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Monkeypox Virus: Current Status And Global Health Ipmlications

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Abstract: Monkeypox virus (MPOV), formerly known as MPOX, is a zoonotic disease agent belonging to the Orthopoxvirus family.. First discovered in monkeys in 1970, the virus was later detected in humans and became endemic in Central and West African countries. In 2022, MPOV turned into a global pandemic and was declared a Public Health Emergency of International Concern by the World Health Organisation. This review article comprehensively examines the current status of MPOV, its transmission routes, prevention strategies and implications for global health. The study highlights areas for future research and emphasizes the importance of global collaboration against this emerging health threat. With the aim of raising awareness about MPOV, supporting informed decision-making and developing intervention strategies to reduce transmission, this review aims to contribute to efforts to protect public health.

Maymun Çiçeği Virüsü: Güncel Durum ve Küresel Sağlık Etkileri

Anahtar kelimeler:
Maymun çiçeği virüsü (MPOV),
Zoonotik hastalık,
Küresel pandemi,
Halk sağlığı acil durumu,
Kontaminasyon önleme

Özet: Önceden MPOX olarak bilinen Maymun çiçeği virüsü (MPOV), Ortopoksvirüs ailesine ait zoonotik bir hastalık etkenidir. İlk olarak 1970 yılında maymunlarda keşfedilen virüs daha sonra insanlarda tespit edildi ve Orta ve Batı Afrika ülkelerinde endemik hale geldi. 2022 yılında MPOV küresel bir pandemiye dönüştü ve Dünya Sağlık Örgütü tarafından Uluslararası Endişe Verici Halk Sağlığı Acil Durumu ilan edildi. Bu derleme makalesi, MPOV'un mevcut durumunu, bulaşma yollarını, önleme stratejilerini ve küresel sağlık üzerindeki etkilerini kapsamlı bir şekilde incelemektedir. Çalışma, gelecekteki araştırma alanlarını vurgulamakta ve bu ortaya çıkan sağlık tehdidine karşı küresel iş birliğinin önemini vurgulamaktadır. MPOV hakkında farkındalığı artırma, bilinçli karar vermeyi destekleme ve bulaşmayı azaltmak için müdahale stratejileri geliştirme amacıyla bu derleme, halk sağlığını koruma çabalarına katkıda bulunmayı amaçlamaktadır.

1. INTRODUCTION

Monkeypox virüs (MPOV) is a zoonotic disease caused by a virus in the Orthopoxvirus family. The disease was first discovered in monkeys in 1970 in countries where cases of monkeypox were monitored, hence the name [1]. The virus was later found in humans and has since become endemic in Central and West African countries. Monkeypox virus can cause significant morbidity and mortality in humans and there is currently no specific treatment [2]. In 2022, monkeypox became a global epidemic when a large number of cases were reported in several countries where the disease had previously been rare or absent. The World Health Organisation declared monkeypox a Public Health Emergency of International Concern as it continued to spread rapidly around the world and public health measures failed to prevent it [3].

It is important to provide a comprehensive overview of MPOV to raise awareness and inform informed decision-making and intervention strategies to reduce transmission and protect public health. In this study, we examined the current status of monkeypox virus, transmission routes, prevention strategies, and global health impacts. Potential areas for future research and the importance of global collaboration to counter this emerging health threat are highlighted.

1.1. History and First Cases of Monkeypox Virus

Monkeypox virus was first discovered in laboratory monkeys at a research center in Copenhagen in 1958, but the first case in humans was detected in 1970 in a 9-year-old boy in the Democratic Republic of Congo (then Zaire) [4]. After this discovery, sporadic cases were reported in Central and West Africa throughout the 1970s. In the 1980s, the incidence of the disease increased and in 2003, the United States experienced an outbreak outside the African continent for the first time [1] and may have arisen as a result of transmission from infected prairie dogs to humans [5].

The geographical distribution and sociocultural implications of monkeypox virus form an important complement to understanding the global health impact of the disease. The virus has historically been endemic in the rainforest regions of Central and West Africa, but has become particularly widespread in the Democratic Republic of Congo, Nigeria and Cameroon [6]. Due to globalization and increased international travel, in recent years, cases have also been seen in Europe, North America and Asia [7]. Thus, geographical spread has also affected the approach of different cultures to the disease. For example, in some African societies, traditional medical practices and the consumption of wild animal meat (bushmeat) play a role in the spread of the disease, while in Western societies the disease is generally perceived as an exotic threat [8]. Misperceptions due to the name of the disease and the conditions under which it was first discovered (in laboratory monkeys) have led to some discriminatory attitudes such as stigmatization in some societies [9].

Over time, with the increase in travel and trade, monkeypox cases have started to be seen in different parts of the world. The patterns of spread of MPOV in different geographical regions reflect the complex interactions between the ecology of the virus, human behaviour and global health systems. These patterns can be summarised as follows:

1.2. Endemic Regions in Africa

MPOV was first detected in the Democratic Republic of Congo (DRC) in 1970 and remained endemic in Central and West Africa for many years [10]. Regular outbreaks have been observed in DRC, Congo Basin and Nigeria. In these regions, the virus is usually spread through zoonotic transmission and is more prevalent in rural areas [11].

1.3. West African Strain and Congo Basin Strain

MPOV has two main genetic clades: West African (WA) and Congo Basin (CB) strains. The CB strain is considered more virulent and infectious [12]. While the WA strain is usually seen in West African countries, the CB strain is more common in Central Africa.

1.4. First Outbreaks Outside Africa

The 2003 outbreak in the USA showed that the virus could spread outside Africa. This outbreak was associated with infected rodents imported from Ghana [5].

1.5. 2022 Global Pandemic

The 2022 pandemic, which started in 2022 and spread rapidly, represents a significant change in the spread patterns of the virus. In this outbreak, the virus emerged simultaneously in many countries, especially in previously non-endemic regions [7].

a) Europe: Cases were seen in many European countries, especially in the UK, Spain, Portugal and Germany [13].
b) North America: A significant number of cases have been reported in the USA and Canada [14].
c) Latin America: Cases have also been detected in countries such as Mexico and Argentina, [15].
d) Asia and Oceania: The number of cases has been relatively low in these regions, but cases have also been reported in countries such as Japan, Australia and New Zealand [16].

1.6. New Propagation Dynamics

In the 2022 outbreak, the spread of the virus occurred mostly through human-to-human transmission. High transmission rates were observed especially in the men who have sex with men (MSM) community [15].

1.7. Global Mobility and Spread

International travel and migration have been effective in the rapid spread of the virus to new regions [6].

1.8. Spread in Urban Areas

Unlike previous outbreaks, the virus was more prevalent in urban areas in the 2022 outbreak [17].

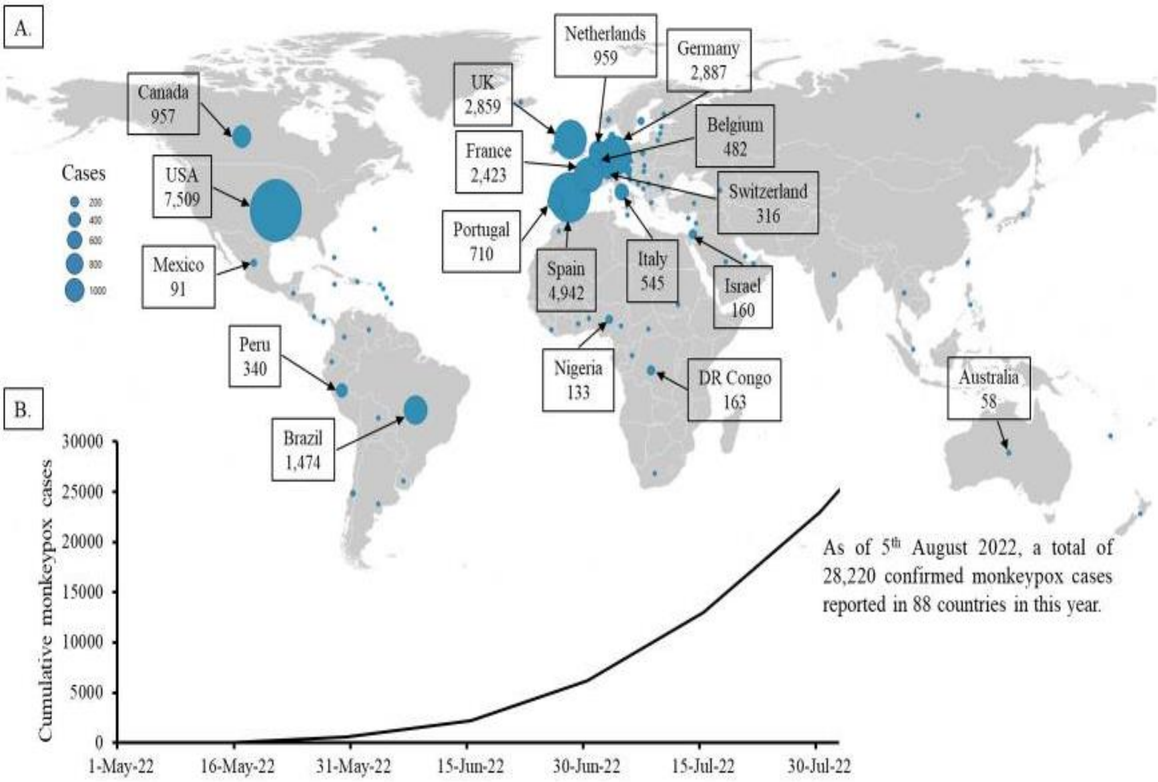

Figure 1. Current global monkeypox (MPOV) infection patterns as of August 5, 2022 [16].

2. BİOLOGİCAL STRUCTURE AND TRANSMİSSİON ROUTES OF MONKEYPOX VİRUS

MPOV is an enveloped DNA virus belonging to the genus Orthopoxvirus of the family Poxviridae. Its genetic structure includes a double-stranded DNA genome of approximately 197 kb in length, characterised by inverted repeat sequences at the ends [18]. The MPOV genome contains approximately 190 protein-coding genes and these genes encode structural proteins, enzymes and immune modulators of the virus [19].

The protein components of the virus are structurally and functionally diverse. Chore proteins package the DNA genome and form the nucleoprotein complex. Membrane proteins are located in the envelope of the virus and play a role in binding to cell receptors. In addition, enzymes encoded by the virus (e.g. DNA polymerase, RNA polymerase) are critical in the replication process [20]. The central core consists of core fibril and viral double-stranded DNA (dsDNA) and is surrounded by the palisade layer, a tightly arranged rod-shaped structure [21](Figure 2).

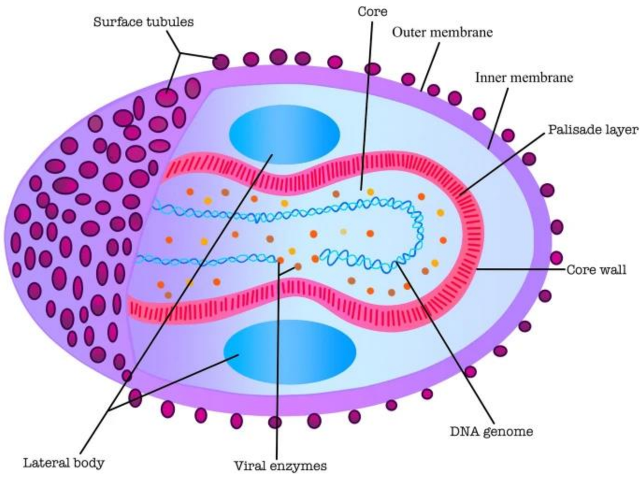

Figure 2. Structure of MPOV [21]

The replication mechanism of MPOV, similar to other poxviruses, occurs entirely in the cytoplasm. This process includes the following steps [22]:

1. Entry of the virus into the cell: This occurs via membrane fusion or endocytosis.
2. Early gene expression: Partial unfolding of viral DNA and transcription of early genes.
3. DNA replication: Replication of viral DNA is carried out by virus-encoded DNA polymerase.
4. Middle and late gene expression: Synthesis of structural proteins and enzymes.
5. Virion assembly and maturation: Formation of new virus particles and their release from the cell.

It covers virus identification, isolation and laboratory diagnostic methods. Identification and isolation of MPOV is usually done with samples taken from lesions. These samples are collected in viral transport medium and processed in biosafety level 3 (BSL-3) laboratories [23].

Virus isolation is performed in cell culture using Vero E6 or BSC-40 cell lines [24]. Laboratory diagnostic methods include polymerase chain reaction (PCR), real-time PCR (RT-PCR), electron microscopy and immunohistochemistry [25]. PCR, especially RT-PCR, is the preferred method due to its high sensitivity and specificity and targets specific gene regions of the virus [26]. Serological tests, especially ELISA and Western blot, are used to detect previous infections, but should be interpreted with caution due to cross-reactivity [27]. Next-generation sequencing technologies are increasingly used for genomic characterisation of the virus and outbreak monitoring [28]. These methods enable rapid and accurate diagnosis of monkeypox infections, which is critical for disease control and management.

When the epidemiological characteristics, transmission routes, host range and spread dynamics of the virus are considered, a complex picture emerges. The routes of transmission of MPOV are diverse: Direct contact with infected animals, close physical contact with infected persons, and contact with contaminated objects are among the main routes [29]. The virus can be transmitted through respiratory droplets, body fluids and material from lesions. Sexual contact has also been identified as an important route of transmission, especially in the global outbreak in 2022 [15]. In terms of host range, MPOV can infect a wide range of mammalian species. The natural reservoir host is thought to be rodents, but primates, squirrels and other small mammals can also be infected [30]. Humans are considered intermediate hosts and are usually infected through contact with infected animals. However, human-to-human transmission is also possible and this type of transmission has come to the fore in recent outbreaks [6]. In terms of spread dynamics, the R_0 value (basic reproduction number) of MPOV is generally estimated to be below 1, indicating that continuous human-human transmission is limited [31]. However, in certain populations and conditions, this value may be higher. For example, in the 2022 outbreak, higher transmission rates were observed within some communities [32]. In terms of geographical distribution, MPOV has historically been endemic in Central and West Africa, but in recent years, cases have been observed in other continents [33]. Factors such as globalization, travel and climate change cause the virus to spread to new regions [34]. In addition, factors such as human behaviour, social networks and the response capacity of health systems also affect the dynamics of spread. Epidemiological surveillance, contact tracing and early warning systems are critical to control the spread of MPOV [35]. In conclusion, the epidemiology of MPOV reflects complex interactions between the ecology of the virus, human behaviour and global health systems, and a holistic understanding of these factors is required to develop effective control strategies.

3. CLİNİCAL SYMPTOMS İN MONKEYPOX CASES

Monkeypox infection usually presents a clinical picture with two distinct stages: the prodromal period and the rash period. The prodromal period follows an incubation period lasting an average of 6-13 days (sometimes 5-21 days) after contact with the virus [24]. During this initial phase, patients typically experience high fever, severe headache, lymphadenopathy (swelling of the lymph nodes), back pain, myalgia (muscle aches) and intense weakness [15]. Lymphadenopathy is an important feature that distinguishes monkeypox from smallpox [36].

The lesions seen in monkeypox infection are remarkable for their characteristic features. They are typically hard or rubbery, well circumscribed and deep-seated. They often develop a punctate structure at the apex of the lesions, which is called an umbilication. The evolution of the lesions occurs in four stages: macular, papular, vesicular and pustular, followed by crusting and shedding. The current global outbreak has revealed some variation in the clinical presentation of monkeypox infection. Lesions are frequently seen on the genital and anorectal areas or in the mouth. Contrary to the classical description, the rash does not always spread to many parts of the body, sometimes limited to only a few lesions or a single lesion. In addition, the appearance of a rash on the palms of the hands and soles of the feet is not observed in all cases in this outbreak [37] (Figure 3).

Figure 3. Mpox Rash [37]

Despite this variable presentation, the development of the lesions usually follows a similar pattern. The lesions start as a maculopapular rash and rapidly progress to vesicular and pustular stages, finally culminating in crusting and shedding [29]. A patient may have lesions in different stages at the same time. The number of lesions may vary from a few to thousands [38]. The clinical course usually lasts 3-4 weeks and most cases heal spontaneously. However, a more severe course may be seen in immunocompromised individuals, young children and pregnant women [6]. In severe cases, skin lesions may coalesce and cover large areas, leading to peeling of the skin [24]. Rare but serious complications include secondary bacterial infections, sepsis, pneumonia, encephalitis and vision loss, especially due to corneal infection [39]. In recent outbreaks, atypical presentations have also been reported, especially in patients infected with the strain of West African origin. These include localised lesions without prodromal symptoms, a single lesion in the anogenital region and oral/perineal lesions suggestive of secondary sexual transmission [40].

The lesions are usually described as painful until the healing phase, when they become itchy [41]. Although fever and other prodromal symptoms (e.g. chills, lymphadenopathy, malaise, myalgia or headache) classically precede the rash, in this outbreak they may also occur after the rash or not at all [42,43].

4. EPİDEMİOLOGİCAL SURVEİLLANCE AND CONTROL STRATEGİES

Epidemiological surveillance and control strategies for MPOV encompass various methods used to monitor, prevent and control the spread of the disease. These strategies can be analysed under the following main headings:

4.1. Epidemiological Surveillance: a) Case Definition and Notification: Using standardized case definitions, suspected, probable and definite cases are rapidly identified and notified [44]. b) Active Surveillance: Active case searches are carried out through health institutions and community-based surveillance systems [45]. c) Laboratory Surveillance: Verification of cases and monitoring of virus strains are ensured by using methods such as PCR tests and genomic sequencing [46]. d) Animal Reservoir Surveillance: Monitoring of potential animal reservoirs and assessment of zoonotic transmission risks [30].

4.2. Control Strategies: a) Case Isolation: Rapid isolation of detected cases and provision of appropriate medical care [47]. b) Contact Tracing: Identifying and monitoring the contacts of the cases and quarantining them when necessary [48]. c) Vaccination: Vaccination of high-risk groups and post-contact cases (e.g. smallpox vaccine or newly developed MPOV vaccines) [49]. d) Risk Communication and Community Engagement: Raising public awareness, informing the public about risk factors and encouraging preventive behaviors [50]. e) Border Controls: Screening and informing international travellers [51].

4.3. Epidemic Management: a) Early Warning Systems: Analysing and interpreting surveillance data for early detection of potential outbreaks [51]. b) Outbreak Response Teams: Formation and deployment of trained teams for rapid response [52]. c) Mobilization of Resources: Rapid mobilization of necessary medical equipment, personnel and financial resources in case of an outbreak [53].

4.4. International Cooperation: a) Data Sharing: Sharing surveillance data between countries and international organizations [7]. b) Capacity Building: Strengthening surveillance and control capacity in low- and middle-income countries [2]. c) Research Collaborations: Coordination of vaccine and antiviral drug development studies [54].

4.5. Technological Innovations: a) Digital Surveillance Tools: Use of mobile applications and artificial intelligence-supported systems [55]. b) Genomic Surveillance: Monitoring virus evolution through the use of next-generation sequencing technologies [56].

Effective implementation of these strategies is critical for early detection, rapid response and effective control of MPOV outbreaks.

5. EVOLUTİONARY BİOLOGY OF MPOV

The origin of the virus, its evolutionary relationship with other poxviruses and its genetic changes over time reflect a complex evolutionary process. Although the exact origin of MPOV is unknown, molecular clock analyses suggest that the virus emerged approximately 70,000 years ago [57]. MPOV is genetically closely related to smallpox virus (Variola virus) and phylogenetic analyses suggest that these two viruses evolved from a common ancestor approximately 3000-4000 years ago [58]. The relationship of MPOV to other poxviruses shows similarities in terms of genomic structure and gene content. For example, the MPOV genome, like other orthopoxviruses, consists of linear double-stranded DNA containing inverted repeat sequences at the ends and is approximately 200 kb in length [18]. In terms of genetic changes over time, two major genetic clades of MPOV have been identified: West African (WA) and Congo Basin (CB) clades. There are significant genetic differences between these two clades and the CB clade is thought to be more virulent [12]. Recent genomic analyses have shown that the rate of evolution of MPOV may be higher than previously thought. In particular, the strains seen in the 2022 pandemic were found to accumulate much more mutations than expected [56]. This rapid evolution may increase the adaptation of the virus to new hosts and potentially increase its infectiousness. Furthermore, its increased circulation in human populations may affect the evolutionary trajectory of the virus and lead to the emergence of new variants [59]. Understanding the evolutionary biology of MPOV is critical for predicting the future behaviour of the virus, developing vaccine and antiviral strategies, and assessing potential zoonotic threats.

6. EFFECTS OF MONKEYPOX VİRUS ON PUBLİC HEALTH AND PUBLİC HEALTH MEASURES

The monkeypox virus outbreak has led to significant social impacts and behavioural changes. Firstly, as with HIV/AIDS virus [60], the faster spread of MPOV among certain groups will increase stigma and discrimination against these groups. Studies of the monkeypox outbreak in 16 countries showed that 98 per cent of cases were gay or bisexual men, 75 per cent of whom were white and 41 per cent were HIV positive [15]. Sexual transmission has emerged as an important route of transmission because lesions are usually seen in the genital and perianal areas and most patients are men who have sex with men [39,61].

However, these data may lead to the association of the disease with certain groups and potentially lead to stigmatization. Jaiswal et al. (2020) highlighted the harmful consequences of labelling the disease as a ‘gay virus’ [62]. This stigmatization can affect not only at-risk groups but also the general population, as people may avoid getting tested or seeking treatment for fear of being stigmatised. Therefore, when presenting and discussing this data, health authorities and the media should use careful language to avoid social stigmatization and make clear that the disease is not limited to any sexual orientation or identity.

The effects of outbreaks can have more devastating effects on vulnerable segments of the population [63]. Without urgent action, they pose a significant risk to immunocompromised groups and families. The health system faces challenges related to diagnosis, treatment and disease prevention during an outbreak. The lives of healthcare workers are at significant risk, especially when the supply chain of healthcare equipment is disrupted [64]. If health workers or their family members become ill, their ability to provide care is also reduced as they will have to look after each other. An outbreak of MPOV could further increase the burden on the health system, which is already facing numerous other problems [65].

Outbreaks of MPOV can lead to lower tax revenues and increased expenditure, causing fiscal stress, especially in low-middle-income countries (LMICs) where fiscal constraints are high and tax systems need to be improved. Therefore, the MPOV outbreak could have short-term fiscal and long-term economic impacts on nations. All efforts to contain the virus will cost a significant amount of resources and will significantly affect the national economy. The productivity of the population is significantly affected, affecting national economies and overall development [65]. In the labour market, there may be productivity losses due to sick or quarantined employees, and increased pressure on health systems may increase the cost of testing and treatment, while the tourism and leisure sectors may also be adversely affected by travel restrictions.

7. CONCLUSİON

MPOV has become a global health threat in recent years and has attracted the attention of the international community. This review comprehensively examined the current status of MPOV, its transmission routes, and its impact on global health. The rapid spread of the virus and the inadequacy of existing public health measures highlight the need for an urgent and coordinated global response.

The following important steps need to be taken to be successful in combating MPOV in the future:

- Research and Development: More resources should be devoted to research to develop effective treatments and vaccines against MPOV. In particular, the focus should be on the development of broad-spectrum antiviral drugs and next-generation vaccines.
- Strengthening Surveillance Systems: Surveillance systems should be improved for early detection and monitoring of MPOV cases globally, especially in high-risk areas.
- International Co-operation: International co-operation should be increased to share information between countries, develop joint research projects and coordinated response strategies.
- Community Education and Awareness: Comprehensive education programmes should be implemented to inform the public about the transmission routes, symptoms and prevention methods of MPOV.
- Strengthening Health Systems: Health systems should be strengthened to diagnose, treat and isolate MPOV cases, especially in resource-limited areas.
- Prevention of Zoonotic Transmission: The risk of zoonotic transmission should be minimised through measures such as reducing human-animal contact and regulating wildlife trade.
- Developing Global Health Security Policies: Global health security policies should be reviewed and strengthened to ensure rapid and effective response to emerging infectious diseases such as MPOV.

To be prepared for similar outbreaks in the future, lessons learnt from the fight against MPOV should be carefully considered and applied.

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