INTERNATIONAL JOURNAL OF CURRENT RESEARCH IN CHEMISTRY AND PHARMACEUTICAL SCIENCES
(p-ISSN: 2348-5213: e-ISSN: 2348-5221)
www.ijcrcps.com
(A Peer Reviewed, Referred, Indexed and Open Access Journal)
DOI: 10.22192/ijcrcps Coden: IJCROO(USA) Volume 10, Issue 1 - 2023

**Review Article**

**DOI:** http://dx.doi.org/10.22192/ijcrcps.2023.10.01.005

# Current Issues on Monkey pox Infection among immunocompromised patients: African Perspectives

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## Abstract

Monkey pox is more prevalent in a subgroup of people who also have HIV, most likely because to sexual transmission and the level of immunosuppression that these patients may display at different stages of their illness. Although monkey pox can spread to everyone who comes into contact with an infected person, the causes of this subgroup's disproportionately high prevalence are yet unknown. HIV-infected individuals are more likely to experience secondary bacterial infections, longer illnesses, and confluent or partly confluent rashes as opposed to discrete lesions. Prognosis is influenced by a number of variables, such as starting health state, concomitant diseases, prior immunisation history and comorbidities. Extended Monkeypox and protracted infection may be more likely to affect those who are immunocompromised due to HIV or other diseases.This seems to occur most frequently in people who have more severe immunosuppression.

**Keywords:** Monkey pox, Immunocompromised patients, HIV, Africa

## Introduction

Monkeypox, which the World Health Organization now refers to as "MPOX" after consulting with numerous international experts, is an uncommon virus that is typically found in forested parts of Central and West Africa(Durski, 2018). Despite having animal origins, the illness has also been linked to human cases in the past 50 years or more(Likos *et al.*, 2005).

The etiologic agent of this illness is the monkeypox virus (MPXV), a DNA virus belonging to the Poxviridae family and Orthopoxvirus genus that shares 96% of its DNA with the variola virus (Am and Ik, 2014). As of August 24, 2022, there were 44,503 confirmed cases worldwide(CDC, 2023). Monkeypox is more prevalent in a subgroup of people who also have HIV, most likely because to sexual transmission and the level of immunosuppression that these patients may display at different stages of their illness(CDC, 2023). Although monkeypox can spread to everyone who comes into contact with an infected person, the causes of this subgroup's disproportionately high prevalence are yet unknown(CDC, 2023). Given the vast range of characteristics recorded in the ongoing outbreak, which vary from localized lesions to potentially fatal generalized dermatoses, there is no longer a typical clinical presentation for this illness(Martínez *et al.*, 2022). All of these individuals have immunosuppression, which is a side effect of HIV infection, in some capacity(Martínez *et al.*, 2022).

There is a dearth of information on the severity of mpox in immunocompromised individuals, especially those with uncontrolled HIV(Am and Ik, 2014). Immunocompromised individuals do appear to be more likely to experience vaccinia inoculation problems following smallpox immunization, larger and more extensive molluscum contagiosum eruptions, and recurrent or massive of virus lesions(Reynolds *et al.*, 2017).

## Monkeypox

Monkeypox is a rare viral zoonotic disease caused by a double stranded DNA virus that belongs to the Orthopoxvirus genus of the Poxviridae family(McCollum and Damon, 2014). The disease presents with symptoms similar to smallpox but with a lesser severity(Nakazawa *et al.*, 2013). Monkeypox was first discovered in 1958 when two outbreaks of a pox-like disease occurred in colonies of monkeys kept for research, hence the name monkeypox(Durski, 2018). The first human case of monkeypox was recorded in 1970 in the Democratic Republic of the Congo (DRC), which has subsequently spread to other central and western African countries(Nakazawa *et al.*, 2013). There are two circulating clades of the monkeypox virus: clade I and clade II(Nakazawa *et al.*, 2013). Genomic studies linked most of the cases from the outbreak 2022 cases in Europe and America to clade II lineage B.1. Clade II was seen in previous years outbreaks in the USA, Israel and Singapore and the 2017-2018(Reynolds *et al.*, 2017). Cameroon is the only country known to harbor both classes(Doty *et al.*, 2017).

The West African strain of monkeypox rarely results in fatal illnesses(CDC, 2023). The likelihood of survival is greater than 99 percent for those who contract the West African variety of monkeypox, which was found in the epidemic of 2022(CDC, 2023). A compromised immune system, being pregnant or nursing, or being under the age of eight all increase your risk of developing a terrible illness and passing away from monkeypox(Am and Ik, 2014). The disease itself is typically not fatal. Monkeypox can occasionally, though infrequently, result in life-threatening complications such as pneumonia, encephalitis of the brain, or eye problems(Doty *et al.*, 2017). Monkeypox normally requires a 2 to 4 week healing period(Doty *et al.*, 2017).

## Monkey Pox and Immunity

According to (Lum *et al.*, 2022) ,Orthopoxviruses (OPVs) are still important public health hazards upwards of 30 years after smallpox was eradicated. Other OPVs, including vaccinia virus (VACV) and monkeypox virus (MPXV), continue to pose a danger. Research on safer, better-defined vaccinations has been sparked by ongoing worries about vaccine safety and the spread of smallpox(Lum *et al.*, 2022). Acam2000 (Acambis) and Imvamune are two examples of 2nd- and 3rd-generation vaccinations that have evolved due to these worries(Adler *et al.*, 2022). However, concerns persist with regard to the breadth and quality of the response, the safety of those who are immunocompromised, and the appropriate usage techniques(Adler *et al.*, 2022). Additionally(Hernandez *et al.*, 2022), the first-generation vaccinations that were used to

 

eliminate smallpox were developed before sophisticated methods for defining precise immune responses were available.

Despite the fact that the virus has been known about for a long time, nothing is known about human immunity to MPXV infection(Hernandez *et al.*, 2022). So, research with VACV and similar orthopoxviruses are frequently used to infer how MPXV interacts with the host immune system(Hernandez *et al.*, 2022). Many innate immune cells, including monocytes/macrophages, neutrophils and natural killer cells, have not yet been well understood in MPXV-infected patients. Identifying these immune cells' roles and finding critical indicators for disease prediction will need identification and profiling of these cells(Karem *et al.*, 2007).

Following an active viral infection, innate immune cells are usually the first line of defence, although certain viruses also employ these cells as targets(Van Damme *et al.*, 2021). Monocytes are the first cells that poxviruses target, according to a number of in vitro and in vivo studies. MPXV infection occurs in cynomolgus macaques, and susceptible monocytes are aggressively attracted to the sites of infection(Van Damme *et al.*, 2021). Inflammatory mouse monocytes that are CD45+CD11b+GR-1int have also been demonstrated to be permissive to VACV replication(Betancort-Plata et al., 2022). Actin tails, cell connections, lamellipodia, and branching structures related with the VACV virions were generated by these primary macrophages after VACV infection, suggesting that these cells may help the virus spread(Betancort-Plata *et al.*, 2022). However, Ly6G+ innate immune cells (neutrophils as well as Ly6G+ monocytes) were in charge of infiltrating and regulating virus-infected cells, hence reducing viral tissue damage(Fischer *et al.*, 2011). Depletion of phagocytic cells, however, was also observed to not completely stop the transmission of VACV in infected mice, indicating that other immune cells than monocytes and macrophages are also capable of promoting viral propagation(Fischer *et al.*, 2011).

It is also important to note that immune cells deployed to the infection site only prevent local pathogenesis and tissue pathology and do not stop viral propagation, necessitating a systemic immune response(Huhn e*t al.*, 2005).

Recently, Gazzani et al. (2017)concluded that Natural killer cells are a crucial part of innate immunity and can direct the course of the adaptive immune response. Prior to this fast expansion, MPXV infection dramatically reduced the ability of the different natural killer cell subsets to migrate. On these cells, it was also noted that chemokine receptors CXCR3, CCR5, CCR6, and CCR7 were downregulated(Gazzani *et al.*, 2017).Natural killer cells from lymph nodes and blood lose their capacity to degranulate and release IFN and TNF(Jahrling *et al.*, 2004). This suggests that IL-15 therapy is beneficial because it boosts the amount of IFN-secreting innate immune cells(Jahrling *et al.*, 2004).

One of the most economical medical procedures available in contemporary society is vaccination(de Sousa *et al.*, 2022). The first human vaccination was a smallpox vaccine, and vaccinia virus (VV), which is credited with eradicating smallpox illness globally, is thought to be the most effective human vaccine(de Sousa *et al.*, 2022). However, it is still unknown how the smallpox vaccination causes individuals to develop an adaptive immune response(Fischer *et al.*, 2011). Due to the potential threat of bioterrorism, interest in smallpox immunity has recently been considerably rekindled(de Sousa *et al.*, 2022).

(Adler *et al.*, 2022) said there are three main immune responses that are each thought to be crucial for long-lasting protection are induced by vaccines: antibodies, memory T cells, and memory B cells. These responses include antibodies, memory T cells and memory B cells. Human smallpox (variola virus) infection can be prevented by antibodies, most likely by neutralising the initial viral inoculum(Adler *et al.*, 2022). Humans who have cellular or humoral immune weaknesses are more susceptible to contracting the poxvirus(Iñigo Martínez *et al.*, 2022). Circulating antibodies are the main sign of

 

protection for the majority of human vaccinations since they represent the body's first line of defence against infection(Townsend *et al.*, 2013). The importance of memory T cells (CD8, CD4, or a mix of them) for defence against a range of infectious illnesses, including poxviruses, has been demonstrated by several investigations(Hernandez *et al.*, 2022). Memory B cells are also likely to play a role in human immunity to smallpox(Lum *et al.*, 2022). Due to their capacity to produce anamnestic antibodies in response to infection, they may replace long-lived plasma cells to maintain sustained serum antibody levels(Lum *et al.*, 2022).

Is there any protection from monkeypox infection provided by distant smallpox vaccination? This is perhaps the most obvious question(Miller, 2022). Distant smallpox vaccination offered 85% protection against monkeypox infection in close family and household connections(Miller, 2022). In the 1990s, a follow-up study in Central Africa estimated that household transmission of monkeypox would increase(Betancort-Plata *et al.*, 2022). This study attributed an increase in disease incidence to a decrease in vaccine-derived protection(Betancort-Plata *et al.*, 2022). Prior immunisation and high IgG levels seem to offer some protection against monkeypox, although not statistically significant levels, and disease severity is reduced(Van Damme et al., 2021). The emergence or alteration of immunological responses to the OPX antigen in household contacts of patients is indicative of an infection that, in previously immunised individuals, may provide a partial defence against illness(Miller, 2022).

The presence of immunological indicators of infection in certain non-vaccinated contacts shows that illness outcome may rely on the kind, dosage, or route of viral exposure(*US Public Health Service*, 2021). Infection with the monkeypox virus during the U.S. outbreak was brought on by exposures to or encounters with animals, mostly prairie dogs (Adler *et al.*, 2022), which may not have been the same as those linked to outbreaks of the disease among humans in Central Africa. Independent of vaccination history(Townsend *et al.*, 2013), the route and dose of exposure may potentially have an impact on the severity of the condition. It is plausible that variations in viral virulence and even differing responses to decreasing vaccine-derived immunity may be reflected in the clinical presentations of the Western and Central African clades of virus(Townsend *et al.*, 2013).

Protective properties of antibodies against EV suggest that a specific group of proteins would be sufficient to provide immunity(Rizk *et al.*, 2022). MV proteins L1, A17, A27, D8 H3, A13, and A28 as well as EV proteins A33 and B5 are all immune response targets(Karem et al., 2007). It is known that the protein targets of humoral immunity after vaccination vary from person to person(Huhn *et al.*, 2005). The mechanisms of protection in recently developed smallpox vaccines will be essential for comprehending novel-vaccine efficacy(Karem *et al.*, 2007). A recent examination of CD8 T cell responses in mice revealed bigger than anticipated variations in MHC-dependent responses between VACV-infected outbred and inbred populations(Petersen, 2016). All of these elements (specific antigen recognition, cellular responses, and diversity of neutralising antibody response) may contribute to the mechanism of protection(Petersen, 2016).
MPXV does not consistently activate TNF-regulated and NF-B-regulated genes, particularly in infected animals, but this is not unexpected given that VARV and other orthopoxviruses include genes that may alter these pathways(Lum *et al.*, 2022). It has been shown that human IFN prevents MPXV replication and dissemination. While host immunity is necessary to fight infections, abnormal immunological signaling can negatively impact the course of illnesses(de Sousa *et al.*, 2022). Cytokines promote monocytosis, which may aid in increased viral transmission through viraemia linked with monocytic cells(Fischer *et al.*, 2011).

## Monkey Pox in Immunocompromised Persons

HIV-infected individuals are more likely to experience secondary bacterial infections, longer illnesses (and hence a longer time of

 

infectiousness), and confluent or partly confluent rashes as opposed to discrete lesions(Miller, 2022). According to a recent U.S. investigation(*US Public Health Service*, 2021), hospitalisations were more frequent among those with HIV than among those without HIV. Several cases of severe mpox among HIV-positive, immunocompromised individuals are known to the CDC(Miller, 2022).

Four of the seven deaths in a 2017–18 case series of 122 Nigerian patients(Iñigo Martínez *et al.*, 2022), with mpox were those with untreated advanced HIV, although information on the general prevalence of patients with HIV was inadequate. According to the information available, individuals with advanced and untreated HIV may be more susceptible to developing severe or protracted mpox(Iñigo Martínez *et al.*, 2022).

Molluscum contagiosum eruptions and massive orf virus lesions (mpox) have been known to occur in immunocompromised individuals, especially those with uncontrolled HIV(Hernandez *et al.*, 2022). A fatal instance of mpox in a kidney transplant recipient has also been previously documented(Davies *et al.*, 2005). It is still unclear if this evidence can be applied to mpox. In two individuals with lupus nephritis and a history of bone marrow transplant, a 2003 mpox outbreak investigation(Davies *et al.*, 2005) found that they recovered without experiencing severe disease. Immunocompromised people may be more prone to disease and infection, although not necessarily with severe consequences(de Sousa *et al.*, 2022).

Mpox(Miller, 2022) can cause a progressive or disseminated rash, extended course, sepsis, ophthalmic disease, encephalitis and death in those with advanced or untreated HIV. Prognosis is influenced by a number of variables, such as starting health state, concomitant diseases, prior immunisation history and comorbidities (Townsend *et al.*, 2013). Extended mpox and protracted infectiousness may be more likely to affect those who are immunocompromised due to HIV or other diseases(Miller, 2022). This seems to occur most frequently in people who have more severe immunosuppression. Patients with CD4 levels below 350/mm3 have seen poor outcomes (who are unlikely to be virologically suppressed)(Petersen, 2016).

## Remedies

According to(Rizk *et al.*, 2022), recent statistics on MVIH (Monkeypox virus in human), adults tend to have a milder case of the condition than children do. Pregnant women are at a higher risk of fetal loss, and immunocompromised patients' outcomes can be poor(Betancort-Plata *et al.*, 2022). Two existing vaccinations based on the vaccinia virus are known to successfully prevent it(Betancort-Plata *et al.*, 2022).

Despite the fact that MVIH is not a new illness, there are still many unanswered questions. The current worldwide epidemic is bigger and more widespread than previously(Gazzani et al., 2017). It's still unclear how the disease will affect a broader population of immunocompromised patients, pregnant women, and patients from places with little resources(Gazzani *et al.*, 2017). Monitoring for post-MVIH sequelae would be necessary, particularly for major issues including sight-threatening corneal opacities and physically crippling scarring(Miller, 2022).

Additionally(Rizk *et al.*, 2022), research is needed to determine the sources and modes of transmission of monkeypox. Animals can contract monkeypox, and animal reservoirs are unknown, hence research on disease frequency in household pets and other animals is necessary(Townsend *et al.*, 2013). In a comparable vein, zoonotic transmission mitigation strategies should be taken into account for reducing monkeypox in animals(Rizk et al., 2022).

Resources for Public health will be challenged as the number of patients rises, with major consequences for public health(Jahrling *et al.*, 2004). The effectiveness and safety of antiviral medications and vaccinations require more research(Petersen, 2016). Frontline healthcare workers should get training on how to identify,

 

isolate and manage patients with MVIH. Innovative therapies and diagnostics, such as the lateral flow test for the detection of orthopoxviruses, also need more investigation(Petersen, 2016).

An individual should be considered while deciding whether to treat and watch over an immunocompromised patient at home or in a hospital(Adler *et al.*, 2022). Consideration may be given to both prolonging the period of therapy and switching from oral to IV administration if the patient does not improve after the recommended course of oral tecovirimat (i.e., 14 days)(Adler *et al.*, 2022). Such decisions should be taken case-by-case, taking into account the patient's health, any coexisting conditions, capacity for oral medicine absorption, and capacity for a substantial, fatty meal(Adler *et al.*, 2022). It may also be explored to add other treatments such VIGIV, brincidofovir, or cidofovir(Rizk *et al.*, 2022). Medical countermeasure usage decisions must be determined individually for each patient and may be influenced by a number of clinical and other factors(Petersen, 2016).

## Conclusion

Monkey pox is more prevalent in a subgroup of people who also have HIV, most likely because to sexual transmission and the level of immunosuppression that these patients may display at different stages of their illness. Prognosis is influenced by a number of variables, such as starting health state, concomitant diseases, prior immunisation history and comorbidities. This seems to occur most frequently in people who have more severe immunosuppression.

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Quick Response Code

DOI: 10.22192/ijcrcps.2023.10.01.005

How to cite this article:

Emmanuel Ifeanyi Obeagu, Godfred Yawson Scott, Felix Amekpor, Valerie Esame Njar. (2023). Current Issues on Monkey pox Infection among immunocompromised patients: African Perspectives. Int. J. Curr. Res. Chem. Pharm. Sci. 10(1): 40-47.

DOI: http://dx.doi.org/10.22192/ijcrcps.2023.10.01.005

 