First-ever Marburg virus disease outbreak in Equatorial Guinea and Tanzania: an imminent crisis in West and East Africa.

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Abstract

The Marburg virus, which is a member of the same virus family as the Ebola virus called Filoviridae, causes the severe infectious disease known as Marburg Virus Disease (MVD). Previously, different outbreaks of MVD have appeared in different African countries, including Ghana, Guinea, Uganda, Angola, the Democratic Republic of the Congo, Kenya, and South Africa. For the first time, Equatorial Guinea and Tanzania are experiencing MVD outbreaks. A total of 15 laboratory-confirmed cases of MVD and 23 probable cases have been reported in Equatorial Guinea since the confirmation of the outbreak on 13 February 2023. The first MVD outbreak in the United Republic of Tanzania was formally confirmed by the Ministry of Health on March 21, 2023. As of 22 March, there were eight cases and five fatalities (case fatality ratio [CFR]: 62.5%). Due to the facts that Ebebiyin and Nsock Nsomo districts, the affected regions of Equatorial Guinea, borders Cameroon and Gabon, and Kagera region, the affected region of Tanzania, borders Uganda, Rwanda and Burundi, there is fear of cross-border spread of MVD due to cross-border migrations, and this can be a great crisis in West and East Africa. Although there are currently outbreaks of MVD in Equatorial Guinea and Tanzania, there is currently no proof of an epidemiological connection between the two outbreaks. The aim of this paper is to describe Marburg Virus Disease (MVD), describe its first outbreak in Equatorial Guinea and Tanzania, explain the efforts being used and the challenges being faced in MVD mitigation, and recommend different measures to be taken to cope with the outbreak of MVD in Equatorial Guinea and Tanzania.

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Keywords: Marburg virus disease, outbreak, Equatorial Guinea, Tanzania

Introduction

A severe infectious disease called Marburg Virus Disease (MVD) is caused by the Marburg virus, a member of the Filoviridae family of viruses that also includes the Ebola virus [1]. Haemorrhagic fever outbreaks in laboratories in Marburg and Frankfurt (in Germany), and Belgrade (in Yugoslavia [Serbia of today]), led to the discovery of the Marburg virus in 1967 [2]. Two viruses, MARV and Ravn, are members of the Marburgvirus genus. The World Health Organization has identified MARV as being of the utmost priority. The virus has a case fatality rate that ranges from 24.0 to 88.0%, showing that it is deadly and that extensive knowledge on it is required [3]. MARV is a single-stranded negative sense RNA virus that is enveloped. It is morphologically similar to silk and has a length that ranges from 800 to 14,000 nm. When it is 790 nm in length, it is most contagious. Seven structural proteins make up MARV. Although having a structure that is remarkably comparable to the Ebola virus, the MARV may cause distinct antibodies in susceptible individuals. MARV is thought to have been the first human-discovered filovirus [4].

The Egyptian fruit bat (*Rousettus aegyptiacus*) serves as the reservoir of the zoonotic virus [5], [6]. Previous research demonstrates that most of the primary infections associated with natural outbreaks of MARV disease to date have been related to human access to caves, for example, cave visitors and mine workers [3]. Following the first human-to-human transmission of a zoonotic disease caused by an infected animal, the disease is subsequently spread more widely via close human-to-human contact. This can happen either directly or by coming into contact with contaminated fomites or bodily fluids [3]. The transmission of Marburg can also occur during burial ceremonies that involve getting into close contact with the corpse of the deceased [7].

The incubation period of the Marburg virus lasts 3–21 days (usually between 5 and 10 days) and is probably influenced by the infectious dose and route [8]. After the incubation period, people often have sudden illnesses with vague symptoms such as fever, chills, headache, odynophagia, myalgia, vomiting, and diarrhea. Early cases can be overlooked because they resemble more widespread infections such as malaria, typhoid, or rickettsial diseases. Early signs of MVD frequently include rash, which is characterized as non-pruritic, erythematous, and maculopapular. It starts out focally before becoming confluent and widespread. During the initial outbreak, the condition starts as a distinctly marked, pin-sized red papule around the hair roots at the buttocks, trunk, and outside of both upper arms between the fifth and seventh day. This papule lasts up to 24 hours before developing into a maculopapular rash, which later coalesce [9].

Since MVD was discovered, there have been two sizable outbreaks that occurred simultaneously, one of which was linked to laboratory research involving African green monkeys that were imported from Uganda. Two unconnected sporadic occurrences of the disease occurred in 2008 in tourists from the Netherlands and the United States while they were visiting a cave in Uganda that was home to a sizable colony of Rousettus bats. Previous reports of MVD outbreaks include Ghana (2022), Guinea (2021), Uganda (2017, 2014, 2012, 2007), Angola (2004–2005), the Democratic Republic of the Congo (1998 and 2000), Kenya (1990, 1987, 1980), and South Africa (1975) [10]. The greatest MVD outbreak to date was in Angola in 2005, where 374 cases and 329 deaths were reported, with an 88% CFR. There have been four previous epidemics in Uganda, with case fatality rates ranging from 27 to 100% in 2007, 2012, 2014, and 2017 [11]. Table 1 shows the history of Marburg Virus Disease outbreaks from 1967 to 2022. Countries reporting outbreaks of MVD until 2023 are shown in Figure 1.

Table 1. History of Marburg Virus Disease Outbreaks from 1967 to 2022

Year(s)	Country	Apparent or suspected origin
2022	Ghana	Ashanti Region
2021	Guinea	Guéckédou
2017	Uganda	Kween
2014	Uganda	Kampala
2012	Uganda	Kabale
2008	Netherlands ex Uganda	Cave in Maramagambo forest in Uganda, at the southern edge of Q
2008	USA ex Uganda	Cave in Maramagambo forest in Uganda, at the southern edge of Q
2007	Uganda	Lead and gold mine in Kamwenge District, Uganda

Year(s)	Country	Apparent or suspected origin
2004 to 2005	Angola	Uige Province, Angola
1998 to 2000	Democratic Republic of Congo (DRC)	Durba, DRC
1990	Russia	Russia
1987	Kenya	Kenya
1980	Kenya	Kenya
1975	Johannesburg, South Africa	Zimbabwe
1967	Germany and Yugoslavia	Uganda

*Numbers reflect laboratory confirmed cases only.

Source: Centers for Disease Control and Prevention, National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), Division of High-Consequence Pathogens and Pathology (DHCPP), Viral Special Pathogens Branch (VSPB)

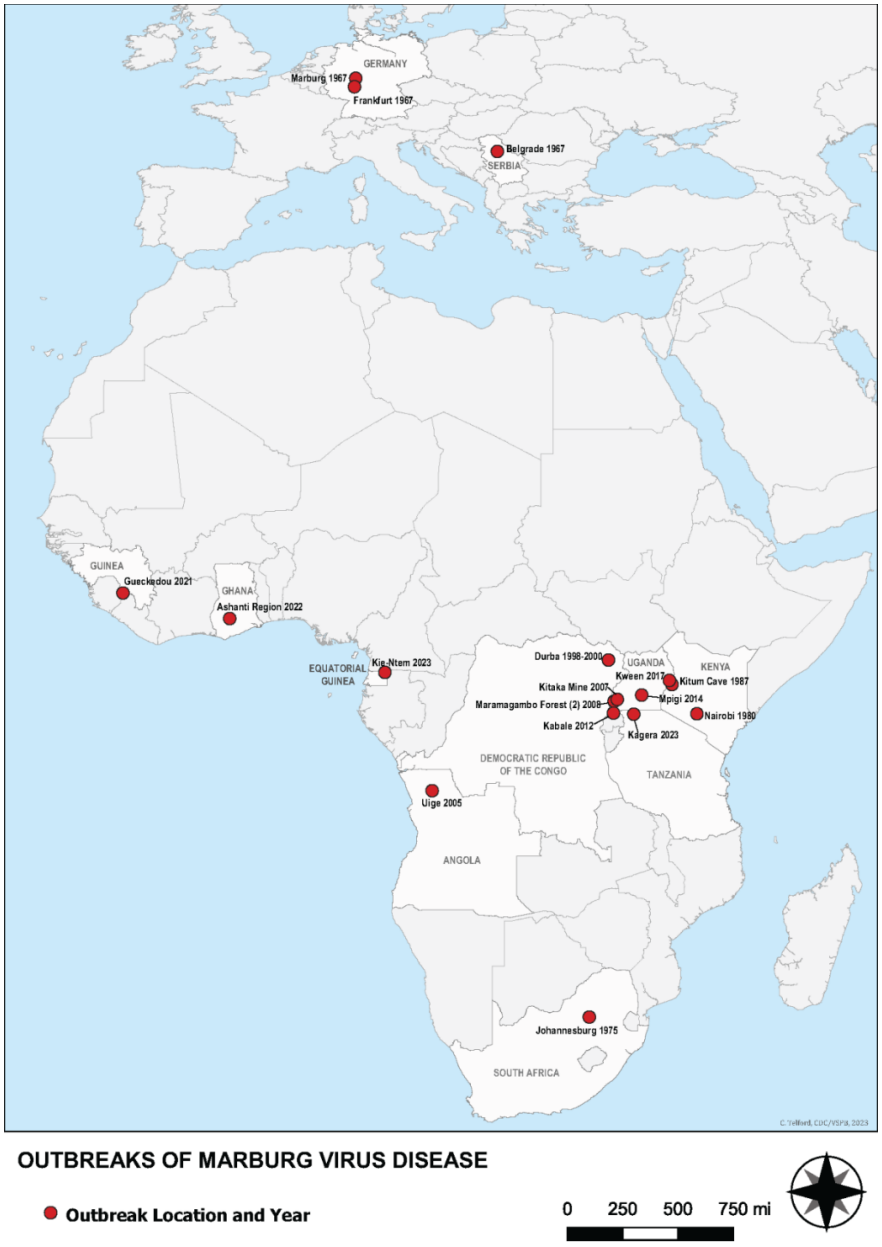

Figure 1. Countries reporting outbreaks of Marburg virus disease.

Source: Centers for Disease Control and Prevention, National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), Division of High-Consequence Pathogens and Pathology (DHCPP), Viral Special Pathogens Branch (VSPB).

For the first time, Equatorial Guinea is facing Marburg virus disease outbreak. The Ministry of Health and Social Welfare of Equatorial Guinea reported the first case on February 7, 2023 [7]. This is the same case in Tanzania: the country is experiencing the first outbreak of the Marburg virus disease. The Marburg virus disease (MVD) outbreak in the United Republic of Tanzania was declared on March 21, 2023, by the Ministry of Health (MoH) of that nation [10]. Although there are currently outbreaks of MVD in Equatorial Guinea and Tanzania, there is currently no proof of an epidemiological connection between the two outbreaks [10].

Outbreak and epidemiology of Marburg virus disease in Equatorial Guinea

In two villages in the district of Nsock Nsomo, eastern province of Kie-Ntem, Río Muni Region, the Ministry of Health and Social Welfare of Equatorial Guinea reported at least eight deaths that occurred between 7 January and 7 February 2023. The cases, according to the current epidemiological study, began with fever that preceded weakness, vomiting, and blood-stained diarrhea. In two cases, skin lesions and otorrhagia also appeared. Eight blood samples from contacts were taken on 9 February 2023, and sent to the Centre Interdisciplinaire de Recherches Médicales de Franceville (CIRMF) in Gabon, where real-time polymerase chain reaction (RT-PCR) testing revealed that they were free of Marburg and Ebola viruses [7].

On 12 February 2023, eight more blood samples were obtained from different contacts and delivered to the Institute Pasteur in Dakar, Senegal. One of these samples came from a suspected case that was RT-PCR verified to have the Marburg virus. The patient had a fever, non-bloody vomiting, bloody diarrhea, and convulsions. On February 10, 2023, the patient passed away at the Ebebiyin District Hospital. Epidemiological evidence connected the case with four other persons of deceased cases from one of the communities in the Nsoc-Nsomo district [7].

By using RT-PCR at a mobile lab at the Regional Hospital of Ebibeyin on 13 March 2023, samples from two more people from the Kié-Ntem province tested positively for MVD. On 15 March 2023, a sample from a person living in Litoral province who was epidemiologically connected to a case that had been confirmed in Kié-Ntem was positive for MVD after being subjected to RT-PCR by the same laboratory. The two provinces (Kié-Ntem and Litoral) are separated by around 150 kilometers and are situated in different regions of the nation. Three other laboratory confirmed positive cases from the Litoral province were reported on March 18 and 20. Two further laboratory-verified cases from the province of Centre Sur were reported on March 20. Since then, six additional cases have been reported. The possibility of unnoticed spread of the virus in the community is suggested by the wide geographic distribution of the cases and the hazy epidemiological connections in the Centre Sur province. Since the outbreak began, a total of 15 laboratory-confirmed cases of MVD and 23 probable cases have been reported. Laboratory-confirmed cases were found to have 11 fatalities (Case Fatality Ratio (CFR) among confirmed cases: 78.6%); all probable cases also had fatal outcomes; one confirmed case had an undetermined result. Healthcare professionals reported four laboratory-confirmed cases (26.6%), including two fatal instances. Three of the confirmed patients have recovered. [12], [13].

Outbreak and epidemiology of Marburg virus disease in Tanzania

On March 16, 2023, the Ministry of Health of the United Republic of Tanzania declared that two villages in Bukoba district, Kagera region, northern Tanzania, had seven cases and five fatalities associated with an unidentified disease. Subsequently, the Tanzanian National Public Health Laboratory used reverse transcriptase-polymerase chain reaction (RT-PCR) to confirm the cases as Marburg virus infection. The first MVD outbreak in the nation was officially confirmed by the Ministry of Health on 21 March 2023. As of 22 March, the Kagera region had eight cases, including five fatalities (case fatality ratio [CFR]: 62.5%). Treatment is still being provided to the three remaining patients. No cases have been documented outside the Bukoba district as of March 22 [10].

The first case of MVD was identified in a person with a travel history on Goziba Island in Lake Victoria in Tanzania and symptoms were developed after the traveler returned to his village of Bukoba. The patient died in the community. Four further cases from the same family as this index case were detected. Also, among the healthcare workers who treated them, there were two cases reported, one of which resulted in death. The eighth case is still under investigation, so no information is available. Fever, diarrhea, vomiting, numerous bleeds, and kidney failure were the patients' reported symptoms. The National Public Health Laboratory tested samples from both dead and living cases and confirmed the Marburg virus [10].

Efforts and challenges to mitigate Marburg virus disease in Equatorial Guinea and Tanzania

Different public health responses are being implemented in Equatorial Guinea and Tanzania, but there are also different challenges. Within Equatorial Guinea, to identify the cause of the outbreak, comprehensive

epidemiological investigations are being conducted. National teams have been sent to affected districts with the purpose of locating and isolating cases and contacts, and treating patients. The WHO has also sent out specialists in epidemiology, case management, infection control, laboratory, and risk communication to aid national response operations and guarantee community participation. Also, 500 health professionals will get a viral hemorrhagic fever kit from WHO that includes personal protective equipment in addition to tents, tools for sample collection and analysis. As efforts are being made to establish laboratory facilities locally, WHO is providing support for the transportation of samples to labs in Senegal and Gabon [12].

Regional and district-level rapid response teams have been sent to Tanzania to conduct investigations and implement response plan. Contact tracking initiatives have also been implemented to keep an eye on others who exhibit comparable symptoms in the local population and medical facilities, including contacts with known patients. On March 21, health workers followed up and monitored 140 of the 161 contacts that had been discovered. In the Kagera region, risk communication initiatives have also been launched to spread messages about health awareness, education, and prevention [10].

Although different measures have been taken against the spread of the Marburg virus in both Equatorial Guinea and Tanzania, there is still fear of cross-border spread of the virus. For instance, in the Equatorial Guinean districts of Ebebiyin and Nsock Nsomo, Cameroon, and Gabon, there are many cross-border people migrations and relatively porous boundaries. This represents a risk of cross-border spread of the virus [12]. The affected area of Tanzania, Kagera region, borders three nations (Uganda to the north, Rwanda and Burundi to the west), as well as Lake Victoria, and cross-border population movements could increase the risk of disease transmission. In addition, the fruit bat species (*Roussettus aegyptiacus)* has been identified in other nearby nations that neighbor the affected Kagera region; as a result, these countries may be attached by MVD as they are home to the same bat species that carry the virus [10]. The risk of spreading MVD in Tanzania at the national level is rated very high due to the high CFR and existing risk of the outbreak spreading to other regions of the country, the insufficient human, financial, and material resources to implement response interventions, and the likelihood that existing capacities will be overwhelmed if cases increase [10].

It is difficult to diagnose Marburg virus disease. Because many other tropical febrile illnesses have some clinical symptoms of MVD in its early stages, it can be challenging to make a clinical diagnosis of the condition. Ebola virus disease, malaria, typhoid fever, leptospirosis, rickettsial diseases, and plague are a few diseases that must be ruled out [12]. This difficulty in the diagnosis of MVD can delay the identification and treatment of a disease, the factor that can increase its mortality rate and the transmission rate.

Except rehydration with oral or intravenous fluids and treatment of specific symptoms that improve survival, no current vaccines or antiviral medications are approved to cure MVD, despite the fact that a variety of potential treatments, including blood products, immune, and drug therapies, are being evaluated [12]. The Marburg virus (MARV) outbreak in Guinea and Ghana led to the formation of the "MARVAC" consortium, which is made up of experts in the field of vaccine research and development. The consortium's goal is to assist in a quick response to the threat posed by this infectious disease. Soon after the virus was identified, work on a MARV vaccine began with only little progress. Several different vaccine platforms for MARV have been tested in rodent models, but only some of these candidate vaccines showed protective efficacy in nonhuman primates (NHPs). However, Currently, there are no MARV vaccines or treatments that have received regulatory agency approval [14].

Recommendations

Controlling the Marburg virus disease outbreak requires a variety of interventions, including social mobilization, case management, surveillance, including contact tracking, good laboratory service, and infection prevention and control, including safe and dignified burials [12]. In all impacted health zones, surveillance and detection efforts—including contact tracing and active case finding—should be stepped up. Identifying those who may have come into contact with someone who has the Marburg virus and tracking their health for 21 days are among the measures to be taken to control MVD outbreaks. Other measures include separating healthy and ill people to stop further transmission, caring for confirmed patients, maintaining good hygiene,

and keeping the environment clean [10].

To prevent contact with patients' blood and other bodily fluids as well as contaminated surfaces and objects, healthcare workers caring for patients with confirmed or suspected MVD should take additional infection prevention and control procedures in addition to conventional safety measures. Furthermore, educating people about the risk factors for Marburg infection and the preventive measures they can take to reduce human exposure to the virus are important steps in reducing human infections and fatalities [10].

Furthermore, WHO advises male MVD survivors to engage in safer sexual activities and maintain good personal cleanliness for 12 months from the onset of symptoms until their semen has tested Marburg virus-free twice. Body fluid contact should be avoided, and cleaning with soap and water is advised. WHO advises against segregating male or female convalescent patients whose blood has been tested negative for the Marburg virus [12].

Conclusions

Equatorial Guinea and the United Republic of Tanzania are experiencing the first ever outbreaks of the Marburg virus. Different public health responses are being implemented in Equatorial Guinea and Tanzania, including treating patients, locating and isolating cases and contacts, case management, infection control, risk communication, and the provision of hemorrhagic fever kits to health professionals who involve in outbreak responses. The unavailability of vaccine and drugs against MVD and the fear of its cross-border spread are major challenges. In affected regions of Equatorial Guinea and Tanzania, surveillance and detection efforts including contact tracing and active case finding are recommended. Furthermore, healthcare professionals dealing with suspected cases of MVD are advised to take additional infection prevention and control procedures in addition to conventional safety measures.

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