Monkeypox among linked heterosexual casual partners in Bayelsa, Nigeria

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Abstract

Introduction

The 2022 outbreak of monkeypox (MPX) in the global north has been linked to sexual networks of gay and bisexual men with high-risk behaviours such as multiple sexual partners (MSP) and condomless casual sex (CCS). Studies describing potential transmissions of the monkeypox virus (MPV) via sexual contact among heterosexuals in MPX-endemic countries are lacking. We report the epidemiological and clinical features of seven cases of MPX in Bayelsa State, Nigeria who were linked heterosexual casual partners.

Methods

We conducted a descriptive cross-sectional study between June and August 18th, 2022, among confirmed and probable MPX cases seen at the Niger Delta University Teaching Hospital (NDUTH), Bayelsa during the study period. The demographic, clinical, exposure, and sexual history of the patients were documented using a structured data entry form. Case definitions were according to the Nigeria Centre for Disease Control guidelines.

Results

The seven participants seen during the study period (six laboratory-confirmed and one probable case), were between 21 to 42 years (mean and SD of 31± 8.6 years) of age, four were males, four (57.1%) were single, and all reported MSP (mean and SD of 3± 1.1 sexual partners) and CCS in the prior three months. There were three pairs of linked heterosexual casual partners who developed symptoms two to 14 days (median of 3 days) after their last sexual activity. About 86% reported a distinct febrile prodrome, and a genital rash was the primary lesion in all cases. Three (42.9%) of the seven cases reported potential exposures to the MPV before the appearance of the genital rash.

Conclusion

Our results support sexual transmission of MPV among a few heterosexual casual partners from a state in Nigeria. Further studies are required to determine the extent of sexual transmission of MPX in Nigeria, including the potential of transmission before appearance of genital rash.

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Introduction

Over 30,000 cases of human monkeypox (MPX) have been reported in 93 countries across the globe as of the 12th of August 2022.[1] About 97% of cases in this current outbreak have been among men who have sex with men (MSM), especially among those who report high-risk behaviours such as multiple sexual partners (MSP), condomless casual sex (CCS) and use of recreational drugs during sex[1][2][3]. It is now established that the major route of transmission of the monkeypox virus (MPV) in the current global outbreak is via sexual contact. While some studies have proposed potential for transmission of the MPV via genital fluids such as semen[2][4][5], the evidence is not conclusive.

As of the 18th of August, about 400 confirmed cases of MPX have been diagnosed in Africa in 2022,[1] but the role of sexual contact in the transmission of the MPV among MPX-endemic countries in Africa is yet to be established. Contact with infected animals has traditionally been the major route of transmission of MPX in some endemic countries such as the Democratic Republic of Congo (DRC) and based on a recently published study from this country[6], it seems this predominant mode of transmission has not changed. However, for Nigeria, which reported the largest outbreak of the Clade 2a of the MPV in 2017-2018, the major source and modes of transmission of monkeypox remain largely unknown.[7]

During the 2017-2018 outbreak in Nigeria, we hypothesized a role of sexual contact in the transmission of MPV among our patients in view of high rates of genitals ulcers, concomitant HIV and syphilis infections, and associated high-risk behaviours such as MSP, CCS, and transactional sex.[8][9] While describing the sexual history of MPX cases seen at our centre between 2017 and 2019[9], apart from a married couple, we could not directly link confirmed cases who were sexual partners as most of the sexual partners could not be contacted or were not available for clinical or laboratory diagnosis. Consequently, we did not provide evidence of linked casual sexual partners who were confirmed to have developed MPX following sexual activity.

In this paper, we present findings of potential transmission of MPV among linked heterosexual casual partners who were all confirmed/probable cases of MPX. To our knowledge, this is the first report of potential heterosexual transmission of MPX from Africa during the 2022 global MPX outbreak.

Methods

This was an observational descriptive study conducted between June and August 2022 at the Niger Delta University Teaching Hospital (NDUTH), Okolobiri, Bayelsa State, Nigeria. We report the clinical and epidemiological findings of a cohort of confirmed and probable MPX cases seen at the NDUTH for clinical care during the study period. The hospital did not report any cases of MPX between January and May 2022.

The case definitions and laboratory diagnosis were based on the Nigeria Centre for Disease Control (NCDC) MPX surveillance and laboratory guidelines. All confirmed cases had polymerase chain reaction (PCR) positive MPV DNA. According to the NCDC guidelines, a probable case is a case that meets the clinical case definition, is not laboratory confirmed, but has an epidemiological link to a confirmed case. We used a structured checklist to document the clinical and epidemiological characteristics of the cases, as well as their sexual history: sexual orientation, number of sexual partners in the prior three months, history of sexual activity before symptoms onset, CCS, and transactional sex. The study was approved by the ethical committee of the NDUTH, and we obtained verbal consent from study participants to take and use their clinical pictures. Study data were presented using descriptive statistics and summarised in Table 1.

Results

A total of eight patients were seen at the NDUTH during the study period, but the 8th case was excluded as the potential source and mode of transmission were unknown following a detailed enquiry. Among the seven cases in this report, six were confirmed by PCR, while the seventh was a probable case that declined laboratory diagnosis. The cases were between 21 to 42 years (mean and SD of 31± 8.6 years) of age, four were males, and four (57.1%) were single. None reported contact with animals or a history of ingestion of bush meat in the prior 1 month before the onset of their illness. All seven cases have been living in the city centre (Yenagoa) in the previous 1 year and did not report travel out of the city in the prior 1 month to their illness. None received a childhood smallpox vaccination or reported a history of associated chronic medical diseases such as Diabetes Mellitus, chronic kidney disease, or cancer. Laboratory tests for HIV, Hepatitis B, and Syphilis (VDRL) were negative in all seven cases.

All seven cases reported MSP (mean and SD of 3± 1.1 sexual partners) and CCS in the prior three months. We identified three pairs of linked heterosexual casual partners who developed symptoms two to 14 days (median of 3 days) after their last sexual activity. Six (85.7%) of the seven cases reported a distinct febrile prodrome before the onset of skin rash, and

a genital rash was the primary lesion in all cases. Three (42.9%) of the seven cases reported potential exposures to the MPV before the appearance of the genital rash.

The details of the epidemiological, clinical, and sexual histories of the seven patients are briefly outlined below and summarised in Table 1.

Case 1. A 31-year-old unmarried lady presented with high-grade fever, headache, sore throat, and malaise, followed three days later with the appearance of a pruritic vulva maculopapular rash. Due to the rapid evolution of the rash to painful vesicles, increase in the number of lesions on the vulva, and foul-smelling vagina discharge, she visited a local chemist where she was given unspecified intramuscular and intravenous medications. A few hours after these injections, she noticed the sudden concurrent appearance of similar rashes in other parts of the body, including the palms, soles, face, limbs, and upper trunk. Skin lesions were discrete, and monomorphic, except on the vulva where they coalesced to form ulcers. She was referred for treatment in our hospital because vulvar ulcers were painful and discomforting. She had a history of MSP, CCS, and had received treatment for an unknown sexually transmitted infection (STI) twice in the last six months. Within the prior 1 month to her presentation, she had CCS with two sexual partners. The sexual activity with the first sexual partner was one week before the onset of her symptoms and the partner was asymptomatic at the time of sexual activity but later complained of fever a few days after she reported her symptoms to him. She could not confirm if he developed a skin rash and this sexual partner declined public health consultation. Sexual activity with the second partner occurred on the second day of her illness when she had febrile symptoms without rash. This second partner is Case 2 described below. During her illness, she lived in a household with her parents (above 50 years) and younger siblings (below 35 years), and, following contact tracing, none were reported to develop symptoms suggestive of MPX.

Case 2. This case was identified following contact tracing of Case 1. He is a 42-year-old married businessman who developed fever, headache, muscle aches, and malaise three days after condomless vaginal intercourse with Case 1. Two days after the onset of the fever, he observed a genital rash, and then a few other discrete pustular lesions on the scalp, trunk, and limbs. He claimed not to have had any sexual intercourse with his wife since the onset of his symptoms, and his wife and three children, who live in the same household with him, did not develop any symptoms of MPX.

Case 3. A 21-year-old single unemployed lady presented with a one-week history of high-grade fever with associated headache, sore throat, and a four-day history of two pruritic rashes on the vulva which progressed from macules, papules, vesicles to pustules. A few hours following unspecified intramuscular injections from a patent medicine store, similar skin lesions appeared concurrently on the other parts of her body, including discrete monomorphic lesions on the limbs and neck. She decided to present for medical care because the vulva lesions were very painful and discomforting. Her symptoms began two days after CCS with Case 4. She also reported multiple sexual partners in the prior three months and CCS. She does not know the current health status of her previous sexual partners. She lives in the same household with her parents (above 50 years), siblings, and relatives (all below 20 years, including a child of 2 years of age). None developed symptoms suggestive of MPX.

Case 4. A 32-year-old married businessman who was identified as a sexual contact of Case 3. Two weeks prior to presentation, he first observed a penile pruritic macular rash and then developed fever, headache, malaise, and sore throat the following day. Rash later evolved into papules, vesicles, and pustules, and then crusted. Similar discrete skin lesions also developed on the limbs and trunk. At the time he presented, most skin lesions had crusted. (See figure 1). About 10 days before the onset of his symptoms, he had unprotected vaginal intercourse with a commercial sex worker. He could not tell if this sex worker had genital rash or fever. He had unprotected sexual intercourse with Case 3 on the second day of his illness. He also reported MSP and CCS in the prior three months. His wife and child remained asymptomatic, and he claimed his last sexual activity with his wife was two months before the onset of symptoms.

Case 5. A 23-year-old single unemployed lady presented on account of a 2-week history of fever associated with headache, malaise, and sore throat. Three days after the onset of the fever, she observed a single pruritic macular vulva rash. A few discrete lesions also appeared on her face and limbs, but after an unspecified intramuscular ingestion received at a patent medicine store, more lesions appeared on the vulva, face, and limbs. The skin lesions evolved from macules to papules, vesicles, and pustules. Her symptoms began two days after unprotected vaginal intercourse with her partner – Case 6. At the time of this sexual activity, the partner had a healed scar on his penile shaft. She also reported MSP in the prior three months and one of her more recent casual sexual partners was said to have also complained of fever and genital rash. However, she declined to provide further information about this partner to enable contact tracing. She lives in a household with two of her sisters (below the age of 35 years) and none of them developed symptoms suggestive of MPX.

Case 6. A 42-year-old married businessman who was a sexual contact of case 5. This one is a probable case as he consented to clinical evaluation and clinical photos but declined laboratory testing. His symptoms began about six weeks before presentation and about two weeks after condomless vaginal intercourse with a casual partner. He claimed this sexual partner was asymptomatic at the time of sexual activity. He developed fever, malaise, and body weakness, accompanied by genital and facial papular skin rashes occurring at about the same time. Skin lesions were discrete and fewer than ten. He sought medical attention from a private hospital and was given several unspecified oral medications and an intramuscular injection for the treatment of a suspected STI. He could not remember if the skin lesions worsened after the intramuscular injection. He claimed all skin lesions had healed (See figure 1) before he had unprotected vaginal intercourse with Case 5. He also reported MSP and CCS in the prior three months, including sex with his spouse about three weeks before presentation. His wife and three children did not report any symptoms suggestive of MPX.

Case 7. A 27-year-old single oil rig worker presented 12-days after the onset of symptoms. He first observed a pruritic macular rash on his penile shaft three days after condomless vaginal intercourse with a commercial sex worker. On the same day he noticed the skin rash, he also developed high-grade fever, malaise, sore throat, and headache. Thereafter, discrete skin lesions appeared on other parts of the body including the face, limbs, and trunk. Skin lesions evolved from macules to papules, vesicles, and pustules, which later crusted. He also developed an episode of watery diarrhoea which

resolved following ingestion of unknown oral drugs. He claimed to have noticed healed hypopigmented scars on the skin of the groin and buttocks of the commercial sex worker during the last sexual activity. He could not provide the required information of this commercial sex worker for contact tracing. He also reported MSP, CCS, and treatment for STI in the prior three months. He stays alone and has shared the same space with colleagues at his office during his illness. However, he is not aware of similar skin lesions among his co-workers.

Discussion

To our knowledge, this is the first report of MPX among linked heterosexual casual partners from Africa.

We believe that all seven cases acquired their infection from sexual activity in view of the temporal relationship between the last sex and development of symptoms, location of primary lesion on the genitals, the predominance of lesions in the genital area, and history of risky behaviours such as MSP, CCS, and transactional sex. Based on the reported clinical symptoms before and during the last sexual activity, it is plausible that transmission via sexual activity occurred in multiple scenarios, including asymptomatically (Case 1 and 7), before the appearance of noticeable genital or skin rash (Case 2), during the early phase of genital rash evolution (Case 3) and after healing of the skin or genital rash (Cases 5 and 7). In an earlier study, we reported potential transmission of MPV before the onset of the skin or genital rash in a couple from Nigeria.[9] If asymptomatic or pre-skin rash transmissions occurred in some of our cases, then it is probable that the MPV was transmitted via infected bodily fluids such as genital secretions or through infected respiratory droplets following prolonged face-to-face contact during sexual activity. Viral shedding from genital skin before the rash becomes noticeable is possible and warrants future investigations. However, it is probable that during the last sexual activity, skin or genital rash was unrecognisable by the patients because lesions were in the very early phase of evolution. The suspected transmissions from healed skin lesions that had apparently desquamated might indicate a potential for viable MPV to persist on the skin even after apparent healing has taken place. However, the reports of desquamated skin lesions were based on the patient's account and therefore subject to recall and observer bias. Independent of genital rash, it is also probable that the virus was also transmitted from infected genital secretions after recovery since prior studies have shown that viral shedding in semen could occur for up to 19 days after the onset of symptoms, and replication-competent virus could persist in the semen for up to six days after symptoms.[4]

Most cases in our study had a distinct febrile prodrome, and a short incubation period: a median of three days (range of two to 14 days) before their first symptom. In the pathogenesis of MPX, viral prodromes have been linked to secondary viraemia[10], and the distinct febrile prodrome observed among our cases could indicate a predominant systemic infection following sexual contact. The shorter IP suggests that secondary viraemia occurred very early after sexual contact possibly because sexual activity might represent a type of 'complex invasive exposure' associated with breaking of skin that was previously proposed to be associated with more pronounced systemic symptoms and shorter IP.[11] The short IP could also indicate early and direct inoculation of the virus to the blood from the genital tract during sexual activity. Recent

reports of asymptomatic detection of MPV in anogenital swabs[12][13], the suspicion of genital reservoirs for the MPV[4], and the apparent overrepresentation of the genital skin in the clinical manifestation of MPX in our patients further expound a role of the genital tract and or genital secretions in the pathogenesis of MPX, deserving further confirmatory studies. The zero secondary attack rate among household members of the MPX cases in our study is noteworthy and could imply a limited role of non-intimate contact in the transmission of MPX within households. However, we could not exclude transmissions that led to asymptomatic or mildly symptomatic MPX infections that were not recognised or reported by household members.

Our findings regarding the number of skin lesions, risky behaviours, and location of primary lesions on the genitals, are comparable to studies from the global north.[2][3][14] However, none of our cases reported anorectal skin rash or proctitis which could imply receptive anal sex was not practiced by the cohort reported in our study. Three of our cases noticed a worsening of their skin lesions following intramuscular injections. It is necessary for future studies to explore the potential of IM injections to cause a flare-up of skin lesions among MPX patients.

None of our patients belonged to the LGBTQ social group and none reported same-sex or bisexual orientation. Our finding of MPX among male and female heterosexuals who report high-risk behaviours is against the notion in some quarters that the current MPX outbreak is only a challenge for gay and bisexual men[15], or that sexual activity plays no role in the outbreak in Africa. Similar notions were held during the early stages of the HIV pandemic[16], but today the challenge of HIV/AIDS is most devastating among heterosexuals in developing countries of Africa.[17] In view of our observations of the refusal of some sexual partners to present themselves for clinical consultation and diagnosis, preference for patent medicine stores for treatment, and atypical presentation of MPX as genital rash, it is probable that many cases of MPX acquired via sexual contact are getting missed in Nigeria. The MPV is probably circulating silently in Nigeria and other African countries, but unfortunately, as it was with antiretroviral drugs and the HIV/AIDS pandemic, it seems that African countries will have access to MPX-countermeasures such as vaccines and therapeutics only after the global north will have controlled their outbreak.

Our study has some limitations. First, we report only seven cases of MPX, which as of the 18th of August is about 4% of the total MPX cases reported in Nigeria in 2022. Although we are not aware of prior published studies investigating transmission of MPV via sexual contact during the 2022 outbreak in Nigeria, our findings from a single centre in Nigeria could be an exception and is therefore not generalisable to the whole country or to Africa. Second, the lack of animal contact does not completely exclude exposure to rodents, which are known to be very prevalent within and around households in Nigeria.[18] Third, we could not confirm MPX via laboratory diagnosis in the probable case and were not able to identify sexual contacts for some cases who had sex with commercial sex workers. Fourth, genomic sequencing results of the cases were not available at the time of this report to confirm similarities in the MPV sequences that would support the same origin viral source among the linked sexual partners.

Conclusion

Overall, our study supports our prior hypothesis in the 2017-2018 outbreak where we proposed transmission of MPX via sexual contact in some parts of Nigeria. Additionally, in this study, we report potential transmission of MPV among linked heterosexual casual partners who report high-risk behaviours. These findings call for more enhanced surveillance to identify and understand the role of sexual activity in the transmission of monkeypox in Nigeria.

Tables and Figures

Table 1. Epidemiological and clinical characteristics of monkeypox in seven linked heterosexual casual partners in Bayelsa, Nigeria

Study variable	Monkeypox cases						
	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Age (years)	31	42	21	32	22	42	27
Sex	Female	Male	Female	Male	Female	Male	Male
Marital status	Single	Married	Single	Married	Single	Married	Single
Time interval between sexual contact and first symptom (IP)	7 days	3 days	2 days	10 days	2 days	14 days	3 days
First symptom	Fever	Fever	Fever	Genital rash	Fever	Fever	Genital rash and fever
Location of initial rash	Genitalia	Genitalia	Genitalia	Genitalia	Genitalia	Genitalia and face	Genitalia
Type of rash	Discrete monomorp hic nongenital lesions, coalescing genital lesions	Discrete monomor phic genital and nongenital lesions	Discrete monomorp hic genital and nongenital lesions	Discrete monomor phic genital and nongenital lesions	Discrete monomor phic genital and nongenital lesions	Discrete monomorp hic genital and nongenital lesions	Discrete monomor phic genital and nongenital lesions
Other body sites affected	Limbs, Trunk, Face, Sole, and Palm	Face, Arm, Trunk, Scalp	Arm, Trunk, Legs	Leg, Arm, Trunk	Scalp, Ear, Arms, Trunk, Limbs	Face, Legs	Arm, Trunk, Legs
Lesion count	80 – 100	<10	50-79	20-49	80 – 100	<10	50-79
Lymphadeno pathy	Inguinal	Submenta l, axillary, inguinal	Submandib ular, axillary, inguinal	Inguinal	Inguinal	Unknown	Inguinal
Complication	Secondary bacterial skin infection	Nil	Nil	Nil	Secondary bacterial skin infection		Nil
Number of sexual partners	3	4	3	3	4	6	3
Sexual History*	MSP, CCS, prior STI, vaginal receptive sex	MSP, CCS, vaginal insertive sex	MSP, CCS, prior STI, vaginal receptive sex	MSP, CCS, vaginal insertive sex	MSP, CCS, prior STI, vaginal receptive sex	MSP, CCS, prior STI, vaginal insertive sex	MSP, CCS, prior STI, vaginal insertive sex
Symptoms of sexual partner before or during last sexual activity	Asymptom atic	Fever	Pruritic macular rash	Unknown	Healed genital rash	Asymptom atic	Healed genital rash

* Sexual history in the prior three months, IP-incubation period, MSP-multiple sexual partners, CCC- condomless casual sex, STI-sexually transmitted infections

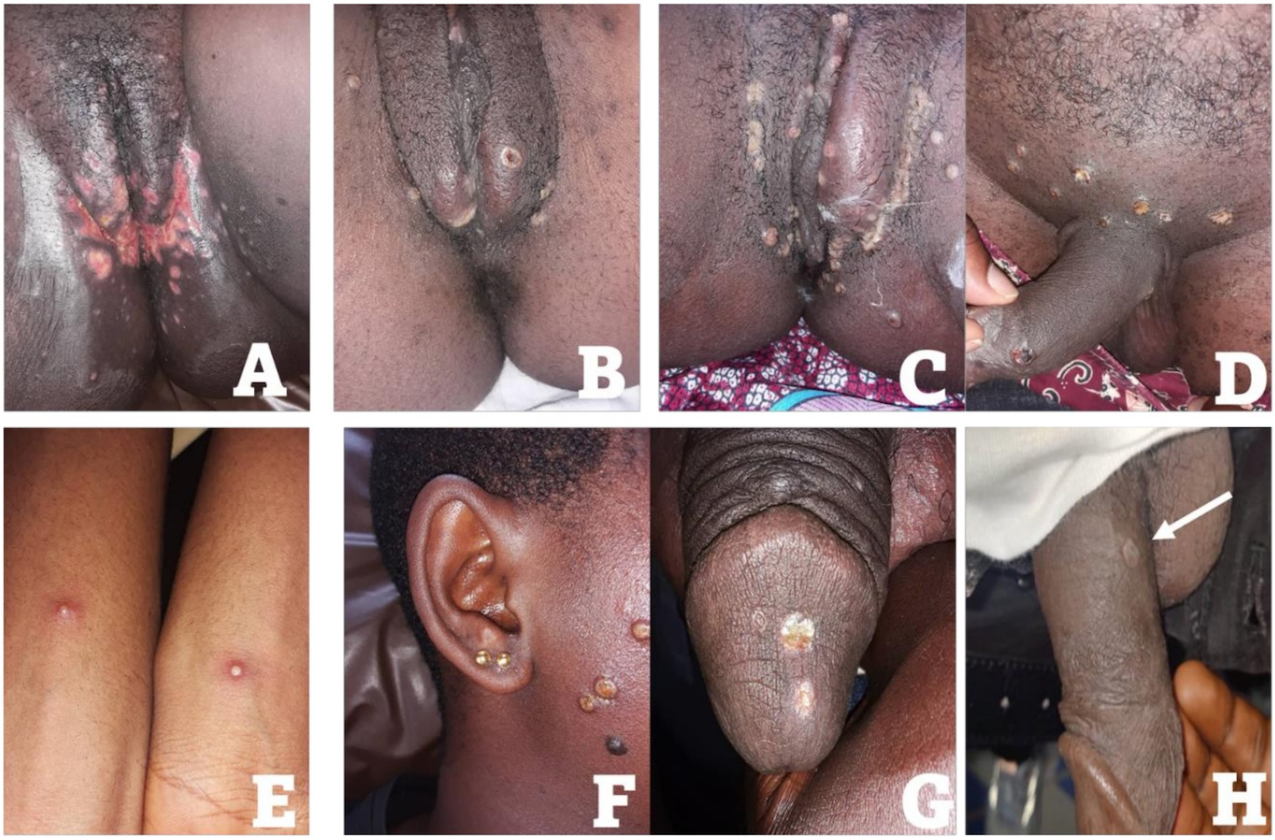

Figure 1. *Genital and non-genital skin lesions of monkeypox among heterosexual casual partners in Bayelsa, Nigeria: A-Case 1- coalescing vulvo-vagina ulcers. B-Case 3, Discrete umbilicated pustular vulva lesions, C- Case 5- Vesiculopustular vulvovaginal lesions with crusting. D-Case 7- Multiple discrete pustular lesions on penile shaft and groin. E-Case 1-Discrete vesiculopustular lesions on lower limbs. F-Case 5-umbilicated crusted pustular lesions on face and ear. G. Case 4- scabbed and desquamating genital lesions. H Case 6- hypopigmented macular scar on penile shaft (arrow) following healing of a previous genital rash.*

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