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Review Article

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An overview of monkeypox: let's be aware of the emerging yet underreported disease

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Abstract

***Background & Aims*:** A lot is being heard regarding monkeypox, which is currently an emerging disease. The sole purpose of this publication is to enlighten the world regarding epidemiology in the context of recent outbreaks, etiopathogenesis, clinical features, diagnosis, and management, depicting an overview of this underreported disease so that the concerned microbiologists and clinicians can diagnose and manage the disease as soon as possible.

Materials & Methods: In this review study, we searched Google Scholar, PubMed, and Scopus databases to keywords regarding the main objective of the study, and collected the most recent and novel studies less than 10 years about the objectives of the study.

Results: Recent outbreaks, etiopathogenesis, clinical features, diagnosis, and management, depicting Monkeypox were collected and categorized to highlight the importance of the disease in recent communities.

Conclusion: Although and underreported disease, Monkeypox is a disease with important effects in today's societies, and it is needed that health officials be aware of its importance and have programs to control it. With improved knowledge, monitoring of the exposed cases, and better infrastructure, we can successfully contain this emerging and potentially re-emerging viral disease.

***Keywords*:** Monkeypox, Mpox, Pox-Like Disease, Virus, Zoonotic

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Introduction

First discovered in 1958, the monkeypox disease is currently in the news due to the recent surge in the number of cases in various parts of the world. It is a pox-like disease caused by the Mpox (monkeypox) virus. It was named monkeypox because of the occurrence of initial outbreaks in colonies of monkeys kept for research purposes (1). The disease is usually self-limiting with low mortality ranging from 0 to 10%. It is characterized by fever, rash, and lymphadenopathy. Molecular methods are the diagnostics of choice in such cases. The recent increase in the number of cases caused by monkeypox is explained by the fact that due to the eradication of smallpox, vaccination against it (smallpox) has also come to a halt, rendering people susceptible to such infections (2). The present study

focuses on epidemiology in the context of recent outbreaks, etiopathogenesis, clinical features, diagnosis, and management, depicting an overview of this underreported disease so that the concerned clinicians and microbiologists can diagnose and manage the disease as soon as possible.

Epidemiology and Recent Outbreaks:

The zoonotic disease 'monkeypox' was first reported in humans in the year 1970 in the Democratic Republic of the Congo (3). The Mpox virus has two distinct genetic clades: the central African (Congo Basin) clade and the West African clade. The Congo Basin clade is known to cause more severe diseases and is said to be more transmissible. Cameroon is known to be the only country where both viral clades have been found in humans (4). The natural animal hosts include squirrels, rodents, and non-human primates. It is still not known how the virus circulates in nature, and it needs to be further explored by enthusiastic researchers. The incubation period ranges between 5 and 13 days. Recently, the case fatality ratio has been approximately 3-6% (4). In the 1970s, the patients were primarily young children, but in recent years, it has been found that confirmed patients are predominantly young adults (5). The virus is known to cause several outbreaks, especially in Central and West Africa. The first monkeypox outbreak outside of Africa occurred in the year 2003 in the USA (the United States of America) and was linked to contact with infected pet prairie dogs (4). In the year 2017, Nigeria experienced a large outbreak with 60 confirmed cases and 228 suspected cases (though between 1970 and 2017, only 3 cases were reported), leading to the re-emergence of the disease (6). Many cases have been reported from non-endemic countries in recent years, posing a global challenge. Between 2010 and 2019, Israel, Singapore, and the United Kingdom reported 1, 1, and 4 outbreaks, respectively. In the year 2020-21, the United States reported 2 outbreaks of monkeypox (7). India reported a monkeypox outbreak in 2022, with confirmed cases from Kerala and Delhi. In July 2022, WHO declared it a public Health Emergency of International Concern (PHEIC) (8). Looking back at the timeline 2017 to 2022, it can be inferred that the virus is continuing to evolve through point mutation in the genes, and hence the world needs to be prepared for the outbreaks possible in the future (9).

Etiopathogenesis:

Mpox virus (enveloped, double-stranded DNA virus), the etiological agent of monkeypox disease, belongs to the genus *Orthopoxvirus* in the family *Poxviridae*. Humans acquire the disease after being in close contact with infected animals or humans. The disease can also be transmitted through contact with lesions, respiratory droplets, body fluids, or contaminated materials such as bedding (4). Innate and acquired immunity plays a crucial role in the containment of the disease. The innate immune response is quicker but non-specific. Type 1 interferons, chemokines, pro-inflammatory cytokines, and other antiviral proteins constitute the first line of host defense. Pathogen-associated molecular patterns (PAMPs) that work through a diverse recognition system named pattern recognition receptors (PRRs) also play an important role in the innate immune response against monkeypox. Cellular immunity is mediated by cytolytic immune cells such as cytotoxic T lymphocytes (CTLs) and natural killer (NK) cells that play an important role in the rapid identification and clearance of virus-infected cells (5). Evasion of antiviral CD4+ and CD8+ T cells occurs by monkeypox virus through MHC Class II downregulation and consequent suppression of T cell activation (5,10). Entry of the Poxviruses into the host cell may occur in three steps: virus attachment (with the help of glycosaminoglycans), binding to the membrane and fusion with the host cell, and core entry, which occurs at the cell membrane or following endocytosis. Once released into the cell's cytoplasm, enzymes and factors present in the virion core initiate transcription. DNA-dependent RNA polymerase plays an important role in viral transcription. This process is followed by the host ribosome-mediated translation of proteins (11). The replication of the monkeypox virus occurs in the cytoplasm of the host cell (unlike other DNA viruses).

Clinical Features:

The clinical features are said to be similar to smallpox with less severity. In suspected cases of travel history and history of sexual/ close contact with a patient having skin lesions should always be inquired about (7). The patient initially develops a fever, headache, myalgia, and lymphadenopathy (develops at the onset of fever). Rash/skin lesions usually develop within 1-3 days of fever and involve various sites such as the face, palm, soles, around the genitals/anus, chest, conjunctiva, or cornea. The rash changes its morphology and evolves through different stages such as macule, papule, vesicles, pustule, and crust formation, dries up and falls off. The duration of infection is between 1 and 4 weeks. The disease is self-limiting but may progress and lead to complications such as secondary bacterial infection, encephalitis, pulmonary distress, conjunctivitis, or pneumonia (5). The severity of the infection and associated complications are more commonly reported in children and immunocompromised patients, though people of all ages have been affected by the disease.

Diagnosis:

The various diagnostic options for the detection of Mpox include polymerase chain reaction (PCR), electron microscopy, serology (anti-Orthopoxvirus IgM and IgG antibodies)/ immunohistochemistry (Orthopoxvirus-specific antigens), and culture. PCR is considered the gold standard test. Other tests can be done if it turns out to be negative and the disease is still suspected based on clinical features (2). Mpox viral PCR testing specimens include swabs of persistent lesions or lesion fluid, upper respiratory tract swabs, EDTA (Ethylenediaminetetraacetic Acid) blood samples, urine samples, etc. (12). It is suggested to take specimens from two separate lesions in the body and then store them in a dry, sterile tube under cold conditions (4,7). If PCR test results are positive, contact tracing, testing, and vaccination of individuals at-risk are recommended (2). As per Centers for Disease Control and Prevention (CDC) case definitions (2022), a confirmed case is one in which monkeypox virus DNA is detected by PCR or next-generation sequencing of a clinical specimen or isolation of Mpox virus in culture from a clinical specimen (13). Serology can be helpful in epidemiological investigations, though it has limitations, such as cross-reactions occurring in persons previously vaccinated with the smallpox vaccine. Characterization of Mpox strains can be done with the help of cell culture technique, but it requires accredited biosafety level 3 reference laboratory facilities (7).

Management:

Smallpox vaccine can also prevent monkeypox with clinical effectiveness of up to 85%, as evidenced by various published literature (3). Second and third-generation (not first-generation due to lack of safety) smallpox vaccines, such as the modified vaccinia Ankara (MVA) vaccine (JYNNEOS) and ACAM2000, can be useful in the prevention of monkeypox. ACAM2000 is a 2nd generation live-attenuated vaccine that is replication-competent. JYNNEOS is a 3rd generation, highly attenuated vaccine that is replication-deficient and safer to use even in immunocompromised patients compared to ACAM2000 (3). As the disease can be transmitted from one person to another, educating the masses and monitoring the exposed persons can be extremely helpful in preventing disease outbreaks (14). The use of personal protective equipment and isolation of the cases are other important measures that must be taken care of. It has been noticed that even after the resolution of skin lesions, prolonged shedding of viral DNA occurs from the upper respiratory tract posing a great challenge in its control (12). Treatment is symptomatic, with most cases being managed by using antipyretics and antiviral drugs. Perzia et al. reported a case of ocular monkeypox in an HIV-positive patient successfully managed by moxifloxacin and 1% trifluridine drops along with oral tecovirimat (15). The authors suggested clinicians raise suspicion of the disease when they examine patients with ocular features (conjunctivitis, eyelid lesions) along with skin lesions and use eye protection in such cases.

Conclusion

Awareness regarding the Mpox is important to prepare ourselves and our future generations for any

outbreak situation before it becomes uncontrollable. With improved knowledge, monitoring of the exposed cases, and better infrastructure, we can successfully contain this emerging and potentially re-emerging viral disease.

Highlights of the Present Study

- The present article covers the epidemiology in the context of recent outbreaks, etiopathogenesis, clinical features, diagnosis, and management, depicting an overview of Mpox.
- PCR is considered the gold standard test for the detection of Mpox. Other diagnostic options include electron microscopy, serology/ immunohistochemistry, and culture.
- Mass education and monitoring the exposed persons can be extremely helpful in preventing disease outbreaks.

Authors' contributions

UH designed the initial study, conducted the research, collected, and organized the data. KP proofread and finalized the manuscript. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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Ethical approval

Not applicable.

Conflicts of interest

The authors have no conflict of interest in this study.

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