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EDITORIAL

Monkeypox: A Rising Threat

Sadia Choudhury Shimmi*

Department of Biomedical Sciences, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, 88400 Kota Kinabalu, Sabah, Malaysia

*Corresponding author's email: shimmi_cmc40@ums.edu.my

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Monkeypox (mpox) has recently emerged as a global health emergency. This zoonotic disease is caused by the monkeypox virus (MPXV), an enveloped double-stranded DNA virus belonging to the Orthopoxvirus genus in the Poxviridae family, which also includes viruses such as variola (smallpox), cowpox, and vaccinia. The monkeypox virus is part of the same family as the virus that causes smallpox. In 1958, two outbreaks of a pox-like disease occurred in colonies of monkeys kept for laboratory research in Denmark. It remains unclear what causes the disease, despite its name. African rodents and non-human primates might transmit the virus to humans, like monkeys. The first recorded human case of MPXV infection occurred in 1970 in the Democratic Republic of Congo (DRC), involving a nine-month-old child. After this initial case, the virus spread to several countries in Central and West Africa, where it became endemic. The spread of the virus has often been linked to travel or the importation of animals from these regions. A significant outbreak in the DRC in 1997 reportedly resulted in 88 infections and three deaths, all among children under the age of three.

In 2022, mpox spread globally, marking a significant shift in its epidemiology. Starting in May of that year, cases were reported in several non-endemic countries, including Sweden, Portugal, Austria, Italy, Germany, France, Germany, Belgium and Spain. Notably, most of these cases indicated a new pattern of transmission with no direct travel history to the endemic areas. As the outbreak progressed, numerous clusters and cases of mpox were

reported simultaneously across both endemic and non-endemic countries, covering vast geographical regions.

The global mpox outbreak a Public Health Emergency was declared by the World Health Organization (WHO) on 23 July 2022 which was International Concern. Between January and October 2022, WHO reported that mpox was in approximately 77,000 cases and 36 deaths from 109 countries. The majority of cases, over 65%, were reported in the Americas, with 32% occurring in Europe. Several mpox-related deaths were due to complications like encephalitis, particularly among immunocompromised patients.

In humans, the febrile rash illness as a first-ever case was reported in Indiana, Illinois and Wisconsin between the end of May and the beginning of June 2003. Prairie dogs (Cynomys) which were purchased recently and housed with recently shipping African rodents were the causes of mostly affected individuals. In April 2023, for the pet trade, these African rodents shipped to the United States were identified as the source of the infection.

From 2022, 1 January to 2024, 30 June, the total number of cases of mpox which were confirmed by the laboratory was 99,176, including deaths, 208 from 116 countries across all WHO regions, according to the United Nations Health Agency. WHO noted that, outside of Africa, "the outbreak continues at a low level of transmission" globally.

Globally, in June 2024 alone, a total of 934 new mpox cases were reported. The highest cases (567 cases) were in Africa. The second highest (175 cases) was in the Americas. Europe reported 100 cases, except for the Eastern Mediterranean region, the Western Pacific reported 81 cases, and Southeast Asia reported 11. During this period, 61% of the cases were reported by the African Region, 19% by the Americas, and European Region 11%.

According to the Africa Centres for Disease Control and Prevention (Africa CDC), in 2024, a total of 17,541 suspected and confirmed mpox cases (14,719 suspected and 2,822 confirmed) have been reported across the African continent. There were more cases of mpox in 2024 rather than in 2023 in African countries with 17,500 cases this year in contrast to approximately 15,000 in 2023. Most vulnerable groups are children, with around two-thirds of infections in the DRC occurring in individuals under the age of 15.

In Malaysia, from July 26, 2023, when the first case was detected to November 2023 when the last case was reported, the total number of cases was nine. The Health Ministry stated that in all cases, there was the involvement of high-risk activities among the affected individuals with fully recovered and no death was reported. "Based on our monitoring, no new imported mpox cases have been reported," the ministry said in a statement on August 15, 2024. The ministry also advised avoiding risky activities and maintaining a healthy lifestyle for those travelling to endemic and non-endemic countries.

Two distinct clades of the MPXV have been recognised: the Congo Basin clade (Clade I) and the West African clade (Clade II). In 2022–2023, the Clade IIb was the primary strain for the mpox global outbreak. In 2024, both Clade I and Clade II have been detected. The case fatality ratio for mpox in Africa is approximately 10% for the Congo Basin clade, with the highest mortality rates occurring in children and individuals without prior vaccination. Outside of Africa, the fatal Clade I was detected in a single patient in Sweden.

Mpox is transmitted to humans through infected animals, physical contact with an infectious person, or contaminated materials. In the current outbreak, most cases were reported among young men, with transmission primarily occurring through skin and mucosal contact during sexual

activities. The most commonly reported sexual orientation among affected individuals is men who have sex with men within connected social-sexual networks. Additionally, a higher prevalence of human immunodeficiency virus (HIV) infection has been reported among patients with mpox.

The incubation period of mpox normally ranges from 6 to 13 days. Although it may vary from 5 to 21 days. Mpox symptoms usually begin within a week after exposure, though they can appear anywhere from 1 to 21 days post-exposure. Mpox symptoms are generally milder than those of smallpox. Usual symptoms are a skin rash or mucosal lesions with 2 to 4 weeks duration, along with fever, low energy, muscle aches, headache, back pain, and obvious swollen lymph nodes.

However, classic mpox infection is divided into two stages: the prodromal stage and the rash stage. The prodromal stage lasts within 1 and 4 days and is characterized by symptoms such as fever (over 38.5°C), headache, sore throat, myalgia, fatigue, and lymphadenopathy. Lymphadenopathy is a key differentiating feature of mpox, distinguishing it from other diseases such as smallpox, chickenpox, hand-foot-and-mouth disease, or measles. Swelling of the lymph nodes may occur on either the bilateral or unilateral side of the submandibular, cervical, axillary, or inguinal regions.

In 1 to 3 days, the rash stage begins after the onset of fever. The rash typically first appears on the face and after that palms and soles to all parts of extremities. The lesions vary in size and shape from vesicles, macules, pustules, and papules to crusts, then scabs and eventually drop off as the skin heals. The rash generally concentrates more on the face (95%) and the palms and soles (75%) than on the trunk, displaying a centrifugal distribution. Skin lesions are often at the same stage of development (monomorphic). This disease affects the conjunctiva, cornea, oral mucosa, and genitalia.

However, in the recent global outbreak, the clinical features of mpox differ from those of previously reported classic cases. Patients are now exhibiting more mucosal lesions, which often localize in the genital, perineal/perianal regions, as well as on the eyes and in the mouth. The rashes may be confined to only a few lesions, may not always appear on the palms and soles, and may present at different stages of evolution. Notably, rashes may develop before the onset of typical prodromal symptoms, such as fever and fatigue. Anorectal pain and bleeding have also been frequently reported, making diagnosis challenging; therefore, a high index of suspicion for monkeypox is required in the current outbreak.

Mpox is generally a self-constraining disease, and its symptoms last from 2 to 4 weeks. Before the rash, from one day to 21 days, infected persons are contagious after the initial symptoms up to all skin scabs have fallen off. However, severe cases occur more commonly among immunocompromised individuals, children, and pregnant women. Complications of monkeypox can include secondary skin infections, keratitis, sepsis, bronchopneumonia, encephalitis, and which may lead to vision loss. Polymerase chain reaction (PCR) is the preferred laboratory test if symptoms are noticed. Specimens are collected from the rash including fluid, skin or crusts by robust swabbing for diagnosis. If no significant skin lesions are present, anal, rectal or oropharyngeal swabs testing is done.

The main principles of mpox management include providing supportive care, preventing complications, and controlling the outbreak. Many patients with mpox experience mild infections and recover without medical intervention. Infected patients should be isolated and adhere to infection control precautions until all skin lesions have dried and fallen off. During

isolation, supportive care-such as adequate hydration, nutritional support, antipyretics, pain control, and psychosocial support-should be provided.

Patients should be advised to stay away from picking or scratching skin lesions to prevent secondary infections. Topical antiseptics can be applied to excoriated skin lesions, and any skin infection or signs of sepsis should be monitored closely. Secondary skin infections should be treated with antibiotics, while warm sitz baths or topical lidocaine may be offered for symptomatic relief of anorectal or genital lesions.

Antivirals such as tecovirimat and brincidofovir, approved for the treatment of smallpox based on animal models and safety trials in healthy individuals, are also predicted to be effective against mpox.

Prevention remains crucial. Mpox is prevented by avoiding physical contact with infected individuals. Some countries approved vaccines and therapeutics that were developed for smallpox that can be used for mpox in certain circumstances. Immunization against mpox was previously achieved with smallpox vaccination. However, due to waning immunity and the cessation of vaccination efforts, mpox has emerged as the most prevalent orthopoxvirus following the eradication of smallpox. Currently, the World Health Organization (WHO) recommends the use of LC16 or MVA-BN vaccines, with the ACAM2000 vaccine as an alternative when the others are unavailable. For individuals at risk, such as close contacts of confirmed mpox cases or in high-risk groups, vaccination is helpful to prevent infection. However, mass vaccination is not yet recommended.

In Malaysia, the Ministry of Health (KKM) has integrated mpox monitoring into the MySejahtera application, amid the spread of this rare but potentially fatal disease in several countries. The health minister announced that the new feature on the government's mobile application includes alerts for travellers arriving in Malaysia from countries where mpox is endemic or where cases have been confirmed. The alert instructs travellers from these regions to monitor themselves for 21 days-the incubation period of mpox-and if they develop symptoms, try to find quick medical attention. The management of mpox follows established guidelines.

On August 14, mpox was again declared a public health emergency worldwide by WHO, just after 15 months the WHO previously declared mpox emergency on July 23, 2022. This declaration calls for global cooperation and resource allocation to enhance surveillance, treat infected individuals, and halt the outbreak. Diagnostics, surveillance, community engagement, and risk communication remain central to stopping the outbreak and eliminating human-to-human transmission of mpox in all contexts. Therefore, it is essential to be vigilant about the transmission, signs, and symptoms of mpox. We must protect ourselves, especially when in close contact with high-risk individuals or travelling to high-risk regions, to prevent this endemic disease from escalating into an epidemic or pandemic.

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