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Article

One Health Response for Rift Valley Fever Outbreak in Sudan

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Abstract: Rift Valley fever (RVF) is a mosquito-borne zoonotic viral disease that infects both human and animals. This is a descriptive study summarizes investigation and response to RVF outbreak, using surveillance data. A RVF outbreak occurred in Berber locality in northern Sudan. We identified 246 cases of RVF including seven deaths among humans, 119 deaths and 82 abortions among Livestock. Our entomological surveillance confirmed the presence of *Anopheles arabiensis*, *An. stephensi*, *Aedes aegypti*, *Ae. vexans*, *Culex pipiens*, *Cx. Quinquefasciatus*, and *Cx. theileri* in the area during the outbreak. In a comparison with another outbreak of Rift Valley fever in nearby area while ago, a multisectoral One Health response strategy has resulted in strengthening the health system through re-innovating health facilities and centres and training about 200 healthcare and emergency responders. Additionally, it reduced cases and fatalities among humans by 78% and 63%, respectively, and loss in livestock due to deaths and/or abortions by 82%. The added-value of implementing One Health strategy was saving more lives and resources, while strengthening the health system. We recommend the systematic institutionalization of One Health strategy in the country as a core part of the national prevention and control strategy for zoonotic diseases epidemics and pandemics.

Keywords: Zoonotic diseases; Arboviruses; Emerging Infectious Disease; Epidemic; Epizootic; Haemorrhagic fevers; Health security; Pandemic preparedness; prevention; and response

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1. Introduction

Arthropod-borne viruses (arboviruses) are group of viruses that are transmitted by diseases vectors, mainly mosquitoes, biting midges, sand flies, and ticks [1,2]. Most of arboviral diseases are zoonotic in nature, therefore they are readily causing a life-threatening illness to humans and animals, as well as reduction in meat and milk production by livestock leading to substantial health and socioeconomic burdens [3–6]. Arboviral diseases such as Rift Valley fever (RFV) are mainly emerging in form of health emergencies including epidemics among humans, epizootic among animals, or outbreaks that affect both human and animal populations [7–10]. These health emergencies usually overtaking health systems, particularly in under-resourced settings that lack early preparedness and response systems [11,6,12]. The geographical distribution, prevalence, morbidity, mortality, and related disability and socioeconomic burden of arboviral diseases are increasingly growing [8,13,14]. This growth is mainly driven by several risk factors including climate

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change, growing size of populations living in humanitarian crisis settings, change in land use and land cover, globalization, and unplanned urbanization [15–21].

Sudan is located in Northeastern Africa and has open borders with seven countries including Chad, Central African Republic, and Libya in the west, Egypt in north, South Sudan in south, and Eritrea and Ethiopia toward the east. Due to the large coastal area on the Red Sea, the country is considered one of the main coastal gates of Africa; therefore, there is high international travel and transportation dynamics of human and animals' populations as well as goods. Additionally, due to the geo-political position and wide space, the country has a wide range of diversity in ecological zones, environmental suitability, disease vectors, and alternative hosts. Therefore, these characteristic altogether make Sudan an epidemic-prone country, particularly, for haemorrhagic fevers including RFV [12]. Furthermore, Sudan is endemic with several arboviral diseases including Chikungunya (CHIK) [22,23], Crimean-Congo haemorrhagic fever (CCHF) [5], dengue (DEN) [20], RVF [8], Zika and West Nile viruses [6]. RVF is endemic in the southern and central regions of Sudan and serological evidence about the local circulation of the virus there goes back to 1936 [24]. The disease has affected both human and animal populations in the country [25–28].

In this study, we report on the investigation and response to an outbreak of RVF in Berber locality, northern Sudan and highlight the added value of implementing One Health approach for the containment and control of the outbreak. We document best practices, success story, and we recommend additional measures to improve the prevention and control of RVF outbreaks.

2. Materials and Methods

Here we analysed secondary anonymised data that was extracted from the outbreak report. Data was collected through the surveillance system. Additionally, we are documenting practices and actions were implemented throughout the investigation and response to the RVF outbreak in the area. In brief, in response to health alerts from the human and animal health authorities in Berber locality (Fig. 1), about unusual increase in non-malaria febrile illness among humans associated with high rate of abortion and deaths among livestock in September 2019, an emergency taskforce was deployed for investigation. This team was technically and logistically supported by the World Health Organization (WHO) to investigate a suspect epidemic of haemorrhagic fever in the area. Diagnostic analyses at the reference National Public Health Laboratory in Khartoum confirmed infections with RVFV among humans. Similarly, Central Veterinary Research Laboratory has confirmed infections with RVF were confirmed among livestock. The Integrated Vectors Management department at the directorate of Environmental Health and Food Control; Federal Ministry of Health has implemented additional investigations to determine the vector composition in Berber locality during the outbreak.

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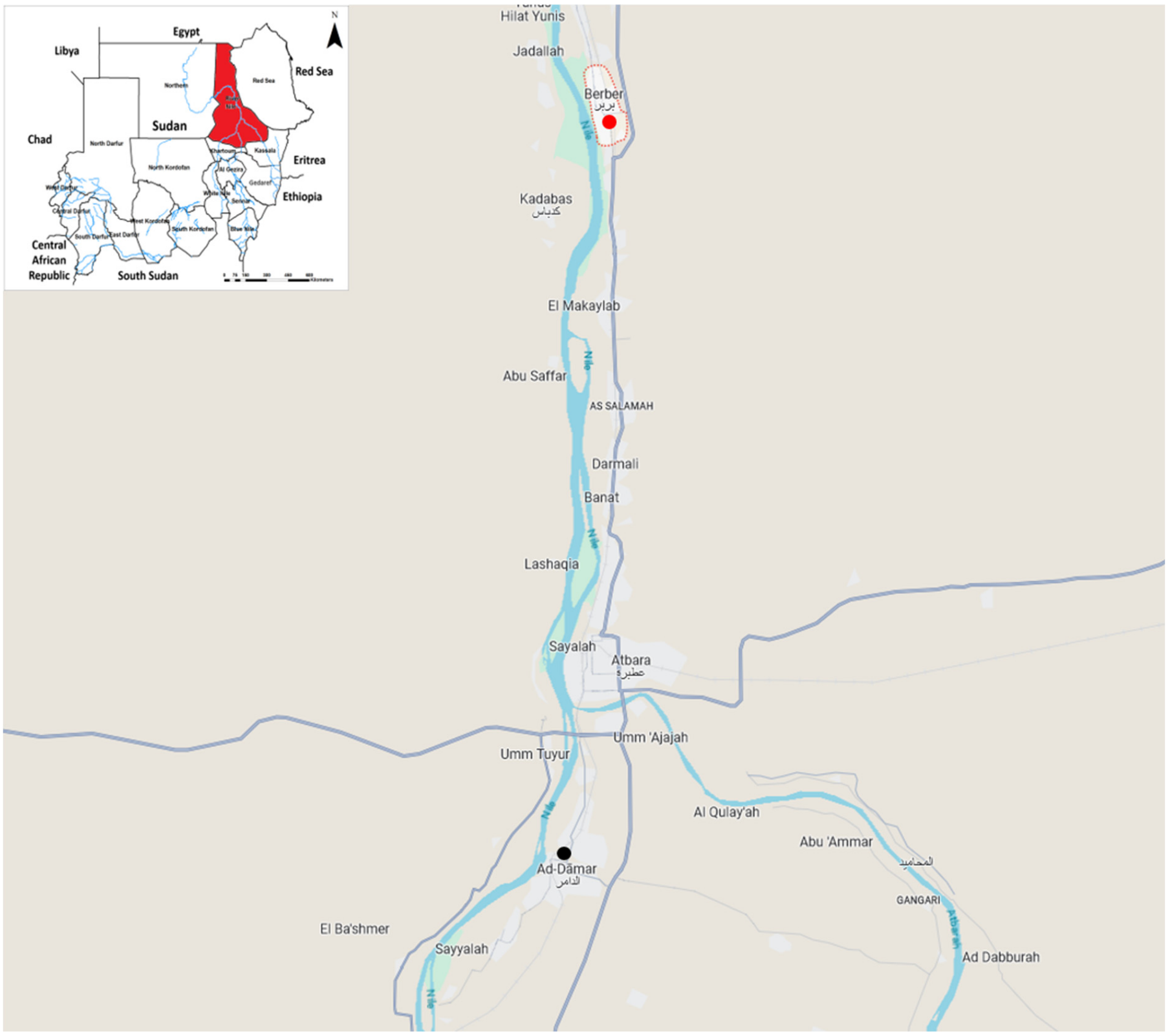

Figure 1. Map indicates the study area highlighted with red sphere, and the place where the previous outbreak of RVF occurred marked with the black sphere.

3. Results

3.1. Literature analysis:

The history of the epidemic in the area was established retrospectively by reviewing and analysing the epidemiological records and previous reports about similar health events in the area. This revealed that RVF virus has emerged in the capital city of the state; Eldamar locality (Fig. 1) over two month ago [7].

Upon increase in reported non-malaria febrile illness among humans and the local people reported increase in mortality and abortions among their domestic animals, sheep and goats in particular, investigations confirmed the emergence of RVF in the area (Table 1).

Table 1. Historical and current overview of the sequential events related to the epidemic development.

Date	Event or action taken
December 2018	Violence escalated throughout the country and increased the dynamic of

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	human and animal populations between RVF-endemic and disease-free areas.
January 2019	Public services totally or partially paralyzed
August - October 2019	Unexpected heavy rains and flash flooding occurred in River Nile
September 11th 2019	Indexed case was reported from Berber locality, River Nile state
September 2019	Alert from the state Ministry of Health
September 2019	Investigation team was deployed and logistic and technical support was provided
September 2019	RVFV infections in human and animal were confirmed
October 2019	RVF epidemic and epizootic were officially declared
October 2019	Ministry of Health, Ministry of Livestock, and WHO joint One Health response and containment mission was launched
January 2020	Successful containment of the outbreak.

3.2. The outbreak:

The development of this outbreak has started with the first index case that was reported in Berber locality on September 8th through January 1st 2020. In total, among humans, we identified 246 cases of RVF infection including seven deaths (Fig. 1). Additionally, 119 deaths and 82 abortions were reported among Livestock (Fig. 2). The outbreak peaked in October with 64% of cases and 86% of deaths among human were reported, also 96% and 94% of animal deaths and abortions respectively were reported during the same period (Fig. 2).

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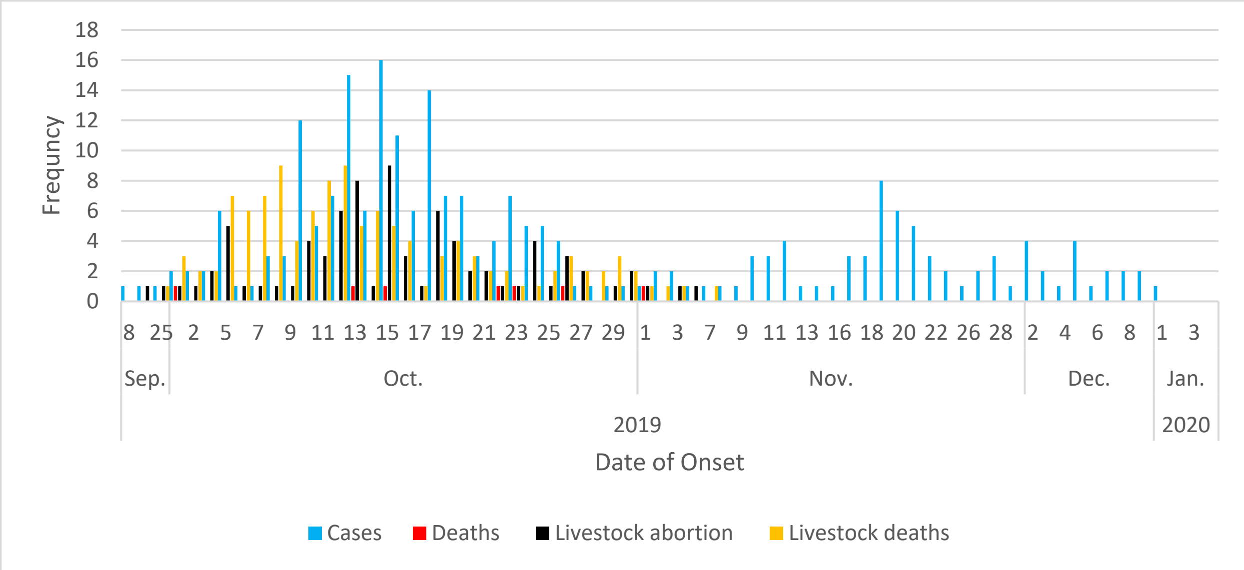

Figure 2. Epicurve of RVF outbreak in Berber locality shows the temporal distribution of cases and deaths among humans as well as abortions and deaths among livestock between September 2019 and January 2020.

The major clinical presentation of RVF in human patients included fever (100%), headache (82%), joint pain (46%), and subconjunctival haemorrhage (5%). A few patients were presented with nose (3%) and gum (1%) bleeding as well as haematemesis (1%) (Fig. 3).

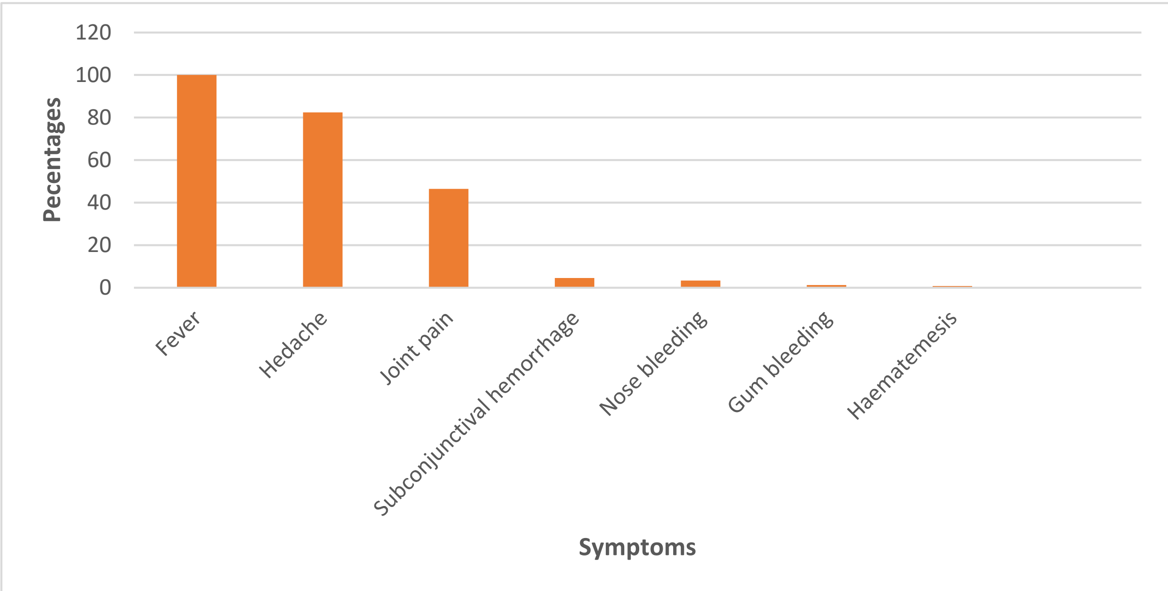

Figure 3. The clinical presentations of Rift Valley fever patients during the outbreak in Berber locality between September 2019 and January 2020.

The demography of cases showed that 2% of patients were under five years old and 8% were children aged between 11 and 15 years old. The majority of patients (51%) were young adults aged between 16 and 40 years old and only 2% of patients were aged between 76 and 80 years (Fig. 4). The male to female sex ratio of cases was 1:1.

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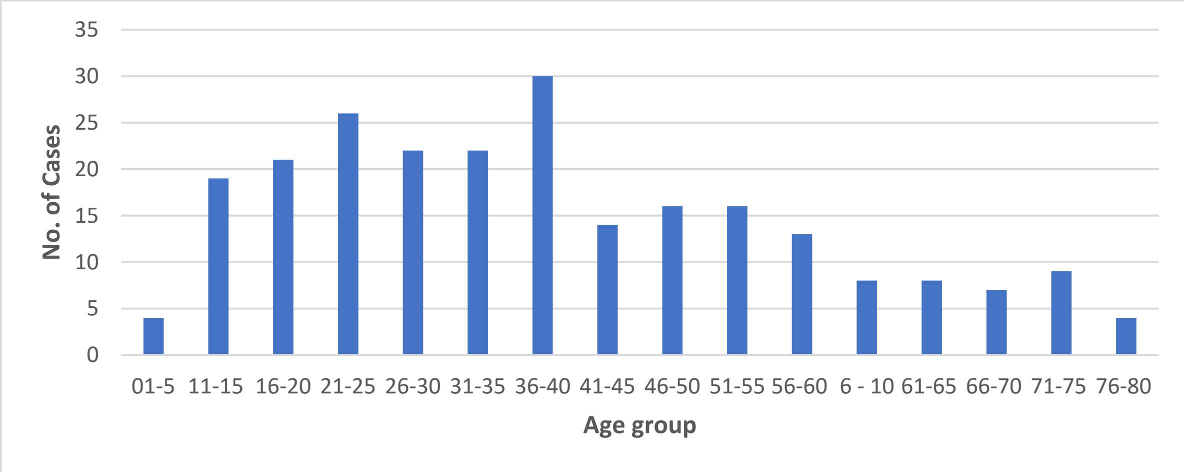

Figure 4. The age structure of Rift Valley fever patients during the outbreak in Berber locality between September 2019 and January 2020.

We further analysed the patients' demographics to investigate any potential occupational hazard. Thirty-three percent of the patients were housewives followed by health workers (18%), farmers (16%). Interestingly, low proportions of the patients were animal breeders, children, and health workers, 10%, 3%, and 1% (Fig. 5).

Figure 5. The distribution of the Rift Valley fever cases by occupation during the outbreak in Berber locality, River Nile state between September 2019 and January 2020.

3.3. The One Health response:

One hindered and eighty-five healthcare providers at the state Ministry of Health received a package of extensive and short training on the active case surveillance and effective management as well as blood samples collection, preservation, and shipment (Fig. 6). Also, 70 public health workers were trained and equipped for the vector inspection, collection, and control. Additionally, 110 health promoters were trained on the risk communication and outreach activities to engage communities at risk and raise their awareness about the risk, prevention and control measures, and what to do to handle infections among humans and animals (Fig. 6).

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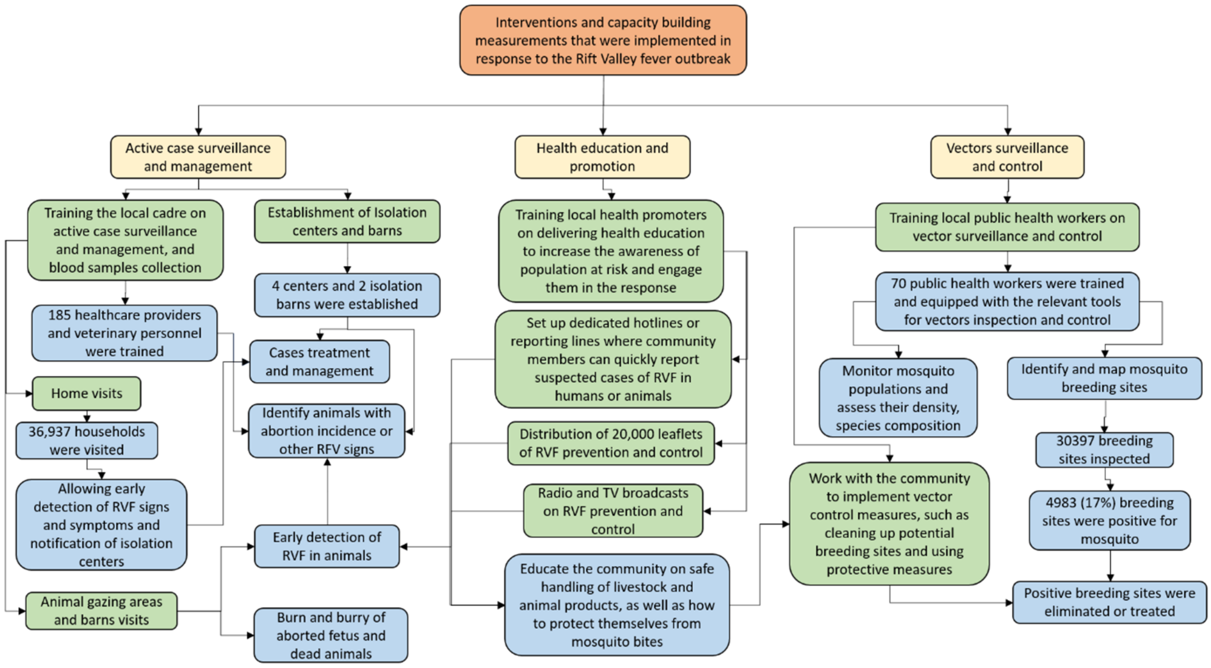

Figure 6. Flowchart explain multisectoral One Health actions and measurements implemented in response to the Rift Valley fever outbreak in Berber locality in 2019.

Entomological surveillance revealed that, the vector composition of mosquito species in Berber locality during the outbreak between September 2019 and January 2020, mainly included *Anopheles arabiensis*, *An. stephensi*, *Aedes aegypti*, *Ae. vexans*, *Culex pipiens*, *Cx. Quinquefasciatus*, and *Cx. theileri*. However, distribution and density of these species was very heterogeneous.

Comparing outcomes of two outbreaks of RVF in similar settings that occurred within less than three months gap in time highlights the added value of implementing multisectoral One Health in the surveillance, preparedness, and response to the disease outbreaks (Table 2). Through the implementation of integrated One Health strategy, about 78% more human case were averted and 63% lives were saved. On the animal side, over 80% loss in livestock resources were prevented (Table 2).

Table 2. A brief comparison between the outcomes of two different response strategies to two outbreaks of RVF in similar settings.

Outcomes	Routine intervention	Integrated One Health intervention	Added value of One Health strategy
Location	Eldamar locality	Berber locality	Health system strengthened
Period	May-July 2019	September 2019-January 2020	Less cases and deaths
Human cases	1,129	246	78% less human cases
Human fatalities	19	7	63% less human deaths

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Death/abortion among animals	At least 1,104 deaths and/or abortions	201 deaths and/or abortions	82% less loss in livestock
Associated vector composition	Not identified	*Anopheles arabiensis*, *An. stephensi*, *Aedes aegypti*, *Ae. vexans*, *Culex pipiens*, *Cx. Quinquefasciatus*, and *Cx. theileri*	Implementation of vector species targeted interventions.

4. Discussion

Here we report a major RVF outbreak in Berber locality, River Nile state, northern Sudan between September 2019 and January 2020. We also document the first implementation of One Health strategy in response to an outbreak of zoonotic disease in Sudan. We identified 246 cases of RVF among humans including seven deaths in the River Nile state between September 2019 and January 2020. We also, detected 119 deaths and 82 abortions due to infections with RVF among livestock. Despite the apparently high number of infections among both, humans and animals, compared with a previous outbreak of RVF in a nearby locality around three months ago, this outbreak resulted in substantially less morbidity, mortality, and loss in livestock in comparison with other outbreaks of RVF in the country [7,29–33]. This underscore the added value of the jointly implemented One Health strategy with an integrated surveillance and response system [34–36]. Nevertheless, RVF outbreaks are serious threat to health and socioeconomic status particularly for poor populations that depend on livestock.

Up to recently, outbreaks of RVF were mainly occurring in the southern region of the country [6,27,30]. However, due to climate change that indicated by extreme weather events including the heavy rains and flash flooding, several vector-borne and zoonotic diseases are increasingly spreading and outbreaking throughout the country [21]. The country has recently suffered from major outbreaks of CCHF [5,37], CHIK [22], Cholera [38], DEN [39,40], hepatitis E [41], malaria [42], and RVF [7,8]. In addition to these challenges, the COVID-19 pandemic and increasing conflicts and humanitarian crisis have further weakened the already fragile health system, making it more difficult to effectively respond to these outbreaks [43–45].

Having the highest prevalence of RVF infections among housewives suggests household exposure and also the involvement of other modes of transmission of RVF such as exposure to raw meat and milk from infected animals [46]. This aligns with the WHO and Centers for Disease Control and Prevention (CDC) evidence that most of RVF infections result from contact with infected animals or their products and fluids [47,48]. The household exposure assumption is supported by the wide range of patients' age, between less than 1 year old and over 80 years old. Nevertheless, this might be driven by the diverse species of vectors that were detected in the area during the outbreak. Particularly that evidence from other countries revealed that *Cx. theileri* was involved in the re-introduction of RVF virus following a long disappearance [49]. While, *Anopheles arabiensis*, *An. stephensi*, *Aedes aegypti*, *Culex pipiens*, and *Cx. Quinquefasciatus* are well known competent vector of RVF [26,50–52], *Ae. vexans* is known as anthropophilic and mammalophilic floodwater, is considered the initial vector of sporadic RVF outbreaks because of it is unique biology and breeding behaviour. *Ae. vexans* lays the eggs on the edge of waterbodies, the eggs need to dry first before it can hatch, therefore, it capable of withstanding draught for years while harbouring the RVF virus [53–55]. According to the Food and Agriculture Organization of the United Nations (FAO), once the infected

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eggs of *Ae. vexan* hatch after years, the emerging adults are readily capable to infects animals upon their first blood-meal [56]. This explains the sporadic nature of RVF outbreaks in endemic countries [57–60]. However, as commonly only small proportion of RVF infections develop symptoms and that most of the clinical presentation of RVF's patients is closely similar to malaria and other prevalent diseases in endemic areas, low transmission and sporadic cases might be missed by the surveillance system or mistakenly identified as a different disease [39,61–63]. For instant, screening blood donated by seemingly healthy individuals for arboviral infections revealed high seroprevalence of arboviruses including Chikungunya, O'nyong'nyong, Zika, and West Nile virus, that was not captured through the routine surveillance and healthcare facility based diagnosis [64,65]. This calls for strengthening the diagnostic capacity and surveillance system for emerging infectious diseases including RVF [66–68]. Particularly in rural areas and humanitarian crisis settings, where populations are underserved and more vulnerable diseases outbreaks [7,42,69,70]. In Sudan, particular attention is urgently needed for the increasingly emerging and spreading invasive diseases vectors including *An. stephensi and Aedes albopictus* and the diseases they transmit, because little is known about their vectorial capacity and susceptibility to the locally implemented vector control interventions [23,71–73].

Changes in the land use and land cover due to climate change and human activities including deforestation, unplanned urbanization, conflicts and human-made humanitarian crisis are the major risk factors for disease outbreaks [21,74–76]. Unfortunately, the size of forcibly displaced population in the country is rapidly growing to over 10 million, this increases the vulnerability of communities to infectious diseases [40,41,76]. These risk factors increase humans and animals movements between endemic and disease-free areas [7,8,22], they also influence the spread of diseases vectors, particularly invasive vectors such as *Aedes albopitcus* and *Anopheles stephensi* [23,71,77,78].

Existed evidence confirms mother to child transmission in humans and animals, transovarial transmission in vectors, and the involvement of RVF in abortion among pregnant women [26,53,79–81]. RVF virus infects wide range of hosts including humans, wildlife and domestic animals particularly livestock, the disease has very devastating impacts on global security, health, socioeconomic, and food safety and security, particularly among poor communities in endemic countries including Sudan [27,30,30]. This underscores the need for implementing multisectoral One Health strategy for the surveillance, prevention, and control of RVF outbreaks [8,82,83]. Such strategy should capitalize on improving the diagnostic capacity and surveillance system, enhance case management and vector control, and more importantly strengthening preparedness, prevention, and response strategies and interventions.

More investment should be made on improving the early detection and surveillance through leveraging the use of diseases vectors as flying needles that naturally collect blood samples randomly from all different hosts in the area including human and livestock to monitor dynamics of diseases and pathogens through what is known as Xenosurveillance [84–87]. This will might offer a robust and cost-effective tool for the early detection of pathogens circulating in a specific area [23]. Integrating molecular Xenosurveillance, community-based syndromic surveillance for humans and animals, and the health facility-based passive surveillance enhanced with genomic analysis will create a powerful collaborative integrated surveillance [10,35,68,86,88]. Appreciating the potential challenges in the field for the implementation of molecular Xenosurveillance, it still could be leveraged as an early warning system that alert the health system to initiate more in depth investigations. Supporting this with a multisectoral One Health strategy for the early preparedness, prevention, and response strategy will substantially reduce the risk of future outbreaks and pandemics [89–91]. Interestingly, blood-fed mosquitoes were proven useful in tracking the community exposure to a non-mosquito-borne virus; namely SARS-CoV-2 in rural areas [92]. This underscores that, Xenosurveillance in addition to its cost-effectiveness in the early detection of vector-borne diseases before they emerge among human and/or animal populations and causing significant health and socioeconomic challenges, it offers a robust and non-invasive approach for tracking the community exposure to pathogens [84,93]. Nevertheless, the feasibility and effectiveness of this approach need to be explored in different settings and for different diseases [85,86].

To strengthen future responses, it is essential to incorporate an animal vaccination program in regions endemic or vulnerable to RVF outbreaks [28]. This proactive measure will add significant value in preventing the recurrence of such outbreaks and minimizing their devastating impacts [94]. Effective preparedness, prevention, and response strategy in countries endemic with or at risk of RVF outbreaks like Sudan should consider vaccinating most at risk human populations using the currently leading candidate vaccine for human use, once it is approved [95]. To maximize the cost-effectiveness, there is a need to establish a coordinated mechanism for joint vaccination campaigns for humans and livestock, this might bring the disease eliminating at sight.

Due to the disease's characteristics including virulence, devastating impacts on health, socioeconomic, and food insecurity, and global health security, RVF is on the high priority lists of Gavi; the Vaccine Alliance, the Coalition for Epidemic Preparedness Innovations (CEPI), and the WHO list for potential involvement of the next pandemic [89,96–98]. Therefore, the world will save more lives and resources by investing in improving the planning and implementation of effective measures of preparedness, prevention, and early responses through a multisectoral and integrated systems One Health strategy [35,90,99–101]. This must include increasing the awareness, engagement, and empowerment of communities at-risk to enhance the implementation of preparedness and prevention measures and facilitate the early notification through a community-based syndromic surveillance and increase the uptake of interventions and services including vaccination [68,102,103].

5. Conclusions

Here we reported an outbreak of Rift Valley fever in Berber locality in the northern region of Sudan. We identified 246 cases of RVF infection including seven deaths among humans, and 119 deaths and 82 abortions among Livestock in the area. Our entomological surveillance confirmed the presence of *Anopheles arabiensis*, *An. stephensi*, *Aedes aegypti*, *Ae. vexans*, *Culex pipiens*, *Cx. Quinquefasciatus*, and *Cx. theileri* in the area during the outbreak. In a comparison with another outbreak of Rift Valley fever in nearby area while ago, a multisectoral One Health response strategy has resulted in strengthening the health system through re-innovating health facilities and centres and training about 200 healthcare and emergency responders. Additionally, it reduced cases and fatalities among humans by 78% and 63%, respectively, and loss in livestock due to deaths and/or abortions by 82%.

This underscore the added value of implementing a One Health strategy including an integrated surveillance and response system for the containment and control of Rift Valley fever outbreak. We recommend the institutionalization of a comprehensive One Health strategy in countries endemic with devastating zoonotic diseases like Rift Valley fever. Such a multisectoral One Health strategy should capitalize on preparedness and prevention include improving the early detection, massive vaccination program for livestock, supporting the development of effective and safe vaccinations to human. This could be enhanced by the implementation of metagenomics-enhanced Xenosurveillance as an early warning system.

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