

Monkeypox Virus: Transmission Pathway, Clinical Manifestation, Predisposing Factors Responsible for the Re-Emergence and Spread in Nigeria

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Monkeypox is a zoonotic viral disease of public health concern, after almost forty years of no case report, its re-emergence in 2017 at Bayelsa state, Nigeria creates public anxiety, morbidity as well as mortality. It affects susceptible individual of all age groups and gender and consequently, the prevalence is continuously increasing. The causative agent of this disease is Monkeypox virus (MPXV), which belongs to the family *Poxviridae* and the genus *Orthopoxvirus*. Its genome is linear double-stranded DNA (~197kb). This article aimed to make an overview on transmission, clinical manifestation, the factors responsible for the re-emergence and spread of Monkeypox virus in Nigeria. It is transmitted through animals to human (zoonotic transmission) and human to human with broad signs and symptoms after short incubation period including headache, fever, swollen lymph nodes,

muscle pain, and tiredness, followed by rashes which develops into blisters and crusts over. Among the predisposing factors of the re-emergence of Monkeypox in Nigeria include but not limited to: Increased bush meat consumption, lack of smallpox vaccination coverage or declined of immunity in vaccinated individual over time and accumulation of young population, climate change and deforestation, inadequate health and research infrastructures. The re-emergence is beyond public health concern for Nigeria but has potential global health threat and implications. It is re-emergence after several years of no case report, further justify the need for the scientific community to extend their research work on this virus, especially for the development of specific preventive measures, therapies, and control strategies.

INTRODUCTION

Monkeypox (MPX) is a Zoonotic viral disease of public health concern, occurring in many countries, resulted in mortality and morbidity especially in Central and Western Africa, Nigeria inclusive. On 23rd July 2022, World Health Organization (WHO) officially placed MPX in the list of “disease of public health emergency of international concern”. The causative agent of the disease is the Monkeypox virus (MPXV), which belongs to the family *Poxviridae*, subfamily *Chordopoxvirinae*, and genus *Orthopoxvirus* [1, 2]. *Variola* virus, *Vicinia* virus, and *Cowpox* are also members of the genus

Orthopoxvirus [3, 4]. The MPXV possess linear double-stranded DNA of approximately 197 kb and it resemble brick in shape or oval in structures measuring 200–300nm under an electron microscope [5, 6, 7]. MPX in human was initially reported in the Democratic Republic of the Congo in 1970 [8, 9]. regulation and programming [7, 8]. MPXV can be transmitted through handling bush meat, suspected reservoir animal bite, bodily fluids, contaminated objects, or intimate contact with an infected human [10]. Its symptoms usually begin with headaches, fever, swollen lymph nodes, muscle pain, and tiredness.

And later followed by rashes that develops into blisters and crusts [11, 7, 12, 13]. The time interval between exposure to MPXV and the onset of symptoms (incubation period) is 7 to 14 days, with a maximum of 21 days. On average, symptoms last about 2-4 weeks [14 .]

Despite the WHO declaration on smallpox being eradicated in 1980, MPX re-emerged in Nigeria in 2017, which lasted from late 2017 to early 2018, causes threat to public health [15, 16] and its now spreading within the country and to several countries in the world, of which majority countries have not historically reported monkey pox, while with few countries (Nigeria Ghana, the Democratic Republic of the Congo, Liberia, and Cameroon) have previously reported monkeypox infection [13]. The re-emergence of MPXV is tied to some biotic, abiotic, and social factors. The re-emergence is beyond a public health concern for Africa alone; rather, it has a global health threat and implication, as there is evidence of MPXV exportation from one country to another by travelers and through the trade of bush meat [17, 7, 18, 19]. Generally, MPX should not be taken as rare disease that is limited to countries in West and Central Africa. This review tends to provide an overview on the transmission pathways, clinical manifestation as well as factors responsible for its re-emergence.

It is re-emergence after several years of no case report, further justify the need for the scientific community to extend their research work on this virus, especially for the development of specific preventive measures, therapies, and control strategies.

Methodology

This article is a narrative review of Monkeypox virus, and the source of data for this article were original and review articles published in English Language, reporting data relating to the transmission, pathogenesis, clinical manifestation and the factors responsible for the re-emergence and spread of Monkeypox virus. The data was searched for on PubMed, Embase, Scopus, Google Scholar and ResearchGate retrieved and reviewed.

Transmission pathway:

There are several modes in which the MPXV is

transmitted, all of which depend on direct exposure with infected reservoir animals or infected humans (Figure 1) [20]. Generally, contact with infected animals have connected to human infections. However, specific exposure to human case can be difficult to determine in communities/areas where contact with animals is common either through household rodent infestations, hunting or preparation of bush meat from a variety of species [21]. Until now, the actual route of MPX transmission is still unclear, but those represented below (Figure 1), considered as the suspected routes of transmission and also highlighted as the risk factors to contract MPX infection [9, 20]. Zoonotic transmission of MPX is considered by direct contact or exposure to bodily fluids such as saliva, respiratory excretions or exudates from cutaneous or mucosal lesions from infected animal. Viral shedding via feces may represent another source of infection [22, 20]. In poor resources and infrastructure setting especially in MPX endemic region of Africa, exposure to the feces of infected animals can be an important risk factor, because in this settings individuals have no options than to live closely to the suspected reservoir animals or visit the forest in search of items for domestic use, where infected animals are much more prevalent [9]. In a community with limited resources, such as food, individuals are left with no option then to feed from small mammals, which in-turn accelerate the risk of exposure to MPX. Despite the fact that transmission from one person to another is less common than zoonotic transmission, it usually through respiratory droplets with closed and prolonged face-to-face contact or contact with lesions from an infected individual [16]. Contaminated objects and surfaces, such as sleeping on the same bedding, living in the same household, or eating or drinking from the same dishes with an infected individual, are deemed a risk factors for MPX transmission among individuals in the same household. Despite the current, ongoing MPX epidemic, whether it's transmitted via sexual contact is not known, as disclosed by the World Health Organization (WHO); however, the transmission can be generally linked to close contact with infected human or animal [23].

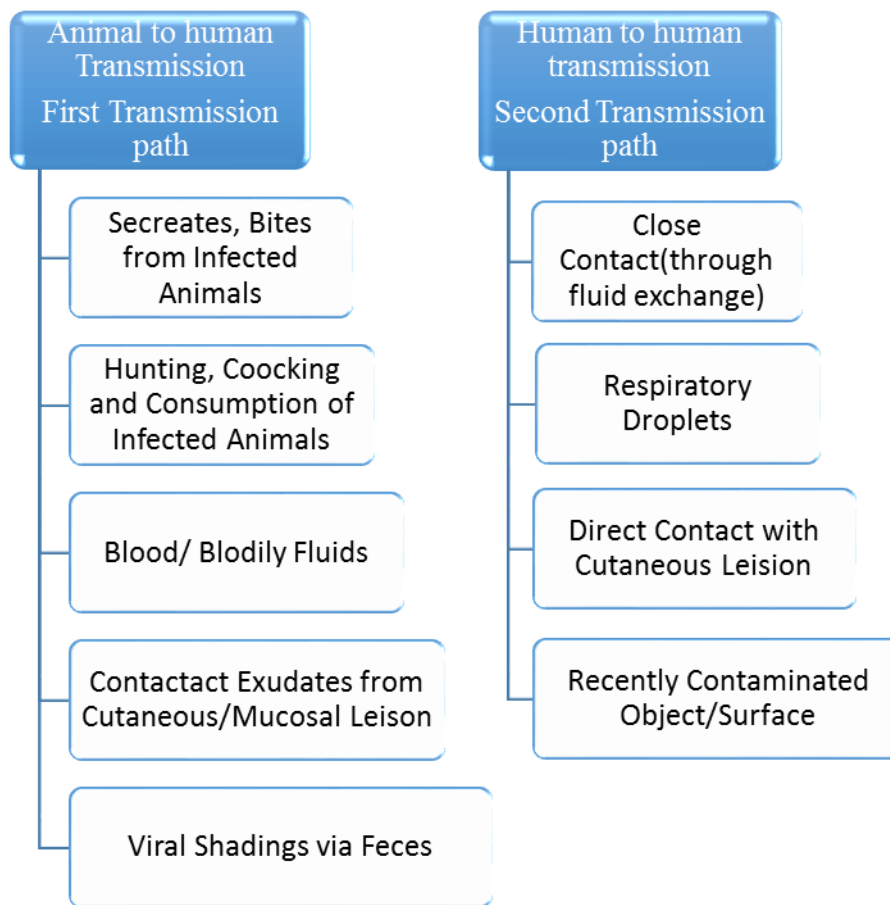


Figure 1: Schematic Illustration of the Monkeypox Virus Transmission

Pathogenesis:

Although individual's transmission of MPX is uncommon, the most common cause considered is respiratory droplets. The pathogenesis of the MPXV follows a similar pattern to that of smallpox, initiating with the exposure of the oropharyngeal or respiratory mucosa of the person infected with the virus [20]. Following entry, Monkeypox virus replicates at the site of inoculation. The respiratory and oropharyngeal mucosa were the sites of inoculation in human-to-human transmission. Following viral replication, in primary viremia, the virus spreads to the local lymph nodes, while in secondary viremia, the virus move to the far lymph nodes and organs through circulation [24]. The outbreak of the MPXV was reported with sustained transmission between men who have engaged in sexual intercourse, especially gay men [25]. The entire process described above represents the period between the exposure to the initiation of symptoms, ideally lasting seven (7)

to fourteen (14) days with maximum of 21 days [20]. It is not contagious at the incubation stage because at this stage, the clinical manifestation of Monkeypox is not visible [20]. The symptoms and clinical manifestations of Monkeypox can be similar to the prodromal stage. During the prodromal stage, secondary viremia occurs from the lymphoid organs to the skin and tertiary organs such as the lungs, eyes, gastrointestinal tract, etc. It is during this state that; an individual confirmed to be highly infectious. This is absolutely due to the appearance of signs and symptoms such as cutaneous lesions and lymphadenopathy, among other non-specific symptoms.

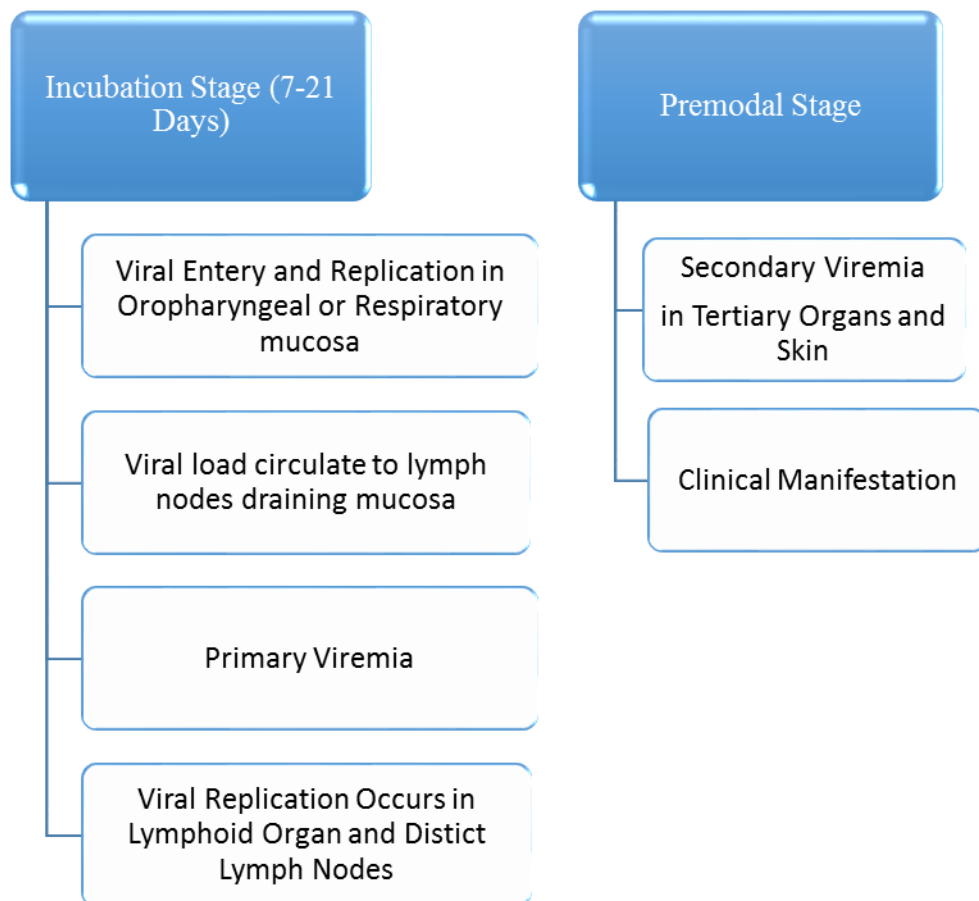


Figure 2: Schematic representation of Monkeypox Virus Pathogenesis

Clinical manifestation:

There are numerous nonspecific symptoms that is shared among an individual infected with MPX. Symptoms begin to develop 7 to 14 days after an individual has been exposed to the Monkeypox virus [26, 20]. Initially, during the prodromal stage, nonspecific symptoms such as fever, headache, backache, exhaustion, chills, rashes, mouth and throat ulcers, lymphadenopathy as well as myalgia manifest, stimulating the infected individual's immune system. As a result of nonspecific nature of these early symptoms, an infected individual may consider these symptoms to other infections such as seasonal flu or the common cold. The activation of the immune system will always cause changes in lymph nodes (enlargement), including maxillary, cervical and inguinal, occurring in synchrony with the onset of fever [23]. In cases before 2022 outbreak in Nigeria, rashes were observed and appeared between 1-3 days after development of fever and

lymphadenopathy. In the emergence of these new cases, Harris states "that for some patients, those prodromal symptoms might be mild, or not even noticed at all, suggesting that some individuals may not be aware of any symptom at all, until the appearance of the rashes" [20]. Fever in typical cases often disappears between the ranges of 1-3days post onset of the rashes [20]. The facial rashes will and concomitantly spread and appear across the entire body [21, 20]. There are lesions usually noticed in the mouth and consequently, these lesions cause difficulties with eating and drinking and thus, affects the feeding habit/nutritional intake of an infected individual. The skin lesions cause an extensive perturbation of the skin, and this creates a chance for secondary bacterial infection of the skin, and this complication has been observed in 19% of unvaccinated Monkeypox-infected individuals [21, 8.]

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The re-emergence has global potential health threat as trade in suspected reservoir animal have exported MPX to the United State of America in 2003 [17, 27], while human travelers from the epicenter (Africa) have also exported the disease to several other countries [28, 29, 30]. The most devastating part is that; researchers observed transmission from one individual to another and vice-versa of West African strain of MPXV in other countries [31, 18]. The re-emergence of MPX after many years of zero case report may be linked to the fact that significant portion of the population is susceptible to Orthopoxvirus infection as they did not receive smallpox vaccination, which cross-protects against MPXV, or smallpox vaccine-induced immunity has been reduced in vaccinated individuals as well as accumulation of young population [32, 16, 33, 34, 35]. There are quite a number of factors that may facilitate the re-emergence and spread of MPX. This article attempted to explore some of them as:

a) Lack of Smallpox Vaccination Coverage

Studies have shown that smallpox vaccination protects against MPX infection [36, 37, 39, 6, 40, 34]. A number of studies and reports from health institutions from different countries reported a significant number of cases from the disease outbreak. Consequently, no single individual among the reported cases received smallpox vaccination, which cross-protects by 85% against MPXV [41, 9, 42, 43, 18, 9]. Likewise, reports from outbreaks in the Democratic Republic of the Congo (1981–2013) [44, 45, 46, 47] and the US [48] showed that the majority of MPX cases was low in vaccinated individuals and ranged between 4–21% [49, 9] indicating that the majority of cases reported, approximately 80–96%, occurred in unvaccinated individuals. A study conducted in Central African Republic on confirmed and suspected cases showed that 19.2% (5/26) received smallpox vaccination, and the overall secondary attack rate was lower among individual who previously received Smallpox vaccination (0.95/1000) compared to unvaccinated individuals (3.6/1000) [50, 9].

b) Increase in Susceptible Population over Time

Over time, an increase in number of individual susceptible to MPXV infection plays a role in the re-emergence and person to person transmission of the virus [51, 52], as the number of people susceptible to smallpox infection has increased

significantly since the cessation of routine smallpox vaccination in 1978, and a threshold has been declined where presently human-to-human transmission of MPXV is observed. And also, the accumulation of young children who were born during the post-smallpox vaccination era [45, 40, 7] has substantially reduced the overall population immunity level within the past 45 years. The former was evidenced using statistical modeling by Nguyen et al. (2021); they reported that, in 2016, a year before the re-emergence of the MPXV in Nigeria, only 10.1% of the present population were vaccinated, and the population immunity was substantially waned down from 65.6% in 1970 to 2.6% in 2016 [33, 34]. By 2018, the vaccinated population had decreased to 9.3%, and the estimated population immunity had declined to 2.2% [33]. And the level of serologic immunity to MPXV for the vaccinated population would continue to decline at a constant rate until it reached 0%, at which point all previously vaccinated populations would be fully susceptible to MPXV [33, 34]. While the latter was evidenced by a higher increase in the number of young people who were born after stoppage of smallpox vaccination in 1980, when smallpox vaccination was ceased as a result of a declaration by the WHO that smallpox was eradicated [45, 53, 47].

c) Inadequate Health and Research Infrastructures

Initially, there was a diagnostic challenge as many individuals, including physicians, had no knowledge of the etiology of the disease condition. This makes laboratory diagnosis, treatment, and prevention of MPX disease difficult [15]. This is because in developing countries' health care settings, especially at the basic health care level, are challenged with limited facilities, staff technical skills, and training needed to diagnose Monkeypox [54]. However, delays in detection, treatment, and management of infection caused by unavailable standard laboratories, especially at the basic health care level, contributed greatly to the re-emergence of the disease [54]. In Africa (especially Nigeria), before the re-emergence of MPXV, it had already been considered a neglected pathogen [54, 31], and a lack of research on it has recently been demonstrated. The relatively scarcity of the disease after smallpox vaccination as well as lack of political

willpower in health care concerns might be the reasons [19.]

d) Increased Bush Meat Trade and Consumption

A number of ecological and behavioral factors contribute to the increased risk of exposure to MPXV through the bush meat trade [55]. Increased human contact with wild animals through hunting, butchering, and consumption of bush meat has led to the cross-species transmission of numerous infectious diseases, several of which have led to devastating outcomes across the globe [56, 1]. Transmission across species through bush meat hunting and butchering has been connected to the outbreaks of MPXV [56]. Monkeypox outbreaks are usually common among residents of small communities who engage in hunting and trade in animals suspected as reservoir of MPX rodents [49], facilitated by the increased demand for and indiscriminate consumption of such animals in Africa [57, 7]. Hunting activities and trade in animals suspected of being reservoirs of MPXV infection lead to excessive bush meat consumption, which in turn might contribute to the re-emergence and spread of MPXV [58]. This evidence is further supported by the higher prevalence observed among men and individuals of higher age groups in majority of the previous outbreaks, because predominantly, men and individuals of higher age groups carry out most high-risk occupations dealing with suspected animals compared to their counterpart women and children [58, 33.]

e) Climate Change and Deforestation

Climate change is assumed to result in changes in the geographic ranges and local prevalence of infectious diseases, including MPX, either through direct effects on the pathogen or indirectly through range shifts in vector and reservoir animals [53, 59]. Environmental stress such as heavy rainfall and flooding, as well as deforestation in the name of clearing bush and forest for urbanization or farming, could expose individuals and also drive the transmission of MPXV [7, 16]. However, extension of developed areas could also increase the possibility of reservoir animals to be displaced from their natural habitat and moving to live with humans, thus increasing interspecies contact [57, 60, 59]. These allow the transmission of the virus from

reservoir host animals to a susceptible human, which consequently hastens the re-emergence and spread of MPX virus [33, 16.]

f) Limited Public Health Awareness

The limited public awareness of the disease in endemic areas has greatly contributed toward its re-emergence [15]. This was evidenced by indiscriminate and caution-less handling and dealing with animals suspected as reservoirs of the Monkeypox [61, 62], with the perception that monkeys are the reservoir of MPXV as the name implies. Other behavioral activities that speed up the risk of exposure to suspected reservoir animals and subsequent risk for zoonotic transmission as a result of limited awareness of the disease and in turn fuel the re-emergence of Monkeypox are: indiscriminate eating of meat from a dead animal from unknown causes of death or eating under-cooked meat [55,47, 54.]

Other predisposing factors may include: Social activities; the current outbreak of the MPXV virus is being reported with sustained transmission between men who have engaged in sexual intercourse with men [25]; social gatherings such as clubs and group sex [7]; tourism, migration, and war, among others, have also been agents for the spread of the virus.

Conclusion:

Monkeypox virus is a very serious emerging and re-emerging pathogen with complex mode of transmission and broad clinical signs and symptoms as well as potential global outreach, it requires critical understanding for improved prevention diagnosis and management/treatment of this viral infection. The re-emergence is beyond a public health threat for Nigeria or other historically MPXV reported countries alone but has global health implications as trade in suspected reservoir animals and travelers have facilitated the exportation of MPX to other countries. However, it is re-emergence after several years of no case report, further justify the need for the scientific community to extend their research work on this virus, especially for the development of specific preventive measures, therapies, and control strategies.

Abbreviations:NA= Deoxyribonucleic acid, kb= Kilo-base, MPX=Monkeypox, MPXV=Monkeypox virus, USA = United State of America, WHO=World Health Organization.

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HIGHLIGHTS:

- 1- Monkeypox virus is a very serious emerging and re-emerging pathogen with complex mode of transmission, broad clinical signs and symptoms with potential global health threat and implications.
- 2- The re-emergence and high spread of MPXV was tied to some biotic, abiotic, and social factors.
- 3- A quit number of factors facilitated the re-emergence and spread of Monkeypox virus in Nigeria, including but not limited to: Lack of Small Pox Vaccination Coverage, Increase in Susceptible Population over Time, Inadequate health and research infrastructures, Increased bush meat trade and consumption, Climate Change and Deforestation.

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