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A Virulent Disease Called Monkeypox: A Case Report of Countries in Africa Where The Disease is Endemic

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ABSTRACT: Cases of Monkeypox continue to rise and the World Health Organization (WHO), declared it a public health emergency of international concern (PHEIC). A virus called monkey pox causes the disease and it is zoonotic. The epidemiological surveillance from 1981-1986 in the Democratic Republic of Congo (DRC) a country in Africa were the disease is endemic, documented only 338 cases. Previously, 90% of the affected persons were children approximately 15 years of age at least in the endemic countries in Africa. Beyond Africa, 99% cases of the current outbreak were found in men and of those, 98% involved men who have sex with men implying it is being transmitted through sexual activities. Crowded living quarters, poor hygiene, discontinuation of the smallpox vaccination, amongst others were implicated in the human to human transmission. The symptoms of the disease includes, viremia with 1-2 days of fever and lymphadenopathy before lesions appear. Patients at this stage may be contagious. For treatments, there are no known clinically proven treatments for the disease. Polymerase chain reaction (PCR) amplification are used for specific diagnosis and smallpox vaccines are effective against the disease. Table 1 shows cases from Africa union member countries (AUMC), and Congo Republic, Cameroon and DRC, have a high cumulative frequency (CFR) of occurrence (43, 5.6 and 4.1%), respectively (see Fig 2). The vaccine is not readily available in these endemic countries thus, donors countries needs to collaborate with researchers and health officials to determine what these endemic countries in the global south requires towards enabling scale up in response to this disease.

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INTRODUCTION

Monkeypox is a viral zoonotic disease, caused by monkeypox virus. There are two known form of monkeypox i.e. West African and Congo Basin clades and after the eradication of smallpox, monkeypox remain an important human pathology of orthopoxvirus origin [1]. The disease was initially found in the rain forest rural areas of Central and Western Africa, until the recent 2022 outbreak. Since the cessation and usage of smallpox vaccine, there has being, rising incidence and outbreaks of this disease with concerns about the future spread of the disease. Despite higher risks in endemic countries/areas, the disease remains under-recognized and underreported [1].

Monkey pox was first identified in 1970. The first known human case occurred in the Equateur province of Zaire (now known as the Democratic Republic of Congo [DRC]) in a 9-year-old boy. Similar cases occurred in 1970-1971 from the Ivory Coast, Liberia, Nigeria, and Sierra Leone. The disease was limited to the rain forests of central and western Africa until 2003, when the first cases in the Western Hemisphere were reported. Since the most recent outbreak in 2022, the number of cases continues to increase rapidly [2].

An outbreak of monkeypox disease, was first confirmed on the 6th of May 2022 [3], in the United Kingdom [4], in an individual with travel links to Nigeria [5]. This outbreak marked the first time monkeypox has spread outside Central and Western Africa. From 18th May onwards, cases were reported from an increasing number of countries and regions, predominantly in Europe but also in North and South America, in Asia, in Africa, and in the Oceania [6]. On 23 July, the World Health Organization (WHO) declared the outbreak a public health emergency of international concern (PHEIC), raising the status of the outbreak to a global health emergency[7,8]. As of 30th July, there were a total of 22,763 confirmed cases in nearly 80 countries, with some of the countries located in the global North [9,10].

This report is on monkeypox as a virulent disease covering countries in sub Sahara Africa (sSA) were the disease is endemic, using cue from the epidemiological surveillance, etiology, pathophysiology/clinical features.

REVIEW OF CURRENT LITERATURE ON MONKEY POX

Epidemiology

Monkeypox was until recently a rare disease, bearing it was indigenous and considered endemic in some parts of the rain forests region of western and central Africa. For instance, the epidemiology surveillance reports on this disease from 1981-1986 documented only 338 cases in the DRC in an estimated population of 5 million as of 1982 [2]. Further, between 1996-1997 in the same DRC, an attack rate of 22 cases per 1000 population was reported. However, in the current outbreak 51 locations has been identified as of June 29, with Five thousand one hundred and fifteen (5115), confirmed cases, with no racial or gender predilection affecting as many male/ female [11]. In the previous outbreak in Africa, it was found that 90% of the affected persons (patients) were children approximately 15 years of age [2]. However, in the 2003 US outbreak, of the confirmed cases (n = 35), 11 patients were younger than 18 years and 24 were older [2].Male gender has also been correlated with infection risk. However, this may have been compounded by the cultural norm that men frequently hunt thus most likely to have contact with wild animals [11].

Etiology

In 1997 animals in the DRC that were caught from the wild, were tested for the monkeypox virus, and the following animals, including; domestic pig (*Sus scrofa*), Gambian rat (*Cricetomys emini*), elephant shrew (*Petrodromus tetradactylus*), Thomas's tree/rope squirrel (*Funisciurus anerythrus*), Kuhl's tree squirrel (*Funisciurus congicus*), and sun squirrel (*Heliosciurus rufobrachium*) [12], were found to have neutralizing antibodies against the monkeypox virus, suggesting a role by these animals to acts as a natural reservoirs [12]. Human to human transmission was observed earlier, but it was not as prominent as animals to humans. Factors implicated in human-human transmission are; crowded living quarters, poor hygiene, discontinuation of the smallpox vaccine, and decreased herd immunity. Moreover, respiratory droplets and direct contact with mucocutaneous lesions or fomites have also been postulated as routes of human-to-human transmission of the disease[2]. It is most probable that the current outbreak may have change the thinking by WHO officials as available evidence suggest that 99% of all the current monkeypox cases beyond Africa were in men and that of those, 98% involved men who have sex with men implying it is being transmitted through sexual activities.

Pathophysiology

The monkeypox virus is a member of the genus orthopox (family Poxviridae); other members of this same family are; cowpox, vaccinia, and variola (smallpox) viruses. It is a zoonotic virus with primary transmission believed to occur through direct contact with infected animals or possibly by the consumption of their inadequately cooked flesh. Inoculation may be from cutaneous or mucosal lesions on the animal, especially when the skin barrier is compromised and this may be secondary to bites, scratches, or other trauma [2].

The pathogenesis of human monkeypox is very similar to that of smallpox, with the exception that for monkeypox, viral entry from a wildlife source may probably occurs via small lesions on the skin or oral mucous membranes. Further, such viral entry may also occur via the respiratory tract in the rare cases of person-to-person transmission [13]. Human-to-human transmission has been confirmed as a major factor in the 2022 outbreak in multiple areas across the world. Sexual transmission of monkeypox has been observed [14]. Following viral entry from any route (oropharynx, nasopharynx, or intradermal), the monkeypox virus replicates at the inoculation site then spreads to local lymph nodes, with an initial viremia leading to viral spread and seeding of other organs. This represents the incubation period and typically this lasts for between 7 to 14 days with an upper limitation of 21 days [15].

The disease symptom onset correlates with a secondary viremia with 1-2 days of prodromal symptoms that includes, fever and lymphadenopathy before lesions appear. Infected patients may be contagious at this time. Lesions start in the oropharynx then appear on the skin. Serum antibodies are often detectable by the time lesions appear [15].

Clinical features

Historical clues for monkeypox infection such as recent travel to endemic areas, interaction with wild animals imported from endemic areas, and providing care to an infected animal or human help build a differential diagnosis, but clinical features are critical [11].

The most reliable clinical sign differentiating monkeypox from smallpox and chickenpox is enlarged lymph nodes, especially the submental, submandibular, cervical, and inguinal nodes [2].

Initial symptoms include fever, headache, myalgia, fatigue, and lymphadenopathy. Lymphadenopathy remain a key

differentiating feature of monkeypox from smallpox. After 1-2 days, mucosal lesions develop in the mouth closely followed by skin lesions of the face and extremities, including palms and soles (see **Figure 1**). The rash may or may not spread to the rest of the body, and the total number of lesions may vary from a small amount to thousands [16]. Unlike smallpox, skin lesions may appear in crops. In contrast to smallpox, the lesions do not have a strong centrifugal distribution. Necrosis, petechiae, and ulceration may be features. Pain is unusual, and, if it occurs, it is often associated with secondary bacterial infection and pruritus may occur [2].

Over the following 2-4 weeks, the lesions evolve in 1 to 2-day increments through macular, papular, vesicular, and pustular phases. Lesions change synchronously and are characterized as firm, deep-seated, and 2 to 10 mm in size [17,18]. Lesions remain in the pustular phase for 5 to 7 days before crusts begin to form. Crusts form and desquamate over the subsequent 7 to 14 days, and the condition resolves around 3 to 4 weeks after symptom onset in most cases. Patients are no longer considered infectious after all crusts fall off [17].

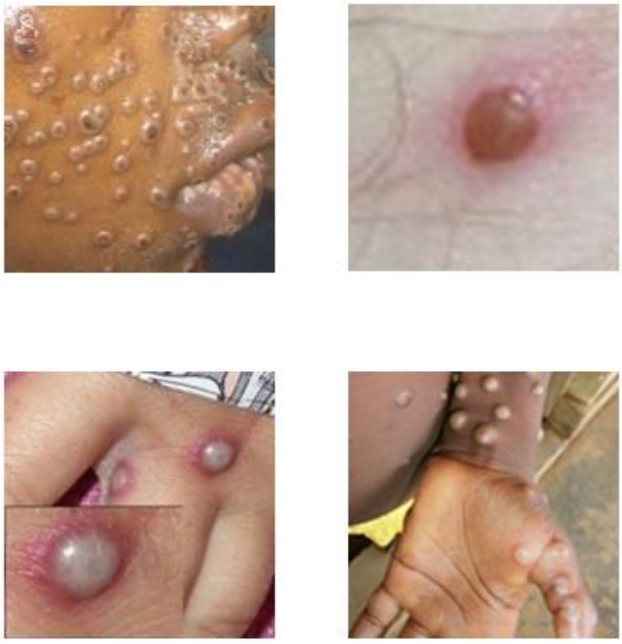

Figure 1: Image of typical monkey pox lesions. Ref: Center of Disease Control. Monkey Pox: Clinical recognition. Available from: https://www.cdc.gov/poxvirus/monkeypox/clinicians/clinical-recognition.html**. Accessed 2022 Aug 07**

TEST AND DIAGNOSIS

Diagnosing monkeypox requires tissue biopsy from an open sore, which is amplify using the polymerase chain reaction (PCR). Similarly, the disease can also be diagnosed via, blood sample to get serum for immunoglobulin (IgG or IgM). Below are some of the diagnosis method current being used. The PCR method remain the only test that distinguishes between monkeypox and related diseases enumerated below.

Differential Diagnosis

The process of diagnosing monkeypox disease is always difficult. Thus, arriving at the correct diagnosis for this disease requires the analysis of the patient history so as to eliminate errors. This is because many other closely related diseases such as; smallpox, generalized vaccinia, disseminated zoster, chickenpox, eczema herpeticum, disseminated herpes simplex, syphilis, yaws, scabies, rickettsialpox, measles, bacterial skin infections and drug-associated eruption [16,18, 19], share similar clinical features and symptoms.

Workup/Diagnosis

Current diagnostic criteria as approved by the Center of Disease control (CDC) includes:

Confirmed case

These are cases that meets one (1) or more of the following laboratory criteria:

- Isolation of the monkeypox virus in media culture from a sample obtained from the patient
- Amplification of the monkeypox virus using a PCR in a specimen obtained from the patient
- Demonstration of the orthopox virus by electron microscopy in samples obtained from the patient in the absence of exposure to other orthopoxviruses
- Demonstration of the monkeypox virus by immunohistochemical methods in samples obtained from the patient in the absence of exposure to another orthopoxvirus

Probable case

This is occurs when the individual has contact that meets current epidemiologic criteria as stated by the CDC. It is the occurrence of fever and vesicular-pustular rash, with the onset of the first sign or symptom at most or within 21 days after the last exposure, meeting the epidemiologic exposure.

Suspected case

This is when the contact that meets current CDC epidemiologic criteria including, the occurrence of fever or unexplained rash and 2 or more other signs or symptoms, with the onset of the first sign or symptom at most or within 21 days after exposure, meeting the epidemiologic criteria. Such symptoms includes; chills and/or sweats, lymphadenopathy, sore throat, cough, shortness of breath, headache and Backache [2, 20].

Moreover it is essential a viral culture is obtained from an oropharyngeal or nasopharyngeal swab. A skin biopsy specimen of the vesiculopustular rash or a sample of the roof of an intact vesiculopustule should be analyzed. PCR amplification from a patient tissue that provide DNA sequence-specific for the monkeypox virus [21,22,23,24]

Paired sera for acute and convalescent titers may be analyzed. Serum collected more than 5 days for IgM detection or serum collected more than 8 days after rash onset for IgG detection

has shown to be most efficient for the detection of the monkeypox virus infection.

A Tzanck smear can help differentiate monkeypox from other nonviral disorders in the differential diagnosis [2]. However, a Tzanck smear does not differentiate a monkeypox infection from smallpox or herpetic infections [2].

Considering the similarities between human monkeypox infection and smallpox, the "Acute, Generalized Vesicular or Pustular Rash illness Protocol" created by the CDC with the addition of lymphadenopathy to requisite primary criteria could be used to determine which patients warrant further testing [16].

TREATMENT/MANAGEMENT

Currently, there are no specific clinically proven treatments for monkeypox infection. As with most viral illnesses, the treatment is supportive symptom management. There are, however, prevention measures that can help prevent an outbreak [11]. Such preventions includes some of these measures below such that;

The infected individual should remain in isolation, wear a surgical mask, and keep lesions covered as much as reasonably possible until all lesion crusts have naturally fallen off and a new skin layer has formed. For severe cases, investigational approach can be considered using materials or compounds with demonstrated benefit against orthopoxviruses in animal studies and severe vaccinia vaccine complications. The oral DNA polymerase inhibitor brincidofovir, oral intracellular viral release inhibitor tecovirimat, and intravenous vaccinia immuno-globulin have not be proven to have known efficacy against the monkeypox virus, but may be used in patients with weakened immune system or likely to have severe illness [14,16].

When an individuals is exposed to the virus, temperature and related symptoms should be monitored twice per day for the next 21 days because that is the accepted upper limit of the monkeypox incubation period. Moreover, the rate of infection of the disease have been shown to aligns with the onset of the symptoms; therefore, someone who had close contacts but is asymptomatic need not to isolate. In some cases, post-exposure vaccination using modified vaccinia, such as Ankara vaccine (smallpox and monkeypox vaccine, live, non-replicating) is recommended. Contact between broken skin or mucous membranes and an infected patient's body fluids, respiratory droplets, or scabs is considered a "high risk" exposure that warrants post-exposure vaccination as soon as possible. According to the CDC, vaccination within four days of exposure may prevent disease onset, and vaccination within 14 days may reduce disease severity [11].

The Ankara vaccine is replication-defective vaccine modified for vaccination treatment against smallpox and monkeypox. The vaccine is a two-shot dosage, taken within four weeks apart. This modified vaccine has shown to have a superior safety profile when compared to first and second-generation smallpox vaccines. Unlike live vaccinia virus preparations, administering modified vaccinia, Ankara does not create a skin lesion or pose a risk of local or disseminated spread [16]. In addition, clinical trials have shown that modified Ankara vaccinia is safe and stimulates antibody production in patients with atopy and compromised immune systems, which are known contraindications to live vaccinia administration [19].

Complications

The complications that have been reported from the African outbreaks includes; pitted scars, deforming scars, hypo or hyperpigmentation, secondary bacterial infection, bronchopneumonia, respiratory distress, keratitis, corneal ulceration, blindness, septicemia, dehydration, vomiting, diarrhea, decreased oral intake due to painful oral lesions, and insensible fluid loss from widespread skin disruption and encephalitis [2, 20].

Prognosis

Mortality rates ranging from 1-10% have been reported in some countries in sub Sahara Africa (sSA), where the disease is endemic. However, during the 2003 outbreak of the disease in the United State of America (USA), no fatalities were reported. Several factors including; health status, co-morbidities, vaccination status, and severity of complications may have influence the prognosis in the United States and sSA as, uncomplicated cases in the USA were resolved within 2-4 weeks, with only pock scars remaining [2].

PREVENTION

Smallpox vaccination is said to confer 85% protection from monkeypox with infection being milder even several years after vaccination, and a reduction was seen in the incidence of complications [21, 22] . The CDC recommended small pox vaccination for individuals who had been in contact with infected animals or humans for even up to 2 weeks after such unprotected exposure [23]. Other preventive measures include- practice of safe sex, avoidance of crowded gatherings etc.

Cases and deaths in endemic African countries

The Africa Centres for Disease Control and Prevention has alerted several members of the African Union in May 2022 about cases of monkeypox. The director of the Africa CDC, Ahmed Ogwell, said that Cameroon, Central African Republic, the Democratic Republic of Congo and Nigeria have reported 1405 cases with 62 deaths during the first five months of 2022. The case fatality rate in these four African countries combined is 4.4% [25], of the total global death cases reported due to this disease.

In an article in "The Conversation", Oyewale Tomori pointed out that the number of monkeypox infections in Nigeria through 2021 is likely to be under-reported, this is because much of the Nigerian population has been avoiding healthcare facilities due to fear of contracting COVID-19 [26]. Nigeria's surveillance of various diseases, including monkeypox

suffered, as the country focused on the global COVID-19 pandemic in 2020 and 2021, missing many cases, resulting in a drop in the official statistics [27].

The British health authorities reported the first case of monkeypox in the UK in May 2022, and the Nigerian government released to the public information and statistics on reported cases and deaths in the country in May 2022 [27]. In the report, the Nigeria center for disease control (NCDC), stated that 230 cases were confirmed across 20 states of the federation and the Federal Capital Territory (FCT) between 2017 and 2022, with Rivers State, a state south of the Niger river being the most affected, followed by Bayelsa and Lagos, all in the south of the country. From 2017 to 2022, the NCDC reported six deaths in six different states, making for a 3.3% case fatality ratio [28]. On the 30th May 2022, the first death from monkeypox following the current outbreak, was reported in Nigeria, bearing the last time a death was reported in the country due to this disease was in 2019 [29]. On the 20th July 2022, the World Health Organization reported 5 deaths across endemic sSA [30].

The following **table 1** shows the 2022 death cases as reported from sSA, including countries with endemic monkeypox outbreak [31, 32, 37-39].

Table 1: Cases Per Country (endemic African countries)

Country	Confirm	Suspected cases	Total	No of Death	Ref
Benin	3	0	3	-	33
Cameroon	7	29	36	2	34, 38
Central African Republic	8	17	25	2	34, 4
Democratic Republic of the Congo	107	2159	2266	93	33, 38, 39
Liberia	1	4	5	-	33, 35
Nigeria	133	370	503	3	4, 33, 36, 37
Ghana	34	0	34	-	38
Morocco	1	0	1	-	38
Sudan	1	0	1	-	38, 39
South Africa	3	0	3	-	39
Congo Republic	2	5	7	3	38, 39
Total Cases = 2879					

Following the **Table 1**, the cumulative frequency of death resulting from monkeypox disease was calculated using the formular;

CFR= Death/(suspected + confirmed) x100.

The results is as represented in the **Figure 2** below. From the CFR calculation Congo Republic (43%), with a distant Cameroon (5.6%) and the Democratic Republic of Congo (4.1%) are the endemic countries with highest mortality rate occasioned by the outbreak of the current monkeypox disease.

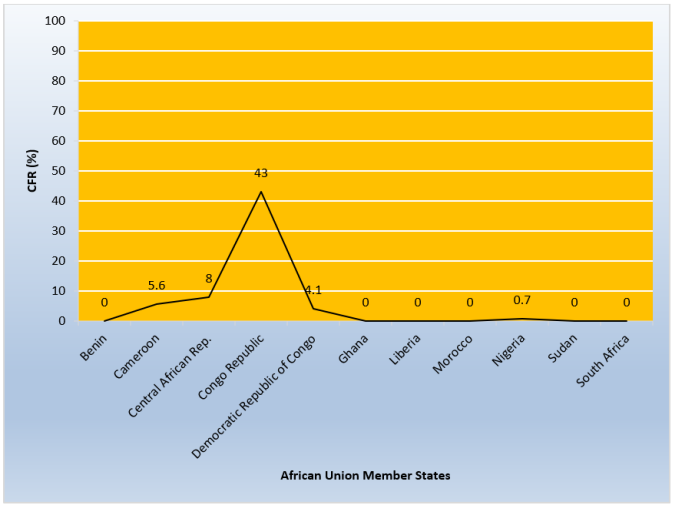

Figure 2: Cumulative frequency (CFR) of death occurrence

CONCLUSION

Some recent reports available in the literature shows the disease is spreading. Thus, it is expected that nations will work together in tackling this current outbreak and to also ensure that sufficient resource and other necessary instruments are made available to low- and middle-income countries (LMICs), especially in sSA where the disease has been known to be prevalent.

Above is even more necessary at this point as the global south especially sSA countries bear most of the burden of this disease. Studies indicated that young children, older people and those with low immunity have a higher risk of developing severe monkeypox disease. Albeit, in the current outbreak available evidence in the global north suggests, the disease has spread mainly through networks of men who have sex with men, implying the disease is spreading as an sexually transmitted infection (STI). There is currently a broad agreement amongst health officials that monkeypox is being transmitted during sexual encounters, albeit leading to

ongoing debate whether it should be classified as sexually transmitted disease (STD), mainly to avoid stigmatization, as gay or bisexual men who have sex with multiple partners seems to be at the highest risk.

The vaccines that offer protection against this disease exist, although in short supply. It is hope efforts will be stepped up for research leading to further development that would enhance prioritizing the needs of those at highest risk and deploying the same for the benefit of all. Wealthy global northern countries must be encouraged to avert vaccine competition, a mistake made during coronal virus-19 (COVID-19) outbreak.

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AUTHOR'S CONTRIBUTION

Author's contributions are as follows;

Kenneth C. Nwachukwu: Draft preparation, Data validation, Data Investigation. **Michael P. Okoh:** Conceptualization, Original draft preparation, Data Investigation, Writing reviewing and editing

ETHICS STATEMENT

The authors have taken all the necessary permissions as per ethical guidelines wherever applicable. The authors will be responsible for all the technical content mentioned in the manuscript. Journal and Publisher will not be responsible for any copyright infringement and plagiarism issue.

CONFLICTS OF INTEREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

DATA AVAILABILITY

All the key information is available in the manuscript.

FUNDING SOURCE

Not applicable

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