gabon	Zaire Ebolavirus	60	45
1996	Gabon	Zaire Ebolavirus	31	21
1996	Russia	Zaire Ebolavirus	1	1
1996	South Africa	Zaire Ebolavirus	2	1
2000	Uganda	Sudan Ebolavirus	425	224
2001	Gabon	Zaire Ebolavirus	65	53
2001	Congo	Zaire Ebolavirus	59	44
2002	Congo	Zaire Ebolavirus	143	128
2003	Congo	Zaire Ebolavirus	35	29
2004	Sudan	Sudan Ebolavirus	17	7
2004	Russia	Zaire Ebolavirus	1	1
2005	Congo	Zaire Ebolavirus	12	10
2007	DRC	Zaire Ebolavirus	264	187
2007	Uganda	Bundibugyo Ebolavirus	131	42
2008	Philippine	Reston Ebolavirus	6	0
2008	DRC	Zaire Ebolavirus	32	15
2011	Uganda	Sudan Ebolavirus	1	1
2012	Uganda	Sudan Ebolavirus	11	4
2012	Uganda	Sudan Ebolavirus	6	3
2012	DRC	Bundibugyo Ebolavirus	38	13
2014	DRC	Zaire Ebolavirus	69	49
2014	West Africa, US, and UK	Zaire Ebolavirus	28,646	11,323
2017	DRC	Zaire Ebolavirus	8	4
2018	DRC and Uganda	Zaire Ebolavirus	3470	2287
2018	DRC	Zaire Ebolavirus	54	33
2020	DRC	Zaire Ebolavirus	130	55
2021	DRC	Zaire Ebolavirus	12	6
2021	DRC	Zaire Ebolavirus	11	9
2021	Guinea	Zaire Ebolavirus	23	12
2022	Uganda	Sudan Ebolavirus	164	55
2022	DRC	Zaire Ebolavirus	5	5
2022	DRC	*Zaire Ebolavirus*	1	1

Source: Centers for Disease Control and Prevention, History of Ebola virus disease outbreaks [4].

significant implications for communities in developing countries. The health of people, animals, and the environment are interconnected and impact each other, making it important to address health issues holistically [18]. Therefore, this review highlights the natural history, epidemiology, pathogenesis, diagnostic techniques, and prevention and control strategies of Ebola virus disease in light of one health approach.

2. The History of Ebola outbreaks

The first known Ebola virus outbreak occurred in 1976, with simultaneous Ebola strain outbreaks in Yambuku, northern Zaire (now the Democratic Republic of the Congo, DRC), and Southern Sudan. The Ebola river was named the *Zaire ebolavirus* [19]. In 1994, an ethnologist fell ill after examining a dead chimpanzee in Tai National Park on the Ivory Coast [5]. The virus was distinct from viruses linked to outbreaks in the DRC and Sudan. Thus, it is referred to as *Tai Forest ebolavirus* [9]. An outbreak of a mystery disease in Reston, Virginia, USA, in 1990 occurred among cynomolgus crab-eating macaque monkeys that were brought from the Philippines. It was later determined to be an Ebola virus strain of Asian origin and named *Reston ebolavirus* [20]. In 2007, a new strain of Ebola virus emerged in Western Uganda in the township of Bundibugyo. This marked the discovery of a fifth strain of the virus, *Bundibugyo ebolavirus* [21]. During the years 2013–2015, Western Africa experienced its deadliest Ebola outbreak. The outbreak, which was first reported in Guinea in March 2014 but was eventually traced back to the end of 2013, was the first time an Ebola virus variant had spread across people for such a long time [22,23]. *Bombali ebolavirus* (*BOMV*) was first discovered in bats in Sierra Leone in 2018; however, it remains unknown whether it causes disease in either animals or people, major cases and outbreaks of Ebola virus disease in human are summarized chronologically (Table, 1) [8].

3. Ebola virus

Ebola virus vary greatly in size, with diameters ranging from 50 to 80 nm and lengths ranging from 10,000 to 14,000 nm. Virions range in shape, from cylinders to branches and loops. However, all filoviruses retain unique thread-like filamentous structures [24]. Ebola virus has a large negative-strand, non-segmented RNA of approximately 19 kb. The RNA genome contains seven genes that are sequentially ordered. The genes included 3′ leader-nucleoprotein (NP) –virion protein(VP) 35, matrix protein VP40, glycoprotein(GP), VP30, VP24, and RNA-dependent RNA polymerase (L)-5′ trailer. Except for GP, which encodes three glycoproteins, each gene encodes a single protein product [25]. The genomes of the six Ebola viruses (*BDBV*, EBOV, *RESTV*, *SUDV*, *BOMV*, and *TAFV*) differ in sequence, number, and location of gene overlaps [8,26].

4. Epidemiology of EVD

4.1. Host and reservoir range

The precise host and reservoir ranges remain unknown. However, there are indications that the primary hosts of Ebola virus are primates, including humans, chimpanzees, gorillas, and monkeys [14,25]. The natural reservoirs of Ebola virus are thought to be the fruit bats of the Pteropodidae family. Duikers, non-human primates, cats, foxes, hogs, antelopes, porcupines, and rodents are among the animals that are considered potential intermediate or incidental hosts of Ebola virus. However, unlike bats, these animals typically suffer from severe and often fatal illnesses when infected. These animals can carry the virus asymptomatically and shed it in their bodily fluids, which can infect humans who come into contact with it through hunting or handling of bushmeat [14,27,28].

Studies have indicated that the virus has the ability to survive in bodily fluids and tissues, such as semen, vaginal fluids, sweat, aqueous humor, urine, and breast milk of individuals who have recovered from the disease [29,30]. A scenario that can result in the recurrence of Ebola virus infection in individuals who had previously recovered from EVD [25].

4.2. Transmission among humans

The Ebola virus is transmitted to humans by coming into contact with the blood, organs, or other bodily fluids of infected animals. The first case of Ebola virus disease during the 2014–2016 West Africa outbreak was traced to exposure to bats [17]. Besides bats, EVD cases have been reported in people who handle infected chimpanzees, gorillas, and forest antelopes, whether alive or dead, in Gabon, the Republic of the Congo, and Cote d'Ivoire [2]. The virus can enter the body through the nose, mouth, eyes, ears, wounds, open wounds, cuts, or mucous membranes [31]. Transmission through sexual contact with a convalescent or survivor of Ebola virus has been documented [32]. Ebola virus is present in all bodily fluids of people with EVD, including blood, vomit, urine, feces, sweat, tears, breast milk, semen, mucus, saliva, and other bodily fluids [33]. Reusing contaminated needles and medical supplies without first sterilizing them can spread the Ebola virus. The virus can survive for weeks on surfaces such as utensils, bedding, clothing, furniture, doorknobs, electrical switches, and other items that can become contaminated by body fluids [28].

4.3. Pathogenesis

The Ebola virus targets the mononuclear phagocytic system. Entry of Ebola virus through the skin or mucosa paves the way for its entry into target monocytes, macrophages, and dendritic cells. These cells play a pivotal role in viral dissemination [13]. Ebola viral spike glycoprotein initially mediates viral entry into macrophages and dendritic cells. There is significant evidence that this is a key

step in disease [34]. As a result, the adaptive immune response fails, including the inability to co-stimulate chemokines, up-regulation of the major histocompatibility complex(MHC), and failure to induce lymphocyte differentiation. In addition, interferon synthesis is inhibited [35,36].

Multiple organ dysfunction syndrome (MODS), which results from persistent severe systemic vascular inflammation is observed in the latter stages of EVD, which is characterized by generalized increased capillary permeability, capillary leak, and edema [37]. Organ dysfunction in MODS is caused by alterations in capillary permeability, changes in blood flow, and the occurrence of microthrombi and microvascular stasis [34].

4.4. Clinical manifestations

Ebola virus disease (EVD) in humans presents with a range of clinical manifestations. Symptoms typically appear abruptly, with an incubation period of 2–21 days after infection. The initial symptoms of EVD include fever, chills, headaches, body aches, and fatigue. These symptoms are often followed by gastrointestinal symptoms such as nausea, vomiting, diarrhea, and abdominal pain [38].

As the disease progresses, patients may develop significant weakness with severe exhaustion and dehydration. This may lead to complications, such as hypotension, shock, and multi-organ failure. In severe cases, patients experience profuse external and internal bleeding, a hallmark of EVD, a condition termed Ebola hemorrhagic fever. Additionally, EVD can cause neurological symptoms such as confusion, seizures, and coma [9]. Symptoms may vary depending on the individual, and some patients may not manifest all the symptoms. However, those who develop symptoms are highly contagious during the acute phase of the disease, making early detection and isolation of cases crucial for preventing the spread of the virus [6].

5. Diagnosis of EVD

5.1. Definitive diagnosis

The most commonly used diagnostic tests for EVD include reverse transcription polymerase chain reaction (RT-PCR) and antigen-capture enzyme-linked immunosorbent assay (ELISA). These tests detect Ebola virus genetic material or protein in the blood or other body fluids. RT-PCR is highly sensitive and can detect viruses even in the early stages of infection. ELISA is less sensitive but can detect antibodies produced by the immune system against the virus [39]. Currently, WHO recommends automated or semi-automated nucleic acid testing (NAT) for regular diagnostic management and rapid antigen detection assays for use in distant locations [40]. Antibody detection does not play a role in the diagnosis of acute EVD but may be useful in epidemiological and surveillance studies. A negative test result within 48 h of exposure to Ebola virus does not exclude infection [41].

5.2. Differential diagnosis

EVD can show symptoms similar to those of other infectious diseases; therefore, a differential diagnosis is essential to eliminate other illnesses with similar clinical symptoms. Diseases that might be considered as differential diagnoses for EVD include malaria, Lassa fever, dengue fever, yellow fever, typhoid fever, cholera, influenza, SARS, and MERS [42]. It is necessary to consider the possibility of EVD in anyone who has traveled to or resided in regions where EVD outbreaks have occurred or who has had close contact with a confirmed EVD case [6,43]. In tropical regions, where various febrile diseases can mimic the symptoms of EVD, immediate diagnosis should be made [44].

6. Treatement of EVD

Currently, two drugs are approved by the U.S. Food and Drug Administration (FDA) to treat EVD caused by Zaire ebolavirus. The first approved drug is Inmazeb (atoltivimab, maftivimab, and odesivimab), a combination of three monoclonal antibodies has been the first FDA-approved treatment for Zaire ebolavirus infection in adult and pediatric patients. Inmazeb targets glycoproteins on the surface of the Ebola virus which aids host cell entry. Inmazeb's three antibodies can bind to this glycoprotein simultaneously, preventing viral attachment and entry [45]. The second approved drug for use in *Zaire ebolavirus* infection in adults and children is ansuvimab (mAb114), a human monoclonal antibody, to be treated for Zaire ebolavirus infection in adults and children. Ansuvimab blocks the binding of the virus to cell receptors, preventing viral entry into the cell [46]. Overall survival was significantly greater in individuals who received either of the two FDA-approved therapies [45].

Furthermore, to maintain optimal organ function, patients need personalized supportive treatment based on their problems [47]. Rehydration with oral or intravenous fluids, as well as the treatment of particular symptoms, increases survival. Analgesics are indicated to reduce pain, whereas intravenous fluids are recommended to maintain osmotic balance. Critically ill patients may require intensive care and support [13].

6.1. Vaccination

Vaccine development has started in the past decades, concurrent with the introduction of the Ebola virus into the human population. However, the first Ebola virus vaccine, Ervebo, a vesicular stomatitis virus-based vaccine, was only recently approved and has proven successful in protecting people against the *Zaire ebolavirus* strain. Ervebo is a live, attenuated vaccine that has been genetically

modified to incorporate a protein from the *Zaire ebolavirus*. It was administered as a single dose. The most commonly reported side effects are pain, edema, and redness at the injection site, as well as headache, fever, joint and muscle aches, and fatigue [48].

The second officially approved vaccine for EVD is a two-dose regimen vaccine named Zabdeno and Mvabea for people aged 1 year and older. The vaccine was administered in two doses: Zabdeno was administered initially, followed by Mvabea, approximately 8 weeks later. As a result, this prophylactic 2-dose regimen is not appropriate for an epidemic response where immediate protection is required [49]. Despite ongoing efforts to develop new vaccines such as *SUDV*, only two vaccines have been authorized for human use [1].

7. Prevention and control

Controlling epidemics necessitates the coordination of medical services, which includes early detection, contact tracing for persons who have been exposed to, treatment for people who have been exposed to Ebola virus, and vaccination of frontline health workers and at-risk individuals [50]. In some countries affected by Ebola virus, multi-level and multi-sectoral approaches have been implemented to prevent the spread of the disease. These measures were not limited to health services and other sectors of society, and all levels of government were involved. A holistic approach enabled countries to enhance their preparedness to combat the outbreak from multiple perspectives and to tackle the different elements that contributed to its expansion [51].

Studying and learning from the successful strategies used during these outbreaks could prove valuable in preparing for future outbreaks and improving our ability to contain them. By adopting a similar multilevel and multisectoral approach, we may be able to generate a more effective response and reduce the impact of future Ebola outbreaks [52]. Public education about this deadly disease is also critical for preventing its spread [53]. Proper monitoring of airports and public places where there is a high risk of infection spread is critical [54]. Patients who become ill should be monitored for at least 21 days to rule out infections. All protective clothing, such as gowns, gloves, face masks, goggles, and respirators, should be worn by healthcare workers and practice nursing barriers. Samples collected for diagnosis should be transported with extreme caution and handled only at Biosafety Containment Level 4 [14]. Because bush meat has been identified as a potential and significant source of epidemics in the past, it is critical to monitor its consumption and illegal export to developing countries [55]. Safe sex practice for recovered individuals and utilization of currently approved vaccines for frontline workers and at-risk individuals is a recommended prevention practice [1].

8. One health approach

The One Health (OH) programme is a collaborative approach that aims to maintain the well-being of humans, animals, and the environment. Since ancient times, animal studies have influenced human medicine. In the past, the fields of human and animal medicine were closely linked; however, owing to the emphasis on specialization during the Industrial Revolution, the connection between these fields gradually decreased in the early 20th century [56]. In the last three decades, it has become clear that most new and emerging infections that can be transmitted from animals to humans have their origins in animals, particularly in wild animals. It is apparent that human activities such as changes in land use, intensification of ecosystems, urbanization, international travel, and trade are the primary causes of their emergence [57]. Studies indicate a correlation between recent deforestation incidents and a greater likelihood of an EVD outbreak occurring in a particular area [58]. To obtain knowledge about each newly emerging zoonotic disease and formulate a plan to respond and control it, a collaborative, interdisciplinary approach that entails animal, human, and environmental health is needed to comprehend the ecology of each disease and carry out risk assessment [59].

The One Health approach emphasizes the impacts, reactions, and measures taken at the interfaces between animals, humans, and ecosystems. This approach is particularly relevant for addressing emerging and endemic zoonoses, with the latter being responsible for a significantly greater disease burden in developing countries and having a significant social impact in areas with limited resources [60]. Zoonosis accounts for up to 60% of emerging infectious diseases reported globally. Understanding the complex interdependence of humans, animals, and the environment is important for the design and implementation of effective interventions for EVD outbreak response [43]. The global economy has enabled rapid movement of people, animals, plants, and agricultural goods worldwide. This has contributed to more frequent outbreaks of zoonotic infections in impoverished populations. Improved coordination across sectors is required to match responses to the current disease ecology [61]. The epidemic response highlights the importance of strong institutional collaborations as well as efficient and effective communication methods, diagnostic tools, and disease prevention strategies [62].

Establishing a prioritized list of zoonotic diseases and committing to sharing resources between participants from various fields, such as humans, animals (domestic and wildlife), and environmental health, simplifies the establishment of multisectoral collaborations [63]. The early involvement of several sectors fosters teamwork and guarantees program ownership [64]. One health approach involves properly measuring the burden of zoonotic diseases, which is a crucial step in setting public and animal health priorities and evaluating the success of prophylactic and control strategies [61]. Effective zoonotic disease prevention, detection, and response necessitate strong coordination across the animal, human, and environmental health sectors, as well as well-defined roles and responsibilities. Countries can consider holding frequent cross-sectoral meetings to foster cross-sectoral and multidisciplinary collaboration, promote transparency, and coordinate activities across agencies. Developing mutually agreed-upon standard operating procedures is critical and can be achieved by establishing a One Health coordination unit and conducting collaborative outbreak investigations and response operations [56,63,64]. Ebola virus is a zoonotic pathogen that can transfer between animals and humans, highlighting the need for a comprehensive One Health approach to understand and manage the transmission of the virus [15,43].

One Health methodology acknowledges the interdependent nature of human, animal, and environmental health, emphasizing the

inefficacy of a disjointed approach in combatting diseases, such as Ebola. For instance, the Ebola outbreak in West Africa between 2014 and 2016 was primarily due to increased interactions between humans and wildlife as a result of farming and deforestation [22,43].

Adopting the One Health approach enables researchers and public health officials to better comprehend the ecology of the Ebola virus and how it can be transferred between various species. In addition, with effective coordination, the One Health approach can identify and address the underlying factors that may contribute to the emergence of viruses and transmission, and develop targeted intervention strategies to contain its spread [43]. Overall, the One Health approach is an invaluable tool for addressing emerging diseases such as Ebola, providing the potential to prevent further outbreaks [15].

9. Conclusion and recommendation

EVD has been known since 1976, but its severity, exceptionally infectious or contagious nature, and acquisition of pandemic status in 2014–2015 have raised numerous concerns among health professionals and policymakers. The emergence of Ebola as a threat has warned us to prepare arsenals for combating Ebola-like diseases through multidisciplinary and collaborative approaches that transcend national boundaries. This is the right time to address the EVD emergency by developing and deploying cutting-edge tools and techniques for confirmatory diagnosis, as well as developing internationally compatible surveillance, monitoring, and networking systems, and identifying animal reservoirs. Effective Ebola virus disease prevention, detection, and control necessitate strong coordination across animal, human, and environmental health sectors, as well as well-defined roles and responsibilities. The WHO is urging public health authorities to remain alert and ready to respond to emergencies. Furthermore, strong surveillance and immediate response capacity need to be upheld, and care, screening, and counseling also need to be provided to survivors. Further research to study and completely comprehend the geographic extent and reservoir species involvement is critical for assessing the risk of future outbreaks.

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The author states that the review meets all the necessary ethical guidelines, including conforming to the legal requirements of the review writing.

Author contribution

Hassan Abdi Hussein: conceived and designed the article, extracted the data, Wrote the article and critically revised its important intellectual content; and finally approved the submitted version.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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