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INTERNATIONAL JOURNAL OF SURGERY

OPEN

Epidemiology, pathophysiology, transmission, genomic structure, treatment, and future perspectives of the novel Marburg virus outbreak

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Dear Editor,

Marburg virus disease (MVD) has been linked to two fatal cases in Ghana's Ashanti region. These cases were reported to the appropriate health authorities on June 28, 2022, as suspected cases of viral hemorrhagic fever, and on July 1, 2022, Marburg virus (MARV) testing was positive. This is the first time MVD has been made known in Ghana, and there has only ever been one earlier outbreak of the disease reported in West Africa. An MVD outbreak could pose a significant risk to the public's health because it is severe and frequently fatal[1]. Three laboratories in West Germany and Yugoslavia reported epidemics of a previously unidentified disease in 1967 that was characterized by high temperature, hemorrhaging, and organ failure[2]. The culprit responsible for the disease was later determined to be a new virus known as MARV, the first described member of the Filoviridae family[3]. The first documented instance of the illness outside of a lab was in Rhodesia (now Zimbabwe) in 1975. Cases of the illness were caused by MARV in 1980 and the Ravn virus, another MARV, in 1987[4]. Recent outbreaks have been linked to higher pathogenicity and ~90% fatality in humans, compared to earlier outbreaks that were linked to 20–40% lethality[5].

Marburg hemorrhagic fever is a condition caused by MARV, which typically enters the body through damaged skin. Inadequate fluid transport, coagulation issues, shock, and multiorgan failures are the most severe clinical characteristics of MVD. Studies on MARV-infected monkeys indicate that macrophages, monocytes, and Kupffer cells are the main targets of MARV infection[6]. In order to cause cellular activation and damage to secondary targets, like endothelial cells, MARV predominantly targets mononuclear phagocytic cells, such as monocytes and macrophages. Shock, which accelerates the development of cytokines and other proinflammatory mediators by activated macrophages and monocytes, is the primary cause of death in MVD[7,8].

Investigations are underway to find out how the virus first spread from its animal host to people. Transmission occurs through interpersonal interaction and many factors, such as (1) Direct contact with any of the following, including cuts, scrapes, or the mucous membranes of the eyes, nose, or mouth, might cause the virus to spread. (2) Blood or bodily fluids from an MVD patient or patient who has passed away from it, including urine, perspiration, feces, vomit, breast milk, amniotic fluid, and semen. (3) Products that have been contaminated with the MVD patient's or the deceased person's bodily fluids, such as clothing, bedding, needles, and medical supplies. (4) Another is sperm from an MVD survivor, such as through oral, vaginal, or anal sex. After MVD recovery, even though a patient no longer displays acute disease symptoms, the virus may still be present in some body fluids (including semen). There is no evidence that engaging with or touching a woman's vaginal fluids while she is infected with MVD can transfer MARV[9,10].

The MARV genome is composed of inversely complementary 3′ and 5′ termini and is negative sense single-stranded (-ssRNA), linear, and nonsegmented. The genome does not have a 5′ cap and is not 3′ polyadenylated. About ~19 kb make up the MARV genome. The genome contains seven genes: 3′-UTR-NP-VP35-VP40-GP1-GP2-VP30-VP24-L-5′-UTR[11]. Highly conserved transcriptions start and stop codon locations make up each gene of the MARV. Each gene contains a 3′OH, an open reading frame, and a 5′ untranslated region. These genes are separated by brief intergenic regions that range in length from 4 to 97 nucleotides. Using five highly conserved nucleotides, the transcription turns off the signal of the upstream gene and turns on the signal of the downstream gene[12]. Seven structural proteins make up the MARV genome, and each one of them makes a unique contribution to the genome. Nucleotide proteins are required for the processes of replication, transcription, RNA genome encapsulation, nucleocapsid synthesis, and budding[13]. While viron protein 40 promotes budding and prevents interferons signaling, viron protein 35 serves as a cofactor for the polymerase, an interferons antagonist, and promotes the production of nucleocapsids. Nucleocapsid formation is a function of viron protein 30, whereas nucleocapsid maturation is a function of viron protein 24. Surface-bound budding glycoprotein facilitates

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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International Journal of Surgery (2023) 109: 36–38

Received 8 October 2022; Accepted 20 November 2022

Published online 27 January 2023

http://dx.doi.org/10.1097/JS9.0000000000000096

fusion, receptor binding, and attachment. The tail L gene affects the activity of RNA-dependent RNA polymerase[14].

Several drugs for MARV infection have been the subjects of recent trials. Remdesivir is a crucial medication that requires additional research after a recent study on it against MARV revealed that it has therapeutic efficacy in cynomolgus macaque models. According to the study, it was therapeutically effective when given once daily in a vehicle in 4 or 5 days after the immunization, for 12 days at a dose of 5 mg/kg, or for 10 days at a dose of 10 mg/kg loading dose and then 5 mg/kg[15]. In vitro activity against the MARV was demonstrated by a different investigation using cholesterol-conjugated fusion inhibitors. 4-(amino methyl) benzamide has recently been shown to be a potent MARV entry inhibitor. Additionally, researchers found 33 compounds that were effective in vitro against MARV and had a variety of pharmacological potential[16]. Efficacy against MARV infection has also been demonstrated for aloperine, favipiravir, and other minor drugs. Once more, a chemical called FC-10696 has just been found to prevent MARV infection[17]. Additionally, it has been suggested that AVI-7288 may have the potential as a post-exposure prophylactic against MARV[18]. Preclinical investigations have demonstrated that recombinant vesicular stomatitis virus (rVSV) vectors are as efficient against MVD in guinea pigs and nonhuman primates as both preventative vaccinations and postexposure therapies (NHPs). The effectiveness of rVSV-based immunizations against MARVs, including the Angola variant, has been demonstrated in preclinical testing, but the precise prophylactic window is still unknown. A 'delta G' rVSV-based vaccination (rVSVG-MARV-GP-Angola), which is comparable to Ervebo, has recently been reported by Marzi and colleagues to fully protect NHPs when administered 7 or 14 days before exposure. When NHPs received the vaccine three days prior to exposure, there was a partial (75%) degree of protection. The same vaccine was shown to be 89% effective in protecting NHPs against a low 50 PFU dose of MARV-Angola in 20–30 minutes following infection. More studies on MARV are still needed to provide exact guidance for the therapeutic care of patients and the creation of vaccines, which could help health professionals and policy makers to prevent and effectively manage future outbreaks. The virus is being studied on a variety of animal models, including NHPs, mouse models, guinea pigs, and hamsters, as part of long-term vaccine testing. Vaccine development should continue until human vaccinations are authorized and made accessible.

Ethics approval

Not applicable.

Sources of funding

None.

Authors' contribution

Md.R.I., S.A.: conceptualization, study design, and writing. Md. M.R., R.S.: writing. R.S.: editing and reviewing.

Conflict of interest disclosure

All authors declare no conflict of interest exists.

Research registration unique identifying number (UIN)

None.

Guarantor

Dr Rohit Sharma (corresponding author) is taking the full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

Availability of data and materials

No new data generated.

Data statement

The data in this correspondence article is not sensitive in nature and is accessible in the public domain. The data is therefore available and not of a confidential nature.

Acknowledgements

None.

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