https://www.banglajol.info/index.php/BJMM/index

Bangladesh Journal of Medical Microbiology

July 2024, Volume 18, Number 2, Page 120-130

ISSN (Print) 2070-1810

ISSN (Online) 2072-3105

Review Article ***Open Access***

Global Patterns and Emerging Challenges of Human Monkeypox Virus: An In-Depth Narrative Review and Analysis

Md. Rakibul Hasan[1], Md. Abdullah Yusuf[2], Whitney T. Rogers[3], Gerald Egbury[4], Moryom Akter Muna[5]

[1]Graduate Research Assistant (Biomedical Health Sciences) and PhD Candidate in Health Promotion & Behavioural Sciences, University of Louisville, United States; [2]Associate Professor, Department of Microbiology, National Institute of Neurosciences & Hospital, Dhaka, Bangladesh; [3]Project Director (School of Medicine), University of Louisville, United States; [4]Senior Lecturer and Supervisor, School of Health, Education, Medicine & Social Care, Anglia Ruskin University, Cambridge, United Kingdom; [5]Residential Medical Officer, Mirpur General Hospital, Dhaka, Bangladesh

Abstract

Monkeypox, caused by the monkeypox virus (MPXV), has reemerged as a significant public health concern, primarily due to reduced immunity following the cessation of smallpox vaccination. The 2024 outbreaks in South Africa and Pakistan underscore the virus's capacity to spread beyond its traditional endemic regions, driven by factors such as increased international travel, urbanization, and closer human-animal interactions. This narrative review consolidates current knowledge on the epidemiology, clinical manifestations, transmission mechanisms, and therapeutic approaches for MPXV. Employing a comprehensive literature review methodology, the study highlights several key findings, including the virus's ability to adapt and spread in new environments, the necessity of monitoring viral evolution, the importance of assessing the long-term effectiveness of existing vaccines, and the critical role of understanding environmental factors influencing viral transmission. Additionally, the review emphasizes the need for effective public health initiatives, such as vaccination strategies and surveillance systems, to mitigate the spread of MPXV. These insights are crucial for informing and shaping global health policies aimed at preventing future outbreaks and enhancing international health security in an increasingly interconnected world. In conclusion, this review suggests several key areas for future research, including the necessity for ongoing surveillance, the enhancement of vaccination strategies, and a deeper understanding of the ecological factors that affect the spread of MPXV.

Keywords: Monkeypox virus (MPXV); emerging epidemics; zoonotic transmission; global health security; vaccine effectiveness; epidemiological patterns

Bangladesh Journal of Medical Microbiology, July 2024;18 (2):120-130

Correspondence: Dr. Md. Rakibul Hasan, MBBS (DU), MPH (Cambridge, UK), Diploma in Neuroscience (UK), MCGP (BD), CCT in Emergency Medicine (University of Glasgow, Scotland), PGT in Healthcare (London); Graduate Research Assistant (Biomedical Health Sciences) and PhD Student in Health Promotion & Behavioural Sciences, University of Louisville, 2301 S 3rd St, Louisville, KY 40292, United States; Former Healthcare Professional, Cambridge University Hospitals, NHS Foundation Trust, UK; Former Teaching Assistant, Cambridge Regional College, UK; Email: mdrakibul.hasan@louisville.edu; drmdrakibul@gmail.com; Cell No: +1 (502) 475-2298; ORCID: https://orcid.org/0000-0002-9152-8753

DOI: https://doi.org/10.3329/bjmm.v18i2.75690

Introduction

Human monkeypox, a zoonotic disease caused by the monkeypox virus (MPXV), is a member of the Orthopoxvirus genus, which also includes notable viruses such as variola (smallpox), vaccinia, and cowpox. Monkeypox was first discovered in humans in 1970 in the Democratic Republic of the Congo (DRC) and has typically been prevalent in areas of Central and West Africa[1]. Recent outbreaks in non-endemic areas, however, have raised worldwide concerns about its potential for broad spread and underlined the changing character of this infectious illness[2].

Although MPXV usually causes a less severe disease, it has numerous clinical traits with smallpox, including a distinctive rash and fever[3]. The comeback of monkeypox, especially in relation to declining population immunity after the smallpox vaccine was stopped, has attracted public and scientific attention in this regard once again. With an eye towards important topics such its epidemiology, clinical aspects, treatment choices, infection rates, and preventative measures, this review seeks to provide a thorough analysis of the body of current research on human monkeypox. It also looks at the virus's possible re-emergence, its global expansion outside of conventional endemic areas, and the important knowledge gaps that must be filled to properly control this newly developing public health hazard. Effective worldwide health policies depend on a better knowledge of these elements as international travel and interactions between humans and animals grow.

Epidemiology

In 1970, the first occurrence of monkeypox in a 9-month-old child was detected in the Democratic Republic of the Congo (DRC), specifically in an area where smallpox had been recently eliminated[4]. Subsequently, the illness has established itself as a prevalent and ongoing issue in several nations in Central and West Africa, such as the Democratic Republic of Congo, Nigeria, Cameroon, and the Central African Republic. Two separate genetic clades of MPXV have been recognized: the Central African (Congo Basin) clade and the West African clade[5]. The Central African clade is linked to more severe illness, increased transmission rates, and a higher case fatality rate (CFR), while the West African clade often results in less severe illness.

The reappearance of monkeypox in Nigeria in 2017, after a period of over forty years without any documented cases, highlights the shifting patterns of the disease's spread[6]. The reappearance of MPXV is likely a result of many causes, such as reduced smallpox vaccine coverage, which formerly offered protection against MPXV, and increasing encounters between humans and animals owing to urbanization encroaching on natural habitats. Moreover, the occurrence of recent outbreaks in non-endemic nations like the United States and the United Kingdom underscores the possibility of worldwide dissemination of monkeypox via international travel[7].

During August 2024, South Africa and Pakistan saw substantial mpox (formerly referred to as monkeypox) epidemics. The epidemic in South Africa has worsened, with a total of 16 confirmed cases and three deaths. The reported instances were mostly seen in males between the ages of 23 and 43, and were distributed throughout the provinces of KwaZulu-Natal, Gauteng, and the Western Cape[8]. South African health officials have been diligently endeavouring to control the epidemic, placing significant emphasis on health education and pushing anyone with symptoms to swiftly seek medical attention (Med Xpress) (SA News).

Pakistan has just announced its first instances of mpox for the year, with nine confirmed illnesses and one fatality. The cases in Pakistan were associated with persons who had returned from the Middle East, suggesting that the virus had not yet spread locally. The National Command and Operation Centre (NCOC) has intensified monitoring, especially at crossings, to closely check arriving passengers for symptoms and prevent any further transmission (Pakistan Today). These outbreaks highlight the continuous worldwide danger of mpox and the crucial need for international collaboration in monitoring, immunization, and public health measures to avoid future escalation.

Geographic Distribution

Although the Democratic Republic of the Congo (DRC) reports the most occurrences since the virus was first discovered in humans, monkeypox is essentially native throughout Central and West Africa[2]. Other nations in the area, including the Central African Republic, Nigeria, and Cameroon, have also had major epidemics. Monkeypox is usually linked in these endemic locations to rural and wooded settings where human-animal contacts are more prevalent. The virus sometimes crosses over to humans but mostly circulates in animal species. Although their extent is usually restricted, in the absence of sufficient public health policies these outbreaks might develop into more significant ones. Monkeypox has lately been recorded in various non-endemic nations, which raises questions over its possible worldwide distribution. Often connected to foreign travel or the importation of diseased animals, notable outbreaks have occurred in the United States, the United Kingdom, and other European nations. Traced back to a shipment of animals from Ghana, the 2003 epidemic in the United States was the first documented incidence of monkeypox outside of Africa, therefore underscoring the dangers connected with international animal

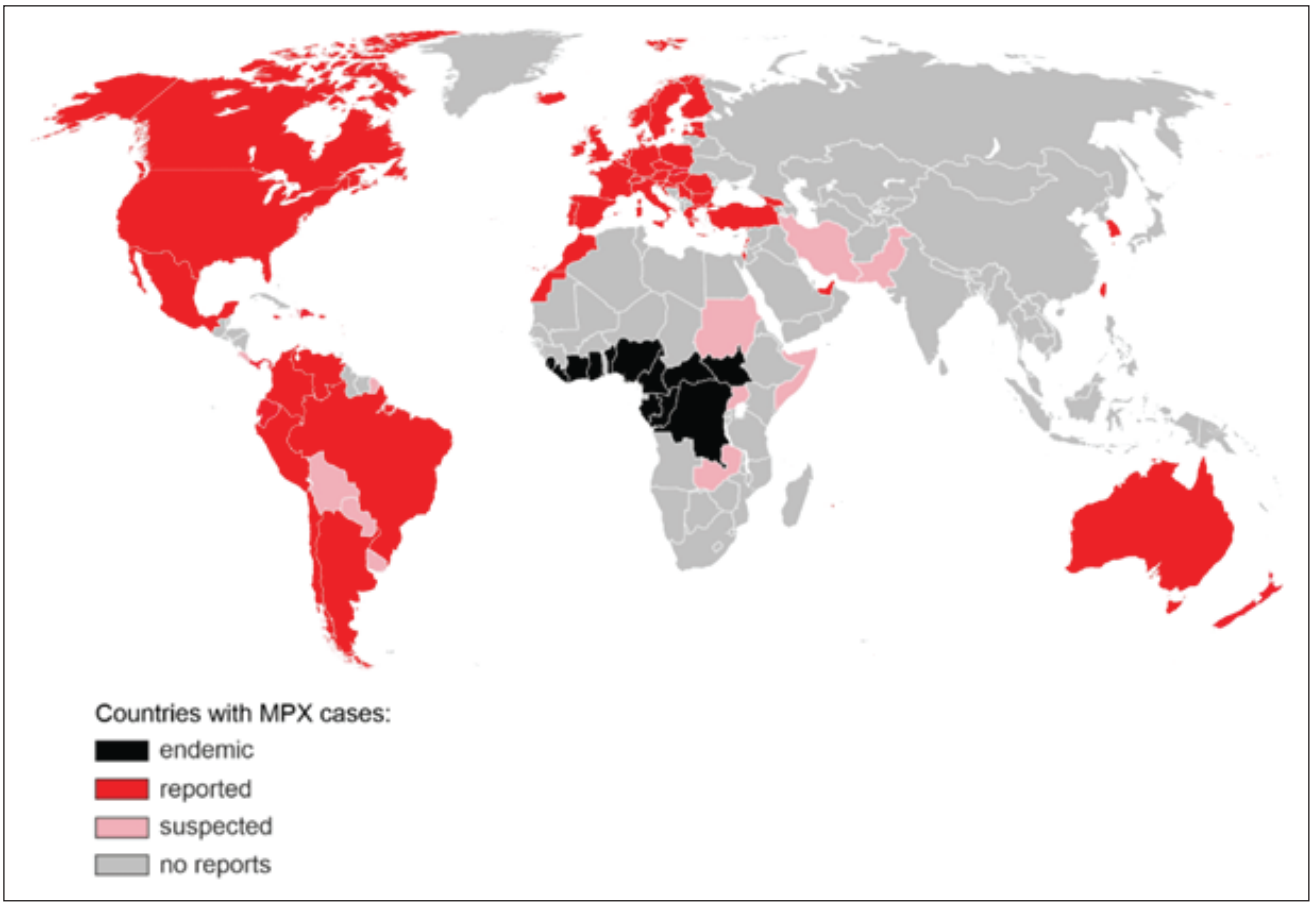

Figure I: Geographic Distribution of MPOX (2022)

trading[9]. Later epidemics in non-endemic areas have included human-to-- human transmission, especially among visitors from endemic areas. These events highlight the importance of strict importation rules and global collaboration in controlling and monitoring monkeypox. Public health authorities in non-endemic areas have to be alert, particularly in regard to screening visitors from endemic areas and reacting quickly to suspected cases.

Transmission and Replication Dynamics

Monkeypox virus (MPXV) is mostly transmitted by direct contact with infected rodents. However, human-to-human transmission may also occur through intimate contact with lesions, bodily fluids, respiratory droplets, and contaminated items. Studies conducted on macaques exposed to aerosolized MPXV demonstrate that the virus first infects the epithelial cells in the lower airway. It subsequently travels to the

Table-1: Stages of Viral Infection and Replication Process

Stages	Description
Attachment	Facilitated by glycosaminoglycans (chondroitin and heparin sulfates)
Entry	Endosomal pathways or direct fusion
Early Transcription	Viral gene transcription and translation
DNA Replication	Takes place in specialized cytoplasmic structures called “factories”
Intermediate Transcription	Intermediate viral gene transcription and translation
Late Transcription	Late viral gene transcription and translation
Assembly	Assembly of viral particles
Morphogenesis	Transformation of viral particles
Envelopment	Envelopment by intracellular membranes
Budding	Release of mature virions to infect neighboring cells

lymph nodes and disseminates throughout the body via monocytic cells[10]. MPX lesions may occur in several organs, such as lymph nodes, thymus, spleen, skin, oral mucosa, gastrointestinal tract, and reproductive system. MPXV has the ability to infect a wide range of mammalian cells under laboratory conditions. This infection is facilitated by glycosaminoglycans such as chondroitin and heparin sulfates, which help the virus bind to the cells[11].

The replication cycle of MPXV consists of several crucial stages: attachment to host cells, entry through endosomal pathways or direct fusion, early viral gene transcription and translation, DNA replication, intermediate and late transcription and translation, assembly, morphogenesis, envelopment by intracellular membranes, and budding. The attachment process is facilitated by viral proteins and cellular glycosaminoglycans, whereas entrance is assisted by a complex of viral membrane proteins. The synthesis of viral DNA takes place inside specialized structures in the cytoplasm called "factories," which undergo a transformation from compact forms to crescent-shaped locations for the assembly of viral particles. Once mature, virions may either stay inside the cell or become encapsulated and leave to infect neighbouring cells[12].

Mechanisms of Immune Evasion, Mutation, and Adaptation

Monkeypox (MPXV) employs many tactics to elude the host's immune system. It suppresses the activation of interferon-stimulated genes and important cytokines like TNF-α, IL-1α, IL-1β, CCL5, and IL-6 as well as phosphorylation of immunological receptors like PKR and eIF2α, therefore compromising the body's antiviral defences[13]. MPXV genes for homolog of D7L, which reduces IL-18 signalling, and B16, which blocks type I interferon signalling, therefore suppressing the normal immunological responses of the host. Furthermore, produced by the virus is a complement control protein (CCP), which stops complement activation. Lower case fatality rate in the West African (WA) clade relative to the Congo Basin (CB) clade explains the lack of CCP in that clade[11].

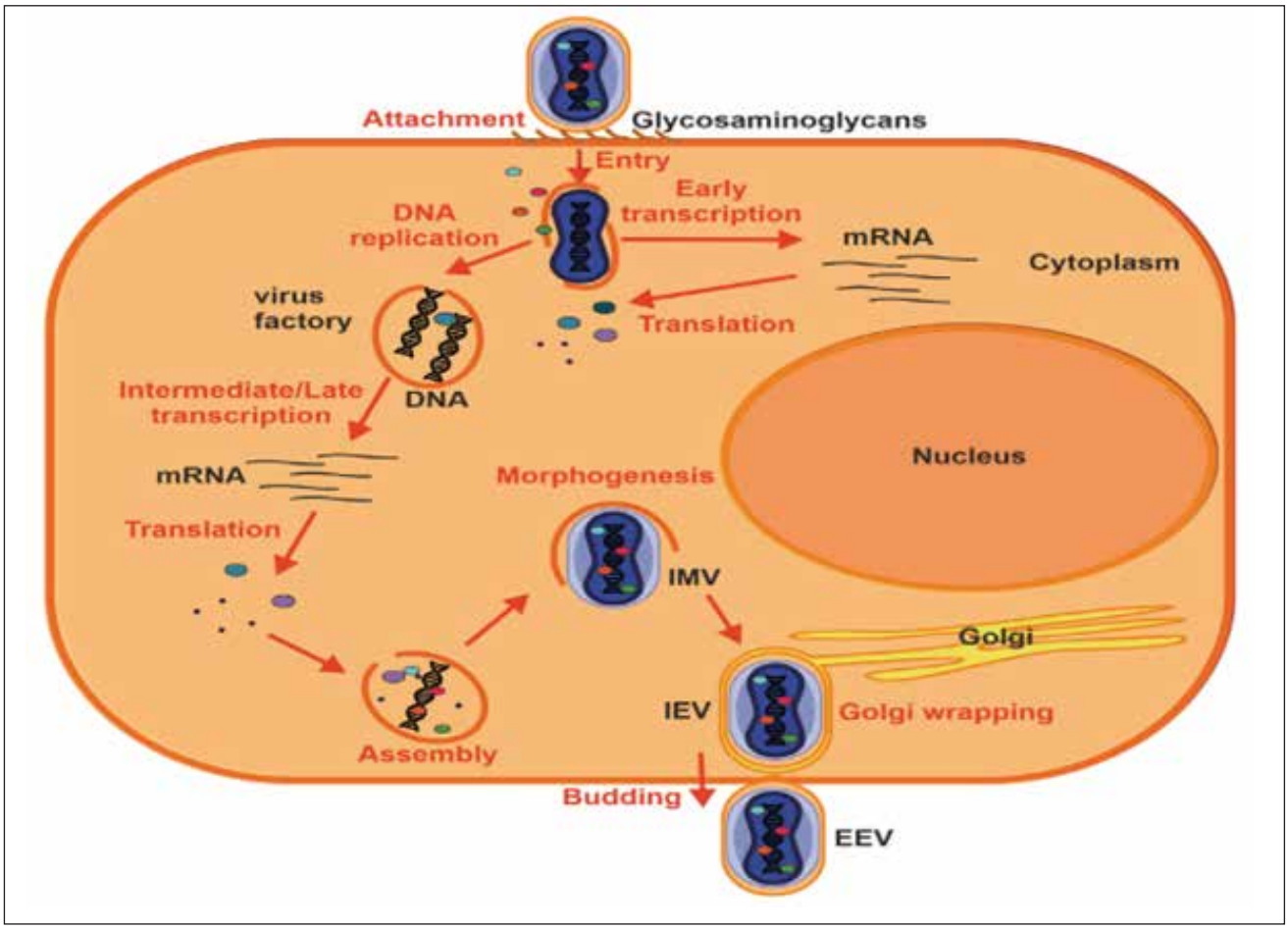

Figure II: Pathogenesis of Monkeypox Virus

With an estimated evolutionary rate of 1–2 nucleotide changes year, MPXV mutates less often than RNA viruses because of the durability of its double-stranded DNA and the proofreading capacity of its DNA polymerase. Analysis of MPXV genomes from the 2022 epidemic showed mutations suggestive of APOBEC3 editing, which drastically changed proteins engaged in viral transcription, DNA binding, entry/fusion, and immune evasion[1]. By means of recombination, poxviruses may also acquire or lose genes, enabling their adaptation to selection forces without appreciable genomic growth. Research on the functional effects of certain mutations discovered in the strains of the 2022 epidemic is still under progress, therefore underscoring the virus's adaptability and evolution in response to environmental factors.

Human Outbreak Patterns of the Monkeypox Virus

Historically rare and limited mostly to the Democratic Republic of the Congo (DRC), monkeypox outbreaks have Still, current patterns suggest that a continuous rise in case count is driving a comeback of monkeypox in Nigeria[14]. This shift points to possible variations in the viral epidemiological tendency. Some plausible causes of this change in population immunity, changes in human behavior, and environmental modifications influencing the distribution and behavior of reservoir species might be each other.

Those who skipped the smallpox vaccine after the disease's eradication in 1980 have become more susceptible to monkeypox[15]. Moreover, perhaps assisting the virus in spreading from animal reservoirs to people include urbanization, changes in land use, and increasing contacts between humans and animals. Especially in areas where the disease is not frequently seen, the current worldwide monkeypox epidemic highlights the need of ongoing surveillance and specific public health interventions to stop the virus from spreading.

Pathogenesis and Clinical Features

Usually starting an incubation period of five to twenty-one days, monkeypox virus (MPXV) infection proceeds with a prodromal phase marked by fever, headache, muscular pains, backache, swollen lymph nodes, chills, and exhaustion. Usually, a rash that begins on the face and extends to other areas of the body including the palms and soles successes this phase. From macules to papules, vesicles, pustules, and finally scabs, the rash moves in phases[12]. Unlike smallpox, lymphadenopathy usually helps to differentiate monkeypox. The viral clade, the patient's immunological state, and other variables may all affect the degree of the rash and general clinical presentation. Typical symptoms include fever, chills, sore throat, malaise, headache and body pains, and a distinct skin rash. Though lymphadenopathy is more prevalent in MPXV infections, the illness might mimic chickenpox and cause possible misdiagnosis. Atypical presentations include few or no lesions localized in the genital or perineal/perianal regions, anal discomfort, and bleeding have been recorded in the 2022 epidemic[8]. Though the condition may be more severe in young children, immunosuppressed patients, and those with HIV-1, who may have longer sickness and increased incidence of subsequent infections, symptoms typically recover 2-4 weeks. MPXV can be passed via the placenta during pregnancy, maybe resulting in fetal mortality. Among the severe effects might include encephalitis, secondary skin infections, bronchopneumonia, sepsis, and vision loss brought on by scarring and corneal infection. Death rates vary; children have more mortality while the Congo Basin (CB) clade differs from West African (WA) clade. Whereas the WA clade is around 3.6%, the CB clade has a case fatality rate of up to 10%. Better access to healthcare makes outcomes in non-endemic areas usually more positive[16]. Recent outbreaks have also recorded unusual presentations including vaginal lesions, which might be confused for sexually transmitted diseases (STIs) including syphilis or herpes simplex virus.

Infection Rate

Several variables, such as population immunization levels, the particular viral lineage, and the degree of human-to-human transmission, impact the infection rate of monkeypox. Unvaccinated persons have an estimated secondary attack risk of about 10%, which is greater in close-contact environments like families and healthcare institutions. The reappearance of monkeypox in different areas highlights the need of understanding these processes in order to enforce efficient public health policies[17]. Factors including as heightened human-animal interactions, urbanization, and changes in land use may promote the transmission of the virus from animal reservoirs to people.

Case Fatality Rate

The case fatality rate (CFR) for monkeypox varies significantly depending on the specific viral lineage and the overall health condition of the patient. The

Central African clade is linked to increased case fatality rates (CFRs), which vary from 1% to 11%[18]. This clade mostly impacts young and immunocompromised people. On the other hand, the West African clade often exhibits lower Case Fatality Rates (CFRs), although it remains a considerable danger, particularly in regions with restricted healthcare availability. The fluctuation in Case Fatality Rate (CFR) emphasizes the need for specific treatments and enhanced healthcare infrastructure to effectively handle and reduce the consequences of monkeypox epidemics. To decrease the occurrence and death rate related to monkeypox, it is essential to implement improved monitoring, vaccination initiatives, and public health awareness programs.

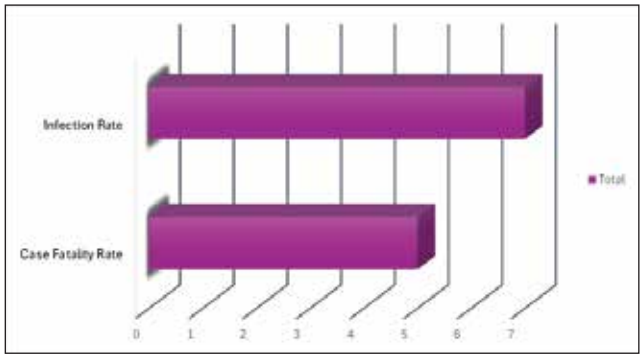

Fig-III: Infection rate and CFR for MPOX among worldwide population in 2022

Complications of Monkeypox Virus (MPXV) Infection

Monkeypox can lead to a range of serious complications, including secondary bacterial infections, respiratory problems such bronchopneumonia, gastrointestinal difficulties, dehydration, encephalitis, and corneal infections that can cause irreversible vision loss[19]. Various variables, including the patient's age, immunological condition, and the particular viral lineage, have an impact on the severity of the illness. The Central African clade is specifically linked to more severe consequences and elevated death rates, particularly among children[20].

Children, especially those with pre-existing diseases such as diabetes, have substantial difficulties in their treatment because of the connection between microbial dysbiosis and viral infections. Dysbiosis, which refers to disruptions in gut microbiota, might hinder the immune system's capacity[21] to fight illnesses like monkeypox. This imbalance may worsen the severity of viral infections, particularly those that impact the gastrointestinal tract, making treatment more complicated and increasing the susceptibility of these young individuals.

Management of Monkeypox Virus (MPXV) Infection

Early post-exposure immunization might be helpful for susceptible individuals considering MPX's somewhat extended incubation periodfive to twenty-days. Research on prairie dogs has shown that post-exposure immunization reduces the severity of MPX illness; non-human primates did not exhibit such advantages[22]. The longer incubation period in the prairie dog model, which more fairly represents human infection and provides enough time for an immune response to develop, may be the cause of this disparity. Close contacts of smallpox cases and immunocompromised patients with progressing vaccinia have utilized passive immunisation with immune sera or vaccinia immune globulin. Vaccinia immune globulin intravenous (VIGIV) is regarded safe and maybe helpful for susceptible people even if clinical trial evidence on its effectiveness against MPX are inadequate[1].

The only FDA and EMA-approved medication for orthopoxvirus infections in humans right now is Tecovirimat (ST-246)[23]. Severe MPX cases have been treated with it; patients have shown recovery. Tecovirimat acts by interfering with the p37 viral envelope protein's cellular location, therefore stopping the generation and spread of enveloped virions[24]. In monkey models devoid of side effects, this medication has shown effectiveness in lowering MPX mortality. Though its efficacy in human MPX patients is still unknown, cidofovir, authorized for cytomegalovirus (CMV) retinitis therapy in AIDS patients, has shown efficacy against deadly MPXV infection in macaques. Given its improved safety profile, brincidofovir a lipid compound of cidofovir is under investigation as a possible MPX treatment[1].

None of any particular antiviral drug is licenced only for monkeypox as yet. Mostly, treatment addresses supportive care to reduce symptoms and avoid consequences. Still, numerous antiviral medications used to treat smallpox including cidofovir and tecelovir have showed promise in treating severe MPX infections[25]. Given the little evidence on their efficacy in people, the use of these medications is probably going to stay restricted to extreme situations.

Prevention Strategies

Public Health Initiatives: Preventive actions aimed at

monkeypox mostly aim to lower the risk of transmission from people and animals. Monkeypox is a zoonotic illness, hence direct contact with possibly infected animals should be avoided especially in endemic areas where animals like rats and primates are known to be viral reservoirs. This includes avoiding touching or eating bushmeat, which has been shown to be a major risk factor for transmission in various African countries[26].

Strictly hygienic practices help to reduce human-to-human transmission. Especially after contact with an infected person or animal or after handling animal products, this entails frequent hand washing with soap and water. Healthcare professionals and caregivers who come into close contact with sick people should wear gloves, masks, and gowns personal protective equipment (PPE). Controlling the virus's spread also depends critically on isolation of verified cases.

Raising knowledge of the dangers of monkeypox and the need of preventative actions depends on educational efforts. Particularly in regions where monkeypox outbreaks are expected to arise, these programs should aim at the general community as well as healthcare professionals. Early identification of suspected illnesses and quick isolation of them should be emphasized in public health messages to help to stop epidemics.

Vaccination Against Monkeypox (MPX): Immunization is a very successful approach to thwart the occurrence of monkeypox. Modified Vaccinia Ankara (MVA-BN), a kind of modern third-generation vaccine, provides cross-protection against the monkeypox virus (MPXV)[27]. Immunization is crucial for those residing in or visiting areas where a disease is often seen, as well as for laboratory workers, healthcare professionals, and others who are at a high risk of coming into contact with the disease. Administering a post-exposure vaccination within a timeframe of four days after exposure may considerably diminish the intensity of monkeypox. Implementing focused vaccination efforts, as advised by the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC), play a vital role in diminishing viral transmission and managing outbreaks[28]. Historical research indicates that smallpox vaccines, because of their resemblance in terms of antigens to MPXV, are efficacious, offering around 85% protection and substantially decreasing the likelihood of infection even after a span of 25 years[29].

There are other vaccine choices, such as ACAM2000 and APSV, which include live, replication-competent vaccinia virus. However, these alternatives are not appropriate for persons with weakened immune systems. The MVA-BN vaccine, which consists of two doses and contains a virus that is unable to replicate, is considered safe for patients with weakened immune systems[27]. The LC16m8 vaccination, which has been authorized for use in Japan, provides an enhanced level of safety. Although the World Health Organization (WHO) does not endorse widespread vaccination, it does encourage immunization for persons who have recently been exposed to a disease, as well as for healthcare professionals and laboratory staff. Certain locations have begun the administration of vaccines to populations at a higher risk, specifically targeting homosexual and bisexual males. In response to the 2022 epidemic, the European Health Emergency Preparedness and Response Authority (HERA) has taken steps to improve the supply of vaccines, despite their restricted availability. As part of these efforts, HERA has ordered 110,000 doses of MVA-BN[30].

Vaccination Strategies: Vaccination remains one of the most effective tools for preventing monkeypox. The smallpox vaccination is crucial because it has been scientifically shown to provide cross-protection against monkeypox, because to the genetic similarities shared by the two viruses. Discontinuing routine smallpox vaccination after the worldwide elimination of the illness in 1980 has made unvaccinated persons more susceptible to monkeypox. Advancements in vaccine research have resulted in the creation of third-generation smallpox vaccinations, including MVA-BN (Modified Vaccinia Ankara-Bavarian Nordic) and LC16m8. These vaccines are safer and have less adverse effects compared to prior versions[30]. The administration of these vaccinations is advised for persons who are at a heightened risk of contracting monkeypox, such as healthcare workers, laboratory personnel who handle Orthopoxviruses, and individuals residing in places affected by epidemics. Ring vaccination, a tactic that involves immunizing individuals who have close contact with confirmed cases, may be used to effectively stop the transmission of an epidemic. This method, which was effectively used during the smallpox eradication effort, has been modified for the purpose of controlling monkeypox epidemics. Nevertheless, the accessibility and use of these vaccinations remain restricted, especially in areas with minimal resources where monkeypox is prevalent. It is crucial to ensure fair distribution and enhance the manufacturing of vaccinations in order to

supply at-risk groups with this vital preventative strategy[31].

Challenges in Vaccine Deployment: Though vaccination is very successful, various obstacles hinder its general use in the prevention of monkeypox. The scarcity of vaccinations is one of the main difficulties, particularly in endemic areas where the infrastructure of healthcare may not have built. Significant obstacles also come from the expense of vaccinations and the difficulties of storing and delivering them in far-off places. Moreover, public reluctance towards vaccination resulting from false information and mistrust of health officials could lower vaccination rates. This is especially alarming in areas where local people have become suspicious and opposed earlier vaccination initiatives based on past events[26]. Dealing with these issues calls for a multifarious strategy including improvements in vaccine manufacturing capacity, enhancement of healthcare facilities, and community involvement campaigns to inspire confidence and therefore advance the advantages of immunization. To guarantee that vaccinations are accessible to those most in need, international cooperation and assistance are also very vital.

Surveillance and Monitoring

Early identification of monkeypox cases and tracking of the virus's transmission depend on effective surveillance systems. Limited resources and poor healthcare facilities in many endemic areas compromise monitoring and cause underreporting of cases and delayed reaction to outbreaks.

Training healthcare professionals to identify monkeypox symptoms, setting explicit reporting rules, and integrating monkeypox surveillance into current infectious disease monitoring systems help to strengthen surveillance systems. By means of digital tools and mobile technologies, data collecting, and real-time reporting may be improved, thus facilitating faster reactions to newly developing epidemic.

Particularly in areas with great people mobility, cross-border cooperation is also very vital for tracking and stopping the spread of monkeypox. By means of information and resource sharing made possible by regional and multinational collaborations, surveillance initiatives' general efficacy may be raised.

Re-Emergence Probability

Factors Contributing to Re-emergence: Many interrelated elements affect the likelihood of monkeypox re-emergence. Among them, the most important one is the diminishing immunity in human populations after regular smallpox vaccination stopped. The number of people vulnerable to MPXV rises as immunity declines, therefore generating more possible hosts for the virus[3]. Driven by changes in land use, deforestation, and urbanization, increasing human-animal interactions also help to re-emerge monkeypox. Zoonotic spillover occurrences increase when human populations encircle wildlife areas, hence increasing human interaction with the MPXV animal reservoirs. Moreover, globalisation and more travel abroad have helped monkeypox to expand beyond its usual endemic areas. Linked to the importation of contaminated animals, the 2003 epidemic in the United States emphasizes the possibility of monkeypox developing in non-endemic regions and the requirement of constant observation and quick reaction capacity all around[4].

Potential for Human-to-Human Transmission

Although zoonotic transmission is still the major way of infection, there is increasing worry about the possibility of continuous human-to-human monkeypox spread. In highly crowded metropolitan areas, where direct interaction among people might help the virus to spread, this issue is especially important. Mostly by respiratory droplets, direct contact with body fluids or lesions, and indirect contact via infected objects like bedding or clothes, human-to-human transmission takes place Among household members of infected people and in hospital environments, where intimate contact with sick patients is more prevalent, the risk of transmission is increased[10]. Particularly in environments with limited healthcare resources and insufficient infection control policies, the possibility for human-to-human transmission raises the risk of epidemics. Dealing with this danger calls for improving infection control and preventive strategies in hospitals, public awareness of transmission hazards, and quick isolation of sick people to stop further spread.

Gaps in Understanding Re-emergence

Though significant gaps in knowledge still exist even with the recognized elements driving the re-emergence of monkeypox. For example, it is not quite clear how animal reservoirs help the virus to survive in the surroundings. Development of focused treatments to lower the risk of zoonotic transmission depends on the identification and research on these reservoirs. Furthermore, little recorded is the long-term efficacy

of smallpox immunizations in preventing monkeypox[18]. Although the vaccinations are known to provide cross-protection, further research on the length of this protection and its effectiveness in other groups is necessary. Particularly since the virus keeps changing, research is also required to investigate the possibility of vaccination resistance to develop over time. Another issue that demands further research is the effect of environmental changes on the epidemiology of monkeypox including habitat degradation and climate change. Predicting and reducing future infections depends on an awareness of how these developments affect the dynamics of viral transmission as well as the distribution and behavior of animal reservoirs.

Gaps in Geographic Knowledge

Although there is much documentation on the geographic distribution of monkeypox in certain areas, there are still notable gaps in our knowledge. Surveillance endeavors are constrained in many nations where a disease is prevalent, especially in rural and undeveloped regions. This results in inadequate reporting and incomplete data about the actual extent of the condition. Enhancing monitoring and reporting systems in these places is essential for acquiring a more precise understanding of monkeypox epidemiology[32]. Moreover, the extent to which the virus might spread to other areas, particularly those with favorable weather conditions and vulnerable people, remains incompletely comprehended. Given the dynamic global climatic and socioeconomic settings, it is essential to perform studies in order to evaluate the likelihood of monkeypox establishing itself in countries outside of Africa. Comprehensive surveillance and prognostic modeling are necessary to assess the probability of the virus spreading to new regions and to formulate measures for prevention and management.

Modern Developments in Monkeypox Research

New insights on the etiology, transmission patterns, and clinical symptoms of the virus have greatly increased our knowledge of monkeypox according to recent studies. Studies have shown atypical presentations that complicate diagnosis include vaginal lesions and odd rashes. More complex tests for MPXV have also been developed, hence improving diagnosis capacity especially in resource-limited environments[33]. Research is also looking at antiviral medicines and new vaccination formulations especially aiming at monkeypox. Targeted treatments especially meant for the prevention and treatment of monkeypox are still much needed even with current antivirals and vaccinations available. Better control of the virus's dissemination depends on these developments.

Gaps in Current Research

Research on monkeypox still lags greatly despite recent developments. One major area of uncertainty is the long-term immunity provided by smallpox vaccinations. Although cross-protection against monkeypox is well-documented, especially in communities inoculated decades ago, the length and strength of this immunity over time call for further research. Furthermore, additional research is needed on the part subclinical or asymptomatic infections play in spreading monkeypox. Developing sensible public health policies and epidemic control plans depends on knowing if asymptomatic carriers may transmit the virus. On the social and behavioral elements affecting monkeypox transmission, further investigation is also required. These covers realizing the elements causing vaccination hesitancy and resistance in impacted groups as well as knowing how cultural activities like hunting and eating bushmeat raise the danger of zoonotic transmission. Improving preventative and control strategies for monkeypox depends on filling up these gaps[34].

Public Health Implications and Future Research

Strengthening Public Health Infrastructure: The resurgence of monkeypox, particularly in regions with inadequate healthcare resources, underscores the need for improved public health infrastructure. This includes enhancing the availability of healthcare services, fortifying surveillance and reporting systems, and ensuring that vulnerable populations have convenient access to immunizations and treatments[29]. International collaboration is essential for effectively addressing the global threat of monkeypox. This includes the exchange of data and resources, coordination of epidemic response, and provision of funds for research programs focused on developing new vaccines, treatments, and diagnostic equipment.

P**rospective Future Research Directions against Monkeypox virus:** In order to successfully combat the persistent menace of monkeypox, future research should give utmost importance to many crucial domains. Longitudinal studies are crucial for assessing the long-term efficacy of smallpox vaccinations in preventing monkeypox, especially across

heterogeneous populations with different age groups, health conditions, and immunization backgrounds. This study aims to get a thorough understanding of the length and effectiveness of immunity that is generated by vaccines. Furthermore, it is essential to closely monitor the genetic development of the monkeypox virus to evaluate its capacity to acquire resistance to existing therapies and vaccinations. Gaining a comprehensive understanding of these genetic alterations will aid in maintaining the ongoing effectiveness of current treatments and enable adjustments to be made in response to newly developing variations[34].

Monkeypox transmission is greatly influenced by ecological and environmental variables. Research should examine the effects of urbanization, deforestation, and climate change on the distribution of animal reservoirs and the resulting danger of zoonotic spillover. Acquiring this information is crucial for predicting and reducing the impact of future epidemics, especially in areas experiencing significant environmental changes[33]. Moreover, it is crucial to tackle the social and behavioral variables that contribute to the transmission of monkeypox. The research should prioritize the investigation of cultural behaviors that contribute to the heightened risk of transmission, as well as the identification of the underlying causes of vaccination hesitation and resistance. Customizing public health interventions based on these variables may efficiently decrease transmission, particularly in regions with little healthcare infrastructure.

The reemergence of monkeypox in both areas where the disease is regularly seen and areas where it is not often found highlights the need of thorough public health measures, which should include educating the public, implementing vaccination campaigns, and fostering worldwide cooperation. Continued study should prioritize investigating the long-lasting nature of protection provided by vaccines, the effectiveness of antiviral therapies, and the impact of environmental variables on the spread of the virus. It is essential to prioritize the development of quick diagnostic tests and the investigation of alternate treatment approaches to effectively manage and prevent future outbreaks of monkeypox[34]. This will ensure that public health systems are well-prepared to handle the changing problems associated with monkeypox.

Limitations of the Study

A number of limitations impede this research, one of which is the lack of thorough data from non-endemic areas, which limits a complete comprehension of the dynamics of the virus's worldwide propagation. In addition, a major gap in the research that affects public health planning is the lack of longitudinal studies on the long-term effectiveness of smallpox vaccinations in preventing monkeypox. The continuous evolution of MPXV poses challenges in maintaining the relevance of current findings, necessitating ongoing research. Furthermore, the study's findings may have limited relevance in low-income regions due to financial limitations, particularly in terms of vaccination and treatment availability. The investigation of environmental and behavioral elements that affect the transmission of the virus is made difficult by the lack of localized data, which might affect the overall comprehensiveness of the research.

Conclusions

Human monkeypox is an emerging infectious disease with the potential for significant public health impact. Along with growing human-animal contacts and globalization, the drop in smallpox immunity has resulted in a comeback of the virus in both endemic and non-endemic areas. Good control of monkeypox epidemics calls for a multimodal strategy comprising public education, early identification, and immunization. Still, there are significant information gaps, especially about the long-term protection smallpox vaccinations provide, the function of subclinical infections, and the environmental elements affecting viral dissemination. Reducing the effect of monkeypox and stopping further outbreaks will depend on closing these gaps by focused study and worldwide cooperation. Public health officials can create more successful plans to stop the virus from spreading and safeguard sensitive people by strengthening on the present knowledge of monkeypox and filling in the noted research gaps.

Acknowledgements
None

Conflict of Interest
There are no any potential conflicts of interest.

Financial Disclosure
The author(s) received no specific funding for this work.

Authors' contributions
Hasan MR, Yusuf MA Concept, literature search, manuscript writings, manuscript revision. Rogers WT, Egbury G, Muna MA manuscript revision. All authors read and approved the final manuscript.

Data Availability
Any inquiries regarding supporting data availability of this study should be directed to the corresponding author and are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate
Not Applicable

How to cite this article: Hasan MR, Yusuf MA, Rogers WT, Egbury G, Muna MA. Global Patterns and Emerging Challenges of Human Monkeypox Virus: An In-Depth Narrative Review and Analysis. Bangladesh J Med Microbiol, 2024;18(2):120-130

ORCID
Md. Rakibul Hasan: https://orcid.org/0000-0002-9152-8753
Md. Abdullah Yusuf: https://orcid.org/0000-0002-8551-7185
Whitney T. Rogers: https://orcid.org/0009-0004-6592-6450
Gerald Egbury: https://orcid.org/0000-0003-2516-6114
Moryom Akter Muna: https://orcid.org/0009-0006-2027-7543

Article Info
Received: 7 February 2024
Accepted: 2 March 2024
Published: 1 July 2024

References

1. Adnan N, ul Haq Z, Malik A, Mehmood A, Ishaq U, Faraz M, et al. Human monkeypox virus: An updated review. 2022;101(35): e30406.
2. Sklenovská N, Van Ranst M. Emergence of monkeypox as the most important orthopoxvirus infection in humans. 2018;6:383729.
3. Rizk JG, Lippi G, Henry BM, Forthal DN, Rizk Y. Prevention and treatment of monkeypox. 2022;82(9):957–63.
4. Ježek Z, Szczeniowski M, Paluku KM, Mutombo M. Human monkeypox: clinical features of 282 patients. 1987;156(2):293–8.
5. Chakraborty S, Mohapatra RK, Chandran D, Alagawany M, Sv P, Islam MA, et al. Monkeypox vaccines and vaccination strategies: Current knowledge and advances. An update–Correspondence. 2022;105:106869.
6. Breman JG. Monkeypox: an emerging infection for humans? 2000;45–67.
7. Poland GA, Kennedy RB, Tosh PK. Prevention of monkeypox with vaccines: a rapid review. 2022;22(12):e349–58.
8. Ellis CK, Carroll DS, Lash RR, Peterson AT, Damon IK, Malekani J, et al. Ecology and geography of human monkeypox case occurrences across Africa. 2012;48(2):335–47.
9. Shchelkunova GA, Shchelkunov SN. Smallpox, monkeypox and other human orthopoxvirus infections. 2022;15(1):103.
10. Alakunle E, Kolawole D, Diaz-Canova D, Alele F, Adegboye O, Moens U, et al. A comprehensive review of monkeypox virus and mpox characteristics. 2024;14:1360586.
11. Subissi L, Stefanelli P, Rezza G. Human mpox: global trends, molecular epidemiology and options for vaccination. 2024;118(1):25–32.
12. Wei H, Huang D, Fortman J, Wang R, Shao L, Chen ZW. Coadministration of cidofovir and smallpox vaccine reduced vaccination side effects but interfered with vaccine-elicited immune responses and immunity to monkeypox. 2009;83(2):1115–25.
13. Petersen E, Zumla A, Hui DS, Blumberg L, Valdoleiros SR, Amao L, et al. Vaccination for monkeypox prevention in persons with high-risk sexual behaviours to control on-going outbreak of monkeypox virus clade 3. 2022;122:569–71.
14. Hasan MR, Yusuf MA. Microbial Dysbiosis in Diabetic Children with Enteric Hepatitis: The Global Phenomenon and Bangladesh's Contextual Significance. 2023;10(2):56–8.
15. Martín-Delgado MC, Sánchez FJM, Martínez-Sellés M, García JMM, Guillén SM, Rodríguez-Artalejo F, et al. Monkeypox in humans: a new outbreak. 2022;35(6):509.
16. Huang Y, Mu L, Wang W. Monkeypox: epidemiology, pathogenesis, treatment and prevention. 2022;7(1):1–22.
17. Nadar S, Khan T, Omri A. Reemergence of monkeypox: prevention and management. 2022;20(11):1425–33.
18. Shafaati M, Zandi M. State-of-the-art on monkeypox virus: an emerging zoonotic disease. 2022;50(6):1425–30.
19. Webb E, Rigby I, Michelen M, Dagens A, Cheng V, Rojek AM, et al. Availability, scope and quality of monkeypox clinical management guidelines globally: a systematic review. 2022;7(8): e009838.
20. Rallapalli S, Razai MS, Majeed A, Drysdale SB. Diagnosis and management of monkeypox in primary care. 2022;115(10):384–9.
21. Ihekweazu C, Yinka-Ogunleye A, Lule S, Ibrahim A. Importance of epidemiological research of monkeypox: is incidence increasing? 2020;18(5):389–92.
22. Kmiec D, Kirchhoff F. Monkeypox: a new threat? 2022;23(14):7866.
23. Baraniuk C. Mpox: two years on. 2024;386.
24. Gruber MF. Current status of monkeypox vaccines. 2022;7(1):94.
25. Bunge EM, Hoet B, Chen L, Lienert F, Weidenthaler H, Baer LR, et al. The changing epidemiology of human monkeypox—A potential threat? A systematic review. 2022;16(2):e0010141.
26. Patel A, Bilinska J, Tam JC, Fontoura DDS, Mason CY, Daunt A, et al. Clinical features and novel presentations of human monkeypox in a central London centre during the 2022 outbreak: descriptive case series. 2022;378.
27. Abdelaal A, Reda A, Lashin BI, Katamesh BE, Brakat AM, Al-Manaseer BM, et al. Preventing the next pandemic: is live vaccine efficacious against monkeypox, or is there a need for killed virus and mRNA vaccines? 2022;10(9):1419.
28. Farasani A. Monkeypox virus: Future role in Human population. 2022;15(11):1270–5.
29. Thornhill JP, Barkati S, Walmsley S, Rockstroh J, Antinori A, Harrison LB, et al. Monkeypox virus infection in humans across 16 countries—April–June 2022. 2022;387(8):679–91.
30. El Eid R, Allaw F, Haddad SF, Kanj SS. Human monkeypox: A review of the literature. 2022;18(9):e1010768.
31. Billioux BJ, Mbaya OT, Sejvar J, Nath A. Neurologic complications of smallpox and monkeypox: a review. 2022;79(11): 1180–6.
32. Gong Q, Wang C, Chuai X, Chiu S. Monkeypox virus: a re-emergent threat to humans. 2022;37(4):477–82.
33. Elsayed S, Bondy L, Hanage WP. Monkeypox virus infections in humans. 2022;35(4):e00092-22.
34. Petersen E, Kantele A, Koopmans M, Asogun D, Yinka-Ogunleye A, Ihekweazu C, et al. Human monkeypox: epidemiologic and clinical characteristics, diagnosis, and prevention. 2019;33(4):1027–43.