



Trends, Manifestations, Issues and Prospects of Chloroquine Resistance in Nigeria: A Structured Narrative Review

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Received 18 June, 2026

Revised 24 August, 2026

Accepted 25 August, 2026

Published 29 August, 2026

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Abstract

Chloroquine was once central to malaria treatment in Nigeria, but widespread resistance prompted its withdrawal as first-line therapy in 2005. This narrative review characterized Nigerian research on chloroquine resistance, examined trends in use and resistance, and assessed evidence of continued use after withdrawal. PubMed and Google Scholar were searched from 1 to 14 August 2025 for English-language studies using terms related to chloroquine, Nigeria, pfcr, K76T, pfmdr1, mutation, polymorphism, and resistance. The search covered publications from 1980 to 2025; the studies meeting the eligibility criteria were published between 1989 and 2025. Of 1,490 records retrieved, 150 full texts were assessed, and 60 studies met the eligibility criteria. Evidence was summarized by design, period, geographical distribution, and level. Observational studies predominated, while randomized trials and systematic reviews were uncommon, indicating that most evidence was surveillance-based rather than trial-based. Research was concentrated in the South West and South-South, with comparatively limited coverage in the South East and North East. Molecular evidence suggests that the prevalence of the pfcr K76T resistance allele has declined in some settings; however, continued informal use, affordability, accessibility, and renewed exposure during the COVID-19 period may sustain drug pressure. The findings indicate uneven surveillance rather than a uniform national picture and do not establish complete restoration of chloroquine susceptibility. Nigeria should strengthen pharmacovigilance, nationwide molecular and genomic surveillance of pfcr and pfmdr1, periodic resistance mapping, enforcement of withdrawal restrictions among Patent and Proprietary Medicine Vendors, and monitoring of informal medicine markets.

Keywords: Chloroquine resistance; Drug resistance; Malaria treatment policy; Molecular markers; Narrative review; Nigeria; *Plasmodium falciparum*

Introduction

In January 2005, the Nigerian Federal Ministry of Health announced a phase-out program for malaria-resistant drugs used in the treatment of uncomplicated malaria, with chloroquine included among them. The program also covered sulfadoxine-pyrimethamine [1,2]. This decision was driven by the emergence of multi-drug resistance in *Plasmodium falciparum*, the protozoan species responsible for severe malaria. Chloroquine was included in the phase-out because of the emergence of chloroquine-resistant (CQR) strains [3,4]. Despite WHO's target of reducing malaria incidence and mortality by 90% in 35 countries by 2030, by 2020 only about a

third of the milestones had been achieved, and the overall target appears unrealistic [5,6].

Chloroquine had long been a drug of choice for malaria treatment due to its ease of use, relatively high efficacy, and cost-effectiveness. Millions of doses were consumed annually, making it a cornerstone of malarial chemotherapy. However, growing concerns over high resistance rates and treatment complications led to its withdrawal as a first-line drug, according to WHO's Guidelines for the Treatment of Malaria (2015) [3,7–10]. CQR was first reported in 1957 in Southeast Asia and spread to Eastern Africa by the late 1970s, before gradually reaching West Africa. In Nigeria, the first documented cases of chloroquine resistance were reported in 1987 in Lagos in the

South West and Calabar in the South-South, after which resistance was reported across the country. Several genes have been implicated in this resistance, but the most widely recognized are *pfCRT* and *pfmdr1*, which encode the chloroquine resistance transporter (pfcRT) and multi-drug resistance transporter (pfMDR1), respectively. The *pfCRT* mutation results in a substitution of lysine with threonine (T76) at position 76, while the *pfmdr1* mutation replaces tyrosine (Y86) with asparagine [3,11,12].

The *pfCRT* T76 mutation serves as a molecular marker for chloroquine resistance and is considered the key determinant of chloroquine sensitivity. Its mechanism involves efficient efflux of protonated chloroquine molecules out of the parasite's digestive vacuole (DV), reducing drug accumulation and impairing its toxic effect on the heme target. Mutations in the *pfmdr1* transporter have also been linked to resistance or sensitivity not only to chloroquine but also to quinine, mefloquine, artemisinin, lumefantrine, and halofantrine [11,13–16].

Withdrawal of chloroquine has been associated with declining resistance in some African regions, including Tanzania, Zambia, and Malawi. More recent studies in Nigeria also suggest a reduction in the prevalence of the *pfCRT* K76T allele, likely due to decreased drug pressure [2,17]. However, other studies still report molecular evidence of persistent resistant strains, driven by continued drug pressure and ongoing chloroquine use among certain groups, particularly patent and proprietary medicine vendors (PPMVs) [3,11].

Although previous studies have documented the emergence and molecular mechanisms of chloroquine resistance in Nigeria, most have been limited to individual locations, specific resistance markers, or isolated epidemiological findings. To date, there is no comprehensive narrative review that merges the geographical distribution, methodological characteristics, extent of continued chloroquine use, policy compliance, and evolving resistance patterns across the country. This gap is particularly important in light of emerging reports of artemisinin-based combination therapy (ACT) resistance and the increasing financial burden associated with ACT use in many low- and middle-income countries. Evidence from countries such as Malawi suggests that sustained withdrawal of chloroquine can restore parasite susceptibility, raising the possibility that renewed chloroquine effectiveness could contribute to future malaria control strategies. For resource-constrained settings such as Nigeria, understanding the current landscape of chloroquine use and resistance has important clinical, public health, and socioeconomic implications. By reviewing the available evidence, this review provides an overview of chloroquine resistance research in Nigeria, identifying methodological and geographical gaps in the existing literature, and as well highlighting priority areas for surveillance, policy implementation, and future research. This narrative review aims to characterize the existing literature on chloroquine use and resistance in Nigeria by synthesizing evidence on study characteristics, trends in chloroquine use and resistance, reported molecular resistance markers, current resistance patterns, and evidence of continued chloroquine use after withdrawal as first-line therapy under the national withdrawal policy.

Methods

Study design and scope

This study was conducted as a structured narrative review of published literature on chloroquine use and chloroquine resistance in Nigeria. The review focused on studies addressing trends, manifestations, molecular markers, treatment response, policy compliance, and continued chloroquine use after its withdrawal as first-line therapy. The search covered studies published between 1980 and 2025 and included research conducted in Nigeria or studies that provided extractable Nigeria-specific data.

Eligibility criteria

Studies were eligible for inclusion if they were published in English, fell within the defined publication period, and addressed chloroquine use, chloroquine resistance, treatment response, molecular resistance markers such as *pfCRT* and *pfmdr1*, or chloroquine-related malaria treatment policy in Nigeria. Studies were excluded if they were not related to Nigeria, did not provide extractable Nigeria-specific data, lacked sufficient information for review, or did not address chloroquine use or resistance in relation to malaria.

Review questions

The review was guided by the following questions:

1. What are the characteristics of published studies on chloroquine resistance in Nigeria?
2. What are the trends in chloroquine use and resistance in Nigeria?
3. What is the current level of chloroquine resistance reported in Nigeria?
4. To what extent does chloroquine continue to be used after its withdrawal as first-line therapy?

Search strategy

PubMed and Google Scholar were searched between 1 and 14 August 2025 for English-language studies published from 1980 to 2025. The search used combinations of Medical Subject Headings, free-text terms, and Boolean operators. Search terms included chloroquine, chloroquine resistance, chloroquine use, Nigeria, malaria, *Plasmodium falciparum*, *pfCRT*, K76T, *pfmdr1*, mutation, polymorphism, and antimalarial. Reference lists of eligible articles and relevant review papers were also screened manually to identify additional studies.

Study selection

The electronic search yielded 1,490 records, comprising 1,410 records from Google Scholar and 80 records from PubMed. Duplicate records were removed before screening. Titles and abstracts were screened against the eligibility criteria, after which 150 articles were selected for full-text assessment. Full texts were then reviewed, and 60 studies met the inclusion criteria and were included in the narrative review. The study selection process is summarized in Figure 1. This matches the manuscript's reported search and screening numbers.

Data extraction and evidence classification

Data were extracted using a standardized data-extraction form. Extracted information included publication year, study design, study location, geopolitical zone, study population, sample size, chloroquine use, treatment response, molecular resistance markers, resistance patterns, and key findings. Formal

independent dual screening and extraction were not undertaken. However, uncertain records and ambiguous extracted data were checked against the full text and resolved through author discussion. The Oxford Centre for Evidence-Based Medicine and Scottish Intercollegiate Guidelines Network frameworks were used to classify the level and hierarchy of evidence. No formal validated study-level risk-of-bias tool was applied.

Data synthesis

A descriptive narrative synthesis was used. Included studies were summarized according to publication period, study design, geographical distribution, study population, evidence level, chloroquine use, treatment response, and molecular resistance markers. Frequencies and percentages were used to summarize study characteristics where appropriate, while key findings were discussed narratively to identify trends, gaps, and implications for chloroquine resistance surveillance and malaria treatment policy in Nigeria.

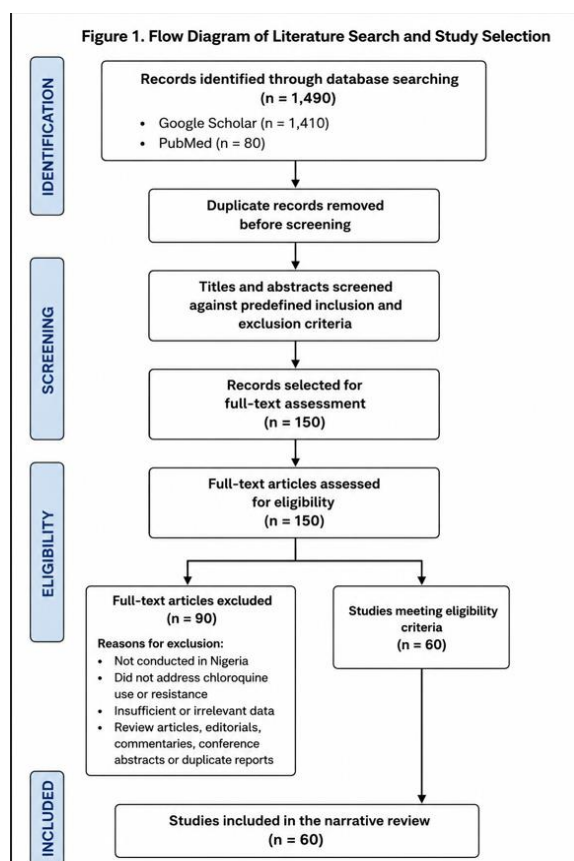


Figure 1. Diagrammatic flowchart of the article selection process for the study

Results

The search yielded 1,490 records, of which 150 full-text articles were assessed and 60 studies met the inclusion criteria. The included studies were summarized by study design, location, publication period, sample size and data source (Table 1). The regional distribution of study locations is presented in Table 2. Study classification using the Oxford Centre for Evidence-Based Medicine and Scottish Intercollegiate Guidelines

Network frameworks is shown in Tables 3 and 4, respectively. The distribution of studies by publication period is presented in Table 5.

A total of 60 studies met the inclusion criteria. Observational designs accounted for 54 studies (90.0%); randomized controlled trials and systematic reviews were uncommon. Because several studies covered more than one geopolitical zone, the geographical analysis produced 69 zone occurrences. The South West had 28 occurrences (40.6%), followed by the South-South with 15 (21.7%), North West with 10 (14.5%), North Central with 9 (13.0%), South East with 5 (7.2%), and North East with 2 (2.9%). Publication-year reconciliation identified 9 studies before 2000, 14 from 2000–2010, 22 from 2011–2020, and 15 after 2020. These findings demonstrate marked geographical and methodological imbalance in the available evidence.

Discussion

Overall, this study aimed to provide a bird's-eye view of research on chloroquine resistance in Nigeria. It highlighted gaps across different geopolitical zones, the characteristics of studies conducted, patterns of chloroquine use, and the current level of resistance. The study was necessitated by the economic need to identify more affordable alternatives, given not only the emerging resistance to ACT-based therapies but also the socio-economic burden they place on average Nigerians, particularly rural dwellers and underserved populations.

The South West recorded the greatest number of geographical occurrences (28; 40.6%), particularly in Ibadan, Lagos, and Osogbo. Studies in this zone frequently examined molecular markers, clinical efficacy, and resistance trends. The South-South followed with 15 occurrences (21.7%), with substantial work in Calabar, Benin, Bayelsa, Rivers, and Delta. Coverage was lower in the North West (10; 14.5%), North Central (9; 13.0%), South East (5; 7.2%), and North East (2; 2.9%). These percentages describe study-location occurrences rather than unique studies because multi-zone studies contributed to more than one category. The observed geographical differences could stem from different factors. Regions such as the South West have historically benefited from stronger academic institutions, established research collaborations, and better access to research funding, making them major centres for malaria research. In contrast, the low number of studies from the Northeast may be due to insecurity, logistical challenges, and limited research infrastructure. These gaps in rural and underserved communities are significant. The surprisingly low coverage in the Southeast, despite its dense population and high malaria burden, also deserves emphasis and may indicate disparities in research prioritization rather than a lower malaria burden. This mirrors findings from other African countries where urban or economically stronger regions have richer datasets, while rural or conflict-affected zones remain underrepresented. This is concerning, as underserved areas typically experience a higher malaria burden and may exhibit different resistance patterns [76]. These geographical imbalances may result in important resistance trends remaining undetected in underserved areas, thereby limiting the representativeness of the available evidence.

Overall, 60 studies were included in this review, most of them observational epidemiological designs, primarily cross-sectional and cohort studies, with very few RCTs, systematic reviews, or case-control studies. This trend is similar to other Sub-Saharan

Table 1: Concise characteristics of studies included in the narrative review

Ref.	Location	Region	Design	Year	N	Data source/instrument
[3]	Anambra, Rivers, Bayelsa	South South, South East	Cross sectional survey	2024	582	Questionnaire
[18]	Zaria	North West	Cross-sectional observational	1989	59	In-vitro assay
[19]	Benue State	North Central	Cross-sectional observational	1990	271	Microscopy; WHO/in-vivo test; Clinical monitoring; Records/audit
[20]	Anambra, Benue	South East, North Central	observational field study	1991	922	Microscopy; WHO/in-vivo test; Clinical monitoring; Records/audit
[21]	Calabar	South South	Cross-sectional observational	1991		Questionnaire
[22]	Calabar	South South	Prospective observational study	1991	33	WHO/in-vivo test; In-vitro assay
[23]	Ibadan	South West	Prospective randomized controlled trial with initial observational cohort	1997	110	Microscopy; In-vitro assay; Clinical monitoring
[24]	Calabar	South South	Prospective observational cohort study	1997	69	WHO/in-vivo test; Clinical monitoring
[25]	Calabar	South South	Prospective Cohort Study	1999	1935	WHO/in-vivo test; Clinical monitoring; Records/audit
[26]	Zaria	North West	Observational molecular epidemiology study	1999	39	PCR; RFLP
[27]	Ibadan	South West	Prospective Randomized Controlled Test	2002	142	Microscopy; Clinical monitoring
[28]	Ibadan	South West	Observational Clinic Study	2002	62	In-vitro assay
[29]	Delta	South South	Prospective observational study	2003	218	WHO/in-vivo test; In-vitro assay
[30]	Ibadan	South West	Observational Study	2003	30	Blood sample; Clinical monitoring
[31]	Ibadan	South West	Observational Study	2003	48	Blood sample; Clinical monitoring
[32]	Ibadan	South West	Prospective observational clinical study	2003	161	Microscopy
[33]	Sokoto	North West	Case Reports	2003	3	Not stated
[34]	Ibadan	South West	prospective cohort study	2005	385	Not stated
[35]	Sokoto and Kebbi State	North West	Prospective Observational Study	2005	559	Blood sample
[36]		South West	Prospective Observational Study	2006	111	Blood sample
[37]	Nil		In vitro experimental laboratory study	2008	Nil	In-vitro assay
[38]	Osogbo	South West	Prospective Cohort Study	2008	116	Blood sample
[39]	Benin	South South	Cross-sectional comparative study	2008	424	Blood sample
[40]	Benin	South South	Cross sectional survey	2009	561	Not stated
[41]	Lagos	South West	Cross-sectional observational study	2011	1211	Blood sample
[42]	Sagamu, Ogun	South West	Cross-sectional study	2011	98	Not stated
[43]	Kano	North West	Mixed-method prospective cross-sectional study (caregiver treatment-seeking behavior and prescriber knowledge/attitudes) combined with retrospective prescription audit	2011	342	Not stated
[44]	Nigeria, Brazil		Cross-sectional study	2012	88	Study records
[45]	Lagos	South West	Cross-sectional study	2014	1527	Blood sample
[46]	Lagos	South West	Cross-sectional study	2015	251	Blood sample
[47]	Ibadan	South West	Prospective Cohort Study	2015	120	Not stated
[48]	Lagos	South West	Cross-sectional study	2016	54	Not stated
[49]	Sagamu	South West	Cross-sectional study	2016	180	Questionnaire

[50]	Sub-Saharan Africa		Narrative Review of Systematic Studies	2016	Does not apply	Narrative synthesis
[51]	Calabar	South South	Cross-sectional study	2017	369	Microscopy
[52]	Kaduna, Jigawa, Kano, Kebbi, Katsina	North West	Cross-sectional study	2017	466	Blood sample
[53]	Uyo	South South	Case Control Study	2017	67	Not stated
[54]	Ogun	South West	Cross-sectional study	2017	249	Blood sample
[55]	Edo, Lagos	South South, South West	Cross sectional Study	2018	151	Blood sample
[56]	Ogbomoso, Oyo State,	South West	Cross-sectional descriptive study	2019	254	Blood sample
[57]	Bayelsa, Rivers, Edo, and Delta, Nigeria	South South	Cross-sectional molecular epidemiological study	2019	846	Blood sample
[11]	Nnewi	South East	Cross-sectional molecular epidemiological study	2019	725	Not stated
[58]	Lagos	South West	Cross-sectional study	2020	1243	Study records
[59]	Akure, Ondo	South West	Case-control study	2020	317	Blood sample
[60]	Kwara	North Central	Cross-sectional Study	2020	187	Blood sample
[61]	Lagos, Osun	South West	Cross-sectional epidemiological study	2020	83	Blood sample
[62]	Adamawa, Sokoto, Kwara, Bayelsa, Imo	North East, North West, North Central, South South, South East	Observational Cohort Study	2021	271	Blood sample
[63]	Port-Harcourt	South South	Observational Study + Post treatment Sampling	2021	459	Blood sample
[64]	New Bussa. Ijeda	North Central, South West	Cross-sectional comparative study	2021	145	Not stated
[65]	Kaduna	North West	Cross-sectional study	2021	300	Questionnaire; Blood sample
[66]	Oyo	South West	Cross-sectional study	2022	316	Questionnaire; Blood sample
[67]	Kano, Jigawa	North West	Observational Study	2023	300	Blood sample
[17]	Ibadan	South West	Observational Study	2024	51	Blood sample
[68]	Ilorin	North Central	Cross-sectional study	2024	103	Blood sample
[69]	Jos	North Central	Cross-sectional study	2024		Not stated
[70]	Enugu	South East	Case-crossover retrospective cohort study	2025	125	Microscopy
[71]	Lagos	South West	Cross-sectional study	2025	178	Not stated
[72]	Benue	North Central	Cross-sectional study	2025	1264	Not stated
[73]	Osun	South West	Cross-sectional study	2025		Blood sample
[74]	Kano, Adamawa, Lagos, Kebbi, Bauchi, Plateau, Ibadan, Calabar	North East, North West, North Central, South West, South South	Cross-sectional study	2025	894	Not stated

Table 2: Regional distribution of study locations in Nigeria (69 zone occurrences across 60 studies; multi-zone studies were counted once in each applicable zone)

Geopolitical Zone	No of Studies(%)	Focus of Studies
South West	28 (40.6)	Chloroquine resistance, molecular markers (Pfcr, Pfmdr1), antimalarial drug efficacy, HIV-malaria co-infection, drug resistance evolution, clinical and molecular epidemiology studies
South South	15 (21.7)	Chloroquine resistance, molecular detection of resistance genes, treatment efficacy, antimalarial drug resistance in pregnant women and HIV patients, clinical and epidemiological studies
North West	10 (14.5)	Chloroquine resistance patterns, molecular marker distributions, in vitro sensitivity assays, treatment outcomes
North Central	9 (13.0)	Chloroquine resistance surveillance, molecular marker studies, treatment response, community and clinical epidemiology
South East	5 (7.2)	Chloroquine resistance clinical and molecular studies, antimalarial use patterns, drug resistance markers
North East	2 (2.9)	Included mainly in multi-zone studies focusing on molecular surveillance of malaria and chloroquine sensitivity

Table 3: Assessment of studies based on Oxford Center for Evidence-Based Medicine's Levels of Evidence from Highest to Lowest [76]

S/N	Level of Evidence	Definition	No of Studies(%)
1	1A	Systematic review of RCTs	1(1.6)
2	1B	Individual RCT	2(3.3)
3	2A	Systematic review of cohort studies	0(0.0)
4	2B	Individual cohort studies, low-quality RCT	50(83.3)
5	2C	Ecological studies	2(3.3)
6	3A	Systematic review of case-control studies	0(0.0)
7	3B	Individual case control studies	5(8.3)
8	4	Case series, poor quality cohort and case control studies	0(0.0)
TOTAL			60 (100.0)

S/N: Serial Number

Table 4: Assessment of studies based on the Scottish Intercollegiate Guidelines Network for hierarchy of Study Type [75]

S/N	Study Types	n (%)
1	Systematic review and Meta-analysis	1 (1.7)
2	Randomized Controlled Trials	2 (3.3)
3	Nonrandomized intervention studies	0 (0.0)
4	Observational studies	54 (90.0)
5	Non experimental studies	1 (1.7)
6	Expert opinion	2 (3.3)
	Total	60 (100.0)

S/N: Serial Number

Table 5: Periodic distribution of research articles

Period	No of studies	Percentage(%)	Focus of studies
Before 2000	9	15.0	Early observational studies; focus on chloroquine efficacy, in vivo and in vitro tests; limited molecular data
2000–2010	14	23.3	Gradual emergence of molecular methods for resistance gene detection (Pfcr, Pfmdr1); coexistence of clinical efficacy trials and observational cohorts.
2011–2020	22	36.7	Increased molecular epidemiological reports, cross-sectional and cohort designs; emphasis on resistance surveillance and policy-driven withdrawal impacts; larger sample sizes typical.
After 2020	15	25.0	Recent studies focus on molecular genetics, population-level data, and qualitative insights on chloroquine use and resistance after withdrawal policy; integration with control interventions.

African countries, where molecular surveillance and cohort studies are common, while large-scale randomized trials are more difficult to implement [77,78]. The predominance of observational studies reflects the challenges of conducting standardized antimalarial trials in endemic settings, where treatment policies evolve rapidly and resources are often limited. While observational studies are helpful for resistance surveillance, they provide weaker evidence than randomized studies, highlighting the need for more robust prospective research to inform treatment policy.

Using the Oxford Centre for Evidence-Based Medicine hierarchy, the evaluation of chloroquine resistance studies in Nigeria showed that most fell into Level 2 or Level 3 evidence, with limited Level 1 studies, reflecting the difficulty of conducting large trials in field settings. Although molecular epidemiological studies offer valuable insights into genetic marker surveillance, they are generally considered lower levels of evidence due to their observational design [79]. Similarly, using the Scottish Intercollegiate Guidelines Network (SIGN) hierarchy, most studies ranked at the fourth level of evidence on a six-point scale. Many were further classified as low quality due to small sample sizes, observational design, or lack of randomization. Only three gold-standard studies (systematic reviews or individual RCTs) were identified, highlighting an important gap [75]. Examining temporal trends, research before 2000 focused largely on clinical effectiveness and early resistance patterns in children and general populations, relying heavily on *in vivo* and *in vitro* assays. Work was concentrated in the Southwest, South-South, and North Central. Between 2000 and 2010, studies expanded to molecular epidemiology, identifying resistance genes such as *pfprt* and *pfmdr1*. Alternative therapies (e.g., chloroquine-chlorpheniramine combinations) were explored, and research expanded to include the Northwest and South East. Attention also grew around HIV–malaria co-infection and vulnerable groups such as pregnant women.

Post-2010, following the 2005 chloroquine withdrawal policy, research shifted toward molecular monitoring, documenting declines in resistance markers and the adoption of ACTs. Studies focused on parasite sensitivity, drug durability, emerging ACT partner drug resistance, and broader multi-zone epidemiological surveys. The Southwest and South-South remained major research hubs. From 2020 onwards, genomic and advanced molecular tools have been employed to track trends and support treatment policy, with coverage expanding to the Northeast. Overall, the evidence shows a shift from clinical and assay-based studies prior to 2000, toward molecular and policy-focused work after 2000, with greater sophistication and broader geographic reach in the last decade. Findings indicate that chloroquine resistance (CQR) in Nigeria began in the late 1980s, driven by mutations such as *pfprt* T76 and *pfmdr1* Y86, mirroring the global timeline with the resistance trend first observed in Southeast Asia in 1957 and arriving in Africa in the late 1970s. A systematic review in East Africa reported similar mutation patterns, underscoring the continent-wide challenge [78].

Despite chloroquine withdrawal in 2005, resistant mutations remain widespread in Nigeria, sustained by continued drug pressure due to chloroquine's affordability compared to ACTs. Similar persistence has been reported in Uganda and other African settings [80–82]. In contrast, countries such as Malawi, Tanzania,

and Kenya documented reductions in chloroquine-resistance markers after stopping chloroquine use [83–89]. Even though some studies, particularly in the South West, suggest declining prevalence of the CVIET haplotype, a key driver of resistance, reports still document ongoing chloroquine prescriptions by physicians, pharmacists, and PPMVs. This persistence may be partly explained by off-label use, including during the COVID-19 pandemic when chloroquine and hydroxychloroquine were promoted for prophylaxis [3,17,90]. A 2011 multi-country African study confirmed the same trend: resistance remained stable where chloroquine use persisted, but fell where its use declined. This highlights that policy shifts alone are insufficient; enforcement and community education are also critical; a challenge echoed across Africa. Several Nigerian studies further recommended tightening restrictions on chloroquine importation and distribution. Nigeria can learn from Malawi's example: after enacting a withdrawal policy in 1993, studies by 2001, just eight years later, reported a chloroquine efficacy rate of 99%. However, though Malawi's experience is informative, differences in population size, health system structure, and overall spread of informal medicine vendors may limit its direct applicability to Nigeria [83,85,88]. The faster recovery observed in these countries is likely attributable to effective implementation of chloroquine withdrawal policies, resulting in a substantial reduction in drug pressure and subsequent restoration of chloroquine-sensitive parasite populations. In contrast, the continued circulation of chloroquine in Nigeria has probably slowed this process, illustrating that withdrawal policies are only effective when accompanied by sustained enforcement, surveillance, and public adherence.

Limitations of the study

This review has several limitations. The search was restricted to PubMed and Google Scholar and to English-language reports, so relevant indexed, non-indexed, unpublished, or non-English evidence may have been missed. Publication bias is possible, particularly because studies reporting resistance may be more likely to appear in the literature. Considerable heterogeneity in populations, locations, follow-up periods, phenotypic tests, and molecular markers prevented quantitative pooling and no meta-analysis was undertaken. Formal independent dual screening and extraction were not undertaken, and the review did not apply a validated study-level risk-of-bias instrument; OCEBM and SIGN classifications indicate evidence hierarchy rather than methodological quality. Geographical counts also reflect available publications, not malaria burden or nationally representative surveillance. Consequently, the findings should be interpreted as a narrative map of the evidence rather than a precise national estimate of chloroquine resistance.

Conclusion

Available studies suggest that chloroquine resistance and continued chloroquine exposure remain concerns in Nigeria, but the geographically uneven and predominantly observational evidence does not support a definitive national estimate or confirm complete restoration of susceptibility. The concentration

of studies in the South West and South-South may reflect differences in research infrastructure, security, funding, laboratory capacity, and institutional collaboration rather than true regional differences in malaria burden. NAFDAC and the National Malaria Elimination Programme should strengthen enforcement and pharmacovigilance, including oversight of Patent and Proprietary Medicine Vendors and informal medicine markets. Future work should establish nationwide, periodically repeated resistance mapping; molecular and genomic surveillance of pfprt and pfmdr1; standardized therapeutic-efficacy studies; and transparent reporting across all geopolitical zones. These measures would support antimalarial stewardship and protect the effectiveness of artemisinin-based combination therapies.

Declarations

Ethical approval

Ethical approval was not required for this study.

Informed consent

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

All data analyzed in this review are contained in the cited publications and the tables presented in this manuscript.

Competing interests/Conflict of interests

The authors declare that they have no competing interests.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Authors' Contributions

BOO conceptualized the review. BOO and OEE prepared the initial draft. DUE and OEE contributed to the literature search and data extraction. BOO, OEE, and DUE drafted and revised the manuscript. BOO supervised the work and completed the final review. All authors read and approved the final manuscript.

Acknowledgements

Not applicable.

Artificial Intelligence (AI) disclosure

Generative artificial intelligence was used to support language editing, consistency checks, and manuscript formatting. The authors critically reviewed and revised all AI-assisted text, independently verified the data, calculations, citations, and references against the source materials, and accept full responsibility for the accuracy and integrity of the manuscript.

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