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Nigeria Mpox clinical characterisation study

Submission date
22/02/2024

Recruitment status
No longer recruiting

Registration date
21/03/2024

Overall study status
Completed

Last Edited
01/04/2026

Condition category
Infections and Infestations

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Mpox virus, formerly known as Monkeypox, is the cause of the most important global human orthopoxvirus disease since smallpox was eradicated in 1979. After the virus re-emerged in Nigeria in 2017, reported cases have continued to increase annually. Since 2017, there have been 2668 suspected cases, 975 confirmed cases and 14 deaths with Lagos and Rivers States accounting for the highest burden of the disease. The 2022 global outbreak which affected over 100 countries, coincided with Nigeria's largest outbreak, with 762 confirmed from more than 2000 suspected cases. Though the increase is likely attributed to improved surveillance (reporting and testing capacities), there are important gaps in clinical and epidemiological knowledge of mpox in Nigeria that are not limited to the hypothesised loss of protection from historical smallpox vaccination, lack of clarity about the actual animal reservoir, and emerging genomics data suggesting transmission may now be entirely human to human. These knowledge gaps in part have hampered the development and deployment of effective control measures.

Before the 2022 global Mpox outbreak, the Nigeria Centre for Disease Control and Prevention (NCDC), the National Veterinary Research Institute (NVRI), the Niger Delta University Teaching Hospital (NDUTH), the Pandemic Sciences Institute at the University of Oxford, the United Kingdom Public Health Rapid Support Team (UK-PHRST - an innovative partnership between the UK Health Security Agency and the London School of Hygiene & Tropical Medicine, funded with UK aid by the UK Department of Health and Social Care), and stakeholders in Lagos, Rivers and Ogun States agreed to collaborate on a multi-disciplinary research project aimed at addressing Mpox knowledge gaps that would improve the public health response to the virus in Nigeria and beyond.

The project aims to provide evidence to strengthen mpox outbreak prevention, response and control in Nigeria and similar endemic settings of the mpox virus, through a research project entitled “Epidemiological and clinical investigation of mpox in Nigeria: A multi-disciplinary research project to inform case management and outbreak prevention and control.” The research project will be completed over two years and will cover thematic areas, including the clinical characteristics and natural history of mpox disease; the essential epidemiological parameters and factors associated with infection and transmission; and, the experience of people infected with mpox and those close to them. There will be two studies, this study is a Clinical Characterisation Study, which will help address knowledge gaps in the clinical understanding of the virus and the natural history of infection. The One Health Study will help to

increase understanding of the dynamics of infection and transmission (human-to-human, animal-to-human, environment-to-human) in the Nigerian context.

Who can participate?
Adults and children with mpox, at hospitals and in the community, across several states in Nigeria

What does the study involve?
Participation is voluntary and potential participants will be identified and invited to participate when they have been identified by public health teams responding to a new diagnosis of mpox. Recruitment opens on 5th February 2024 at the first site (Port Harcourt, Rivers) and clinical data including signs and symptoms of mpox, information on general health and medical conditions, and possible ways in which the patient was exposed to mpox virus, will be recorded using a structured case report form. Data will be collected at recruitment and then at a series of follow-up visits over subsequent weeks, to see how the illness progresses over time, identify any complications of infection, and determine the outcome of the illness.

Where feasible, blood samples, throat swabs and mpox lesion swab samples will be collected, as baseline and then at follow-up visits where possible. This will allow measurement of the virus in different samples over time, determine the clade (strain) of the infecting mpox virus, and provide samples to look for changes in the genetic sequence of the virus over time. Routine clinical tests such as measuring the number of blood cells, and liver and kidney function, will be performed as part of the study and the results will be shared with the patient's clinicians, to help with clinical management. A blood culture sample (to look for bacterial infection) will be performed if these tests are clinically indicated for the patient.

What are the possible benefits and risks of participating?
Participants will not be identifiable, individual participant data are treated as confidential, and all records and data are maintained securely. There are no direct benefits for an individual participant, although they may benefit if they have clinical tests performed as part of the study, such as routine blood tests or chest x-rays, tests may inform their clinical care but they could not arrange and/or pay for the tests themselves. Otherwise, participation in the study will help improve national and global knowledge about mpox and its effects on human health.

Participants in the Clinical Characterisation Study will be invited to participate in the associated - but separate - One Health Study. Participation in the One Health study is voluntary and it is possible to participate in the Clinical Characterisation Study but decline participation in the One Health Study.

There is minimal risk in participating in the study. Participants may find some questions asked during the interview or via telephone call uncomfortable. It is also possible that the time of assessments might be inconvenient or too lengthy for the participants. There is also the likelihood of experiencing some discomfort when blood samples are taken for mpox antibody testing. Participants will be made to understand that they are free to opt out of the study at any time, and they can choose to not answer any of the questions at any time or ask not to be contacted via telephone, and that all information they with share study staff is treated in the strictest confidence.

Where is the study run from?
The Clinical Characterisation Study is run jointly by the Nigerian Centre for Disease Control and Prevention (NCDC), the London School of Hygiene and Tropical Medicine on behalf of the UK

Public Health Rapid Support Team, the Pandemic Sciences Institute at the University of Oxford, and Niger Delta University. The study is sponsored by the London School of Hygiene and Tropical Medicine, London, UK.

When is the study starting and how long is it expected to run for?
August 2022 to March 2026

Who is funding the study?
The study is funded by UK Government Overseas Development Assistance via UK-PHRST research funds.

Who is the main contact?
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Additional identifiers

Protocol serial number
UKPHRST_NMCCS_1.0

Study information

Scientific Title
Mpox clinical characterisation protocol (Nigeria)

Acronym
NMCCS

Study objectives
This observational study aims to address the following research questions:
1. Which groups of people get infected by mpox (previously called monkeypox) currently in Nigeria, including but not limited to analyses of sex (male:female) differences, age when infected, underlying health status (any chronic health conditions including immune-compromising diseases)?
2. What are the signs, symptoms, common laboratory findings, radiological findings, clinical course, complications and clinical outcomes of contemporary mpox in people infected with mpox virus in Nigeria, across all levels of severity of illness; hospitalised and non-hospitalised cases?
3. What are the virological features of mpox virus infection in Nigeria, including the clade and sub-clades/lineages of infecting viruses, the viral loads in different sample types, and the viral replication trajectories over the course of illness (by sample type)?
4. Are certain patterns of mpox disease, including rash distribution and areas of the body most affected or more severely affected, associated with different types of exposure/transmission, such as confirmed or assumed sexual transmission?
5. Do different types of immune response seen in mpox, including anti-orthopoxvirus antibody production and inflammatory immune responses, vary between individuals and correlate with the severity of disease, complications, and the presence of certain chronic health conditions (such as HIV-associated immunosuppression)?
6. Does the mpox virus infecting one individual have genetic differences depending on the site

of the body sampled, particularly differences between the primary infection site (the part of the body originally exposed to the virus and that became infected) and secondary infection sites (other parts of the body where mpox lesions occur, representing the spread of the virus within the body or an alternative exposure site).
7. Does the mpox virus' genetic code change during illness within an infected individual?

Ethics approval required
Ethics approval required

Ethics approval(s)
1. Approved 06/09/2023, National Health Research Ethics Committee of Nigeria (NHREC) (Department of Health Planning, Research and Statistics, Federal Ministry of Health, Federal Secretariat Complex Phase III, Ahmadu Bello Way, Abuja, 900242, Nigeria; +234 09 523 8367; secretary@nhrec.net), ref: NHREC/01/01/2007-06/09/2023

2. Approved 16/10/2023, London School of Hygiene and Tropical Medicine Observational /Interventions Research Ethics Committee (Keppel Street, London, WC!E 7HT, United Kingdom; +44 (0)20 7636 8636; ethics@lshtm.ac.uk), ref: 28801

3. Approved 30/10/2023, Government of Rivers State of Nigeria Health Research Ethics Committee (Rivers State Hospitals Management Board, 26 Okoroma Street, Port Harcourt, PMB 6083, Nigeria; 084-230828; rshmbph@yahoo.com), ref: RSHMB/RSHREC/2023/052

Primary study design
Observational

Study design
Multi-centre prospective observational cohort study with longitudinal biological sampling

Study type(s)
Other

Health condition(s) or problem(s) studied
Clinical characterisation of mpox (monkeypox) affecting people in Nigeria

Interventions
Clinical and demographic data will be collected at recruitment and at follow-up visits, using a structured case report form. Where feasible, biological samples will be taken at recruitment and follow-up visits, for virological and immunological analyses. This includes venous blood samples, throat swabs, and swabs of mpox lesions. Research laboratory analyses include quantitative PCR of mpox virus and clade-typing, and routine clinical assays such as full blood count, CRP, renal and liver profiles, and quantification of anti-orthopox antibodies in blood. Chest radiographs will be performed if clinically indicated. Blood culture samples will be obtained for any patient with suspected sepsis. Where possible, viral genomic sequencing will be performed on mpox-positive samples that are suitable for sequencing. If possible, a selection of cytokines and chemokines will be measured in plasma/serum. Host genomic sequencing will not be performed. There are no pharmaceutical interventions in this study.

The primary outcomes comprise a descriptive analysis of common clinical haematology and biochemistry variables, including inflammatory markers and markers of end-organ abnormalities, in patients in the acute phase of mpox and, where longitudinal samples are available, analysis of

changes in common haematology and biochemistry variables during illness. There will also be the quantification of monkeypox virus (MPXV) present in different samples, where longitudinal samples are obtained, how these change over time and how the dynamics relate to the observed clinical course, severity of mpox and clinical outcomes.

Secondary outcomes investigate the immune response and genetic dynamics associated with Monkeypox Virus (MPXV) infection through various methodologies. Firstly, it involves quantifying multiple soluble immune mediators in blood using high-sensitivity assays, comparing levels in longitudinally obtained samples to discern innate and adaptive responses to MPXV infection and their correlation with disease manifestations and outcomes. Secondly, it assesses the levels of anti-orthopox antibodies over time in response to natural infection and their relationship with clinical courses and viral replication dynamics. Additionally, it examines the baseline levels of anti-orthopox antibodies and their connection to subsequent clinical courses and viral dynamics. Furthermore, the study incorporates genetic sequencing of lesion-swab and blood samples to identify within-host genetic changes in MPXV, considering factors like host immunodeficiency states and drug-selection pressure, and their impact on the disease course. Moreover, it compares sequences from different anatomical sites within individuals to discern variations and their association with disease severity. Finally, it explores the variability of MPXV clades and sub-clades within the study population through viral genome sequencing and bioinformatics, cross-referencing with published sequences from previous and contemporary MPX cases in Nigeria.

Intervention Type
Other

Primary outcome(s)
1. Common clinical haematology and biochemistry variables, including inflammatory markers and markers of end-organ abnormalities, in patients in the acute phase of mpox and, where longitudinal samples are available, analysis of changes in common haematology and biochemistry variables during illness.
2. Quantification of MPXV present in different samples using quantitative/semi-quantitative PCR and, where longitudinal samples are obtained, how these change over time and how the dynamics relate to the observed clinical course, severity of mpox and clinical outcomes.

Key secondary outcome(s)
1. Quantification of multiple soluble immune mediators (cytokines and chemokines) in blood and blood markers using high-sensitivity assays, including comparisons of levels in longitudinally obtained samples, to better understand the nature of the innate and adaptive responses to MPXV infection and how these may be associated with disease manifestations and outcomes.
2. Levels of anti-orthopox antibodies (IgM, IgG, total Ab, measured by ELISA) in response to natural infection over time and how these relate to differences in clinical courses and viral replication dynamics in infected individuals.
3. Quantification of anti-orthopox antibodies at baseline (recruitment) and how these relate to the subsequent, observed clinical course of mpox and the viral dynamics in the infected individuals.
4. Genetic sequencing of lesion-swab samples and blood samples containing viral DNA to look for within-host genetic changes in MPXV over time, whether this is influenced by non-viral factors such as host immunodeficiency states (e.g. severe immunosuppression) and/or drug-selection pressure (should anti-orthopox antivirals be administered as part of routine clinical care), and how any viral genetic changes detected relate to the observed course of the disease.
5. Comparison of sequences obtained from two different anatomical sites within an individual to

see if these differ and whether they are associated with different patterns or severities of mpox disease at those different anatomical sites.
6. Variability of mpox virus clades and sub-clades within the study population, assessed by viral genome sequencing and bioinformatics, with cross-referencing of published sequences from previous and contemporary samples from mpox cases in Nigeria.

Completion date
31/03/2026

Eligibility

Key inclusion criteria
Case definitions are informed by NCDC case definitions for mpox but some may have been amended for recruitment to this study. See note at the end about preferred recruitment of confirmed cases only.

1. Confirmed case of mpox: a clinically compatible case where mpox infection has been confirmed by laboratory testing
2. Probable case of mpox: a clinically compatible case with epidemiological linkage but where laboratory confirmation of infection could not be obtained
3. Suspected case of classical mpox according to the extant NCDC case definition (current definition: a person with acute illness with fever >38.3°C, intense headache, lymphadenopathy, back pain, myalgia, and intense asthenia followed one to three days later by a progressively developing rash often beginning on the face (most dense) then spreading elsewhere on the body, including soles of feet and palms of hand) or suspected non-classical / atypical mpox based on a clinician's assessment (e.g., absence of prodromal illness but mpox lesions are present, or mpox lesions with a more localised distribution, or predominantly genital/anorectal mpox lesions)

Note:
The recruitment of laboratory-confirmed cases is preferred over the recruitment of probable and suspected cases; however, probable and suspected cases may be recruited at the discretion and direction of the study's central coordinating team if real-time laboratory diagnosis is not possible or proves to be too slow to facilitate timely recruitment of participants. If suspected cases are recruited, subsequent analyses of data will recognise the important differences between confirmed, probable, and suspected cases and, accordingly, separate analyses of a single sub-cohort (e.g., confirmed cases only, suspected cases only) or combined sub-cohorts (e.g., confirmed and probable cases) will be performed when necessary. If suspected cases are recruited, data from those participants where mpox is subsequently and confidently excluded by laboratory testing may provide a useful control group and/or reveal common alternative diagnoses in suspected mpox cases, which could help refine case definitions and clinical diagnostic guidance. However, the primary purpose of this study is to clinically characterise confirmed cases of mpox. A recruited suspected case may later become a confirmed case if laboratory testing is delayed; all sub-cohort analyses will use participants' final mpox status based on data available at their outcome assessments.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
All

Lower age limit
0 Years

Upper age limit
120 Years

Sex
All

Total final enrolment
70

Key exclusion criteria
1. Confirmed diagnosis of a pathogen unrelated to the objectives of this study and there is no indication or likelihood of co-infection with MPXV
2. Mpox is not suspected clinically and there is no laboratory evidence of MPXV infection

Date of first enrolment
05/02/2024

Date of final enrolment
30/01/2026

Locations

Countries of recruitment
Nigeria

Study participating centre
Port Harcourt University Hospital
East-West Road, Port Harcourt
Rivers
Nigeria
6173

Sponsor information

Organisation
London School of Hygiene & Tropical Medicine

ROR

https://ror.org/00a0jsq62

Funder(s)

Funder type
Government

Funder Name
UK Public Health Rapid Support Team (UK-PHRST) through UK Official Development Assistance (ODA)

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the study will be stored in a non-publicly available repository maintained by NCDC. All individual participant-stored data will be pseudonymised, so individuals cannot be identified by those accessing the data. Use of any stored data or residual biological samples by other researchers will be controlled by a data and materials access committee. The committee will have scientist members and advisers from Nigeria and the UK, and processes will be in place for making requests to access data or materials, and for reviewing and approving or rejecting requests.

IPD sharing plan summary
Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet		05/01/2024	19/03/2024	No	Yes
Protocol file	version 1.0	31/07/2023	19/03/2024	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes