

Review Article

Monkeypox Virus, A Global Public Health Concern and Challenge for Low-income Countries including Pakistan: A Right Time to Nip the Evil in the Bud

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Abstract

Monkeypox is a rare zoonotic infection originating in the regions of Central and West Africa. The global threat has been arising since monkeypox is spreading outside of the endemic regions. Pakistan has recently exhausted health funds in a quarrel against SARS-CoV-2, by supplying expensive COVID-19 vaccines to the general public, free of cost. Pakistan's government has remarkably contributed to lowering the suffering of COVID-19-affected patients by granting the Sehat Sahulat Programme and similar health initiatives to restrict viral propagation in the general public. However, despite all efforts the major constraints are a lack of international funds and limitations on the budget of healthcare systems and medical facilities. Newly emerged cases of monkeypox are very threatening to Pakistan's economy and health. Therefore, it is very necessary that healthcare authorities take effective measures like surveillance, early identification, separation, monitoring of contacts, immunization, and public awareness in order to stop the spread of the virus and control monkeypox outbreaks.

Introduction

Monkeypox disease

Monkeypox (Mpx) is categorized as a zoonotic disease affecting humans with symptoms of rash, skin lesions, upper respiratory symptoms, headache, lymphadenopathy, oral ulcers, and conjunctivitis [1]. Mpx is primarily found in isolated areas of Central and West Africa, in 1958, the first instance of this disease was reported when monkeys used for research exhibited symptoms similar to that of pox [2]. The Democratic Republic of the Congo witnessed the initial occurrence of the disease in 1970 when the first human contracted the disease. Since that time several African nations have experienced intermittent occurrences of Mpx [3-5].

Monkeypox Virus (MPXV), is classified under the genus Orthopox and Poxviridae family [2]. This virus bears a resemblance to the smallpox-causing variola virus, albeit less severe and with a lower fatality rate [6,7]. Humans can contract the virus from animals, particularly rodents and primates, by coming into contact with their bodily excretions such as blood, urine, or fecal matter, or through bite [8]. Human transmission can occur through various means, primarily by inhaling respiratory droplets, extended face-to-face contact, direct contact with bodily fluids or infectious skin lesions, or touching contaminated surfaces. Viral transmission can also occur by sharing contaminated household surfaces such as sleeping in the same bed, eating or drinking from the same dishes, or sharing fomites with an infected person [9]. The virus may be transmitted from the mother to the fetus through the placenta and also causes fetal death [10,11].



Occurrence of monkeypox

MPXV is classified into three clades (1, Ha, and 1lb). Clade I is characterized as the “Congo Basin Glade”; while clades Ha and Lib are characterized as the “West Africa Glade” [12]. The occurrence of Mpox is irregular and varies across different regions. Mpox is most commonly found in countries located in central and West Africa, but there have been occasional occurrences of outbreaks in other parts of the world as well. Mpox has been documented in numerous other African nations since that time. As per the World Health Organization (WHO), various African nations such as Cameroon, Central African Republic, Democratic Republic of Congo, Ivory Coast, Liberia, Nigeria, Republic of the Congo, Sierra Leone, and South Sudan have been affected by outbreaks of Mpox [13].

The ailment is a cause of worldwide worry because there is a possibility of the virus spreading beyond Africa, as evidenced by an incident in the United States in 2003, where infected rodent species imported from West Africa came in direct contact with prairie dogs imported from Ghana. The virus was transmitted to almost 40 humans through these prairie dogs marking this the first outbreak of Mpox outside its endemic zone of Africa [14,15].

In 2017, Nigeria experienced its most extensive Mpox epidemic, with numerous states reporting more than 300 cases. The spread of the disease was attributed to the ingestion of wild animals and exposure to contaminated creatures. Nigeria has experienced a number of subsequent instances of disease outbreaks, while other African nations have also reported smaller occurrences [16].

To sum up, although Mpox is not widely prevalent, it continues to pose a major threat to public health, particularly in secluded regions of Central and West Africa. More than 85,000 people have been affected by the disease with cases documented in 110 countries (Multi-Country Monkeypox Outbreak).

The genetic composition of the monkeypox virus

MPXV contains a double-stranded DNA genome of approximately 197,000 kb in size and contains more than 190 Open Reading Frames (ORFs) that encode diverse viral proteins [17,18]. The virus bears a strong resemblance to the variola virus that leads to smallpox infection and also shares similarities with other orthopoxviruses like the vaccinia virus, cowpox virus, and camelpox virus [19].

The central coding region of the genome is highly conserved and flanked by inverted terminal repeats. 90 ORFs are obligatory for the replication and morphogenesis of poxvirus. Other non-essential ORFs play an important role in host tropism, pathogenic behavior, or immunomodulation, and the functions of many ORFs are yet to be identified [20]. MPXV virions contain DNA-dependent RNA polymerases and related transcriptional enzymes for over 30 structural and membrane viral proteins [21,22].

The MPXV genetic makeup encompasses multiple genes that code for proteins responsible for host range and virulence aspects. A gene that is similar to the C7L gene found in the vaccinia virus has been identified, and it codes for a protein that hampers the interferon response in the host [23]. One specific gene, referred to as the ortholog of the A35R gene found in the vaccinia virus, produces a type of protein that hinders the process of complement-mediated lysis in cells that have been infected [24].

The genome of MPXV has been sequenced from various sources, comprising cases of human infection, animal epidemics, and laboratory variants. Different clusters have been distinguished through analysis of the genome sequences of MPXV isolates, indicating, a genetic variation among them. The: variation is assumed to: stem from separate viral strains circulating in distinct African areas, as well as the potential for transmission between different species [25].

Monkeypox in Pakistan

In view of the burden that has been caused by the COVID-19 pandemic, Pakistan is already stressed with healthcare systems [26,27]. The health systems of Pakistan faced various obstacles during the COVID-19 pandemic and a shortage of health facilities such as adequate manpower, laboratory equipment, hospital beds, and ventilators makes the situation worse [28]. The scarce budget for health care and poor medical facilities would collapse further if Mpox started to spread in Pakistan. Mpox cases have been officially confirmed in Pakistan. Pakistan recorded the first instances of Mpox in April 2023, with two cases reported. As per media sources, individuals who had traveled from Saudi Arabia to Islamabad, Pakistan were identified with Mpox following the manifestation of corresponding symptoms, the samples were sent to the National Institute of Health Islamabad which confirmed the viral infection (Express Tribune). The two cases of Monkeypox in Pakistan were reported in individuals who had traveled from Saudi Arabia to Islamabad. This indicates a possible importation of the virus from a region where Monkeypox is not typically found. It's essential to investigate the source and transmission dynamics of these cases to prevent further spread. Individuals who tested positive for Monkeypox would have been isolated in a medical facility to prevent transmission to others. Close contacts of infected individuals would have been quarantined and monitored for symptoms. Currently, there is no specific antiviral therapy for Monkeypox. Therefore, supportive care is essential. This includes providing fluids, oxygen, and medications to alleviate symptoms such as fever and discomfort. It's crucial for Pakistan's healthcare system to collaborate with international health organizations like the World Health Organization (WHO) to enhance surveillance, containment, and prevention measures for Monkeypox.

Managing the symptoms and effects of monkeypox

Pakistan's healthcare system needs to effectively handle



Mpox. It requires a blend of strategies geared towards curtailing the spread of the infection and alleviating the, accompanying symptoms of the illness. To manage Mpox, a multi-faceted approach is necessary to both limit the transmission of the virus and address the various symptoms associated with the illness. Some crucial elements of managing illnesses include; Individuals who may have contracted or tested positive for Mpox should be placed in a medical facility in order to contain the virus' transmission to others. Individuals who have been in close proximity with those who have contracted an infection must undergo quarantine and regular symptom monitoring. Assistance in managing symptoms is currently the only option available for treating Mpox, as there is no targeted antiviral therapy. To address the symptoms of the disease, care that offers support is given. One of the ways we can help is by supplying necessary substances such as fluids, oxygen, and drugs to manage the symptoms of fever and discomfort. Mpox can be prevented by administering a potent vaccine that is known to be effective against the disease. It is advisable for individuals who are highly susceptible to contracting the virus, including laboratory personnel, veterinary practitioners, and healthcare professionals, to receive the vaccine. To curb the virus's spread, it is crucial to detect and keep a watchful eye on individuals who have had contact with infected ones through contact tracing. Effective surveillance mechanisms should be established to promptly identify Mpox outbreaks in order to thwart their propagation. It is recommended that public awareness programs be organized to educate individuals on the indications and manifestations of Mpox, its mode of transmission, and ways to avoid contracting it. Pakistan has a huge number of flights coming from Mpox-inflicted regions, hence screening for infection or virus should be obligatory at the airport. Suspected or confirmed cases should be quarantined. Control measures for animals: The primary mode of transmission of the virus to humans is through direct exposure to contaminated animals, especially rats and monkeys. To contain the virus, it may be essential to employ animal control tactics like trapping, testing, and culling.

Managing Monkeypox involves a combination of strategies supported by scientific evidence to prevent transmission and alleviate symptoms. Isolation and quarantine of confirmed cases and close contacts form a foundational approach to disease management, as seen in various infectious disease outbreaks. This practice helps break the chain of transmission and is supported by guidelines from health organizations like the CDC. Supportive care, another crucial aspect of managing Monkeypox, involves providing symptomatic relief to patients, especially when specific antiviral treatments are unavailable. Research and clinical guidelines recommend the use of fluids, analgesics, and antipyretics in viral infections.

Viral infections are increasing day by day [29-31]. There is an immediate need to adopt viral prevention strategies [32-

34]. Vaccination has shown promise in preventing Monkeypox. Vaccines based on the smallpox vaccine, such as Modified Vaccinia Ankara (MVA), have demonstrated effectiveness in clinical trials. Scientific literature, including studies published in medical journals, documents the development and efficacy of Monkeypox vaccines. Contact tracing, an essential epidemiological practice, helps identify and isolate potentially exposed individuals, thereby reducing disease spread. Numerous epidemiological studies and textbooks provide scientific evidence supporting the effectiveness of contact tracing. Public awareness campaigns play a critical role in educating the population about viral symptoms, transmission modes, and prevention [35-40]. Behavioral science research informs the design of effective health communication campaigns and measures their impact. Lastly, animal control measures are vital, especially in areas where transmission from animals to humans is a concern. Scientific studies on zoonotic diseases and control measures provide evidence for the role of animal control in preventing Monkeypox outbreaks. In summary, these strategies, backed by scientific evidence and guidelines from organizations like the WHO and CDC, form a comprehensive approach to managing Monkeypox and curbing its spread.

Modified Vaccinia Ankara (MVA) Vaccine is based on a modified form of the smallpox vaccine virus, and was in clinical trials for Monkeypox. MVA had shown promise in early-phase trials and demonstrated efficacy against Monkeypox in non-human primate models. The vaccine aimed to provide protection against Monkeypox, similar to its success in preventing smallpox. Cidofovir and Brincidofovir antiviral drugs have been studied for their effectiveness in treating Monkeypox. While not vaccines, they are important in managing the disease once contracted. Clinical trials have explored the use of cidofovir and its oral prodrug, brincidofovir, in Monkeypox treatment. Brincidofovir or CMX001, a lipid-conjugated derivative of cidofovir, was being evaluated in clinical trials for its potential to treat Monkeypox. This drug inhibits viral replication and has shown promise in vitro and in animal models against poxviruses, including Monkeypox. Tecovirimat or ST-246 is an antiviral compound that targets the intracellular mature virus form of poxviruses, including Monkeypox. Clinical trials have assessed its efficacy in treating Monkeypox. Vaccinia Immune Globulin (VIG), a type of immunotherapy, was studied as a potential treatment for Monkeypox. It contains antibodies against the vaccinia virus and related orthopoxviruses. VIG is administered to individuals who have been exposed to Monkeypox to reduce the severity of the disease.

Pakistan is a third-world country and already is struggling with poor healthcare systems and collapsed health facilities. The significance, of implementing effective monitoring and control strategies to control the transmission of contagious viral infection has been brought to the forefront by the



recent incidents in Pakistan [41-47]. According to reports, Pakistani health officials are taking action to detect and isolate possible instances of Mpox while also educating the public about the disease. Effective measures like surveillance, early identification, separation, monitoring of contacts, immunization, and public awareness are essential in curtailing the spread of the virus and controlling outbreaks.

Conclusion

Mpox is seen as an uncommon illness, and the real count of instances may be underestimated as a result of restricted monitoring and diagnostic capabilities in numerous nations that are affected. The World Health Organization acknowledges that monkeypox is a disease that is either newly emerging or re-emerging and is thus a cause for concern. Initiatives are currently underway to enhance monitoring and management strategies in order to deter the virus from spreading any further.

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