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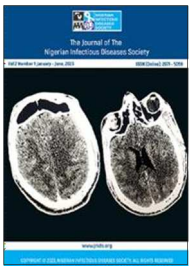

Short Communication

Clinico-epidemiological Study of Mpox in a Tertiary Hospital in Benin City, Nigeria.

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Abstract

Background: Mpox, a re-emerging outbreak-prone viral zoonosis has been reported from healthcare facilities in Nigeria. This study aims to describe a series of mpox cases seen at a tertiary hospital in Nigeria and surveillance activities undertaken in response to an outbreak in 2022.

Methods: Epidemiologic and clinical data of patients suspected to have mpox were collated using a standardised case investigation form. Appropriate specimens were taken and transported for real-time PCR diagnosis at the National reference laboratory. Data were analysed and summarized using descriptive statistics.

Results: Sixteen suspected cases reported from April 1 to December 31, had a mean age of 34.1 ± 11.5 years. Mean turn-around time for laboratory results was 10.6 ± 4.9 days. Mpox was confirmed in 7 (43.5%) cases, amongst whom the mean age was 42.3 ± 10.2 and 5/7 (71.4%) were males. Travel and animal contact history were non-contributory. Only one (14.3%) had epidemiological links with someone with rash. One (14.3%) had concurrent human immunodeficiency virus infection while three others were co-infected with varicella zoster virus. All cases presented with rash distributed variously on the face, scalp, limbs, trunk and genitals. Three (42.9%) patients had mild lesions, one (14.3%) was moderate, one (14.3%) severe and two (28.6%) serious. Three patients were hospitalised including two patients who had serious rash and one who also had neurological manifestation of headache and seizures. No deaths or secondary transmissions occurred within the hospital.

Conclusion: This study describing self-limiting disease in predominantly male urban dwellers with undetermined exposure sources contributes to the literature on mpox in Nigeria. Facility response was hampered by laboratory diagnostic delays. Decentralised testing and further research to understand transmission mechanisms of mpox are recommended.

Key words: Mpox, Epidemiology, Nigeria, Outbreak, Zoonosis

INTRODUCTION

Mpox (formerly known as monkeypox), caused by monkeypox virus (MPXV), is an outbreak-prone zoonosis endemic in Central and West Africa.[1,2] The natural reservoir of MPXV is unknown but it has a wide host range that includes rodents and non-human primates.[1] Mpox was first described in 1958, among monkeys acquired for research purposes in Denmark, and later in humans, in 1970.[3, 4] Since then, mpox outbreaks have been reported in several Central and West African countries, including Nigeria, where the disease re-emerged in 2017 after a 39-year hiatus.[5]

Human mpox is primarily contracted through the bite or scratch of infected animals and consumption of wild game including giant rats and monkeys.[1] Secondary human to human transmission occurs via close contact with skin lesions, fomites and surfaces contaminated by an infected person and respiratory droplets.[6] Studies have shown the presence of cultivable virus in semen and vaginal secretions, thus supporting a possible role for sexual transmission.[7] However, close contact, whether sexual or non-sexual, remains the dominant means for human-to-human spread.

Mpox is a deep-seated rash variously affecting the face, limbs, palms, soles and genital region. It is preceded by a flu-like prodrome of fever, intense headache, muscle aches, malaise and lymphadenopathy lasting 1-5 days.[1] The disease is self- limiting without treatment in most cases with the rash evolving sequentially from macules to papules, vesicles, pustules, and crusts which eventually dry up and fall off over the course of 2 to 4 weeks. Management, mainly supportive, reduces symptoms and averts complications including secondary bacterial skin infections, bronchopneumonia, encephalitis, keratitis, corneal ulceration and rarely blindness and permanent skin scarring. Antiviral agents that have activity against MPXV include cidofovir, brincidofovir (a lipid- conjugate prodrug of cidofovir), and tecovirimat, although these drugs are available only in developed countries.[1]

Two MPXV clades, I and II, exist, differing in human-to-human transmission potential, disease severity and case, fatality with Clade II which is found in West African countries, including Nigeria, displaying milder virulence with respect to these parameters.[1]

Hospitals are often the first location where infectious disease outbreaks are identified.[8] Therefore, these healthcare facilities must be prepared to respond in a co-ordinated fashion that promptly detects threats, provides care for the afflicted, prevents disease transmission to the workforce and other patients within the facility, and notifies appropriate public health authorities to stem community spread.[8] The re-emergence of mpox in Nigeria was detected in a tertiary hospital.[9] Nevertheless, facility-level response to this disease is sparsely documented since occurrence has been sporadic. However, with an unprecedented number of cases detected in 2022 alone, the likelihood of encountering this disease in Nigerian hospitals appears higher than ever.[10] The objective of this study is to describe mpox cases seen at the University of Benin Teaching Hospital (UBTH) in Edo State, Southern Nigeria and highlight the response activities at the facility.

MATERIALS AND METHODS

A descriptive study of all suspected cases of mpox that presented at UBTH, Benin City from April 1st to December 31st, 2022 was conducted. Benin City is the capital of Edo state in Southern Nigeria and is bounded by latitudes 6°11´ and 6°29'N and longitude 5°33' and 5°47'E. The Benin City metropolis spans across four of the 18 local government areas (LGA) in Edo state namely Oredo, Ikpoba-okha, Egor and Ovia North East.[11] The UBTH, situated in Egor LGA, is a federal tertiary hospital serving Edo and surrounding states. The hospital has an active infection prevention and control committee and undertakes disease surveillance activities through its Public Health and Community Medicine Department. It also hosts a molecular diagnostic and virology laboratory testing for several viruses, including measles, rubella, human immunodeficiency virus, hepatitis B virus, and severe acute respiratory syndrome coronavirus-2. In response to the coronavirus 2019 (COVID-19) pandemic in 2020, the hospital constituted a coordinated multi-pillared response team which was leveraged for the management of the 2022 human mpox outbreak.[12] The multi-disciplinary team was constituted with pillars for infection prevention and control/surveillance, case management, and diagnostics.

Case definitions proposed by the Nigeria Centre for Disease Control (NCDC) were used to classify suspected, confirmed, and probable cases, as well as contact persons and mpox deaths.[13] Suspected cases were defined as individuals with a history of fever, rash, and other clinical symptoms suggestive of mpox. Data including sociodemographic and clinical features of suspected cases were collected using a standardized case investigation form which was modified to include history of sexual contact with an individual with skin lesions.[13]

The facility surveillance officer was responsible for receiving reports of suspected cases, which were then notified to the state disease surveillance notification officer and the World Health Organisation state co-ordinator. All specimens were collected by trained laboratory scientists observing standard and contact transmission-based precautions. Swabs were collected from pustular lesions, and crusts were unroofed and collected using a scalpel and placed in o-ring tubes. All specimens were immediately transported to the facility molecular virology laboratory for triple packaging before referral to the National reference laboratory, Abuja, through a designated transport and logistics company.

At the National reference laboratory, swabs and crusts were subjected to real time Polymerase Chain Reaction (PCR) to detect MPXV and varicella zoster virus (VZV). Results were reported as confirmed, negative, or inconclusive for mpox with or without concurrent VZV infection. Results were transmitted electronically to the molecular virology laboratory onsite, and the turnaround time was recorded as the number of days between dispatch of patient samples and receipt of results from the National reference laboratory.

All socio-demographic, clinical, and laboratory data were entered into SPSS version 22.0 for analysis. Descriptive statistics were used to summarize the data, including means (standard deviation) and median (interquartile range) for continuous variables and frequencies and percentages for categorical variables.

This study was conducted in accordance with ethical principles outlined in the Declaration of Helsinki and approved by the Research Ethics Committee of the University of Benin Teaching Hospital. Patient identifiers were anonymized to maintain confidentiality, and data were kept in a secure location, accessible only to authorized research team members.

RESULTS

Outbreak response: Health-worker sensitization, disease surveillance, laboratory turn-around time and case management

Following an outbreak declaration by the NCDC, a one-day sensitization workshop was conducted by the outbreak response team for all cadres of health workers at UBTH, including doctors, nurses, pharmacists, laboratory workers, physiotherapists, and interns. The staff was trained on clinical presentation and recognition of mpox, specimen collection and handling, infection prevention and control (IPC) measures, and disease surveillance and notification. Attendees were encouraged to disseminate the training to their departments, particularly among clinical units.

Between epidemiological weeks 14 and 52 of 2022, 16 suspected cases of mpox were flagged by doctors in UBTH with the surveillance and case management teams duly notified. **Figure 1** shows the distribution of suspected mpox cases seen in the facility.

The male to female ratio was 1.3:1 and age range of suspected cases was 13-52 years with a median (IQR) of 34 (19) years. Seven (43.5%) cases were confirmed positive for mpox, seven (43.5%) tested negative for mpox, one (6.3%) was inconclusive and one (6.3%) patient declined testing. Table 1 shows the epidemiological profile of suspected and confirmed cases seen in UBTH.

Laboratory turn-around time ranged from 3 to 20 days with a mean duration of 10.6±4.9 days.

Five (31.3%) suspected cases (three of which were later confirmed to have mpox) were admitted on account of symptom severity and managed in isolation bays with strict barrier nursing precautions as well as linen and waste management protocols observed. Management was supportive with analgesics for pain relief and antibiotics to prevent secondary bacterial infections. All others were seen on outpatient basis and admonished to self-isolate at home. Case fatality rate was 0% as all patients recovered without sequelae. There were no reports of secondary transmission to healthcare providers or other patients.

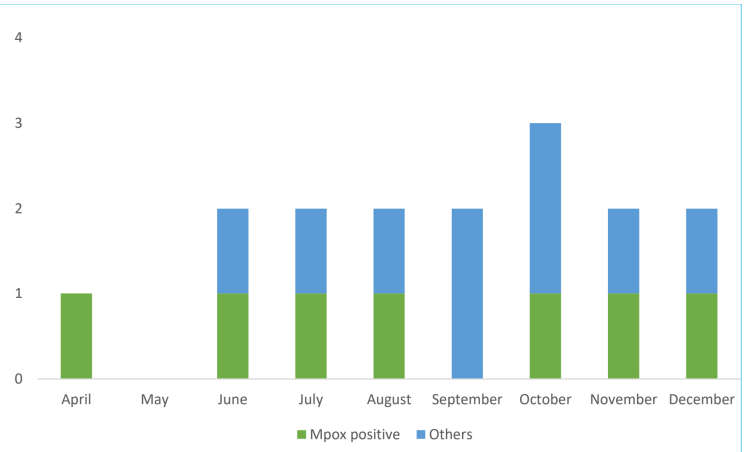

Fig. 1: Temporal distribution of suspected mpox in UBTH, April-December, 2022

Table 1: Epidemiological profile of suspected cases of mpox in UBTH, April-December, 2022

Variable	Frequency (%)	
	All suspected cases n=16	Confirmed mpox cases n=7
Mean age ± S.D (years)	34.1 ± 11.5	42.3 ± 10.2
Age group		
1-20	2 (12.5)	0 (0.0)
21-40	9 (56.3)	2 (28.6)
41-60	5 (31.3)	5 (71.4)
Sex		
Male	9 (56.3)	5 (71.4)
Female	7 (43.8)	2 (28.6)
Marital status		
Single	7 (43.8)	1 (14.3)
Married	9 (56.3)	6 (85.7)
Ethnicity		
Edo	6 (37.5)	3 (42.9)
Others[a]	10 (62.5)	4 (57.1)
LGA of residence		
Egor	7 (43.8)	3 (42.9)
Ikpoba Okha	3 (18.8)	1 (14.3)
Oredo	3 (18.8)	2 (28.6)
Ovia North East	3 (18.8)	1 (14.3)
Significant exposure risk[b]		
Present	6 (37.5)	3 (42.9)
Absent	10 (62.5)	4 (57.1)
VZV infection		
Positive	9 (56.3)	3 (42.9)
Negative/Inconclusive/Not tested	7 (43.8)	4 (57.1)

[a]Others= Owan, Etsako, Urhobo, Igbo, Efik
[b]Significant exposure risk include occupation involving work in bushes, contact with persons with similar rash
VZV= *Varicella zoster* virus

Table 2: Case series of mpox seen in UBTH, April-December, 2022

S/No	Sex	Age	Marital status	Level of Education	Occupation	Presentation	Admission	Co-infections	Outcome
1.	M	44	Married	Primary	Lumberjack	5-day history of fever and generalized painful rashes which were first observed on the genitalia with subsequent involvement of the trunk, upper/lower limbs and scalp. At presentation, rashes were widespread crusted papular lesions Lesion count: 250-300	Admitted	HIV (newly diagnosed)	Rash resolved about 24 days after onset
2.	M	40	Married	Primary	Bush Inspector/Community Land Salesman	5-day history of rashes on the genitalia (penile shaft) which later involved the trunk, axilla, face and the upper limbs. Rashes on the genitalia evolved into clear fluid containing lesions and later pustular lesions which ruptured resulting in erosion/ulcer formation with associated crusting of the lesions. There was associated swelling of the penile shaft. Lesion count: 250-300	Admitted	Nil	Rash resolved within 15 days of onset of lesions
3.	F	21	Single	Secondary	University Student	Headache (7days), Fever (7 days), Rashes (5 days) and Seizures (2 days) Headache was global, throbbing, constant but no associated redness of the eyes, tearing, photophobia or vomiting. No features of meningeal irritation. Fever was insidious in onset and became high grade but without chills or rigors Rashes were first observed on her genitalia with subsequent involvement of the scalp, face, upper limbs, the hands and feet. Rashes were pustular all at same stage of evolution. Seizures occurred 2 days before presentation, were generalized tonic-clonic with post ictal sleep. Lesion count: 50-100	Admitted	Nil	Rashes resolved within 16 days of onset
4.	F	52	Married	Primary	Petty trader (Wholesale Fufu Seller)/Trades from her home	Lesion count: Less than 25 Rash was distributed on upper limbs and face.	Outpatient	Nil	Rashes resolved within 14 days of onset
5.	M	44	Married	Secondary	Manual labourer	Lesion count: Less than 25. Rash was distributed on upper limbs and face.	Outpatient	VZV	Rashes resolved within 14 days of onset
6.	M	45	Married	Tertiary	Healthcare worker	Lesion count: Less than 25. Rash was distributed on upper limbs and face.	Outpatient	VZV	Rashes resolved within 14 days of onset
7.	M	50	Married	Secondary	Security guard	Presented with rashes on the head, face, forearms, legs and genitalia of 6 days duration and fever also of 6 days duration. Rashes said to have been observed first on the scalp, face with subsequent involvement of the genitalia, trunk, upper and lower limbs. Rashes at presentation were largely crusted erosive lesions more widely distributed on the scalp, and face with sparse crusted pustular rashes on the trunk, upper and lower limb. A solitary crusted ulcerated lesion was noted on the shaft of the penis. Lesion count: 150-200	Outpatient	VZV	Patient refused admission and was lost to follow-up

HIV= Human immunodeficiency virus, VZV= Varicella zoster virus

DISCUSSION

From April to December, 2022, we mounted a multidisciplinary response to human mpox in our healthcare facility. We carried out health worker sensitisation, recorded seven laboratory confirmed cases of mpox out of 16 suspected cases and no nosocomial transmission occurred. All confirmed cases resided in Benin City, highlighting the need for heightened mpox awareness and surveillance in the community. Between 2017 and 2021, only 10 cases of mpox were reported from Edo state (4 cases in 2017, 1 in 2018, 1 in 2019, none in 2020 and 4 in 2021).[15] This skyrocketed to 27 in 2022 alone, placing Edo 9th among states with the most confirmed cases in Nigeria.[10] Thus, about a quarter of all mpox cases detected in Edo state in 2022 (7 out of 27) were seen in our facility.

The clinical features seen in this case series are mostly similar to previously described cases of mpox recorded in Nigeria.[16] Besides the rash present in all cases, we saw a patient with seizure who was never previously known to have seizure disorder.

This presentation, though rare, has been reported sporadically including one case in Nigeria and a couple in the United States.[16, 17] Data from animal studies show that MPXV can cross the blood–brain barrier causing neuroinvasive disease although neurotropism in human subjects is not fully understood.[17]Suggested routes of entry into the central nervous system are through the olfactory epithelium and hematogenous penetration through infected monocytes/macrophages. Other serious neurological manifestations in mpox include encephalitis and coma but these were not seen in the index series.

Mpox cases seen in UBTH were predominantly adult male urban dwellers. This is in tandem with findings from a previous nationwide outbreak analysis (2017-2018) which showed a predominance of cases in urban areas involving young adult males.[18] However, compared to the nationwide analysis where the median age was 29 years, majority of cases seen in our facility were slightly older with a median age of 44 years. From the outbreak report of 2017-2018, more than 70% of the cases had no known exposure source.[18] Likewise, we were unable to ascertain how majority of cases seen in our facility contracted the disease. Two cases, being forest workers, were at high risk of occupational exposure but could not recount any direct contact with animals. Only one reported casual, non-sexual contact with someone with a similar rash. Although the data collection tool used for mpox surveillance in Nigeria does not probe for sexual exposure and practice, we specifically enquired about sexual contact with persons having a similar rash because several cases presented with genital lesions and in three cases, rash was first noticed in the genital area.

During the timeframe covered by our report, there was a concurrent global outbreak of human mpox with over 80,000 confirmed cases reported across 110 countries including many where the disease is not endemic.[1, 8] Over 90% of mpox cases recorded outside endemic regions involved gay and bisexual men within interconnected sexual networks.[19] Despite the links with sexual exposure established during the multi-country outbreak, our study did not reveal any role for sexual contact in transmission of mpox. This is possibly a limitation of the small number of confirmed cases seen in our facility.

A recent Nigerian study, however, showed a good number of affected persons reporting high risk sexual behaviour such as condomless casual sex, multiple sexual partners and transactional sex, thus supporting a role for sexual contact in disease transmission.[20] In consonance with these findings and in light of the links to sexual contact established in the global setting, it is imperative that the case investigation form currently used in Nigeria be updated to include a section that probes sexual history including high-risk sexual behaviour as this could provide the basis for public health interventions.

In this study, VZV infection was common highlighting the importance of the laboratory in making clear distinctions between mpox and similar skin lesions for both clinical and surveillance purposes. Of all differentials, VZV infection is the condition most likely to be confused with mpox.[21] Lymphadenopathy and pre-eruptive fever distinguish the exanthem of mpox from VZV but may not always be present as highlighted in our case series.[1] Additionally, VZV is characterised by regional pleomorphism whereby rashes are in varied stages of evolution; yet atypical presentations could occur.[1] Thus, reflex laboratory testing for VZV on all specimens submitted for mpox diagnosis in Nigeria is judicious, more so as co-infection with both viruses appears to be a common phenomenon as we discovered in this case series. Cases of co-infection have also been reported from elsewhere in Nigeria during the 2022 mpox outbreak and the phenomenon has been observed in a study from the DRC where mpox is caused by the more virulent Clade II strain.[22, 23]. Compared to high income countries, the burden of VZV in Nigeria and most parts of Africa is poorly characterized and there are no formal surveillance systems.[24] However, primary infection of VZV tends to occur at a later age in tropical and subtropical climates compared to temperate climates.[25] Safe and effective vaccinations for the virus exist, but are not among the routine immunizations in Africa. The decision to introduce these vaccines could be potentially guided by data on the burden of VZV in Nigeria sourced from add-on testing for VZV in suspected mpox cases.

The gains of laboratory diagnosis notwithstanding, prolonged turn-around time for laboratory confirmation of cases posed a significant challenge to our response efforts. Prompt diagnosis and expedient public health actions such as contact tracing are necessary for curbing transmission within the community.[26] In non-cases, prompt exclusion of the disease allows reappraisal of the diagnosis and further testing to ascertain the actual cause of a patient's ailment. Currently in Nigeria, a centralised approach to mpox diagnosis is adopted whereby specimens collected from peripheral facilities are sent to the National Reference Laboratory in the Federal Capital Territory. This introduces delays that undermine both clinical and public health action. The drawback of centralised, and in effect limited, testing was also experienced in high income settings during the multi- country outbreak of 2022 with sporadic testing cited as an impediment to case detection in the United States (US). This led to the US CDC's authorization of 5 commercial laboratories to commence testing and supporting them by providing the necessary test kits.[26] Nigeria, having endured a more protracted outbreak, should have by now expanded and streamlined access to testing in clinical settings.

Going forward, the country can leverage the capacity for molecular diagnosis built during the COVID-19 pandemic, [27] as well as novel, accessible technologies (such as the new mpox cartridge with recent regulatory approval for use on widely available GeneXpert testing platforms) to provide decentralised testing in states that are endemic while sporadic cases from non-endemic states are handled at a central or regional laboratory. Prompt laboratory confirmation will not only improve clinical management and contact tracing, it will strengthen surveillance and provide a more accurate picture of the burden of mpox in the country.

Diagnostics are not the only weak link in the response to mpox in endemic countries. As depicted by this study, medical countermeasures such as antiviral therapeutics and vaccines for prevention in susceptible individuals and close contacts are also lacking and were not used in any of the cases managed. Although mpox is typically self-limiting, complications can occur. There is a dire need for antiviral agents, such as tecovirimat, and vaccines, such as Jynneos, to be made available for clinical trials in the regions where they are most needed. Again, as illustrated during the COVID-19 pandemic, collective regional and global partnership, leadership commitment and investment are required for equitable distribution of countermeasures to the less developed endemic regions as the disease constitutes a global health security issue.

In conclusion, we have described a series of self-limiting mpox cases encountered in a tertiary facility in Benin City, southern Nigeria thereby contributing to the literature on disease clinic-epidemiological profile in the country. Characteristics were similar to previously reported cases in Nigeria. We leveraged on our experience with COVID-19 to tackle the mpox outbreak with satisfactory outcomes. However, health facility response could improve if testing is decentralised to allow for prompt diagnosis. Increased awareness and surveillance for the disease at both healthcare facility and community levels are highly recommended.

DECLARATIONS

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Authors' Contributions: **E.O.O**-Conceptualization, Methodology, Formal analysis, Writing-Original Draft, Writing-Review and Editing; **I.I.O**- Conceptualization, Methodology, Formal analysis, Writing-Original Draft, Writing- Review and Editing; **E.S.E**-Investigation, Resources, Data Curation, Writing-Review and Editing; **I.O.I**- Investigation, Resources, Data Curation, Writing-Review and Editing; **B.U.O**- Investigation, Resources, Validation, Writing- Review and Editing; **G.F.I**-Data Curation, Validation, Writing-Review and Editing; **D.E.O**-Resources, Validation, Supervision, Writing-Review and Editing. All authors have reviewed and approved the final manuscript.

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