

Monkeypox (mpox) Outbreak

More queries posed as cases soar globally

*Salah T. Al Awaidy,¹ Faryal Khamis,² Malik Sallam,³ Ramy M. Ghazy,⁴ Hassan Zaraket⁵

EMERGING AND RE-EMERGING OUTBREAKS of infectious diseases are on the rise, with devastating effects on people's health, society and the economy.¹ An outbreak of human monkeypox (Hmpox) in multiple non-endemic countries was announced by the World Health Organization (WHO) in May 2022 with the majority of cases having no confirmed travel to endemic countries.² The monkeypox virus (mpoxv) was isolated for the first time in 1958 by the Staten's Serum Institute in Copenhagen, Denmark.³ The virus is classified as a species within the *Orthopoxvirus* genus together with the variola virus, the causative agent of smallpox.⁴ The mpoxv causes similar, albeit less severe clinical manifestations compared to smallpox with a lower case-fatality rate (CFR).⁴

A zoonotic disease transmitted from animals to humans with limited chains of human-to-human transmission, cases of Hmpox infections were frequently detected near tropical rainforests, the habitat of a variety of animals known to harbour the mpoxv.⁵ Examples of these animals include squirrels, Gambian rats, dormice, monkeys of various species, however, the definitive animal reservoir of mpoxv remains unknown.^{4,5} Prior to the current outbreak in non-endemic countries, Hmpox has been endemic to Central and West Africa.⁴ Occasional outbreaks outside the African continent were linked to a history of travel or imported animals from endemic regions.^{4,5}

Hmpox is a contagious infection that leaves a distinctive rash, following exposure via close contact with an infected animal's bodily fluids or through a bite. It can also be acquired through preparation of bush meat or contact with infectious sores, scabs or body fluids (in human-to-human transmission), or through respiratory secretions. The incubation period ranges from five to 21 days.^{6,7} The prodromal phase, which may not manifest in all cases, resembles influenza illness and includes fever, headache, backache, lymphadenopathy and fatigue.⁸ Following the prodromal phase, the affected individuals develop a rash, initially macular, that evolves into papules, vesicles and then pustules within 1–5 days.⁶ The skin

lesions could be present on the hands, feet, chest, face, genitalia or the anus.^{6,8} Before healing, the pruritic skin lesions evolve through a number of phases, eventually forming scabs.⁸ Enanthema involving the mouth, vagina or anus could occur as well.⁸ Complications such as sepsis, pneumonia, bacterial super-infection, vision loss, skin scarring, encephalitis, dehydration, skin pigmentation and death may also occur.⁹

The smallpox vaccines used in the past are 85% effective in preventing Hmpox. However, the use of this vaccine has been ceased since the eradication of smallpox.¹⁰ More recently, a novel, two-dose vaccine based on the modified attenuated vaccinia virus was approved. Additionally, antivirals licensed by the European Medicines Agency in 2022, such as tecovirimat, are available, albeit with limited or no human safety and efficacy data.¹¹

GLOBAL BURDEN OF HMPOX

Before the ongoing 2022 Hmpox outbreak, the majority of infections that were reported in the endemic regions were caused by animal to human spillover, with rare cases of human-to-human transmission that primarily involved household contacts.⁷ However, the present epidemic serves as a reminder of how viruses capable of sustained human transmission can emerge suddenly.¹²

Until recently, Hmpox was limited to West and Central Africa—where the virus can be found in several animal species—and dominated by two separate clades, one of which is exclusive to the Congo Basin and the other is prevalent in West Africa.^{4,5,13} The Congo Basin lineage of the virus is expected to be more contagious and has historically been associated with more severe illness and a higher case fatality rate (CFR = 10.6%, 95% CI: 8.4–13.3%).^{4,11}

It has been confirmed that the West African clade is indeed the clade associated with the current Hmpox outbreak and is characterised by a lower CFR (3.6%, 95% CI: 1.7–6.8%).^{11,14} An important and urgent call for modification of the mpoxv clades' nomenclature has been advocated for in order to make it non-discriminatory and non-stigmatising with reliance

¹Office of Health Affairs, Ministry of Health, Muscat, Oman; ²Adult Infectious Diseases, Department of Medicine, Royal Hospital, Ministry of Health, Muscat, Oman; ³Department of Pathology, Microbiology and Forensic Medicine, School of Medicine, University of Jordan, Amman, Jordan; ⁴High Institute of Public Health, Alexandria University, Egypt; ⁵Department of Experimental Pathology, Immunology and Microbiology, American University of Beirut, Lebanon

*Corresponding Author's e-mail: salah.awaidy@gmail.com

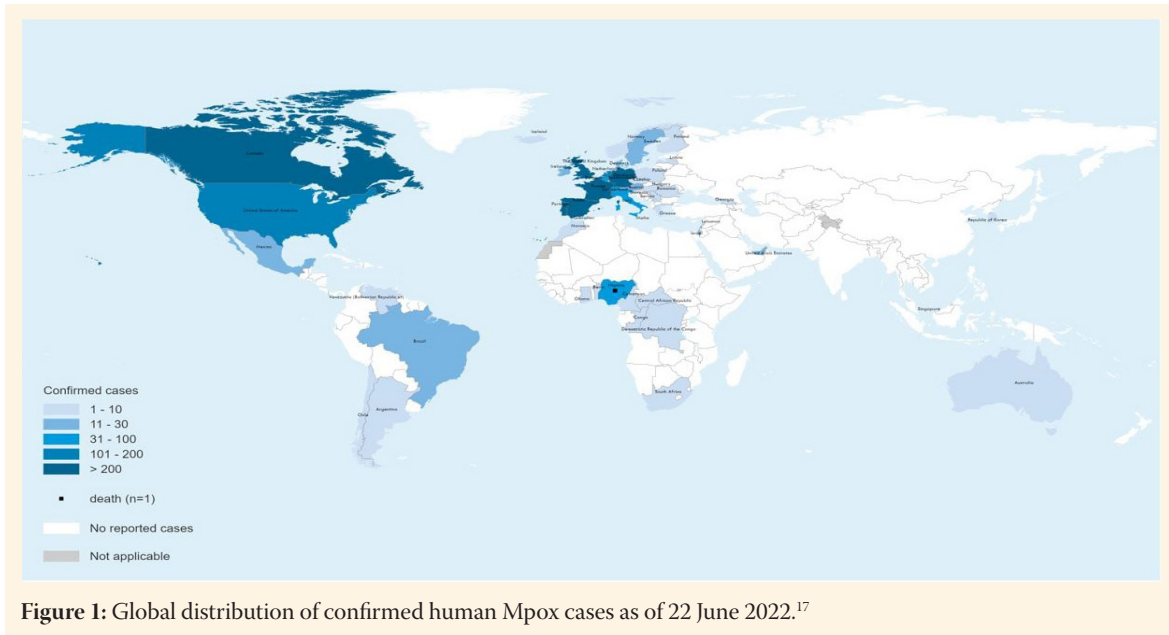


Figure 1: Global distribution of confirmed human Mpox cases as of 22 June 2022.¹⁷

on Arabic numerals for clade assignment rather than geographic location.¹⁵

The cumulative number of confirmed Hmpox cases that have been reported to the WHO exceeded 3,400 with one fatality being reported from across 50 countries between January and June 2022.¹⁶ These cases (many of which were from countries where the mpox is not endemic) were reported from a total of five different WHO regions: the Region of the Americas, the African, European, Eastern Mediterranean and Western Pacific Regions.¹⁶ The vast majority of confirmed Hmpox cases were reported from the WHO European Region and the Region of the Americas [Figure 1].¹⁷

The second meeting of the WHO held on 23 June 2022, concurred with the International Health Regulations (IHR) Emergency Committee that the multi-country Mpox outbreak did constitute a Public Health Emergency of International Concern (PHEIC). The Hmpox outbreak, in that regard, presented a moderate danger to global public health according to the WHO as of June 2022.² Contrary to the previous Hmpox cases reported from the endemic regions, no linkages to animals have been traced amid the ongoing outbreak. Furthermore, the initial cases were reported in Europe, hinting that the virus could have been circulating between people for months and gone unnoticed.^{6,18}

Since the first recorded case in April 2022, no fatalities had been recorded amid the ongoing outbreak in previously non-endemic countries as a result of the disease, as of June 2022.² Males constituted a majority of the confirmed cases of Mpox and the majority of these cases were among males who had had sex with males (MSM) in densely populated

metropolitan settings.² Additionally, more cases of Hmpox have been recorded in the African Region, with 1,408 suspected cases since the start of the year 2022, of which 44 cases have been confirmed and 66 fatalities have been recorded.² It is worth mentioning that contrary to the relatively high CFR in Africa, the lack of fatalities in the current outbreak outside Africa could be linked to early detection of cases and quality of health care including the use of antivirals and prophylactic vaccines.

The ongoing detection of the virus and the reported deaths in several African countries underpin the urgent need to better understand the source and the transmission dynamics of the disease and to provide people with the knowledge and resources they would need to safeguard themselves and others in a variety of situations.

REQUIRED MEASURES TO MITIGATE AND STOP THE SPREAD

The public health hazards of Hmpox is on rise with the ongoing transmission of the virus and potential spread to populations vulnerable to the development of severe illness including pregnant women, young children and immuno-compromised individuals, as the virus seizes the opportunity to establish itself as a resident human pathogen.¹⁹ In context of the current multi-country Hmpox outbreak, it is vital to establish reliable and efficient surveillance at a national level at this stage, since failure to do so raises the risk of undetected cases and uncontrolled spread of the outbreak to additional regions/countries.

Another issue to be considered is that the majority of cases have been reported among MSM or in healthcare settings. Therefore, it is recommended

that the countries seek out overlooked cases while conducting contact tracing. Testing and identification of suspected cases are essential to monitor the progress of the outbreak and to direct the vaccination programs.²⁰ Moreover, since a majority of emerging infectious disease incidents that afflicted humans in the recent era were zoonotic in nature, the importance of proactive zoonotic and animal surveillance activities should be highlighted.²⁰

Regarding the utility of smallpox vaccinations for the prevention of Hmpox, the WHO released interim recommendations stating that vaccination should only be used when necessary and emphasised that it does not advocate widespread Hmpox immunisation.²¹ In order to learn more about the effectiveness of vaccines as they are used in the current situation, countries are required to cooperate in the adoption of standardised research protocols tackling this aim.

The WHO endorsed the use of post-exposure preventive vaccines in the fight against the outbreak for contacts of cases, provided preferably within four days of the initial exposure in order to avoid illness in these contacts and as primary preventive (pre-exposure) vaccination for health care workers, researchers dealing with orthopoxviruses and clinical lab technicians.²¹

In January 2022, the European Medicines Agency authorised tecovirimat, an antiviral originally designed to fight smallpox, for the treatment of mpox. However, in the context of a mpox epidemic, there is limited experience with these therapies.²¹ In addition to the need for information on Hmpox vaccinations and their usage, proper recommendations for exposed individuals, more information on antivirals and the necessity to deploy these vaccines and antivirals need to be disseminated. Additionally, it is crucial to improve laboratory and diagnostic capabilities, the clinical management and measures to prevent and control infections in health care and community settings.

CONCLUSIONS AND THE WAY FORWARD

The rapid transmission of Hmpox and its widespread detection across various countries worldwide can be viewed as an emergency of international concern.² The current multi-country outbreak of the disease is evolving, with potential risk of further spread if swift containment interventions are not promptly devised and followed.

The CFR observed in the African region in contrast to what is being observed outside of Africa

highlights the need for assistance involving all response components, including but not limited to raising awareness at the community level, risk communication, human and animal surveillance, diagnostic and laboratory assistance and regional research and analysis of antivirals and vaccines. This is critical not only to curbing the current outbreak but also to preventing future ones at their source. Both countries that have recently been impacted by Hmpox and those that have experienced it for a long time need vigilant intervention measures.

It is essential that urgent actions be called for in order to contain mpoxv transmission and interrupt the chains of virus spread in non-endemic and endemic countries. Special attention should be paid to ensuring effective surveillance among highly vulnerable groups in terms of exposure or disease severity with a cautious approach that ensures that the potential stigmatisation of these groups is avoided.²² Currently, it is recommended that the global and regional public health authorities: (1) amend the law to enable it to list Hmpox as a notifiable disease; (2) ensure robust surveillance with an emphasis on surveillance of zoonotic disease in all countries, including appropriate contact-tracing, isolation and care of patients; (3) call for immediate involvement by the national advisory committees and panels of scientific experts and groups to formulate the roadmap necessary to limit and contain the threat of Hmpox. The WHO recommends that potential cases should be reported immediately and investigated within 48 hours. Health professionals also need to be made aware of and involved in developing an epidemic management framework that has proven successful in other contexts to ensure effective planning and response owing to the nature of disease propagation in an outbreak environment.²³

Without increased and efficient efforts, entire communities could risk losing all of the progress being made towards controlling the Hmpox outbreak worldwide. Collaborative efforts, especially at the national level, are urgently needed in order to provide accurate and reliable information about the disease to the general public in service of halting the spread of this disease.

AUTHORS' CONTRIBUTIONS

SA and FK conceptualised the idea. All authors were involved in the information extraction and literature review for this manuscript. All authors were also involved in designing, structuring and revising this manuscript. All authors approved the final version of the manuscript.

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