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NARRATIVE REVIEW

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Prediction of potential public health risk of the recent multicountry monkeypox outbreak: An update after the end declaration of global public health emergency

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Abstract

Background and Aims: A double-stranded DNA virus called monkeypox virus (MPV) belonging to the Poxviridae family and Orthopoxvirus genus causes monkeypox (mpox) infection. This virus used to infect only Central, East, and West Africa. However, it has spread to an extent outside Africa recently. The range of MPV outbreaks was so high that on July 23, 2022, the World Health Organization (WHO) declared it a Public Health Emergency of International Concern (PHEIC). About a year later, the WHO notified the end of a global public health emergency for mpox on May 11, 2023. Here, we aimed to assess the current pathogenicity and potential risk of MPV causing public health emergencies.

Methods: We searched information from published articles available in PubMed, Scopus, and ScienceDirect. We used monkeypox, mpox, monkeypox outbreak, and monkeypox virus as keywords during the literature search.

Results: Many new variants of MPV have emerged throughout the world that created PHEIC for mpox. Considering the low lethality and transmission rate, mpox is no longer a global public health threat. In addition, the availability of therapeutic and preventive measures helped the healthcare authorities fight the mpox infection in an efficient manner. In this review, we have portrayed the history and evolution of mpox from past to present and an idea of its future outcomes. Also, we have discussed the symptoms related to mpox and approved antiviral treatment strategies to fight off the infection in this piece. This review also emphasized the preventive guidelines set by the WHO for patients, caregivers, and healthcare providers to control the outbreak of mpox infection.

Conclusion: We believe this article would give an idea about the potential public health threats of the recent multi-country monkeypox outbreak to the healthcare authorities for taking measures accordingly.

KEYWORDS

monkeypox, monkeypox virus, mpox, orthopoxvirus, poxvirus, zoonotic disease

1 | BACKGROUND

The monkeypox (mpox) virus (MPV) was first discovered in 1958 in the laboratory monkeys of Denmark.[1] The first human case was discovered in 1970 in a 9-month-old child from the Democratic Republic of the Congo. After 1970, the Clade I variant affected Central and East Africa, whereas the Clade II variant primarily affected West Africa.[2] Within the years 1981–1986, around 37 cases of mpox infection were identified in the Democratic Republic of Congo, in most parts of the Zaire area. Between the years 1996 and 1997, the infection was widely spread in the region of Zaire. From February to August of 1996, there were 71 clinical cases reported, including six fatalities, in 13 communities, mostly in the Zaire region.[3] This disease, which was formerly restricted to the continent of Africa, has now spread outside its borders, causing harm to other nations.[4] In 2003, the outbreak of mpox gained widespread global attention as it was the first outbreak of the disease outside of Africa. The outbreak affected 47 individuals throughout six US states: Illinois, Indiana, Kansas, Missouri, Ohio, and Wisconsin.[5] The probable reason was considered to be the shipment of MPV-infected mammals from Ghana and West Africa to the United States.[6] In October 2018 and May 2019, one traveler in Israel and another in Singapore were found to be affected by mpox respectively, during their travels from Nigeria.[7] In the Democratic Republic of the Congo, over 3000 suspected cases were recorded annually in 2018. By 2020, there were 6216 cases and 222 fatalities. Moreover, 78 cases in the Central African Republic (CAR), nine cases in Cameroon, 138 cases in Nigeria, two cases in Sierra Leone, and eight cases involving men traveling from Nigeria between the ages of 30 and 50 have been reported to be affected by MPV from 2018 to 2021.[8] Similarly, cases of mpox infections were reported in numerous nations in 2021 and 2022, mostly affecting travelers who had recently traveled to parts of Africa. During this mpox outbreak in 2022, predominantly this infection was prevalent in a group of males who were engaged in sexual activities with other males. This referred MSM group (Men Who Have Sex with Men) had some common symptoms like inguinal lymphadenopathy and lesions in the genital, perineal, or perianal areas. A cohort study of mpox infection conducted in Spain has shown that out of 595 confirmed cases, 99% were among the MSM group. Similarly, out of 1304 confirmed cases reported in Germany on July 6, 2022, most of the infection was within the MSM population.[9]

An article published by Cambridge University has brought out how the factors of the environment are affecting the mpox spread. The ongoing deforestation is making the mpox spread more likely to happen due to increased human and infected animal interaction. Besides, the article pointed out that the increased number of pollutants is also another reason for the spread. A study conducted in the United Kingdom, Spain, France, Germany, Italy, the Netherlands, Switzerland, and Portugal showed that the mpox spreading chance multiplies by 29.6%, 9.7%, 13%, and 80.6% for every 10-unit rise in PM2.5, PM10, NO2, and O3 levels respectively. So, rapid industrialization or fuel consumption is also to some extent responsible for mpox.[10] The rapid global spread of mpox prompted the World Health Organization (WHO) to designate it as a public health emergency of international concern (PHEIC) on July 23, 2022. The declaration highlighted how critical it is to address the problem and place safety measures forward to stop mpox from spreading and becoming a pandemic.[11]

2 | A BRIEF HISTORY OF MONKEYPOX INFECTION

The MPV, a subtype of the genus Orthopoxvirus which is a member of the Poxviridae family, causes mpox infection. MPV is a double-stranded DNA virus with an outer covering, or envelope, with protein spikes on top, holding inside all of the virus's genetic information-carrying materials.[12] The size range of MPV is within 200–250 nm when observed under an electron microscope. The virion is formed of five regions made of nucleic acids (DNA), a double-concave dumbbell-shaped core, a palisade layer, a bilayered inner and outer membrane made of lipoproteins, and 10 nm long surface tubules. The double-stranded 197 kb long linear genome of MPV consists of a central region of approximately 101 kb and two terminal variable regions with an inverted terminal repeat (ITR) of 6.4 kb at each end. The central region codes for structural proteins and essential enzymes whereas the ITR consists of ORFs, hairpin loops, and short tandem repeats that are responsible for virtual transcription and replication.[13] MPV is available in two variants: Clade I and Clade II. Originating in Central Africa, the Clade 1 has been responsible for about 10% of deaths.[14] Meanwhile, the Clade II variety, or more precisely the Clade IIb subtype, which originated from West Africa has been found to affect humans more during the years 2022–2023. The Clade IIb variety rarely kills humans; typically, more than 99% of infected individuals by Clade IIb recover.[15] However, those who fall under certain categories young children, children or infants of breastfeeding mothers, eczema sufferers, and those with severely compromised immune systems, like HIV-positive individuals are more likely to suffer from severe illnesses that might prove fatal.[16] Furthermore, the MPV can be transmitted to fetuses from infected expectant mothers, and evidence has shown this has led to many pregnancy complications such as stillbirth and miscarriages.[17]

The MPV usually enters through the nasopharynx, oropharynx, or intradermal pathways when a healthy person comes into close contact with an infected animal or person.[18] Moreover, humans can contract mpox through sexual contact, skin-to-skin contact, or other face-to-face interactions with infected humans. Further, the MPV can be transmitted to fetuses from infected expectant mothers, and evidence has shown this has led to many pregnancy complications including stillbirth and miscarriages. Interaction of infants before and during birth with an infected mother can lead to MPV transmission but transmission through breast milk or amniotic fluids is still not known yet.[17] The mpox symptoms first start to develop during the 3rd week after being exposed to the virus.[19] A mpox infection usually appears as severe or itchy rashes on the face, palms of hands, soles of

feet, groin, genital areas, and anal areas that resemble pimples or blisters. There may also be lesions on the rectum, vagina, anus, mouth, throat, or eye. Again, fever, headache, soreness in the muscles, back pain, fatigue, and enlarged lymph nodes are some other symptoms associated with rashes.[20] Usually, rashes last up to 2–4 weeks, and proper medication symptoms can be handled. On the other hand, in severe cases, the common symptoms are accompanied by a bacterial infection in the brain, skin, blood, lungs, or genitals causing encephalitis, myocarditis, pneumonia, balanitis, proctitis, urethritis, and sometimes eye problems. In this case, hospitalization, supportive care, and antiviral medication are recommended.[21]

3 | EPIDEMIOLOGY OF RECENT OUTBREAK

The WHO published a report on September 19, 2023, affirming that 90,439 mpox cases have been found globally in 115 countries up to September 11, 2023, from January 1, 2022. In that report, 22 countries out of 115 were newly affected within 21 days.[22] Another recent report by the WHO published on October 20, 2023, stated that since January 1, 2022, up to September 30, 2023, there have been 91,123 confirmed cases of mpox infection in 115 countries, resulting in 157 deaths overall. Among these, 10 countries most affected are the United States of America, Brazil, Spain, France, Colombia, Mexico, Peru, The United Kingdom, Germany, and China.[22] According to another recent report by WHO, in total, 668 cases from 29 countries have been confirmed globally till October 2023. The most cases were observed from the Western Pacific and European regions. Apart from this, eight new cases from African Regions and one new case from the Eastern Mediterranean Region have been recorded. Through the latest global observance, it's been revealed that the MPV infection has less propagation in the European and American countries compared with Western Pacific and Southeast Asia areas. Apart from this, in the Democratic Republic of the Congo, 12,569 cases have been suspected and 581 deaths are documented. The latest report of the WHO published on December 22, 2023, stated that around 92,783 confirmed cases with 171 deaths have been recorded from January 1, 2022, to November 30, 2023. Among this in November, 906 cases of mpox infection were confirmed from 26 countries. As per the report, the infection spread extensively in the European Region and in the Region of the Americas with 26,654, and 60,400 confirmed cases respectively.[23] On the other hand, the CDC confirmed that since January 1, 2023, the Democratic Republic of Congo has reported 12,569 suspect cases and 581 deaths due to mpox till February 8, 2024.[24]

Currently, the MPV spread is more common in human-to-human compared to animal-to-human. A MaxEnt model was used for detecting which populations are at high-risk zones and it showed that the mpox infection has spread at an alarming rate in Europe and North America. Other than that Central Africa plus East and South Asia regions are also affected by mpox infection compared to other regions. Spain, France, Britain, and Germany from European countries and the United States, Canada, and Mexico of North America have a high susceptibility towards mpox infection as confirmed cases are increasing in these areas. The possible reasons might be mpox transmission from transportation hubs or greater population travel and migration from one country to another. Additionally, the weather also to some extent affects the MPV spread. Enhanced precipitation in the driest season, increases the chances of the infection.[25]

Due to the sudden rise of mpox infection in recent years, some therapeutic approaches have been fully or partially approved under some restrictions and guidance for treatment purposes.[26] Moreover, these measures aim to offer patients effective treatment options considering the condition and progression of infection in the patient.[27]

4 | UPDATES ON DIAGNOSTIC, THERAPEUTIC, AND PREVENTIVE MEASURES

Polymerase chain reaction (PCR), reverse-transcription polymerase chain reaction (RT-PCR), isothermal amplification (loop-mediated amplification & recombinase polymerase amplification), CRISPR, immunological methods (ELISA detection, haemagglutination inhibition test, western blot, and radioimmunoassay), whole genome sequencing and MPV isolation and culture techniques are the identified methods still now for MPV detection.[28] Among the diagnostic methods of MPV, RT-PCR has been one of the most effective techniques till now due to its higher sensitivity, specificity, rapidity, and accurate outcomes. Nevertheless, for better understanding and further study of MPV transmission and mutation, the Genome Sequencing method needs to be applied in a more accessible and cost-effective manner. A competitive binding inhibition assay (CBIA) test was conducted to analyze the serums of MPV-infected patients and then it was found that the MPV interacted plus formed a bond with monkeypox-specific monoclonal (MAb) antibody H12C1 but not with MAb G6C6 which is a vaccinia-specific monoclonal antibody (ref). Similarly, another experiment was conducted in which MPV proteins A29, A35, B6, and M1 along with VACV containing A27 were tested for binding with the monoclonal antibody (mAb 69-126-3-7). The result showed that the monoclonal antibody binding was specific for only MPV protein A29.[29] So, the use of monoclonal antibodies is one of the effective techniques for distinguishing MPV from another Orthopox vaccinia virus. Nowadays "Monkeypox Antigen Rapid Test Kits" from different brands are available in the market. The main advantages of these kits are they are highly sensitive, accurate, and can be easily operated to give results within 10–20 min.

In January 2022, the European Medicines Agency (EMA) authorized the utilization of the oral or intravenous antiviral drug tecovirimat for mpox treatment due to the similarity of mpox with smallpox.[20] The use of tecovirimat is not recommended for everyone since the chances of MPV growing resistant to this drug can't be unseen.[30] Currently, three vaccines MVA-BN, LC16, and

OrthopoxVac have been approved to treat mpox in case of serious conditions or those who are more exposed to the virus but the use of these vaccines at the mass level hasn't been recommended yet.[31] Moreover, the FDA has authorized a standard dosage regimen of the JYNNEOS, a 3rd generation MVA-BN vaccine to be used in the USA. In Canada and the European Union, this same vaccine is approved under the trade names IMVAMUNE and IMVANEX, respectively.[32] 0.5 mL of this JYNNEOS vaccine can be given to people below 18 years or above 18 years, subcutaneously in two doses, separated by a period of 28 days. An alternative regimen has also been authorized in which individuals who are 18 years of age or older can receive 0.1 mL of it intradermally in two doses spaced between 28 days apart.[23] 2 weeks after the second dose, maximum protection is achieved against MPV. Furthermore, it is carefully observed if there is any severe allergic reaction evident after the first dose of JYNNEOS is injected.[33] If a condition like anaphylaxis is observed in that case, a second dose isn't recommended.[34] ACAM2000, a second-generation, live attenuated, vaccinia virus-containing vaccine was approved in 2015 by FDA to be used for people of age between 18 and 64 years old. It is a single-dose vaccine that develops immunity against MPV within 28 days from the date of administration.[35] Vaccinia immune globulin intravenous (VIGIV, CNJ-016) is also approved by the FDA to be used in children and the elderly in serious cases of mpox under the Expanded Access IND protocol.[36] Application of Cidofovir both topically and intravenously has provided a positive efficacious response against MPV in immunocompromised people. Cidofovir complex binds with MPV DNA Polymerase Holoenzyme at the SER552, ASP753, and GLU792 by Hydrogen bond (H-bond) and ARG634 plus LYS638 by salt-bridge.[37] This drug gets activated into the phosphorylated form by cellular kinases. The active diphosphate derivatives act as an inhibitor to terminate functions of viral DNA polymerase and DNA polymerase 3′–5′ exonuclease enzyme.[38] Brincidofovir is the lipid conjugative of Cidofovir and for this lipidic nature, it penetrates better in the cell membrane and provides greater oral bioavailability. Brincidofovir binds with the DNA Polymerase Holoenzyme to exhibit its antiviral action. Mainly Brincidofovir interacts with residues SER552, ASP549, and ASP753 by Hydrogen bond (H-bond), and ARG634 plus LYS638 interacts with it by salt-bridge.[39] Once the Brincidofovir enters the targeted cell, it liberates the cidofovir molecules after being cleaved by the phospholipase enzyme. The liberated Cidofovir molecule further gets activated into Cidofovir diphosphate by two phosphorylation steps to give the therapeutic effect against MPV.[40] Under special consideration and with FDA approval, physicians recommend the use of investigational medication Brincidofovir in emergencies. Even though Brincidofovir is the prodrug of cidofovir, cidofovir isn't normally advised because it is less safe compared to its prodrug. However, both aren't recommended at the same time.[41]

It is always known that prevention is better than cure so the risk of getting affected by mpox can be prevented by getting the full course of the JYNNEOS vaccine, avoiding skin-to-skin contact or any kind of sexual activity with an MPV-infected person, avoiding touch of any object used by an MPV-infected person, limiting contact with MPV carrier wild animals and avoiding raw meat consumption.[42] Lastly, building the habit of washing hands often with soap and water or an alcohol-based sanitizer after interaction with infected patients is very important.[43] It's better suggested to completely isolate an infected person in a separate room unless he fully recovers. Besides, healthcare professionals must be extra cautious during the diagnosis of mpox, especially when handling needles or swabs and during the time of providing treatment.[44] In addition, the deceased body should be transferred to the morgue as early as possible by properly wrapping it with cloth or shroud to prevent fluid leakage or keeping lesions open to the environment.[45] To prevent the spread of mpox from hospitals other than patient isolation or gown, gloves, PPE use, instructions on room cleaning, or specimen handling were adopted in many hospitals. For example, collected swabs were inserted into a closed-cap container and kept inside two plastic bags. The outermost plastic pack had a biohazard sign and then it was put inside a plastic container with a screw top for ensuring maximum safety and better transport into the laboratory. Besides, the cleaning protocol recommended the use of hypochlorite solution (1000 ppm) for cleaning the occupied or suspected mpox patient rooms. Other than this shared equipment was rubbed with chlorine wipes and those that are susceptible to chlorine were cleaned two times with Quaternary ammonium wipes.[46]

5 | EVALUATION OF VIRAL GENETIC MUTATIONS AND POTENTIAL THREATS

The sudden and extensive appearance of the Clade IIb strain of MPV on a global scale provoked substantial concerns regarding the health and safety of people all around the world. However, the cases of mpox infection declined gradually on May 23, 2023, and it was no longer a PHEIC.[47] Even though the number of cases has declined in the present, the potential threats associated with it in the future can't be overlooked. The mpox virus has been divided into three clades. Clade I represent the lineage from the Congo Basin, Clade II is the lineage from West Africa, and Clade III causes the current mpox infection outside of Africa. The alteration of the coding region involving the H3L and B21R antigens in the virus is primarily responsible for the evolution and variations across these Clades. The B.1 lineage which is primarily linked to the present cases of mpox infection has undergone microevolution giving rise to numerous clusters including B.1.1, B.1.2, B.1.3, B.1.4, B.1.5, B.1.6, B.1.7, and B.1.8.[48] Another finding demonstrated that the mean nucleotide substitution rate for the A.2 lineage is 5.53×10^{-5} substitutions per base/year, while the B.1 lineage has 1.13×10^{-4} substitutions per base/year. This suggests that the B.1 lineage has undergone more alterations than the A.2 lineage.[49] Moreover, 10 proteins OPG210, OPG188, OPG153, A27L-like, D2L-like, OPG109, OPG105, OPG071, OPG047, and OPG023 were observed to be more susceptible to changes due to assigning mutation in 187 open reading frames (ORFs) of the MPV genome. Particularly OPG210 and OPG105 have several nucleotide substitutions in the recent strains of MPV and got mutated along many lineages of the MPV.[50]

The Apolipoprotein B MRNA Editing Enzyme Catalytic Subunit 3G (APOBEC3), a cytidine enzyme, has caused around 42 nucleotide changes in the virus by conversion of GA to AA or from TC to TT. This evolution is also leading to human-to-human transmission of the MPV. The influence of APOBEC3 has caused around 46 B.1-specific single-nucleotide polymorphisms (SNPs) till now. Among these polymorphisms, four intergenic, 18 synonymous, and 24 nonsynonymous mutations are found. Among 10 genes particularly these six genes OPG003, OPG093, OPG098, OPG110, OPG185, and NBT03_gp174), genes related to the B.1 lineage have undergone mutation under the influence of APOBEC3 enzyme. These 6 proteins are responsible for determining virulence factors plus immune evasion. Other non-APOBEC3 mutations include changes in D209 N, P722S, and M1741I amino acids present in genes responsible for creating OPG210 or B22R immunogenic surface glycoproteins. Likewise, in MPV, a mutation in the OPG176 gene coding for a BCL-2-like protein which disrupts the host immune response is also observed.[51]

The 2022 outbreak of mpox contained the mutation in the L108 residue of the MPV F8L gene. The phenyl group of L108F is closer to the flipped nucleotide and this enhances the binding affinity of polymerase enzyme and triphosphate due to the rise in hydrophobicity. Thus, this whole phenomenon enhances the processivity, alters the sensitivity towards the nucleoside inhibitors, and helps in further DNA synthesis. Emerging since 2018, the W411 mutation has managed to keep evolving up to the 2022 outbreak. In the F8L insert 2, W411 remains exposed to the surface and influences insert 2 to more feasibly interact with the regulatory factors of MPV.[52] Furthermore, S30L and D88N mutations in the G9R gene were evident in the 2022 outbreak. There are possibilities that this mutation may affect the G9R and E4R (uracil DNA glycosylase) and cause functional variations in other proteins.[53] For the past decades, MPV has been seen to survive and adapt even after multiple mutations in its genes. The multiple mutations are responsible for the transmission of this infection rapidly in non-endemic areas. In comparison to RNA viruses, DNA viruses like MPV are slow and less fatal. Nevertheless, mutational features of MPV can't be neglected since mutations can lead to the risk of immunity evasion, increased virulence, and drug/vaccine resistance.[54] Therefore, it is important to look into the risks of future MPV mutations to stop massive outbreaks and prevent mpox infection from becoming a worldwide health problem.

6 | RECOMMENDED ACTIONABLE ITEMS FOR GLOBAL PREPAREDNESS

The WHO published guidance on 10 June 2022 to clinically manage, prevent, and control the MPV infection. For example, the WHO recommends hospitalization for patients such as small children, expectant mothers, and immunocompromised individuals so that they continue to receive clinical and supportive care while being appropriately isolated to prevent the spread of the virus. Additionally, suspected or confirmed patients are recommended to undergo continuous follow-up and counseling to monitor any changes in their physical or mental health.

In the case of mild and noncomplicated patients, isolation at home is possible by maintaining some instructions related to Infection Prevention and Control (IPC).[55] This involves having a skilled health worker inspect the house to determine whether it is suitable for isolating the patient and whether it has the necessary amenities present, such as enough food, water, and a sanitary system; it also includes checking if the facility of contacting the patient by a phone call or telemedicine is available or not; and lastly, it includes carefully assessing whether other healthy people or vulnerable people could still become infected with MPV even after the patient has been isolated. If the chances of infection spreading remain then the patient must be kept in an alternate location away from healthy individuals. Moreover, only one caregiver should be appointed and the caregiver must maintain at least a 1-m distance from the patient while being present in the isolation room. Even if isolation isn't possible then also at least 1 m distance needs to be kept between patients in a single room. In case, the caregiver needs to get considerably closer than proper masks, disposable gloves, and well-fitted clothes should be worn. Similarly, each health worker must also wear PPE before examining or collecting any samples from patients like gloves, mask, gown, eye protection, respirator, and footwear. Furthermore, patients should notify the hospital before the visit so that all required arrangements can be made in advance to properly deliver necessary treatment to the patient along with limiting the access of virus to the surrounding area. Besides, the formation of an mpox management team compromising young and experienced employees would be a wise decision for the hospitals to cope in case of any major mpox pandemic. Young and immunocompetent health workers below ≤ 45 years of age with proper training are suitable to be chosen in the mpox management team as they have a lower risk of contracting serious MPV infection. The hospital staff based on their expertise can be divided into numerous groups to ensure workers safety and round-the-clock service for patients' betterment.

Management of mpox would be a lot easier if mass people were made aware and given proper education and instructions related to stress managing techniques, self-management ways, stigma mitigating mentality, and details concerning home care. Besides, the deceased body should be transferred to the morgue as early as possible by properly wrapping it with cloth or shroud to prevent fluid leakage or keeping lesions open to the environment. On the other hand, the evolution of the MPV, its susceptibility to existing treatments, stability of new variants, the appearance of unknown symptoms, duration, and mode of transmission need to be continuously tracked to find better ways to fight off the infection.[56]

In the current situation, the availability of vaccines is also an important factor to be considered for mitigating the mpox infection worldwide. The disparity between rich and low and middle-income countries (LMICs) is once again evident due to the inequality of this vaccine distribution. The affluent countries like the United States,

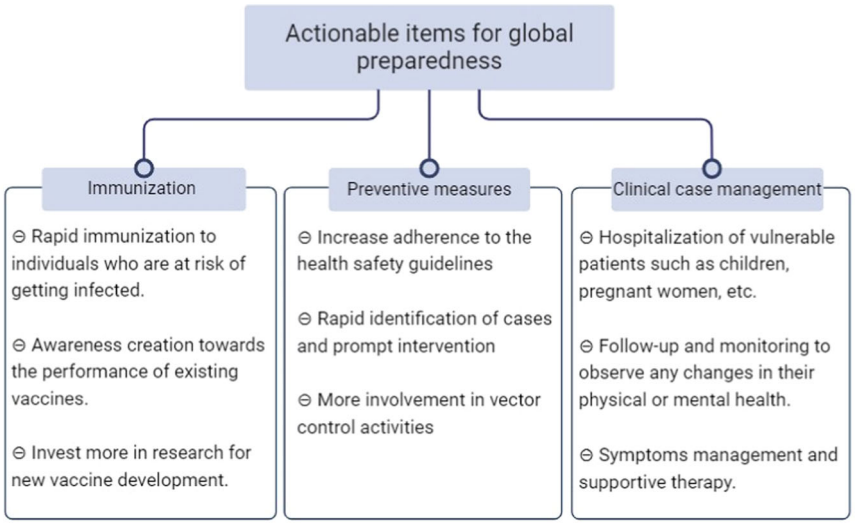

FIGURE 1 Therapeutic and preventive measures suggested for the global healthcare authorities to fight mpox infection.

European Union, Britain, and Canada have seemed to be at the forefront when it comes to having access to MPV vaccines. One of the main reasons for the unavailability of such vaccines is due to its limited production. Africa doesn't have the proper infrastructure and qualified personnel for its vaccine production. Out of 12 production facilities, only six countries South Africa, Egypt, Algeria, Senegal, Rwanda, and Morocco are contributing to vaccine production which is also less than 1%. Around 1.2 billion people in South Africa have no access to the mpox vaccine yet. Again, only Japan is responsible for the current production of LC16m8 and no other countries are producing it in the global market. Moreover, even after the availability of 100 million doses of ACAM2000, it raises concerns about immunocompromised people's safety as previously many side-effects have been recorded for this particular vaccine. As per WHO, 35 countries are fighting for 16.4 million currently available doses of the JYNNEOS vaccine. The only European manufacturer of this vaccine, Bavarian Nordic has halted production in 2022. This highlights the fact that amidst the rising confirmed cases of mpox, it's still uncertain that how much percentage of people in low and middle-income countries will have the opportunity to get vaccinated. We have summarized the actionable items for global preparedness to fight mpox in Figure 1.

7 | CONCLUSION

Mpox has been a part of global talk after it suddenly started spreading in nonendemic areas in the year 2022. Due to its huge outbreak outside Africa, it was formerly considered and declared as a matter of global health concern. Again, many new variants of MPV have emerged throughout recent years which also put forward possible risks of adverse conditions in the upcoming future. Yet, due to being less lethal as well as having a slower transmission rate, mpox is no longer considered an upcoming reason for pandemics like COVID-19. In addition, the availability and approval of the use of vaccines and oral medication have made it possible to treat the mpox viral infection in a much more efficient manner. Besides, maintaining the guidelines provided by the WHO for both patients and healthcare providers the reduction of mpox infection in large communities is possible. In brief, indeed the prevailing cases of mpox is not as deadly as the COVID cases but by ensuring proper treatment and awareness among the mass population it is possible to control the infection to a greater extent.

AUTHOR CONTRIBUTIONS

Md. Aminul Haque: Conceptualization; data curation; writing—original draft. **Angelina Samantha Halder**: Conceptualization; data curation; writing—original draft. **Md. Jamal Hossain**: Conceptualization; supervision; visualization; writing—review & editing. **Md. Rabiul Islam**: Visualization; writing—review & editing; supervision; conceptualization.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

TRANSPARENCY STATEMENT

The lead author Md. Rabiul Islam affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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REFERENCES

1. Islam MR, Asaduzzaman M, Shahriar M, Bhuiyan MA. The spreading of monkeypox in nonendemic countries has created panic across the world: could it be another threat? *J Med Virol*. 2023;95(1):e27919. doi:10.1002/jmv.27919
2. World Health Organization. Mpox (monkeypox). Accessed on October 8, 2023. https://www.who.int/news-room/fact-sheets/detail/monkeypox
3. Ligon BL. Monkeypox: a review of the history and emergence in the Western hemisphere. *Semin Pediatr Infect Dis*. 2004;15(4):280-287. doi:10.1053/j.spid.2004.09.001
4. Rabiul Islam M, Hasan M, Rahman MS, Rahman MA. Monkeypox outbreak - no panic and stigma; only awareness and preventive measures can halt the pandemic turn of this epidemic infection. *Int J Health Plann Manage*. 2022;37(5):3008-3011. doi:10.1002/hpm.3539
5. Centers For Disease Control and Prevention. Past U.S. cases and outbreaks. Accessed on October 8, 2023. https://www.cdc.gov/poxvirus/mpox/outbreak/us-outbreaks.html
6. Ahmed SH, Shahabi M, Malik H, Abid S, Hasibuzzaman MA. Mpox virus: a growing threat to fragile healthcare systems in Pakistan. *Ann Med Surg*. 2023;85(11):5842-5844. doi:10.1097/MS9.0000000000001378
7. National Library of Medicine. Mpox (Monkeypox). Accessed on October 8, 2023. https://www.ncbi.nlm.nih.gov/books/NBK574519/
8. World Health Organization. Weekly epidemiological record (WER), 20 January 2023, Vol. 98, No. 03, pp. 29-40[EN/FR]. Accessed October 8, 2023. https://reliefweb.int/report/world/weekly-epidemiological-record-wer-20-january-2023-vol-98-no-03-pp-29-40-enfr
9. Sarker R, Roknuzzaman ASM, Shahriar M, Bhuiyan MA, Islam MR. The WHO has ended public health emergency of international concern for mpox: assessment of upside and downside of this decision. *Int J Surg*. 2023;109(10):3238-3239. doi:10.1097/JS9.0000000000000545
10. Singh A, Shaikh B. The impact of pollutants and deforestation on the spread of monkeypox: an unintended consequence of progress. *Disaster Med Public Health Prep*. 2023;17:e464. doi:10.1017/dmp.2023.128
11. Levitt VC, Tran KQ, Hraky H, Mazer-Amirshahi M, Pourmand A. Emergency department approach to monkeypox. *World J Emerg Med*. 2023;14(5):341-348. doi:10.5847/wjem.j.1920-8642.2023.098
12. Sohan M, Akter MS, Islam MR. Expedition of monkeypox virus from Africa to rest of the world: what has made this old foe so powerful? *Ann Med Surg*. 2022;82:104688. doi:10.1016/j.amsu.2022.104688
13. Li H, Huang QZ, Zhang H, et al. The land-scape of immune response to monkeypox virus. *EBioMedicine*. 2023;87:104424. doi:10.1016/j.ebiom.2022.104424
14. Chowdhury PPD, Haque MA, Ahamed B, Tanbir M, Islam MR. A brief report on monkeypox outbreak 2022: historical perspective and disease pathogenesis. *Clin Pathol*. 2022;15:2632010X221131660. doi:10.1177/2632010X221131660
15. Centers For Disease Control and Prevention. Accessed October 8, 2023. https://www.cdc.gov/poxvirus/mpox/about/index.html#:~:text=Mpox%20
16. Sarker R, Roknuzzaman A, Nazmunnahar B, Islam MR. Risk evaluation and mitigation strategies for potential outbreaks of adenovirus infection: evidence from the recent incidences in West Bengal, India. *Clinical Pathology*. 2023;16:2632010X231205672. doi:10.1177/2632010X231205672
17. Centers For Disease Control and Prevention. Clinical Considerations for Mpox in People Who are Pregnant or Breastfeeding. Accessed October 8, 2023. https://www.cdc.gov/poxvirus/mpox/clinicians/pregnancy.html#:~:text=Mpox%20virus%20can%20be%20transmitted,confirmed%20mpox%20infection%20during%20pregnancy
18. McCollum AM, Shelus V, Hill A, et al. Epidemiology of human mpox - worldwide, 2018-2021. *MMWR Morb Mortal Wkly Rep*. 2023;72(3):68-72. doi:10.15585/mmwr.mm7203a4
19. Centers For Disease Control and Prevention. Signs and symptoms. Accessed on October 8, 2023. https://www.cdc.gov/poxvirus/mpox/symptoms/index.html
20. Islam MR, Hossain MJ, Roy A, et al. Repositioning potentials of smallpox vaccines and antiviral agents in monkeypox outbreak: A rapid review on comparative benefits and risks [published correction appears in Health Sci Rep. 2022 Nov 1;5(6):e897]. *Health Sci Rep*. 2022;5(5):e798. doi:10.1002/hsr2.798
21. Dhama K, Nainu F, Frediansyah A, et al. Global emerging omicron variant of SARS-CoV-2: impacts, challenges and strategies. *J Infect Public Health*. 2023;16(1):4-14. doi:10.1016/j.jiph.2022.11.024
22. World Health Organization. Multi-country outbreak of mpox, External situation report#28: 19 September 2023. Accessed on October 23, 2023. https://www.who.int/publications/m/item/multi-country-outbreak-of-mpox–external-situation-report-28—19-september-2023
23. World Health Organization. Multi-country outbreak of mpox. External situation report#31: 22 December, 2023. https://www.who.int/publications/m/item/multi-country-outbreak-of-mpox–external-situation-report-31—22-december-2023
24. Centers For Disease Control and Prevention. Outbreak in DRC. Accessed on April 16, 2024. https://www.cdc.gov/poxvirus/mpox/outbreak/2023-drc.html#:~:text=The%20Democratic%20Republic%20of%20Congo,mpox%20cases%20and%20581%20deaths
25. Gao S, Zeng Z, Zhai Y, et al. Driving effect of multiplex factors on Mpox in global high-risk region, implication for Mpox based on one health concept. *One Health*. 2023;17:100597. doi:10.1016/j.onehlt.2023.100597
26. Bruno G, Buccoliero GB. Antivirals against monkeypox (Mpox) in humans: an updated narrative review. *Life*. 2023;13(10):1969. doi:10.3390/life13101969
27. Akter MS, Sohan M, Islam MR. The rapid spreading of monkeypox virus is a threat for global public health: what should we do to fight this old enemy? *Health Sci Rep*. 2022;5(6):e876. doi:10.1002/hsr2.876
28. Zhou Y, Chen Z. Mpox: a review of laboratory detection techniques. *Arch Virol*. 2023;168(8):221. doi:10.1007/s00705-023-05848-w
29. Ichihashi Y, Oie M. Epitope mosaic on the surface proteins of orthopoxviruses. *Virology*. 1988;163(1):133-144. doi:10.1016/0042-6822(88)90240-1
30. Centers For Disease Control and Prevention. Patient's guide to mpox treatment with tecovirimat (TPOXX). Accessed on October 23, 2023. https://www.cdc.gov/poxvirus/mpox/if-sick/treatment.html
31. Sauerbrei A, Meier C, Meerbach A, Wutzler P. Inhibitory efficacy of cyclosal-nucleoside monophosphates of aciclovir and brivudin on DNA synthesis of orthopoxvi ruses. *Antiviral Chem Chemother*. 2006;17(1):25-31. doi:10.1177/095632020601700104
32. Panda K, Mukherjee A. Is monkeypox a threat to another pandemic? *Front Microbiol*. 2022;13:983076. doi:10.3389/fmicb.2022.983076
33. Centers For Disease Control and Prevention. JYNNEOS vaccine. Accessed on October 24, 2023. https://www.cdc.gov/poxvirus/mpox/interim-considerations/jynneos-vaccine.html
34. Centers For Disease Prevention and Control. Mpox vaccination basics. Accessed on October 24, 2023. https://www.cdc.gov/poxvirus/mpox/vaccines/index.html
35. Abdelaal A, Reda A, Lashin BI, et al. Preventing the next pandemic: is live vaccine efficacious against monkeypox, or is there a need for killed virus and mRNA vaccines? *Vaccines*. 2022;10(9):1419. doi:10.3390/vaccines1009141937

36. Centers For Disease Control and Prevention. Expanded access IND protocol: use of vaccinia immune globulin intravenous (VIGIV, CNJ-016) for treatment of human orthopoxvirus infection in adults and children. Accessed on October 24, 2023. https://www.cdc.gov/poxvirus/mpox/data/VIGIV-Protocol.pdf
37. Russo AT, Berhanu A, Bigger CB, et al. Co-administration of tecovirimat and ACAM2000™ in non-human primates: effect of tecovirimat treatment on ACAM2000 immunogenicity and efficacy versus lethal monkeypox virus challenge. *Vaccine*. 2020;38(3):644-654. doi:10.1016/j.vaccine.2019.10.049
38. Sudarmaji N, Kifli N, Hermansyah A, Yeoh SF, Goh BH, Ming LC. Prevention and treatment of monkeypox: A systematic review of preclinical studies. *Viruses*. 2022;14(11):2496. doi:10.3390/v14112496
39. Kumari S, Chakraborty S, Ahmad M, Kumar V, Tailor PB, Biswal BK. Identification of probable inhibitors for the DNA polymerase of the monkeypox virus through the virtual screening approach. *Int J Biiol Macromol*. 2023;229:515-528. doi:10.1016/j.ijbiomac.2022.12.252
40. Ghosh N, Chacko L, Vallamkondu J, et al. Clinical strategies and therapeutics for human monkeypox virus: a revised perspective on recent outbreaks. *Viruses*. 2023;15(7):1533. doi:10.3390/v15071533
41. Centers For Disease Prevention and Control. Treatment information for healthcare professionals. Accessed on October 24, 2023. https://www.cdc.gov/poxvirus/mpox/clinicians/treatment.html
42. Khan MR, Hossain MJ, Roy A, Islam MR. Decreasing trend of monkeypox cases in Europe and America shows hope for the world: evidence from the latest epidemiological data. *Health Sci Rep*. 2022;6(1):e1030. doi:10.1002/hsr2.1030
43. Islam MR, Nowshin DT, Khan MR, Shahriar M, Bhuiyan MA. Monkeypox and sex: sexual orientations and encounters are key factors to consider. *Health Sci Rep*. 2023;6(1):e1069. doi:10.1002/hsr2.1069
44. Weber DJ, Rutala WA, Sickbert-Bennett E. Emerging infectious diseases, focus on infection prevention, environmental survival and germicide susceptibility: SARS-CoV-2, Mpox, and Candida auris. *Am J Infect Control*. 2023;51(11S):A22-A34. doi:10.1016/j.ajic.2023.02.006
45. World Health Organization. Clinical management and infection prevention and control for monkeypox. Interim rapid response guidance. Accessed on April 16, 2022. https://iris.who.int/bitstream/handle/10665/355798/WHO-MPX-Clinical_and_IPC-2022.1-eng.pdf?sequence=1
46. Safir A, Safir M, Henig O, et al. Nosocomial transmission of MPOX virus to health care workers -an emerging occupational hazard: a case report and review of the literature. *Am J Infect Control*. 2023;51(9):1072-1076. doi:10.1016/j.ajic.2023.01.006
47. Pan American Health Organization.WHO declares end of mpox emergency, calls for sustained efforts for long-term management of the disease. Accessed on October 25, 2023. https://www.paho.org/en/news/11-5-2023-who-declares-end-mpox-emergency-calls-sustained-efforts-long-term-management-disease#:~:text=May%2011%2C%202023%2D%20The%20Emergency,General%20accepted%20the%20Committee%27s%20advice
48. Li H, Zhang H, Ding K, et al. The evolving epidemiology of monkeypox virus. *Cytokine Growth Factor Rev*. 2022;68:1-12. doi:10.1016/j.cytogfr.2022.10.002
49. Azzi A. Unusual monkeypox virus outbreak in 2022: phenotypic and molecular characteristics. *Aspects Mol Med*. 2023;1(2023):100001.
50. Forni D, Cagliani R, Molteni C, Clerici M, Sironi M. Monkeypox virus: the changing facets of a zoonotic pathogen. *Infect Genet Evol*. 2022;105:105372. doi:10.1016/j.meegid.2022.105372
51. Luna N, Muñoz M, Bonilla-Aldana DK, et al. Monkeypox virus (MPXV) genomics: A mutational and phylogenomic analyses of B.1 lineages. *Travel Med Infect Dis*. 2023;52:102551. doi:10.1016/j.tmaid.2023.102551
52. Kannan SR, Sachdev S, Reddy AS, et al. Mutations in the monkeypox virus replication complex: potential contributing factors to the 2022 outbreak. *J Autoimmun*. 2022;133:102928. doi:10.1016/j.jaut.2022.102928
53. Jin Y, Asad Gillani SJ, Batool F, et al Structural and molecular investigation of the impact of S30L and D88N substitutions in G9R protein on coupling with E4R from monkeypox virus (MPXV). *J Biomol Struct Dyn*. Published online January 4, 2024. doi:10.1080/07391102.2023.2291159
54. Nazmunnahar B, Haque MA, Ahamed B, Tanbir M, Suhee FI, Islam MR. Assessment of risk perception and subjective norms related to mpox (monkeypox) among adult males in Bangladesh: a cross-sectional study. *Health Science Reports*. 2023;6(6):e1352. doi:10.1002/hsr2.1352
55. Islam MR, Haque MA, Ahamed B, et al. Assessment of vaccine perception and vaccination intention of mpox infection among the adult males in Bangladesh: a cross-sectional study findings. *PLoS One*. 2023;18(6):e0286322. doi:10.1371/journal.pone.0286322
56. World Health Organization. Clinical management and infection prevention and control for monkeypox. 2022. Accessed on October 26, 2023. https://iris.who.int/bitstream/handle/10665/355798/WHO-MPX-Clinical_and_IPC-2022.1-eng.pdf?sequence=1

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