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"From Endemic Regions to Global Outbreaks: Monkeypox Virus and Its Challenges"

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Abstract:
A zoonotic virus belonging to the Orthopoxvirus genus, monkeypox has resurfaced as a global health concern outside of its endemic areas in central and western Africa. Symptoms of the virus appear 6–13 days after contact and include fever, rash, lymphadenopathy, and serious consequences in immunocompromised patients. The Central African clade, one of the two primary clades, has a greater mortality rate than the West African one. Since the first human case occurred in 1970, outbreaks have been documented on several continents, especially after smallpox vaccination campaigns were discontinued. Recent worldwide outbreaks, which have included thousands of cases documented in Europe, Africa, and the Americas, highlight the significance of effective antiviral therapies, immunisation programs, and surveillance. Since 2022, a number of cases have been confirmed in India, and efforts are still being made to enhance public health response and readiness. In order to shed light on the changing nature of monkeypox and methods for lessening its effects, this short communication explores the epidemiology, clinical presentation, immunisation, and treatment techniques. Controlling future epidemics and halting broad transmission requires improved research, more public awareness, and targeted immunisation for high-risk groups.

Keywords: Monkey pox, Outbreaks, Vaccination for Mpox, zoonotic disease

1. Introduction:

A member of the same genus as Orthopoxvirus in the Poxviridae family, monkeypox virus is a double-stranded DNA virus with an envelope that spreads through zoonotic infection (1,2). In central and western Africa, incidences of monkeypox are typically seen in close proximity to tropical rainforest regions (3). Therefore, instances outside Africa are believed to be associated with recent international travel to endemic regions or the importation of animals. The monkeypox virus, also known as the mpoxvirus (MPXV) (4), is a zoonotic virus that mostly affects rats and other animals that inhabit African rainforests.

Initially, MPXV was described into two clades (1). About 11% of deaths are caused by lineage 1 (the ex-Central Africa lineage), which is linked to the majority of outbreaks in Africa. Clade 2, the ex-West African clade, is the most exported lineage and has a lower death rate (1%–6%) (5). Usually the symptoms emerge between 6–13 days (and sometimes up to 21 days) following infection. Clinical signs of the illness include fever, sores on the mucosa (such as the mouth, nose, throat, or digestive tract), a rash on the skin called a papule, back discomfort, and muscle aches (6).

After the rash first appears, it can spread swiftly within three days and eventually develop into tiny sacs filled with fluid that are called vesicles. Hand and foot soles may also be affected if the rash disseminates throughout the body (6). Most people experience a full recovery after two to four weeks of mild to moderate symptoms. MPXV is spread to humans by items contaminated with the virus or by intimate contact with animals or people who are sick. The mucous membranes or skin wounds, which are frequently undetectable, are the entry points for it into the body. Sexual interaction is a potential means of transmission of the mpox virus (6).

Though it was believed that hMPXV infection was similar to smallpox in terms of symptoms, severity, and fatality, it was linked to lower mortality and poor transmissibility between humans. 90% of mpox patients experience unilateral or bilateral lymphadenopathy, which can affect any combination of the cervical, postauricular, axillary, inguinal, or submandibular lymph nodes (1,7,8).

There has been evidence to suggest that individuals with HIV infection and young infants are more vulnerable to severe consequences (1,7,9). A severe necrotising form of monkeypox appears to mimic the clinical features of a disorder that defines acquired immunodeficiency syndrome (AIDS) in situations of advanced immunosuppression. This includes a high frequency of severe systemic and dermatological symptoms, which frequently have lethal

consequences (10). Pneumonitis, encephalitis, keratitis, and subsequent bacterial infections are among the consequences of multiple mpox (7,11).

2. Epidemiology and Global Spread of Monkeypox:

It was initially found in a Danish animal facility in 1958 while conducting research on polio vaccines using colonies of monkeys (1,12). There have been around 16,500 cases globally since the first human case, which involved a 9-month-old baby boy in Zaire in 1970 (12), was documented.

There were 59 instances of human monkeypox reported in west and central Africa in the ten years after the first incidence in 1970, with a 17% fatality rate in children under the age of ten. With the goal of reducing population vulnerability to the monkeypox virus, the World Health Organisation (WHO) tracked incidences of human monkeypox following the eradication of smallpox and the consequent suspension of routine smallpox immunisation in 1980.

Three spatiotemporal clusters suggestive of outbreaks of probable monkeypox cases were identified in the Democratic Republic of the Congo between 2000 and 2015 (9). Between 2005 and 2007, 760 cases were confirmed in laboratories. Moreover, after nearly 40 years without any reported cases, monkeypox has been on the rise in Nigeria since 2017 (12), as highlighted in a WHO report from 2022. While rates continue to rise in endemic countries, there have also been several isolated cases and outbreaks of monkeypox in non-endemic countries, including the United Kingdom, the United States, Israel, and Singapore.

In the United States, prairie dogs that had come into contact with African rodents were linked to 71 cases of human illness in 2003 (35 of which were confirmed in a laboratory). Seven cases of monkeypox were reported in the UK between 2018 and 2021, four of which were linked to travel from endemic countries. Two Nigerian travellers who were returning were diagnosed with monkeypox in Texas and Maryland (USA) in July of 2021 (13).

3. Outbreaks and trends:

When exotic animals were brought from Ghana in 2003, the United States became the site of the first known human case of mpox (hMPXV) outside of Africa. Since then, intermittent outbreaks have been reported in many parts of the world, all of which can be linked back to the endemic African regions. Over 24,000 confirmed cases of mpox, as well as over 600 suspected cases, have been reported from Member States of the Africa Union in 2024, furthermore, Morocco returned a case on September 12, 2024 (6).

Sweden reported the first case of mpox imported into the EU/EEA caused by MPXV clade I on August 15, 2024 (6). There have been no reports of secondary cases as of September 15th. Between January 2022 and July 31, 2024, 121 countries recorded 1,03,048 cases of Mpox worldwide, with 229 deaths, according to the WHO. 3,900 confirmed cases have been reported from 15 African nations as of September 1, 2024. Nigeria, Burundi, and the Democratic Republic of the Congo are with the highest number of cases this year.

The monthly reported new case count as of July 2024 is 8.8% higher than the previous month. The African Region (54.9%) and the Region of the Americas (24.2%) accounted for the majority of cases reported in the previous month. Since January 1, 2022, the following ten nations have experienced the greatest levels of suffering worldwide: the United States (n = 33,556), Brazil (n = 11,841), Spain (n = 8,104), the Democratic Republic of the Congo (n = 4,385), France (n = 4,283), Colombia (n = 4,256), Mexico (n = 4,132), the United Kingdom (n = 4,018), Peru (n = 3,939), and Germany (n = 3,886). All of these make up to 80% of instances that are reported worldwide (14). The literature underscores the role of global interconnectedness in mpox dissemination, necessitating robust surveillance systems, timely diagnostic measures, and targeted public health interventions to mitigate its spread.

4. Methodology

This review synthesizes findings from peer-reviewed studies, WHO reports, and national surveillance data to present an integrated perspective on MPXV epidemiology, pathophysiology, and management strategies. Existing literature was critically analyzed to elucidate the virus's clinical features, zoonotic transmission patterns, and implications for public health. Future research methodologies must validate findings through longitudinal studies, randomized controlled trials on antiviral efficacy, and improved genomic surveillance to track viral mutations and assess vaccine performance comprehensively.

5. hMPXV cases in India:

Kerala reported the first case of hMPXV in India on July 14, 2022 (1), and on 27th March 2024, Kerala additionally reported the final case on March 27, 2024 (15).
Many of them had travelled abroad in the previous twenty-one days. Remarkably, the deceased displayed signs of encephalitis and exhaustion instead typical mpox symptoms (16,1). 18 states and Union Territories in India provided 96 samples of probable mpox cases to the Indian Council of Medical Research (ICMR) as of September 18, 2022. On 27th March 2024, the last case was also reported from Kerala (15).

The cases were all immunocompetent, free of comorbidities, and showed up with a brief prodromal phase of fever, myalgia, and vesiculopustular rash, mostly on the face, trunk, and extremities (17).

6. Vaccination:

There are presently three mpox vaccines with licenses: 1) Highly-attenuated replication-deficient vaccinia virus vaccine, known as modified vaccinia Ankara-BN (also known as MVA-BN or JYNNEOS, Imvamune or Imvanex), a 2-dose third-generation smallpox vaccine licensed in the United States, Canada, and Europe; 2) LC16-KMB (licensed in Japan); and 3) OrthopoxVac (licensed in the Russian Federation). Based on currently assessed risks and benefits, mass vaccination is NOT recommended by WHO for Mpox at this time. WHO recommends vaccination for individuals who are at high risk of exposure, such as those with certain occupations or circumstances, and travellers who may be at risk, as determined by a healthcare provider. As of right now, India has also not released any advisories regarding the Mpox vaccination (18). Further clinical trials are essential to validate the efficacy of these interventions in diverse patient populations.

7. Treatment:

The use of antivirals that are active against the monkeypox virus is combined with general supportive care in the clinical management of monkeypox cases (1,3). During the outbreak, around half of the patients needed painkillers (for example, for oral or anogenital sores). Warm baths and oral antihistamines may help alleviate pruritus, while stool softeners and topical lidocaine have been used to treat proctitis (19). Supportive care, including catheterization, may benefit individuals who are dehydrated or at risk of dehydration, those requiring more intensive pain management, and those with severe illnesses or complications.

Drainage, debridement, and wound care are necessary for patients with large genital ulcers or abscesses; antibiotics are indicated for subsequent bacterial infections. Monkeypox may be treated with three antivirals: tecovirimat (oral and intravenous), cidofovir (topical and intravenous), and brincidofovir (oral). It is anticipated that these antivirals, which have been licensed for the treatment of smallpox based on safety data in healthy persons and animal models, will also work against monkeypox. (20,21) The best treatment for monkeypox is tecovirimat, which is advised for a subset of patients who have a history of severe illness (such as encephalitis, pharyngitis, eye infections, or severe proctitis) or who are at risk of developing

a serious illness (such as immunocompromised individuals, children under the age of eight, patients with atopic dermatitis, expectant mothers, and nursing mothers).(22,23)

In patients with severe immunocompromised conditions, such as those with HIV who have a CD4 count of less than 200, early initiation and prolonged therapy should be taken into consideration. At this time, tecovirimat is only accessible in an emergency. There are ongoing clinical trials to assess its effectiveness in treating human monkeypox. While the Centres for Disease Control and Prevention in the USA have an expanded access protocol, the use of cidofovir for monkeypox is prohibited in the EU. Because there is not enough data on cidofovir, only tecovirimat is advised in the UK. Human studies have shown some improvement in symptoms and viral clearance. (23,24)

8. Preparedness for mPox

The protocols for managing patients in India include isolation, masking, protecting mucosal membranes and skin lesions (such as ulcers and conjunctivitis), rehydrating patients with nutritional supplements, and managing symptoms such as fever, itching, nausea, vomiting, headaches, and more. Although the guidelines recommend antibiotic treatment for skin rash-related secondary infections, they offer no guidance on prevention or antiviral therapy. The guidelines take into account destigmatization when discussing homosexual, bisexual, and men who have sex with men in the context of good risk communication. They are also aware of the dangers the illness presents to medical personnel (18).

Beyond the recommendations, the Indian Council Medical Research - National Institute of Virology (ICMR-NIV) has educated fifteen strategically located and dispersed geographically to detect monkeypox viruses. This is part of the organization's preparatory measures. The federal government has also made contact with state authorities to inform them of the necessity of reorienting and orienting stakeholders for a number of items mentioned in the guidelines as the global spread of monkeypox evolves. These items include scaling up hospital resources and services to manage probable or confirmed cases of monkeypox, as well as screening, testing, and patient isolation (15,17). Nonetheless, gaps remain in addressing antiviral access, prevention strategies, and community education, underscoring the need for coordinated efforts to bolster response frameworks.

9. Conclusion:

While MPXV appears less lethal than other orthopoxviruses, its expanding geographic reach, evolving epidemiology, and potential for severe outcomes in vulnerable populations make it a formidable public health threat. Current strategies focus on containment, symptomatic management, and high-risk immunization. However, there is an urgent need for interdisciplinary research to elucidate viral pathophysiology, optimize therapeutic interventions, and develop context-specific public health policies. The global health community must prioritize mpox research and preparedness, leveraging lessons from recent outbreaks to strengthen response mechanisms and enhance health outcomes across diverse settings. A balanced interpretation of results, coupled with rigorous methodological validation, will ensure the development of actionable insights to combat MPXV effectively. Awareness and health education among population along with immunisation of high-risk individuals would help us gain a deeper understanding of vaccination and appropriate academic preparation for medical professionals can help handle cases of monkeypox.

Abbreviations: hMPXV- Human Monkey pox Virus, MPXV- Monkey pox Virus, EEA- European Economic Area, EU- European Union, OPVX- Orthopoxvirus, CPVX- Cowpox virus.

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