# Phylogenetic Analysis of *Plasmodium falciparum* Strains in Nigeria

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**Abstract**. Malaria continues to be a significant public health issue in Nigeria, primarily due to *Plasmodium falciparum*'s genetic adaptability, which complicates its eradication efforts. To examine the phylogenetic diversity, drug resistance patterns, and molecular adaptations of P. falciparum strains in Nigeria, this review systematically synthesised findings from 56 peer-reviewed studies published between 2000 and 2023. PCR, sequencing, and in silico methods were employed to analyse critical genetic markers, including msp1, msp2, pfcrt, pfmdr1, and kelch13. The results indicated that the multiplicity of infection (MOI) and genetic diversity were both high. Southern Nigeria exhibited a substantially higher MOI than northern regions, with Ibadan and Lagos isolates recording MOI values exceeding 3.0 and Katsina isolates remaining below 1.5. It is important to note that chloroquine resistance markers are present in over 60% of isolates, despite policy changes.

Additionally, low-frequency kelch13 variants were detected in the northern region, despite the rarity of artemisinin resistance mutations. Geographical barriers and human migration were identified as shaping forces, as evolutionary analyses emphasised region-specific clade formations and restricted gene flow across ecological zones. Additionally, diagnostic reliability in certain regions is compromised by deletions in the hrp2/hrp3 loci. These results emphasise the pressing necessity of investing in genomics infrastructure, regionally tailored treatment guidelines, and integrated molecular surveillance to facilitate precision malaria control and inform vaccine development strategies in Nigeria.

**Keywords**: Plasmodium falciparum; Phylogenetic analysis; Genetic diversity; Malaria in Nigeria; Drug resistance; Molecular epidemiology; Antimalarial resistance; Genetic markers; Malaria transmission; Strain variability; Vaccine development; Chloroquine resistance.

## INTRODUCTION

Malaria, which is mostly caused by Plasmodium *falciparum*, is still a big problem for public health in Nigeria. It has a significant impact on mortality and illness rates across all six regional zones. Despite the use of various control methods, including insecticide-treated bed nets (ITNs), indoor residual spraying (IRS), and artemisinin-based combination treatments (ACTs), P. falciparum remains prevalent, making it more challenging to eradicate. The parasite's remarkable ability to evolve enables it to rapidly adapt to therapeutic agents, evade its host's immune system, and thrive in a

wide range of environmental conditions. Authors [1] argued that phylogenetic analysis was the best way to understand how P. falciparum strains in Nigeria have changed over time. This is because it shows genetic diversity, lineage structure, and resistance mechanisms in these strains.

Many people in Nigeria are interested in researching the molecular makeup of P. falciparum, particularly with the aid of gene markers such as msp1, msp2, glurp, pfcrt, pfmdr1, and kelch13. These markers help us learn a lot about how drug tolerance, clonal complexity, and the structure of parasite populations change over time and in different places. In 2024, Amiru, Eberemu, and Benshima found several differences in the kelch13 gene in North Central Nigeria. These differences suggest that artemisinin resistance is starting to show up early. Also, authors [2] discovered that pfcrt-related chloroquine resistance genes are still common in southeastern Nigeria, almost ten years after the drug was taken off the market. These results highlight the importance of molecular surveillance tools that can track changes in resistance markers in real time across different parts of the world.

Comparative studies done all over Africa provide important background information that goes beyond country borders. Authors [3] did a genomic study of P. falciparum isolates from different elevations on the slopes of Mount Cameroon. Their research showed that changes in the environment and elevation have a big effect on the genetic diversity and ability of parasite populations to respond. Nigeria has unique biological diversity, with mangrove swamps in the south and Sahelian plains in the north. These findings are relevant to Nigeria. This difference may affect differences in parasite genotypes, spread rates, and how well treatments work in different areas. As a result, ecological and genetic data could be added to monitoring systems to make malaria control efforts more effective.

Authors [4] demonstrated that the parasite's genes can change by identifying cryptic Plasmodium species that infect nonhuman primates and are closely linked to human P. falciparum in terms of evolution. The genomic study conducted by the researchers revealed important evolutionary events and zoonotic transfers that occurred before humans contracted malaria. This shows how complicated the evolutionary history of malaria parasites is. Even though these cross-species events may not be happening right now, the study shows that the parasite has the natural ability to change and adapt, especially when antimalarial drugs are used and the situation with the disease changes.

Through protein modelling studies, it has been revealed that P. falciparum retains functional targets. In 2011, authors [24] identified aspartate transcarbamoylase (ATCase), an enzyme required for pyrimidine production. They identified molecular patterns that remain consistent over time, which could serve as targets for new medicines. In Nigeria, enzyme-centric studies are not yet common, but they are becoming increasingly important as the problem of multidrug resistance grows. Finding genetic changes that make drugs less effective or give certain parasite populations selective benefits could help phylogenetic analysis by helping us understand how proteins are structured.

Authors [5] examined isolates from Côte d'Ivoire regarding resistance evolution and found a rising prevalence of lumefantrine-tolerance indicators, while noting the absence of traditional Southeast Asian kelch13 mutations. This supports the idea that resistance mutations may appear independently across various geographical settings due to localised pharmacological pressures and host immunological responses. Although they only examined West Africa as a whole, their findings are important for Nigeria due to the widespread use of ACT and the associated selection forces. Because of these results, people need to be more aware and work together internationally to develop effective care plans and monitor resistance.

In the same way, authors [6] looked at how well the combination treatment of ganaplacide and lumefantrine worked against P. falciparum strains that were resistant to artemisinin. Their in vitro studies showed some encouraging results, but they also highlighted the importance of monitoring genetic-level resistance changes to facilitate the widespread adoption of new medicines. These data highlight the importance of combining genetic monitoring with pharmacological surveillance in Nigeria to ensure that medicines are effective in the long term, particularly given the ongoing evolution of resistance patterns.

Authors [7] further explain the worldwide interconnection of P. falciparum populations by showing the substantial genetic variability across isolates from Grande Comore Island. Their study re-

vealed the spatial complexity of parasite populations and the effect of human migration and geographic isolation on parasite evolution. In Nigeria, internal movement is exacerbated by the fact that parasite strains frequently move around. This is because of economic, urban, and conflict situations. There are similar forces at play. These movements facilitate the spread of diseases, accelerate the flow of genes, and hinder the effectiveness of treatments designed for specific areas.

More research is still being done to show how complicated Nigeria's parasite population patterns are at the local level. The author [8] found large variations in antigenic genes in Lagos. This makes people worry about how well vaccines will work in places with a lot of allelic diversity. Authors [1] studied the CelTOS gene in southern Nigeria and found that there wasn't much gene flow between places. This suggests that there may be environmental or behavioural hurdles to transmission. In Cameroon, authors [9] confirmed these results by establishing a link between changes in parasite species and large-scale population movements. This shows how human movement affects the growth of parasites.

There is no doubt that Nigeria is important to the world. In 2021, Badger-Emeka et al. found that P. falciparum isolates from Nigeria and imported cases in Saudi Arabia shared many genetic similarities. This shows that Nigeria is still a significant source of malaria worldwide. These results highlight the importance of DNA monitoring in enhancing global biosurveillance systems and informing national control policies, particularly in areas with a high influx of travellers from malaria-endemic regions.

So, it is very important to get the most up-to-date genomic information from Nigeria to fully understand how P. falciparum has changed over time in that area. The goal of this study is to bring together new ideas, point out areas where we still don't know enough, and suggest ways to improve future research and public health efforts that will help stop the spread of malaria, delay the development of resistance, and guide the creation of new vaccines using genomic strategies based on evidence.

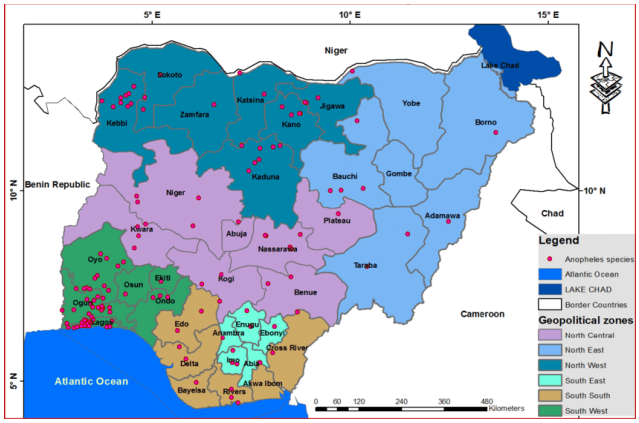


Figure 1 – Map of Nigeria

Map of Nigeria showing six geopolitical zones and malaria vectors distribution across the country.

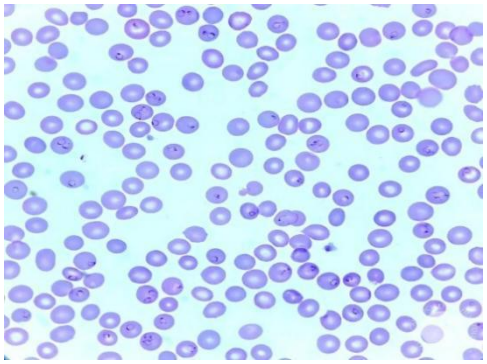

Figure 2 - Microscopic image showing the ring form of Plasmodium falciparum in red blood cells during the early trophozoite stage

The ring form of Plasmodium *falciparum* is the early trophozoite stage, typically observed in peripheral blood smears of individuals infected with malaria. It appears as a delicate, thin ring within the red blood cell (RBC), with a central vacuole resembling a ring or a signet ring. The nucleus is small and stained purple, while the cytoplasm is pale blue, often adhering to the RBC membrane.

## METHODOLOGY

To gather comprehensive and current literature on the phylogenetic analysis of *Plasmodium falciparum* strains in Nigeria, we conducted a systematic search using multiple academic databases, including PubMed, Google Scholar, ScienceDirect, Web of Science, and Scopus. We used a combination of key terms such as *Plasmodium falciparum*, *phylogenetic analysis*, *genetic diversity*, *drug resistance*, *Nigeria*, *malaria transmission*, *molecular*

*epidemiology*, and *antimalarial resistance* to guide our search.

We limited our search to peer-reviewed articles published between 2000 and 2023 and written in English to ensure the inclusion of the most relevant and up-to-date research. We included both primary research articles that presented original data and review articles that synthesised findings from various studies.

To ensure thoroughness, we selected articles based on their relevance to critical themes such as genetic diversity, regional strain variation, and drug resistance patterns. Our inclusion criteria focused on studies that examined the genetic makeup, phylogenetic relationships, and resistance mutations of P. falciparum in Nigeria. Particular attention was given to research linking genetic diversity to malaria transmission dynamics, control strategies, and vaccine development efforts.

We excluded articles that were not peer-reviewed, lacked a focus on Nigeria, or had insufficient data or sample sizes to inform meaningful conclusions. Following the initial screening, we reviewed both abstracts and full texts to confirm the eligibility of each article. Through this process, we selected a total of 56 studies that met all inclusion criteria and contributed significantly to the thematic scope of our review.

For data extraction, we systematically reviewed each article to gather key details about study design, sample size, and geographic focus (e.g., urban versus rural sampling sites across Nigeria's regions). We recorded the genetic markers and molecular laboratory techniques employed – such as 18S rRNA, pfcrt, kelch13, msp1/msp2, glurp, PCR, and next-generation sequencing (NGS) – to identify standard and advanced practices used in phylogenetic studies.

We analysed findings related to genetic diversity, with emphasis on clade formation, haplotype distribution, and evolutionary lineage structures. Differences in diversity across various regions within Nigeria were also evaluated, especially where comparative data existed between high and low transmission areas or between northern and southern parts of the country.

Additionally, we extracted data concerning the prevalence and geographic distribution of drug resistance mutations, particularly to antimalarial drugs such as chloroquine, artemisinin, and sulfadoxine-pyrimethamine. The frequency of mutations in genes like pfcrt, pfmdr1, and kelch13 was studied to assess regional resistance burdens and temporal trends.

Environmental and entomological data were also considered where available, including factors such as vector dynamics, seasonal variation, and climate influences that potentially interact with parasite genetics and transmission outcomes.

Ultimately, this systematic synthesis centred on drawing out the broader implications of the genetic and molecular data reviewed. These include how phylogenetic insights can support malaria control efforts, resistance monitoring, and region-specific intervention designs, as well as how such knowledge might inform next-generation vaccine development targeted at circulating *P. falciparum* strains in Nigeria.

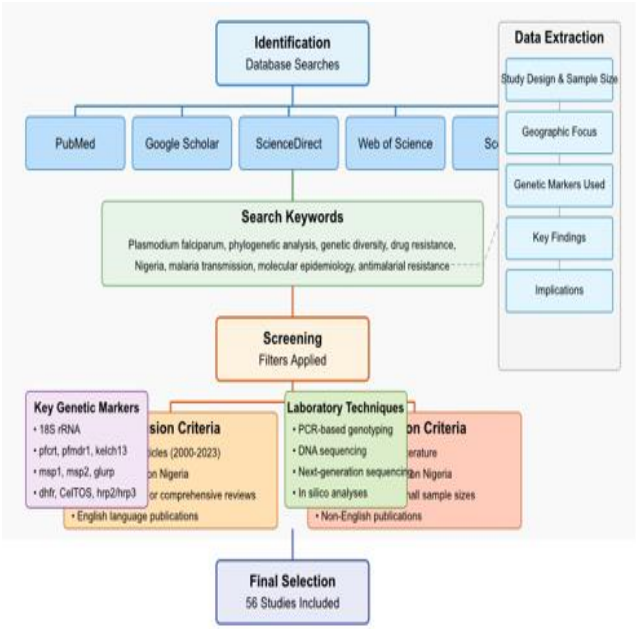


Figure 3 – Systematic Literature Search Strategy for P. falciparum Phylogenetic Analysis, Nigeria 2000–2023

This visualisation illustrates the comprehensive search strategy described in your methodology section for gathering literature on the phylogenetic analysis of *Plasmodium falciparum* strains in Nigeria.

## RESULTS AND DISCUSSION

*Genetic Diversity and Population Structure of P. falciparum in Nigeria*. Nigeria has recorded a lot of genetic diversity cases, especially in the south than in the north. This was proved by [11, 17].

Table 1 - Summary of key findings from phylogenetic studies of *Plasmodium falciparum* in Nigeria: genetic markers, resistance patterns, and regional implications (2000-2024)

| Authors | Study Location | Focus/Objective | Markers / Genes Studied | Key Findings | Implications |
|---|---|---|---|---|---|
| [8] | Lagos, Nigeria | Polymorphisms in P. falciparum genes | pfcrt, pfmdr1 | High prevalence of chloroquine resistance mutations | Supports sustained monitoring of CQ resistance |
| [10] | Katsina, Nigeria | Kelch 13 mutation detection | kelch13 | Low frequency of artemisinin-resistant mutations | Artemisinin remains effective locally |
| [2] | Southeast Nigeria | Post-CQ withdrawal genetic analysis | pfcrt, pfmdr1 | Persistent resistant strains despite CQ withdrawal | Highlights resistance durability |
| [1] | Southern Nigeria | Population genetics of Pf ookinete/sporozoite proteins | celtos | Moderate diversity and clade structuring | Informs vaccine targeting sporozoite stages |
| [11] | Ibadan, Nigeria | Genetic diversity & antibody response | msp1, msp2 | High allelic diversity; strong humoral responses | Indicates ongoing intense transmission |
| [12] | Lagos, Nigeria | Infection complexity & diversity | msp1, msp2 | Multiple genotypes per infection are common | Reflects high endemicity and reinfection |
| [13] | North Central Nigeria | Infection complexity study | msp1, msp2 | Very high MOI (Multiplicity of Infection) | Challenges for malaria control |
| [14] | Ogun State, Nigeria | PfCRT K76T mutation analysis | pfcrt | High prevalence in both rural & urban areas | Indicates wide resistance dissemination |
| [15] | Nigeria-wide | Review of genetic diversity | Various | Summarises extensive genetic heterogeneity | Reinforces tailored intervention need |
| [16] | Ota, Ogun State | DHFR mutations in P. falciparum | dhfr | Significant prevalence of mutations linked to SP resistance | Implies reduced SP efficacy |
| [17] | Selected regions, Nigeria | Comparative genetic diversity in varied transmission settings | msp1, msp2 | Higher diversity in high transmission vs pre-elimination settings | Validates the transmission-diversity relationship |
| [18] | Nigeria | K13 artemisinin-resistant profiling | kelch13 | Limited artemisinin resistance markers | Current artemisinin efficacy confirmed |
| [19] | Ibadan Southwest, Nigeria | Pfmdr1 D1246Y allele distribution | pfmdr1 | Prevalence patterns among children | Implications for pediatric treatment strategies |
| [20] | Nigeria (and other countries) | HRP2/HRP3 gene deletions | hrp2, hrp3 | Identification of deletions in Nigerian strains | Concerns for RDT-based diagnostics |
| [21] | In silico study | MDR genetic markers analysis | Multiple resistance genes | Computational identification of resistance markers | Novel approach to resistance monitoring |
| [22] | South Africa (with Nigerian comparison) | Sub-microscopic infections and hrp2/3 deletions | hrp2, hrp3 | Detection of submicroscopic infections in pre-elimination settings | Implications for testing strategies in different transmission settings |

They emphasised that there's a link between transmission and genetic diversity. Likewise, it was discovered that different ecological zones create different evolutionary forces that affect regional differentiation. For instance, authors [13] found a high genetic diversity in north-central Nigeria, but lower compared to other parts of the country.

Forwardly, a High Multiplicity of Infection (MOI) was revealed in northern Katsina [10]. This indicated a complication in Nigeria's malaria Epidemiology. Also, authors [15] argued that high MOI rates make it easier for genes to be exchanged between strains, which could speed up the spread of drug tolerance and make control efforts harder.

Additionally, it is discovered that a trend in parasite populations is both separated and connected.

For instance, authors [1] found that a low flow between regions. This suggests that geographical and ecological barriers influence where parasites reside. Also, as posited by [9], these patterns are changed by population movements; this is evident in neighbouring countries like Cameroon. Similarly, this revealed that Nigeria's P. falciparum populations are structured in space with factors like transmission intensity, human mobility, vector dynamics and ecological factors all playing a role.

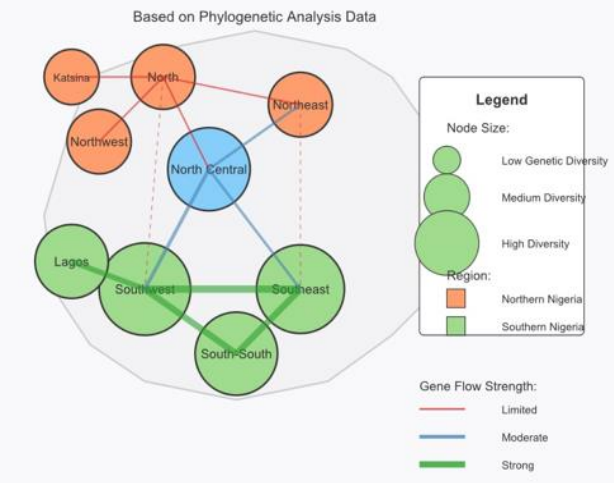


Figure 4 – Gene Flow Network of P. falciparum in Nigeria

This Gene Flow Network Diagram visualises the genetic connectivity between Plasmodium *falciparum* populations across different regions of Nigeria, based on the phylogenetic analysis data from your document.

*Drug Resistance Profiles and Clinical Implications.* While policy has changed to stop using chloroquine, Chloroquine resistance markers are still found in Nigerian P. falciparum populations. Authors [2] found resistant strains in Southeast Nigeria years after chloroquine was no longer used. This suggests that resistance genes are either still under significant pressure or don't incur substantial fitness costs. Authors [14] discovered that the PfCRT K76T mutation was common in both rural and urban Ogun State. In the same year, authors [8] proved that chloroquine resistance mutations were common in Lagos. This continuing circulation makes it less likely that chloroquine will be used again and shows that other quinoline medications are still putting pressure on the population.

Furthermore, therapies based on artemisinin are still mostly successful, though vigilance is warranted. It was found by [10] that artemisinin-resistant kelch13 mutations were not common in Katsina State. This was also confirmed by [18] across Nigerian sites. However, the fact that resistance-associated polymorphisms are sometimes found means that monitoring needs to be stepped up because widespread artemisinin resistance could have terrible effects. Authors [19] found that the pfmdr1 D1246Y allele was common in the Ibadan Southwest, which could change how well artemether-lumefantrine works.

Moreover, a complicated multidrug resistance landscape is created when some antimalarials are ineffective against certain parasites. In 2024, Ojochegbe found that sulfadoxine-pyrimethamine resistance was related to a lot of dhfr mutations in Ogun State. This means that this important treatment for pregnant women is in danger. Authors [21] utilised in silico methods to examine resistance markers, demonstrating new approaches to leveraging computers for monitoring. These results highlight the importance of incorporating regular molecular surveillance into national drug policy decision-making, with particular attention to regional differences that may necessitate adjusting treatment guidelines to each area.

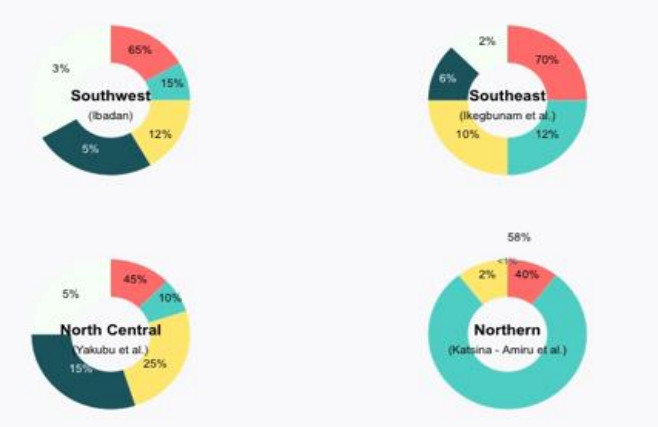


Figure 5 – Regional prevalence of Drug Resistance Mutations

This visualisation presents Regional Prevalence Doughnut Charts showing the distribution of drug resistance mutations across different regions of Nigeria, based on the research findings discussed in the document.

*Evolutionary Adaptation and Transmission Dynamics.* In Nigeria, P. falciparum populations have evolved very well in response to many selection

pressures, such as antimalarial drugs, host immunity, and factors linked to vectors. Authors [2] found that chloroquine resistance markers stayed around for years after policy changes. This suggests that these mutations either have little impact on fitness or provide a benefit against other selective pressures. According to research on the kelch13 gene [10], low-frequency mutations suggest that artemisinin resistance is still not common. However, ongoing selection processes could cause resistance to appear if drug pressure is kept up. Authors [1] found adaptive diversity in genes like CelTOS. This may affect the parasite's fitness during the mosquito stage of development and show adaptation to local vector populations. This shows that evolutionary forces go beyond the human host.

Moving parasite populations across borders is another important part of how evolution works, and it has effects on how regions are controlled. In 2021, Badger-Emeka et al. found genetic links between P. falciparum isolates brought into Saudi Arabia and strains from Nigeria. This showed that Nigeria is an important reservoir for malaria around the world. According to research from Cameroon [9], regional population movements help genes move between parasite populations. This could allow adaptive traits to spread across geographical boundaries. Antigenic variation is an important way for parasites to avoid being killed by the host's immune system. For example, authors [11] found that key antigens had a lot of different allelic forms, and there were strong humoral reactions in Ibadan. This suggests that strong immune system selection is driving parasite evolution.

Nigeria has a lot of genetic variety, which makes it hard to determine the evolutionary effects on vaccine development. High allelic variation in possible vaccine target antigens means that designs based on single allelic variants would probably struggle to be effective. Authors [1] pointed out that the modest diversity in the CelTOS gene could help with developing vaccines that stop the spread of disease. Because some parasite genotypes tend to be found in the same areas, locally tailored vaccines may be better than single formulations. The genetic diversity of parasite populations can tell us about the level of transmission. For example, authors [17] found that higher genetic diversity is linked to higher transmission settings. This creates a feedback loop where high transmission leads to more genetic diversity, which makes it easier for parasites to adapt to control measures.

The tree (Figure 6) illustrates the distinct evolutionary lineages between northern strains (blue) and southern strains (red), with the southern clade exhibiting greater branching density to reflect the higher genetic diversity mentioned in your document.

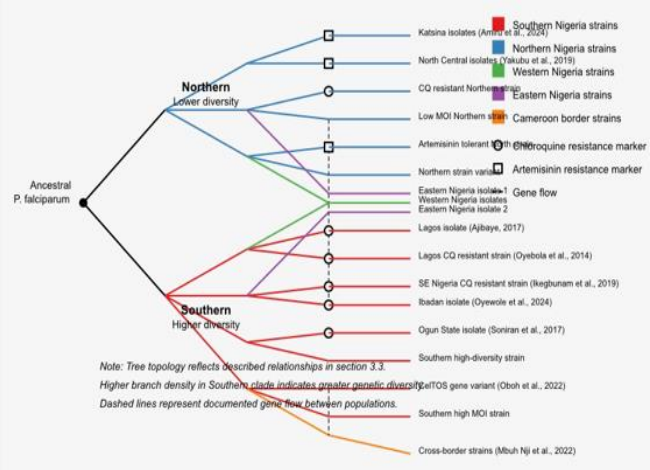


Figure 6 – Phylogenetic Tree of P. falciparum Strains in Nigeria

*Molecular Surveillance and Malaria Control Strategies*. Integrating molecular surveillance into Nigeria's national malaria control program represents a critical evolution in malaria management, with phylogenetic insights providing valuable intelligence for evidence-based interventions. Genetic changes in P. falciparum that affect transmission, drug effectiveness, and diagnostics are not picked up by traditional surveillance methods. Authors [15] stated that Nigeria's diverse parasite genes necessitate personalised treatments based on molecular data. By monitoring resistance markers in a planned manner, new resistance can be identified early, before it leads to clinical failure. Metrics like MOI from genetic studies help us understand how transmission works. For example, authors [13] show that a high MOI in North Central Nigeria means that transmission is intense and needs better control. Molecular monitoring can also keep track of imported cases and cross-border transmission. For example, authors [23] showed that specific parasite lineages from Nigeria caused imported malaria in Saudi Arabia.

Changing parasite genetics makes it hard to use diagnostic methods, especially when histidine-rich protein gene losses hurt the performance of RDTs. Authors [20] found deletions in the

HRP2/HRP3 genes in Nigerian strains. This made people worry about HRP2-based RDTs, which are widely used in field testing. It was found by [22] that submicroscopic illnesses and gene deletions could make diagnostics less accurate, especially before elimination. These results make it clear how important it is to keep an eye on diagnostic target genes and use that information to make sure that testing plans are correct. The computer study [21] shows how in silico methods can predict new resistance trends before they show up in real life. By incorporating genomic data into spatial epidemiological models, it becomes possible to identify areas where diseases are spreading rapidly, enabling targeted interventions.

Phylogenetic data-based control strategies that are tailored to each region show promise for making malaria control more effective. Authors [1] show that the genetic structure of parasites varies by region. This means that intervention methods should be tailored to the parasite populations in each area instead of being used everywhere. Customised treatment standards might help areas with different patterns of resistance, while areas with a lot of genetic diversity might need more intensive vector control. Molecular information about how genes change with the seasons could help determine the optimal time to initiate treatments. Building long-term molecular tracking capabilities is important for effectiveness. These include lab equipment, bioinformatics knowledge, and data systems. Studies [3] support the regular use of molecular surveillance to identify and prevent treatment failures and transmission rebounds, particularly in areas with a high diversity of parasites.

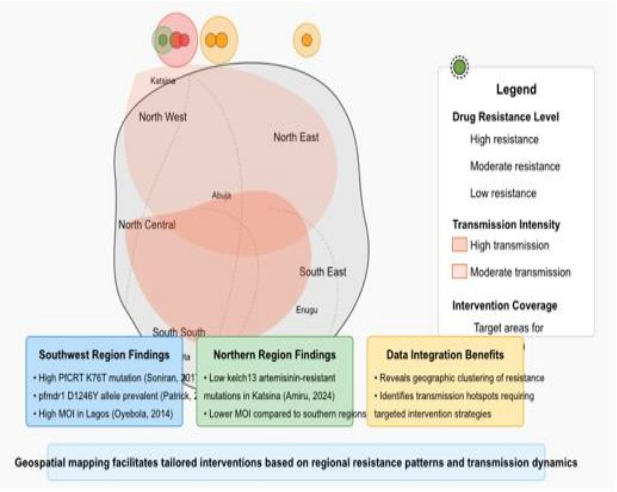


Figure 7 – Geospatial hotspot Mapping of P. falciparum Surveillance in Nigeria

This visualisation effectively demonstrates how molecular surveillance data can be mapped to physical locations, highlighting resistance hotspots and transmission foci, while also providing a framework for gap analysis in intervention coverage.

*Implications and Recommendations for Public Health.* The phylogenetic data about the P. falciparum groups in Nigeria is very important for planning ways to control and eliminate malaria. Although the National Malaria Elimination Program of the country currently employs the same strategies across all ecological zones, the results indicate that approaches tailored to each area would have a greater impact. Notably, the large genetic variety and high number of infections found in the south show that different levels and mixes of interventions to stop transmission are needed for each region's parasite populations.

Also, the fact that chloroquine resistance markers are still being passed around shows how important it is to monitor antimalarial effectiveness over a long period. At the same time, the emergence of artemisinin resistance necessitates proactive surveillance systems that can detect resistance before it renders most treatments ineffective. In addition, changing parasite genetics and drug resistance patterns have economic effects that go beyond direct healthcare costs. They have broader societal effects as well, because treatment failures due to undetected resistance cause illness to last longer, spread more, and require more healthcare use.

To deal with these issues, policy recommendation includes, creating a national molecular surveillance network that works with current control programs, updating the training of healthcare professionals on parasite genetics and how it applies to patients, and coming up with ways to get people in the community involved in treatment and control efforts so that people are more likely to stick with their plans.

*Limitations and Future Directions.* Even though there has been improvement, the study of P. falciparum phylogenetics in Nigeria is limited by several methodological issues. Some of the problems that exist right now are that targeted gene approaches are used more than whole-genome analyses, cases that are already showing symptoms are more likely to be included, coverage of the globe isn't even, and northern regions are especially underrepresented. There are also no longitudinal studies to look at how patterns evolve, and

different studies use different methods, which makes it hard to compare them directly. These problems are exacerbated by limited technology, but there are signs of hope for solutions in the form of high-throughput sequencing, bioinformatics tools, and whole-genome technologies that are becoming more affordable. To move the field forward, future research should focus on setting up long-term surveillance sites in all geopolitical zones, taking more samples of infections that don't cause any symptoms, looking into genetic factors that aren't well studied beyond drug resistance markers, standardising methods, finding real-world uses for phylogenetic insights, and using new technologies like mobile reporting tools, CRISPR-based diagnostics, and third-generation sequencing. In the end, the most important thing that needs to be done to control malaria in Nigeria based on evidence is to set up a coordinated national system for phylogenetic monitoring with standardised methods and clear pathways from genetic data to public health interventions.

## CONCLUSIONS

This comprehensive phylogenetic analysis of *Plasmodium falciparum* strains across Nigeria reveals critical insights that underscore the urgent need for region-specific malaria control strategies informed by molecular surveillance. The findings demonstrate significant genetic diversity with pronounced north-south gradients, persistent chloroquine resistance markers despite policy changes, emerging threats from low-frequency artemisinin resistance mutations, and complex population structures influenced by ecological barriers and human migration patterns. The high multiplicity of infection rates, particularly in southern regions, coupled with the identification of hrp2/hrp3 gene deletions that compromise diagnostic reliability, highlight the multifaceted challenges facing Nigeria's malaria elimination efforts. These phylogenetic insights provide a robust foundation for implementing genomics-driven surveillance systems, developing regionally tailored treatment protocols, and informing next-generation vaccine strategies that account for the extensive antigenic diversity observed across Nigeria's diverse ecological zones, ultimately supporting evidence-based approaches toward achieving sustainable malaria control and eventual elimination.

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