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Review Article

Public Health

Mpox A - Global Public Health Threat

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Abstract: Mpox also known as monkeypox, is a zoonotic viral disease instigated by the Mpox virus, a double-stranded DNA virus related to smallpox. The disease typically presents with flu-like symptoms and a characteristic rash that progresses through distinct stages, including painful lesions and scabs. Two recognized clades, Clade I and Clade II, show regional prevalence in Central and East Africa, respectively, with varying severity and mortality rates. Efforts to combat Mpox include targeted vaccinations, such as MVA-BN and LC16, prioritized for high-risk groups and regions. Recent research advances have identified G-quadruplex structures within the viral genome, enabling more precise diagnostic tools using fluorescent probes. Countries have implemented diverse strategies to curb Mpox spread, including intensified screening of travelers, enhanced laboratory diagnostics, and public health campaigns. While nations like the Democratic Republic of Congo (DRC) face severe outbreaks, others such as Indonesia, China, and Kenya emphasize rigorous surveillance and border controls. The evolving epidemic highlights the critical need for international collaboration, rapid diagnostic innovation, and equitable vaccine distribution to mitigate the global impact of Mpox. This review on Mpox (formerly monkeypox) should comprehensively address its recent epidemiology, including global incident trends, outbreak hotspots, and the factors driving its spread and explore vaccination efforts, focusing on the efficacy and availability of smallpox-based vaccines used against Mpox. Recent advancements in diagnostics, including novel detection methods like rapid molecular assays, should be highlighted. The review examines preventive measures undertaken by affected countries, such as contact tracing, isolation protocols, and public health campaigns.

Keywords: Mpox, monkeypox, Clade I, Clade II, virus, global health

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1. INTRODUCTION

Mpox, also referred to as monkeypox, is a virus-induced illness. It typically results in flu-like symptoms and a rash. The dermatitis is comparable to that induced by smallpox, a virus that is related. MPox is an endemic disease that is frequently encountered in certain regions of Africa[1]. However, epidemics occasionally occur in other regions of the globe. An outbreak is characterized by an increase in the number of instances or a higher number of cases than anticipated. During an outbreak of MPox, public health officials must work quickly to contain the spread of the virus and prevent further transmission. This often involves implementing quarantine measures, conducting contact tracing, and providing medical treatment to those affected. In some cases, vaccination campaigns may also be necessary to protect at-risk populations. The goal is to control the outbreak and prevent it from becoming a larger epidemic that could pose a significant threat to public health.

2. MPOX Types

- **Clade I**. Central Africa is the region in which Clade I is found. It has a propensity to induce more severe illness than clade II. Clade I infections have been less lethal in recent years[2]. This may be due to increased immunity and improved healthcare practices in the region. However, continued monitoring and research are necessary to understand the changing dynamics of Clade I infections and to ensure that appropriate measures are in place to prevent outbreaks and effectively treat those who become ill. The findings from these studies will be crucial in developing targeted interventions and vaccination strategies to further reduce the impact of Clade I viruses in Central Africa.
- **Clade II**. East Africa is the sole location where Clade II is found. Since 2022, there has been a worldwide incidence of clade II mpox. It is less probable to result in death than clade I[3]. However, it is still highly contagious and can spread rapidly through populations. In East Africa, public health officials have been working tirelessly to contain the spread of clade II mpox through vaccination campaigns and strict quarantine measures. Despite its lower mortality rate, the virus still poses a significant threat to public health and efforts to monitor and control its spread continue to be a top priority for health authorities worldwide.

3. SYMPTOMS

The dermatitis that results from mpox can manifest as lesions on the mouth, face, hands, feet, penis, vagina, or anus (butthole). Individuals may exhibit a widespread dermatitis, while others may only have a few lumps or lesions. Treatment for mpox-related dermatitis typically involves topical corticosteroids to reduce inflammation and itching. In severe cases, oral antihistamines may be prescribed to help alleviate symptoms. It is important to avoid scratching the affected areas to prevent further irritation and potential infection. Practicing good hygiene and keeping the skin clean and dry can help promote healing and prevent recurrence of the dermatitis. Mpox rash may progress through numerous phases over a period of two to four weeks:

- The ridges become elevated.
- It may initially manifest as scarlet, flat lumps. These can be excruciating.
- The nodules develop into ulcers.
- Pus accumulates within the lesions.
- The lesions develop a crust and eventually detach.

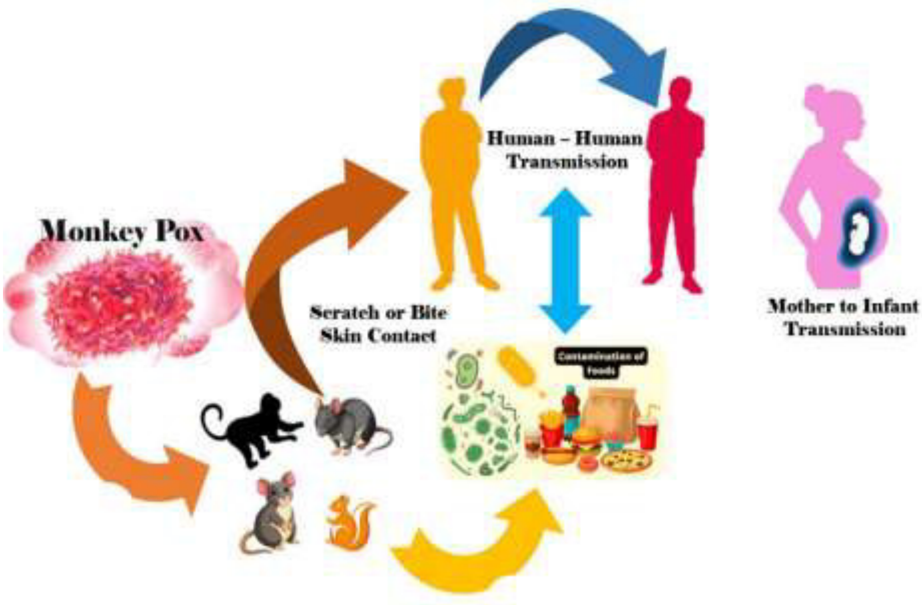

Fig 1: Depicts the global genomic transmission of MPX

4. SPREADING OF M POX

Human-to-human transmission: Physical contact, sexual activity, and close conversation or breathing with an individual infected with mpox may produce infectious respiratory particles; however, more study is required to understand the virus's transmission dynamics during epidemics across many environments and circumstances, according to the WHO[4]. Scientists are aware that the virus may remain viable for a duration on clothes, bedding, towels, items, gadgets, and surfaces that have been in contact with an individual infected with mpox. Individuals who handle these products may get an infection if they do not wash their hands prior to contacting their eyes, nose, or mouth. The virus may transmit to the fetus during pregnancy, during or post-delivery by skin-to-skin connection, or from a parent with mpox to an infant or kid via intimate connection[5]. While transmission of mpox from an asymptomatic individual has been documented, there is little data on the potential for the virus to be transferred by an individual before to the onset of symptoms or subsequent to the healing of lesions. Individuals with mpox are considered infectious until all lesions have crusted, scabs have detached, an additional layer of skin has developed beneath, and all lesions in the eyes and body (including the mouth, throat, eyes, vagina, and anus) have also healed, typically requiring 2 to 4 weeks. The virus may also endure for a while on clothes, bedding, towels, items, gadgets, and surfaces that have been contacted by an individual with mpox. Individuals who handle these materials may get an infection, especially if they possess any wounds or abrasions or contact their eyes, nose, mouth, or other mucous membranes without prior handwashing. Sanitizing surfaces and objects, as well as washing hands following contact with potentially contaminated items, might mitigate this mode of transmission. The virus may also transmit to the fetus during pregnancy, during or after delivery by skin-to-skin contact, or from a parent with mpox to an infant or kid via intimate contact[6]. While transmission of mpox from asymptomatic individuals has been documented, there are few data about the potential for viral spread from individuals before to symptom onset or after the resolution of their lesions. While live virus has been extracted from semen, the degree to which infection may disseminate via semen, vaginal fluids, amniotic fluids, breast milk, or blood remains uncertain. Human to animals: Numerous animal species exhibit susceptibility to the virus, indicating a possibility for spillback from people to animals in numerous surroundings[7]. Individuals with established or alleged mpox should exhortation from neighboring somatic connection with animals, especially pets such as gerbils, hamsters, dogs and cats well as cattle and wildlife animals. Such transmission occurs when infected humans come into close contact with susceptible animal species. Domestic pets like dogs and rodents, as well as wild animals, may be at risk if exposed to contaminated materials such as bedding, or through direct contact with infected individuals. Viral shedding via skin lesions, respiratory droplets, or bodily fluids can facilitate this cross-species transmission. The risk of establishing new animal reservoirs in non-endemic regions is significant, as it could perpetuate the virus's circulation and lead to recurrent outbreaks. Preventative measures include strict isolation of infected individuals, avoiding contact with animals during the infectious period, and disinfecting contaminated environments. Veterinary surveillance and public health collaborations are essential to monitor and mitigate the risks of reverse zoonosis. Understanding the dynamics of human-to-animal transmission is critical for preventing the establishment of persistent reservoirs and ensuring long-term control of Mpox. Animals to Humans: An individual who has direct contact through an animal harboring the virus, such as some monkey species or telluric rodents like tree squirrels, might similarly get mpox. Exposure may ascend via bites or nicks, or during accomplishments like chasing, peeling, duping, or food preparation[8]. The virus might also be transferred by the ingestion of inadequately cooked infected meat. Humans typically acquire the infection through direct contact with infected animals, their bodily fluids, or contaminated materials such as bedding[9]. Handling or consuming undercooked meat from infected animals also poses a risk. Key modes of animal-to-human transmission include bites or scratches from infected animals, direct contact with lesions, or exposure to respiratory secretions during close interaction. Factors such as habitat destruction and increased human-animal interactions have heightened the risk of zoonotic spillover. This is particularly concerning in regions where subsistence hunting and wildlife trade are common. Preventing animal-to-human transmission involves educating at-risk populations about safe handling practices, reducing contact with wildlife, and strengthening surveillance in animal reservoirs. Ongoing research is essential to identify potential new reservoirs and understand the virus's ecological dynamics. Efforts to control zoonotic transmission are vital to reducing the risk of human outbreaks and mitigating the global health impact of Mpox.

4.1. Incidents

The Mpox virus was identified in Denmark in 1958 in monkeys maintained for scientific purposes[10]. The primary documented human instance of mpox occurred in a 9-month-old male infant in the Democratic Republic of the Congo in 1970[11]. Subsequent to the elimination of smallpox in 1980 and the cessation of global smallpox immunization, mpox progressively surfaced in western Africa, eastern, and central[12]. Since 2005, hundreds of cases have been recorded annually in the Democratic Republic of the Congo. Mpox resurfaced in Nigeria in 2017 and endures to blowout among the population and in travelers to additional locations[13]. In May 2022, an epidemic of mpox materialized abruptly and swiftly spread over Europe, the Americas, and subsequently all six WHO regions[14]. The worldwide pandemic has mostly impacted homosexual, bisexual, and other males who engage in sexual relations with men, spreading via person-to-person contact within sexual networks. In 2022, clade I mpox epidemics transpired in immigrant campsites in the Republic of the Sudan. Since 2022, there has occurred an increase in mpox circumstances and fatalities in the Democratic Republic of the Congo. In some regions of the nation, a novel branch of clade I, designated clade Ib, has remained dissemination by human transmission. By mid-2024, the clade has been documented in other nations. More than 120 nations have documented mpox from January 2022 to August 2024, with over 150,000 laboratory established illnesses and more than 220 fatalities between verified cases[15].

4.2. Vaccination

Vaccines are offered primarily to those at elevated risk or those who have had intimate contact with an infected individual. The WHO has urged pharmaceutical companies to provide their vaccinations for emergency use, albeit pending official clearance. Japan and the United States are delivering vaccinations to the Democratic Republic of Congo, where officials want to immunize 2.5 million people[16]. The Africa CDC has committed to provide 10 million immunizations by 2025[17]. The WHO anticipated that the declaration of a continent-wide public health emergency would enhance the influx of medical supplies and assistance into impacted regions, facilitating governmental coordination of their response. The UN health agency endorses many vaccinations for the prevention of mpox. Currently, mass vaccination initiated during the COVID-19 worldwide pandemic is not advised[18]. Extensive research over many years has resulted in the creation of improved and safer vaccinations for the eliminated illness smallpox. Several of these vaccinations have received approval in several countries for the prevention of mpox. The WHO now recommends the use of MVA-BN or LC16 vaccinations, or the ACAM2000 vaccine in the absence of the former options[19]. According to the WHO, immunization should be limited to those at risk of exposure to mpox.

Travelers identified as at risk via a personal risk assessment with their healthcare physician may seek immunization.

4.3. Recent novel detection

Scientists have discovered a new method for comprehending the virology of Monkeypox Virus (MPV) and creating sophisticated diagnostic tools, as well as uncovering new therapy avenues. The Mpox virus, formerly known as MPV, has been designated a Public Health Emergency of International Concern (PHEIC) on two occasions in the last three years owing to its unforeseen worldwide proliferation[20]. This has elicited considerable apprehension, since the mechanisms of transmission and symptoms are not understood. A profound understanding of its virology, along with the rapid development of efficient diagnostic and treatment approaches, is essential. MPV is a double-stranded DNA (dsDNA) virus, and the identification of its extracellular viral protein gene using polymerase chain reaction (PCR) is a recognized method for detecting MPV in clinical samples[21]. Conventional PCR techniques, which amplify double-stranded DNA using fluorescent probes, exhibit sensitivity to DNA concentration but encounter difficulties in distinguishing between particular and non-specific amplification products. Conversely, some distinctive DNA configurations referred to as noncanonical nucleic acid conformations diverge from the traditional double-helix configuration. These typical DNA configurations, including G-quadruplexes (GQs), provide opportunities as targets for small-molecule fluorescence probes, therefore enhancing the reliability of diagnostic procedures. Researchers at the Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR), an independent entity under the Department of Science and Technology (DST), have located and characterized four highly conserved G-quadruplex-forming DNA regions within the MPV genome. Employing a customized fluorescent small-molecule probe, scientists effectively identified a particular GQ sequence, marking a significant advancement in the accurate identification of MPV. This study emphasizes the therapeutic potential of targeting atypical nucleic acid structures.

5. COUNTRIES MEASURES TO PREVENT SPREAD

5.1. Democratic Republic of Congo (DRC)

The DRC is now undergoing its most severe Mpox epidemic, characterized by a 160% escalation in cases and a 19% increase in fatalities relative to the previous year[22]. The Democratic Republic of Congo (DRC), a hotspot for Mpox (monkeypox), has implemented multifaceted measures to control its spread. In December 2022, the Democratic Republic of the Congo announced a nationwide outbreak of mpox, and an incident management system has been operational since February 2023 because to the rising number of reported cases. From September 2023, an mpox epidemic in South Kivu province has persisted and lately extended to adjacent North Kivu, facilitated by sexual contact transmission. A novel variation of clade I MPXV has been identified in South Kivu. It typically exhibits APOBEC3-type alterations, indicating the virus's adaptability resulting from human transmission. It is expected that it originated around mid-September 2023, with human-to-human transmission persisting since that time. This is the initial recorded instance of prolonged community transmission of the virus inside the nation. The transmissibility and severity of this variation compared to other clade I MPXV strains remain uncertain. Recognizing the endemic nature of the disease in its rural regions, the DRC has emphasized enhanced surveillance and community-based health education[23]. Surveillance systems have been bolstered to ensure timely reporting and accurate case identification, particularly in regions with high transmission risk. Health authorities in the DRC have prioritized vaccination campaigns targeting high-risk populations, such as healthcare workers and those with direct exposure to confirmed cases[24]. Leveraging the cross-protective benefits of smallpox vaccines, these efforts aim to curb further outbreaks. Additionally, mobile health units have been deployed to remote areas, improving access to diagnostics and treatment while raising public awareness about Mpox prevention. Quarantine protocols have been strengthened for suspected and confirmed cases to reduce human-to-human transmission. These measures are complemented by campaigns to educate communities about reducing contact with wildlife, which is a significant transmission vector in the DRC. International partnerships with organizations like the World Health Organization (WHO) have provided critical support in terms of resources and technical expertise. Despite these efforts, challenges remain, including limited healthcare infrastructure and persistent underreporting, necessitating sustained focus and global cooperation to contain Mpox effectively.

5.2. Indonesia

The Health Ministry of Indonesia has implemented rigorous health screening measures for international travelers. Upon entrance, travelers are now required to submit paperwork detailing their medical history and current travel activities. The Ministry has appointed 12 state labs throughout the country to monitor and detect suspected Mpox cases for early identification[25]. Indonesia has implemented comprehensive measures to control the spread of Mpox. All travelers need to complete the SATUSEHAT Health Pass (SSHP), a multilingual web-based health declaration system, and present its QR code upon arrival. Thermal scanners have been installed at international airports and ports, complemented by enhanced visual surveillance by officers. Vaccination efforts have been intensified among high-risk populations, and the government has revived its health tracking system for Mpox. Additional measures include screening suspected or self-referred cases at entry points, establishing management plans for potential cases on flights, cruises, and ships, and reactivating the MySejahtera application for Mpox surveillance[26]. Public awareness campaigns target communities such as gay, bisexual, and other men who have sex with men, as well as sex worker organizations and networks.

5.3. The People's Republic of China

Chinese authorities have enforced stringent travel restrictions on those exhibiting Mpox symptoms. Augmented airport monitoring protocols have been implemented to identify and assess impacted travelers. Individuals exhibiting symptoms such as fever, headache, myalgia, or rash are required to report their status upon entrance. These remedies will be effective for a duration of six months[27]. Despite no sustained community transmission, the number of patients with mpox in China has significantly increased since February 2023. The WHO reports that mpox cases continue to increase, indicating a risk of an outbreak in China. To contain potential transmissions, China needs to learn from countries that have successfully contained mpox and improve its sensitivity to identify patients and build contact-tracing systems. Strengthening health education and screening populations at high risk is also crucial. Smallpox vaccinations for populations at high risk have been shown to be effective in preventing mpox in the USA. To control the potential outbreak of mpox, China needs to list mpox as a notifiable disease, review the COVID-19 outbreak, and learn from successful experiences of other countries, including efficient medical systems and targeted vaccination programs. China has implemented a multi-faceted approach to control the spread of Mpox (formerly monkeypox) in response to global outbreaks. Early detection and swift containment were central to the country's strategy, with the government enhancing surveillance systems for early identification of suspected cases. China has utilized advanced diagnostic tools, including PCR testing, to rapidly detect Mpox cases and trace potential contacts[28]. Quarantine measures have been enforced for individuals with exposure to infected persons, while close contacts are closely monitored for symptoms. To prevent further spread, public health campaigns have been launched to raise awareness about Mpox transmission and preventive measures. These campaigns are aimed at educating the public on reducing risk through hygiene, avoiding contact with sick animals, and practicing safe behaviors in high-risk environments. In addition, China has coordinated with the World Health Organization (WHO) and other global health bodies, ensuring a data-driven response. Vaccination efforts have been crucial in controlling the virus; although Mpox is primarily found in regions outside China, vaccines such as the smallpox vaccine, which provides cross-protection, have been deployed among at-risk groups, particularly healthcare workers[29]. Preventive travel measures have also been adopted, including health checks at international airports and other transport hubs to limit the spread of the virus. These efforts are part of China's broader commitment to preventing emerging infectious diseases.

5.4. The Republic of South Africa

South Africa has initiated a new airport screening program designed to detect and manage suspected Mpox cases among incoming travelers. This proactive initiative is integral to a comprehensive approach aimed at improving early diagnosis and control of the infection[30]. South Africa has reported 20 confirmed mpox cases between May and July 2024, including three deaths, in three provinces. These are the first cases since 2022. The affected men are aged 17-43, with 11 self-identifying as men who have sex with men. At least 15 cases are living with HIV, have advanced HIV disease, and have diabetes. Sexual contact is the primary exposure contact. The risk to public health remains low, but for vulnerable groups like gay men, bisexual men, trans and gender-diverse people, and sex workers, the risk is moderate. The global mpox outbreak linked to clade IIb monkeypox virus remains ongoing. The South African Medical Research Council (SAMRC) is focusing on educating the public on effective prevention strategies for the Mpox outbreak in the Democratic Republic of Congo (DRC)[31]. The Global Research Collaboration for Infectious Disease Preparedness (GloPID-R) Africa Hub has led discussions with stakeholders and funders to gather real-time information on the outbreak. This information has been used to create an evidence briefing document, which is shared with the European & Developing Countries Clinical Trials Partnership (EDCTP) to advise funders on necessary interventions to stop the spread of measles[32]. Cochrane South Africa is also collaborating with other partners to compile evidence for the National Immunisation Technical Advisory Groups (NITAGs) to make informed recommendations for the public health response and vaccine introduction across the African region. The SAMRC aims to ensure a coordinated and effective response to the Mpox outbreak, grounded in the latest scientific research and public health best practices.

5.5. Kenya

Kenya has implemented testing protocols for incoming travelers to detect Mpox cases and mitigate their transmission. Despite the detection of just moderate cases to yet, these precautions are seen as essential for overseeing and controlling the epidemic[33]. Kenya has implemented various measures to control the spread of Mpox, particularly following the resurgence of cases in 2022. The Kenyan Ministry of Health swiftly activated its emergency response mechanisms, focusing on surveillance, awareness campaigns, and strengthening diagnostic capabilities. The country began enhanced monitoring at entry points, such as airports and border posts, to prevent the importation of cases. Health officials worked closely with the World Health Organization (WHO) and other global partners to improve case detection, isolate confirmed cases, and identify contacts for timely follow-up. Public health campaigns, including mass media outreach, were employed to educate citizens on recognizing symptoms, preventing transmission, and seeking medical care promptly. This effort was critical in addressing stigma and misinformation surrounding the virus. Kenya prioritized strengthening its healthcare infrastructure, providing adequate personal protective equipment (PPE) for frontline workers, and ensuring that diagnostic tools for Mpox were readily available. Vaccination was also considered part of the strategy, with Kenya evaluating the use of smallpox vaccines for high-risk groups, although vaccine availability remained a challenge. Local health authorities continued to collaborate with international partners for the provision of vaccines and further research. These measures were critical in mitigating the spread and minimizing the impact of Mpox outbreaks. Kenyan health officials have instituted a series of readiness and reaction measures to promptly identify and mitigate the spread of mpox, verified in the nation on 31 July 2024. Kenya, along with Burundi, Rwanda, and Uganda, has verified instances of the clade Ib mpox variant, first identified in the Democratic Republic of the Congo, which is thought to be more virulent and transmissible[34]. The rapid proliferation of haplogroup Ib contributed to the World Health Organization's (WHO) designation of the mpox epidemic as a public health emergency of worldwide significance on 14 August 2024[35]. As of 2024, 14 nations in the African area are reporting instances, with the Democratic Republic of the Congo representing around 90% of all cases. Kenya has reported five instances of mpox, with no fatalities. Four of the five cases were imported from adjacent nations, whereas the fifth case is linked to one of these instances, indicating potential community transmission inside the country.

5.6. Nigeria

Nigeria has instituted a compulsory declaration procedure for travelers destined for certain African areas. Travelers are required to submit a declaration form, either at the airport or online, to facilitate the monitoring and management of Mpox transmission. Border Health Services in Pakistan have advocated for increased surveillance and protective protocols. Authorities are meticulously observing travelers and enforcing stringent health assessments to mitigate the transmission of

Mpox[36]. Nigeria has implemented a range of measures to control the spread of Mpox (formerly monkeypox) following its re-emergence in 2017. The country has strengthened its surveillance systems, improving early detection and rapid response to suspected cases. The Nigerian Centre for Disease Control (NCDC) has been at the forefront, working in collaboration with local and international partners to track outbreaks[37]. Key strategies include enhanced case detection through active surveillance, contact tracing, and testing in high-risk areas, especially in states with frequent human-animal interactions. Public awareness campaigns have been vital in educating the population about the transmission and prevention of Mpox, particularly emphasizing avoiding close contact with infected animals and individuals. Healthcare facilities have been equipped with protective equipment, and healthcare workers trained in managing suspected cases. Nigeria has worked with global organizations, including the World Health Organization (WHO), to increase access to vaccines for high-risk groups, leveraging smallpox vaccination as a preventive measure against Mpox. In response to confirmed outbreaks, isolation of infected individuals, along with community-level containment measures, has been implemented to limit the virus's spread. Nigeria's approach highlights the importance of community engagement, surveillance, and international cooperation in managing emerging infectious diseases.

6. CONCLUSION

Mpox represents a significant global health challenge due to its increasing spread and diverse transmission pathways. While historically endemic to specific African regions, the recent global outbreaks highlight the need for enhanced surveillance, public awareness, and international cooperation. Advances in diagnostic methods, such as the identification of unique DNA configurations, offer promising avenues for early detection and targeted treatments. Vaccination initiatives, particularly in high-risk areas, are critical but must be coupled with education and strict preventive measures to curb transmission effectively. Countries are adopting varied strategies, from rigorous health screenings and travel restrictions to large-scale immunization campaigns, reflecting the urgency of a coordinated global response. With over 120 nations reporting cases since 2022, addressing mpox demands sustained research, resource allocation, and a robust public health infrastructure to mitigate its impact and prevent future outbreaks.

7. AUTHORS CONTRIBUTION STATEMENT

Dr. John Abraham contributed to the study's conceptualization, study design, and manuscript drafting. Dr Krishna Agarwal contributed to the literature review, data interpretation, and manuscript editing. All authors have read and approved the final version of the manuscript and agree to be accountable for all aspects of the work.

8. CONFLICT OF INTEREST

Conflict of interest declared none.

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