

## **MONKEYPOX: AN EMERGING AND RE-EMERGING THREAT IN NIGERIA**

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### **ABSTRACT**

*Monkeypox (MPX) is a viral zoonosis that mostly prevalent in tropical rainforests of Central and West Africa and can also be found in other parts of the world. Only three (3) cases have been documented in Nigeria before 2017, with the first occurrence being in 1971. There have been 558 suspected cases reported from 32 states from 2017-2022. In 22 states, 241 (43.2%) of the reported cases have been confirmed. However, between September 2017 and April 30th, 2022, eight (8) deaths (CFR= 3.3%) were reported in six states. MPXV is transmitted from one person to another by close contact with lesions, body fluids, respiratory secretions and infected materials such as bedding. Common symptoms are fever, rash, and enlarged lymph nodes, which can lead to a variety of medical conditions. The incubation period lasts 7–14 days on average. MPX has a similar clinical presentation to smallpox. Since Nigeria is a resource-poor country with inadequate infrastructure, technical skills, and training, laboratory diagnosis, along with prevention and management of MPX infection, remains difficult in Nigeria. Vaccines used during the smallpox eradication programme, however, still provide protection against MPX. The MPXV potential to mutate, it is possible bioweapons threat, and its re-emergence in Nigeria all add to the urgency of better understanding the symptoms and prevention of MPX infection.*

**KEYWORDS:** *Monkeypox, Smallpox, Infection, Monkeypox virus, Nigeria*

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## INTRODUCTION

Monkeypox (MPX) is an uncommon disease caused by a monkeypox virus. Monkeypox virus (MPXV) is a member of the *Orthopoxvirus* genus in the Poxviridae family. Other members of the *Orthopoxvirus* genus include Variola virus (which causes smallpox), vaccinia virus (used in the smallpox vaccine), and cowpox virus (CDC, 2021). MPX is a zoonotic disease which can be transmitted from animals to humans, presenting symptoms that are comparable to those observed in smallpox patients in the past, but it is less severe clinically. It has emerged as one of the most significant *orthopoxvirus* after the elimination of smallpox in 1980 and the consequent termination of smallpox immunisation. MPX is prevalent in Central and West Africa, usually near tropical rainforests (WHO, 2019). Symptoms usually begin with headaches, fever, swollen lymph nodes, muscle pains, and tiredness. Thereafter, it is followed by a rash which develops into blisters and crusts over. The time interval between exposure to MPXV and to the onset of symptoms is around ten (10) days. On average, symptoms last about two to four weeks (CDC, 2015). MPXV can be transmitted through handling bushmeat, an animal bite or scrape, bodily fluids, contaminated objects, or intimate contact with an infected human. The virus is thought to generally circulate in Africa among specific rodents (WHO, 2021). MPX infection can be confirmed by isolating MPXV DNA from a patient's sample and growing it in a viral culture (Moore and Zahra, 2021). The condition might resemble

chickenpox in appearance (McCollum and Damon, 2014).

The smallpox vaccination is thought to protect against infection (CDC, 2018). MPXV infection currently has no documented, safe therapy. Smallpox vaccination, antivirals, and vaccinia immune globulin (VIG) can or have been utilised to suppress a MPX outbreak in the United States. The usefulness of cidofovir and brincidofovir in treating human instances of MPX is unknown. Both, however, have been shown to be effective against poxviruses in both in vitro and animal trials (CDC, 2021). Those who are infected have a 10% chance of dying (Hutin *et al.*, 2001).

The disease was first discovered in experimental monkeys in 1958. The first human cases were reported in the Democratic Republic of Congo in 1970 (Bunge *et al.*, 2022). Despite the WHO declaring smallpox eradicated in 1980, MPX still occurs on occasion in Central and West Africa (WHO, 2016). In 2003, an epidemic in the United States was linked to a pet business that sold rodents imported from Ghana (CDC, 2018).

The previous MPX outbreak in Nigeria, which lasted from October 2017 to February 2018, was a threat to public health (Fowotade *et al.*, 2018). A MPX incident was recently recorded in a UK citizen who landed in Nigeria on April 20, 2022, travelled to Lagos and Delta States during his stay in Nigeria, departed Lagos on May 3, 2022, and returned to the UK on May 4, 2022 (Muanya and Onyedika-Ugoeze, 2022). There was an early diagnostic challenge since many people, including physicians, had no idea of what was causing the disease. According to

NCDC (2022), owing to the re-emergence of MPX in Nigeria in September 2017, the country has continued to report occasional instances of the virus from states throughout the country. A total of 558 cases and eight fatalities have been reported from 22 states between September 2017 and April 30, 2022. A total of 46 suspected cases were recorded between January 1st and April 30th, 2022. There have been 15 confirmed cases from seven (7) states: Adamawa (3), Lagos (3), Cross River (2), FCT (2), Kano (2), Delta (2), and Imo (1), but no deaths have been reported (NCDC, 2022).

MPXV is a possible biological warfare tool since its aggressiveness is

second only to Variola virus, the agent of smallpox, with a 10% death rate (McCollum and Damon, 2014). As a result, physicians and the general public must be educated on the diagnosis, care, and control of this disease.

Table 1: Monkeypox virus classification

Realm:	Varidnaviria
Kingdom:	Bamfordvirae
Phylum:	Nucleocytoviricota
Class:	Pokkesviricetes
Order:	Chitovirales
Family:	Poxviridae
Genus:	<i>Orthopoxvirus</i>
Species:	Monkeypox virus

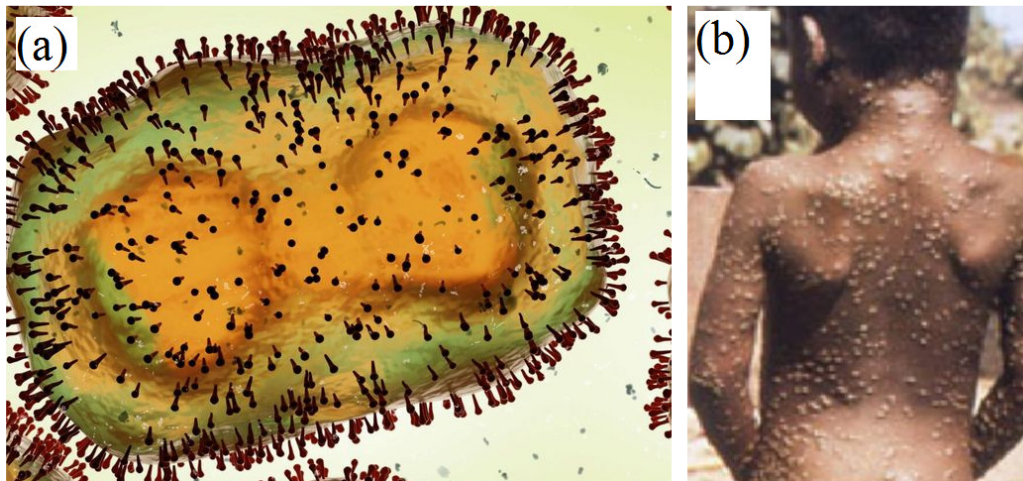


Fig. 1: (a) Microscope micrograph of MPXV (Barnett, 2021)

(b) A young boy infected with MPX

### EPIDEMIOLOGY

Monkeypox (MPX) is exclusively found in the rainforests of Central and West Africa (Reynolds *et al.*, 2019). Ten cases of human MPX infection were documented in Sierra Leone, Nigeria, Liberia, and Côte d'Ivoire between 1970 and 1986 (Pal *et al.*, 2017; Fowotade *et al.*, 2018).

Surveillance data in the Democratic Republic of Congo revealed 338 cases between 1981 and 1986. Another epidemic occurred in the Democratic Republic of Congo from 1996 to 1997, with an attack rate of 22 cases per 1000 population and occasional occurrences in neighbouring countries (Pal *et al.*, 2017; Fowotade *et al.*, 2018). Human

MPX infection was first reported outside of Africa in 2003 in the United States, following the export of rodents from Ghana to Texas. This epidemic resulted in 81 cases of MPX, with 41% laboratory confirmed. In 2003, the Democratic Republic of Congo recorded 11 cases of MPX and 1 death, while Sudan reported 10 cases in 2005 (Fowotade *et al.*, 2018).

The greatest known outbreak occurred in Nigeria in 2017, 40 years after the previous verified case. Between September and December 2017, Nigeria reported 88 confirmed MPX cases from 15 of the 36 states (NCDC, 2022). MPXV studies have revealed at least two genetic varieties (clades) of the virus, both of which segregate geographically, with one type present in West Africa and the other in Central Africa (Fowotade *et al.*, 2018). This epidemic was linked to the West African clade. The majority of confirmed cases were among people aged 21 to 40, with a male to female ratio of 2.5:1. Six deaths were reported, with 4 of them having history of immunosuppression (Yinka-Ogunleye *et al.*, 2017; NCDC, 2018).

Before 2017, only 3 cases have been documented in Nigeria. The first incidence was recorded in 1971 in a 4-year-old child from the country's southeastern region, and the final case was reported in 1978 (Eke, 2017). MPX has not been recorded in Nigeria since 1978, prior to the 2017 epidemic. Similarly, Liberia, a West African country,

reported 2 confirmed cases of MPX in November 2017 (Fowotade *et al.*, 2018).

Nigeria has been reporting rare cases of MPX since 2017. The MPX National Technical Working Group (TWG) has been keeping track of cases and improving prevention and response capabilities (NCDC, 2022). According to NCDC (2022), a total of 46 suspected cases have been reported between January 1st to April 30th, 2022. Of the suspected cases, 15 were confirmed from seven (7) states (Table 1) including; Adamawa (3), Lagos (3), Cross River (2), FCT (2), Kano (2), Delta (2) and Imo (1). However, no deaths have been reported. From September 2017 to April 30th, 2022, a total of 558 suspected cases have been reported from 32 states out of the 36 states in the country including the Federal Capital Territory, Abuja. Furthermore, of the reported cases, 241 (43.2%) have been confirmed in 22 of the 36 states namely; Rivers (52), Bayelsa (43), Lagos (33), Delta (31), Cross River (16), Edo (10), Imo (9), Akwa Ibom (7), Oyo (6), FCT (8), Enugu (4), Abia (3), Plateau (3), Adamawa (3), Nasarawa (2), Benue (2), Anambra (2), Ekiti (2), Kano (2), Ebonyi (1), Niger (1) and Ogun (1). A total of eight (8) deaths have been recorded (CFR= 3.3%) in six states, namely Edo (2), Lagos (2), Imo (1), Cross River (1), FCT (1) and Rivers (1) from September 2017 to April 30th, 2022 (NCDC, 2022).

Table 2: Nigeria confirmed MPX cases by state, September 2017 - April 2022

State	2017	2018	2019	2020	2021	2022	Total
Abia	1	2	0	0	0	0	3
Adamawa	0	0	0	0	0	3	3
AkwaIbom	6	0	1	0	0	0	7
Anambra	0	1	1	0	0	0	2
Bayelsa	19	11	7	0	6	0	43
Benue	2	0	0	0	0	0	2
Cross River	9	3	1	0	1	2	16
Delta	3	6	10	1	9	2	31
Ebonyi	0	0	0	1	0	0	1
Edo	4	1	1	0	4	0	10
Ekiti	2	0	0	0	0	0	2
Enugu	1	2	1	0	0	0	4
FCT	5	0	0	0	1	2	8
Imo	5	2	1	0	0	1	9
Kano	0	0	0	0	0	2	2
Lagos	4	1	15	4	6	3	33
Nasarawa	1	1	0	0	0	0	2
Niger	0	0	0	0	1	0	1
Ogun	0	0	0	0	1	0	1
Oyo	1	3	2	0	0	0	6
Plateau	0	2	0	1	0	0	3
Rivers	25	14	7	1	5	0	52
<b>Total</b>	<b>88</b>	<b>49</b>	<b>47</b>	<b>8</b>	<b>34</b>	<b>15</b>	<b>241</b>

Adapted from NCDC (2022)

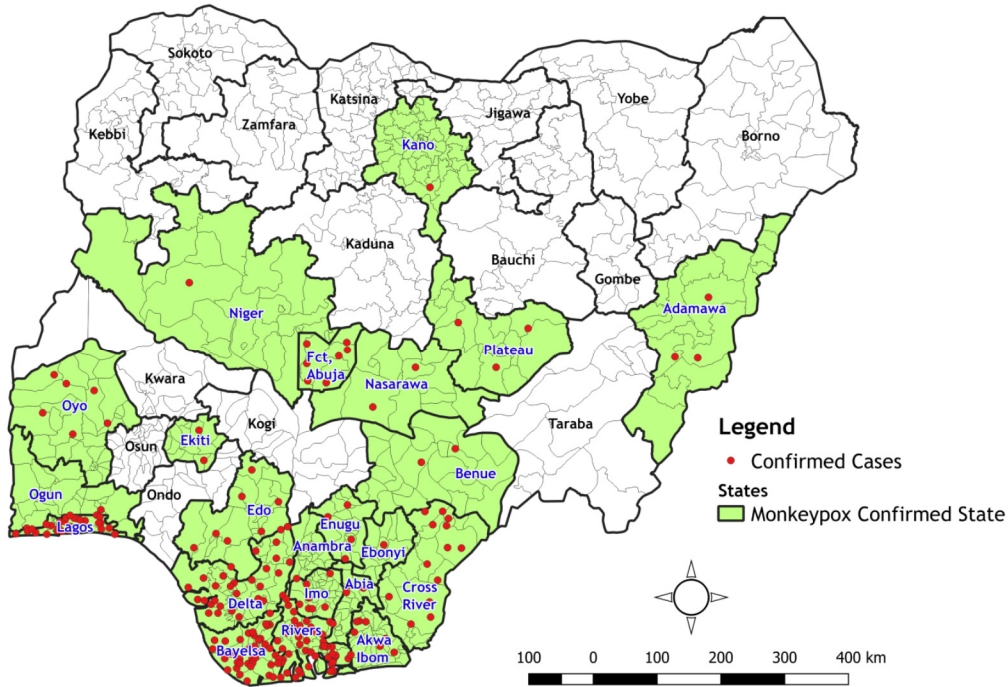


Fig. 2: Map of Nigeria Showing States with Confirmed MPX Cases from September 2017 – April 2022 (NCDC, 2022)

Figure 2 shows that confirmed MPXV cases were more prevalent in the southern region, as well as the federal

capital territory Abuja, whereas just a few cases were confirmed in the western and eastern parts of the country.

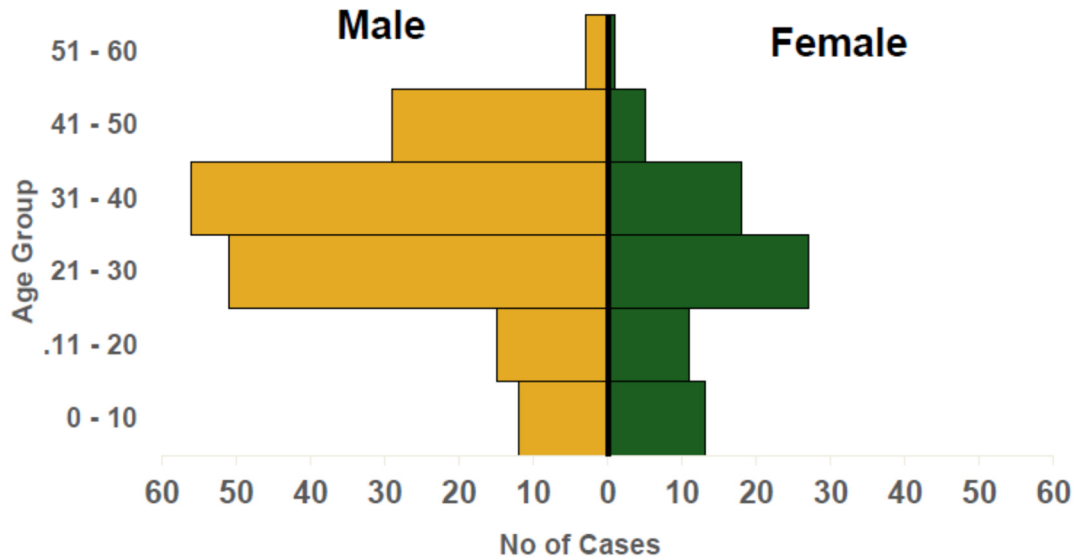


Fig. 3: Age and sex distribution of Nigeria confirmed MPX cases between September 2017 - April 2022 (NCDC, 2022).

Sutcliffe *et al.* (2012) revealed that, transmission occurs all year in endemic nations, with no peak month or season. Males (especially those aged 21-40) have been observed to have a higher rate of MPX infection (Figure 3) than females, with no tribal preference. The majority of patients in Nigerian epidemics were male (over 75 percent) and aged 21–40 years old (median 30

years). Children under the age of 10 were also afflicted, with 25 confirmed cases (10 males and 15 females) over a 5-year period (2017-2022), which might be connected to the end of smallpox immunisation. Furthermore, there was a distinct difference in the number of confirmed cases for those under the age of 20, with the lowest confirmed cases recorded among those aged 51-60.

Table 3: Age distribution of confirmed MPX cases from September 2017 – April 2022

Age Group	2017	2018	2019	2020	2021	2022	Total
0-10 Years	7	5	1	0	1	1	15
11-20 Years	12	4	1	0	4	2	23
21-30 Years	34	13	13	4	10	5	79
31- 40 Years	26	17	22	4	13	5	87
41-50 Years	9	10	9	0	5	2	35
51-60 Years	0	0	1	0	1	0	2
Total	88	49	47	8	34	15	241

Source: NCDC, 2022

Table 3 shows that the age distribution of confirmed MPX cases, it was observed that age group 31-40 years was the most affected by MPXV with 87 confirmed cases, followed by 21-30 years with 79 confirmed cases, 35 confirmed cases in the 41-50 years age group, 23 confirmed cases in the 11-20 years age group, and 15 confirmed cases in the 0 – 10 years age group, but the age group 51-60 years was the least affected with 2 confirmed cases.

**Modes of Transmission**

Handling infected animals; direct contact with blood or body fluids; inoculation from mucocutaneous lesions on an infected animal, especially when the skin barrier is broken due to scratches, bites, or other trauma, or ingestion of inadequately cooked meat from infected animals are all ways for the virus to reach humans (Sutcliffe *et*

*al.*, 2012; Pal *et al.*, 2017). Handling of infected monkeys, Gambian giant squirrels, rats, rabbits, dormice, porcupines, gazelles, and prairie dogs have been recorded as a means of transmission (Pal *et al.*, 2017). MPX outbreaks are most common among residents of small communities that engage in hunting and gathering, with close physical contact being the most significant risk factor for infection. Although no specific species has been established as its natural reservoir, rodents are being explored. Large respiratory droplets can transmit disease from person to person during persistent face-to-face contact. MPX infection can potentially be transmitted through the placenta (Pal *et al.*, 2017).

Regarding transmission from infected animals or people, MPX infection begins with infection of the

dermis or respiratory epithelium. The virus spreads from the lymphatic system to the blood, resulting in primary viraemia and systemic infection. Secondary viraemia arises, resulting in epithelial infection and resulting skin and mucosal sores. The virus replication on mucosal surfaces can lead to transmission to close contacts via oropharyngeal secretions. Although the MPXV has evolved strategies to evade the host immune response, the density of viruses in oropharyngeal secretions, closeness and length of contact, and virus survival likely impact the probability of virus transmission (Sutcliffe *et al.*, 2012).

#### **Clinical Manifestation**

According to the WHO (2018), the clinical features of probable MPXV are similar to that of normal distinct smallpox. Following infestation, there is an incubation period of 7-14 days on average. The prodromal stage begins with the onset of first symptoms such as fever, malaise, headache, and weakness (the period one develops an early set of symptoms).

The development of enlarged lymph nodes is a hallmark that separates MPXV infection from smallpox infection (lymphadenopathy). Lymph node swelling can be widespread (affecting many distinct parts of the body) or localised (affecting only a few places) (for example, neck and armpit).

A rash emerges shortly after the prodrome (MPX patients acquire an early set of symptoms). Lesions on any area of the body usually start developing and evolving at the same time. Before scabbing over and disappearing, lesions develop through four stages: macular, papular, vesicular, and pustular.

This process requires about 2-3 weeks to complete. The depth of disease is determined by the individual's initial health, the route of exposure, and the virus strain infecting them (West African vs. Central African virus genetic groups or clades). MPXV in West Africa is characterised by a mild illness, low mortality, and less human-to-human transmission. Human infections with the Central African monkeypox virus clade are often more severe and have a greater mortality rate than those with the West African virus clade. The Central African MPXV is known to be transferred from person to person (WHO, 2018).

#### **Laboratory Diagnosis**

Diagnosis of MPXV infection can be carried out by cell culture, polymerase chain reaction (PCR), enzyme linked immunosorbent assay (ELISA), or Western blotting, with PCR being utilised for final diagnosis (McCullum and Damon, 2014; Mullendore *et al.*, 2016). During specimen collection, standard contact and droplet precautions must be followed, and any samples that might be contaminated with the MPXV should be handled in biosafety level 2 facilities. Tonsillar tissue, oropharyngeal tissue, or nasopharyngeal tissue swab, punch biopsy kit, lesion fluid, lesion roof, scab/crust, whole blood, acute and convalescent phase sera are some of the specimens that may be acquired to help with diagnosis (Fowotade *et al.*, 2018). For viral culture, MK2 cells, LLCMK2 cells, and Vero E6 cells can be used to acquire oropharyngeal or nasopharyngeal swabs for viral culture. The presence of cytotoxic effects, such as multinucleated syncytial



keratinocytes, can be used to identify growth. This cytopathic impact, however, is also present in the Vaccinia and cowpox viruses, making it difficult to distinguish these viruses in cell culture. The virus from the culture may be identified by DNA restriction analysis (Pal *et al.*, 2017).

Swabs of the lesion's exudates, scabs, a skin biopsy of the vesiculopustular rash, or a sample of the roof of an intact vesiculopustule can all be used to make the diagnosis. The monkeypox extracellular-envelope viral protein gene and the conserved portion of the DNA polymerase gene (E9L) may be examined using PCR (Breman *et al.*, 1980; Bayer-Garner, 2005). If a cold chain is not accessible at the time of specimen collection, the viral DNA in the specimen can be kept stable for a long time if preserved in a cool, dark area. The use of ELISA to detect antibodies such as immunoglobulin M (IgM) or immunoglobulin G (IgG) in serum or plasma is an efficient way to diagnose monkeypox infection (Karemet *et al.*, 2005). IgM is detectable in the serum approximately 5 days after the rash appears, whereas IgG is discovered after more than 8 days. Increased titre values in paired sera for IgG and IgM titers can be used to identify seroconversions, which are used as a sign of recent monkeypox infection (Fowotade *et al.*, 2018). The Tzanck smear can be used to distinguish monkeypox infection from other nonviral illnesses, but it cannot distinguish it from smallpox or herpetic infections. Stern *et al.* (2016) reported that an immunofiltration technology based on gravity-driven flow-through antigen capture ELISA called Antibody

Immuno Column for Analytical Processes (ABICAP) has been developed. It is a mobile laboratory diagnostic test that may be used on humans and animals.

Inverse electron microscopy with negative staining can reveal a huge brick-shaped particle with rounded corners, which is indicative of a poxvirus in biopsy specimens from lymph nodes or scab material, vesicular fluid, blood specimens, or viral culture (Mullendore *et al.*, 2016). On electron microscopy, round-to-oval intracytoplasmic inclusions with core sausage-shaped features spanning 200–300 nm can also be detected. These inclusions are widespread in Orthopox viruses, making it easier to distinguish them from herpes and parapox viruses (Pal *et al.*, 2017).

Bayer-Garner (2005) reported that, in carrying out histological analysis of papules, the analysis may reveal acanthosis, individual keratinocyte necrosis, and basal vacuolation, as well as a superficial and deep perivascular, lymphohistiocytic infiltration in the dermis. The vesicles' histology may exhibit spongiosis, ballooning, and reticular degeneration. Pustules may exhibit epidermal necrosis with many eosinophils and neutrophils, many of which have karyorrhexis. The necrosis may run the length of the epidermis with a distinct lateral demarcation from the neighbouring healthy epidermis. Secondary vasculitis may be indicated by a perivascular infiltration containing eosinophils and neutrophils, as well as lymphocytes and histiocytes. The presence of amphiphilic intranuclear structures inside the keratinocytes may indicate the presence of viral inclusions.

Within the keratinocytes, eosinophilic Guarnieri-type intracytoplasmic inclusions can also be detected (Bayer-Garner, 2005). Immunohistochemistry staining can be used to evaluate orthopox viral antigens, although it is only available in a few reference laboratories.

#### **Treatment**

Since MPX is self-limiting, it is usually treated with bed rest and supportive care. In extreme situations, however, hospitalisation and maybe even critical care may be required. Nursing should be done in a negative pressure environment with airborne and contact precautions to reduce the transmission of the disease. Isolation of affected individuals is another important precaution in preventing infection spread, and it must be maintained until the final crust is shed, as direct contact with skin lesions and fomites is considered contagious (Fowotade *et al.*, 2018).

There is currently no established therapy for human illness, but in vitro and animal researches have revealed that cidofovir and brincidofovir (CMX-001) have anti-monkeypox viral activity (Weinstein *et al.*, 2005). Upon intratracheal infection of cynomolgus monkeys, cidofovir was found to reduce mortality more than the therapeutic use of smallpox vaccination (Stittelaar *et al.*, 2006). For those with severe MPX infection, the CDC recommends cidofovir. However, brincidofovir has a better safety profile than cidofovir because it has less kidney toxicity when used to treat cytomegalovirus infection. In vitro and in animal tests, tecovirimat (formerly known as ST-246) has efficacy against orthopoxviruses,

including MPX, although its usefulness in people is uncertain (Jabeen and Umbreen, 2017).

Vaccinia Immune Globulin (VIG) is a blood product that is high in antibodies against the Vaccinia virus and is made from the pooled blood of people who have had the smallpox vaccination. Although, there is no evidence that VIG is beneficial in preventing or treating symptoms of MPX infection, it may be explored in individuals with severe infection. The CDC recommends using VIG as a preventive measure in people who have been exposed to the virus but have significant cellular immunodeficiency, making smallpox vaccine contraindicated (Fowotade *et al.*, 2018).

#### **Prevention and Control**

The restriction of monkey and small African animal travel may help to keep the MPXV from spreading outside of Africa (Fowotade *et al.*, 2018). Animals with probable MPX infection (as evidenced by rhinorrhea, respiratory distress, mucocutaneous lesions, eye discharge, and/or lymphadenopathy) should be confined and kept away from humans, especially bites and scratches, as well as exposure to bodily fluids and secretions. Animals that have come into contact with an infected animal must be confined for 30 days and monitored for MPX signs. Handling ill animals or slaughtering operations with gloves and protective clothes, as well as thoroughly boiling all animal products before consuming them, reduces the risk of infection (Fowotade *et al.*, 2018). Avoiding contact with any substance that has come into contact with an infected animal, as well as exercising excellent hand hygiene after coming

into contact with sick animals or people reduces the risk of infection and dissemination (Pal *et al.*, 2017).

Preexposure smallpox immunisation is recommended for field investigators, laboratory professionals, veterinarians, and healthcare workers investigating or caring for patients with probable MPX in the case of considerable unprotected exposure to an infected animal or human. Likewise, smallpox immunisation should be given within two weeks after exposure, ideally within four days (Fowotade *et al.*, 2018). Due to the scarcity of MPX infection, vaccination of an entire population is unusual, and vaccination in groups with a high frequency of HIV infection should be approached with caution due to the danger of consequences (Pal *et al.*, 2017).

#### ***Addressing Gaps in Knowledge and Strengthening Public Health Preparedness***

The majority of MPX data now available originates from individual case or outbreak reports, as well as voluntary periodic surveillance, none of which provides a clear overall picture. The Nigerian CDC's prompt reaction to the ongoing MPX epidemic (NCDC, 2018) is an example of how a locally driven integrated human-animal disease surveillance and response system may be utilised effectively to characterise the outbreak, and it serves as a model for other African nations. Nigeria's information is very valuable for regional training and network development to increase surveillance potential, laboratory diagnosis, best public health and clinical practise, and regional competencies, to launch locally driven and responsive operations. This

will help to meet the requirement for Africa to develop public health and surveillance capacity, to lead proper surveillance, data collection, prevention, preparation, and response operations in the face of MPX and other emerging and re-emerging illnesses with epidemic potential. Increasing public health readiness and linking aggressive surveillance initiatives with priority research will necessitate concerted, domestically interdisciplinary efforts that are tightly linked to capacity building and training.

#### ***Challenges with Diagnosis, Management and Prevention of Monkeypox in Nigeria***

In Nigeria, laboratory diagnosis, treatment, and prevention of MPX disease remain difficult. Nigeria is a resource-poor country with limited facilities, technical skills, and training needed to make a diagnosis. This might be due to the disease's relative scarcity as well as a lack of political willpower in health care concerns. There is a need to promote awareness among the general population, including physicians, by disseminating correct information on the disease's risk factors, symptoms, signs, prevention, and control through legitimate channels. Handling caution should be used while dealing with animals, and these animals should be thoroughly cooked before eating. In addition, beliefs concerning MPX disease must be dispelled in diverse groups and states.

Furthermore, in order to facilitate early detection, treatment, and management of the infection, everyone should have access to basic health care through health insurance plans. It is also vital to improve political willpower in

health care concerns through legislation, infrastructure funding, staff training, and research.

### CALL TO ACTION

1. The government, at all levels, must take proactive measures to counteract the re-emergence of MPXV. States in Nigeria should get off-site assistance.
2. To assist state and LGA surveillance teams, community and LGA surveillance officers should be engaged.
3. All states should train and retrain healthcare staff on MPX Surveillance and Management.
4. In facilities and localities where positive cases have been recorded, an aggressive case search should be done.

### CONCLUSION

MPXV infection is uncommon and typically self-limiting. The infection has the potential to expand to many regions of the world in the time of globalization, with greater human mobility and cross-border animal transportation. The virus propensity to develop, the fear of it being used in bioweapons, and its re-emergence in Nigeria all add to the need for a deeper knowledge of MPX infection.

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