

Minireview Article

India in the midst of another epidemic with Monkeypox

Comment [MM1]: The title should be a review on India in the midst of another epidemic with Monkeypox.

Abstract

Monkeypox virus is an Orthopoxvirus of the Poxviridae family that is of zoonotic origin. It is a double-stranded DNA virus similar to the eradicated smallpox virus. Monkeypox disease caused by this virus is mainly endemic to western and central African region. The disease has now garnered the attention of global public health as it has been declared monkeypox as a disease of Global Health Emergency of International Concern on 23rd July 2022, due to an explosion of non-endemic cases in 78 Member states across all 6 WHO regions, including India which has recorded 5 cases till date. Increased surveillance and detection of cases are essential to understanding the continuously changing epidemiology of this resurging disease. . The Smallpox vaccine is the most readily available protective agent against this disease, and it needs to be stockpiled to be deployed in case of an outbreak in the country. The disease is neither novel nor very mutable, so if our country is adequately prepared, there is less chance of this becoming a big public health concern. Viral behaviour is worrying, but nothing can substitute full-fledged preparation after two years of an intensive phase of the health system through COVID-19. Monkeypox can also be controlled and perhaps one day, like Smallpox, can be eradicated from this world with vaccination, appropriate treatment and personal protective measures.

Comment [MM2]: Make your abstract a single paragraph and keywords below it.

Introduction

Monkeypox virus is an Orthopoxvirus of the *Poxviridae* family that is of zoonotic origin. It is a double-stranded DNA virus similar to the eradicated smallpox virus. Monkeypox disease caused by this virus is mainly endemic to western and central African region.^{1,2} The disease is dubbed the “miniature smallpox”. In endemic regions of Africa, there are several reservoirs of this virus like wild rodents, mainly squirrels and Gambian pouched rats, and certain monkey species like cynomolgus monkeys from where the virus was first isolated. This zoonotic disease can accidentally cross-over to humans, resulting in epidemics of fatal nature. Throughout history, only two clades of monkeypox virus have been identified: the West African clade, and the Congo Basin (Central African) clade.³

The name monkeypox is because of the discovery of the virus in monkeys in a Danish laboratory in 1958. The first human case was identified in 1970 in a 9-year-old boy in the Democratic Republic of the Congo, where smallpox had been eliminated in 1968.^{2,4} Till 1986, cases had mostly occurred in children or adolescents under age of 16 in Central Africa, accounting for 85% of total cases, and from West Africa. The human monkeypox disease in West Africa have been found to occur in hot and humid forest weather conditions, and at lower elevations than in the Congo Basin.⁵ The disease usually affected immunologically naive subjects as only 13% of infected subjects presented vaccination scars from Smallpox.³ The recorded cases were caused by primary exposure to common animal source or human-to-human secondary transmission, and coincided with the period of most intensive human activity outdoors namely hunting and agricultural activities. An epidemiological investigation done by WHO in 1997 in Kasai region revealed risk factors for Monkeypox to be skinning and handling wild animals, close contact with a case and not being vaccinated against smallpox.⁶ There have been frequent outbreaks in 11 countries of Africa over the last

40 years. Ever since 2017, Nigeria has experienced a large outbreak with over 500 suspected and 200 confirmed cases, with a case fatality ratio of 3%.² All such minor zoonoses (monkeypox, cow-pox, camel-pox) which are re-emerging in the world could occupy the ecological niche that remained vacant after the disappearance of smallpox.⁷

Characteristics of the disease

The symptoms and signs noticed first in suspected individuals are vesicular rash with or without other symptoms such as fever, respiratory signs and lymphadenopathy (swollen lymph nodes). The eruption of rashes usually begins within 1–3 days of fever. They spread from the face, towards the limbs and finally the trunk, and usually clears in 2-4 weeks. The oral mucous membranes, conjunctivae, cornea and genitalia are affected in several cases. Monkeypox can cause complications including secondary infections, bronchopneumonia, sepsis, encephalitis, and loss of vision. The clinical difference of Monkeypox from Smallpox was the presence of lymphadenopathy, and a low case fatality rate (3-6%). Monkeypox is spread through close physical contact, such as lesions, body fluids, respiratory droplets, sexual contact and contaminated materials, even with mild illness.⁸ The incubation period is usually from 6 to 13 days, but it can range from 5 to 21 days, which is why the suspected cases are being quarantined at global transit points for 21 days to prevent transmission. The disease is said to be self-limiting but those with immune suppression, like children, pregnant women or persons suffering from other health conditions, can have severe disease. Cases have been identified including but not limited to amongst men who have sex with men (MSM) seeking care in primary and sexual health clinics. A study done between April to June 2022 in the UK showed that 98% of the persons with infection were gay or bisexual men, and 41% had human immunodeficiency virus infection.⁹ Monkeypox in these individuals can also occur commonly in co-infection with hepatitis A, B, or C.¹⁰ During human monkeypox outbreaks, having close contact with infected persons is the most significant risk factor for infection, with Health workers and household members being at a greater risk. For prevention purposes, isolation of infected patients, no contact with suspected animals and fomites along with good hand hygiene are of utmost importance.¹¹ Smallpox vaccination is considered 85% effective, however persons younger than 40 years of age in India are more susceptible to monkeypox due to cessation of smallpox vaccination campaigns after its eradication.¹²

Present global scenario

The disease has now garnered the attention of global public health as there recently has been reporting of several cases outside Africa. The first reported case was in the United States of America in 2003 which was linked to contact with infected pet prairie dogs. The patients reported fever with rashes evolving from a macule, papule, vesicle, then to pustule, finally forming dried crusts before falling off. On electron microscopy from the skin lesion of a patient and a tissue lymph node of the “prairie dog”, the virus was confirmed. Consequently, there were 79 cases in six states of the country, with 29 confirmed by laboratory results.³ Monkeypox has also been reported in travelers from Nigeria to Israel and the United Kingdom from 2018 till 2022, to Singapore in 2019, and to the United States of America in 2021. This disease has seen an huge uptick of cases since 1990.¹³ Even the reservoir animals of the virus in Africa and other countries are different. The encroachment of humans into forested areas, growing international travel and cessation of smallpox vaccination programmes are the main factors found in the epidemiology of monkeypox virus outbreaks.¹³ Monkeypox has been declared monkeypox as a disease of Global Health Emergency of International Concern on 23rd July 2022¹⁴, due to an explosion of non-endemic cases in 78 Member states across all 6 WHO regions, including India which has recorded 5 cases till date. Till 26th July 2022, around 18,880 cases of monkeypox have been globally confirmed, including 5 deaths in Africa.^{15,16} This demands our attention to prepare

for increased transmission within India at the time of worldwide rise of emerging zoonotic viruses.^{2,17} This is a highly unusual caseload for the disease. In order to control the transmission of the disease in these outbreak regions, continuous detection of the virus are being done by established surveillance mechanisms along with contact tracing, clinical management, isolation, laboratory investigation, genomic sequencing of DNA (where available) and implementation of infection prevention and control measures. IEC materials, infographics are being used to raise awareness, while these countries are on the fast-track to procure vaccines. A new two-dose vaccine (MVA-BN) based on the Ankara strain of the attenuated vaccinia virus was approved for the prevention of monkeypox in 2019. Most of the monkeypox virus genes detected belong to the West African clade. Two types of vaccines (ACAM-2000 and MVA-BN) are being currently deployed for prophylaxis in case of close contacts. But their availability remain very limited.^{2,3,17} Right now, Bavarian Nordic remains the only company with stockpile of Monkeypox vaccines which are already being procured by the developed nations such as USA and UK-NHS.¹⁸ Government of India has invited expression of interest (EOI) by August 10th 2022, from vaccine manufacturers and in-vitro diagnostic kit manufacturers for collaborating in production of vaccine against monkeypox virus (MPXV).¹⁹

Position of India

WHO has now defined international guidelines and case definitions to detect MPXV. It has recommended to mount a coordinated response to stop transmission, engage and protect the vulnerable populations in the society, intensify surveillance, strengthen infection control and management, and finally accelerate research into use of vaccines and therapeutics.²⁰ A person of any age presenting in a non-endemic country with an unexplained acute rash unrelated to any known clinical cause, along with either headache, acute fever onset, lymphadenopathy, myalgia, asthenia and back pain, is a *Suspected case*. Such a suspected case having epidemiological link or direct contact, travel history to endemic country within previous 21 days, has had multiple sexual partners within 21 days before symptom onset, hospitalized or having a positive serological result is a *Probable case of Monkeypox*. Finally, the cases who had been detected by unique viral DNA sequencing by real-time polymerase chain reaction (PCR) are *Confirmed cases of Monkeypox*.⁴ In India, the National Institute of Virology, Pune has released updated case reporting form of fever with rashes through the Integrated Disease Surveillance Programme portal. One sample from the regional IDSP will be accepted for MPXV testing at VRDL, second referred to NIV Pune, and third stored for future testing.²¹ The NCDC, MoHFW has emphasized on several public health actions in the event of suspected cases being reported from India. They are:

- i. Health facilities are to keep heightened suspicion in people who are suspected or a probable case of Monkeypox.
- ii. All suspected cases to be isolated until all lesions have resolved OR until the treating physician decides to end isolation.
- iii. All such cases are to be reported to the District Surveillance officer of the IDSP.
- iv. Infection control practices should be maintained while treating patients.
- v. Laboratory samples such as fluid from vesicles, blood, sputum are to be sent to NIV Pune, and in case a positive case is detected, the contacts of the patient within 21 days are to be determined and quarantined.¹²

There are a number of factors which may render Monkeypox as a serious public health problem in India, starting with the subtropical climate, and overpopulation with high transmission rates. The first laboratory-confirmed case was reported on July 14th 2022 in a 35 year-old male from Thiruvananthapuram, Kerala, upon returning from UAE.²² The next two cases were also confirmed from Kerala on July 18th and 22nd.²³ New Delhi reported its first

MPXV case in a 34 year-old man on July 24th with no history of travel, unlike the previous cases.²⁴ The area continues to be on high alert as a 47-year-old woman has approached the health department on July 26th and is currently the 5th in the growing list as a suspected case of MPXV.²⁵ There is currently an ongoing surveillance in the community, primary care, fever clinics, sexual health clinics, infectious disease units, obstetrics and gynecology, and dermatology clinics. Contact tracing should be initiated as soon as there is suspected case identification. The patients are to be interviewed to elicit the names and contact information of all contacts, who should be notified within 24 hours of identification. The contacts would then be kept in isolation for 21 days.²⁶ But we need to address the elephant in the room, that is, our vulnerability to the disease which has been spreading across geographical barriers quite rapidly. A huge section of the Indian population (40%) are young (13-35 years)²⁷ and not immunized against it. The Smallpox vaccine is the most readily available protective agent against this disease, and it needs to be stockpiled to be deployed in case of an outbreak in the country. The disease is neither novel nor very mutable, so if our country is adequately prepared, there is less chance of this becoming a big public health concern. Healthcare workers should wear the personal protective equipment (PPE) while dealing with a Monkeypox patient. The patient should also be instructed to wear a medical mask when they come within 1 metre of health workers or other patients. According to WHO, an antiviral agent (Tecovirimat) has also been developed for the treatment of Monkeypox in 2022. However, this drug and the new vaccine MVA-BN are not available en-masse, so India needs to be prepared by monitoring the transit points of global and domestic travels, and making the citizens aware about the disease epidemiology and signs.⁴ ICMR has published guidelines for symptomatic treatment by managing protection of compromised skin and mucous membranes, rehydration and nutritional therapy along with other symptom alleviation.²⁶

Increased surveillance and detection of cases are essential to understanding the continuously changing epidemiology of this resurging disease. The need for *One Health* is now more than ever. A Clinical Trial named “A One Health Study of Monkeypox Human Infection (AFRIPOX)” by Institut Pasteur de Bangui in Central African Republic is currently underway.²⁸ The identification of risk factors for zoonotic and human-to-human transmission of the virus, animal reservoirs, post-vaccination immunity status of individuals vaccinated against Smallpox, the comparison of circulating strains between human and animal populations, development of diagnostics and next-generation sequencing are all required for tackling this disease in India.²⁹ The Healthcare workers could use a method called ‘ring vaccination’ that would vaccinate the close contacts of people who have been infected with monkeypox to cut off any routes of transmission. The Ministry of Agriculture and Ministry of Fisheries, Animal Husbandry and Dairy are involved with MoHFW to formulate an integrated action plan against any scenario possible. WHO has also recommended consultations with the Strategic and Technical Advisory Group on Infectious Hazards (STAG-IH), the SAGE working group on smallpox and monkeypox vaccines, Advisory Committee on Variola Virus Research, the Scientific Advisory Group for the Origins of Novel Pathogens (SAGO), the Emergencies Social Science Technical Working Group, and the WHO Research & Development Blueprint consultation regarding Monkeypox research.³⁰

Conclusion

With Monkeypox spreading globally, the number of cases detected outside of Africa in the last week alone has crossed the total number detected outside the continent since 1970.³¹ Since ethnicity, health behaviour, hygienic conditions and transmissibility are very different in our country from the West and African regions, we need stringent preparations tailored to our needs to combat this virus in India. Viral behaviour is worrying, but nothing can substitute full-fledged preparation after two years of an intensive phase of the health

system through COVID-19. Monkeypox can also be controlled and perhaps one day, like Smallpox, can be eradicated from this world with vaccination, appropriate treatment and personal protective measures.

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