Journal of Pharmacological Biomolecules and Therapeutics

ETERNO PRESS

Review

Transmission, Preparedness, and Pharmacological Interventions for a Monkeypox Outbreak: An Overview

Chandni Hayat[1], Muhammad Riaz[2], Muhammad Fawad Ali[1], Abdul Wadood[1,*]

[1]Department of Biochemistry, Abdul Wali Khan University Mardan, Mardan-23200, Pakistan

[2]Government Degree College Garhi Kapura, Mardan, KPK, Pakistan

[*]Corresponding author: Abdul Wadood, awadood@awkum.edu.pk

Abstract

Monkeypox, caused by the monkeypox virus (MPXV), has become a growing global health concern due to its increasing prevalence and potential for widespread transmission. MPXV, a member of the Orthopoxvirus family, spreads through direct contact with infected individuals, contaminated objects, respiratory droplets, and potentially through sexual transmission. Recent outbreaks have highlighted the need for enhanced surveillance, vaccination strategies, and pharmacological interventions to mitigate its impact. This review examines the transmission pathways, pathogenesis, and clinical manifestations of MPXV, as well as current and emerging treatment options. Antiviral agents such as Tecovirimat and Brincidofovir show promise in mitigating disease severity, though further clinical trials are required to establish their efficacy. Vaccination remains a crucial tool, with JYNNEOS™ and ACAM2000® being the primary vaccines available. However, challenges such as accessibility and vaccine hesitancy persist. The review also underscores the importance of public health interventions, including quarantine measures, rapid diagnostic testing, and global coordination in controlling outbreaks. Future research should focus on improving antiviral effectiveness, understanding long-term immunity, and enhancing outbreak preparedness to minimize the impact of future epidemics.

Keywords

Monkeypox, Zoonotic, Virus, Outbreak, Antiviral drugs, Pharmacological drugs, Treatment

Article History

Received: 18 February 2025 Revised: 1 September 2025

Accepted: 2 September 2025 Available Online: 2 September 2025

1. Introduction

Monkeypox is a zoonotic viral disease caused by the monkeypox virus (MPXV), first identified in 1958 in laboratory monkeys in Denmark, hence the name “monkeypox [1]. Monkeypox virus belongs to the genus *Orthopoxvirus*, which is a group of DNA viruses within the family *Poxviridae* known for infecting both humans and animals [2]. MPXV is a double-stranded DNA virus with a relatively stable genome compared to RNA viruses, but it still exhibits genomic mutations over time. Recent studies have shown that MPXV is evolving, with mutations affecting viral replication efficiency and potential host adaptation. The virus has a brick-shaped virion with a lipoprotein envelope, and have a characteristics dumbbell-shape nucleoprotein core containing viral genome. MPV is relatively stable in the environment and can survive on surfaces for extended periods [3].

Orthopoxvirus genus comprised of variola virus, causative agent for smallpox disease. In human, symptoms of smallpox and monkeypox are relatively same, but monkeypox has low mortality rate [4]. Other body fluids, scabs, shared clothing/bedding and infectious sores. The symptoms of monkeypox are lymphadenopathy, flu and fever, which are relatively similar, but severity rate is lower than smallpox. Once begins, patients are considered as infectious [5]. Here, we discuss transmission and immunopathogenesis and pathological characteristics of MPXV noted in current outbreak, also discuss therapeutics, and vaccines against monkeypox.

1.1 Transmission Route and Pathogenesis

Monkeypox virus (MPXV) transmission routes have been identified, this infection affects various animals, both humans and monkeys are accidental hosts [6]. There are different transmission routes such as animal bite, contact infected animals, minimally processed meat or consumption of raw. Intensity of animal contact resembles with severity of clinical manifestations. MPX transmission in human has attributed to intimate or direct contact with body fluids, scabs, and infectious sores. Another study reported that direct transmission may be through placenta, (mother to fetus route) [7]. A case report among 4 MPXV infected pregnant women indicated that just 1 baby was healthy one after birth in the Democratic Republic of the Congo. Although, small pox vaccine is not recommended in pregnancy. Extra research are needed for assessment of MPX effects in pregnancy [8]. Indirect transmission has also reported via contaminated clothes sores or infectious materials. Furthermore, this virus may spread because of respiratory secretions [9]. Although prevalence of MPVX is less than small pox in human, the virus transmissibility in unvaccinated people is seems to be more severe attack than vaccinated [10]. Infectiousness period of virus and viral shedding are not cleared yet. On the basis of symptoms, person is considered infectious [11].

1.2 Clinical Manifestation

Although MPX's clinical presentation often mimics that of smallpox but MPX has a distinctive characteristic: lymphadenitis, particularly in the sub-mental, sub mandibular, cervical, and inguinal areas [12]. Most MPXV patients exhibit a moderate illness; nevertheless, in some cases such as pregnancy or immunodeficiency, MPXV can result in severe disease areas [13]. Clinical indications of MPX infection frequently appear after an incubation period of 5 to 21 days, and it is normally a self-limited illness. When monkeypox virus enter into body through nose, mouth and pharynx, it frequently spread through local lymph nodes and then damage other organs and tissues which is monkeypox incubation period. The prodromal phase of MPX infection lasts for around 0–3 days. At that stage, maculopapular rash frequently begins at the site of initial infection and quickly spreads to other regions of the body three days following symptoms. The face (>90%), palms and soles of the feet (75%), oral mucosa (70%), genitals (30%), and conjunctiva (20%) are the usual sites of the rash's concentration and lasting 7–21 days is characterized by fever, fatigue, headache, chills, back pain, and muscular pains. In prodromal phase, fever is one of common symptom, in which temperature of body is approximately 101.3–104.9 ◦F [14]. Nearly, 37% patients suffered from secondary fever (2 to 3 days) [15,16]. Additionally, fever was also considered as first system in US and Congo. However, from 2017-18 in Nigeria, 65% patient suffered from rash and 34.3% suffered from fever and 2 cases were reported as genital rash with ulcers noted as first manifestation. In their research, it was found that infected patients with no fever might be caused though various transmission routes [5]. Lymphadenopathy is also one of essential characteristic manifestation for monkeypox, which are utilized as crucial sign to differentiate monkeypox infection from smallpox, varicella and other infectious diseases [17]. According to several reports, 90% monkeypox infections are at early stage, cause lymphadenopathy, occasionally one or two days after fever and mostly one or two days after rash [18]. The diameter of enlarge lymph nodes are 1 to 4 cm, which are hard, accompanied through pain and local tenderness. Mostly occur in groin, neck, sub mandibular, retro auricular, and can spread throughout full body [19]. The lymphadenopathy presence can present that immune system has effective immune recognition as well as response towards monkeypox than other infection; however, the hypothesis still requires to be confirmed through further research.

However, in rash period, usually rash appears within 1 to 3 days after suffering from fever and less infected patients have fever and rash at same time. The common area of skin lesions are torso (92.5%), face (97.5%), palms (55%), genitals (67.5%), Scalp (62.5%), legs (85%), eyes (25%) and mouth (37.5%). There are no such definitive evaluation for scalp involvement, however, present study might be available on the basis of clinical study reports [20].

Additionally, in early African outbreak, rashes were mostly found on limbs and face, but, in 2022, skin lesions around testicles, vagina, penis and labia were common [21].

Regarding the laboratory findings, the available literature is inadequate. It is well known that early detection of hematologic abnormalities such as lymphocytes and thrombocytopenia has occurred in severe confluent kinds of smallpox infection. Hematologic or liver test abnormalities should prompt an instant addition of MPX to the differential diagnosis, much like the aforementioned clinical signs. Rarely, MPX cases in individuals might develop more serious symptoms: in endemic regions, consequences can include conjunctivitis, pneumonia, keratitis, encephalitis, dehydration, and secondary bacterial infections of the skin. despite the fact that the fatality rate in a number of prior MPX epidemics involving humans in central Africa reached up to 10.6% [22]. The current outbreaks case mortality ratio fluctuates between 3% and 6%. In the Democratic Republic of the Congo, WHO reported 67 deaths from 1st January to 1st May 2022. It is crucial to take into account MPX's neuropsychiatric symptoms. A variety of neurological and psychiatric MPX manifestations are supported by early research (from common yet severe neurological consequences like encephalitis and seizures to general neurological symptoms like myalgia and headache). During monkey pox outbreak, researcher identified some data regarding monkey pox infected patient with neurological disorders. For example, in USA, several severe cases of monkey pox infection with myalgia and severe headache were reported. In addition, 7 other monkey pox cases reported with fatigue, myalgia and headache in Western hemisphere. In USA (Midwestern), family is badly affected in which 2 of them have mild skin rash and 1 patient had encephalitis. Different neurological manifestations such as seizure, myalgia, fatigue, headache and confusion were reported in various cases. Neurological examination determined low consciousness level, optic disc edema, and pupillary dilatation. In addition, through magnetic resonance imaging, hyper intensity was confirmed in brainstem and thalamus with vasogenic and cytotoxic brain edema. By analyzing, cerebrospinal fluid, Pleocytosis was also detected. In USA, several other studies reported that because of confusion and seizure, various other neurological disorders including, myalgia and headache were noted. Additionally, in Nigeria, the cross-sectional study reported, several neurological disorders including photophobia, myalgia, pain, and headache [23]. However, in the current MPX outbreak, there is little information on the mental side effects and nervous system manifestations that may necessitate surveillance [24]. Unfortunately, despite the WHO's recent request for increased focus on mental health issues and suicide prevention during epidemics, the psychological impact of MPX is not as well understood. Further study is require [14]. The latest outbreak is revealing deficiencies in the knowledge of MPX. For an instance, in some circumstances, herald skin lesions were exclusively present at the site of sexual encounters while premonitory indications seemed absent [25]. It implies that a significant reason in the present pandemic is human-to-human acquisition via intimate physical interaction in sexual networks. Moreover, asynchronous skin lesions may emerge in rare circumstances, casting aspersions on the lesions' synchronous progression. 528 cases were identified between April 27, 2022, and June 24, 2022, according to a global collaboration including 16 countries [26]. In this study, these individuals exhibited anogenital lesions in 73% patients, mucosal lesions in 41%, and rashes in 95% patients. 54 people (10%) had just one genital lesion. This may indicate that the infection can spread through close skin-to-skin or mucosal contact. In order to prevent diagnostic errors, the existing worldwide clinical diagnosis has to be updated to include these uncommon appearances [27]. Information on MPXV/HIV co infection is scarce. According to earlier research conducted in Africa, HIV-infected individuals had more large and persistent lesions, more comorbidities, and a worse prognosis overall [13]. There are currently just a few reported cases or case studies, however, a comprehensive review showed that this co infection may manifest with a variety of unusual symptoms, such as pale papules arranged in the shape of kissing lesions in the perianal region [28]. The biggest analysis of verified MPX cases to date discovered no connection between HIV status and the severity of monkey pox [26].

2. MPXV Pathogenesis

In vertebrate host, orthopoxviral pathogenesis depend on entry route utilized through virus in order to establish infection [29]. For highly contagious MPXV, and VARV, oral/respiratory cavity is the possible entry way such as inhale of aerosolized respiratory secretions or bodily fluids ingestion from infected individuals [30]. For primary infection, upper, lower and middle airway epithelium along with respiratory/oral tract mucosae are important targets [31]. This infectious is called asymptomatic (no symptoms of oropharyngeal lesions). Additionally, B cells, macrophages, monocytes, and dendritic cells are enrol in virus infection [32]. However, main mechanisms where MPXV, and VARV, relocate from initial phase to final phase (lymph nodes) are still matter of debate. It has noted that VACV-infected cells for example, dendritic cells move from lung epithelium towards lymph nodes, in order to play vital role in virus dissemination [33]. Conversely, VACV infection has severely affect maturation and migration of dendritic cells [34]. Importantly, VACV relocation lymph nodes in some hours of inoculation showed viral access towards lymphatic vessels [35].

Different studies indicate that lymphoid tissues in throat and neck are main targets for MPXV replication. These studies were supported via cynomolgus macaque model of aerosolized where mediastinal, mandibular lymph nodes and tonsils were represented as active regions in virus replication. In lymphoid tissue, Pox virus tropism linked with infected dendritic cells, macrophages, activated T cells, and B cells which might be main targets for MPXV [36]. The methods that are leading to abnormal lymph node because of MPXV are still not elucidated yet; in experimental analysis infection of such non-human primates along with MPXV indicated massive cell growth and accumulation of NK cells in lymph nodes. After the development of infected lymphoid tissues, MPXV may disseminate to various organs through

lymphohaematogenous route [37]. After the lymphatic spread in monkey pox models, liver and spleen can be targets for speeding infection. In liver and spleen, virus infection releases viraemia wave, which affect kidneys, skin, intestines, and lungs. In MPXV infection, viral antigen was reported in Kupffer cells, and enlarge liver spleen was observed. Because of orthopoxviruses, skin infection and skin lesions are develop [38]. However, this is still not confirmed how virus reach skin layers. Infiltration of dendritic cells, $CD3^+$ T cells and macrophages has been noted in infective pustule, other factor anathema also appear in pharynx, trachea, oesophagus, larynx and oropharyngeal mucosa during MPXV infection [39]. Infection may also affect through skin. Recent study postulated that infection in macrophages, Langerhans cells, dermal keratinocytes and fibroblasts can occur and these cells migration contribute to virus dissemination through lymphatics [40]. Recent data in mouse model observed that migration of dendritic cell is impaired from skin to lymph nodes on VACV [41]. Monkey pox sexual transmission has also speculated [42], monkey pox cases with genital lesions also noted, hat denoted MPXV tropism in testes [43], testes play role in MPXV infection, however, need further investigation. Recently new animal report indicate that VACV may exhibits tropism in ovarian and testicular tissues. Some data showed that HIV patients act as reservoir for MPXV [44]. Recent report [45], indicate that in MSM rectal mucosa immune environment differ from heterosexual.

2.1 Monkey Pox Association with Other Cases

On the basis of various studies, monkey pox has more severe complication as well as high mortality rate than adult in people with HIV, pregnant women, and children [46] (Table 1).

Table 1. Association of Monkeypox Complications with HIV-Infected Individuals, Children, and Pregnant Women.

Population	Complications	Key Findings	References
HIV-Infected	- Larger lesions - Increased lesions count - Higher mortality	- Severe lesions, prolonged illness, higher risk of complications in HIV-positive individuals.	[44]
Children	- Severe dehydration - Encephalitis - Pneumonia - Higher mortality	- Higher infection rates and complications in children; mortality rate of 1.5-1.7%.	[47]
Pregnant Women	- Abortion - Fetal death - Premature birth	- Increased risk of miscarriage, vertical transmission, and fetal death during infection.	[48]

2.2 Association of Monkey Pox Complication with HIV

Different studies on monkey pox did not determine HIV as an essential co factor in clinical manifestations for monkey pox [10]. From 1996 to 1998, only 3 combine cases were reported in Congo. In 2003, no such combined cases were reported in United States. From 2017-18, retrospective study in Nigeria reported nine cases with monkey pox, which co-infected with HIV.

The researcher determines that, by comparing with normal people, the skin lesions diameter was more than (2cm) as well as number of skin lesions was 100 or more than 100. The skin lesions were mostly semi-fused, presented perianal and genital skin lesions, also represent high rate of skin infection. The possibility of mortality and complications rate was higher than ordinary patients of monkey pox. It observed that combine infection of HIV and monkey pox has change the history.

In monkey pox epidemic which were reported in 2022, there were 96 confirmed reports with HIV infection, was characterized through inguinal lymphadenopathy, local rash and fever. First the skin lesions found in genitals, perianal area, then effect mouth, face, and other body parts. According to Cohen MS et al.the dense skin lesions appearance around anus might be because of monkey pox inoculation and in HIV infection, skin lesions mostly aggravated through immune system dysfunction [49]. However, Thornhill, J.P et al. speculated that 41% monkey pox patients were infected with HIV during the onset of disease and 95% cases were receiving antiretroviral therapy. Thornhill, J.P did not consider significant difference in monkey pox severity with or without HIV infection. It was also noted in monkey pox infection with sexually transmitted infections (STI) might increase HIV risk. Previous report indicated that 10% of HIV cases may be attributed to STI including gonorrhea and chlamydia. Mathematical models which explore relationship among MPXV co infection and HIV considered that HIV has vital role in monkey pox transmission and vice versa [50]. In addition, HIV patients give attention towards small pox vaccination. Since AIDS epidemic found after eradication of smallpox stopped by utilizing replicative smallpox vaccine, but still it is not clear, AIDS affected patients have complications after using replicative vaccine. According to several reports, people who diagnosed with HIV but not infected with AIDS have no such complications, however, AIDS infected patients may develop disseminated vaccinia infection after using vaccine. Some studies report that 30–50% of monkeypox cases occur in people living with HIV, especially among MSM communities. HIV-positive individuals with low CD4 counts may experience more extensive lesions, prolonged illness, and increased risk of secondary infections. However, those on antiretroviral therapy often have similar outcomes to HIV-negative individuals [44]. Thus, as the epidemic progresses, educating people about complications against live viral vaccination and probability of monkey pox should have focus of public advocacy.

2.3 Children

Children are considered as one of main group with monkey pox disease in Africa. From 1970-89, median age for monkey pox cases were approximately four to five years old, among them, 80% cases were considered under fifteen years old. However, from 2000-2019, median age for monkey pox were 10-21 years [42]. In Nigeria the median age for monkey, pox cases were 29 years. In 2022, the high rate of monkey pox reports was noted in adults. According to WHO report in 2022, in monkey pox patients with respect to age information, 96% patients were under 18 age, in which 42% were hospitalized because of proper treatment or isolation [47]. According to epidemiological data, monkey pox infected patients without vaccinated were more like to be transmitted easily because of family environmental contact in children. In Congo outbreak, approximately more than 90% children under 15 years and deaths under three months to eight years were recorded. In children the mortality rate were from 1.5-1.7% recorded and such severe complication including, severe dehydration, encephalitis, septicemia, pneumonia, and blindness were recorded in children. In many developed countries, children were more affected and have severe complications. The epidemic of 2003 in US, most of children were hospitalized in ICU with some severe complications including retro pharyngeal abscess, corneal ulcer, and corneal ulcer. The rate of children in hospital is higher than adults. In Spanish epidemic, 16 reported cases under 18 years were recorded in which 1 patient had bacterial super infection and needed abscess drainage. Mostly children inevitably be exposed to school, family and other environments and may also affected via sexual contact. Recent study reported that newborns can be effected with monkey pox virus because of prenatal contact with mother [51].

2.4 Pregnant Female

During pregnancy, decline for body·s immune system makes pregnant female so susceptible towards monkey pox. In pregnancy, there are only few cases in early African outbreaks, and after monkey pox infection, limited attention has paid to changes in pregnancy outcomes. Four pregnancy cases with monkey pox infection were found in which 2 of them were aborted, one pregnant female at eighteen weeks of gestation delivered dead fetus because of fetal heart stop [48]. During monkey pox infection, the risk of abortion is 25 to 30%. A recent study found that increase in monkey pox virus transmission have the ability to release cytokines in female placenta, result in severe cell damage. After performing various tests, in dead fetus, several characteristics of monkey pox infection were noted, in which histological, serological and virological evidence determined that there was vertical transmission. Some other reports for smallpox and vaccinia viruses indicated that pregnant female have increase morbidity, premature and still birth rates, abortion, and also increase risk of hemorrhagic smallpox and mortality. Pregnant female infected with monkey pox are serious than non-pregnant female. However, little information is available on effect of monkey pox in pregnant women, vertical transmission of monkey pox are found to be linked with fetal death.

3. Prevention

Data indicate that immunization with effective smallpox vaccine can protect against monkey pox virus [52]. In US, three smallpox vaccines, JYNNEOSTM, ACAM2000® and Aventis Pasteur Smallpox Vaccine are available. JYNNEOSTM vaccine was approved by FDA and attenuate orthopoxviruses [53]. The JYNNEOSTM vaccine prevented monkey pox and smallpox disease in 18 or older than 18 years people. Historical record suggest that smallpox vaccine against monkey pox was 85% effective [54]. The vaccine IMVANEX® for smallpox was approved by Europe. However, in case of monkey pox, UK has utilized it off-label. ACAM2000® comprised of live vaccinia virus, approved by FDA, replacing Dryvax® vaccine. ACAM2000® represent active immunization against smallpox. During an outbreak, CDC allows ACAM2000® vaccine against monkey pox [5]. There are various differences in both vaccines; JYNNEOSTM is replication-deficient modified vaccinia whereas ACAM2000® is replication-competent vaccinia virus. ACAM2000® forms cutaneous reaction at inoculation site whereas JYNNEOSTM cannot. FDA assessed ACAM2000® effectiveness by comparing different immunologic responses ACAM2000® to Dry vax [55]. The FDA also assessed JYNNEOSTM by comparing immunologic response of JYNNEOSTM to ACAM2000®. ACAM2000® is administered percutaneously in a single dose, whereas, JYNNEOSTM is given subcutaneously in two doses, twenty-eight days apart. Aventis Pasteur Smallpox Vaccine (APSV) can be utilized under Emergency Use Authorization or an IND to protect against smallpox in case licensed vaccines are contraindicated or unavailable. Still it is not confirmed is this vaccine can be utilized against monkey pox.

4. Treatment

4.1 Care

Patients infected with monkey pox mostly recover without use of medical treatment. Patients with vomiting, diarrhea need intravenous/oral rehydration to lower gastrointestinal fluid losses [5].

4.2 Antiviral

Different antivirals (drugs approved for smallpox management) can be effective against monkey pox. Dose studies for these agents were conducted in human, but drug efficacy were not checked thoroughly [56]. Brincidofovir and tecovirimat (dual therapy) can be used in severe disease.

4.3 Tecovirimat

Tecovirimat drug utilized for smallpox treatment in pediatric and adults patients [57]. A smallpox antiviral drug approved by the FDA in 2018.It Inhibits viral maturation and spread by targeting the orthopoxvirus VP37 protein. It is well-tolerated in human clinical trials, with mild adverse effects such as headache and fatigue. A study in non-human primates demonstrated that Tecovirimat reduced mortality from 100% to 0% when administered within 72 hours of infection. Different studies indicated improved survival against monkey pox in tecovirimat-treated animals as compared with placebo-treated animals [13]. Both vaccinia immune globulin and tecovirimat were used in combination for smallpox vaccine (eczema vaccinatum) [58].

4.4 Brincidofovir and Cidofovir

Brincidofovir drug approved for management of smallpox from 2021 in US. Brincidofovir is an analogue for cidofovir drug, compared with cidofovir, having less renal toxicity and effective safety profile [59]. Both agents inhibits viral DNA polymerase. However, brincidofovir used against monkey pox are scarce in animal model, brincidofovir are effective for treatment of orthopoxviruses. Clinical data of cidofovir for monkey pox is not available in human, yet in vivo and in vitro efficacy against were reported.

4.5 Vaccinia Immune Globulin (VIG)

It is hyper immune globulin approved via FDA for management of several complication of vaccinia vaccination such as vaccinia infections, severe generalized vaccinia, progressive vaccinia and eczema vaccinatum and other aberrant infections caused by vaccinia virus except ocular infection. However, potential treatment, on VIG against smallpox or monkey pox has not tested yet in humans [60].

5. Conclusion

Monkeypox virus (MPXV) has emerged as a significant global health threat, particularly in the wake of its re-emergence in non-endemic regions and its potential for rapid human-to-human transmission. The expanding clinical spectrum, rising incidence in immunocompromised individuals, and association with comorbidities such as HIV highlight the urgency of a coordinated global response. This review consolidates current knowledge on MPXV, encompassing its transmission mechanisms, clinical manifestations, pathogenesis, and potential complications in vulnerable populations including children, pregnant women, and HIV-infected individuals. Despite the availability of antiviral agents like Tecovirimat and Brincidofovir, clinical evidence for their efficacy in human monkeypox cases remains limited. These drugs, while promising, necessitate further rigorous clinical trials to assess their safety profiles and optimize dosing regimens, especially in special populations. Furthermore, the development of next-generation antivirals and therapeutic antibodies should be prioritized to broaden treatment options.

Vaccination remains a cornerstone of MPX prevention. The deployment of non-replicating vaccines such as JYNNEOS™ offers a safer alternative to traditional live vaccines like ACAM2000®, especially for immunocompromised individuals. However, logistical challenges including vaccine availability, public hesitancy, and disparities in access must be addressed through strategic policymaking and global health equity initiatives.

Importantly, monkeypox is not just a virological or clinical concern but also a societal and behavioral one. Stigmatization, particularly among MSM and HIV-positive communities, may hamper surveillance and hinder access to healthcare. Public health messaging should therefore be inclusive, evidence-based, and sensitive to cultural and social dynamics to ensure high-risk populations are protected without being marginalized.

Looking ahead, it is imperative to strengthen surveillance systems, enhance diagnostic capacity, and invest in research exploring viral evolution, immune response dynamics, and long-term immunity. Multidisciplinary collaboration between virologists, clinicians, epidemiologists, and policymakers will be key to anticipating and mitigating future outbreaks. As with all emerging zoonotic diseases, a One Health approach that integrates human, animal, and environmental health will be crucial in understanding the reservoirs, spillover dynamics, and preventing future pandemics.

In conclusion, MPXV presents a complex and evolving challenge. Combating this threat requires a combination of scientific innovation, public health vigilance, and global solidarity. Future efforts must be proactive, not reactive, ensuring the world is better prepared for potential MPXV resurgence and other zoonotic threats on the horizon.

Data Availability Statement

Dr. Abdul Wadood should be contacted for data and material or other information.

Informed Consent

Not applicable

Conflict of Interest

The authors declare that they have no known competing financial interests.

Consent for Publication

Not applicable

Acknowledgement

The authors appreciate the support and guidance of Dr. Ajmal Khan, University of Nizwa, Sultante Oman in preparing this article.

Funding

Not applicable

Use of Gen AI

The authors declare that no Gen AI was used in the creation of this manuscript.

Reference

[1] Khalil A, Samara A, O'Brien P, Morris E, Draycott T, Lees C, et al. Monkeypox vaccines in pregnancy: lessons must be learned from COVID-19. The Lancet Global Health. 2022, 10(9), e1230-e1231. DOI: 10.1016/S2214-109X(22)00284-4

[2] Sevindik M, Yazar M, Polat AO, Karatepe HK, Uysal İ, Özdemir B, et al. MONKEY POX (M-Pox/MPXV): Epidemiology, transmission, clinical findings, treatment and herbal treatment. Indian Journal of Natural Products and Resources. 2024, 15(4), 473-490. DOI: https://doi.org/10.56042/ijnpr.v15i4.13951

[3] Alakunle E, Kolawole D, Diaz-Cánova D, Alele F, Adegboye O, Moens U, et al. A comprehensive review of monkeypox virus and mpox characteristics. Frontiers in Cellular and Infection Microbiology. 2024, 14, 1360586. DOI: 10.3389/fcimb.2024.1360586

[4] Liu Q, Fu L, Wang B, Sun Y, Wu X, Peng X, et al. Clinical characteristics of human Mpox (monkeypox) in 2022: a systematic review and meta-analysis. Pathogens. 2023, 12(1), 146. DOI: 10.3390/pathogens12010146

[5] Durski KN, McCollum AM, Nakazawa Y, Petersen BW, Reynolds MG, Briand S, et al. Emergence of monkeypox in West Africa and Central Africa, 1970-2017. Weekly Epidemiological Record. 2018, 93(11), 125-133.

[6] Sousa ÁFL, Sousa AR, Fronteira I. Monkeypox: between precision public health and stigma risk. Revista Brasileira de Enfermagem. 2022, 75(5), e750501. DOI: 10.1590/0034-7167.2022750501

[7] Pfeiffer JA, Collingwood A, Rider LE, Minhaj FS, Matheny AM, Kling C, et al. High-contact object and surface contamination in a household of persons with monkeypox virus infection—Utah, June 2022. MMWR. Morbidity and Mortality Weekly Report. 2022, 71(34), 1092-1094. DOI: 10.15585/mmwr.mm7134e1

[8] Sookaromdee P, Wiwanitkit V. Neonate, infected mother and monkeypox: the present concern. Journal of Perinatal Medicine. 2022, 51(3), 437-437. DOI: 10.1515/jpm-2022-0256

[9] El Eid R, Allaw F, Haddad SF, Kanj SS. Human monkeypox: A review of the literature. PLoS Pathogens. 2022, 18(9), e1010768. DOI: 10.1371/journal.ppat.1010768

[10] Hutin YJ, Williams RJ, Malfait P, Pebody R, Loparev VN, Ropp SL, et al. Outbreak of human monkeypox, Democratic Republic of Congo, 1996 to 1997. Emerging Infectious Diseases. 2001, 7(3), 434-438. DOI: 10.3201/eid0703.010311

[11] Adler H, Gould S, Hine P, Snell LB, Wong W, Houlihan CF, et al. Clinical features and management of human monkeypox: a retrospective observational study in the UK. The Lancet Infectious Diseases. 2022, 22(8), 1153-1162. DOI: 10.1016/S1473-3099(22)00228-6

[12] Girometti N, Byrne R, Bracchi M, Heskin J, McOwan A, Tittle V, et al. Demographic and clinical characteristics of confirmed human monkeypox virus cases in individuals attending a sexual health centre in London, UK: an observational analysis. The Lancet Infectious Diseases. 2022, 22(9), 1321-1328. DOI: 10.1016/S1473-3099(22)00411-X

[13] Del Río García V, Palacios JG, Morcillo AM, Duran-Pla E, Rodríguez BS, Lorusso N. Monkeypox outbreak in a piercing and tattoo establishment in Spain. The Lancet Infectious Diseases. 2022, 22(11), 1526-1528. DOI: 10.1016/S1473-3099(22)00652-1

[14] Yinka-Ogunleye A, Aruna O, Ogoina D, Aworabhi N, Eteng W, Badaru S, et al. Reemergence of human monkeypox in Nigeria, 2017. Emerging Infectious Diseases. 2018, 24(6), 1149-1151. DOI: 10.3201/eid2406.180017

[15] Brown K, Leggat PA. Human monkeypox: current state of knowledge and implications for the future. Tropical Medicine and Infectious Disease. 2016, 1(1), 8. DOI: 10.3390/tropicalmed1010008

[16] Gong Q, Wang C, Chuai X, Chiu S. Monkeypox virus: a re-emergent threat to humans. Virologica Sinica. 2022, 37(4), 477-482. DOI: 10.1016/j.virs.2022.07.006

[17] Sale TA, Melski JW, Stratman EJ. Monkeypox: an epidemiologic and clinical comparison of African and US disease. Journal of the American Academy of Dermatology. 2006, 55(3), 478-481. DOI: 10.1016/j.jaad.2006.05.061
[18] Damon IK. Status of human monkeypox: clinical disease, epidemiology and research. Vaccine. 2011, 29(4), D54-D59. DOI: 10.1016/j.vaccine.2011.04.014
[19] Antinori A, Mazzotta V, Vita S, Carletti F, Tacconi D, Lapini LE, et al. Epidemiological, clinical and virological characteristics of four cases of monkeypox support transmission through sexual contact, Italy, May 2022. European Communicable Disease Bulletin. 2022, 27(22), 2200421. DOI: 10.2807/1560-7917.ES.2022.27.22.2200421
[20] Huhn GD, Bauer AM, Yorita K, Graham MB, Sejvar J, Likos A, et al. Clinical characteristics of human monkeypox, and risk factors for severe disease. Clinical Infectious Diseases. 2005, 41(12), 1742-1751. DOI: 10.1086/498115
[21] Erez N, Achdout H, Milrot E, Schwartz Y, Wiener-Well Y, Paran N, et al. Diagnosis of imported monkeypox, Israel, 2018. Emerging Infectious Diseases. 2019, 25(5), 980-983. DOI: 10.3201/eid2505.190076
[22] Sallam M, Al-Mahzoum K, Al-Tammemi AB, Alkurtas M, Mirzaei F, Kareem N, et al. Assessing Healthcare Workers' Knowledge and Their Confidence in the Diagnosis and Management of Human Monkeypox: A Cross-Sectional Study in a Middle Eastern Country. Healthcare. 2022, 10(9), 1722. DOI: 10.3390/healthcare10091722
[23] Sepehrinezhad A, Ashayeri Ahmadabad R, Sahab-Negah S. Monkeypox virus from neurological complications to neuroinvasive properties: current status and future perspectives. Journal of Neurology. 2023, 270(1), 101-108. DOI: 10.1007/s00415-022-11339-w
[24] Badenoch JB, Conti I, Rengasamy ER, Watson CJ, Butler M, Hussain Z, et al. Neurological and psychiatric presentations associated with human monkeypox virus infection: a systematic review and meta-analysis. EClinicalMedicine. 2022, 52, 101644. DOI: 10.1016/j.eclinm.2022.101644
[25] Davido B, D'anglejan E, Jourdan J, Robinault A, Davido G. Monkeypox 2022 outbreak: cases with exclusive genital lesions. Journal of Travel Medicine. 2022, 29(6), taac077. DOI: 10.1093/jtm/taac077
[26] Thornhill JP, Barkati S, Walmsley S, Rockstroh J, Antinori A, Harrison LB, et al. Monkeypox virus infection in humans across 16 countries—April–June 2022. New England Journal of Medicine. 2022, 387(8), 679-691. DOI: 10.1056/NEJMoa2207323
[27] Wise J. Monkeypox: New clinical symptoms are identified in confirmed cases. British Medical Journal Publishing Group. 2022, 378, o1845. DOI: 10.1136/bmj.o1845
[28] de Sousa D, Patrocínio J, Frade J, Correia C, Borges-Costa J, Filipe P. Human monkeypox coinfection with acute HIV: an exuberant presentation. International Journal of STD & AIDS. 2022, 33(10), 936-938. DOI: 10.1177/09564624221114998
[29] Stanford MM, McFadden G, Karupiah G, Chaudhri G. Immunopathogenesis of poxvirus infections: forecasting the impending storm. Immunology and Cell Biology. 2007, 85(2), 93-102. DOI: 10.1038/sj.icb.7100033
[30] Nalca A, Rimoin AW, Bavari S, Whitehouse CA. Reemergence of monkeypox: prevalence, diagnostics, and countermeasures. Clinical Infectious Diseases. 2005, 41(12), 1765-1771. DOI: 10.1086/498155
[31] Zaucha GM, Jahrling PB, Geisbert TW, Swearengen JR, Hensley L. The pathology of experimental aerosolized monkeypox virus infection in cynomolgus monkeys (Macaca fascicularis). Laboratory Investigation. 2001, 81(12), 1581-1600. DOI: 10.1038/labinvest.3780373
[32] Engelmayer J, Larsson M, Subklewe M, Chahroudi A, Cox WI, Steinman RM, et al. Vaccinia virus inhibits the maturation of human dendritic cells: a novel mechanism of immune evasion. The Journal of Immunology. 1999, 163(12), 6762-6768. DOI: 10.4049/jimmunol.163.12.6762
[33] Beauchamp NM, Busick RY, Alexander-Miller MA. Functional divergence among CD103+ dendritic cell subpopulations following pulmonary poxvirus infection. Journal of Virology. 2010, 84(19), 10191-10199. DOI: 10.1128/JVI.00892-10
[34] Walzer T, Galibert L, Smedt TD. Poxvirus semaphorin A39R inhibits phagocytosis by dendritic cells and neutrophils. European journal of immunology. 2005 35(2), 391-398. DOI: 10.1002/eji.200425669
[35] Hickman HD, Reynoso GV, Ngudiankama BF, Rubin EJ, Magadán JG, Cush SS, et al. Anatomically restricted synergistic antiviral activities of innate and adaptive immune cells in the skin. Cell Host & Microbe. 2013, 13(2), 155-168. DOI: 10.1016/j.chom.2013.01.004
[36] Chahroudi A, Chavan R, Kozyr N, Waller EK, Silvestri G, Feinberg MB. Vaccinia virus tropism for primary hematolymphoid cells is determined by restricted expression of a unique virus receptor. Journal of Virology. 2005, 79(16), 10397-10407. DOI: 10.1128/JVI.79.16.10397
[37] Chapman JL, Nichols DK, Martinez MJ, Raymond JW. Animal models of orthopoxvirus infection. Veterinary Pathology. 2010, 47(5), 852-870. DOI: 10.1177/0300985810378649
[38] Harrison SC, Alberts B, Ehrenfeld E, Enquist L, Fineberg H, McKnight SL, et al. Discovery of antivirals against smallpox. Proceedings of the National Academy of Sciences of the United States of America. 2004, 101(31), 11178-11192. DOI: 10.1073/pnas.0403600101
[39] Institute of Medicine (U.S.). Committee on the Assessment of Future Scientific Needs for Live Variola Virus. Assessment of future scientific needs for live variola virus. Washington (DC): National Academy Press(US). 1999. DOI: 10.17226/6445
[40] Cann JA, Jahrling PB, Hensley LE, Wahl-Jensen V. Comparative pathology of smallpox and monkeypox in man and macaques. Journal of Comparative Pathology. 2013, 148(1), 6-21. DOI: 10.1016/j.jcpa.2012.06.007
[41] Aggio JB, Krmeská V, Ferguson BJ, Wowk PF, Rothfuchs AG. Vaccinia virus infection inhibits skin dendritic cell migration to the draining lymph node. The Journal of Immunology. 2021, 206(4), 776-784. DOI: 10.4049/jimmunol.2000928
[42] Bhunu CP, Mushayabasa S, Hyman JM. Modelling HIV/AIDS and monkeypox co-infection. Applied Mathematics and Computation. 2012, 218(18), 9504-9518. DOI: 10.1016/j.amc.2012.03.042
[43] Forrester JV, Mölzer C, Kuffova L. Immune privilege furnishes a niche for latent infection. Frontiers in Ophthalmology. 2022, 2, 869046. DOI: 10.3389/fopht.2022.869046
[44] Khoury G, Fromentin R, Solomon A, Hartogensis W, Killian M, Hoh R, et al. Human immunodeficiency virus persistence and T-cell activation in blood, rectal, and lymph node tissue in human immunodeficiency virus–infected individuals receiving suppressive antiretroviral therapy. The Journal of Infectious Diseases. 2017, 215(6), 911-919. DOI: 10.1093/infdis/jix039
[45] Cuérel A, Favre G, Vouga M, Pomar L. Monkeypox and pregnancy: latest updates. Viruses. 2022, 14(11), 2520. DOI: 10.3390/v14112520
[46] Brewer MG, Monticelli SR, Ward BM. Monkeypox: considerations as a new pandemic looms. The Journal of Investigative Dermatology. 2022, 142(10), 2561-2564. DOI: 10.1016/j.jid.2022.08.030

[47] Aguilera-Alonso D, Alonso-Cadenas JA, Roguera-Sopena M, Lorusso N, Miguel LGS, Calvo C. Monkeypox virus infections in children in Spain during the first months of the 2022 outbreak. The Lancet Child & Adolescent Health. 2022, 6(11), e22-e23. 10.1016/S2352-4642(22)00250-4
[48] Ammon Avalos L, Galindo C, Li DK. A systematic review to calculate background miscarriage rates using life table analysis. Birth Defects Research Part A: Clinical and Molecular Teratology. 2012, 94(6), 417-423. DOI: 10.1002/bdra.23014
[49] Cohen MS, Shaw GM, McMichael AJ, Haynes BF. Acute HIV-1 infection. New England Journal of Medicine. 2011, 364(20), 1943-1954. DOI: 10.1056/NEJMra1011874
[50] Alakunle E, Moens U, Nchinda G, Okeke MI. Monkeypox virus in Nigeria: infection biology, epidemiology, and evolution. Viruses. 2020, 12(11), 1257. DOI: 10.3390/v12111257
[51] Wang X, Lun WH. Skin Manifestation of Human Monkeypox. Journal of Clinical Medicine. 2023, 12(3), 914. DOI: 10.3390/jcm12030914
[52] Hammarlund E, Lewis MW, Carter SV, Amanna I, Hansen SG, Strelow LI, et al. Multiple diagnostic techniques identify previously vaccinated individuals with protective immunity against monkeypox. Nature Medicine. 2005, 11(9), 1005-1011. DOI: 10.1038/nm1273
[53] Chong AC, Visitsunthorn K, Ong PY. Genetic/Environmental Contributions and Immune Dysregulation in Children with Atopic Dermatitis. Journal of Asthma and Allergy. 2022, 15, 1681-1700. DOI: 10.2147/JAA.S293900
[54] Fine PE, Jezek Z, Grab B, Dixon H. The transmission potential of monkeypox virus in human populations. International Journal of Epidemiology. 1988, 17(3), 643-650. DOI: 10.1093/ije/17.3.643
[55] Ansari Z, Ramzan H, Shakeel R. Is there a need of monkeypox vaccine amidst the hesitancy of COVID-19 immunization in Pakistan? Annals of Medicine and Surgery. DOI: 10.1016/j.amsu.2022.104391
[56] Chowdhury SR, Datta PK, Maitra S. Monkeypox and its pandemic potential: what the anaesthetist should know. British Journal of Anaesthesia. 2022, 129(3), e49-e52. DOI: 10.1016/j.bja.2022.06.007
[57] Zimmermann P, Curtis N. Monkeypox—What Pediatricians Need to Know. The Pediatric Infectious Disease Journal. 2022, (12), 1020-1031. DOI: 10.1097/INF.0000000000003720
[58] Grosenbach DW, Honeychurch K, Rose EA, Chinsangaram J, Frimm A, Maiti B, et al. Oral tecovirimat for the treatment of smallpox. New England Journal of Medicine. 2018, 379(1), 44-53. DOI: 10.1056/NEJMoa1705688
[59] Chittick G, Morrison M, Brundage T, Nichols WG. Short-term clinical safety profile of brincidofovir: A favorable benefit–risk proposition in the treatment of smallpox. Antiviral Research. 2017, 143, 269-277. DOI: 10.1016/j.antiviral.2017.01.009
[60] Wittek R. Vaccinia immune globulin: current policies, preparedness, and product safety and efficacy. International Journal of Infectious Diseases. 2006, 10(3), 193-201. DOI: 10.1016/j.ijid.2005.12.001