**Basic Mini Review**

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# Monkeypox scenario in India: a review study

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**Abstract:** The monkeypox virus, which causes the viral zoonotic disease, is known as the most significant orthopoxvirus infection following the elimination of smallpox. The monkeypox virus, which was previously exclusive to West and Central African nations and caused endemic diseases in monkeys and people, has recently been linked to human infections in non-endemic areas including the United States of America (USA) and more than 30 additional countries. Guidelines for the diagnosis and treatment of monkeypox have also recently been made available by the Ministry of Health and Family Welfare of India and the Indian Government. The monkeypox outbreak continues to be a worldwide health emergency, the highest degree of alert recognised by the World Health Organization. The Centers for Disease Control and Prevention (CDC) advises vaccination for those who have been exposed to the disease as well as those who may be at higher risk of contracting it, such as those who have been identified by public health officials as a contact of someone who has the disease.

**Keywords:** monkeypox; polymerase chain reaction; vaccination; virus.

## Introduction

Monkeypox, a DNA virus belonging to genus Orthopoxvirus, is a zoonotic disease which was first noticed in Congo as the human infection [1]. World Health Organization (WHO) has declared monkeypox as the danger to life on 23rd June 2022 due to the reporting of successive increase to about 3,000 cases in as much as 50 countries [2, 3].

There have been various factors which are responsible for the human transmission which includes contact with the fluids of body, lesions in cutaneous region. Transmission from infected animals through respiratory droplets is also responsible for infection either through direct contact or contaminated passive vectors (fomites). As the herd immunity is getting lower, there has been spike in the terror due to Monkeypox infection [4]. The practice of isolation in the hospital settings with provision of negative pressure room and awareness of standard Contact and droplet precautions has been under strong recommendation by the Centers for Disease Control and Prevention (CDC).

The monkeypox virus enters the human body through any of the routes like oropharynx, nasopharynx, or intradermal. After entering the body, the replication begins at the site of viral inoculation from where the virus enters the lymph nodes present locally. The other organs also get infected gradually due to viremia. The maximum incubation period of the infection is 21 days with usual range of 7–14 days [5]. There have been reports with cases of vertical transmission and death of fetus [6]. There has been increase in Monkeypox cases in males having sex with other males (MSM). The experts have raised worry also that this would lead to discrimination against gay men [7]. The sexual behaviour of the four Italian cases [8] and the initial distribution of lesions, primarily in the anal and vaginal regions, all point to the importance of intimate contact during sexual activity for virus transmission.

The Congo Basin (CB) clade, also known as the Central Africa clade, and the West African (WA) clade are two additional genetic subgroups of the monkeypox virus [9]. While the WA clade has been documented from Western Cameroon to Sierra Leone, the CB clade has been found from Central and Southern Cameroon to the Democratic Republic of the Congo. The CB clade is thought to be more virulent with extremely high rates of interhuman transmission, serial transmission events, and secondary attack rates, whereas the WA clade is the milder one [10].

Infection with the monkeypox virus activates cellular and humoral immune responses that limit the replication of virus and create long-lasting protection in patients who have recovered. After a natural infection with monkeypox the body produces orthopoxvirus-specific IgM and IgG antibodies against a variety of antigen targets, along with long-lasting residual IgG-memory B cells [11–13] that guard against re-infection or the onset of severe disease.

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A rapid increase in activated effector CD4+ and CD8+ T cells is a hallmark of the cellular immune response following monkeypox infection or vaccination against the vaccinia virus [12, 14, 15]. This increase is followed by a gradual decline that typically returns to normality 12–20 days after the onset of symptoms [12]. The majority of patients have specialised T cells that may release a variety of Th1 inflammatory cytokines (including MCP-1, IFN-, IL-1, IL-6, and IL-8).

## History

Several more outbreaks of monkeypox were documented in captive monkey colonies in the US and Netherlands between 1960 and 1968 [16]. Despite the deaths of many infected animals during these epidemics, no human cases were found, suggesting that people were immune to monkeypox [16]. In 1970, the national smallpox surveillance and eradication programme was started in Africa where the first case of monkeypox in a human was reported [1]. The patient was a 9-month-old boy with fever, which was followed by centrifugal rash after two days (i.e., a rash with the majority of lesions on the arms and legs). Six further cases of monkeypox were found in humans in West African nations between September 1970 and March 1971. None of these patients had received a smallpox vaccination, and the majority were young children [17].

## Epidemiology

In the current outbreaks being reported, the WHO claims that this is the first time that chains of transmission have been reported in Europe without known epidemiological connections to West or Central Africa. In several other central and western African nations, including Cameroon, Central African Republic, Cote d'Ivoire, Democratic Republic of the Congo, Gabon, Liberia, Nigeria, Republic of the Congo, and Sierra Leone, monkeypox has been documented as being endemic. The United States, the United Kingdom, Belgium, France, Germany, Italy, the Netherlands, Portugal, Spain, Sweden, Australia, Canada, Austria, the Canary Islands, Israel, and Switzerland are just a few of the non-endemic nations where this has been documented. As of May 31st, 2022, India has not had any cases of the monkeypox virus reported [18]. With the first case in India, there has been progressive rise in the cases in various parts of India. There were 10 cases in India as reported till August 13th 2022 with 30 % cases (3/10) who do not have history of travel or close contact with each other (Table 1). The state-wise distribution till August 13 is shown in Table 2 in which it is shown that the States of Uttar Pradesh, Bihar, and Telangana also reported numerous suspected cases, however the only states with lab-confirmed monkeypox (MPX) cases are Delhi and Kerala. Figure 1 shows the epidemic curve of the suspected and confirmed cases of monkeypox.

## Diagnostic approach

When rash diseases including syphilis, measles, chickenpox, bacterial skin infections, scabies, and drug allergies are present, it is possible to make a clinical diagnosis of monkeypox infection. One distinguishing hallmark of monkeypox infection from chickenpox or smallpox infection is the presence of lymphadenopathy during the prodromal stage of illness. The polymerase chain reaction (PCR), the standard laboratory test for skin lesion samples, can be used to check for the monkeypox virus in order to confirm the diagnosis. Since the virus cannot persist in blood for an extended period of time, PCR blood tests are typically inconclusive. To interpret test results, it is necessary to know the patient's age, the date the fever first appeared, the rash's current stage, and the date the samples was taken [30]. The majority of positive PCR results (97 %) came from cutaneous or anogenital lesions; fewer samples were taken from other sites. The percentages of positive PCR results for nasopharyngeal specimens (26 %), urine specimens (3 %), and blood specimens (7 %), respectively, were reported. A total of 32 people from five clinical sites had their semen examined, and a total of 29 of them had PCR positive results (4 of these instances have previously been reported) [8].

In contrast, tests which can demonstrate the presence of orthopoxvirus in a patient specimen and has the potential to prohibit the exposure of the monkeypox infected person to another virus of the same genus, can form important part of the diagnosis. These tests include detection by electron microscopy, staining methods for orthopoxvirus antigens such as immunohistochemical staining, and diagnosis of antibodies: anti-orthopoxvirus IgM and IgG for recent exposure and vaccination/past exposure respectively [30]. If the patient has not been exposed to another orthopoxvirus of the same genus, serum anti-orthopoxvirus IgM antibody testing may be sufficient for diagnosis in low-income nations [31].

The cases of the monkeypox virus are categorised as suspected, probable, and verified according to Indian criteria of Ministry of Health and Family Welfare (MOHFW). Any individual, regardless of age, who has been to one of the affected nations during the preceding 21 days and has an unexplained rash in addition to one or more of the crucial

**Table 1:** Demographic details of monkeypox confirmed cases in India (July to August 2022).

| No. | Gender | Age | Region of positivity | Date of diagnosis | History od travel in last 21 days | Authors |
|---|---|---|---|---|---|---|
| 1 | Male | 35 years | Kollam, Kerala | 14th July 2022 | Yes (travelled from UAE) | Philip Shaju [19] |
| 2 | Male | 31 years | Kannur, Kerala [20] | 18th July | Yes (travelled from Dubai) | – |
| 3 | Male | 35 years | Malapurram, Kerala | 22nd July | Yes (from UAE) | Philip Shaju [21] |
| 4 | Male | 34 years | Paschim Vihar, New Delhi | 25th July | Yes (from Himachal Pradesh, India not overseas) | Jha Nandan Durgesh [22] |
| 5 | Male | 22 years | Thrissur, Kerala [23] | 31st July | Yes (from UAE) | – |
| 6 | Male | 35 years | New Delhi | 1st August | No (Nigerian person resident of Delhi, India) | Bhardwaj Shalini [24] |
| 7 | Male | 30 years | Malapurra, Kerala [25] | 2nd August | Yes (travelled from UAE) | – |
| 8 | Male | 35 years | New Delhi | 2nd August | No (Nigerian person resident of Delhi, India) | Pillai Saumya [26] |
| 9 | Female | 31 years | New Delhi | 3rd August | No (Nigerian person resident of Delhi, India) | Sharma Milan [27] |
| 10 | Female | 22 years | New Delhi | 13th August 2022 | Yes (travelled from Nigeria) | Pillai Saumya [28] |

UAE, United Arab Emirates.

**Table 2:** Distribution of suspected and confirmed cases of monkeypox according to states of India [29].

| State | Suspected cases with negative PCR result | Confirmed cases with positive PCR result | Total cases |
|---|---|---|---|
| Kerala | 0 | 05 | 05 |
| Delhi | 01 | 05 | 06 |
| Telangana | 01 | 0 | 01 |
| Uttar Pradesh | 04 | 0 | 04 |
| Bihar | 02 | 0 | 02 |
| Total | 08 | 10 | 18 |

signs and symptoms is deemed to be a suspected case (fever, headache, body ache, swollen lymph nodes, and weakness). The word “potential case” refers to a suspected case with a clinically comparable illness and denotes a probable epidemiological relationship, such as direct contact with skin or skin lesions, sexual intercourse, or contact with contaminated clothing, utensils, or bedding. A monkeypox case is considered to be validated if it has been identified using PCR or sequencing [18].

According to Indian recommendations, even one case of monkeypox will be regarded as an outbreak. These guidelines also include specific surveillance measures to quickly identify and control cases and clusters of infection as soon as feasible. In addition to contact tracing and testing of all symptomatic cases after the detection of probable or confirmed cases, the core surveillance tactics include hospital-based and targeted surveillance [32].

## Complications

The presence of swollen glands helps to distinguish the sickness from chickenpox, measles, and smallpox. Early symptoms often include a headache, muscle aches, fever, and fatigue. After a few days of the fever, lesions frequently start on the face and then spread centrifugally to other parts of the body, like the soles of the feet and palms of the hands [33–35]. Before converting into scars when the lesions have healed, they may leave behind pale traces [35]. Possible consequences include pneumonia, encephalitis, blindness, and subsequent infections. There’s a chance of

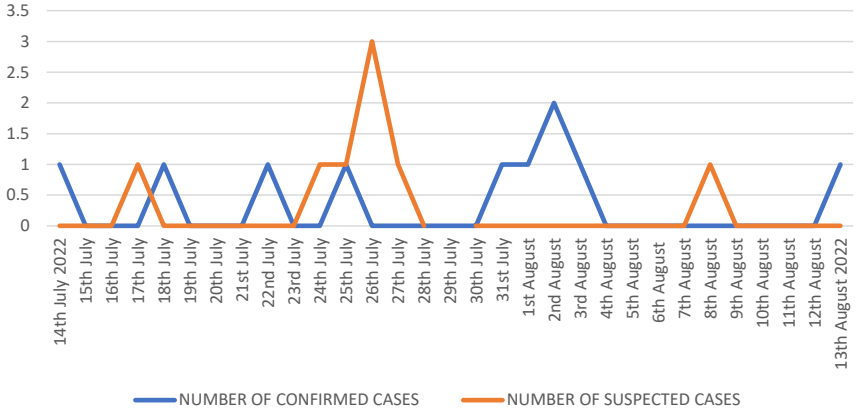


**Figure 1:** Epidemic curve with confirmed (n = 10) and suspected (n = 8) cases of monkeypox till 13th August 2022.

stillbirth or birth defects if an infection develops during pregnancy [36]. In people who received a smallpox vaccination as youngsters, the illness might be less severe [37].

## Treatment

As first-line antiviral therapy and supportive care, British Medical Journal (BMJ) Best Practice suggests using the two Food and Drug Administration-approved medications tecovirimat or the smallpox medicine brincidofovir (including oxygenation, antipyretic, and fluid balance) [38]. If a bacterial infection or subsequent varicella-zoster is suspected, aciclovir or empirical treatment may be used [39]. The United States Food and Drug Administration (USFDA) and CDC have licenced the antiviral Tecovirimat (a protein inhibitor that targets the gene encoding p37—an envelope protein) [40] for the treatment of patients of monkeypox [41]. Also, because both viruses are members of the same family (Orthomyxovirus), prior studies and fieldwork have demonstrated that the smallpox vaccine may be quite helpful in preventing occurrences of monkeypox [42]. The Indian Council of Medical Research (ICMR) in India has asked pharmaceutical companies to develop diagnostic tools and vaccinations for monkeypox.

India has so far primarily advised supportive management and isolation of the confirmed cases, including protection of the compromised mucous membranes and skin (rash, conjunctivitis, oral, and genital ulcers), oral rehydration and adequate nutrition, and symptom relief for fever, nausea/vomiting, pruritus, malaise/headache, and other symptoms using paracetamol, antihistaminics, topical ointments, antiemetics, etc. Close monitoring of the side effects, such as eye pain or blurred vision, dyspnea, changed consciousness, seizures, poor oral intake of meals, and excessive lethargy, is also necessary [18].

## Prevention

### General measures

The management of monkeypox cases is possible by proper academic training for medical practitioners. It is necessary to promote health in vulnerable populations with targeted testing and education that is compassionately supported. To ensure that public health measures are appropriate and nonstigmatizing and to avoid messaging that will push the outbreak underground, communities must be involved from the beginning in structuring their implementation. Following infection, condom use is encouraged according to UKHSA guidelines for 8 weeks; however, further research is needed to determine the probable length and contagiousness of viral shedding in semen [43].

### Vaccination

In the UK, New York City, and Canada, vaccines are currently being provided to people who are at a high risk of contracting an infection [39]. Anybody who has had close or personal contact with monkeypox-infected people or animals is also advised to get vaccinated [44].

ACAM2000 and MVA-BN are the available vaccines for controlling the current outbreak. The Food and Drug Administration (FDA) has given the second generation live, attenuated vaccinia virus vaccine ACAM2000 (Emergent BioSolutions) approval for use either before or after exposure to monkeypox. Although there is a chance of cardiac complications, it is effective [45]. The JYNNEOS vaccine, which is presently being used to treat monkeypox, was developed using the modified vaccinia ankara (MVA) employed in the 1970s German smallpox eradication campaign to immunise more than 100,000 people [46]. Developed by Bavarian Nordic, MVA-BN is a third-generation live, attenuated, nonreplicating, modified vaccinia Ankara vaccine. The vaccine was granted FDA approval in 2019 for use in preventing monkeypox in addition to the prevention of smallpox in the United States and Europe [47].

## Major initiatives in India

Ministry of Health and Family Welfare (MOHFW) had proposed guideline to tackle monkeypox in three significant government hospitals in Delhi—Vardhman Mahavir Medical College (VMMC) Safdarjung, Ram Manohar Lohia (RML) Hospital, and Lady Hardinge Medical College. The government had also taken steps to make isolation rooms operational. It was then enlarged to include three additional hospitals: the Dr. Baba Saheb Ambedkar Hospital, the Lok Nayak Jai Prakash Narayan (LNJP) Hospital, and the Guru Teg Bahadur (GTB) Hospital (10 rooms). In India, National Institute of Virology (NIV) Pune has been the nodal centre for monkeypox diagnosis by RT-PCR [48, 49]. With due course of time, ICMR has given permission to 15

additional institutions to conduct the RT-PCR test for confirmation [50, 51]. All of the recovered monkeypox virus (MPXV) sequences from India are lineages of the A2 which is of clade 2b, according to ICMR research.

## Future perspectives

No matter how the monkeypox medications are approved, randomised clinical trials are required to assess their efficacy. Such experiments are being carried out by the WHO and various nations, particularly using tecovirimat [52, 53]. This assessment needs to be carried out not only in the nations where the present outbreak is occurring, but also in regions where the illness is endemic. Given the possibility for first-line medicines to develop resistance, availability of second-line medications may be crucial. In the United States, Vaccinia immune globulin, pure plasma gamma globulins extracted from individuals immunised with live vaccinia virus vaccine [54], is approved for the treatment of smallpox vaccination sequelae. Monoclonal antibodies and chemical compounds are two other treatments that are currently in development. Phase 1 studies for the synthetic tecovirimat counterpart NIOCH-14 were successful [55]. Preclinical trials for monoclonal antibodies are already underway in numerous facilities [55].

## Conclusions

In some areas where the disease is endemic, an increase in the prevalence of monkeypox may be partially explained by a gradual loss of immunity to smallpox. But the present pandemic serves as a timely reminder that viral emergence is a constant phenomenon without bounds that is frequently unforeseen in its origin, aim, and scale. There is need to further have in depth understanding of vaccination which is possible by encouragement of manufacturers to routinely test dosage administration in next clinical vaccine trials and vaccination of high risk patients.

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