QIU
QUEST INTERNATIONAL UNIVERSITY

Quest International Journal of Medical and Health Sciences – [Online]

SHORT COMMUNICATION

Unveiling the enigma: The pathophysiology and risk assessment of the Marburg Virus Disease (MVD) outbreaks

Ratnadeep Saha[1*], Yupa Min[2]

Corresponding author:

[1]Dr. Ratnadeep Saha, Ph.D., Senior Lecturer, Newcastle University Medicine Malaysia (NuMed), 1, Jalan Sarjana 1, Educity, 79200 Iskandar Puteri, Johor, Malaysia

Email: accessrdx@gmail.com [ORCID]

[2]Dr. Yupa Min, MBBS, M.Med.Sc
Professor and Head of Pathology, Faculty of Medicine, Quest International University, No. 227, Plaza Teh Teng Seng (Level 2), Jalan Raja Permaisuri Bainun, 30250 Ipoh, Perak Darul Ridzuan, Malaysia [ORCID]

Information about the article:

Received: April 8, 2024
Accepted: June 12, 2024
Published online: July 1, 2024
DOI: https://doi.org/10.5281/zenodo.13140724

Publisher

Quest International University (QIU), No.227, Plaza Teh Teng Seng (Level 2), Jalan Raja Permaisuri Bainun, 30250 Ipoh, Perak Darul Ridzuan, Malaysia

e-ISSN: 2636-9478

ABSTRACT

Introduction:
Marburg virus disease (MVD) is caused by the Marburg virus (MARV) of the Filoviridae family, causing acute hemorrhagic fever in humans. Similar to the pathogenesis of Ebola, MVD enters the body through skin cracks or mucous membranes and attacks macrophages and dendritic cells, damages cell membranes and causes cell death. In 2023, nine cases were reported in Tanzania and 17 in Equatorial Guinea. MVD remains a threat due to undetected viral spreading because of unidentified chains of transmission and potential interaction with animal reservoirs. The long presence of MVD in body fluids highlights the importance of a survivorship program.

Conclusion:
Marburgviruses are emerging due to bat distribution, environmental factors, and human behavior. The high mortality rate echoes the West African Ebola epidemic. Early diagnosis is challenging, and careful history-taking is necessary to differentiate MVD from other tropical febrile illnesses. Global agencies like WHO play a pivotal role in diagnosis and treatment.

Keywords
Cells, immune, infection, outbreak, risk, spread, viral

Introduction

Marburg virus disease (MVD) is a highly fatal viral disease caused by infection with the Marburg virus (MARV), a member of the Filoviridae family. Like other filoviruses, MARV causes acute and lethal hemorrhagic fever in humans, with high case fatality rates ranging from 24% to 90%. [1] Approximately 20 MARV outbreaks have been documented. [2] The Egyptian fruit bat, *Rousettus aegyptiacus*, is the primary natural reservoir of MARV.

The first significant outbreak of Marburg and Ravn viruses was recorded in 1998–2000 in the Democratic Republic of the Congo, where the infected bats spread. The largest human-to-human disease transmission and outbreak documented in Angola (2004–2005) was a severe public health concern. MARV has historically received less attention than Ebola, although this is beginning to change. The media frequently reports on the MARV's rapid spread to new nations, such as Tanzania, Guinea, Ghana, and Equatorial Guinea, seriously threatening public health. This article briefly summarized the pathogenesis, recent updates, and countermeasure development (Figure 1). [3]

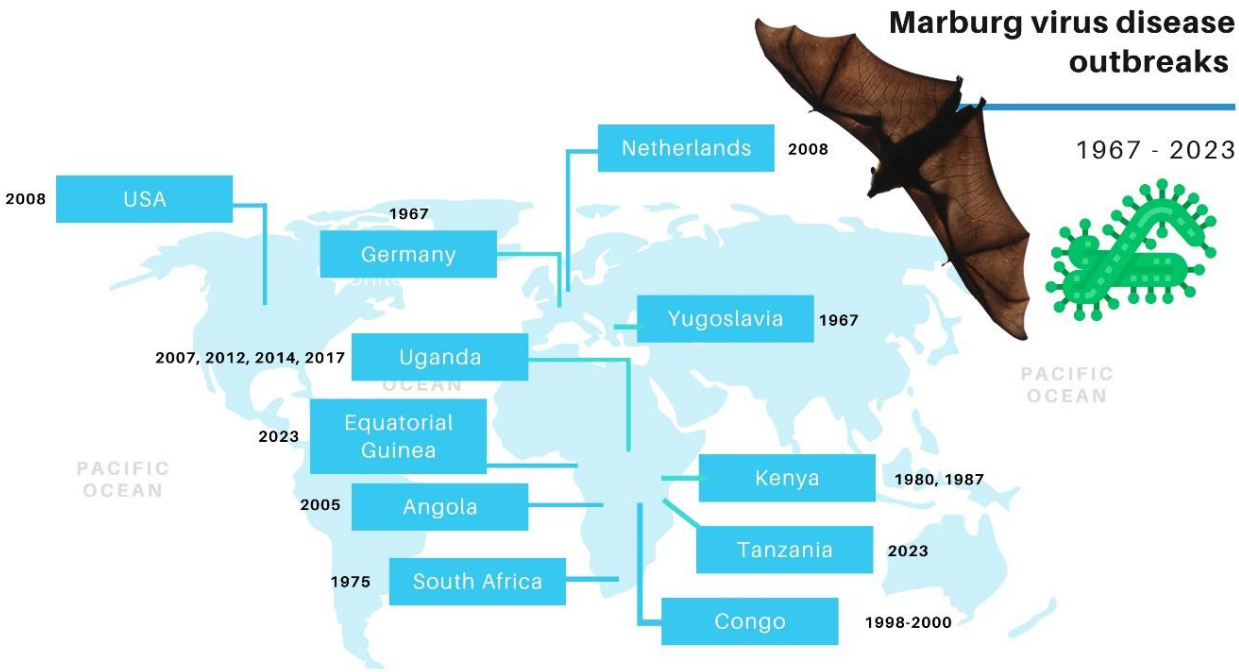

Figure 1: MVV outbreak from 1967-2023 [3]

Pathogenesis

The pathogenesis of the MARV is similar to that of the Ebola virus [4], where the entry begins via mucous membranes or piercing through the cracked skin with a direct motive to corrupt the immune cells, namely macrophages, and dendritic cells. The filovirus hides and replicates efficiently in the host cells, evading the activity of the immune system and producing a massive number of new viral elements in the body fluid once the membranes and cell organelles are necrosed. This unleashes an initial span of viral infection with cell membrane damage and dysfunction and eventually cellular deaths. The virus stations from local to regional lymph nodes and, in such a course, is cloned further to propagate infection to the bloodstream to affect fixed and mobile immune cells of various organs such as the liver, spleen, and lymphoid tissues. When the virus releases the viral proteins (VP24 and V35), they tend to make infections spread faster because type I interferons and other immune cells stop being proactive against pathogens. [5] Eventual spreading, in due course, impacts various other cells and enables extensive tissue damage in other organs, namely the spleen and kidney, causing mortality.

Systemic inflammation

Vascular malfunctioning, fluid imbalance, coagulation complications, shock, multi-organ failures, and death profoundly and critically impact the infected population group. Blood-disseminated inflammation is a distinct route for taking those things into effect. Generally, primary immune cells, especially macrophages, release profuse proinflammatory materials (cytokines, chemokines, etc.), including the target cells, which synergically act in the presence of various pro vascular chemicals such as nitric oxide, prostacyclin, and different vasoactive substances to enhance vessel permissibility and thus compromise vascular integrity. [5, 6] The situation is further eroded when certain tissue factors are unpacked by

the virally rotten cells presented to the site to provoke disseminated intravascular coagulation processes. [7]

Incapacitated immunity

Adaptive immunity acts closely by recognizing the pathogens and transferring the signal to initiate clonal selection for producing antibodies, in conjunction with enhancing the activities of various T cell types to neutralize the foreign body. The adaptive immunity process is exclusively tailored and integrated with immune cells, signalling molecules, and being sentinel to multifarious antigens whenever the demand persists. A filovirus-infected person is unlikely to express a robust antibody response [8], possibly reflecting an attack on the immune system in diversified ways. This could directly affect primary immune cells (dendrites), which are otherwise vested with the responsibility to initiate adaptive immune reactions (by chemokine production). They are slaughtered due to necrosis by a viral infection, along with a prodigious loss of lymphocytes, which undergo bystander apoptosis indirectly due to an overwhelming inflammatory reaction executed by various mediators or dysregulated signalling systems usually provided by dendritic cells. [9]

Current outbreaks

In 2023, between March 21 and May 31, nine cases were reported in the United Republic of Tanzania. 17 confirmed and 23 probable cases were reported from Equatorial Guinea. The Centers for Disease Control and Prevention have declared travel advisory level 1 and level 2 for Tanzania and Equatorial Guinea, respectively. There is no advisory for international travel and/or trade restrictions by the WHO, although it considers the risk high, moderate, or low as a precautionary measure. This outbreak is alarming but does not go to the extreme. [10, 11]

Risk assessment from a current outbreak perspective

Although the Ministry of Health of both Tanzania and Equatorial Guinea within the first two weeks of June 2023 declared this epidemic to bring under control but evidence-based studies on previous outbreaks of filovirus disease suggest that MVD can potentially resurrect with a dreadful impact.

Undetected viral spreading throughout the nation is quite possible since not all chains of transmission are conclusively connected. The original outbreak source in Equatorial Guinea remains unidentified, and interaction with animal reservoirs remains a potent future risk factor. Although the risk of MVD is low at the national, regional, and global levels, the long presence of viruses in body fluids, like blood, saliva, mucus, tears, vomit, semen, and feces emphasizes the importance of the survivorship programme. [12]

The differential diagnosis of MVD is challenging at the early stage compared to other tropical febrile illnesses such as malaria, typhoid fever, and dengue due to common clinical symptoms. The only way out is through careful history-taking, such as exposure in a bat-infested mining area or a cave, as in the United Republic of Tanzania, especially the Kagera region, which houses *Roussettus aegyptiacus*. [10, 11] The risk assessment may be affected by environmental destruction caused by clear-cutting, habitat invasion, urbanisation, and travel to infected areas. Tracking the bat is one method of measuring the risk and forecasting future MVD epidemics.

Conclusion

Marburgviruses are emerging in Africa due to reservoir bat distribution, environmental factors, and human behaviour. Although the risk level is currently low, looking at the high mortality rate, the situation should not be underestimated. The echoes of history resound once more as the current situation recreates the same scenario seen before the West African Ebola epidemic. Crucial components of response activities include contact tracing, contact isolation, contact surveillance, and social outreach programmes. As in African countries, resources and infrastructure are limited, so global agencies like WHO should play a pivotal role in diagnosis and treatment. Countermeasures in the field should be brought to bear to control the MVD in Africa, overcoming social and economic barriers.

Abbreviations

Marburg virus (MARV), Marburg virus disease (MVD), viral proteins 24 and 35 (VP24 and V35)

Acknowledgments

None.

Funding

No funding was received.

Availability of data and materials

Not applicable.

Competing interests

The authors declare no competing interests.

Publisher's Note

QIU remains neutral with regard to jurisdictional claims in published maps and institutional affiliations. The publisher shall not be legally responsible for any types of loss, actions, claims, proceedings, demand, or costs or damages whatsoever caused arising directly or indirectly

in connection with or arising out of the use of this material.

References

1. Languon S, Quaye O. Filovirus disease outbreaks: A chronological overview. Virology (Auckl) 2019;10:1178122X1984992 https://doi.org/10.1177/1178122X19849927
2. CDC. History of Marburg Disease Outbreaks. Marburg Virus Disease 2024. https://www.cdc.gov/marburg/outbreaks/index.html (accessed March 1, 2024)
3. Marburg virus disease. WhoInt n.d. https://www.who.int/news-room/fact-sheets/detail/marburg-virus-disease (March 1, 2024).
4. Rougeron V, Feldmann H, Grard G, Becker S, Leroy EM. Ebola and Marburg haemorrhagic fever. J Clin Virol 2015;64:111–9. https://doi.org/10.1016/j.jcv.2015.01.014
5. Messaoudi I, Amarasinghe GK, Basler CF. Filovirus pathogenesis and immune evasion: insights from Ebola virus and Marburg virus. Nat Rev Microbiol 2015;13:663–76. https://doi.org/10.1038/nrmicro3524
6. Martines RB, Ng DL, Greer PW, Rollin PE, Zaki SR. Tissue and cellular tropism, pathology and pathogenesis of Ebola and Marburg viruses: Ebola and Marburg viruses. J Pathol 2015;235:153–74. https://doi.org/10.1002/path.4456
7. Geisbert TW, Young HA, Jahrling PB, Davis KJ, Larsen T, Kagan E, *et al*. Pathogenesis of Ebola hemorrhagic fever in primate models: evidence that hemorrhage is not a direct effect of virus-induced cytolysis of endothelial cells. Am J Pathol 2003;163:2371–82. https://doi.org/10.1016/S0002-9440(10)63592-4
8. Ksiazek TG, Rollin PE, Williams AJ, Bressler DS, Martin ML, Swanepoel R, *et al*. Clinical virology of Ebola hemorrhagic fever (EHF): virus, virus antigen, and IgG and IgM antibody findings among EHF patients in Kikwit, Democratic Republic of the Congo, 1995. J Infect Dis 1999;179 Suppl 1:S177-87. https://doi.org/10.1086/514321
9. Mahanty S, Hutchinson K, Agarwal S, McRae M, Rollin PE, Pulendran B. Cutting edge: impairment of dendritic cells and adaptive immunity by Ebola and Lassa viruses. J Immunol 2003;170:2797–801. https://doi.org/10.4049/jimmunol.170.6.2797
10. Marburg virus disease - Equatorial Guinea. WhoInt n.d. https://www.who.int/emergencies/disease-outbreak-news/item/2023-DON472 (accessed March 1, 2024).
11. Marburg virus disease - the United Republic of Tanzania. WhoInt n.d. https://www.who.int/emergencies/disease-outbreak-news/item/2023-DON471 (accessed March 1, 2024).
12. Eshun G, Haruna UA, Chinnam S, Sah S, Mehta V, Mohanty A, *et al*. Marburg virus disease in Equatorial Guinea: The need for one health approach. Travel Med Infect Dis 2023;53:102571. https://doi.org/10.1016/j.tmaid.2023.102571