

Monkeypox: Endemic to Epidemic

A review of the current scenario of Monkeypox disease outbreak

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Abstract - The recent outbreak of Monkeypox disease in different parts of the world has drawn attention and concerns of the scientific communities, medicine world and the governments. The world has witnessed what havoc a virus can cause if it jumps from an animal to human beings. Are we moving towards the next pandemic? How safe are the use of animals in medicine and biological research? What will be the consequence of this new zoonotic disease? To avoid another pandemic, it is important that we watch the progress of this disease closely and understand the causes, consequences, treatment, and possible control before it gets out of hands. This article is a compilation of all the information about Monkeypox disease that is available in different domains, to give an overview of the current scenario of the disease.

Index Terms – Monkeypox, virus, MPV, epidemiology of MPV

I. INTRODUCTION

Monkeypox is a viral, zoonotic (transmitted to human from animals), and rare disease that is caused by infection with monkeypox virus (MPV or MPXV) with symptoms close to smallpox but not as severe as smallpox. Monkeypox was first discovered in 1958, when outbreaks of a pox-like disease occurred in monkeys used for research. About a few thousand cases occurred in Africa especially in central and western parts of the African continent [1]. The cases outside Africa were limited to a small number with a travel history of people visiting Africa or with the import of the infected animals.

In 1970, the Democratic Republic of the Congo reported the first human case of monkeypox. Since then, many cases have been reported from various central and west African countries. Most cases are reported from poorest and most marginalised communities in the world [2][3]. Incidents of MPV infections are on a rise since early May 2022. About 19 countries across the world have reported confirmed or suspected cases of monkeypox to the WHO. Since the reports are from different parts of the world, this can no longer be considered endemic to the African region [14].

The cases detected outside the endemic places in the early May 2022 has surpassed the total number detected and this rapid spread has put the scientists worldwide on high alert. There has been a sudden and unexpected occurrence of monkeypox simultaneously in many non-endemic countries, which suggests that there is a possibility of some undetected transmissions for an unknown duration of time followed by recent amplifying events [14].

Epidemiological investigations are going on, however, from the various cases that are reported, so far, no established travel links to endemic areas has been established. Based on currently available information, a unique observation has been established which highlights the possibility of the spread of the disease, mainly but not exclusively, amongst men who have sex with men (MSM) and are seeking primary care in primary clinics or sexual health clinics. A scientific clinical link has yet to be established.

II. WHAT IS MPV?

Monkeypox virus is a double stranded DNA virus which belongs to genus *Orthopox virus* belonging to the Poxviridae family. The *Orthopox virus* genus also includes variola virus responsible for smallpox and cowpox virus. Various animal species have been known to be susceptible to the monkeypox virus. The natural reservoir of monkeypox has been a question of interest from many scientists since its discovery. However, it has been detected from rodents of African region, non-hominids primates such as monkey (hence the name 'Monkeypox'). Further research is needed to know the exact reservoir/s of the virus and the route of its entry into the human population.

III. PATHOGENESIS

Pathogenesis is the progression of an infection which leads to disease. The general viral pathogenicity includes (a) implantation of virus at the portal of entry, (b) viral replication in the host cell [3], spread of viral agent to target organs causing the disease and (c) migration of virus to sites of shedding into the environment.

Factors that affect the pathogenic mechanisms are (a) accessibility of host tissue to the virus (b) host cell susceptibility to virus multiplication, and (c) virus susceptibility to host defences. Low-virulent strains of pathogenic virus strains are favoured by natural selection forces.

In case of monkeypox, infection may begin from the respiratory epithelium or the dermis. The virus further progresses and enters the lymphatic system leading to the swelling of the lymph nodes. Other organs that are susceptible to infected are mucus lining of nose and buccal cavity.

IV. TRANSMISSION OF DISEASE IN HUMAN POPULATION

There are various modes of infection of MPV [6][7]. The virus can spread from an infected person to a healthy person through:

- direct contact with the infection site (i.e., saliva, rashes, scabs, or body fluids of infected person)
- respiratory secretions during extended face-to-face contact, or intimacy during physical contact, such as hugging, kissing or sexual intercourse
- touching infected items (such as clothing or linens)
- placenta, infected pregnant women can spread the virus to their foetus.

Monkeypox infection also spreads among human population by infected animals either by being scratched or bitten by them. Eating infected meat or using products from an infected animal can also cause disease in man.

A person infected from monkeypox can spread the infection from the time of the onset of symptoms start until the rash has fully healed and a fresh layer of skin has formed. This can take several weeks. People without monkeypox symptoms, do not spread the virus to others. The spread of infection through semen or vaginal fluid has not been confirmed [4].

In comparison to smallpox, the fatality rate of monkeypox is relatively low. According to the data obtained by CDC (Centre for Communicable Diseases), the monkeypox has case fatality of less than 4%.

V. COMMON SYMPTOMS

In humans, the monkeypox symptoms are of milder nature as compared to smallpox. It begins with fever, chills, headache, backache, tiredness, swelling of lymph nodes (lymphadenopathy) [4]. The incubation period varies from 7 to 14 days in most of the cases. However, incubation period in some cases may extend from 5-21 days. Monkeypox differs from the smallpox in its severity. Swelling of lymph nodes is also observed in monkeypox infection which is not seen in smallpox.

The infection starts with fever followed by skin eruption within 1–3 days. The patient develops rashes usually on the face in the beginning which later spreads to other parts of the body. It affects the face (in 95% of cases), and palms of the hands and soles of the feet (in 75% of cases). In about 70% of cases, the mucous membrane of mouth, genitalia (30%), conjunctivae (20%) and cornea, are also affected [4].

Macules (lesions with a flat base) are formed in the initial stages of disease, which eventually evolves into rashes. The rash sequentially progresses into papules (slightly raised firm lesions), which are further filled with clear fluid forming vesicles that develops into pustules (lesions filled with yellowish fluid), and crusts which dry up and fall off [15].

Apart from the pox-like symptoms of its own, many secondary complications [3][5] are associated with the monkeypox, including encephalitis, pneumonitis, and bacterial infections.

VI. CHRONOLOGY OF PAST OUTBREAKS

The first case of monkeypox in humans was reported in 1970 from the Democratic Republic of Congo. A nine-year-old boy became infected. Smallpox was eradicated from the Congo region two years before.

Since 1970, most cases of the cases of monkeypox occurred in regions around the Democratic Republic of Congo. The disease was considered endemic to this region, until 2003, when an outbreak of monkeypox was reported in the United States. The giant Gambian rat was determined to be the source of this outbreak, which spread to Indiana, Illinois, and Wisconsin. One case appeared in New Jersey. This outbreak in the United States Midwest was attributed to prairie dogs that had become infected by a Gambian pouch rat that had been imported. This outbreak, however, did not result in any fatalities.

Another outbreak occurred in Unity, Sudan in 2005, followed by another in 2009, again in the Democratic Republic of Congo. In 2016, cases of monkeypox outbreak were reported from the Central African Republic and resulted in 2 deaths out of 26 cases. Later in September 2018, monkeypox was reported in Israel, where the source was traced to travellers from Nigeria. Furthermore, cases were reported from Singapore in May 2019, and from different parts of United Kingdom in September 2018, December 2019, May 2021. Most recently being May 2022.

VII. THE PRESENT SCENARIO: NO MORE CONFINED TO ENDEMIC REGIONS

Since early May 2022 as many as 23 countries have confirmed cases of monkeypox. Czech Republic, United Arab Emirates have become the latest countries to report monkeypox cases to the WHO. Czech Republic saw its first case in a woman coming from a festival in Belgium. As on 4th June 2022, 24 countries have confirmed cases of monkeypox virus (Table 1). The disease is also reported to be spreading in its endemic regions since 2022. 1,365 confirmed cases and 69 deaths have been reported from the endemic region between Dec 2021 to May 2022, with a sharp rise between 1st Jan 2022 to 8th May 2022 (Table 2). No case from India has been reported yet.

The spread of monkeypox disease in the non-endemic parts of the world has become a rising concern for the medical and scientific fraternities as the disease was considered as endemic to the African countries (Fig.1). Governments of countries across the world have become vigilant about the course of spread of MPV.

In a latest development, an emergency meeting of International Health regulation (IHR) was held on 23rd June 2022 in Geneva, by WHO to assess the threat of the disease on a global level and to decide its status of concern to the world. After looking into the details of the spread of the disease and its consequences and threat to the different parts of the world, The Director-general of the WHO announced that in the current pretext, the world-wide monkeypox outbreak does not qualify for a Public Health Emergency of International Concern (PHIEC) [14]. Therefore, it is not given the status of a pandemic. However, the IHR committee has recommended that the threat for a deadlier spear persists and there is a need of a collaborative efforts of the countries for understanding and controlling the spread of the disease.

	Country	Confirmed	Probable cases
Americas	Argentina	2	
	Canada	110	
	Mexico	1	
	United States of America	40	
Eastern Mediterranean	Morocco	1	
	United Arab Emirates	13	
Europe	Austria	1	
	Belgium	24	
	Czechia	6	
	Denmark	3	
	Finland	3	
	France	66	
	Germany	113	
	Hungary	2	
	Ireland	9	
	Israel	2	
	Italy	29	
	Latvia	2	
	Malta	1	
	Netherlands	54	
	Norway	2	
	Portugal	191	
	Slovenia	6	
	Spain	256	
	Sweden	6	
	Switzerland	12	
The United Kingdom	321		
Western Pacific	Australia	6	1
Cumulative	28	1285	1

Table 2. Cases of monkeypox in WHO African Region reported since January 2022, as of 8 June 2022 [14].

Country	Confirmed cases	Suspected cases	Deaths
Cameroon	3	28	2
Central African Republic	8	17	2
Republic of Congo	2	7	3
Democratic Republic of the Congo	10	1356	64
Liberia	0	4	0
Nigeria	31	110	1
Sierra Leone	0	2	0
Ghana	5	12	0
Cumulative	59	1536	72

VIII. DISCUSSION

Scientists worldwide are of the belief that the risk to the whole population is low and the recent outbreak of monkeypox virus cannot become pandemic as the case was with Covid 19. The main reason behind this is that the MPV does not spread as easily as SARS-COV2.

Dr David Heyman, who heads the WHO's expert advisory committee, is of the view that monkeypox virus spreads only if there is a very close contact with the infected person. Sexual contact has amplified the transmission of the disease. In countries like Spain, Britain UAE, Portugal, Czech Republic, the authorities are of opinion that most cases in Europe have been observed among males. However, experts believe that anyone can become infected through close contact, sharing of bed sheets or any other clothing.

A surprising trend have been notices about the transmission. Few reports have claimed that the disease is more transmissible among homosexual men. This, however, has no scientific evidence. According to Dr Jake Dunning, an infectious diseases researcher at University of Oxford is of the opinion that it is unfortunate that this unreasonable tag has been associated with the homosexual community, which could just be a means to deter such people form indulging in homosexual relationships. In the

present time, the monkeypox virus is not confined to the endemic regions, but it is spreading in different parts of the world. There may be various reasons attributed to the increase incidence in other countries apart from the endemic places [8].

Possible causes of the worldwide spread of Monkeypox disease

i. **Cessation of smallpox vaccination:** Scientists across the world are of view that the vast spread of the monkeypox virus and a sudden surge in the new cases that to in non-endemic regions may be due to the cessation of smallpox vaccination. It could be the waning effect of smallpox vaccination in turn creating immunologic niche for the monkeypox virus leading to sudden rise in the monkeypox virus incidences [9].

ii. **Deforestation:** Deforestation can also be a factor for the sudden increase in the incidence of occurrences of monkeypox [10]. The possible explanation for this could be the loss of habitat of wildlife leading to their closer interaction with human population, resulting in more zoonotic diseases.

iii. **Genetic Evolution of the Monkeypox virus:** Mutation can also be a factor for the resurgence of the monkeypox virus. A viral genome diversity of 60 samples was obtained from infected individuals from Sankuru District, Congo. The study led to the discovery of four distinct lineages within the Central African clad. The study revealed a gene loss in 17% of the samples that seemed to correlate with human-to-human transmission [11].

iv. **Increase in human-to-human transmission rate:** Monkeypox virus is well known to spread through close contact with lesions, respiratory droplets and body fluids of the infected person. But the most alarming cases came to light among men who have sexual relationship with men (MSM) [14]. The linking of monkeypox virus to sexual activity does not mean that the virus is more contagious, but it can be interpreted that virus spreads through close contact.

v. **Immuno-suppressed population:** The immune suppressed host may provide a good platform for the monkeypox virus to acquire mutations thereby increasing its fitness in the human hosts leading to increase transmission, the pathogenic capacity and the virulence. There are three possibilities which exist for the potential transmission or decline of a disease depending on the R_0 value

- a. If R_0 —is less than 1, each infection causes less than one new infection.
- b. If R_0 —is equal to 1, then each existing infection causes one new infection.
- c. If R_0 —is more than 1, then each existing infection causes more than one new infection.

In 1918 there was a worldwide outbreak of the swine flu killing about 50 million people. According to a study published in BMR MEDICINE the R_0 value of that pandemic was between 1.4 -2.8. The disease resurged again in 2009, and its R_0 value was reported to be between 1.4 -1.6. The decline in the R_0 was attributed to the vaccines and anti-viral drugs making the outbreak less deadly [12].

In case of monkey virus, the R_0 is nearly equal to 1, giving it an edge to retain higher transmissibility because there is lengthening of transmission chains as each existing infection causes one new infection.

Diagnostic capacity advancement and greater focus on health care education, and development of new molecular techniques have led to accurate and rapid diagnosis and reporting of the monkeypox cases. From the lessons learnt during the COVID 19 pandemic, in recent years there is an increased focus on health care sectors and health education of the frontline workers i.e the general public and the medical workers [13]. There is an increased awareness amongst the general public and the governments have become more vigilant about the spread and control of diseases. This is the reason for the attention that this viral disease is getting.

IX. CONCLUSION

The waning population immunity associated with discontinuation of smallpox vaccination has established the landscape for the resurgence of monkeypox virus.

Until 4th June 2022, 400 case of monkeypox has been reported across 24 countries. Though the numbers are low, the world is alert about course of its spread. While it is too early to declare it a pandemic, the WHO has warned that monkeypox cases may increase in near future. Further, the appearance of cases outside of Africa highlights the risk of geographical spread and the global relevance of the disease. The possibility for human-to-human transmission is a concern not only for the communities, but also for the health care providers in hospitals. Considering the current environment for pandemic threats, the public health importance of monkeypox disease should not be underestimated. Support from international bodies for an increased surveillance and rapid detection of monkeypox cases, can be instrumental for understanding the continuously modifying epidemiology of this disease. Appropriate and effective global intervention is the need of the hour to prevent increased transmission efficiency and virulence of MPV. Monkeypox virus is the most important orthpox virus in humans, certainly in the endemic areas and perhaps globally. Monkeypox is not a rare disease anymore and needs more attention.

Though WHO has not yet declared the disease as a pandemic and a disease of global concern, it has emphasised on the need of a collective and collaborative international response to the outbreak. The developed countries should come forward and give a hand to the developing countries in combating and controlling the outbreak before it gets out of hands. The effectiveness of the control measures depends on the public health monitoring which includes contact tracing, surveillance, isolation and care of the patients, and judicious use of vaccines which can support the onward spread of the disease. The success of effective vaccination program has been evident in controlling the COVID outbreak on a global level by bringing down the mortality rate. Therefore, to control the spread of MPV, it is recommended that efficient vaccination programmes along with information campaign, pharmacovigilance should go in hand together.

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