



Review

Insights into the emergence and evolution of monkeypox virus: Historical perspectives, epidemiology, genetic diversity, transmission, and preventative measures



Smriti Krishna^{a,1}, Chhaya Kurrey^{b,1}, Manisha Yadav^a, Shakuntala Mahilkar^c,
Subash Chandra Sonkar^{a,d,*}, Naveen Kumar Vishvakarma^b, Anand Sonkar^e, Lal Chandra^f,
Bidhan Chandra Koner^{a,f,*}

^a Multidisciplinary Research Unit, Maulana Azad Medical College and Associated Hospital, New Delhi 110002, India

^b Department of Biotechnology, Guru Ghasidas Vishwavidyalaya, Bilaspur, Chhattisgarh 495009, India

^c Vector-borne Diseases Group, International Center for Genetic Engineering and Biotechnology (ICGEB), New Delhi 110067, India

^d Delhi School of Public Health (DSPH), Institute of Eminence, University of Delhi, New Delhi 110007, India

^e Department of Botany, Hansraj College, University of Delhi, New Delhi 110007, India

^f Department of Biochemistry, Maulana Azad Medical College and Associated Hospital, New Delhi 110002, India

ARTICLE INFO

Keywords:

Orthopoxvirus

Monkeypox outbreak 2022

Clade IIb

Transmission

Vaccines

ABSTRACT

In 2022, just before the COVID-19 pandemic ended, many countries noticed a viral monkeypox outbreak. Monkeypox virus, a zoonotic pathogen, causes a febrile illness in humans and resembles smallpox. Prevention strategies encompass vaccination, strict infection control measures, and avoiding contact with infected persons. As monkeypox and related poxviruses continue to pose challenges, ongoing surveillance, early diagnosis, prompt isolation, and effective control measures are crucial for limiting transmission and mitigating the impact of outbreaks on public health. This review provides valuable insights into the evolution of the monkeypox virus and its various modes of transmission, including postmortem transmission, and offers an overall perspective on the guidelines issued by the Government of India to prevent and effectively control the spread of this disease.

1. Introduction

Monkeypox, or “mpox”, is caused by the monkeypox virus (MPXV), a member of the subfamily Chordopoxvirinae and genus *Orthopoxvirus* within the family Poxviridae [1,2]. The Poxviridae family is a family of large, complex, double-stranded DNA viruses infecting various vertebrate hosts, including humans. *Orthopoxvirus* is the most studied genus and includes the variola and vaccinia, camelpox, cowpox, canarypox, raccoonpox, deerpox, and goatpox viruses. All of the members of this family are zoonotic viruses except the variola virus and molluscum contagiosum virus, which primarily infect humans

[1,3]. Members of this family are characterized by a brick-shaped structure, and these entities possess an extensive genome that encodes a diverse array of both structural and non-structural proteins [1,4]. In 1958, the virus was initially recognized in Denmark within research monkeys utilized as animal models, which led to it being labelled “monkeypox”. Subsequently, the first incidence in humans was documented in 1970 in the Democratic Republic of the Congo (DRC) [5]. In recent years, there has been an increasing occurrence of monkeypox cases in countries where the disease is not endemic. Notably, in the year 2022, India reported its first documented case of monkeypox [6].

Abbreviations: MPXV, Monkeypox virus; ITR, Inverted terminal repetitions; ORF, Open reading frames; MOGAD, Myelin oligodendrocyte glycoprotein antibody-associated disease; CSF, Cerebrospinal fluid; APOBEC3, Apolipoprotein B editing complex.

* Corresponding authors.

E-mail addresses: dsph.scsonkar@ioe.du.ac.in (S.C. Sonkar), bc.koner@nic.in (B.C. Koner).

¹ These authors contributed equally to this study.

<https://doi.org/10.1016/j.imj.2024.100105>

Received 9 October 2023; Received in revised form 15 February 2024; Accepted 28 March 2024

2772-431X/© 2024 The Author(s). Published by Elsevier Ltd on behalf of Tsinghua University Press. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

Monkeypox is transmitted through a dual route involving viral transfer from animals to humans and between humans. The virus resides in its natural reservoir in small mammals such as rodents and monkeys. Humans can contract the virus through direct interaction with infected animals, including activities like handling or consuming their flesh, as well as through exposure to contaminated materials or surfaces [7–9]. The symptoms of monkeypox virus infection resemble those of a less severe form of smallpox, with fever, rashes, and fatigue, which then advance to a state of profound weariness [10–13]. Prompt and accurate monkeypox diagnosis is pivotal in efficiently controlling disease outbreaks and epidemics. At present, polymerase chain reaction (PCR) is the diagnostic assay recommended by the World Health Organization (WHO) and Ministry of Health and Family Welfare (MoHFW) of the Government of India [14,15]. This comprehensive review encapsulates insights into the virus, its evolutionary trajectory, modes of transmission, diagnostic approaches, and preventive strategies. By delving into these facets, we will be poised to enhance our preparedness and substantially mitigate potential future outbreaks.

2. Epidemiology

Monkeypox virus was initially identified in 1958 among captive *Macaca fascicularis* monkeys in Copenhagen, Denmark. However, the actual origin of the virus remains a topic of debate due to the fact that the monkeys introduced to Denmark in 1958 were sourced from Singapore rather than Africa, which is traditionally associated with the virus [5]. The initial presentation consisted of a generalized petechial rash that quickly progressed into a maculopapular eruption. Lesions were observed across the entire torso, tail, face, and limbs of the animals. In these areas, the papules were relatively large and exuded fluid resembling pus. The clinical symptoms observed for the disease strongly indicated a potential relationship between the causative agent and viruses belonging to the variola-vaccinia group. Consequently, several experiments were conducted to investigate the antigenic similarity between the isolated strain and the vaccinia virus [7]. Later in 1970, the first human case of monkeypox was reported in the DRC in a 9-year-old boy with fever and chicken pox-like symptoms. A monkeypox-like virus was isolated and, despite early detection, the patient succumbed.

Seventy-two percent of monkeypox cases have been attributed to zoonotic transmission, with the majority occurring in children of an average age of 4.4 years [16]. A significant 20-fold increase in the number of cases in DRC was documented from the 1980s to the mid-2000s [17]. Cases have been reported in distinct African nations, including Benin, Cameroon, the Central African Republic, the Democratic Republic of the Congo, Gabon,

Liberia, Nigeria, the Republic of Congo, Sierra Leone, Zaire, and the Ivory Coast [5]. While the majority of monkeypox cases have been concentrated in Africa, there have been sporadic instances of limited viral spread to regions beyond the continent, including Europe and North America. An unusual disease pattern was observed in non-endemic countries such as the United Kingdom, the United States, Singapore, India, and others, which led the World Health Organization (WHO) to declare monkeypox a Public Health Emergency of International Concern (PHEIC) in May 2022 [17]. These cases were often linked to individuals who have travelled from areas where monkeypox is endemic, highlighting the potential for international transmission. Nonetheless, it is important to note that the overall incidence of monkeypox outside of Africa remains relatively low compared to its prevalence within the continent [7].

3. Virology

3.1. Virus structure and life cycle

Poxviruses have a unique structure compared to other viruses (Fig. 1A). The life cycle of poxviruses involves several stages, including entry into host cells, replication of viral DNA, assembly of viral components, and release of mature virions (MV). During the assembly stage, the viral particles go through a process called morphogenesis, when they acquire their final structure and become infectious. This process takes place within the cytoplasm of infected cells. MV are typically brick-shaped or ovoid in appearance, with a size of 200–250 nm, and have a complex structure. They each consist of an outer envelope derived from the host cell's plasma membrane, which surrounds a core containing the viral genome, enzymes, and structural proteins. The core is further organized into the viral genome and lateral bodies, which are involved in viral replication and morphogenesis. Once the virions are fully assembled, they are released from the infected host cell by cell lysis or through a process called budding, at which point they acquire their envelope from the cellular membrane. These mature virions can then infect neighboring cells or be transmitted to new hosts, initiating the infection cycle [1,4] (Fig. 1B).

3.2. Viral genome

The viral genome is large, ranging from 130 to 300 kilobase pairs (kbps) and has inverted terminal repetitions (ITRs), which are a characteristic feature of poxviruses (Fig. 2). Within the ITRs of poxvirus genomes, there is a conserved region of fewer than 100 base pairs that contains an A+T-rich hairpin loop. This hairpin loop, characterized by incomplete base pairing, plays a crucial role in maintaining the stability of the viral genome.

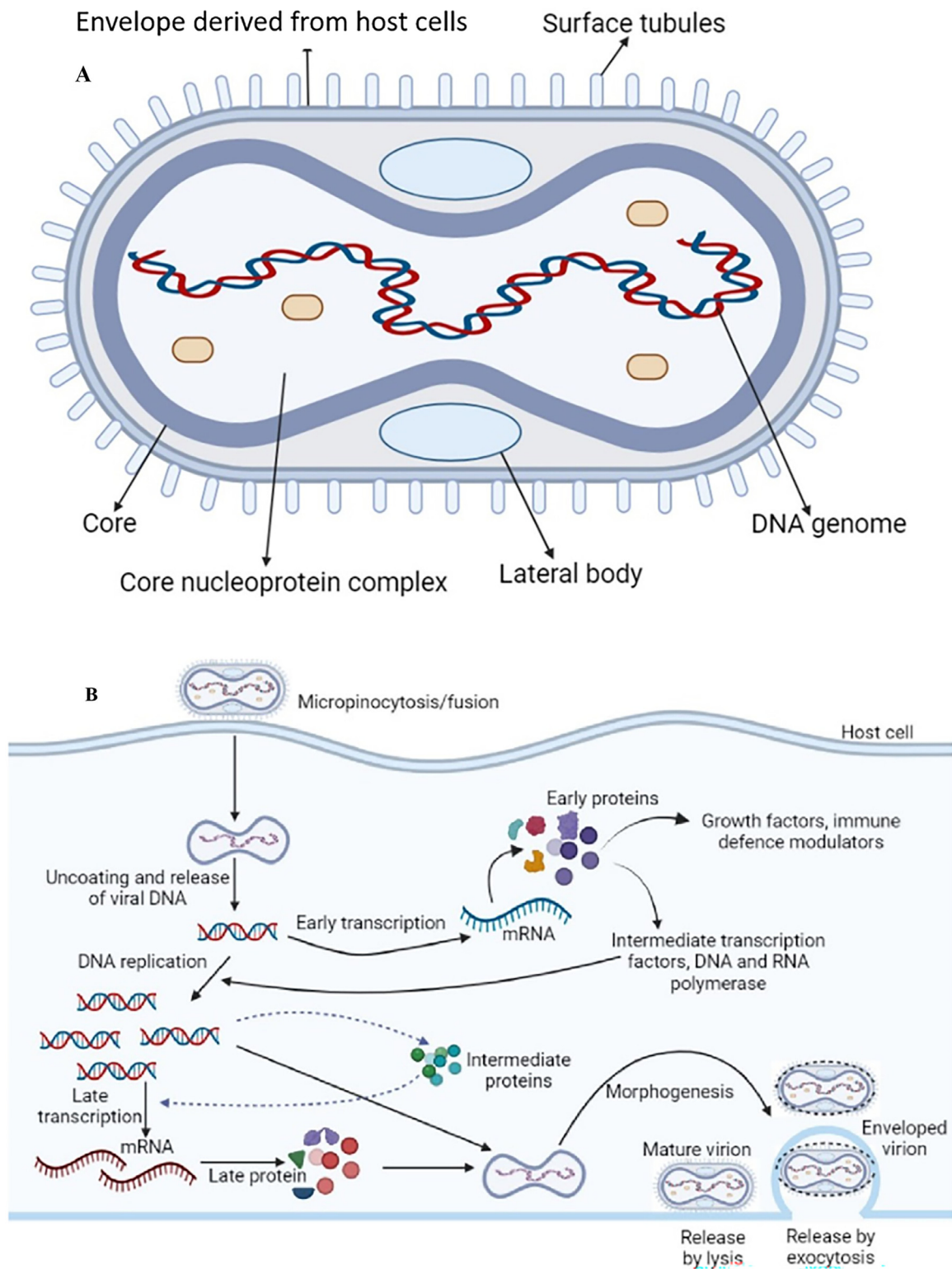


Fig. 1. (A) The general structure of the Poxviridae family is a brick-shaped outer membrane with dsDNA genome present in the core. (B) Viral pathogenesis begins with viral entry into the host cell membrane, followed by transcription, translation, replication, and the release of mature virions, facilitating further viral spread.

The ITRs may include one or several open reading frames (ORFs), which are regions of DNA that can potentially encode proteins. The ORFs within the ITRs may have various functions, such as regulating viral gene expression or modulating host immune responses [1].

4. Evolution

Epidemiologically, MPXV has evolved into two clades, West African and Congo Basin. The epidemiological and clinical characteristics of the diseases caused by these

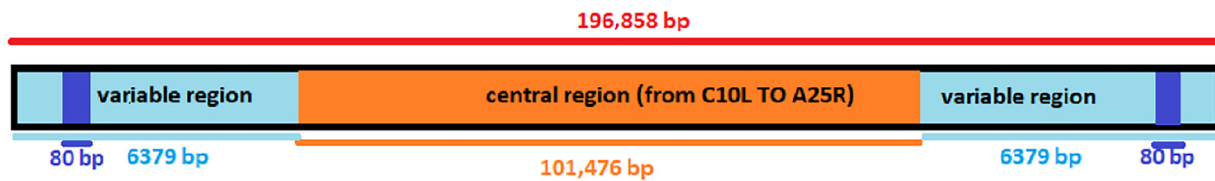


Fig. 2. The genomic structure of the monkeypox virus comprises approximately 196,858 bp, with the central genomic region spanning 101,476 bp. The terminal ends of the genome exhibit variability and include a 6379-bp terminal inverted repetition (ITR) containing a hairpin loop of approximately 80 bp.

two monkeypox virus clades differ significantly. Clade I (Congo Basin Clade) exhibit a case-fatality rate of up to 10%, whereas Clade II (West African Clade) has a much lower case-fatality rate of approximately 1%. The West African Clade is the most widespread and commonly reported variant of monkeypox. It is primarily found in West and Central African countries, including Nigeria, Cameroon, and the DRC. The Congo Basin Clade is primarily found in the central regions of the DRC, particularly in the Congo Basin forested areas. It has been associated with more severe and extensive disease manifestations compared to other variants [5,16]. Clade II includes the IIa and IIb subclades. Clade II is linked to less severe illness, lower mortality rates, and a reduced capacity for human-to-human transmission in comparison to Clade I [18,19]. The Clade IIb virus has been further classified into A.1, A.1.1, A.2, A.2.1, A.2.2, A.3, and B.1 lineages [20]. The primary distinctions between these clades are found in the coding regions, particularly those related to immunomodulatory factors and host-pathogen interaction. This significant divergence and the initial indications of sub-clustering might be linked to the various epidemiological conditions observed during outbreaks [21].

4.1. Re-emergence of the monkeypox virus

In May 2022, several countries in Europe and Australia reported monkeypox infections, prompting Belgium to implement a mandatory 21-day quarantine for monkeypox. In late May, the United Arab Emirates (UAE) confirmed its first case from West Africa. Over 6000 cases of monkeypox were reported across 60 countries in the year 2022. The source of the outbreak is yet to be confirmed, but the evolving nature of monkeypox suggests possible human-to-human and/or animal-to-human transmission was involved. It is believed that the causative agent of the current outbreak belonged to Clade II (West African Clade) of the group [22,23].

In November 2023, a total of 906 new laboratory-confirmed cases of monkeypox emerged across 26 countries worldwide. The areas most affected, ranked by the number of confirmed cases, were the WHO's Region of the Americas, the European Region, the Western Pacific Region, the South-East Asia Region, and the African Region. According to global surveillance data, the mpox outbreak persists across most WHO regions, with low transmission

levels noted in the Western Pacific and South-East Asia. Conversely, the European Region and the Region of the Americas exhibit more widespread transmission, while the African Region reports a comparatively lower count of confirmed laboratory cases [24].

4.2. Monkeypox outbreak in India

The first case of monkeypox in the WHO's South-East Asia Region was reported in India, when a 35-year-old man from UAE arrived in Kerala. The person had a fever and rashes, which eventually healed, and the person completely recovered. Following this, a total of 25 cases were reported in different parts of India, including New Delhi, Uttar Pradesh, Bihar, Telangana, and Rajasthan. Most of the affected individuals had an international travel history. To date, there has been a single recorded fatality, which involved a 22-year-old male. He had been living in the UAE and was in close contact with a confirmed monkeypox case. He returned to his hometown in Kerala, where he unfortunately succumbed to encephalitis [14,25]. Previously, encephalitis resulting in fatality had been reported as a complication of monkeypox. However, cases of encephalitis associated with the monkeypox virus in immunocompetent individuals are rare and can be attributed to either direct infection or autoimmune encephalitis, such as myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) triggered by viral infections. In this particular case, the clinical and neuro-imaging features strongly suggested direct monkeypox encephalitis rather than MOGAD. However, the possibility of MOGAD could not be definitively ruled out due to the unavailability of serum and cerebrospinal fluid (CSF) specimens for further testing. Extensive testing was conducted to exclude other common causes of encephalitis, including the Japanese encephalitis virus, West Nile virus, and Nipah virus [14].

4.3. Genetic diversity

Double-stranded DNA viruses like MPXVs exhibit a slow rate of evolution, but they have been observed to undergo microevolution, involving amino acid point mutations, to adapt to human hosts. The virus has undergone divergence into distinct lineages, and this divergence can be correlated with geographic and demographic characteristics [26,27]. In the case of the 2022 global outbreaks,

Table 1
Emergence of monkeypox across the globe over the years [26,28].

Year	Country	Clade	Accession number
1970	Liberia	Clade IIa	DQ011156-1
1971	Nigeria	Clade IIb-A	KJ642617
1979	Zaire	Clade I	DQ011155-1
1985	Democratic Republic of the Congo	Clade I	KP849471-1
1988	Gabon	Clade I	KJ642619-1
2003	United States	Clade IIa	DQ011157-1
2005	Sierra Leone	Clade IIa	AY741551-1
2006	Democratic Republic of the Congo	Clade I	JX878407-1
2007	Democratic Republic of the Congo	Clade I	JX878419-1
2008	Democratic Republic of the Congo	Clade I	KP849469-1
2017	Nigeria	Clade IIb-A	MG693723-1
2018	Nigeria	Clade IIb-A	NC063383-1
2018	United Kingdom	Clade IIb-A.1	MT903343-1
2018	Israel	Clade IIb-A.1	MN648051-1
2018	Nigeria	Clade IIb-A.1	MT903341-1
2019	Singapore	Clade IIb-A.1	MT903342-1
2019	United Kingdom	Clade IIb-A.1	OL504742-1
2021	United States	Clade IIb-A.1.1	ON676708-1
2021	United States	Clade IIb-A.2	ON676707-1
2022	United States	Clade IIb-A.2	ON675438-1
2022	United States	Clade IIb-B.1	ON676704-1
2022	France	Clade IIb-B.1	ON602722-2
2022	Germany	Clade IIb-B.1	ON853661-1
2022	Portugal	Clade IIb-B.1	ON649722-1
2022	United Kingdom	Clade IIb-B.1	ON619838-2
2022	Italy	Clade IIb-B.1	ON644344-1
2022	Australia	Clade IIb-B.1	ON631963-1
2022	India	Clade IIb-A.2	EPI_ISL_15008575
2022	India	Clade IIb-A.2	EPI_ISL_15022589
2022	India	Clade IIb-A.2	EPI_ISL_15022590
2022	India	Clade IIb-A.2	EPI_ISL_15008576
2022	India	Clade IIb-A.2	EPI_ISL_15008577
2022	India	Clade IIb-A.2.1	EPS_ISL_13953611
2022	India	Clade IIb-A.2.1	EPS_ISL_13953610
2022	India	Clade IIb-A.2.1	EPI_ISL_14952916
2022	India	Clade IIb-A.2.1	EPI_ISL_15008573
2022	India	Clade IIb-A.2.1	EPI_ISL_15008574

Clade IIb or Clade 3 was identified as the responsible lineage. Most countries have reported monkeypox cases associated with Clade IIb-B.1. However, isolates in India exhibited divergence towards Clade IIb-A.2 and Clade IIb-A.2.1 [28]. Table 1 shows the genetic diversity of the monkeypox virus from 1970 to 2022.

Since 2017, the genomes within Clade IIb have been consistently accumulating apolipoprotein B editing complex (APOBEC3)-type mutations, which are induced as a defense mechanism by the host against viruses. These molecules target the viral genome during replication when single strands are exposed. Through multiple replication cycles, either strand can undergo deamination, causing changes, such as cysteine to thymine or guanine to adenine, on the positive strand. Consequently, APOBEC3-mutated genomes are probably non-viable. Yet, occasionally, a genome moderately affected by APOBEC3 might persist and get transmitted. Due to the irreversible nature of APOBEC3, continuous evolution within the human population might lead to a potential decline in the virus's fitness. However, the timeline for this process remains uncertain, and additional evolutionary factors such as recombination could counteract this decline and restore fitness [29].

Genomic studies of the 2022 MPXV outbreak have garnered significant interest by revealing the global divergence of lineage B.1 from the A.1 lineage observed in the 2018–2019 outbreaks; investigating the introduction of lineage A.2 in India has become a pivotal area for further exploration. There is also a need for further research into the mechanisms governing genome evolution and the significance of gene functions to gain a deeper understanding of MPXV's evolutionary processes [28].

5. Transmission

The transmission of monkeypox involves both animal-to-human and human-to-human transmission. Humans can become infected through direct contact with infected animals, such as when handling or consuming their meat, or through contact with contaminated materials or surfaces. Close contact with infected animals or their body fluids, such as blood, saliva, or urine, is a major method of the transmission of monkeypox from animals to people [7,8]. The virus can enter the body through broken skin, the respiratory tract, or mucous membranes such as the eyes, nose, or mouth [30]. In addition, people who come into contact with objects contaminated with the virus, such as bedding or clothing, can also get infected [31]. The virus can survive outside the body for several hours, and therefore, objects contaminated with the virus can remain infectious for some time. Therefore, it is essential to disinfect or discard any objects that come into contact with infected animals or their bodily fluids [32]. The risk of transmission from animals to humans is higher in areas where people hunt or trade wild animals for food or medicine [33]. Therefore, people who live in or travel to areas where monkeypox is endemic should take precautions to reduce their risk of infection. They should also wear protective clothing, such as gloves and masks, while handling animals or their bodily fluids.

Human-to-human transmission of monkeypox can occur through close contact with infected individuals. The virus can be transmitted through respiratory droplets, contact with skin lesions or bodily fluids, and, rarely, through aerosolized respiratory secretions. Recent studies revealed that the outbreak exhibits a significant bias in the distribution of cases, primarily affecting young men under the age of 40. These men account for over 95% of the reported cases. The transmission of the virus has been identified among men who have sex with men. However, it is crucial to also consider heterosexual intercourse as a potential mode of transmission [34,35]. It is important to highlight that the accidental introduction of this infection into the broader community could occur through transmission through heterosexual intercourse [36]. Previous studies suggest the possibility of sexual transmission among infected individuals with groin and genital lesions [37]. The incidence of monkeypox cases can vary

over time, with periodic outbreaks occurring in affected regions [5,22]. The mortality rate associated with monkeypox ranges from 1% to 10%, depending on the infecting strain's clade and the availability of modern health-care [23].

Monkeypox is a highly contagious viral disease that can spread from person to person through respiratory droplets or contact with the bodily fluids and skin lesions of infected individuals [22]. While the virus can cause severe illness and even death in humans, it is not known to survive for long periods outside of the human body [9].

After death, the body undergoes a process of decomposition, which involves the breakdown of tissues and the release of various bodily fluids. While it is possible for some infectious agents to survive in the body after death, including some bacteria and viruses, the risk of contracting monkeypox from a deceased individual is considered to be low [38–40]. For a considerable length of time, it has been extensively documented that poxviruses exhibit remarkable stability in the environment, making them potential sources of transmission [41]. However, the specific risks associated with transmission from deceased individuals or animals with monkeypox are not well-defined.

Proper precautions should be taken when handling deceased individuals or animals suspected of having monkeypox to minimize the risk of transmission. This includes using personal protective equipment like gloves, masks, and gowns, and implementing appropriate infection control measures [42]. Environmental factors, such as temperature, humidity, and sunlight exposure, can also affect the survival and transmission of the virus. However, the specific impact of these factors on monkeypox transmission from deceased individuals or animals has not been extensively studied [31].

6. Signs and symptoms

The clinical manifestations of monkeypox virus infection resemble those of a milder form of smallpox, with the notable difference being the presence of lymphadenopathy, which is not observed in smallpox. It is primarily a disease of the skin and mucous membranes, as well as the respiratory and lymphatic systems [10,11]. After the virus enters the body through the respiratory tract or broken skin, it replicates in the epithelial cells of the skin and mucous membranes, leading to the development of characteristic skin lesions [12]. The onset of monkeypox infection is characterized by symptoms such as fever with chills, headache, muscle aches, and fatigue, progressing to a state of exhaustion. Monkeypox has an average incubation period of 7 to 14 days, occasionally extending up to 21 days. Following the onset of fever, a rash first appears on the face and subsequently spreads to other parts of the body. Most lesions are 3–15 mm in diameter. In young individuals, the lesions may appear as non-specific erythe-

matous papules with a width ranging from 1 mm to 5 mm, resembling arthropod bite reactions. These papules may exhibit a subtle umbilicated appearance [34]. Pain associated with monkeypox infection is typically rare and often arises as a result of secondary bacterial infections [13].

7. Laboratory diagnosis

The timely diagnosis of monkeypox is crucial for effectively managing and containing outbreaks and epidemics of the disease. Molecular diagnostic methods such as PCR target B6R (envelope protein), E9L (DNA polymerase), RP018 (DNA-dependent RNA polymerase subunit 18), and C3L (complementary binding protein). Whole-genome sequencing is considered the gold standard method to distinguish monkeypox from other poxviruses. An enzyme-linked immunosorbent assay (ELISA) is also available for the detection of specific IgM and IgG antibodies in the serum of monkeypox patients after 5 and 8 days of infection, respectively. A 4-fold increase in serum antibodies during both the acute and convalescent stages serves as a diagnostic indicator for the infection. However, the ELISA lacks specificity due to antigenic cross-reactivity between monkeypox and other poxviruses [16].

The Ministry of Health and Family Welfare (MoHFW) of the Government of India developed the diagnostic algorithm shown in Fig. 3. Sample collection for suspected cases is based on the following criteria:

- Asymptomatic: It is advised to closely monitor individuals for any signs and symptoms of monkeypox for a period of 21 days following exposure. If any signs and symptoms do appear, appropriate specimens should be collected based on the duration of the illness.
- Symptomatic/rash phase: Samples should be collected from lesions (lesion roof, scrapings, crust, or fluid) present at multiple sites into a plain collection tube. A nasopharyngeal swab (NPS) or oropharyngeal swab (OPS) can be collected in a plain tube with viral transport medium (VTM). It is suggested that blood samples (4–5 mL) are collected in a serum separation gel tube or in an EDTA tube, and 3–5 mL of urine can also be collected as a sample in a sterile urine container.
- Symptomatic/recovery phase: A blood or urine sample is enough for diagnosis [14,43].

8. Prevention

Preventing monkeypox involves several measures, including avoiding contact with infected animals; practicing good hygiene; wearing protective clothing; vaccination, isolation, and quarantine; and avoiding travel to areas where monkeypox is known to occur. The isolation and quarantine of infected individuals are essential to prevent the spread of monkeypox. People who have been di-

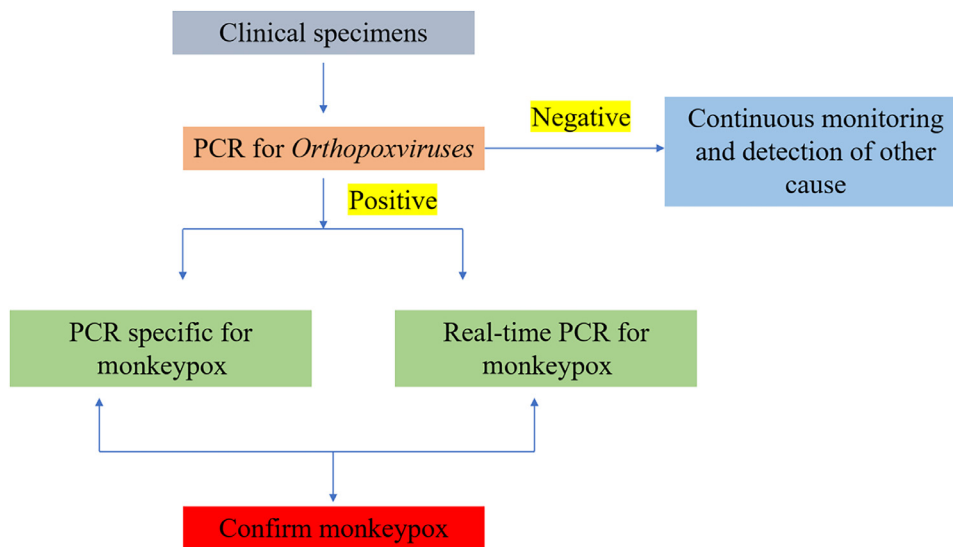


Fig. 3. Diagnostic algorithm defined by the Ministry of Health and Family Welfare.

agnosed with monkeypox should be isolated to prevent the spread of the disease to others. Infected individuals may be quarantined to prevent further close contact and transmission of the virus. Lastly, it is advisable that travel to areas where monkeypox is known to occur is avoided, particularly for individuals with a weakened immune system or at high risk of complications from the disease. If travel is necessary, taking precautions such as avoiding contact with wild animals, practicing good hygiene, and wearing protective clothing can help minimize the risk of exposure to the virus [44].

Utilizing knowledge from previous experiences with smallpox, researchers have identified a potential approach to preventing monkeypox [45]. By leveraging similarities in immune responses to smallpox and monkeypox, researchers have developed animal models to study smallpox infection and test vaccines and antivirals [46,47].

In the US Strategic National Stockpile (SNS), there are currently three smallpox vaccines available that provide cross-protection against the monkeypox virus. These include JYNNEOSTM (also known as IMVAMUNE, IMVANEX, MVA-BN), ACAM2000, and the Aventis Pasteur Smallpox Vaccine (APSV) [5,48]. Studies suggest that the JYNNEOSTM and ACAM2000 may confer a certain degree of cross-protection against monkeypox due to the similarities between the two viruses [49,50]. However, the level and duration of this cross-protection may vary among individuals [48,51].

Managing monkeypox disease involves several key components to ensure the effective treatment and prevention of further spread. The following are guidelines implemented by the Indian Council of Medical Research (ICMR) and MoHFW of the Government of India for disease management and surveillance:

- The foremost priority in managing monkeypox disease is ensuring patient isolation. Isolating infected individ-

uals serves as the primary measure to prevent the further transmission of the disease. It is advised that these individuals wear triple-layer masks and cover their lesions properly by wearing long-sleeve clothes to avoid transmission to healthy individuals.

- The administration of rehydration therapy and nutritional support is essential.
- Continuous monitoring is needed to ensure the person does not develop any complications, such as chest pain, seizures, etc. If any of the aforementioned symptoms manifest, it is crucial for the patient to promptly seek medical attention from a nearby healthcare facility or specialist.
- The surveillance strategy has several objectives, including the swift identification of cases and infection clusters, as well as the sources of infection. Firstly, it focuses on promptly isolating confirmed cases to prevent the onward transmission of the disease. Secondly, it aims to ensure that affected individuals receive optimal clinical care for their condition. Additionally, the strategy emphasizes the identification and management of contacts, minimizing the potential spread of infection. Moreover, it prioritizes the protection of frontline health workers who are at the forefront of managing and responding to cases. Lastly, by identifying the routes of transmission, the surveillance strategy enables the implementation of effective control and preventive measures. By fulfilling these objectives, the proposed surveillance strategy aims to control the spread of the disease and safeguard public health [43].

9. Conclusion

The monkeypox virus was first identified in 1958 in cynomolgus monkeys in Copenhagen, Denmark, and the first human case was identified in 1970 in The Democratic Republic of the Congo (DRC). Subsequently, similar out-

breaks have been reported in different African countries. In recent years, monkeypox disease has been increasingly documented in other parts of the world, including India in 2022 [5]. The virus can be transmitted from animals to humans or humans to humans by direct contact or by contact with body fluids. Studies indicate the environmental stability of poxviruses, which raises concerns about their potential for transmission. However, the precise risks associated with postmortem transmission remain uncertain and require further clarification [39]. The 2022 outbreak witnessed a genetic divergence from lineage A.1 to B.1 worldwide, and to A.2 in India, and is an area for further exploration. The emergence of APOBEC3 within the population might reduce the fitness and virulence of the virus [29]. Currently, there are no specific vaccines or targeted medications for monkeypox; hence, it is crucial to implement rigorous measures for disease prevention and control. As a prophylactic measure, the smallpox vaccine is recommended as a preventive option for monkeypox. The ICMR and MoHFW of the Government of India have documented guidelines for the diagnosis and management of monkeypox disease; however, there is a need for the development of antivirals and vaccines specifically targeting the monkeypox virus to control the disease and reduce fatalities.

Funding

None.

Author contributions

B.C.K., L.C., S.C.S., M.Y., and N.K.V. conceived and designed the study. S.K., C.K., S.M., and A.S. analyzed the data, created figures and prepared the manuscript. B.C.K., S.C.S., and M.Y. finalized the manuscript. All authors contributed to the article and approved the submitted version.

Acknowledgments

We are grateful to the Multidisciplinary Research Unit at Maulana Azad Medical College, the Vector-borne Diseases Group at the International Center for Genetic Engineering and Biotechnology, and the University of Delhi, New Delhi. Additionally, we would like to acknowledge the Department of Biotechnology at Guru Ghasidas Vishwavidyalaya, Chhattisgarh, for their support.

Declaration of competing interest

The authors report no conflict of interest.

Data available statement

There is no data for this review.

Ethics statement

Not applicable.

Informed consent

Not applicable.

References

- [1] B. Moss, I.K. Damon, in: D.M. Knipe, P.M. Howley (Eds.), *Fields Virology*, 2, sixth ed., Wolters Kluwer, Philadelphia, 2013, pp. 2129–2160.
- [2] World Health Organization, WHO recommends new name for monkeypox disease, 2022. Available at: <https://www.who.int/news/item/28-11-2022-who-recommends-new-name-for-monkeypox-disease>. Accessed May 30, 2023.
- [3] A. Saghazadeh, N. Rezaei, Poxviruses and the immune system: implications for monkeypox virus, *Int. Immunopharmacol.* 113 (2022) 109364, doi:10.1016/j.intimp.2022.109364.
- [4] S.J. Flint, L.W. Enquist, V.R. Racaniello, *Principles of Virology*, fourth ed., American Society for Microbiology, New York, 2015.
- [5] J.P. Shabaaz Begum, L. Ngannom, P. Semwal, et al., Emergence of monkeypox: a worldwide public health crisis, *Hum. Cell* 36 (3) (2022) 877–893, doi:10.1007/s13577-023-00870-1.
- [6] World Health Organization, Mpox (monkeypox) outbreak 2022, 2022. Available at: <https://www.who.int/emergencies/situations/monkeypox-oubreak-2022>. Accessed July 25, 2023.
- [7] P.V. Magnus, E.K. Andersen, K.B. Petersen, A pox-like disease in cynomolgus monkeys, *Acta Pathologica Microbiologica Scandinavica* 46 (2) (1959) 156–176, doi:10.1111/j.1699-0463.1959.tb00228.x.
- [8] C.L. Hutson, V.A. Olson, D.S. Carroll, et al., A prairie dog animal model of systemic orthopoxvirus using West African and Congo Basin strains of monkeypox virus, *J. Gen. Virol.* 90 (Pt 2) (2009) 323–333, doi:10.1099/vir.0.005108-0.
- [9] J. Quarleri, M.V. Delpino, V. Galvan, Monkeypox: considerations for the understanding and containment of the current outbreak in non-endemic countries, *Geroscience* 44 (4) (2022) 2095–2103, doi:10.1007/s11357-02200611-6.
- [10] A.A. Sergeev, A.S. Kabanov, L.E. Bulychev, et al., The possibility of using the ICR mouse as an animal model to assess antimoneypox drug efficacy, *Transbound. Emerg. Dis.* 63 (5) (2016) e419–e430, doi:10.1111/tbed.12323.
- [11] A. Nalca, V.A. Livingston, N.L. Garza, et al., Experimental infection of cynomolgus macaques (*Macaca fascicularis*) with aerosolized monkeypox virus, *PLoS One* 5 (9) (2010) e12880, doi:10.1371/journal.pone.0012880.
- [12] G.M. Zaucha, P.B. Jahrling, T.W. Geisbert, et al., The pathology of experimental aerosolized monkeypox virus infection in cynomolgus monkeys (*Macaca fascicularis*), *Lab. Invest.* 81 (12) (2001) 1581–1600, doi:10.1038/labinvest.3780373.
- [13] M.J. Moore, B. Rathish, F. Zahra, Mpox (monkeypox), 2023. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK574519/>. Accessed July 20, 2023.
- [14] P.D. Yadav, M. Vasu, F. Abubaker, An imported case of fatal encephalitis associated with mpox virus infection, India, July 2022, *J. Med. Virol.* 95 (4) (2023), doi:10.1002/jmv.28755.
- [15] H. Adler, S. Gould, P. Hine, et al., Clinical features and management of human monkeypox: a retrospective observational study in the UK, *Lancet Infect. Dis.* 22 (8) (2022) 1153–1162, doi:10.1016/S1473-3099(22)00228-6.
- [16] Q. Gong, C. Wang, X. Chuai, et al., Monkeypox virus: a re-emergent threat to humans, *Virology* 537 (4) (2022) 477–482, doi:10.1016/j.virus.2022.07.006.
- [17] A.W. Rimoin, P.M. Mulembakani, S.C. Johnston, et al., Major increase in human monkeypox incidence 30 years after smallpox vaccination campaigns cease in the Democratic Republic of Congo, *Proc. Natl. Acad. Sci. USA* 107 (37) (2010) 16262–16267, doi:10.1073/pnas.1005769107.
- [18] A. Alcami, Pathogenesis of the circulating mpox virus and its adaptation to humans, *Proc. Natl. Acad. Sci. USA* 120 (13) (2023) e2301662120, doi:10.1073/pnas.2301662120.
- [19] J. Kaler, A. Hussain, G. Flores, et al., Monkeypox: a comprehensive review of transmission, pathogenesis, and manifestation, *Cureus* 14 (7) (2022) e26531, doi:10.7759/cureus.26531.
- [20] BMJ Best Practice, Mpox (monkeypox) etiology, 2023. Available at: <https://bestpractice.bmj.com/topics/en-us/1611/aetiology>. Accessed August 29, 2023.
- [21] N. Luna, A.L. Ramirez, M. Munoz, et al., Phylogenomic analysis of the monkeypox virus (MPXV) 2022 outbreak: emergence of a novel viral lineage? *Travel. Med. Infect. Dis.* 49 (2022) 102402, doi:10.1016/j.tmaid.2022.102402.
- [22] N. Kumar, A. Acharya, H.E. Gendelman, et al., The 2022 outbreak and the pathobiology of the monkeypox virus, *J. Autoimmun.* 131 (2022) 102855, doi:10.1016/j.jaut.2022.102855.
- [23] A. Adajia, T. Inglesby, A novel international monkeypox outbreak, *Ann. Intern. Med.* 175 (8) (2022) 1175–1176, doi:10.7326/m22-1581.
- [24] World Health Organization, Multi-country outbreak of mpox, 2023. Available at: https://www.who.int/docs/default-source/coronaviruse/situationreports/20231222-mpox-external-sitrep-31.pdf?sfvrsn=7545c953_9&download=true. Accessed December 28, 2023.
- [25] T. Singh, P. Baskaran, P. Raghav, et al., Monkeypox: current situation in India: an old virus, a new menace? *Indian J. Community Med.* 47 (4) (2022) 628–630, doi:10.4103/ijcm.ijcm_719_22.

- [26] P.A. Desingu, T.P. Rubeni, N.R. Sundaresan, Evolution of monkeypox virus from 2017 to 2022: in the light of point mutations, *Front. Microbiol.* 13 (2022), doi:10.3389/fmicb.2022.1037598.
- [27] J. Isidro, V. Borges, M. Pinto, et al., Addendum: phylogenomic characterization and signs of microevolution in the 2022 multi-country outbreak of monkeypox virus, *Nat. Med.* 28 (10) (2022) 2220–2221, doi:10.1038/s41591-022-02036-2.
- [28] A.M. Shete, P.D. Yadav, A. Kumar, et al., Genome characterization of monkeypox cases detected in India: identification of three sub clusters among A.2 lineage, *J. Infect.* 86 (1) (2023) 66–117, doi:10.1016/j.jinf.2022.09.024.
- [29] Á. O'Toole, R.A. Neher, N. Ndodo, et al., APOBEC3 deaminase editing in mpox virus as evidence for sustained human transmission since at least 2016, *Science* 382 (6670) (2023) 595–600, doi:10.1126/science.adg8116.
- [30] N. Dar-Odeh, S. Abu-Hammad, O. Abu-Hammad, The emerging monkeypox outbreak: a cause for concern among craniofacial surgeons, *J. Craniofac. Surg.* 34 (1) (2022) 11, doi:10.1097/scs.0000000000008907.
- [31] C.N. Morgan, F. Whitehill, J.B. Doty, Environmental persistence of monkeypox virus on surfaces in household of person with travel-associated infection, Dallas, Texas, USA, 2021, *Emerg. Infect. Dis.* 28 (10) (2022) 1982–1989, doi:10.3201/eid2810.221047.
- [32] Centers for disease control and prevention, Cleaning and disinfecting your home, workplace, and other community settings, 2023. Available at: <https://www.cdc.gov/poxvirus/mpox/if-sick/cleaning-disinfecting.html>. Accessed September 15, 2023.
- [33] M.M. Islam, P. Dutta, R. Rashid, et al., Pathogenicity and virulence of monkeypox at the human-animal-ecology interface, *Virulence* 14 (1) (2023) 2186357, doi:10.1080/21505594.2023.2186357.
- [34] A. Antinori, V. Mazzotta, S. Vita, Epidemiological, clinical and virological characteristics of four cases of monkeypox support transmission through sexual contact, Italy, May 2022, *Euro. Surveill.* 27 (22) (2022), doi:10.2807/1560-7917.ES.2022.27.22.2200421.
- [35] J. Heskin, A. Belfield, C. Milne, et al., Transmission of monkeypox virus through sexual contact—a novel route of infection, *J. Infect.* 85 (3) (2022) 334–363, doi:10.1016/j.jinf.2022.05.028.
- [36] J.P. Thornhill, S. Barkati, S. Walmsley, et al., Monkeypox virus infection in humans across 16 countries—April–June 2022, *N. Engl. J. Med.* 387 (8) (2022) 679–691, doi:10.1056/NEJMoa2207323.
- [37] D. Ogoina, I.H. James, Mpox in a female sex worker in Nigeria: a case report, *IJID Reg.* 7 (2022) 143–145, doi:10.1016/j.ijregi.2022.12.004.
- [38] D. Kopec, M. Thompson, Infection and disease transmission: pandemics, epidemics, and outbreaks, in: A. Bliss, D. Kopec (Eds.), *Architectural Factors for Infection and Disease Control*, first ed., Routledge, New York, 2022, pp. 1–12.
- [39] S. Kulshrestha, A. Rastogi, A. Goel, Monkeypox virus: lessons learnt, *J. Pure Appl. Microbiol.* 16 (suppl 1) (2022) 3072–3082, doi:10.22207/jpam.16.spl1.17.
- [40] J. Louten, Virus transmission and epidemiology, *Essent. Hum. Virol.* (2016) 71–92, doi:10.1016/B978-0-12-800947-5.00005-3.
- [41] A. Atoui, F. Jourdain, D. Mouly, et al., A review on mpox (monkeypox) virus shedding in wastewater and its persistence evaluation in environmental samples, *Case Stud. Chem. Environ. Eng.* 7 (2023) 100315, doi:10.1016/j.csee.2023.100315.
- [42] M. Jeyaraman, P. Selvaraj, M.B. Halesh, et al., Monkeypox: an emerging global public health emergency, *Life* 12 (10) (2022) 1590, doi:10.3390/life12101590.
- [43] Ministry of health and family welfare, Guidelines for management of monkeypox disease, 2022. Available at: <https://main.mohfw.gov.in/sites/default/files/Guidelines%20for%20Management%20of%20Monkeypox%20Disease.pdf>. Accessed June 23, 2023.
- [44] J. Guarner, C. Del Rio, P.N. Malani, Monkeypox in 2022—what clinicians need to know, *JAMA* 328 (2) (2022) 139–140, doi:10.1001/jama.10802.
- [45] E.M. Bunge, B. Hoet, L. Chen, et al., The changing epidemiology of human monkeypox—a potential threat? A systematic review, *PLoS Negl. Trop. Dis.* 16 (2) (2022) e0010141, doi:10.1371/journal.pntd.0010141.
- [46] T.M. Mack, J. Noble Jr, D.B. Thomas, A prospective study of serum antibody and protection against smallpox, *Am. J. Trop. Med. Hyg.* 21 (2) (1972) 214–218, doi:10.4269/ajtmh.1972.21.214.
- [47] J.K. Sarkar, A.C. Mitra, M.K. Mukherjee, The minimum protective level of antibodies in smallpox, *Bull. World Health Organ.* 52 (3) (1975) 307–311.
- [48] G.A. Poland, R.B. Kennedy, P.K. Tosh, Prevention of monkeypox with vaccines: a rapid review, *Lancet Infect. Dis.* 22 (12) (2022) e349–e358, doi:10.1016/S1473-3099(22)00574-6.
- [49] S.A. Meo, A.A. Al-Masri, D.C. Klonoff, et al., Comparison of biological, pharmacological characteristics, indications, contradictions and adverse effects of JYN-NEOS and ACAM2000 monkeypox vaccines, *Vaccines* 10 (11) (2022) 1971, doi:10.3390/vaccines10111971.
- [50] B.E. Katamesh, M. Madany, F. Labieb, et al., Monkeypox pandemic containment: does the ACAM2000 vaccine play a role in the current outbreaks? *Expert Rev. Vaccines* 22 (1) (2023) 366–368, doi:10.1080/14760584.2023.2198600.
- [51] J.G. Rizk, G. Lippi, B.M. Henry, et al., Prevention and treatment of monkeypox, *Drugs* 82 (9) (2022) 957–963, doi:10.1007/s40265-022-01742-y.