Nigerian Medical Journal
NIGERIA MEDICAL ASSOCIATION
Print ISSN 0300-1652, E-ISSN 2229-774X

Review Article

Systemic and Dermatologic Impact of Mpox: An Overview of Guideline-Based Management for Nigerian Healthcare Workers

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Abstract

Monkeypox/Mpox is an Orthopoxvirus infection of the skin and mucous membranes in the same family as smallpox virus. Infection mainly affects the skin, but the eyes, lungs, brain, gastrointestinal tract, and other organs may also be involved to varying degrees. This narrative review on the systematic and dermatologic impact of Mpox is meant for healthcare workers, providers of social services, community leaders, religious leaders, staff of schools, influencers, and institutions. This is in a bid to bring them up to date with the clinical protocol involved in the diagnosis, management, and prevention of the spread of Mpox.

Data and other pieces of information used in this review were accessed from PubMed, Google Scholar, and situation reports from the website of the Nigerian Centre for Disease Control (NCDC), the World Health Organization (WHO), and the Centre for Disease Control and Prevention (CDC). The search date was from 1980 to May 2022. Prompt recognition and diagnosis were found to be predicated on a high index of clinical suspicion while diagnosis can be confirmed through viral DNA polymerase chain reaction tests.

The management of Mpox involves a multidisciplinary approach with Dermatologists playing a central role alongside other specialists and experts as it affects diagnosis, management, and follow-up. The Government should provide an enabling environment for surveillance, notification, and research of this global infection. Since the clinical presentation of Mpox is regularly changing, a regular review of the available guidelines is recommended.

Keywords: Dermatology; Mpox; Skin Health Advisory.

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How to cite this article: Oiwoh SO, Ibekwe.PU, Ajani A.A, Cole-Adeife O M, Olanrewaju F.O, Oripelaye MM, Akinboro AO, Akinkugbe AO, Mohammed TT. Systemic and Dermatologic Impact of Mpox: An Overview of Guideline-Based Management for Nigerian Healthcare Workers. Niger Med J 2023;64(1):4-12

Quick Response Code:

Introduction

The term "Mpox" refers to a viral skin infection that was initially identified as a smallpox-like skin condition in experimental monkeys in Denmark in 1958 [1] The virus belongs to the genus orthopoxvirus, the same as the smallpox virus that was eradicated over 40 years ago.[2-4] Mpox mainly affects the skin and mucous membranes, but the eyes, lungs, brain, gastrointestinal tract, and other organs may also be involved.[3]

It was recently declared a public health emergency of international concern although it has been endemic in Nigeria and Africa with epidemic potentials debated. [5-10] With a surge in the national and global burden, there is a need for a well-written review of the literature on Mpox. This is a narrative review of the systematic and dermatologic impact of Monkeypox, which aims to bring health workers and stakeholders up to date with the clinical protocol involved in the management of Mpox. The target audience includes healthcare workers (primary and secondary healthcare levels), medical health educators, providers of social services like the staff of prisons, hospice facilities, and orphanages, community leaders, religious leaders, management and staff of schools, influencers, and institutions.[11]

Methods

PubMed, Google Scholar, and situation report from the websites of the Nigerian Centre for Disease Control (NCDC), World Health Organization (WHO), and Centre for Disease Control and Prevention (CDC) were reviewed from 1980 to May 2022. Search terms such as “Monkeypox”, “Monkeypox outbreak”, “Monkeypox and Nigeria”, “Monkeypox and skin”, “Monkeypox skin health advisory”, “Monkeypox public health advisory”, “management of Monkeypox for health workers” were used. Case reports and situational and technical reports on Monkeypox with specific information about the Nigerian population were juxtaposed with the national guideline to provide the needed insight.

Discussions

How Is Mpox Transmitted?

Mpox can be spread from one infected person or animal to another through face-to-face contact (via salivary and respiratory secretions), contact with fluids or crust from broken skin/sores, contaminated surfaces (including clothing and beddings that have been in contact with the infected rashes or raw areas), and sexual contacts have also been documented.[3,4] Spread from infected animals to humans occurs through bites and scratches, inappropriate handling of meat from infected animals (like bush meat), and consumption of inadequately cooked meat of an infected animal. It must be noted that Mpox rashes remain contagious till they are cleared. [3,11]

What Are the Possible Reservoirs of the Infection?

The reservoir of the Mpox virus is still unclear, but the virus has been isolated from rope squirrels and mangabey monkeys.[12,13] Other suspected reservoirs are Gambian pouched rats, dormice, and non-human primates.[14]

Risk factors of the Mpox Infection

Risk factors for Mpox infection include forested areas, males, persons younger than 15 years, and those without prior history of smallpox vaccination. Occupational risks include hunting, trading in wild animals, people who prepare these animals for sale, and healthcare workers especially those who interact with Mpox virus-infected patients and their samples (doctors, nurses, and medical laboratory scientists, among others).[3,5,15]

Populations at risk of severe Mpox infection include pregnant women, the immunocompromised, those with background some skin disorders, and those co-infected with other viruses or bacteria. Skin disorders that can predispose to severe Mpox infection include atopic dermatitis, psoriasis, and exfoliative dermatitis. Viral co-infection including herpes simplex virus, varicella-zoster virus, and human immunodeficiency virus (HIV) have also been documented as a risk for severe Mpox infection.[16]

The Skin and Mpox

Mpox infection is mainly observed on the skin; thus, patients stand a great chance of stigmatization and disfiguring scars if prompt and adequate care is not taken. Additionally, its tendency to cover the entire skin surface can create a lot of anxiety and emotional distress for the patient.

For a better understanding of the infection and its associated complications, knowledge of the skin's structure and function is imperative. The skin is the largest organ in the body and, among other things, acts as a barrier and defence. Any breach of these functions puts the entire body at risk. Furthermore, the skin can fail, just like other internal organs.[17]

To maintain health and proper function, the skin is in a perpetual state of self-renewal. Its outermost (corneal) layer is shed and replaced by new cells from the innermost (basal) layer outwards through a process called keratinization. This process normally takes about 28 days, and this possibly explains the duration from eruption to resolution in promptly treated Mpox infection. [3,18] The process of healing can however be prolonged if the skin is perturbed in other ways, for instance by scratching or secondary bacterial infections.

Among the cells of the skin are melanocytes, which produce the pigments that are responsible for skin colour. The release of melanin from melanocytes, due to manipulations that follow the itching, can explain the subsequent post-inflammatory hyperpigmentation (darkening of the skin after the infection).[19]

What Are the Points of Entry to Healthcare workers?

Patients with Mpox can get into health facilities through the following clinics: dermatology, sexually transmitted infections, general outpatient, paediatrics, obstetrics and gynaecology, medical outpatients, and surgical outpatients' clinics [11] They may also be admitted through emergency departments and primary health centres.

What Are the Clinical Manifestations of Mpox that Health Professionals Should Pay Attention to?

Constitutional (non-specific) symptoms, such as fever, body ache, lymph node enlargement (lymphadenopathy), sore throat, body weakness, vomiting, muscle pain, back pain, and headaches (which may be intense) are usually the first symptoms of the disease. Thus, at the onset, the symptoms of Mpox may resemble those of other common infectious conditions, such as malaria and respiratory tract infections. This is called the prodromal phase of the infection, and the severity of these symptoms varies from person to person, depending on age and level of immunity. After 0–5 days of this phase, the characteristic skin rash occurs.[1,3] However, there are few reports of patients who did not experience this prodromal phase.[1]

Typically, the skin rashes begin on the face and subsequently extend to the legs, chest, back, arms, palms, private parts (genitals), and bottoms of the feet. Mpox affects the palms and soles in 75% of cases.[3] It can also affect the conjunctiva of the eyes. Typically, the rashes begin as macules (small, flat rashes), and then evolve to become papules (small, raised rashes without fluid), then vesicles (raised rashes that contain fluid), before finally proceeding to the desquamation stage (during which the skin peels and is shed).[3] Mpox lesions are usually at the same stage on the body region on which they appear, and they slowly progress to the next stage, unlike chickenpox, in which the lesions are at different stages of development.[3,11,19]

The distinctive typical rash pattern (starting on the face), involvement of the palms and soles, and enlarged lymph nodes (particularly on the neck) all work together to aid in diagnosis. Those who have engaged in sexual activity with an infected person may also have the rash begin on their genitalia. [3,11,19] The symptoms and signs of Mpox typically take 2–4 weeks to resolve, but they may take longer if the patient is immunosuppressed.[19,20] Until the crusts and scabs clear, the patient can still infect others.

Mpox infection can get complicated when the lungs, brain, and eyes are involved. Such infection further worsens bacterial infection (sepsis) that may be superimposed on the rash.[3] Other factors that can

predispose to the severe disease include the involvement of a large body surface area, immunosuppression (as in infection with HIV), and varied morphology (appearance) of the rash, with particular reference to nodules. [3,19,20]

What Are the Uncommon Presentations of Mpox?
Genital rashes, solitary rashes, a non-centrifugal pattern of rashes, and anal mucositis and bleeding are some of the recently reported atypical manifestations. [19] Genital ulcers have been documented among Nigerians in the past and have recently appeared in literature from non-endemic regions of the world. [1,19] These atypical presentations call for a circumspect review of patients who present to primary, secondary, or tertiary health facilities.

What Is the Fate of People with Mpox Infection?
Typically, the infection follows its course and ends on its own with little to no fatality. This is especially true for the types of Mpox that are seen in this environment (clade IIa) which can be associated with significant morbidity. This morbidity can cause absenteeism from work and school, loss of income, social stigma, depression, and isolation.

What Are the Strategies for Safe Clinical Evaluation and Disease Control?
All healthcare workers are expected to apply all infection prevention and control (IPC) precautions by the Nigeria Centre for Disease Control (NCDC) in the triage, diagnosis, and management of all suspected and confirmed cases of Mpox infection. [3] Additionally, the reviewing clinician must conduct an in-depth review of all cases. Case investigation and notification must be performed for all confirmed, probable, and suspected cases of Mpox. [3] This will allow proper cataloguing of cases and the institution of appropriate protocols to prevent further spread. The case investigation form of the NCDC [3] is recommended as a guide for this process although it needs to be reviewed to accommodate the changing epidemiological pattern, increasing incidence of the disease in persons with homosexual orientation, and atypical presentations.
How Should Mpox Be Clinically Managed?

The management of Mpox involves the acquisition and management of patient information, determination of patient's immunity status, clinical history taking, examination, evaluation of comorbidities, disease treatment, and vaccination among others. The framework of the public health response and guidelines by NCDC in 2019 and WHO in 2022 have provided templates for management.

Patient's information/Sociodemographic Data
Patients need to be assured of the confidentiality of their information. They also need to give consent for its extraction and use. Since pictures or videos may need to be taken to aid diagnosis, the patient needs to give consent for his/her photograph to be taken and/or published or presented at scientific gatherings that are aimed at information sharing as a strategy for controlling this outbreak. For home-based care through teledermatological consultation, videos or photographs should be reviewed with the patient for comparison of the rash at each consultation for the patient's assurance and needed clinical progress.

Pregnancy status, gestational age during infection, fetal death, and stillbirths, need to be documented. If death occurs, the date and place of death, and the number of days spent on admission (if admitted) need to be stated. Detailed information on death is indispensable, as a rapid increase in death may be a quick signal to possible infection with the more severe clade 1. However, all patients reported in Nigeria have been infected with clade 2a.[15] History of smallpox vaccination, complications, and vaccination scar are equally important. The scar is indicative of immunity to smallpox and likely cross-immunity to Mpox. If the patient was referred from a facility outside the reporting hospital, the location of the referring facility should be specified.

Clerkship of the patient

Because of the nature of this infection and its many mimics, some salient features should be noted during quick clerkship and examination. This will help to ensure a more focused consultation or review, depending on the point of entry of the patient.

Information on location, history of travel and type of contact (direct or indirect) need to be stated clearly. Direct contact includes contact with secretions (respiratory droplets, blood, fluid from rash, urine, semen, and saliva), while indirect contact occurs through infected belongings, clothing and linen, etc. Questions about sexual transmission and the sexual activities the patient has engaged in should be asked. This should include sexual orientation (heterosexual or homosexual), the date of the last contact, the presence of a cutaneous eruption/rash, the date of onset of the rash, history of preceding fever, date of onset of the fever, and the number of days fever stays before or after the onset of rash in the patient and their contact(s).
Examination of the Mpox patient.

Mpox lesions can present as either primary or secondary lesions, each type with its peculiar impact on the disease outcome. Primary skin lesions of Mpox include macules, papules, vesicles, pustules, and nodules. Pustules are often due to bacterial infection of the rash and can be associated with background papules, and vesicles; hence, the vesiculopustular designation of the rashes of Mpox. They may also be associated with nodules (raised rash without fluid that is more than one centimetre) and pustules, in which case the rash can be described as a nodulopustular eruption. The extent of Mpox infection, involvement of the skin, and associated comorbidities can determine the nature of the rash. Nodular involvement is not frequently reported, although some Nigerian reports have documented this morphology. [19,20] These researchers found nodular Mpox rashes to be associated with HIV infection when they are larger and last longer [19,20]

The severity of Mpox infection has also been related to the number of lesions; therefore, particular attention should be paid to the number of skin lesions present during the examination, which should be done under bright light. The lesions may be solitary or multiple on various parts of the body. The number may be grouped as follows: 0–10, 11–20, 21–30, 31–40, 41–50, 51–100, 101-250, 251-500, 501–1000, and >1000. The rash burden will help with prognostication of the infection. [1,19,20]

The rashes may be monomorphic (lesions of the same form) or polymorphic (various forms).[19] Their morphology, symmetry, distribution, and body parts that are exempt from the rashes are also important features that will help to differentiate Mpox from its various mimics. For instance, chickenpox is known to occur in crops at various stages of development, although papules and vesicles are the major findings. Contrariwise, Mpox has been documented to occur in crops of the same morphology on the same body parts at the same time.[3]

Secondary lesions can be useful in the diagnosis and prognosis of infection. They also give an insight into the degree of manipulation of the primary rash that can occur through scratching, hot fomentation, scraping, or peeling. Examples of secondary lesions include crusts and scabs, excoriations, vegetations, lichenifications, and post-inflammatory discolourations. These, as well as scars, should be documented if present. Lichenification is the leathery appearance of the skin, which may occur in patients with longer duration or prominent itching and scratching of the rashes. Post-inflammatory changes include hyperpigmented (darker than normal skin) or hypopigmented (lighter than normal skin) macules and patches, and atrophic scars. Pitted scars, hypertrophic scars, and keloidal transformation can also complicate Mpox rashes.[19]. Oral ulcers and sore throat can also occur, hindering swallowing and the adequate nutrition that is needed for an appropriate immune response to such a self-limiting viral infection as this. Anal mucosal ulcerations, proctitis and anal bleeding associated with Mpox virus infection have been documented in patients who engage in anal intercourse which results in severe pain and difficulty with defecation. [21]
Lymphadenopathy is of diagnostic importance [3,22-25], especially in association with the typical rash and its distribution on the palms and soles. Cervical, inguinal, or axillary lymph nodes may be involved. For a

wider perspective, it is good to note that secondary bacterial infection of any rash can also present with regional lymphadenopathy.

How Is Mpox Diagnosed?
A high clinical index of suspicion is the first step in the diagnosis of Mpox. Diagnosis is confirmed by polymerase chain reaction. Other tests are virus isolation by cell culture, enzyme-linked immunosorbent assay, and antigen detection tests.[3]

Whom Are Those Involved in the Detection and Treatment of the Disease?
The detection and treatment of Mpox is a collaborative effort of health professionals that cuts across humans, animals, and the environment - One Health approach. This transdisciplinary approach is important for disease-effective surveillance and control.[3] Concerted efforts by these teams will ensure a timely break in the chain of transmission.

What Role Does a Dermatologist Play in the Diagnosis and Management of Infection?
For successful national and global Mpox diagnosis, care, control, and eradication efforts, Dermatologists play leading roles. [22] This is more imperative, bearing in mind the recent increase in the reports of atypical cases outside Nigeria, and the plethora of differentials that may mimic the disease.[22]

Depending on its stage of development, Mpox rash may mimic various other skin rashes, such as measles, scabies, chickenpox, impetigo, syphilis, and molluscum contagiosum. With facial involvement, acne vulgaris, particularly nodulocystic acne (that affects the face, upper chest, and back), lepromatous leprosy (nodular involvement of the face), an acute flare of rosacea, and neurofibromatosis may be close differentials. Fulminant acne, with its similar symptoms to the prodromal symptoms of Mpox, may also be confused with Mpox at the early stage of facial involvement (that is, before centrifugal involvement of other parts of the body). With secondary lesions like crusts forming on the face, rashes with impetiginisation and centrofacial orientation (such as rosacea, leishmaniasis, and trichoepithelioma) may be close differentials. The differentiating features therein include loss of sensation in Hansen's disease, involvement of other seborrheic (oil-bearing) areas in acne vulgaris, café au lait macules in neurofibromatosis, and Shagreen's patch and ash leaf macules in tuberous sclerosis.

Similarly, knowing that umbilicated rashes are not exclusive to Mpox, other differentials of umbilicated rashes should also be considered. These include molluscum contagiosum, cutaneous cryptococcosis, disseminated histoplasmosis, smallpox, and penicilliosis.[21] However, the differentiating factor is the immunosuppression that is more commonly associated with disseminated histoplasmosis and cutaneous cryptococcosis. Furthermore, if Mpox presents with only genital rashes or genital ulcers (following ruptured lesions), it needs to be differentiated from other mimics of genital ulcer disease, like genital herpes, secondary syphilis, lymphogranuloma venereum, and chancroid. Associated pain, ulcers, and groups of rashes tilt the diagnosis toward genital herpes. Moreover, genital herpes is not known to affect the palms and soles. Syphilis can present with a solitary ulcer like in some cases of Mpox,[11] and the base of a syphilitic ulcer is not as clean as what is seen in genital herpes. Like Mpox, secondary syphilis affects the palms, but syphilis does not involve the face as seen in Mpox. Non-infectious causes of genital ulcers like Behçet syndrome, Stevens–Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN). However, for SJS and TEN, a history of drug use (penicillin, sulfonamides, nonsteroidal anti-inflammatory drugs, anticonvulsants, etc.) can easily be elicited; the rashes may affect a relatively larger body surface area.

What Are the Principles of Management?
Generally, the care for patients with Mpox should focus on the structural and functional integrity of the skin and mucous membranes, rehydration, symptomatic treatment, adequate dietary intake, treatment of complications, psychosocial support, treatment of comorbidities/co-infections and post-mortem care. [3] Particular attention should be given to the intertriginous areas which are relatively prone to macerations, hence appropriate vehicles of topical medications must be chosen. Powder as a vehicle of drug delivery may

be better for those areas prone to maceration than creams. Rehydration and symptomatic treatment of patients is crucial as Mpox like most viral infections is self-limiting in nature. Particular knowledge of the relatively increased transepidermal water loss is also important for successful management even in the absence of diarrhea and vomiting. This is important to forestall complications like acute kidney injury among others.

Adequate dietary intake cannot be overemphasized considering the catabolic state of the infection and the need for healing of the raw areas/ulcers, consultation with a nutritionist is advised. Similarly, an adequate diet including proteins, fruits, and vegetables can boost immunity against viral infection and also prevent complications. Psychosocial support is required to prevent and manage depression, loneliness during isolation, impaired quality of life (during and after clearing of the rashes), and the stigma that can arise from this disease condition.[3] Thus, the involvement of Psychiatrists and Clinical Psychologists is very expedient in the successful management of these patients.

What Are the Roles of the Government?

The government should establish platforms of control, demonstrate unequivocal political will, and strengthen the active surveillance system. Every state and its health facilities must have a technical team to respond appropriately, guide policy decisions, release protocols, and ensure partnership with the NCDC and other relevant agencies. There is a need to facilitate information sharing, research collaboration, and clinical trials for the possible development of indigenous treatment. Furthermore, people should be made to take responsibility for their health, and proper infodemic management should be ensured as a risk communication strategy.

What Precautions Should Be Taken by the Public?

Anyone with rashes or the aforementioned symptoms should present to the hospital for evaluation, diagnosis, and treatment. Additionally, it's crucial to prevent unprotected contact with sick animals/humans, the rash, bedding, and clothing. Direct contact with secretions and fluids from infected animals and humans should also be avoided. Rodents, the meat of game animals, and animal products should be appropriately handled and prepared. Regular hand washing with soap and water or using an alcohol-based sanitiser when water is not available should be used to guarantee proper hand hygiene. Surfaces in contact with infected animals or humans (bedding, clothing) should be regularly decontaminated with chlorinated water (0.5%). It is pertinent to avoid stigmatization of persons who are infected with Mpox.

Intentional effort must be put in place to avoid spreading false information and rumours. It is also imperative to advise the populace to verify information with healthcare providers as well as from the NCDC and World Health Organisation platforms. The public should be advised to contact the hospital, state Mpox team, or other designated members about suspected cases in their neighbourhood. Public health enlightenment on Mpox should be prioritized from the community level to states and regions in an understandable language and terms the populace can easily assimilate.

Is There a Vaccine for Mpox?

Some vaccines (ACAM2000 and JYNEOS), based on replicating and non-replicating viral components, respectively) have been approved for immunization but none of them is Mpox-based. [9,11] They are vaccinia-based vaccines, previously used for smallpox, and have been found to be protective against Mpox.[9,11]

Conclusion

Monkeypox/Mpox is a public health emergency of international concern; therefore, stronger and better surveillance is imperative for its control and eradication. A better understanding of the skin as well as the rash needs to be elucidated. With changing presentations of the disease, regular review of the NCDC guidelines is germane. Collaborative effort through the One Health approach is indispensable in the successful surveillance and eradication of Mpox in Nigeria and the globe.

Acknowledgement
Sincere appreciation to Dr Adegbosin Bola for helping with the final editing of the work.

Conflicts of Interest
The authors hereby declare no conflict of interest.

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