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Viral Hemorrhagic Fever: A Literature Review

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Abstract

Viral Hemorrhagic Fever (VHFs) is a diverse group of systemic diseases mediated by RNA viruses with significant morbidity and mortality rates and represents a major public health concern caused by four families of viruses- Arenaviridae, Bunyaviridae, Filoviridae, and Flaviviridae. It can harm the walls of small blood vessels, making them leak, and it can prevent blood from clotting. VHFs are a disease that is classified into a variety of deadly viral diseases characterized by severe internal or external hemorrhage or bleeding into the skin. Fever, malaise, muscle soreness, vomiting, and shock are common clinical signs of viral hemorrhagic fever, though they might vary depending on the type. Internal bleeding that results is typically not fatal, but the illness itself may be. Viral hemorrhagic fevers (VHFs) represent a group of severe, systemic feverish diseases. This review aims to shed light on viral hemorrhagic fevers in terms of their causes, symptoms, transmission methods, prevention, and available treatment, to raise awareness about their danger and enhance preventive efforts to combat their spread. Hemorrhagic fever is a serious disease that affects humans and causes a high mortality rate due to its pathogenicity. These viruses infect insects or rodents, so the focus is on staying away from rodents or insects that carry the virus. Therefore, it is necessary to adhere to the procedures of Islam and prepare. These procedures allow for preparation for the future. disease outbreaks and preparation reduce the impact of diseases on humans. Scientific research is still ongoing to develop more effective vaccines and treatments that may contribute to reducing the negative effects of these viruses.

Keywords: Viral Hemorrhagic Fever (VHF), Hemorrhagic fever viruses (HFVs), Arenaviridae, Bunyaviridae, Filoviridae, Flaviviridae.

1. Introduction

Hemorrhagic fever viruses (HFVs) are RNA viruses that are extremely contagious and can cause viral hemorrhagic fever (VHF) in humans are a diverse group of systemic diseases with significant mortality and morbidity rates. Some viral hemorrhagic fevers include Dengue, Ebola, Lassa, Marburg, and yellow fever. Because these viruses have the potential to be employed as biological weapons [1, 2] and to generate outbreaks with high mortality rates, they pose a serious threat to global public health.

The most common viral hemorrhagic fevers are Dengue and Yellow fever, caused by viruses of the subfamily. Type of viral hemorrhagic fevers as a group are caused by viruses from four families - Arenaviridae, Bunyaviridae, Filoviridae, and Flaviviridae [3]. The symptoms of these viruses include circulatory instability, coagulopathies, altered mental status, and, in extreme cases, death. There is a

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vast range in the intensity of disease; While some viruses can be fatal, others only produce minor illnesses [4].

Some VHF are transmitted by mosquito or tick bites, or by touch or inhalation of contaminated substances from animal reservoirs or arthropod vectors. The most common way that viruses linked to arthropod vectors propagate is through human bites from mosquitoes or ticks. However, some of these vectors perhaps transmit the virus to animals and Livestock and then infect humans when they groom or slaughter the animals. Livestock (cattle, sheep, camels, and goats) can carry the Bunyaviridae that causes VHF. However, it is possible for most HFVs through contact with infected blood and other body fluids to spread from human to human [5, 6]. In Iraq, infections with hemorrhagic fever are concentrated among animal breeders and meat sellers. Contact with infected animals is the basis for the transmission of the disease. This review aims to provide a comprehensive overview of viral hemorrhagic fevers, including epidemiological aspects, characteristics, pathogenesis, identification, and diagnostic methods. This research seeks to enhance the scientific understanding of these diseases and provide information to support future research and public health interventions to control their spread and reduce their impact.

2. Classification

Viruses cause the types of viral hemorrhagic fever in four families: Arenaviridae, Bunyaviridae, Filoviridae, and Flavivirus [3].

Table 1: Haemorrhagic fever (HF) viruses and the diseases they cause

Family	Virus	Disease
Arenaviruses	Lassa virus	Lassa fever
Filoviruses	Ebola virus	Ebola haemorrhagic fever Marburg haemorrhagic fever
	Marburg virus	
Flavivirus	Yellow fever virus	Yellow fever
Bunyaviruses	Crimean-Congo haemorrhagic fever virus	Crimean-Congo haemorrhagic fever (CCHF)

3. VHFs Share a Number of Common Characteristics

They are all lipid-enveloped, single-stranded RNA viruses that can be vector-borne or zoonotic. They require an animal or insect host to survive. Geographically, viruses are limited to the regions in which their host species reside. None of these viruses have a natural reservoir in humans. Human cases happen occasionally. They may result in severe, potentially fatal diseases. All require an animal or insect host (known as a natural reservoir) to survive**.**

4. Epidemiology

4.1 Lassa virus (LASV)

LASV belongs to the virus family Arenaviridae are enveloped, single-stranded, negative-sense RNA viruses [7]. Lassa virus causes Lassa fever. It is an acute viral disease that occurs in West Africa. The infection was first described in 1969 after cases in Lassa when two nurses died in Nigeria [8]. Nigeria, Guinea, Liberia, and Sierra Leone are among the West African countries where the illness is extensively endemic, with an estimated 100,000 to 500,000 cases of the disease annually [9]. Lassa fever is imported from time to time to other countries through travel. Sporadic cases were imported

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to Britain, the United States, Japan and Canada [10], and at least four imported cases, all fatal reported during the year 2000 [11]. During the dry season (January–April), nosocomial outbreaks and endemic transmission are more common. Infection occurs through inhalation of aerosols, and ingestion of food contaminated with rodent droppings, Infection also occurs when rodents are captured for consumption [12]. Spread to people with rodent to human transmission being the most common mode of transmission of the virus [11]. Among all known viral hemorrhagic fevers, Lassa fever is considered one of the greatest global burdens and is second only to dengue fever, which affects approximately 390 million people annually [13]. In rodents, particularly Mastomys natalensis, the causative agent, which belongs to the arenavirus group, is known to be enzootic.

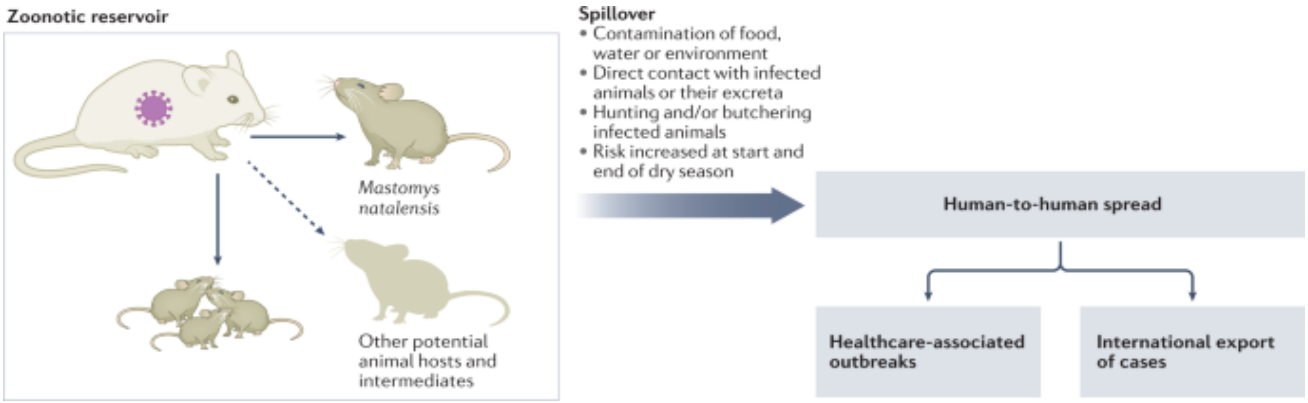

Fig. 1 Lassa virus transmission [14].

4.2 Ebolaviruses and Marburgvirus's

Ebola and Marburg viruses, which are among the most virulent pathogens of humans [15], are zoonotic viruses that cause clinically similar diseases characterized by severe or fatal hemorrhagic fever and capillary leak are caused by members of the genera Ebolavirus and Marburgvirus, respectively, in the family Filoviridae. They were discovered in bats in Africa [16]. Bats are believed to be the reservoir host for all of these viruses. Transmission occurs by direct contact with blood or other bodily fluids, such as feces or vomit from infected humans or animals, or by indirect contact with contaminated objects and surfaces like bedding, clothes, and medical equipment [17]. Once humans are infected, it can spread from person to person [18].

The Ebola virus was identified in 1976 in the Democratic Republic of the Congo for the first time. The Ebola virus infection is just a little more virulent than the Marburg virus [19] and consists of six species: Zaire, Sudan, Bundibugyo, Tai Forest, Reston, and Bombali [20]. Ebola virus disease (EVD), a hemorrhagic fever, is caused only by the first four species [21]. The first Ebola virus to be discovered was the Zaire species [22]. The greatest outbreak of the Zaire ebolavirus since it was discovered in 1976 in Yambuko, Democratic Republic of the Congo, was reported in March 2014 [23] and was responsible for the additional epidemic, including several outbreaks in Yambuko, Democratic Republic of the Congo [24]. During the 2014 outbreak, the Mortality rate for hospital admissions was as high as 64.3% [25] and in some treatment centres in West Africa, it was as low as 31.5% [26] and about 20% in patients treated outside of West Africa [27]. Sudan virus (SUDV; *Sudan ebolavirus*) was first isolated during an outbreak in Nzara, Sudan, in 1976 [23]. The Mortality rate of the Sudan virus was as low as 39% to 65% in previous outbreaks [28], with the largest outbreaks occurring in Uganda (425 cases) in 2000 [29]. Reston virus, which has been found in pigs in the Philippines, causes the virus Reston disease in non-human primates and pigs, while Bombaili virus, which has been identified as viral RNA in African bats. The mortality rate reaches

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80%-90% in the Democratic Republic of the Congo [30]. In recent outbreaks, in the Democratic Republic of the Congo, the mortality rate was 42% in 2020 in Equateur province [31] and 100% on April 23, 2022 [32], in the same province, while in North Kivu province, the mortality rate was 50% in 2021 [33], with one case reported on 21 August 2022 [32].

Marburg virus was first identified in 1969 when outbreaks of hemorrhagic Fever struck Frankfurt and Marburg, Germany, at the same time, as Belgrade in the former Yugoslavia and Serbia [33]. is a serious, frequently fatal disease that affects people. In low-income nations, the death rate from Marburg hemorrhagic fever is very high, at 82% [34]. Approximately 500 to 600 human cases of Marburgviruses have been reported to date, globally [35]. Two major epidemics occurred, one in the Democratic Republic of the Congo among gold miners and involving 154 cases and 128 deaths (cases mortality rate 83% from 1998 to 2000 [36] and the other in Uig province in Angola involving 374 cases and 329 deaths (cases mortality rate 88%) in the period from 2004 to 2005 [35]. Small outbreaks were also reported in Uganda between 2007 and 2017 [37]. In Guinea, one case was reported in August 2021 and in Equatorial Guinea and Tanzania in the Kagera region in February and March 2023, respectively [38].

4.3 Yellow virus

Yellow fever, caused by the flavivirus, was isolated by Adrian Stokes in 1927 from a patient known as Asibi from Ghana [39]. It is a viral disease that is transmitted by a bit of type of infected mosquitoes (such as Haemagogus and Aedes spp) found in South America and tropical regions of Africa. It causes fatal outbreaks of necrotizing hepatitis in South America, East and West Africa. Death occurs in 20%- 50% of people who develop Hepato-renal failure [40]. According to the World Health Organization, as of 2023, there are 13 nations in Central and South America and 34 countries in Africa where yellow fever is endemic or has endemic regions. There is a cheap and safe vaccine to prevent yellow fever. To provide lifetime protection, a single dose of the yellow fever vaccination is adequate. Since yellow fever is widespread in 34 countries, there are over 200,000 cases and 78,000 fatalities every year on the African continent alone, even though there is an efficient and affordable vaccination for the illness [41].

4.4 CCHF virus is a bunyavirus of the genus *Nairovirus*

Crimean-Congo hemorrhagic fever (CCHF) is a disease caused by the Crimean-Congo hemorrhagic virus (CCHV) of the genus *Nairovirus of the* Bunyavirus family. It is endemic to Africa, the Balkans, the Middle East, and Asia. Has a case mortality rate of 40% [42].

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Fig. 2 The Pattern of CCHF distribution in Middle Eastern and Asian nations [43].

Ticks and livestock animals are the main source of transmission. Hyalomma ticks are widely distributed throughout Africa, Asia, the Middle East, and Eastern Europe considered one of the most important vectors for the transmission of many diseases [44]. Livestock animals such as cows, goats, sheep, and camels are considered a reservoir for this infection [45]. Transmission occurs through contact with the blood or tissue of infected ticks, virus patients, and viral livestock. Human-to-human transmission is possible between healthcare workers or relatives. Once a person is infected, they can pass the virus on to others through the blood or other bodily fluids of people with CCHFV [46].

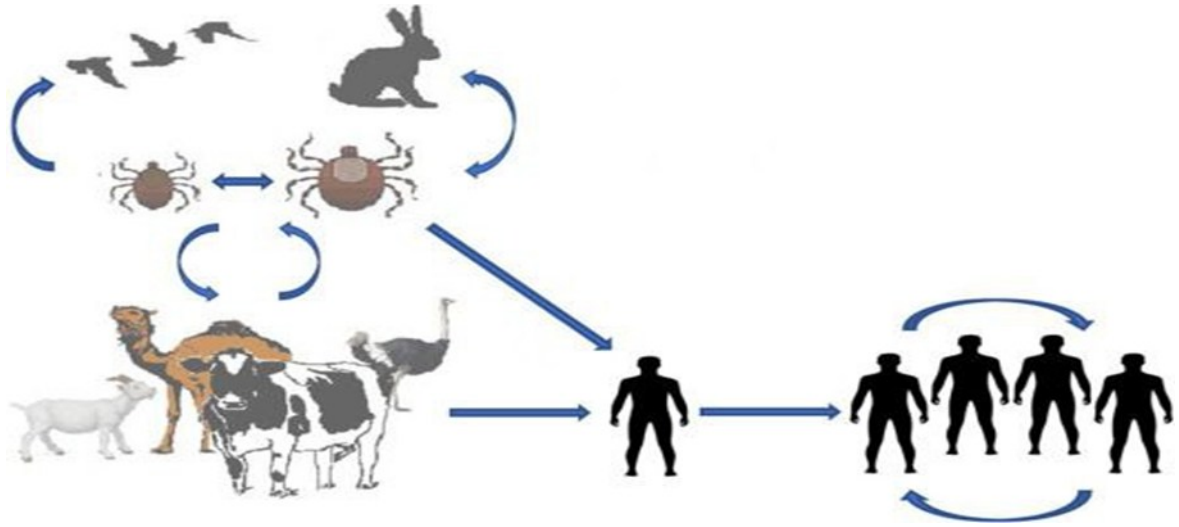

Fig. 3 Transmission of CCHF virus [47].

To date, there are no vaccines or treatments available for humans and animals [48]. For this, it is difficult to contain and prevent outbreaks. Sporadic human cases and outbreaks of CCHF have been reported in the past, from Iraq, Kuwait, Oman, United Arab Emirates, Saudi Arabia, Sudan, Afghanistan, and Iran [42] while in Europe reports have so far been restricted to the Balkan region, Spain, Russia and Turkey.

The first ever case of CCHF was reported in Pakistan in 1976 [49] and has since spread throughout the country when a CCHF patient underwent a laparotomy at Rawalpindi General

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Hospital. It then resulted in 11 secondary cases in the same hospital and ultimately led to the death of 3 people. From the beginning of 2014 to 2020, 356 cases of CCHF were reported [50]. As for the first six months of the year 2022, when 11 cases of CCHF were reported, 4 of them were during the first five months of the year, and the percentage of cases increased during June and reached seven cases, six in Khyber Pakhtunkhwa [51] and one in Balochistan [52]. As for the year 2023, specifically the period from January to June, reported a total of 84 cases of CCHF were reported by public health authorities in Pakistan, of which 81 were in Balochistan and 3 in Khyber Pakhtunkhwa. Five of these died

CCHFV is endemic and widespread in Afghanistan. The first case was reported in 1998. A CCHF outbreak occurred in the western region's Herat district in 2009, with 30 human cases documented, including nine (30%) fatalities. [54]. According to what was stated in the World Health Organization, the total number of suspected cases and reported deaths during 2017 and 2022 was 1,971 and 207, respectively. Of those aged five and older, females made up 25.9% and 97.5%, respectively. It was found that the most frequently reported occupational groups are those reported were those dealing with animals (farmers, animal dealers, herders, and butchers), with a percentage of 37.7% (743), followed by housewives at 23.2% (457). Since the beginning of 2023, the percentage of suspected CCHF cases and associated deaths has reached 668 and 67. Of the total 668 cases.667 (99.9%) were over 5 years old and 192(28.7%) were female [55]. Particularly during Eid al-Adha, when Muslims worldwide sacrifice animals like cattle, sheep, goats, or camels, the frequency of CCHF cases in Afghanistan rises [56].

While Iraq was recovering from the COVID-19 pandemic, Crimean-Congo Hemorrhagic Fever disease appeared in the south again and then spread to many provinces. The lack of preventive veterinary activities during the two years of the COVID-19 pandemic (2020-2021) resulted in the largest outbreak of CCHF in Iraq since 1979 [57]. The disease was discovered that year in ten patients. The percentage of cases reported between 1989 and 2009 was six, and there were 11 recorded occurrences in 2010, and three fatal ones in 2018, and in 2021, 33 confirmed cases were reported, including 13 deaths (mortality rate of 39%). Health authorities in the Republic of Iraq reported to WHO during 2022, specifically the period between January 1 and May 22, 2022, 212 cases, of which 115 (54%) were suspected and 97 (46%) were laboratory confirmed [42]. The number of reported cases in the first five months of 2022 is much higher than what has been reported in 2021, when 33 laboratory-confirmed cases were reported 2021[42].

As for the year 2023, according to the Iraqi Ministry of Health, since the start of 2023, more than 35 fatalities and more than 250 cases of Crimean-Congo hemorrhagic fever have been documented in all of the nation's governorates. With 67 cases and 10 fatalities, the Dhi Qar Governorate had the most hemorrhagic fever infections. Basra, Maysan, the Al-Rusafa side of Baghdad, Al-Muthanna, Wasit, Babil, and the Al-Karkh side of Baghdad were next in line. Sheep and cattle breeding is very common in Iraq, as studies have shown that these animals are regularly infected with various types of Ticks, especially Hyalomma spp., which are the main vector of CCHF.

The first cases of CCHF were detected in 1995. During 2013 and 2017, 80 cases were reported and 48 (60%) of the total instances involved Omani citizens while the foreign-born population made up 32(40%) of the cases that have been reported, 16 (50%) are from Bangladesh, 8 (25%) are from Pakistan, 5 (16%) are from Yemen, and 1 is from India, Somalia, and Sri Lanka. The majority of the incidents included either working directly with animals or in a slaughterhouse [58]. During the year

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2019, specifically during Eid Al-Adha between August 17 and August 23, the directorate of disease control received reports of 4 individuals with CCHF from different places in northern Oman [59].

CCHF was first reported in the United Arab Emirates (UAE) in hospitals in Dubai in 1979. Five cases were reported among hospital staff, two of whom died [60]. After that, no further case was noted until 1994 when it was reported. Epidemic in the UAE among slaughterhouse workers [61]. Five cases and two deaths were reported between the time frame from 1998 to 2013[54]. According to a genomic analysis, this outbreak had several origins in Pakistan, Madagascar, and Somalia, most likely as a result of the importation of diseased cattle from these regions.

5. Pathogenesis

Viral hemorrhagic fevers (VHFs) are a group of diseases caused by multiple separate virus families. Infection with haemorhagic fever viruses occurs through the exposure of mucous membranes or cracks in the skin to an infectious virus such as Ebola virus, through exposure to infected rodent excreta, as in the case of Lassa virus, or through the bite of an infected insect, as occurs in YFA [62]. Cytokine storm, vascular endothelial growth factor-induced increased permeability, complement activation, disseminated intravascular coagulation in one or more hemorrhagic fevers, and hepatocellular necrosis-induced lack of hepatic synthesis of coagulation factors are just a few of the many pathogenic mechanisms [63].

The pathogenesis of VHF involves a complex interplay between the virus and the human immune system, resulting in a range of symptoms and potential complications. The pathogenesis typically begins with the introduction of the virus into the human body, often through contact with infected animals (zoonotic transmission) or through direct contact with the bodily fluids of infected individuals is possible for most HFVs. Once inside the body, the virus begins to replicate, primarily targeting immune system cells and endothelial cells that line blood vessels [64]. An infection's initial targets are DCs and macrophages. In addition to supporting productive growth, macrophages and dendritic cells facilitate systemic dissemination by trafficking to local lymph nodes as well as other tissues and organs [62]. This viral replication triggers an immune response characterized by the release of inflammatory molecules (cytokines) and the activation of immune cells. This immune response, while aimed at controlling the infection, can sometimes become dysregulated and contribute to the severity of the disease.

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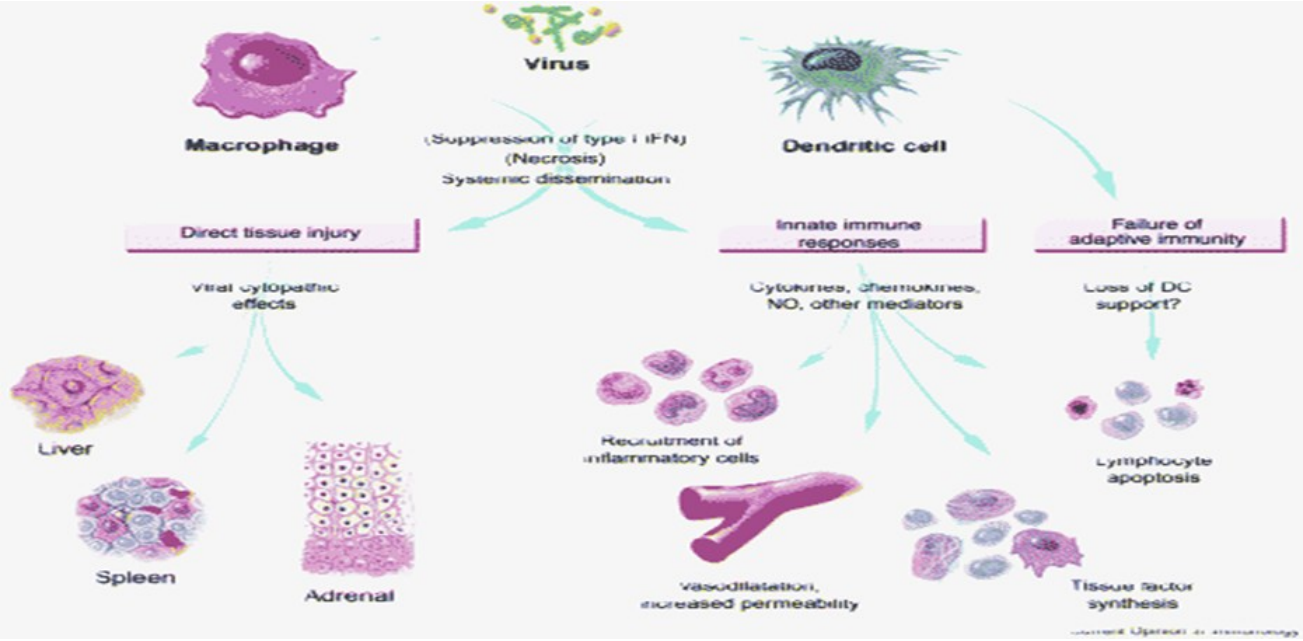

Fig. 4 Pathogenesis of severe viral hemorrhagic fever [65].

6. Diagnosis

VHFs are diagnosed by the detection of specific antibodies (IgM antibody testing paired with acute-convalescent serum serologies), viral antigens (ELISA), immunohistochemistry methods, electron microscopy, and reverse transcriptase polymerase chain reaction (RT-PCR) on blood samples [66].

6.1 Virus Culture and Electron Microscopy

Virus culture is one of the traditional methods that help identify and characterize new or branched viruses, but is rapidly challenged by PCR and next-generation sequencing (NGS) as they are faster and more reliable ways to identify these viruses[67]**.** Diagnostic electron microscopy is a useful technique for identifying viruses associated with human disease [67]. Electron microscopy was an essential component of viral diagnosis until highly sensitive nucleic acid amplification techniques (NAT) were developed. It has been instrumental in identifying the causative agent of several disease outbreaks caused by previously unknown viruses based on structural features from clinical or culture material [68]. However, in many situations, growing live viruses and preparing samples for EM require access to highly specialized laboratories, and these processes can be time-consuming, requiring weeks to grow the virus and additional time for microscopy. As a result, these methods are no longer used as first-line diagnosis [69].

6.2 Nucleic Acid Detection

This method is one of the common methods used to diagnose VHF. This test is performed to detect DNA and RNA from viruses by polymerase chain reaction (PCR), which is one of the molecular techniques used to diagnose VHF. This test is done by taking a sample of RNA and checking for the presence of the virus. Once the virus is confirmed in the RNA, the person is diagnosed with viral hemorrhagic fever. PCR modifications, such as real-time PCR, can be used to determine viral load in addition to detecting viruses in sera from patients [70]. Real-time PCR and reverse transcription PCR are the most common molecular diagnostic tools for identifying viral diseases, including viruses causing VHF [66]. Since VHF can spread easily, these tests are performed in special laboratories, especially if the symptoms are severe.

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6.3 Enzyme-linked immunosorbent assay

It is an immunoassay commonly used for antibody detection [71]. ELISA is used to detect IgM and IgG antibodies in suspected patients. When diagnosing acute VHF, serology is not helpful because IgM antibody levels can indicate various illness stages or presymptomatic or asymptomatic infection. However, sometimes the ELISA may lack specificity and exhibit a high level of reactivity between viruses that are closely related, especially Flavivirus and Bunyavirus [72].

6.4 Immunohistochemistry

Skin biopsy samples were tested for the presence of the Ebola virus using an immunohistochemical assay. Formalin was used to fix the skin biopsy, making the virus non-infectious. It is regarded as an easy, secure, and accurate method for laboratory confirmation of Ebola virus disease [73]. Although a quick diagnosis is not possible due to the specialized laboratory procedures needed for this operation, they can be utilized as a monitoring tool or as a substitute for an autopsy on the deceased patient.

7. Symptoms

Clinical signs and symptoms of Crimean haemorrhagic fever are often nonspecific. The initial symptoms of the disease may resemble those of other common tropical diseases including typhoid and malaria, such as fever and general malaise. Even after the onset of the fulminant disease process, the diagnosis of viral haemorrhagic fever remains difficult because of its rarity and the inability to differentiate its symptoms [74]. In the initial stages of infection, general symptoms similar to other diseases such as influenza appear and include fever, sudden high temperature, fatigue and general tiredness, muscle and joint pain, severe headache, dizziness and general malaise, loss of appetite, nausea and vomiting, abdominal pain and diarrhoea, which may be bloody in some cases. As the disease progresses, more serious and potentially life-threatening symptoms appear and include spontaneous bleeding including bleeding from the gums, nose, nosebleeds, gastrointestinal tract, bloody vomiting, black stools, and skin, the appearance of bleeding spots under the skin, blood clotting disorders such as internal bleeding or uncontrolled bleeding due to impaired clotting process, swelling and pain in soft tissues, yellowing of the skin and eyes, jaundice due to liver involvement, acute renal failure leading to decreased urine output, low blood pressure and circulatory shock, deterioration of the neurological condition, confusion, delirium, convulsions and coma, multiple organ failure due to involvement of the liver, kidneys, heart and lungs, and death occurs in some cases as a result of severe bleeding or multiple organ failure.

The incubation period for the Ebola virus ranges from 2 to 21 days. The symptoms, which include fever, headache, sore throat, joint and muscle discomfort, and weakness, startup abruptly. Later on, there is typically rash, diarrhea, and vomiting along with compromised liver and renal function. Internal or external bleeding may occasionally happen, usually starting five to seven days after the first symptoms appear [75]. Marburg virus Symptoms can begin 2 to 21 days after exposure to the virus. Symptoms begin suddenly and the disease progresses rapidly. Fever, chills, headaches, and muscle aches are among the early symptoms. Yellow fever takes three to six days to incubate. Many folks have no symptoms at all. Fever, headaches, muscle aches, appetite loss, and nausea or vomiting are typical symptoms. Usually, the symptoms disappear in three to four days. Lassa fever symptoms often manifest one to three weeks following viral exposure. About 80% of Lassa fever infections in endemic countries may have minimal symptoms and go undetected. These symptoms include mild fever, headache, and malaise. Depending on how the virus was acquired, the incubation period for Crimean-type hemorrhagic fever can vary in length. The incubation period, which begins

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three to nine days after a tick bite, is when the disease is typically spread. Contact with infected blood or tissue can spread the viruses, and the incubation period for these viruses can be anywhere from 5 to 6 days, up to 13 days [76].

8. Management

Ebola, Marburg, Lassa, and Crimean-Congo hemorrhagic fever are among the severe illnesses known as viral hemorrhagic fevers (VHFs), which are brought on by a number of viruses. The abrupt onset of fever, muscle soreness, bleeding, and, in extreme situations, shock and organ failure are the hallmarks of these illnesses. Healthcare workers should quickly recognize the clinical symptoms associated with VHFs and conduct a risk assessment to determine the likelihood of infection. Isolation of suspected patients in designated facilities is recommended to prevent transmission to others. Currently, there are no FDA-approved treatments for most VHFs. Therefore, supportive care is vital, including maintaining fluid and electrolyte balance. Monitoring vital organ functions.

Treating symptoms such as fever and pain. Preventing and treating secondary infections. Use appropriate personal protective equipment (PPE), including gloves, gowns, and face masks, or goggles. Follow strict infection control protocols when handling patients or biological specimens. Ongoing training in infection prevention and control procedures. In some cases, antiviral drugs such as ribavirin may be helpful, especially in cases of Lassa fever and Crimean-Congo hemorrhagic fever. Research is underway to develop specific vaccines and treatments for certain types of VHFs. Given their potential severity, the risk of secondary spread, and the high degree of public scrutiny and lack of familiarity on the part of most clinicians, infectious disease specialists or other clinicians with expertise in the diagnosis and treatment of viral hemorrhagic fevers should be consulted when the diagnosis is suspected. Early diagnosis is critical for the appropriate treatment of patients suspected of having viral hemorrhagic fevers, as it can improve survival rates and prevent hospital-acquired infections [77].

9. Prevention and treatment

Avoiding direct contact with infected individuals or animals carrying the virus, wearing respirators for laboratory workers, gloves for hunters, masks for agricultural workers in endemic areas, and wearing appropriate clothing for the general public or nylon clothing for those living in focal sites are all ways to prevent and lower the risk of contracting OHFV. Other preventive measures include putting in place infection control procedures, using personal protective equipment, and getting vaccinated when vaccines are available [78]. Treatment is based on supportive care such as fluid replacement and symptom control, and antivirals may be used for some types. Viral hemorrhagic fevers are deadly diseases that require early recognition of symptoms and strict preventive measures to limit their spread. Isolation, supportive care, and providing appropriate treatment when available are key factors in improving the chances of survival. Research is ongoing to develop effective vaccines and treatments to combat these serious diseases. One of the first and most effective vaccinations against hemorrhagic fever viruses is the YF vaccine. It was initially created in the 1930s by attenuating the wild-type Asibi strain by circulating it 176 times through the embryonic tissue of mice and chickens. Unlike YF EVD and HTNV, there isn't a commonly used vaccine for Lassa fever; however, a number of potential ones are being developed [79]. The mainstay of treatment for HFRS is supportive care, which may involve oxygen, dialysis, and shock therapy, depending on the disease's clinical signs. There is no particular treatment offered. The antiviral medication ribavirin

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(1-beta-D-ribofuranosyl 11, 2, 4-triazole-3-carboxamide) has reduced the morbidity and death rates among individuals with HFRS [80].

10. Conclusions

Hemorrhagic fever is a serious disease that affects humans and causes a high mortality rate due to its pathogenicity. These viruses infect insects or rodents, so the focus is on staying away from rodents or insects that carry the virus. Therefore, it is necessary to adhere to the procedures of Islam and prepare. These procedures allow for preparation for the future. disease outbreaks and preparation reduce the impact of diseases on humans. Scientific research is still ongoing to develop more effective vaccines and treatments that may contribute to reducing the negative effects of these viruses.

Conflict of Interest

There is no conflict of Interest

References

[1] Al-Abri, S., Al A, I., Fazlalipour, M., Mostafavi, E., Leblebicioglu, H., Pshenichnaya, N, & *et al*. (2017).Current status of Crimean-Congo haemorrhagic fever in the World Health Organization eastern Mediterranean region: issues, challenges, and future directions. *Int. J. Infect. Dis*.,*58*, 82–89.

[2] Hickman, R., Saunders, L., Bigger, A., Kane, D., & Iversen, L.(2022). The development of broad-spectrum antiviral medical countermeasures to treat viral hemorrhagic fevers caused by natural or weaponized virus infections. *PLoS Negl. Trop. Dis.*, 16, e0010220.

[3] Racsa, D., Kraft, S., Olinger, G., & Hensley, E.(2016). Viral Hemorrhagic Fever Diagnostics. *Clin Infect Dis*.,62(2),214-9.

[4] Mangat, R., Louie, T.(2023). Viral Hemorrhagic Fevers, National library of medicine.

[5] Marty, A. M., Jahrling, P. B., and Geisbert, T. W.(2006). Viral hemorrhagic fevers. *Clin. Lab. Med.*, *26*, 345–386.

[6] Koehler, C., Di Cristanziano, V., Späth, M., Hoyer-Allo, R., Wanken, M., Müller, U., & *et al*.(2022). The kidney in hantavirus infection—epidemiology, virology, pathophysiology, clinical presentation, diagnosis and management. *Clin. Kidney J.*, 15, 1231–1252.

[7] Buchmeier, J., de la Torre, C., & Peters, J.(2007). Arenaviridae: the viruses and their replication, 5th ed, vol 2 Lippincott Williams & Wilkins, Philadelphia, PA.

[8] Frame, D., Gocke, J., Baldwin, M., *et al.* (1970).Lassa fever, a new virus disease of man from West Africa. *Am J Trop Med Hyg*.,19(4),670–676.

[9] Ogbu, O., Ajuluchukwu, E., Uneke, CJ. (2007).Lassa fever in West African sub-region: an overview. *J Vector Borne Dis*.,44,1–11.

[10] Freedman, O., & Woodall, J.(1999). Emerging infectious diseases that concern travelers. *Med Clin North Am.,* 83 (4), 875-7

[11] World Health Organization. Outbreak news. (2000). Lassa fever, imported case, Netherlands. *Wkly Epidemiol Rec*.,75 (33), 265-72

[12] Asogun, A., Günther, S., Akpede, O., Ihekweazu, C., & Zumla, A.(2019). Lassa Fever: Epidemiology, Clinical Features, Diagnosis, Management and Prevention. *Infect Dis Clin North Am*., 33(4),933-951

[13] Lukashevich, S., Paessler, S., de la Torre, J.C.(2019). Lassa virus diversity and feasibility for universal prophylactic vaccine. *F1000Research, 8*, 1–12.

[14] Garry ,F.(2023). Lassa fever — the road ahead. *Nature Reviews Microbiology*,21, 87–96

[15] Bray, M., Chertow, D.(2016). Filoviruses. In: Clinical Virology, 4th edition, American Society of Microbiology.

DOI: 10.69946/ojms/2025.03.004, pp (36-49)

[16] Ftika, L., & Maltezou, HC.(2013). Viral haemorrhagic fevers in healthcare settings. *J Hosp Infect.*,83(3),185–192. https://doi/org/10.1016/j.jhin.2012.10.013.
[17] European Centre for Disease Prevention and Control hweeesdfdA-E-a-M-p. (2021).Ebola and Marburg virus diseases - Annual Epidemiological Report for 2019.
[18] Baseler, L., Chertow, S., Johnson, M., Feldmann, H., Morens, M . (2017).The Pathogenesis of Ebola Virus Disease. *Annu Rev Pathol*.,12,387.
[19] Yuill, T.(2023). Marburg and Ebola Virus Infections, PhD, University of Wisconsin-Madison.
[20] Goldstein, T., Anthony, J., Gbakima, A., Bird, H., Bangura, J., and *et al*.(2018). *Epidemiology and pathogenesis of Ebola virus disease*. *Nat Microbiol.,*3(10),1084.
[21] Jain, S., Martynova, E., Rizvanov, A., Khaiboullina, S., Baranwal ,M. (2021).Structural and Functional Aspects of Ebola Virus Proteins. *Pathogens.,* 10, 1330.
[22] Bull World Health Organ.(1978). Ebola haemorrhagic fever in Zaire, 1976.*Pub med,*56(2),271.
[23] Shears, P., & O'Dempsey, T.J. (2015). Ebola virus disease in Africa: Epidemiology and nosocomial transmission. *J. Hosp. Infect.*, 90, 1–9.
[24] Erb-Alvarez, J., Wendelboe, M., & Chertow, S.(2020).Ebola Virus in the Democratic Republic of the Congo: Advances and Remaining Obstacles in Epidemic Control. *Clinical Care, and Biomedical Research*. *Chest*.,157(1),42.
[25] WHO Ebola Response Team. (2014). Ebola virus disease in West Africa: the first 9 months of the epidemic and forward projections. *N Engl J Med.*,371(16),1481-95
[26] Ansumana, R., Jacobsen, H., Idris, M., & *et al*. (2015).Ebola in Freetown area, Sierra Leone - a case study of 581 patients. *N Engl J Med.*,372(6):587-8
[27] New York Times. (2015). How many Ebola patients have been treated outside of Africa? [internet publication].
[28] World Health Organization. (2023).Disease outbreak news. Ebola disease caused by Sudan ebolavirus – Uganda. [internet publication].
[29] Roddy, P., Howard, N., Van Kerkhove ,MD., & *et al*.(2012). Clinical manifestations and case management of Ebola haemorrhagic fever caused by a newly identified virus strain, Bundibugyo, Uganda, 2007-2008. *PLoS One*.,7(12),e52986.
[30] Rougeron, V., Feldmann, H., Grard, G., Becker, S., and Leroy, M. (2015).Ebola and Marburg haemorrhagic fever. *J Clin Virol.*,64,111-9
[31] World Health Organization. (2020).Disease outbreak news: Ebola virus disease - Democratic Republic of the Congo.
[32] World Health Organization.(2022). Ebola virus disease - Democratic Republic of the Congo. [internet publication].
[33] World Health Organization. (2021).Disease Outbreak News. Ebola - Democratic Republic of the Congo.
[34] Iannetta, M., Di Caro, A., Nicastri, E., Vairo, F., Masanja, H., Kobinger, G., Mirazimi, A., Ntoumi, F., Zumla, A., Ippolito, G. (2019).Viral Hemorrhagic Fevers Other than Ebola and Lassa. *Infect Dis Clin North Am*., 33(4),977-1002.
[35] Centers for Disease, C., (2005).Prevention. Outbreak of Marburg virus hemorrhagic fever--Angola, October 1, 2004-March 29, 2005. *MMWR Morb Mortal Wkly Rep*.,54(12),308-9
[36] Zeller, H. (2000).Lessons from the Marburg virus epidemic in Durba, Democratic Republic of the Congo (1998-2000).*Med Trop (Mars).*,60(2),23-6
[37] World Health Organization. (2017).Uganda ends Marburg virus disease outbreak. [internet publication].
[38] World Health Organization. Marburg virus disease .(2023). August 2021 Centers for Disease Control and Prevention. History of Marburg virus disease (MVD) outbreaks. [internet publication].
[39] Litvoc ,M. , Novaes1, C. and Lopes,M. (2018).Yellow fever , Once again on the radar screen in the Americas. *N Engl J Med*.,376(15),1397-9.

[40] World Health Organization.(2019). Yellow fever. Geneva: World Health Organization.
[41] Simon, S., Amaku ,M., and Massad, E. (2023).Effects of migration rates and vaccination on the spread of yellow fever in Latin American communities. *Rev Panam Salud Publica*.,47,e86.
[42] World Health Organization.(2022).Crimean-Congo haemorrhagic fever (CCHF).
[43] Aslam, M., Abbas, R., **&** Alsayeqh, A. (2023). Distribution pattern of Crimean-Congo Hemorrhagic Fever in Asia and the Middle East. *Front Public Health*.,11,1093817.
[44] Ceylan, O., Uslu, A., Ceylan, C., and Sevinc, F.(2021). Predominancy of Rhipicephalus turanicus in tick-infested sheep from Turkey: a large-scale survey. Pak Vet J.,41,429–33.
[45] Fhogartaigh, N., & Aarons, E.(2015). Viral haemorrhagic fever. *Clin Med (Lond).*,15(1),61-6.
[46] Maltezou, C., Maltezos, E., & Papa, A. (2009). Contact tracing and serosurvey among healthcare workers exposed to Crimean-Congo haemorrhagic fever in Greece. *Scand J Infect Dis*.,41,877–80
[47] Spengler, R. , Bente, A. , Bray, M. , Burt, F. , Hewson, R., Korukluoglu, G. , & *et al.*(2018). Second International Conference on Crimean-Congo Hemorrhagic Fever. *Antiviral Res*., 150,137-147
[48] Tipih, T., & Burt, J. (2020). Crimean-Congo Hemorrhagic fever virus: Advances in vaccine development. *Biores Open Acces*s., 9 (1), 137–150. doi: 10.1089/biores.2019.0057
[49] Abbas, T., Younus, M., & Muhammad, A.(2015). Spatial cluster analysis of human cases of Crimean Congo hemorrhagic fever reported in Pakistan. *Infect Dis Poverty*.,4(1),1-5
[50] Ahmed, A., Saqlain, M., Tanveer, M., & *et al.* (2021).Knowledge, attitude and perceptions about Crimean Congo Haemorrhagic Fever (CCHF) among occupationally high-risk healthcare professionals of Pakistan. *BMC Infect Dis*.,21(1):35
[51] AAJ, V. (2023). Six cases of Congo fever reported in Khyber Pakhtunkhwa. Cited June 29, 2022. Accessed February 20.
[52] Pakistan Today. (2023).Congo virus case reported in Quetta hospital. Cited June 29, 2022. Accessed February 20.
[53] National Institute of Health-Pakistan. (2023). Advisory for Prevention and Control of Crimean Congo Hemorrhagic Fever (CCHF).
[54] Ince, Y., Yasa, C., Metin, M., Sonmez, M., Meram, E., Benkli, B., & *et al*.(2014). Crimean-Congo hemorrhagic fever infections reported by ProMED. *Int J Infect Dis.*,26,44– 6
[55] WHO.(2023).Outbreak of Crimean Congo Hemorrhagic Fever (CCHF)
[56] Al-abri S,S., Hewson, R., Al-kindi, H., and *et al*.(2019). Clinical and molecular epidemiology of Crimean-Congo hemorrhagic fever in Oman. *PLoS Negl Trop Dis*. *13*(4), e0007100
[57] Alhilfia, R., Khaleel, H., Raheem, B., Mahdi, S., Tabche, C., & Rawaf, C. (2023). Large outbreak of Crimean-Congo haemorrhagic fever in Iraq 2022. *IJID Regions*, 6,76-79
[58] Awsidy, S., & Hashami, H. (2019). Zoonotic Diseases in Oman: Successes, Challenges, and Future Directions. *Vector-Borne and Zoonotic Diseases*, 20,1-9
[59] Alsaadi, S., Abd-Ellatif, E., Alhashmi, F., Almoqbali, A., & Vaidya, V.(2022). Crimean-Congo Hemorrhagic Fever Outbreak in the North Region of Oman in August 2019, Case SeriesStudy. *JMIR journal*., 8(1),e36495
[60] Suleiman, H., Muscat-Baron, M., Harries, R., Satti,O., Platt, GS., Bowen, W., & *et al*.(1980). Congo/Crimean Haemorrhagic Fever in Dubai. *An Outbreak at the Rashid Hospital*.,2(8201),939-41
[61] Khan, S., Maupin, O., Rollin, E., Noor, M., Shurie, H., Shalabi, A., & *et al*.(1997). An outbreak of Crimean-Congo hemorrhagic fever in the United Arab Emirates, 1994–1995. *Am J Trop Med*.,57, 519–25.
[62] Basler, F. (2017). Molecular pathogenesis of viral hemorrhagic fever. *Semin Immunopathol*,39(5),551-561.
[63] Juan, C ., Dermot, C., & Maria, S. (2014). The Role of Platelets in the Pathogenesis of Viral Hemorrhagic Fevers. *PLOS Neglected Tropical Diseases*.,8,6

[64] Koehler, C., Di Cristanziano, V., Späth, M R., Hoyer-Allo, K ., Wanken, M., Müller, R-U., & *et al*.(2022). The kidney in hantavirus infection—epidemiology, virology, pathophysiology, clinical presentation, diagnosis and management. *Clin. Kidney J., 15*, 1231–1252.

[65] Bray, M. (2005).Pathogenesis of viral hemorrhagic fever. *Current Opinion in Immunology*,17(4), 399-403.

[66] Mariappan, V., Pratheesh, P., Shanmugam, L., Rao, S., **&** Pillai, A.(2021). Viral hemorrhagic fever: Molecular pathogenesis and current trends of disease management-an update. *Current Research in Virological Science*., 2, 100009

[67] Goldsmith, S., Ksiazek, G., Rollin, E., & *et al*. (2013). Cell culture and electron microscopy for identifying viruses in diseases of unknown cause. *Emerg Infect Dis*, 19, 886–91.

[68] Möller, L., Holland, G., & Laue, M. (2020).Diagnostic Electron Microscopy of Viruses With Low-voltage Electron Microscopes. *Journal of Histochemistry & Cytochemistry*, 68(6), 389-402.

[69] Racsa, D., Kraft , S., Olinger, G., & Hensley, E.(2016). Viral Hemorrhagic Fever Diagnostics. *Clin Infect Dis*.,62(2), 214-9.

[70] Hwang, K. , Ahn, J., & Nam, J . (2018). Diagnosis of Viral Infection Using Real-time Polymerase Chain Reaction. *Journal List J Bacteriol Virol*., *48*(1), 1034277

[71] Emmerich, P., von , PR., Deschermeier, C., Ahmeti, S., & *et al*. (2021). Comparison of diagnostic performances of ten different immunoassays detecting anti-CCHFV IgM and IgG antibodies from acute to subsided phases of Crimean-Congo hemorrhagic fever. *PLoS Negl Trop Dis*., 15, e0009280.

[72] Fajfr, M., & Ruzek, D. (2014). Laboratory diagnosis of viral hemorrhagic fevers. In: Singh S, Ruzek D, eds. Viral hemorrhagic fevers. *Boca Raton, FL: CRC Press*, 183–203.

[73] Zaki, R., Shieh, J., Greer, W., & *et al*.(1999). A novel immunohistochemical assay for the detection of Ebola virus in skin: implications for diagnosis, spread, and surveillance of Ebola hemorrhagic fever. *J Infect Dis.*, 179 (1), 36-47

[74] Srivastav, Y., Kumar, A., Singh, J., Srivastav, A., & Ahmad, M. (2024).Compendium: Management of Viral Hemorrhagic Fever (Viral Fever), Involving Its Pathogenesis. *Asian Journal of Research in Infectious Diseases,* 15(3),17-25.

[75] Mustafa, M., Yusof, M., Kassim, M., Jeffree, MS., Illzam, EM., & Sharifa, AM. (2016).Ebola Virus Disease, Management, and Prevention. *IOSR J Dent Med Sci*.,15,142-8

[76] Travassos, TC., De Oliveira, JMI., Selegatto, IB., & Reis, LO. (2021).COVID-19 impact on bladder cancer-orientations for diagnosing, decision making, and treatment. *Am J Clin Exp Urol*. ,9,132-139.

[77] Mangat, R.(2024). Louie T. Viral Hemorrhagic Fevers. [Updated 2023 Aug 28]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; Available:https://www.ncbi.nlm.nih.gov/books/NBK560717/. 2024;560717.

[78] Diani, E., Cecchetto, R., Tonon, E., Mantoan, M., Lotti, V., Lagni, A., Palmisano, A., Piccaluga, P. P., & Gibellini, D. (2025). Omsk Hemorrhagic Fever Virus: A Comprehensive Review from Epidemiology to Diagnosis and Treatment. *Microorganisms*, *13*(2), 426. https://doi.org/10.3390/microorganisms13020426

[79] Sulis,G., Peebles, A., & Basta, N.E.(**2023**) Lassa fever vaccine candidates: A scoping review of vaccine clinical trials. *Trop. Med. Int. Health* , *28*, 420–431. [**Google Scholar**] [**CrossRef**]

[80] Tariq, M., & Kim, M. (2022). Hemorrhagic Fever with Renal Syndrome: Literature Review, Epidemiology, Clinical Picture and Pathogenesis. *Infection & Chemotherapy*, *54*(1), 1. https://doi.org/10.3947/ic.2021.0148.