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Transmission Dynamics and Genomic Evolution of Monkeypox Virus in Nigeria Across Pre- and Post-COVID-19 Periods

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Abstract

The COVID-19 pandemic altered human civilization, healthcare systems, and disease surveillance, potentially influencing the transmission and evolution of zoonotic pathogens such as monkeypox virus (MPXV). However, changes in MPXV transmission dynamics and genomic evolution in Nigeria across pre- and post-COVID-19 periods remain poorly understood. To infer the transmission dynamics of the virus as influenced by the COVID-19 pandemic, we analyzed whole genomic sequences, and their associated metadata to reveal host range, circulating clades, and seasonal factors that could be implicated in its transmission. From the NCBI, MPXV sequences were retrieved together with their metadata. The whole genome sequences were categorized into pre, during, and post-COVID-19 periods. Neighbour joining trees were used infer the relationships between circulating clades during both periods. Principal component analysis (PCA) was used to evaluate how genome size, season, State of origin, and sample type influenced MPXV transmission dynamics across Nigeria. A total of 172 MPXV sequences from Nigeria (1971 to 2023) were retrieved, with outbreak peaks observed in 2017 to 2019 and 2022. Most cases were recorded in the months of September and October, followed by January to March, with southern States such as Bayelsa and Rivers reporting the highest numbers. Sample data lacked standardization, and seasonal analysis showed a weak correlation between outbreaks and seasons. PCA revealed the year of isolation as the most influential variable in transmission patterns. Phylogenetic analysis confirmed Clade IIb persistence across all periods, with links to exported cases in Singapore (2019), the UK, and the USA (2020 and 2022). There is a need to strengthen routine surveillance, standardize reporting, and targeted interventions.

1.0 Introduction

The monkeypox virus (MPXV) is a unique virus that possesses a double-stranded DNA genome and belongs to the genus *Orthopoxvirus* within the family *Poxviridae* [1]. So far, two clades have been identified: the West African clade (also called Clade IIa and IIb, which causes less severe infection) and the Congo Basin clade (also called Clade I, and causes more severe infection) [1]. The MPXV is a close relative of the variola virus, which causes smallpox, but MPXV infections are generally less severe [2]. The virus was first identified in 1958 following outbreaks in monkeys kept for research; however, the index case occurred in 1970 in the Democratic Republic of the Congo (DRC) [3]. Since then, MPXV has spread to various countries, particularly in Central and West Africa. These countries include Nigeria [4–6], Cameroon [7–8], Ghana [9], and Ivory Coast [10]. Collectively, MPXV has been circulating both within and outside Africa since the index case [11–12] but identification of animal reservoir has been a challenge [13].

Amidst the spread of MPXV in Nigeria, the index case of COVID-19 in the country was reported on 27 February 2020 [14]. As expected, the COVID-19 pandemic disrupted the surveillance, detection, and diagnosis of other zoonotic infections, including Lassa fever virus and MPXV [15]. The severity of the pandemic overwhelmed healthcare facilities, sociowelfare structures, and resources in both developed and developing countries, leading to the reallocation of efforts and time towards combating it[16]. This

resulted in the suspension of surveillance for other infectious diseases, such as monkeypox [17]. Consequently, monkeypox cases were underreported and neglected across Nigeria during the COVID-19 pandemic [18–20]. This situation was further exacerbated by public fear of contracting COVID-19, which may have discouraged individuals or cases from accessing and seeking medical care, thereby contributing to missed or delayed diagnoses of monkeypox. Collectively, these factors including closure of borders may have limited the spread of monkeypox virus beyond Nigeria and other African countries to Europe and other regions, while at the same time fuelling and sustaining local transmission of MPXV during the COVID-19 period [18–20].

Approximately a year before the World Health Organization (WHO) declared monkeypox a Public Health Emergency of International Concern (PHEIC), Nigeria had gradually eased her lock down measures initially enforced to contain the spread of COVID-19. This development may have further contributed to the spread of the virus in the country. Meanwhile, imported cases of the virus into other parts of the world have also been reported [11–12]. Given the significance of the re-emergence and global spread of monkeypox, particularly outbreaks of lineages capable of human-to-human transmission through sexual networks, the WHO declared it a PHEIC in 2022 [21]. In their evaluation of the dynamics of MPXV infection in Nigeria, Cadmus et al. [22] identified several contributing factors, including poverty, inadequate basic healthcare facilities, and unsafe sexual practices. The authors further indicated that MPXV spread from the southern part of Nigeria towards the north, with 30 out of the 36 States already having reported at least one case of the virus [22]. However, other important dynamics, such as the circulating clades, as well as the specific months and years during which the virus spread across various states remain unknown.

Intensification of animal source surveillance is also critical to answer many research questions regarding zoonotic spill over from ecological niches [13]. We speculate that the COVID-19 pandemic may have altered MPXV transmission dynamics across Nigeria and West Africa. Supporting this speculation, a case of MPXV imported from Nigeria was reported in the United Kingdom in 2022 and initiated a global transmission [23]. Nigeria is widely believed to be the epicentre of the 2022 global outbreak [24–25], indicating an underling, sustained spread of the virus in Nigeria. To better understand the spread of MPXV during the COVID-19 period, we analysed genomic sequences and metadata of MPXV from the pre-COVID-19, during-COVID-19, and post-COVID-19 periods deposited in the National Centre of Biotechnological Information (NCBI). The study aimed to achieve the following: (1) map the geographical distribution of cases across Nigerian states during these periods; (2) investigate the factors involved in its transmission dynamics; and (3) perform phylogenetic clustering of whole MPXV genomes to identify circulating clades in Nigeria.

2.0 Methods

2.1 Source and processing of meta-data

From the National Centre for Biotechnology (NCBI) database, using “monkeypox, complete genome, Nigeria” as search term, the MXPV sequence data and their accompanying metadata were retrieved. The search was conducted on April 11th 2025. The search returned a total of 238 sequences with accession numbers and these were screened to remove partial sequences and unverified sequences. The step-by-step process leading to the retention of the metadata and sequences was conducted as previously reported [25] (Fig. 1).

2.2 Statistical analysis

The metadata, including the year and month of sequence collection, diversity of sample types, and seasonal distribution of the isolated sequences, were transformed and visualized using descriptive statistics such as bar charts, scatter plots, and pie charts in Microsoft Excel. The geographical distribution of cases across Nigerian States was illustrated using a map of Nigeria. To further explore the influence of seasons (dry and wet) on the outbreaks, the year and monthly outbreak data were categorized into dry (October to March) and wet (April to September) seasons. These were plotted on an X-Y scatter graph with a trend line with an R^2 value to assess potential correlation. Additionally, Principal Component Analysis (PCA) was employed to transform the metadata comprising months (categorized into dry and rainy seasons), genome size, sample types, and month of isolation to identify the factors driving MPXV outbreaks in Nigeria. The PCA was conducted as previously described, using OriginPro 2024.

2.3 *Bioinformatics analyses*

Phylogenetic analysis of selected whole genomes from Nigeria and across the globe, representing all the various clades, was conducted to perform phylogenomic clustering. Briefly, the sequences in FASTA format were first aligned using the MAFFT alignment tool version 7 (https://mafft.cbrc.jp) [26–27], with the sequence type set to nucleic acid and Kimura selected as the scoring function, while other parameters were kept at their default settings. The phylogenetic tree was then constructed using RAxML [28], and the resulting tree was visualized using PHYLOViZ [29].

3.0 Results

The results of the metadata analysis of the retrieved monkeypox virus sequences from Nigeria, spanning 1971 to 2023, are presented in Figs. 1A to E. The monthly spread shows that in January, February, March, April, May, June, July, August, September, October, November, and December, the number of sequences were 18, 9, 12, 5, 4, 4, 2, 2, 53, 41, 4, and 6, respectively. The results further reveal that September and October had the highest number of isolates, with 53 and 41 sequences, respectively, followed by January, February, and March. The months with the fewest isolates were June and July, with 2 sequences each (see Fig. 1A). The yearly representation of the sequences indicate that the 2017, 2018, 2019, 2022, and 2023 recorded higher occurrences than the other years, with 17, 17, 17, 95, and 19 sequences, respectively (Fig. 1B). Notably, 2022 had the highest number of sequences, totaling 95. The years 1971 and 1978 each had 1 sequence, while 2020 and 2021 recorded 0 and 5 sequences,

respectively. No sequences were documented between 1971 and 1978, nor between 1978 and 2017 (see Fig. 1B).

To explore potential factors influencing the outbreaks, the months were categorized into dry (October to March) and wet (April to September) seasons (Figs. 1C and D). The years were transformed into numerical codes (1 to 8) representing 1971, 1978, 2017, 2018, 2019, 2021, 2022, and 2023, respectively. Scatter plots showed R^2 values of 0.286 and 0.203, suggesting a very weak positive correlation between the seasons and the yearly number of reported cases in Nigeria (see Figs. 1C and 1D). Figure 1E presents the various sample types from which the isolates were obtained. The generic terms "clinical sample" and "swabs" were the most common, with 112 and 22 samples, respectively. Pustule swabs, crust/cotton, serum, and naso swab/liquid accounted for 20, 3, 2, and 1 sample, respectively. Thirteen deposited isolates lacked clearly defined sample types.

Figure 1A: Bar chart representation of the meta data showing monthly representations of sequences.

Figure 1B: Bar chart representation of the meta data showing yearly representations of sequences.

Figure 1C: A scatter plot of cases year by year versus occurrence for dry season.

Figure 1D: A scatter plot of cases year by year versus occurrence for dry season.

Figure 1E = Pie chart representation of the diverse sample types. NS = Not stated; NA = Not assigned a sample type.

Figure 2: Distribution of the MPXV sequences according to geographical zones in the country. Key: GPZ = Geopolitical zones

Figure 2 illustrates the geographical distribution of the sequence data in Nigeria, showing presence across 22 States, including the Federal Capital Territory (FCT). All southern States reported cases, except Osun and Ekiti. The top five states were Bayelsa, Rivers, Imo, Akwa Ibom, and Lagos, with 18, 17, 16, 15, and 9 sequences, respectively. A total of 26 cases had no State attributes to them and as a result are not indicates in the map.

Figure 3: Principal component analysis showing the factors influencing the outbreak of MPXV in Nigeria. Key: Samp. type = Sample type; Mpoc = Monkey pox virus; Gen. Sz = Genome size; Sta = State

The PCA analysis illustrating the impact of isolation year, isolation month, sample type, state, and genome size on the monkeypox outbreak, is presented in Fig. 3. In PCA, the closer the absolute value of the loading scores is to 1, the stronger the influence of the parameter on the variable in this case, the monkeypox outbreak. The PCA revealed that the first two principal components (PC 1 and PC2) accounted for 73.26% of the total variance (PC1: 57.74%, PC2: 15.52%) (Fig. 3). Based on PC1, isolation state, isolation month, sample type, and isolation year all showed a positive relationship with the monkeypox outbreak (as indicated by the acute angles between their vectors and that of the outbreak).

Among these, isolation year exhibited the strongest association, as shown by the length of its vector, indicating it was the primary driver of monkeypox outbreaks in Nigeria. While isolation state, month, and sample type also contributed, their influence was comparatively lower. PC2 was associated only with genome size, suggesting that genome size had no significant influence on the monkeypox outbreaks in Nigeria. Figures 4 and 5 indicates that before, during and after COVID-19, the West African clade was persistently the only clade in Nigeria. Furthermore, the exported cases in Asia, UK and USA were also of the same clade.

4.0 Discussion

The MPXV metadata revealed a temporal trend as well as the re-emergence of the virus. In particular, the resurgence of MPXV cases in Nigeria after decades of dormancy between 1978 and 2017 is notable. The absence of sequences from 1978 to 2017 may indicate either a true absence of cases or significant under-reporting of the virus during that period, potentially due to limited surveillance capabilities at the time. However, the re-emergence of MPXV in Bayelsa in 2017, and the reports of exported cases in 2018 and 2019 from Nigeria, have raised concerns that MPXV may have emerged to occupy the ecological and immunological niche vacated by the smallpox virus [30]. The absence of MPXV cases during the COVID-19 pandemic may be attributed to the diversion of efforts and resources towards pandemic response activities, which likely resulted in reduced surveillance for other infectious disease agents, such as MPXV [17]. Alongside the fears that accompanied the COVID-19 pandemic, MPXV cases were under-reported [18–20]. The re-emergence of the monkeypox virus in 2017 and the subsequent reported cases in 2018, 2019, and 2022 align with findings from the Nigeria Centre for Disease Control (NCDC), which reported increased case numbers during these years [31]. Of particular concern is the fact that recent MPXV cases stem from lineages characterised by human-to-human transmission, which could potentially trigger a pandemic. This aligns with the World Health Organization's declaration of MPXV as a pathogen of public health concern in 2022. However, the zoonotic factor must not be over looked as it takes only a single case of spill over from animal reservoir to trigger series of human-to-human transmission. This is also of particular importance given the propensity for ecological encroachment and it is instructive that most cases in Nigeria (by sequence data) fall within the forest zone of the Niger delta (Fig. 3).

Our metadata further revealed seasonal variation, with more cases recorded in the months of September and October, suggesting potential seasonal patterns. These findings align with the report by Precious et al. [32], who observed higher MPXV case numbers in September, October, November, and December of 2017, but a steady number of cases across the rest of the months in 2017 and throughout 2018, 2019, 2020, 2021, and 2022. The presence of reported cases for 2022 in the study by Precious et al. [32] may indicate either an absence of appropriate metadata for those sequences or non-deposition of such sequences. Our findings also corroborate those of Yinka-Ogunleye et al. [4], who reported a higher incidence of MPXV in September 2017. The multi-country outbreak of 2022 reached its peak around August which was one of the months with the lowest cases of MPXV in cases recorded in Nigeria. While our monthly trend shows increased cases in September, October, January, February, and March

indicating a greater prevalence during the dry season compared to the rainy season our metadata analysis revealed only weak positive correlations. This suggests that factors beyond seasonal variation may play a more significant role in outbreak dynamics. Previous studies have highlighted the role of environmental conditions, human behaviour, and ecological factors in shaping the transmission patterns of the virus [4][30][31]. Furthermore, cultural practices and the consumption of bush meat as a source of protein in various communities in developing countries where the virus is endemic have also been linked to MPXV transmission [34–36][22]. In addition, recent studies indicate the absence of surveillance in endemic ares as well as commercial nature of some States could also be driving the pandemic [24–25].

Analysis of the sample types indicates the dominance of generic terms such as “clinical sample” and “swabs” in the sample descriptions. This suggests a lack of standardized data documentation during the collection or submission of metadata when sequences were deposited in GenBank. The absence of detailed sample information may hinder the identification of the diverse sources from which MPXV can be isolated. Available metadata from deposited sequences reveal other sample types, including pustule swabs, crust/cotton, serum, and nasal swab/liquid, with pustule swabs and nasal swab/liquid representing the most and least common, respectively, excluding generic entries such as “clinical sample” and “swab”. The isolation of MPXV from pustules which are small, raised, blister-like lesions characteristic of monkeypox infection highlights these and other sample types as potential sources of transmission. This aligns with the findings of Palich et al. [37], who reported a higher incidence of MPXV in skin lesions than in other sample types. Beeson et al. [38] and Hernaez et al. [39], through their review and cross-sectional studies, also provided evidence supporting the possibility of nasal droplets as a route of virus transmission. The possibility of transmission via respiratory droplets, particularly at close range, has been recognized by the Centers for Disease Control and Prevention [40]. Although sexual fluids were not among the sources of MPXV isolates in our study, recent large longitudinal studies have demonstrated that sexual fluids can be a source of the virus, providing further evidence of the role of sexual contact in MPXV transmission [37]. Taken together, these findings underscore the importance of accurate documentation of sample types for reliable diagnosis, improved understanding of transmission dynamics, and the implementation of effective control measures. A lack of such detail may impede epidemiological analyses and hinder the development of targeted interventions.

Our metadata further indicates that MPXV was reported in a total of 22 States, including the Federal Capital Territory. Although more cases were observed in the southern states, which are technically and administratively classified as South South, South East, and South West Nigeria, the findings suggest a widespread distribution of MPXV across the country, spanning 22 States including the Federal Capital Territory. The report of cases aligns with the findings of Cadmus et al. [22] who reported MXPV in 30 States out 36 in Nigeria. Our findings felled short of this as we utilised only metadata of submitted isolates to GenBank 16 isolates had no State metadata in their submission. This underscores the virus’s extensive reach within Nigeria. The higher number of cases in southern states such as Bayelsa, Rivers, Imo, Akwa Ibom, and Lagos aligns with previous reports that identified these regions as hotspots during the 2017 outbreak in Nigeria [4] and suggest possible primary exposure to animal source in the equatorial rain forest zone akin to experience in other central and west African countries. Our findings

further posits with an earlier finding that speculated that the MPXV spread may have spread into the Northern part of the country from the south through travels as there were more cases in the South than North [22]. The abundance of cases in the southern states may also be attributed to the closer proximity of individuals, driven by higher population density compared to the northern states, which typically have larger land masses and lower population densities. Alternatively, the lower numbers reported in the northern states could reflect under-reporting. The spread of the virus in the southern region could also be influenced by unique climatic factors, such as greater rainfall, compared to the northern states. A comprehensive understanding of these geographical patterns is essential for effective surveillance planning, resource allocation, and the development of targeted public health interventions.

To further understand the interplay of these factors in driving MPXV cases, we conducted a Principal Component Analysis (PCA). The PCA revealed several notable findings. Firstly, the year of isolation had the most substantial influence on MPXV outbreaks. This is significant and aligns with the years in which outbreaks have been reported. Secondly, genome size had minimal influence on outbreak patterns. The genome size of the MPXV whole genome ranged from 180,828 to 197,792 base pairs, which is consistent with previous reports [1]. The PCA also indicated that sample type, state of isolation, and month were important factors influencing the occurrence of MPXV cases in our study. This supports our metadata analysis, which highlighted that Southern States, certain months of the year, and specific sample types were particularly associated with increased case numbers in Nigeria. However, the strongest influence was attributed to the year of outbreak, likely due to the episodic nature of MPXV resurgence in the country. Overall, these findings suggest that temporal factors, possibly including changes in surveillance efforts, levels of public awareness, and viral evolution, play a significant role in shaping the dynamics of MPXV outbreaks.

The hypothesis that the COVID-19 pandemic may have altered Monkeypox virus (MPXV) transmission dynamics across Nigeria and West Africa is both timely and compelling, particularly in light of the post-pandemic resurgence of MPXV globally. To explore this, phylogenetic analyses were conducted to infer the circulating clades of MPXV before and after the COVID-19 pandemic. The results consistently identified the classical West African clade reclassified under newer nomenclature as Clade IIb as the dominant lineage, both pre- and post-COVID-19. This finding is consistent with earlier studies which confirmed Clade IIb as the dominant variant in Nigeria and West Africa [4][31][41]. The clustering of Clade IIb with sequences from exported cases to Singapore (2019), the United Kingdom (2021), and the United States (2022) provides compelling evidence of Nigeria's role as a hotspot for global MPXV transmission. This pattern of exportation underscores the transboundary nature of the virus and highlights systemic gaps in local containment and international biosecurity.

According to Walter et al. [42], weaknesses in surveillance systems, underreporting, and delays in accurate diagnosis have facilitated the silent persistence and episodic export of MPXV from Nigeria other countries such as Asia, Europe, and the Americas. Notably, the 2019 Singapore case marked the first genetically confirmed link between a monkeypox case in Asia and a Nigerian strain, thereby reinforcing the interconnectedness of global health in the context of international travel and trade [43–

44]. The COVID-19 pandemic catalyzed global attention towards pathogen surveillance, particularly concerning zoonotic viruses. As Mbim et al. [45] argued, COVID-19 exposed the fragility of global health systems and spurred renewed interest in One Health approaches to infectious disease management. Despite this, our post-COVID-19 phylogenetic findings indicate that the MPXV strains exported from Nigeria continued to belong to the same West African clade circulating prior to the pandemic. This continuity points to persistent gaps in public health responses within endemic regions, particularly regarding surveillance, diagnostic capacity, and community engagement. Importantly, genomic evidence suggests that while the exported MPXV strains belong to the same clade, they may harbour subtle mutations. For instance, the United States' 2022 MPXV outbreak strain exhibited GA-to-AA mutations, indicative of APOBEC3-mediated cytosine deaminase activity potentially a marker of human adaptation [46]. These findings raise concerns about the possible evolution of the virus under selective pressures, particularly if outbreaks continue to occur in under-monitored and resource-limited settings and enzootic, silent circulation in animals. This further suggests the virus's increasing fitness and ability to adapt to environmental conditions, spill over transmission, potentially driving its continued spread within human populations. Although this clade is considered less fatal compared to the Central African Clade (Clade I), it nevertheless poses a significant public health challenge [47], requiring continuous surveillance and monitoring molecular dynamics.

Conclusion

This study provides critical insights into the re-emergence and epidemiological patterns of monkeypox virus (MPXV) in Nigeria, revealing temporal, geographical, and sample-type trends from the available metadata. The resurgence of MPXV following decades of apparent dormancy, coupled with its exportation to other countries, underscores Nigeria's pivotal role in the global transmission dynamics of the virus. The seasonal variations observed particularly peaks during the dry season and the predominance of cases in southern states suggest that both climatic and other factors may influence the observed outbreak patterns. However, weak correlations with seasonal data highlight the need to explore additional determinants, including human behavior, environmental interactions, human-animal interface and healthcare access. The analysis further revealed inconsistencies in sample documentation, with the dominance of generic and non-specific terms such as "clinical sample" and "swab" dominating metadata entries in GenBank. This lack of standardization hampers effective epidemiological interpretation and calls for improved data collection protocols including nomenclatures during sample submission. Our PCA analysis reinforced the significant influence of temporal factors, especially the year of outbreak on MPXV case distribution, while also acknowledging the roles of state of isolation, sample type, and month of occurrence. Phylogenetic analysis confirmed the dominance of the West African lineage (Clade IIb) before and after the COVID-19 pandemic, revealing Nigeria as a recurrent source of exported cases. While the viral clade remains consistent, the possibility of minor mutations signals the virus's adaptive potential, raising concerns about its continued evolution. Collectively, these findings emphasise the urgent need for strengthened surveillance, standardized

reporting, and integrated One Health strategies to effectively monitor, contain, and respond to MPXV outbreaks in Nigeria and beyond.

Declarations

Ethical approval -

Not Applicable

Consent to participate -

Not Applicable

Consent to publish -

Not Applicable

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Authorship Contributions:

Conceptualization: UOE and CM. Methods, software, and validation: KAO, AJ, MZA, OH, FN, CM and UOE. Screening of meta: UOE and CM. Supervision: CM. Draft manuscript: AA, CM and UOE. Approval: All the authors.

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Author Contribution

Conceptualization: UOE and CM. Methods, software, and validation: KAO, AJ, MZA, OH, FN, CM and UOE.. Screening of meta: UOE and CM. Supervision: CM. Draft manuscript: AA, CM and UOE. Approval: All the authors.

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Data Availability Statement-

The data that support the findings of this study are available from the corresponding authors upon reasonable request.

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Figures

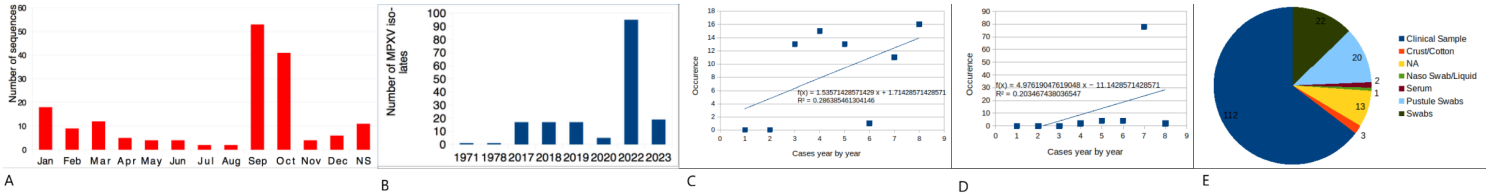


Figure 1

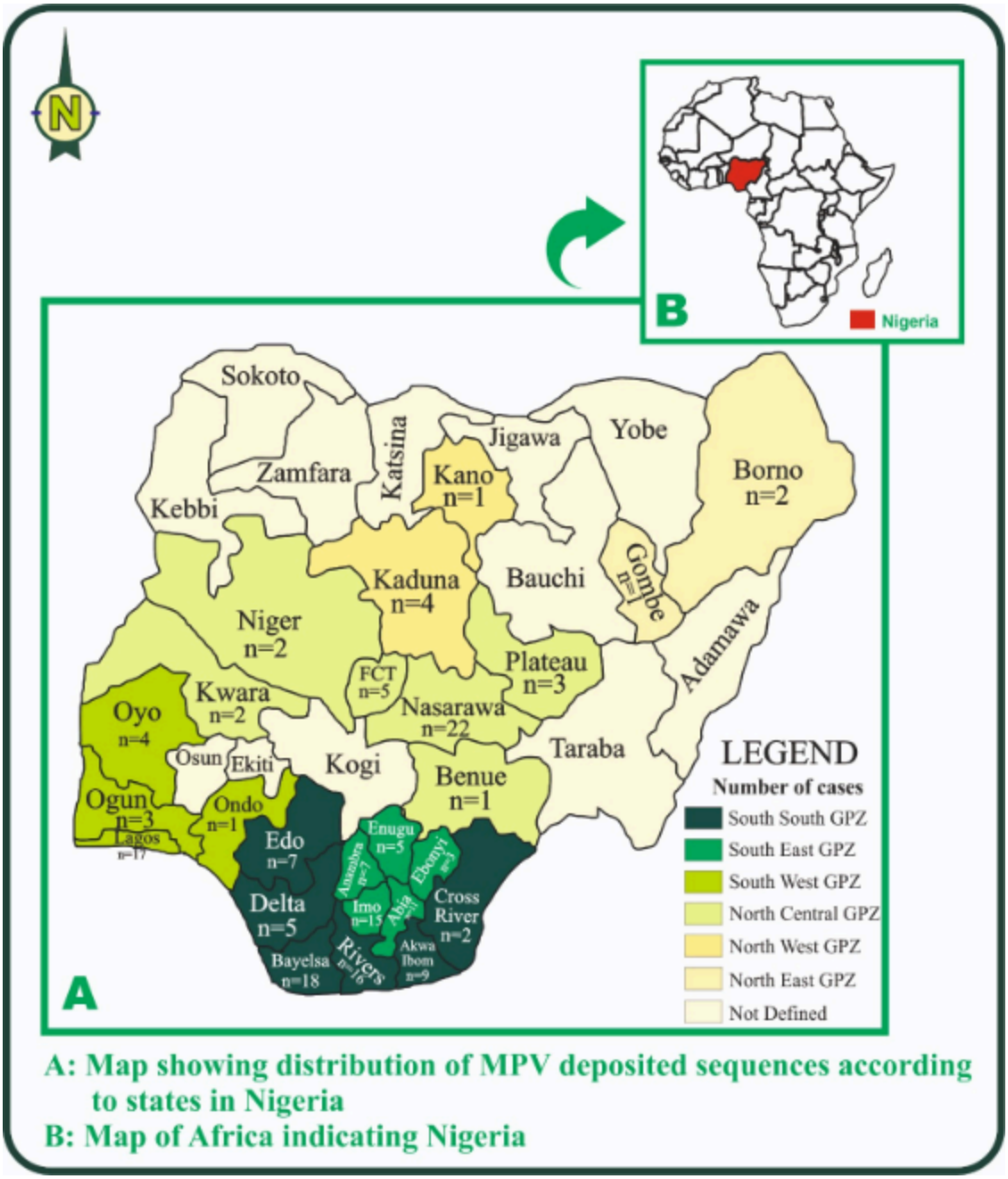
A: Bar chart representation of the meta data showing monthly representations of sequences.

B: Bar chart representation of the meta data showing yearly representations of sequences.

C: A scatter plot of cases year by year versus occurrence for dry season.

D: A scatter plot of cases year by year versus occurrence for dry season.

E = Pie chart representation of the diverse sample types. NS = Not stated; NA = Not assigned a sample type.



A: Map showing distribution of MPV deposited sequences according to states in Nigeria

B: Map of Africa indicating Nigeria

Figure 2

Distribution of the MPXV sequences according to geographical zones in the country. Key: GPZ = Geopolitical zones

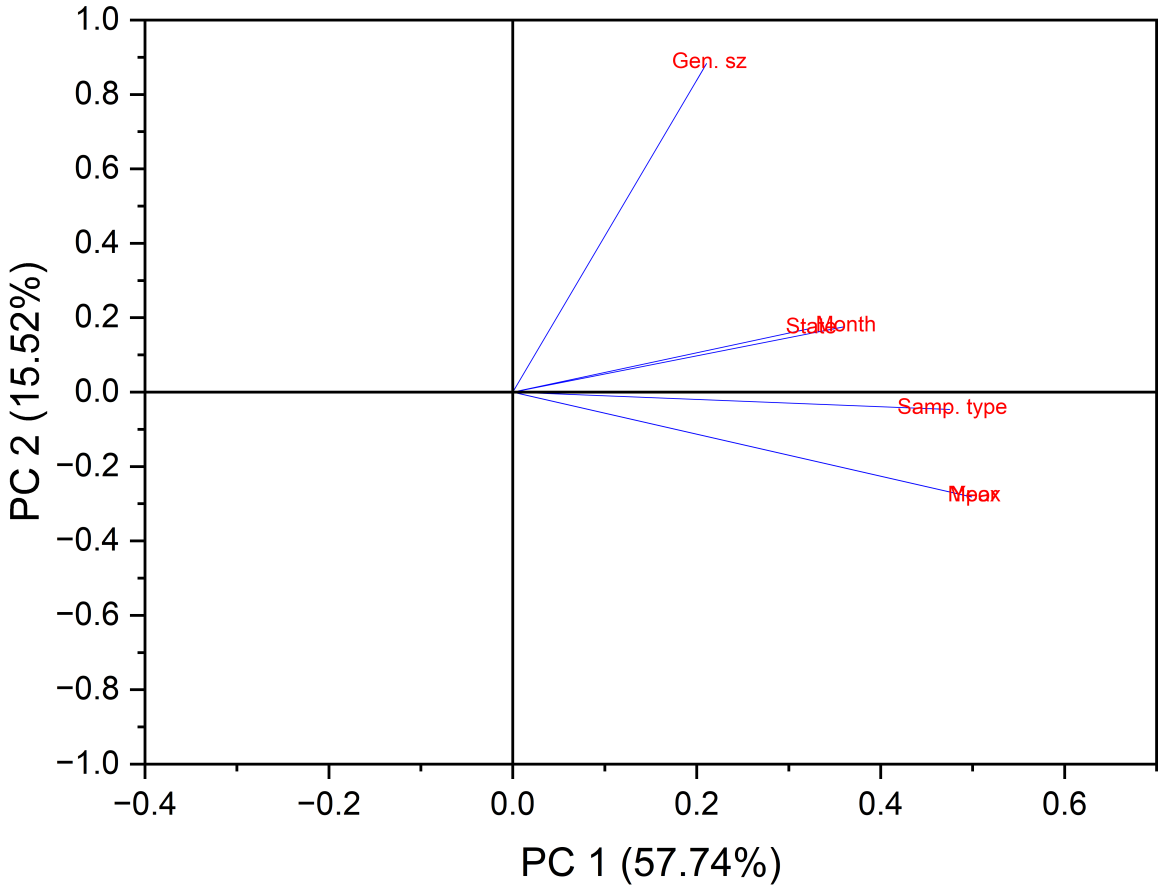


Figure 3

Principal component analysis showing the factors influencing the outbreak of MPXV in Nigeria. Key: Samp. type = Sample type; Mpoc = Monkey pox virus; Gen. Sz = Genome size; Sta = State

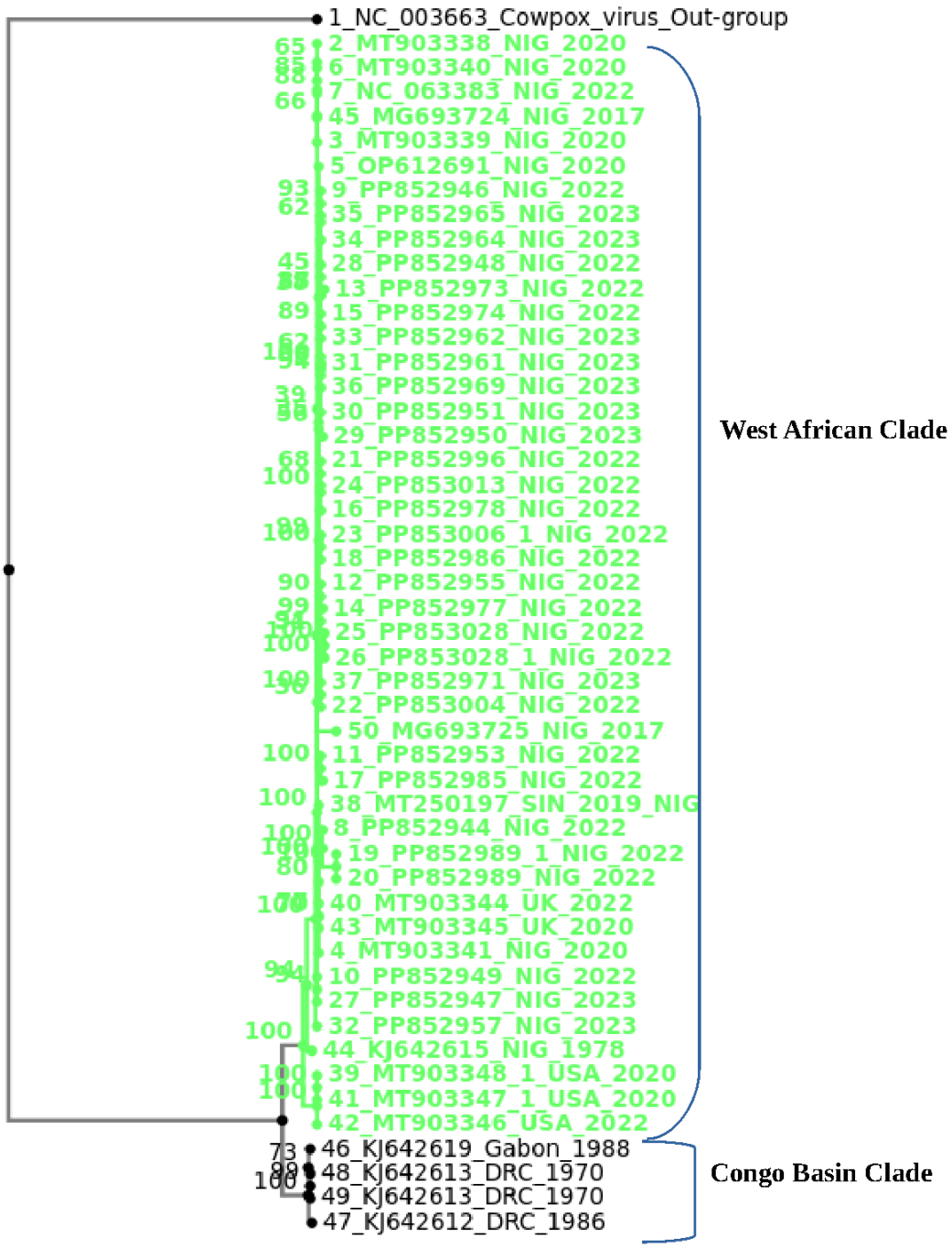


Figure 4

Phylogenetic relationship of retrieved whole genome sequences of MPXV isolate from Nigeria from 2022 to 2023. Key: The phylogenetic tree was constructed following maximum multiple alignment by the Maximum Likelihood (ML) method with the reliability of individual tree nodes kept at 1000 bootstrap pseudo replicates.

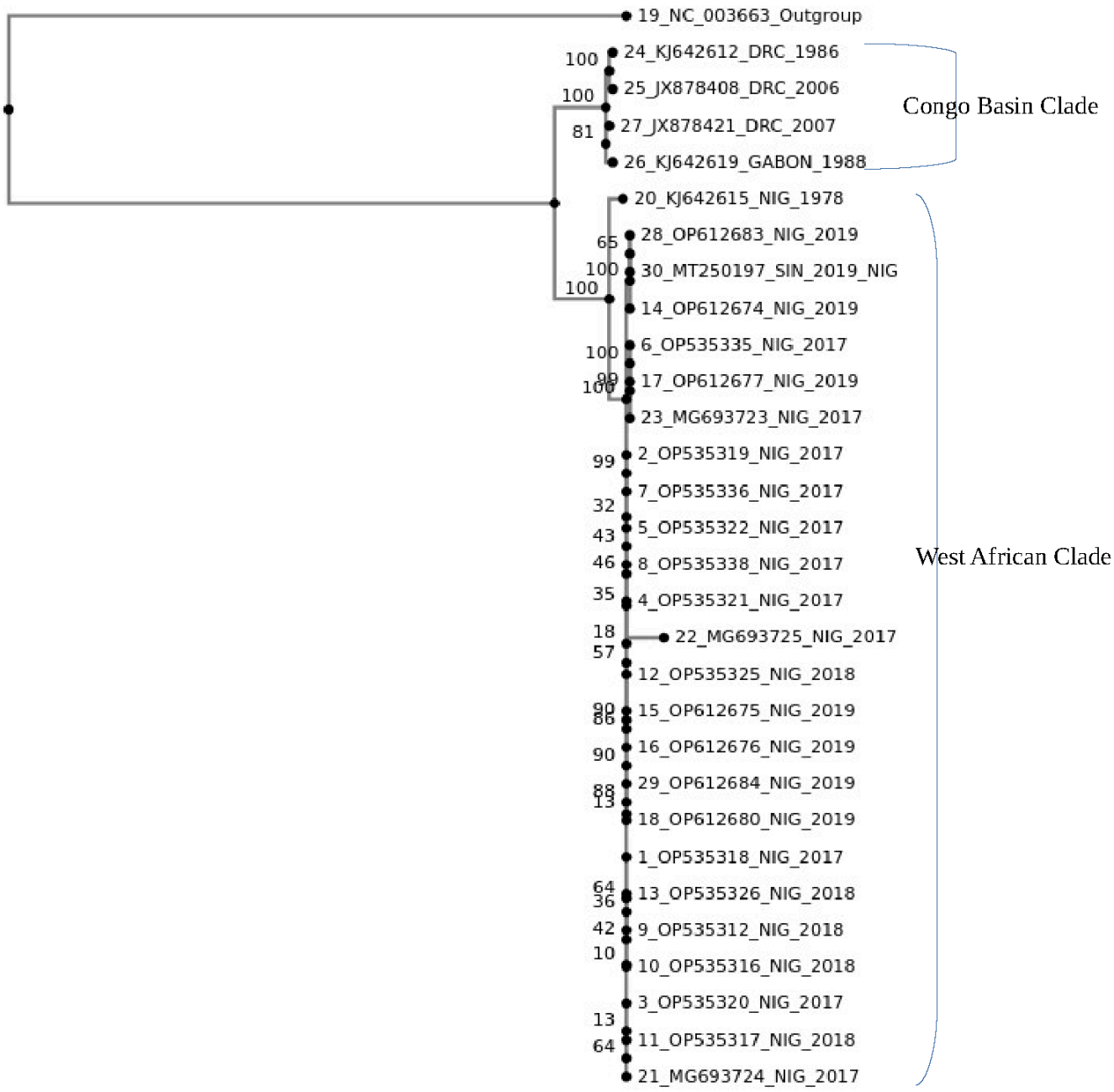


Figure 5

Phylogenetic relationship of retrieved whole genome sequences of MPXV isolate from Nigeria from Pre-Covid-19. Key: The phylogenetic tree was constructed following maximum multiple alignment by the Maximum Likelihood (ML) method with the reliability of individual tree nodes kept at 1000 bootstrap pseudo replicates.