Mpox Outbreak in Previously Non-Endemic Countries: A Review on Impact on Asia

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Madushani Wickramasinghe[1], Manjula Weerasekera[2] and Nilanka Perera[3]

[1]Department of Microbiology, Faculty of Medicine, Wayamba University of Sri Lanka, Kuliyapitiya, Sri Lanka. [2]Department of Microbiology, Faculty of Medical Sciences, University of Sri Jayewardenepura, Gangodawila, Nugegoda, Sri Lanka. [3]Department of Medicine, Faculty of Medical Sciences, University of Sri Jayewardenepura, Gangodawila, Nugegoda, Sri Lanka.

ABSTRACT: Mpox (human mpox) is an opportunistic viral zoonosis that bears a strong resemblance to smallpox. The virus is divided into 2 distinct clades, clade I and clade II, which were originally confined to the moist forest regions of Africa. However, due to air travel and the exotic pet trade, these clades have spread globally. As immunity from smallpox vaccination declined, Mpox emerged as the most significant viral infection affecting humans within the Orthopoxvirus genus. While sporadic cases occurred worldwide, the largest Mpox outbreak outside Africa took place in 2022, prompting the WHO to declare a global public health emergency. Asia plays a pivotal role in both hosting and contributing to the spread of Mpox, driven by socio-economic factors such as high population density, widespread illegal wildlife trade, and a continuous rise in air travel. The increasing number of Mpox cases in Asia poses a significant challenge to healthcare systems, especially during times of global economic crisis. Strengthening diagnostic capabilities and infrastructure, while sustainably utilizing available resources to target high-risk populations, will be essential in addressing the Mpox threat in the region.

KEYWORDS: Mpox in Asia, *Orthopoxvirus*, Zoonosis, *Poxviridae*, human Mpox

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CORRESPONDING AUTHOR: Madushani Wickramasinghe, Department of Microbiology, Faculty of Medicine, Wayamba University of Sri Lanka, Labuyaya, Kuliyapitiya 60200, Sri Lanka. Email: madushani@wyb.ac.lk

Introduction

Human Mpox is a viral zoonosis that shares clinical and immunopathological similarities with smallpox.[1] Currently, it is the most significant Orthopoxvirus infection affecting humans.[2] The virus was first isolated in 1958 from *Macacus cynomolgus* monkeys that were kept in captivity for polio vaccine production and research in Copenhagen.[3] Mpox was identified as a human pathogen in 1970 when a 9-month-old infant in the Democratic Republic of Congo was investigated for a vesicular rash.[4] This occurred during the final stages of the global smallpox eradication campaign.[2,5] In the 1980s, 2 genetically distinct and geographically related clades were identified: clade I (formerly the Central African clade) and clade II (formerly the West African clade).[4,6] It was observed that clade II resulted in less severe disease and lower human-to-human transmission compared to clade I.[4,6] Mutational analysis has revealed ongoing microevolution of the Mpox virus, with evidence suggesting the involvement of the host's APOBEC3 enzyme in viral evolution.[7] Despite this, sporadic cases of imported human Mpox outside Africa have been linked to clade II.[8,9]

Human Mpox infections can occur due to zoonotic exposure, such as being bitten or scratched by an infected animal, consuming contaminated animal meat, or using infected animal products.[4,10-13] While the specific animal reservoirs for the Mpox virus have not yet been identified, non-human primates are considered incidental hosts of the virus.[12,14,15] Human-to-human transmission can happen through direct contact with body fluids, lesion exudate, crusts, respiratory droplets, saliva, or indirect contact through contaminated objects (fomites).[4,12,15-17] Due to the heaviness of the droplets and their limited transmission range, typically just a few feet, prolonged exposure is necessary for person-to-person spread.[11] As a result, individuals at higher risk include household members of infected individuals, healthcare workers, and veterinarians who have extended direct contact with infected humans or susceptible animals.[11]

There have also been reports of transplacental transmission resulting in fetal death.[18] However, transmission via semen or vaginal secretions remains unconfirmed, despite the presence of Mpox DNA in seminal fluid.[19] Airborne transmission is considered important, as evidence shows that Mpox viral DNA can be shed from the upper respiratory tract for an extended period, even after skin lesions have resolved.[20] Moreover, some studies indicate that Mpox is resistant to degradation in aerosolized form.[21] Additional potential transmission routes, including percutaneous, injectable exposure, and reverse zoonosis, were considered during the recent outbreak.[15]

Mpox is generally a self-limiting disease that resolves within 2 to 4 weeks.[2,11,20,22,23] The incubation period ranges from 7 to 21 days, followed by a prodromal phase characterized by fever, malaise, headache, sore throat, and generalized or regional lymphadenopathy.[2,11,20,22,23] Lymphadenopathy is a key distinguishing feature of Mpox compared to smallpox.[2,23] The rash appears after, or in rare cases with, the prodromal phase, progressing from enanthem to pustules, macules, papules, and vesicles, with the first lesions typically occurring on the tongue and inside the mouth.[10,19,20] The rash tends to follow a centrifugal distribution pattern.[10] According to the European Centre for Disease Prevention and Control (ECDC), the West African clade identified in Europe has an estimated mortality rate of about 3.6%, based on studies conducted in African countries.[4] Children, young adults, and immunocompromised individuals are at higher risk of mortality.[4,24,25]

The current outbreak caused by Clade II is the largest spread of Mpox reported outside of Africa.[9] The World Health Organization (WHO) declared it a public health emergency of international concern in 2022 when the number of cases surpassed 16 000 across 75 countries. According to WHO, as of July 31, 2024, there were 103 048 laboratory confirmed cases in 121 countries.[26] According to CDC data as of August 06, 2024, majority of the cases (95 196, or 95.65%) occurred in 115 countries with no prior history of Mpox, while 4.35% were identified in 7 countries that had reported cases in the past and 31 deaths in 6 countries with previous Mpox cases, and 176 deaths in 22 countries without a known history of the disease.[27]

A notable feature of this multi-country outbreak is the lack of an identifiable point of origin.[11] Historically, diseases often emerge or spread during times of war, conflict, and natural disasters.[9] In addition to the ongoing Russo-Ukrainian war and the associated displacement of refugees, factors such as male gender, deforestation, climate change, demographic shifts, and migration have been suggested as potential contributors to the resurgence of Mpox.[9]

The clinical profile of the current outbreak differs from previous ones. There has been a notable concentration of cases among men who have sex with men.[15,19] Specific symptoms, such as single ulcers, anal lesions, mouth sores, and anal or rectal pain, were considered as characteristic of this outbreak.[19] A study, spanning 16 countries, found that 98% of participants were gay or bisexual men, with 41% also diagnosed with Human Immunodeficiency Virus (HIV).[19] Despite this transmission pattern, Mpox can infect and spread among individuals of any sexual orientation or behavior, indicating that sexual activity is not the exclusive mode of transmission.

This review aims to highlight the impact of Mpox in Asia.

Impact on Asia

Asia covers 29.4% of the Earth's land area. According to the 2022 World Population Prospects from the United Nations, the 2 most populous regions—Eastern and South-Eastern Asia—account for 2.3 billion people, or 29% of the global population.[28] Together with the 2.1 billion people in Central and Southern Asia, these areas represent 59.74% of the world's population.[28] As of July, 2024, 940 laboratory-confirmed cases of Mpox were reported from South-East Asia.[29] South Asia, home to 24.89% of Asia's population, has a population density of 303 people per square kilometer, with India playing a key role in Mpox spread due to its proximity to other countries and its high population density of 424.79 people per square kilometer.

The reason for the concentration of Mpox cases in Israel remains unclear. However, the rising number of cases in Asia is alarming, especially given the factors that may contribute to the rapid spread of the virus across the continent. These include socio-demographic factors like high population density, which increases the risk of human-to-human transmission, and urbanization combined with deforestation, which heightens human contact with wildlife. This interaction raises the likelihood of zoonotic infections emerging and persisting.

Additionally, the expanding middle class in Asia has increased air travel affordability, contributing to a 10% annual growth rate in aviation.[30] United Nations data shows that 40% of global international migrants originate from the Asia-Pacific region, further raising the risk of Mpox importation and spread from Central and West Africa. Asia is also the largest hub for

Table 1. Number of laboratory- confirmed Mpox cases in Asia as at 14th of October, 2022 and 5th of September 2024.

COUNTRY	NUMBER OF CASES AT 14.10.2022	NUMBER OF CASES AT 5.9.2024
	N = 383	N = 5351
Israel	254	317
Singapore	19	61
United Arab Emirates	16	28
India	12	27
Saudi Arabia	8	763
Hong Kong	1	
Thailand	10	820
China	1	2567
Jordan	1	1
Bahrain	1	2
Lebanon	14	27
Cyprus	5	5
Vietnam	1	203
Japan	7	247
Philippines	4	9
Qatar	5	5
Taiwan	4	
Georgia	2	2
Indonesia	1	88
Turkey	12	12
Iran	1	1
Russia	2	4
South Korea	2	161
Sri Lanka		4

Source: Center for Disease Control; https://www.cdc.gov/poxvirus/Mpox/response/2022/world-map.html, World Health Organization; https://worldhealthorg.shinyapps.io/mpx_global/#1_Overview.

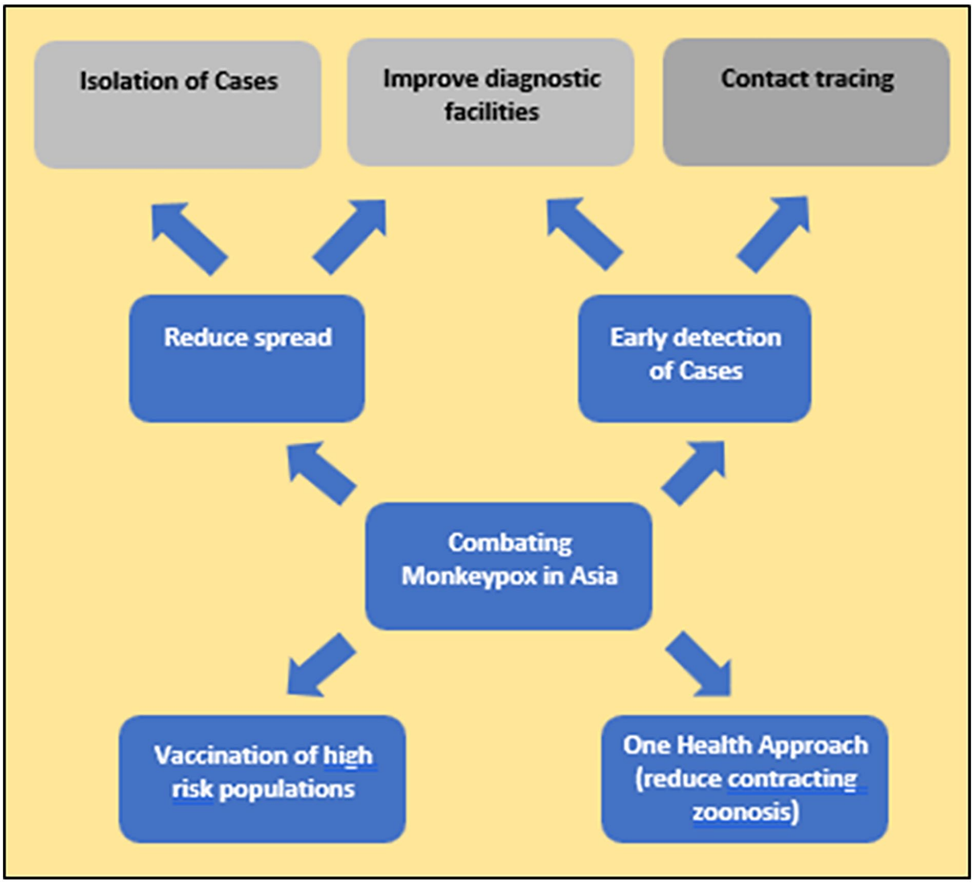

Figure 1. Combating Mpox in Asia. This figure summarizes the measures that could be adopted to combat Mpox case detection, containing the spread and avoid emergence of cases.

illegal wildlife trade, where wildlife is often used in traditional medicine or as symbols of wealth.[31] These practices increase the risk of zoonotic diseases and their introduction to human populations. Implementing a "One Health" approach, which recognizes the interconnectedness of human, animal, and ecosystem health, could benefit Asia in tackling zoonotic diseases. However, economic and social challenges in some nations have hindered the policy's full implementation.

Sexually transmitted infections (STIs) also play a critical role in the spread of Mpox in Asia, as they increase vulnerability to other infections. STIs and related complications are prevalent in Southeast Asia and the Western Pacific.[32] By 2017, the Asia-Pacific region had an estimated 5.2 million HIV-positive individuals, 75% of whom were concentrated in India, China, and Indonesia.[32] This population includes men who have sex with men, who have been shown to be at higher risk of Mpox, raising concerns for continued spread in Asia.[32] Effectively using available resources to control Mpox among high-risk populations is crucial, especially in resource-poor settings in Asia. Ring vaccination—vaccinating close contacts of infected individuals—has been recommended as an effective containment strategy.[33] Israel, for instance, prioritized vaccinating HIV-positive men born after 1980, the year smallpox vaccination ceased, providing a model for optimizing resources in countries with limited facilities.

Across Asia, the prevalence of diseases that mimic Mpox, such as varicella, measles, bacterial skin infections, scabies, and syphilis, varies. While some Asian countries have incorporated varicella immunization into their national programs, others with fewer resources have lagged behind. This increases the risk of undetected Mpox cases due to limited diagnostic capabilities, such as Polymerase Chain Reaction (PCR) testing. Mpox is confirmed through PCR of viral swabs from vesicles or ulcers, but blood tests are typically inconclusive due to the short duration of viremia. Antigen and antibody tests also fail to confirm Mpox due to cross-reactivity among orthopoxviruses.[23] This places additional strain on healthcare systems already weakened by the COVID-19 pandemic, while also negatively impacting the mental health of healthcare workers.

Asia is diverse in terms of economic, social, and healthcare systems, and regions like South Asia have not yet modernized their diagnostic infrastructure to meet the needs of their growing populations.[34] This has a significant impact on Mpox containment efforts, as early identification and isolation are crucial to stopping the spread. High population density, low socioeconomic status, and overcrowded living conditions exacerbate the situation. The entire continent must work together to tackle the threat of Mpox.

The rising spread of Mpox in Asia, as outlined in Table 1, is a cause for serious concern. Prompt and effective public health measures, including early detection, contact tracing, quarantine, and vaccinating close contacts, are essential to breaking the transmission chain and controlling the outbreak (Figure 1).

Conclusions

Asia is experiencing a rise in Mpox cases, with increasing numbers across the region. Factors like high population density, deforestation, a rise in air travel, extensive illegal wildlife trade, and a poorly implemented "One Health Approach" are heightening the risk of Mpox spread, particularly in South Asia. This situation poses a significant challenge to healthcare systems. There is an urgent need to effectively utilize available resources to address this threat.

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Author Contributions

MW, MMW, and NP were involved in conceptualization, retrieval of information. MW drafted the manuscript. MMW and NP have critically revised the manuscript. All authors have reviewed the final draft of the manuscript.

ORCID iD

Madushani Wickramasinghe https://orcid.org/0000-0001-6378-3135

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