Rapid Risk Assessment: Marburg virus in Rwanda

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I. Background

(a) The Event

On 27-Sep-2024, the Ministry of Health in Rwanda declared a Marburg virus disease (MVD) outbreak. This marks the first MVD outbreak in Rwanda and the fourth historical outbreak in West Africa. The outbreak is geographically spread across 7/30 districts (1) across 4/5 provinces: Kigali Province (Gasabo, Kicukiro, Nyarugenge), Eastern Province (Gatsibo, Nyagatare), Southern Province (Kamonyi), and Western Province (Rubavu) (2). As of 3 October, a total of 36 cases, and 11 deaths have been reported (3). Over 70% of those affected are healthcare workers. Authorities are intensifying response efforts and investigating the infection's origin.

Authorities have identified and are monitoring around 300 contacts, 2 of them had traveled internationally, the first has traveled to an unspecified location but completed the monitoring period without presenting any symptoms (2). The other contact traveled to Germany. He and one of his contacts exhibited flu-like symptoms during a train ride from Frankfurt to Hamburg, but tested negative for Marburg virus as of 3 October (4,5). WHO assesses the risk of this outbreak as very high at the national level (Rwanda), high at the regional level, and low at the global level. Investigations are ongoing to determine the full extent of the outbreak, and this risk assessment will be updated as more information is received.

(b) The Hazard

Marburg virus (MARV) is a zoonotic emerging pathogen belonging to the Filoviridae family, which includes also the Ebola virus . The clinical manifestations of MVD are similar to Ebola virus disease (EVD) with a typical sudden onset of fever, chills, diarrhea (that can be bloody), and vomiting. Other possible signs and symptoms include anorexia, severe headache, and myasthenia; hemorrhagic signs and symptoms are considered rare in the early stages. Laboratory findings in patients are similar to those seen in EVD patients and include, among others, leukopenia, thrombocytopenia, and increases in serum transaminase levels. The incubation period ranges from 2 to 21 days (mean 4 to 9 days). The case fatality rate is often high, ranging from 24 to 80 percent. The virus spreads among humans through person-to-person direct contact or contact with contaminated equipment or other material with droplets of bodily fluids (e.g, blood, urine, saliva, sweat, feces, vomit, breast milk, amniotic fluid, and semen) of infected persons (including deceased) with MVD, or sexual intercourse (2). There are no approved specific medical treatments for MVD. Case management is based on clinical supportive care for EVD patients. The same infection prevention and control precautions as for EVD should be used to prevent transmission. There are no approved vaccines for MVD (6).

II. Epidemiological Situation

(a) Globally

The first recognized MVD outbreaks in humans were documented in 1967 when several workers involved in poliomyelitis vaccine development fell ill with a severe and often lethal novel disease at three different locations in Europe (Marburg and Frankfurt in Germany and Belgrade in Former Yugoslavia), the infection source appeared to be from African green monkeys imported from Uganda for research purposes. Since then, all known human infections have occurred in Africa, except an outbreak in Russia in 1990 that occurred through laboratory contamination, there was one case, and the patient died (7). Marburg virus outbreaks are rare but have a high case fatality rate; there have been 15 major Marburg virus outbreaks reported since 1967 (Table 1). The MVD outbreak in Angola (2004-2005) remains the largest event documented **(8)** with more than 250 confirmed cases and an important nosocomial component in terms of spread. The last cases of MVD were identified in Equatorial Guinea in February and continued to June 2023. This was the country's first Marburg disease outbreak. Also, the same year in Tanzania (9), an outbreak was declared in March 2023, and ended in May 2023; cases were reported from Tanzania's northwest Kagera region, which borders Rwanda. Neither of those outbreaks exported cases to other countries, and it is unknown if they were related.

Table 1: History of Marburg virus outbreaks (1967-2024)

Year	Location	Cases (confirmed)
1967	Germany	29 cases and 7 deaths (8)
1967	Yugoslavia	2 cases and 0 deaths (8)
1975	South Africa	3 cases, 1 death (8)
1980	Kenya	2 cases, 1 death (8)
1987	Kenya	1 fatal case (8)
1998-2000	Democratic Republic of Congo	154 cases, 128 deaths (8)
2005	Angola	252 cases, 227 deaths (8)
2007	Uganda	4 cases, 2 deaths (8)
2008	Netherlands, USA	2 cases, tourists from the Netherlands (fatal) and USA after a trip to Uganda and contact with a Python cave (8)
2012	Uganda	18 cases, 9 deaths (8)
2014	Uganda	1 fatal case (8)
2017	Uganda	3 cases, 3 deaths (8)
2021	Republic of Guinea	1 case (8)
2022	Ghana	3 cases, 2 deaths (10)
2023	Equatorial Guinea	17 cases, 12 deaths
2023	Tanzania	9 cases, 6 deaths (9)

(b) GCC countries

There has never been a case of the Marburg virus detected in GCC countries.

III. Risk Assessment

(a) RRA risk questions

What is the risk of one case of Marburg virus being imported into the GCC Region from Rwanda in the upcoming one month, in terms of the likelihood and impact of the importation?

(b) Likelihood

The likelihood of importation of one infected Marburg virus case from Rwanda to GCC countries in the upcoming month is **unlikely**, based on the following aspects:

Importation through airline routes

According to official IATA data on air travel and BlueDot's modeling projections (Table 1), the forecasted number of travelers from Rwanda to each GCC country is very low. UAE and Qatar have the highest passenger volumes as Doha and Dubai airports are major transit hubs and have direct flights from Kigali.

Table 1. Probability of an infected case imported to a GCC country with Marburg virus from Rwanda in the next 30 days (Using Modelling of BlueDot and IATA data*), September 2024

Countries	Forecasted Passenger Volume traveling from Rwanda	Likelihood of Marburg virus importation from Rwanda
United Arab Emirates	2570	**0.13%**
Bahrain	12	0.00%
Saudi Arabia	132	0.00%
Oman	62	0.00%
Qatar	689	**0.04%**
Kuwait	15	0.00%

* Connections between the above-mentioned countries and the region are primarily counted based on airline data and historical passenger volumes including both direct and indirect passengers. Connections between the above-mentioned countries and the region are primarily counted based on airline data.

Zoonotic transmission

Marburg virus has been documented in Egyptian fruit bats (*Rousettus aegyptiacus*) captured in a mine in Uganda where numerous cases had occurred (11). The wide geographical dispersion of MVD cases in African countries suggests that the virus is present among chronically infected bats throughout sub-Saharan Africa. This has been recently confirmed by the identification of the virus in apparently healthy fruit bats in Sierra Leone, South Africa, and Zambia (11). This species has also been identified in the southern parts of the Arabian Peninsula in the UAE, Saudi Arabia, Oman, and Yemen (12) (Annex 2). Although this species of bats is not migratory it is also possible that other migratory bats could transmit MARV to the bats in GCC and pose a threat of zoonotic spillover. However, there is no data to confirm the presence or lack of MARV in bats in the GCC areas. As such, the likelihood of zoonotic transmission

is unknown. Moreover, the documented transmission route from animal to human was found in mine workers and tourists visiting caves inhabited by these bats as an environmental spill (13,14). Also, it has been suspected that Egyptian fruit bats' urine, saliva, feces, and Marburg virus-contaminated fruits are the most likely transmission sources in humans and primates (15). A study in 2023 demonstrated evidence of Marburg virus transmission through fruit consumption and handling. The study found that the virus can remain stable for at least six hours on two types of fruit (mangoes and bananas) commonly consumed by Egyptian fruit bats and primates, including humans, in sub-Saharan Africa (16). As mentioned earlier, this is because the fruits get the virus either due to feeding, biting, or spatting the fruit or through contaminated secretions by the infected bat. These findings highlight the urgent need for preventive measures in Rwanda, such as the consumption or handling of bitten fruits, spat-out fruit, or dropped fruits could be a significant risk factor for spreading Marburg disease.

Rwanda's Capacities and Outbreak Escalation Potential

As this is Rwanda's first-ever Marburg virus outbreak, there may have been delays in initial detection due to unfamiliarity with the disease. The rapid spread of cases across multiple areas, including the capital, makes contact tracing challenging and increases the risk of further transmission. Also, the outbreak origin is unknown, which suggests that the number of cases and close contacts to investigate is higher than currently understood and current case counts may be underreported. These challenges along with the long incubation period, routes of transmission, and the virulent nature of the virus might contribute to the possibility of cross-border transmission, including to the GCC. Nevertheless, Rwanda is rapidly responding to the outbreak since its detection. The health authorities issued guidelines to curb Marburg spread and implemented various public health measures (17), including isolation of cases, enhanced sanitation, implementation of strict protocols in healthcare facilities, making efforts to increase awareness among healthcare workers, communicating the risk to the public, and urging citizens to avoid physical contact, wash their hands, and report suspicious symptoms, and restricted funeral sizes for fatal cases up to 50 people, and prohibited hospital visitations for the next 14 days (2). Moreover, in support of the ongoing efforts, WHO is mobilizing expertise and outbreak response tools, including emergency medical supplies. A consignment of clinical care and infection prevention and control supplies is being prepared and will be delivered to Kigali in the coming days from WHO's Emergency Response Hub in Nairobi, Kenya (1). WHO is also coordinating efforts to reinforce collaborative cross-border measures for readiness and response in countries neighboring Rwanda to ensure timely detection and control of the virus to avert further spread. Also, the US CDC has offered additional support to Rwanda, by deploying subject matter experts to assist with the country's investigation and response to this outbreak (18).

(c) Impact

Although the disease severity and CFR for MVD are high, and no licensed vaccination or antivirals exist to date, the impact of the importation of one Marburg virus case in the GCC countries is considered **minor** given that the GCC countries have high reported capacities for detecting and responding to epidemic-prone diseases, the GCC health systems have been exposed to scenarios of importation of viral hemorrhagic fever since the Ebola virus outbreak in West Africa, which means that similar control measures and precautions will likely be implemented for the current outbreak. Notably, MARV transmission has previously occurred in healthcare settings in non-GCC countries with poor infection prevention and control (IPC) measures, as the GCC countries all have high IPC standards, this chance of nosocomial infections is low. Additionally, based on the mapping exercise of the public health reference laboratories conducted by the Gulf CDC, in August 2024, all GCC countries have the capacity to test for Marburg by PCR in-country while some have the next-generation sequencing capacities; in addition, some GCC countries have noted establishing referral mechanisms to reference laboratories internationally where needed.

(d) Level of confidence

The level of confidence in the assessment is moderate. The available data provides a reasonable basis for the assessment, but there is some uncertainty due to the lack or late receiving of information on the progression of the outbreak in Rwanda.

(e) Overall risk level and statement

Risk assessed					
Negligible	Very Low	Low	Moderate	High	Extreme
*Based on the available data at this point of time, within the next one month, the overall risk of a Marburg virus case importation into the GCC countries is assessed as **very low**.*					
*The probability of a Marburg virus importation into the GCC countries from Rwanda is **unlikely** due to the current scale of the outbreak, and the limited direct travel links to GCC.* *The magnitude of the impact of Marburg virus case importation into the GCC on the general population is **minor** driven by the severity and high CFR of the disease, but high preparedness measures in place. There is a Moderate level of confidence due to lack or late receiving of information of data on the outbreak progression in Rwanda.*					

IV. Recommendations

Surveillance

1. Establish communication with the IHR focal point in Rwanda (and WHO IHR) to request updated information on the outbreak progression and exit screening measures;
2. Disseminate a Marburg case definition to relevant surveillance staff and clinicians and send an alert to clinicians and points of entry staff to maintain a high suspicious level for Marburg cases;
3. Review and disseminate viral haemorrhagic fever guidance (guidelines, case definitions, and investigation forms) to all stakeholders involved in healthcare providers, surveillance, and contact tracing;
4. Strengthen disease surveillance systems to quickly detect and respond to any imported cases of MVD, for early detection and notification;
5. Ensure availability and readiness of the diagnostic PCR for MVD nationally, or ensure the established referral mechanisms to reference laboratories in GCC countries or internationally;
6. Consider conducting a simulation or tabletop exercise to assess the national capacities to detect, notify, and control in case of importing viral haemorrhagic case

Risk Communication and Travel-related measures

7. Enhance risk communication strategies at point of entry regarding the MARV infection to raise awareness of travelers to Rwanda (including aircraft personnel) of the risk factors for MVD and the protective measures (IPC) individuals can take to reduce exposure in affected geographic areas;
8. Enhance implementation of airline policies of refusing embarkation of acutely ill passengers at Kigali airport or any other airports of an affected area.

Clinical management and IPC in healthcare facilities

9. Enhance IPC measures for viral hemorrhagic fever in all healthcare facilities;
10. Raise health awareness and education among healthcare workers about the MVD and route of disease transmission training
11. Train and equip hospitals and other health facilities to strengthen the IPC measures, isolation, and other services such as Laundry and medical waste management

Other

12. Consider contributing to global efforts in supporting Rwandan authorities and international organizations in mounting an effective response in Rwanda.

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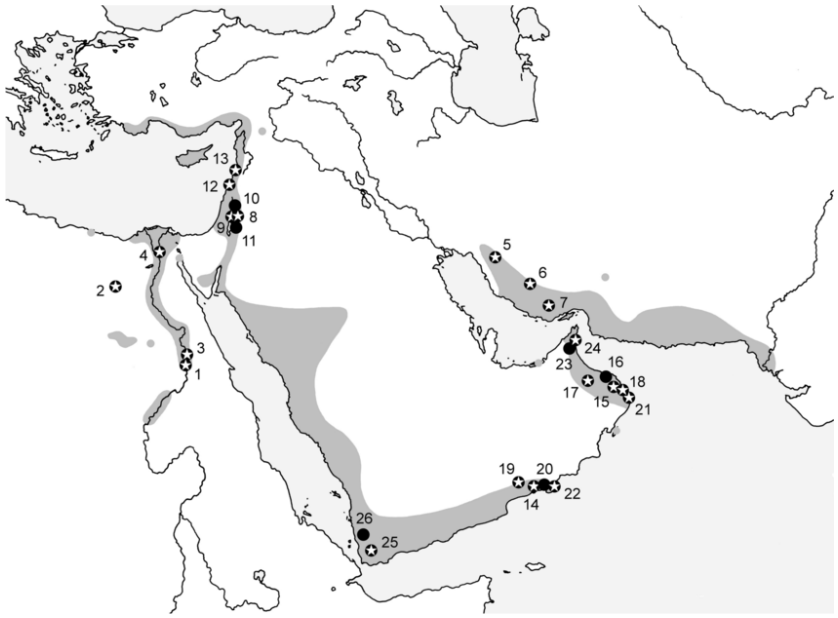
VI. Annexes

Annex 1. Gulf CDC Risk Characterization Matrix

Likelihood	Impact				
	Negligible	***Minor***	***Moderate***	***Major***	***Severe***
Negligible	*Negligible*	*Negligible*	*Negligible*	*Negligible*	*Negligible*
Unlikely	*Negligible*	**VERY LOW**	**LOW**	**LOW**	**MODERATE**
Likely	*Negligible*	**LOW**	**LOW**	**MODERATE**	**MODERATE**
Highly likely	*Negligible*	**LOW**	**MODERATE**	**MODERATE**	**HIGH**
Almost certain/sure	*Negligible*	**MODERATE**	**MODERATE**	**HIGH**	**CRITICAL**

Annex 2. The dark grey area shows the distribution range of Rousettus aegyptiacus in the Middle East reconstructed after Benda et al (12)**. (2011, 2023)**



VII. Acknowledgements

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