Review Article

Marburg Virus Disease: Latest Outbreak and Current Research Review

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ABSTRACT

The Marburg virus disease (MVD) is a severe and deadly viral hemorrhagic fever caused by the Marburg virus. Recent outbreaks have raised global concerns due to the severity of the disease, high mortality rate, and limited treatment options. This review provides an overview of the latest outbreak and current research on MVD, including efforts to understand the virus's epidemiology, transmission, pathogenesis, and diagnosis, as well as the development of antiviral therapies and vaccines. Advances in diagnostic techniques and experimental antiviral drugs show promising results. However, controlling outbreaks remains challenging due to various factors such as limited access to affected areas, inadequate healthcare infrastructure, and community resistance to interventions. Therefore, a multidisciplinary approach involving public health measures, clinical care, and research efforts is crucial in mitigating the impact of MVD outbreaks and improving patient outcomes. Further research and collaborative efforts are needed to develop effective strategies for preventing and managing MVD and protecting public health.

Key words: Marburg virus disease (MVD), viral hemorrhagic fever, Outbreaks, Antiviral therapies, Vaccines.

Marburg virus disease (MVD) is a severe and often fatal viral illness caused by the Marburg virus (MARV), a member of the Filovirus family [1]. In August 1967, an epidemic in Frankfurt am Main and Marburg a der Lahn, West Germany (Germany), led to the discovery of MVD for the first time. Since then, several outbreaks of MVD have been reported in Africa, with the most recent outbreak occurring in 2022. MVD shares similarities with Ebola virus disease (EVD) in terms of its clinical presentation, transmission, and high mortality rate [2].

The Marburg virus is an enveloped, negative-sense RNA virus that has a close resemblance to the Ebola virus [1]. It is transmitted to humans from infected animals, particularly fruit bats, through contact with bodily fluids or contaminated surfaces. Once the virus enters the human body, it can cause severe systemic disease with a wide range of clinical manifestations [3]. MVD is characterized by a sudden onset of fever, headache, myalgia, and malaise, which may progress to more severe symptoms such as hemorrhagic manifestations, including petechiae, ecchymoses, and mucosal bleeding. Gastrointestinal symptoms such as nausea, vomiting, and diarrhea are also common. Severe cases of MVD can lead to multiorgan failure, shock, and death, with mortality rates ranging from 24-88% depending on the outbreak and population affected [4,5].

Diagnosing MVD can be challenging, as the early symptoms are nonspecific and can resemble other febrile illnesses. Laboratory testing, including PCR-based methods, antigen detection, and serological assays, are used for confirmation [6]. However, access to these diagnostic tools may be limited in resource-limited settings where MVD outbreaks often occur. There is no specific antiviral treatment for MVD, and supportive care remains the cornerstone of management. This includes strict infection control measures, fluid and electrolyte management, and organ support as needed. Experimental treatments, including antiviral drugs and immunotherapies, have been used in some cases, but their efficacy and safety are still being evaluated through ongoing research efforts [7].

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Since the identification of MARV, significant research efforts have been directed toward understanding the virus and developing strategies for its prevention, diagnosis, and treatment. Advances in our understanding of MARV epidemiology, viral pathogenesis, and host immune response have shed light on the complex interplay between the virus and the host, and have informed public health measures to control outbreaks [8]. In recent years, the emergence of new outbreaks of MVD, including the most recent one in 2022, has renewed the focus on this deadly disease. Ongoing research efforts are aimed at improving diagnostics, understanding the factors driving the emergence and spread of MVD, developing effective treatments, and advancing vaccine development [9].

In this review, we will provide an overview of the latest outbreak of MVD, and summarize the current understanding of the virus, including its epidemiology, clinical features, diagnostics, treatment, and ongoing research efforts. We will review the existing literature and highlight key findings, discuss challenges and future directions in MVD research, and emphasize the need for continued efforts in understanding and controlling this menacing virus.

Epidemiology of Marburg Virus Disease

The epidemiology of Marburg virus disease (MVD) involves studying its distribution, patterns, and determinants within populations. MVD is primarily endemic to Africa, with sporadic outbreaks occurring in countries like Uganda, Angola, Kenya, and the Democratic Republic of Congo. Fruit bats are believed to be the natural reservoir of the virus, transmitting it to humans through direct contact or exposure to infected animals' bodily fluids or tissues. Understanding MVD epidemiology is challenging due to sporadic outbreaks linked to activities such as cave exploration, mining, or handling infected animals. International collaboration, led by organizations like the WHO, plays a crucial role in responding to MVD outbreaks. Ongoing research aims to improve our understanding of the virus's transmission dynamics, and host reservoirs, and develop effective prevention and control strategies [2,10,11].

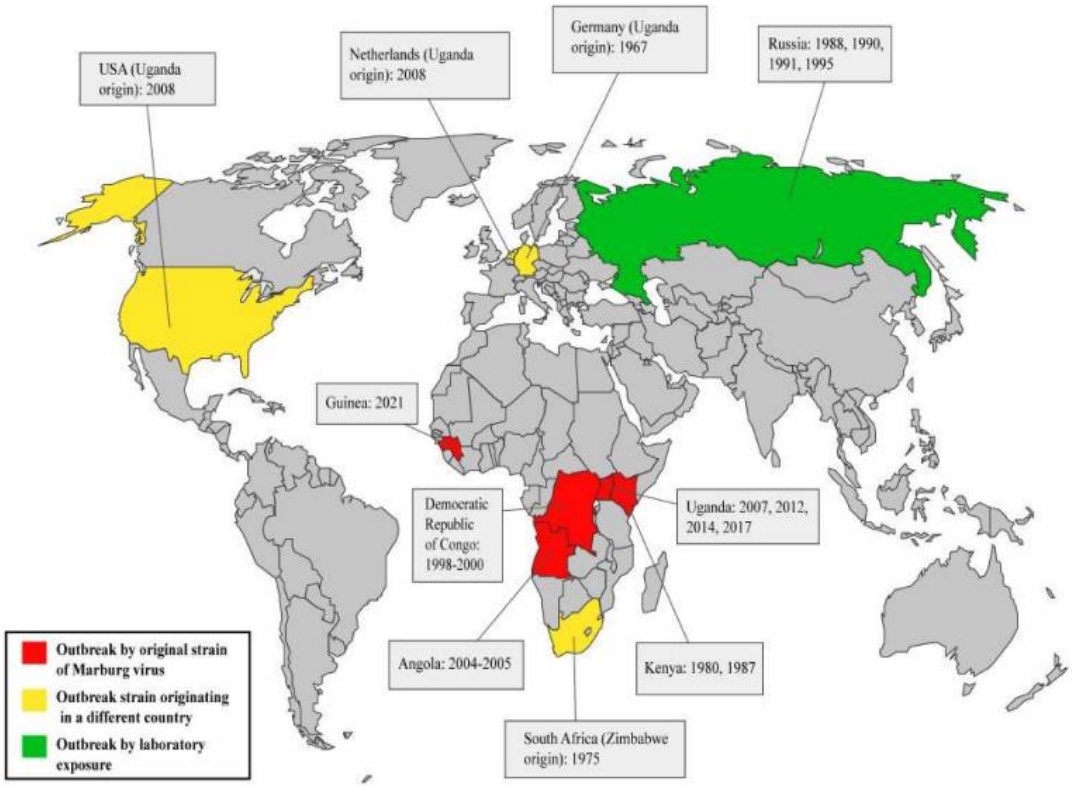

Figure 1: Marburg virus outbreaks in the past [10].

PATHOGENESIS

Marburg virus disease (MVD) is a severe and often fatal illness caused by the Marburg virus. The pathophysiology involves the virus entering the body and infecting immune cells, leading to their destruction and facilitating viral spread. The virus causes dysfunction of endothelial cells, increasing vascular permeability and causing leakage of fluid and clotting factors. This results in disseminated intravascular coagulation (DIC), abnormal blood clotting,

and bleeding. Multiple organ systems, including the liver, spleen, lymph nodes, and adrenal glands, are affected, leading to organ failure. Immune dysregulation and a cytokine storm contribute to systemic symptoms.

The precise mechanisms are still being studied, but these processes collectively contribute to the severe illness and organ damage seen in MVD [12].

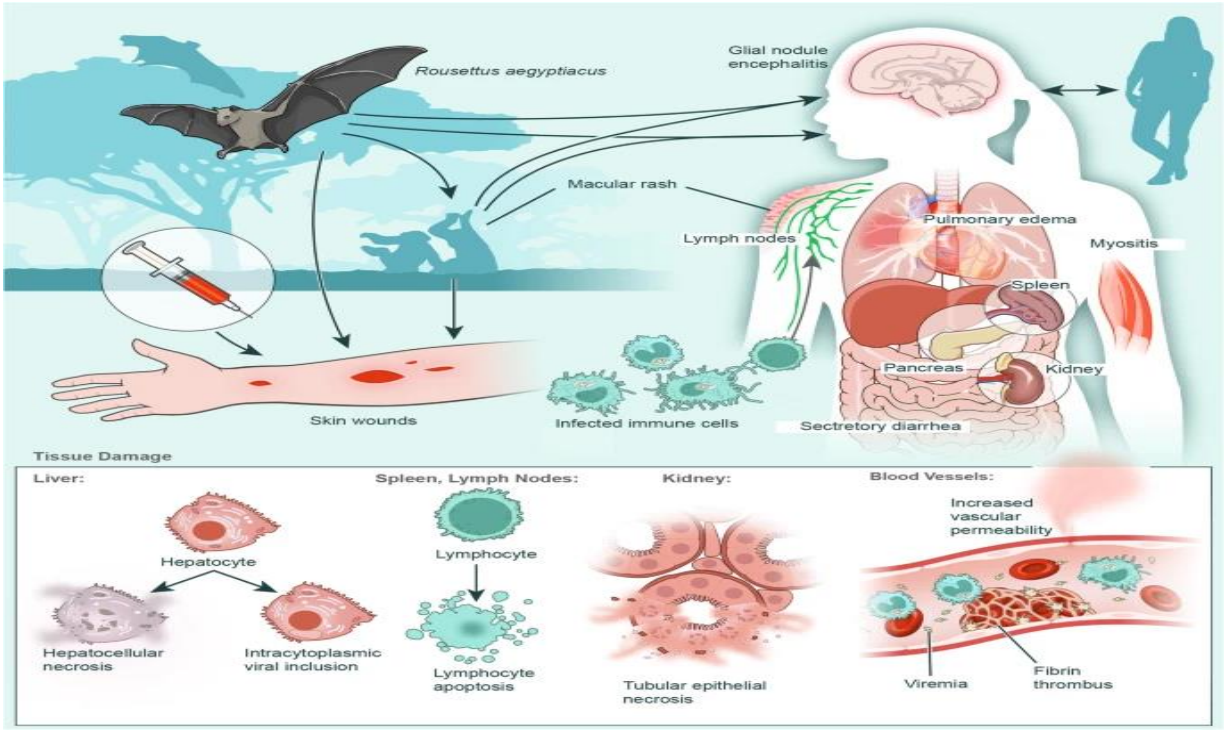

Figure 2: Pathogenesis of Marburg virus disease [13]

Clinical Features of Marburg Virus Disease (MVD)

Marburg virus disease (MVD) is a severe and often fatal viral hemorrhagic fever, shares similarities with Ebola virus disease. The incubation period ranges from 2 to 21 days, with an average of 5-10 days, during which individuals may remain asymptomatic. The disease typically begins with a prodromal phase characterized by sudden onset fever, chills, headache, muscle aches, fatigue, and gastrointestinal symptoms. As MVD progresses, hemorrhagic manifestations occur, including bleeding from gums, nose, gastrointestinal tract, and injection sites, along with petechiae and ecchymosis. Multi-organ dysfunction follows, leading to liver damage, kidney failure, and DIC, which causes simultaneous clotting and bleeding. Severe cases involve central nervous system involvement with confusion, irritability, aggression, delirium, seizures, coma, and neurological deficits. The disease progression can lead to shock, with low blood pressure, rapid heart rate, and poor organ perfusion. Despite supportive care, MVD has a high mortality rate ranging from 24% to 88% depending on the outbreak and healthcare resources available [1].

Prognosis of Marburg Virus Disease (MVD)

The prognosis of Marburg virus disease (MVD) remains poor as there is currently no approved treatment available, and only supportive care can be provided. Optimal management requires specialized biocontainment units to ensure the safety of healthcare personnel. Strict adherence to proper personal protective equipment (PPE), hand hygiene practices, and safe handling of needles and sharps is essential to minimize the risk of occupational exposure. Controlling future outbreaks is crucial in preventing primary infections and secondary transmission. The variability in disease severity observed in different outbreaks is believed to be influenced by factors such as the availability of medical care, infectious dose, route of infection, the virulence of the virus strain, and overall population health [1,5].

Treatment & Management of Marburg Virus Disease

The Marburg virus has no currently approved therapies. During outbreaks, supportive treatment is the primary strategy, and it's essential to take infection control precautions to stop the virus from spreading. Many pharmacological substances are being researched as potential treatments. An evaluation of the safety and pharmacokinetics of the antiviral nucleoside analog

Galidesivir (BCX4430), which has shown promise in animal models, was completed. Interferon-beta and other antivirals such as favipiravir and remdesivir have also been researched, but neither has shown any appreciable survival advantages [14].

Antibody therapy has been researched in animal models and is slated for human use. The monoclonal antibody MR 191-N has demonstrated effectiveness in preventing Marburg virus infection in rhesus macaques. Due to the similarities between the Marburg virus sickness and the Ebola virus disease, antibodies have been utilized successfully in the treatment of both diseases [15]. Additionally, work is being done to create a vaccine that is effective against filoviruses like the Marburg virus. Clinical trials are looking into several vaccine modalities, including inactivated viruses, replication-incompetent vaccines, viral vectors, DNA-based vaccines, and virus-like particles. After the 2013 Ebola virus pandemic, the need for effective immunization grew, but it will take time and more research to assess the value and efficacy of these vaccine candidates [16-18].

Future Directions

Future directions for Marburg virus disease (MVD) involve key areas of focus, including the development of specific antiviral treatments and vaccines, enhanced surveillance and early detection systems, and investment in public health infrastructure. Continued research is needed to develop targeted therapies and safe, effective vaccines against MVD. Improving surveillance capabilities and diagnostic methods will enable early detection and timely response to MVD outbreaks. This includes strengthening laboratory capacity for prompt identification of cases and implementing robust surveillance networks to monitor disease trends [19]. In addition, research efforts should prioritize the development of specific antiviral treatments that target the Marburg virus. Identifying novel drug targets and conducting clinical trials to assess their safety and efficacy are crucial steps in improving treatment options for MVD. This involves collaboration between scientists, pharmaceutical companies, and regulatory agencies to accelerate the development and approval of potential therapies [19,20].

Furthermore, the development of safe and effective vaccines is paramount in preventing and controlling MVD. Ongoing research should explore different vaccine platforms, such as viral vectors and protein subunits, to elicit robust immune responses and provide long-term protection against the Marburg virus. Conducting rigorous preclinical and clinical studies, and ensuring regulatory compliance, are essential for advancing vaccine candidates toward licensure and deployment [20,21]. Enhanced surveillance and early detection systems are critical in managing MVD outbreaks. Strengthening surveillance capabilities involves establishing efficient reporting mechanisms, improving laboratory diagnostics, and enhancing data sharing between countries and international organizations. Early detection enables timely implementation of public health measures, such as case isolation, contact tracing, and infection control protocols, to prevent further transmission and contain outbreaks [20,22].

Investment in public health infrastructure is vital for effective prevention and management of MVD. This includes establishing specialized treatment centers equipped with isolation units and trained healthcare professionals experienced in handling viral hemorrhagic fevers. Adequate resources, including personal protective equipment, laboratory facilities, and medical supplies, must be available to support the response to MVD outbreaks [23]. Furthermore, the development of safe and effective vaccines is paramount in preventing and controlling MVD. Ongoing research should explore different vaccine platforms, such as viral vectors and protein subunits, to elicit robust immune responses and provide long-term protection against the Marburg virus. Conducting rigorous preclinical and clinical studies, and ensuring regulatory compliance, are essential for advancing vaccine candidates toward licensure and deployment [18].

Thus, the future directions for MVD encompass the development of specific antiviral treatments and vaccines, enhanced surveillance and early detection systems, and investment in public health infrastructure. Continued research, collaboration, and investment in these areas are essential for improving the prevention, diagnosis, and management of MVD, ultimately reducing its impact on global public health.

CONCLUSION

MVD is a highly virulent viral hemorrhagic fever caused by the Marburg virus. Its diagnosis, treatment, and prevention pose significant challenges. Current management primarily involves supportive care, while research focuses on developing specific antiviral treatments and vaccines. Early detection, rapid response, and improved healthcare infrastructure are crucial to curtail outbreaks. International collaboration, surveillance strengthening, and public health investment are vital for addressing MVD globally. Despite the grim prognosis,

ongoing research, collaboration, and public health efforts offer hope for improving outcomes and minimizing the impact of MVD. Advancing knowledge, developing treatments, and implementing possible prevention strategies are very important to lower the threat of MVD and to safeguard the affected individuals/group.

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