

Socio-Behavioral and Clinical Predictors of Suspected Artemisinin Resistance in *Plasmodium falciparum* in Dutse Northern Nigeria

Babayaro, R.U¹., Balogun, J.B^{1*}., Dawaki, S.S.¹., Ibrahim, A.A²., Haruna, A¹., Dauda.H³ and Abbas, N.¹

¹Department of Animal and Environmental Biology, Federal University Dutse.

²Department of Public and Environmental Health, Federal University Dutse.

³Department of Animal and Environmental Biology, Borno State University.

*Corresponding Author's Email: joshufeli@gmail.com

ABSTRACT

Background: Artemisinin-based combination therapies (ACTs) remain the cornerstone of treatment for *Plasmodium falciparum* malaria. However, the emergence of artemisinin resistance threatens malaria control efforts, particularly in sub-Saharan Africa. While molecular markers of resistance have been widely studied, limited evidence exists on the socio-behavioral and clinical factors contributing to suspected resistance in Nigeria. A cross-sectional study was conducted among 384 patients presenting with suspected malaria in Dutse, northern Nigeria. Among these, 145 patients with microscopy-confirmed *Plasmodium falciparum* infection were included in the socio-behavioral and clinical analysis. Data were collected using structured interviewer-administered questionnaires and clinical records. Logistic regression analysis was used to identify predictors of resistance-related infections based on clinical and treatment outcome indicators. Treatment difficulty requiring multiple treatment courses was the strongest predictor of resistance-related infections (OR = 4.050; 95% CI: 2.1–7.8; $p < 0.001$). Completion of the full ACT treatment course was associated with significantly lower odds of resistance-related infections (OR = 0.158; 95% CI: 0.07–0.35; $p < 0.001$). Regular use of malaria preventive measures also showed a protective effect (OR = 0.283; 95% CI: 0.12–0.65; $p = 0.002$). Repeated malaria episodes were associated with increased likelihood of resistance-related infections, suggesting that frequent infections and repeated treatment exposure may contribute to resistance development. Self-medication and suspected use of substandard antimalarial drugs showed positive associations but were not statistically significant. The findings suggest that socio-behavioral and clinical factors play an important role in the emergence and spread of suspected artemisinin resistance in northern Nigeria. Treatment difficulty and repeated malaria episodes were major predictors, while treatment adherence and preventive measures were protective. Malaria control strategies should therefore integrate treatment adherence programs, drug quality regulation, preventive interventions, and resistance surveillance to sustain ACT effectiveness.

Keywords: *Plasmodium falciparum*, Artemisinin resistance, ACT adherence, Socio-behavioral factors, Drug resistance, Nigeria



Graphical Abstract

1.0 INTRODUCTION

Malaria remains a major global public health concern, with the heaviest burden occurring in sub-Saharan Africa (Oladipo et al., 2022). The World Health Organization (WHO) estimated that in 2022 there were approximately 247 million malaria cases worldwide,

leading to about 619,000 deaths. Over 90% of these infections and fatalities occur in Africa, where *Plasmodium falciparum*—the most virulent malaria parasite—predominates. Nigeria is particularly affected, contributing nearly one-third of the global malaria case load (Dzianach et al., 2023). Beyond its substantial impact

on morbidity and mortality, especially among children under five years of age and pregnant women, malaria also imposes significant economic consequences by reducing workforce productivity and placing considerable strain on healthcare systems (Souza et al., 2024).

1.1 Evolution of Antimalarial Drug Resistance

A central barrier to malaria control has been the evolution of drug resistance. In the mid-20th century, chloroquine was the mainstay of malaria treatment due to its affordability and effectiveness (van der Pluijm et al., 2020). However, resistance emerged and spread rapidly across Africa and Asia, rendering chloroquine largely ineffective (CDC, 2024). Similarly, sulfadoxine-pyrimethamine (SP), once widely deployed as an alternative, also succumbed to resistance (Azmi et al., 2023). These developments led to widespread treatment failures and prompted policy shifts toward artemisinin-based combination therapies (ACTs).

Artemisinin-based combination therapies (ACTs), introduced in the early 2000s, consist of rapidly acting artemisinin derivatives paired with longer-acting partner drugs. These therapies are currently considered the cornerstone of malaria treatment worldwide and are recommended by the World Health Organization (WHO) as first-line treatment for uncomplicated *Plasmodium falciparum* malaria (Eastman & Fidock, 2009). However, the long-term effectiveness of ACTs is increasingly under threat. Evidence of delayed parasite clearance and reduced therapeutic efficacy was first reported in Southeast Asia, particularly within the Greater Mekong Subregion, and has been strongly linked to mutations in the *pfkelch13* propeller domain (Azmi et al., 2023; Eastman & Fidock, 2009). These developments have raised significant concerns about the potential global spread of resistance, reminiscent of the historical dissemination of chloroquine and sulfadoxine-pyrimethamine resistance.

Emergence of Artemisinin Resistance in Africa

Until recently, Africa was considered relatively unaffected by artemisinin resistance. However, growing evidence now suggests that the threat is real and emerging. Several studies have documented *pfkelch13* mutations in East, Central, and West Africa, with varying prevalence (Zhao et al., 2021). In Nigeria, early reports detected *pfkelch13* polymorphisms of uncertain significance, while recent surveys suggest that mutations potentially linked to reduced ACT efficacy may already be circulating (Amusan et al., 2025). The detection of these markers in the continent's most malaria-burdened country underscores the urgent need for comprehensive monitoring.

The implications are profound: should resistance spread widely across Africa, the effectiveness of ACTs could be compromised, leading to increased treatment failures, higher transmission rates, and greater malaria-related mortality. Moreover, given that no new first-line antimalarial is currently available at scale, preserving ACT efficacy is critical to sustaining malaria control gains (Yang et al., 2020).

Socio-Behavioral and Clinical Drivers of Resistance

While molecular studies have provided essential insights into genetic mechanisms of resistance, they represent only part of the picture. Drug resistance does not emerge in a vacuum; it is influenced by human behaviors, clinical practices, and health system factors that determine how drugs are used in real-world settings. Several socio-behavioral and clinical determinants have been proposed as contributors to resistance dynamics:

1. **Incomplete adherence to ACTs:** Patients often fail to complete the full prescribed regimen due to symptom relief after a few doses, cost considerations, or lack of awareness. This exposes parasites to sub-therapeutic drug levels, fostering survival of partially resistant strains (Winstanley et al., 2004).
2. **Self-medication and informal drug use:** In many parts of Nigeria, antimalarial drugs are readily available without prescription through informal vendors. This practice increases the risk of inappropriate drug selection, under-dosing, and the use of counterfeit or substandard medicines (Cox-Singh et al., 2008).
3. **Repeated malaria episodes:** In high-transmission settings, individuals frequently experience multiple malaria episodes each year. Repeated exposure to treatment cycles increases the probability of selecting resistant parasites, especially when adherence is poor (White et al., 2009).
4. **Use of substandard or counterfeit drugs:** Nigeria has documented circulation of poor-quality antimalarials. Substandard formulations contain insufficient active ingredients, which can accelerate resistance by allowing partial parasite clearance (Johnston & Holt, 2013).
5. **Limited preventive measures:** Insufficient use of insecticide-treated bed nets, repellents, and indoor residual spraying increases exposure to mosquito bites, resulting in more frequent infections and treatment cycles that increase selective pressure for resistance (Ngonghala et al., n.d.).
6. **Clinical management practices:** Delays in diagnosis, misclassification of febrile illnesses, and inadequate monitoring of treatment outcomes in health facilities can hinder the early detection of resistance-related cases (Anyasodor et al., 2023a).

These factors collectively highlight the role of human behavior and health system dynamics in shaping the evolution and spread of resistance. While several studies from Southeast Asia and parts of Africa have documented their importance (Anyasodor et al., 2023b; Sharrow et al., 2022), there remains a significant paucity of systematic evidence from Nigeria.

The Nigerian Context

Despite extensive research on molecular markers of artemisinin resistance, relatively little attention has been paid to the socio-behavioral and clinical factors that

influence drug pressure and parasite selection in endemic setting. In Nigeria, where malaria burden is among the highest globally, understanding how patient behavior and treatment practices contribute to potential resistance development remains critically important. Within this complex context, resistance surveillance has been predominantly molecular, with limited integration of patient-level behavioral or clinical data. This creates a critical blind spot: while mutations may indicate emerging resistance, the socio-behavioral pathways through which resistant strains spread remain underexplored. Without this understanding, interventions risk focusing narrowly on genetic monitoring without addressing the behavioral drivers that sustain resistance selection (Nsanjabana, 2019).

Rationale and Study Objectives

There is an urgent need to bridge the gap between molecular surveillance and socio-behavioral determinants of resistance in Nigeria. Understanding how treatment practices, prevention strategies, and clinical outcomes intersect with molecular findings can inform more effective malaria control strategies. Dutse, in Jigawa State, northern Nigeria, provides an important case study as it represents a high-burden setting with perennial malaria transmission and diverse health-seeking behaviors.

This study therefore aims to investigate the socio-behavioral and clinical determinants of artemisinin resistance among *P. falciparum*-positive patients in Dutse. By combining epidemiological survey data with clinical indicators of treatment outcomes, the research seeks to:

1. Identify socio-behavioral and clinical predictors of resistance-related infections.
2. Quantify the protective effect of preventive measures in reducing resistance risk.
3. Highlight pathways through which patient behaviors may facilitate or hinder resistance emergence.

Through these objectives, the study provides evidence on the non-genetic drivers of artemisinin resistance and offers recommendations for strengthening Nigeria's malaria control strategies.

2.0 MATERIAL AND METHOD

2.1 Study Area

The study was carried out in Dutse Local Government Area, (11°42'04"N and 9°20'31" E), located in Jigawa State

in northern Nigeria. The region falls within the Sudan savannah ecological zone and has a tropical climate characterized by two main seasons: a rainy season extending from May to October and a dry season from November to April. Malaria transmission occurs year-round in this area, with higher transmission rates observed during and immediately following the rainy season (Balogun et al., 2021). Three healthcare facilities within the metropolis, representing different tiers of healthcare services, were selected for inclusion in the study.

2.2 Study Design and Population

A cross-sectional descriptive study was conducted among patients presenting with symptoms suggestive of uncomplicated malaria in Dutse Local Government Area, Jigawa State, Nigeria. The study population consisted of patients aged 1–70 years who attended selected healthcare facilities and were laboratory-confirmed for *Plasmodium falciparum* infection by microscopy.

Inclusion criteria

Presentation with fever or malaria-related symptoms
Laboratory confirmation of *Plasmodium falciparum* infection
Provision of informed consent (or parental/guardian consent for minors)

Exclusion criteria

Severe or complicated malaria requiring hospitalization
Patients who declined participation

2.3 Sampling Method and Sampling Strategy

A facility-based sampling approach was used for participant recruitment. The study employed a convenience sampling method with proportional allocation across selected healthcare facilities. Patients who met the inclusion criteria were consecutively recruited as they presented to the healthcare facilities during the study period until the required sample size was achieved.

The calculated sample size of 384 participants was proportionally distributed among the three selected healthcare facilities based on average patient attendance:

Dutse General Hospital

Federal University Dutse Teaching Hospital

Kudai Primary Health Centre

This approach ensured representation across primary, secondary, and tertiary healthcare levels within the study area.

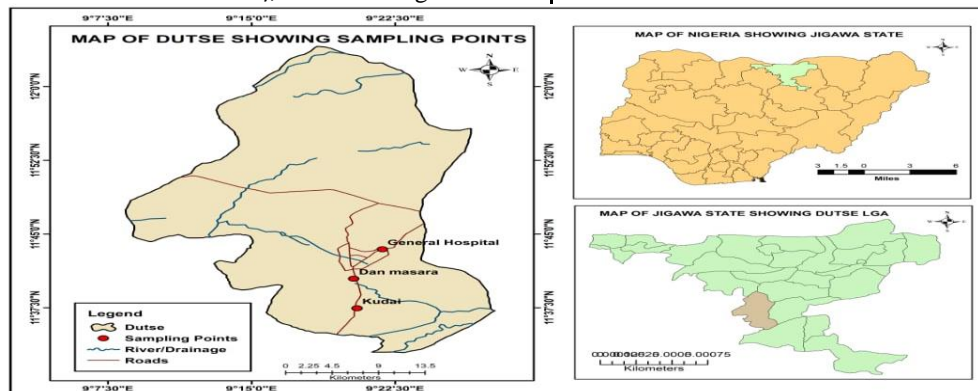


Figure 1: Map Of Dutse Showing The Sampling Point (Source: GIS LAB FUD)

2.4 Sample Size Determination

The sample size was determined based on the malaria prevalence rate in Jigawa State, Nigeria, which was reported to be 51% by (Jennifer & Dogara, 2016). To calculate the required sample size, a standard epidemiological formula (Fisher's Equation) for a cross-sectional descriptive study was applied as follows:

$$N = \frac{Z^2 P (1 - P)}{d^2}$$

Where:

- (n) = required sample size
- (Z) = standard normal deviation at 95% confidence level (1.96)
- (p) = estimated malaria prevalence in Jigawa State (51%)
- (d) = margin of error (0.05)

The minimum calculated sample size was 384 participants.

2.5 Data Collection

Two categories of data were collected: clinical data and socio-behavioral data.

Clinical Samples

Venous blood samples were collected from each participant. Thick and thin blood smears were prepared and examined microscopically to confirm malaria infection and parasite species. Confirmed *P. falciparum*-positive samples were retained for further molecular analysis of artemisinin resistance markers (pkelch13).

Questionnaire Data

Socio-behavioral and clinical information were collected using a structured interviewer-administered questionnaire. The questionnaire captured information on:

- 1 Completion of prescribed ACT treatment courses
- 2 History of self-medication or use of unprescribed antimalarials
- 3 Use of malaria preventive measures (e.g., insecticide-treated nets, repellents, indoor spraying)
- 4 Frequency of malaria episodes in the past year
- 5 Reported treatment difficulties

Questionnaire Validation and Reliability

The questionnaire was developed based on previously published malaria socio-behavioral and treatment adherence studies and aligned with World Health Organization malaria treatment and prevention guidelines to ensure content validity.

A pilot study was conducted among 20 malaria patients in a health facility outside the study area to evaluate clarity, relevance, and consistency of the questionnaire. Feedback from the pilot study was used to revise ambiguous questions and improve the structure of the questionnaire.

To assess reliability, internal consistency of questionnaire items related to treatment adherence, preventive practices, and treatment history was evaluated using Cronbach's alpha, which yielded a reliability coefficient of 0.78, indicating acceptable reliability for socio-behavioral research. Data from the pilot study were not included in the final analysis.

Data Reliability and Quality Control

To ensure data reliability and accuracy:

Questionnaires were interviewer-administered by trained research assistants.

Completed questionnaires were checked daily for completeness and consistency.

Data were double-entered and cross-checked to minimize data entry errors.

Microscopy was performed by trained laboratory personnel using standard procedures.

A subset of slides was re-examined for quality control.

2.6 Ethical Considerations

Ethical approval was obtained from the Jigawa State Ministry of Health Ethical Committee (Ref: MOH/SEC/1.S/858/V1). Written informed consent was obtained from all adult participants. For children under 18 years, parental or guardian consent was secured. Participation was voluntary, and confidentiality was maintained throughout the study.

2.7 Data Analysis

Data were entered into Microsoft Excel and exported to SPSS version 26 for statistical analysis. Descriptive statistics were used to summarize demographic, behavioral, and clinical characteristics. Logistic regression analysis was used to identify predictors of resistance-related infections among *Plasmodium falciparum*-positive patients. Associations were expressed as odds ratios (OR) with 95% confidence intervals (CI), and a p-value < 0.05 was considered statistically significant. Odds ratios (OR) greater than 1 were interpreted as indicating increased odds (risk factors) for resistance-related infection, while odds ratios less than 1 were interpreted as protective factors associated with reduced odds of resistance-related infection.

Definition of Resistance-Related Infection

In this study, artemisinin resistance was not defined solely by molecular markers but by clinical and treatment outcome indicators consistent with suspected reduced drug efficacy. A resistance-related infection was operationally defined as a *Plasmodium falciparum* infection in which the patient reported treatment difficulty, required multiple treatment courses for the same malaria episode, experienced persistent symptoms after completion of ACT, or had recurrent malaria within a short period after treatment. These indicators are commonly used in clinical and epidemiological studies as proxy indicators of suspected antimalarial drug resistance where molecular confirmation is limited.

3.0 RESULTS

3.1 Study Population

A total of 384 patients presenting with symptoms of suspected malaria were recruited across the three healthcare facilities. Of these, 145 (37.8%) were confirmed *Plasmodium falciparum*-positive by microscopy and included in the socio-behavioral and clinical survey. These 145 patients formed the study population for analysis of predictors of artemisinin resistance.

Socio-Behavioral and Clinical Predictors

Logistic regression analysis identified four key factors significantly associated with resistance-related infections (Table 1).

- **Patients who completed ACT treatment** were significantly less likely to experience resistance-related infections (OR = 0.158).
- **Repeated malaria episodes** also showed a strong association. Individuals who reported more than one malaria episode in the past year had higher odds of resistance-related infection (OR = 0.157; 95% CI: 0.07–0.36; $p < 0.001$).
- **Use of preventive measures** (bed nets, repellents, indoor residual spraying) was

negatively associated with resistance. Regular use was protective, reducing the likelihood of resistance-related infections (OR = 0.283; 95% CI: 0.12–0.65; $p = 0.002$).

- **Treatment difficulty**, defined as requiring multiple treatment courses for a single episode, was the strongest predictor. Patients with reported treatment difficulty were four times more likely to have resistant infections (OR = 4.050; 95% CI: 2.1–7.8; $p < 0.001$).

Other factors, such as **self-medication** (OR = 2.248; $p = 0.082$) and **suspected use of low-quality antimalarials** (OR = 2.299; $p = 0.082$), showed positive associations but did not reach statistical significance.

Table 1. Logistic Regression Analysis Of Socio-Behavioral And Clinical Factors Associated With Artemisinin Resistance Among Plasmodium Falciparum-Positive Patients In Dutse (N = 145).

Predictor Variable	Yes (n)	No (n)	Odds Ratio (OR)	95% CI	p-value
Completed full ACT course	90	55	0.158	0.07–0.35	<0.001*
Multiple malaria episodes (past year)	89	56	0.157	0.07–0.36	<0.001*
Regular use of preventive measures	93	52	0.283	0.12–0.65	0.002*
Treatment difficulty (multiple courses)	90	55	4.050	2.1–7.8	<0.001*
Use of unprescribed malaria drugs	55	90	2.248	0.9–5.3	0.082
Use of suspected low-quality drugs	54	91	2.299	0.9–5.5	0.082

*Statistically significant at $p < 0.05$

Abbreviations: ACT = Artemisinin-based Combination Therapy; OR = Odds Ratio; CI = Confidence Interval.

3.3 Discussion

Logistic regression analysis identified several socio-behavioral and clinical factors associated with resistance-related infections (Table 1).

Treatment difficulty requiring multiple treatment courses was the strongest predictor of resistance-related infections (OR = 4.050; 95% CI: 2.1–7.8; $p < 0.001$), indicating that patients who required multiple treatments were approximately four times more likely to have resistance-related infections compared to those who responded to a single treatment course.

Completion of the full ACT treatment course was significantly associated with lower odds of resistance-related infections (OR = 0.158; 95% CI: 0.07–0.35; $p < 0.001$), suggesting that adherence to ACT treatment had a protective effect against resistance development.

Similarly, regular use of malaria preventive measures such as insecticide-treated bed nets, repellents, and indoor residual spraying was associated with reduced odds of resistance-related infections (OR = 0.283; 95% CI: 0.12–0.65; $p = 0.002$).

Repeated malaria episodes were also associated with resistance-related infections, indicating that frequent infections and repeated treatment exposure may contribute to the selection of resistant parasite strains.

Self-medication and suspected use of low-quality antimalarial drugs showed increased odds of resistance-related infections, although these associations were not statistically significant

This study demonstrates that socio-behavioral and clinical factors play an important role in the emergence and spread of suspected artemisinin resistance in Plasmodium falciparum in Dutse, Nigeria. The findings indicate that treatment difficulty requiring multiple treatment courses was the strongest predictor of resistance-related infections, suggesting possible reduced drug efficacy, treatment failure, or circulation of resistant parasite strains.

Completion of the full ACT treatment course was associated with significantly lower odds of resistance-related infections, highlighting the importance of treatment adherence in preventing the selection of resistant parasites. When patients fail to complete treatment, parasites are exposed to sub-therapeutic drug levels, which increases the likelihood that partially resistant parasites survive and multiply.

Regular use of malaria preventive measures was also protective against resistance-related infections. Preventive measures reduce infection frequency and therefore reduce the number of treatment cycles, which in turn lowers drug pressure on parasite populations and slows the development of resistance.

Repeated malaria episodes were associated with higher likelihood of resistance-related infections. In high-transmission areas, repeated exposure to antimalarial drugs increases selective pressure for resistant parasite strains, particularly in settings where adherence is poor or substandard drugs are used.

Although self-medication and suspected use of low-quality antimalarial drugs were not statistically significant predictors, their positive association with resistance-related infections suggests that informal drug use and

3.4 Interpretation of Key Findings

substandard medications may contribute to resistance development and should not be overlooked in malaria control strategies.

Implications for Malaria Control

The findings suggest three major priorities for malaria resistance containment: improving treatment adherence, strengthening drug quality regulation, and developing integrated resistance surveillance systems that combine molecular, clinical, and socio-behavioral data. Addressing these three areas simultaneously may significantly slow the emergence and spread of artemisinin resistance in high-burden malaria settings.

3.5 Strengths and Limitations

A major strength of this study is the combined assessment of socio-behavioral and clinical predictors of resistance in a Nigerian population, filling a critical evidence gap. The use of logistic regression provided robust estimates of associations, and the inclusion of multiple healthcare facilities enhanced representativeness.

This study has some limitations. First, the cross-sectional design limits the ability to establish causal relationships between socio-behavioral factors and resistance-related infections. Second, the study used facility-based convenience sampling, which may limit generalizability to the wider community population. Third, treatment adherence and preventive practices were self-reported and may be subject to recall or social desirability bias. Finally, resistance classification was based primarily on clinical and treatment outcome indicators rather than molecular confirmation alone, which may limit definitive classification of artemisinin resistance. Despite these limitations, the study provides important insights into the socio-behavioral and clinical factors associated with suspected resistance in a high malaria burden setting. The definition of resistance in this study was based on clinical and treatment outcome indicators rather than molecular confirmation alone, which may limit the ability to definitively classify resistance. However, these indicators are useful for identifying suspected resistance patterns in resource-limited settings

3.6 Future Research

Future studies should expand geographic coverage across different ecological zones of Nigeria to identify broader trends in socio-behavioral determinants of resistance. Longitudinal cohort designs could provide stronger evidence of causality, while integrating molecular markers such as *pfkelch13*, *pfcr1*, and *pfmdr1* would capture the full spectrum of multidrug resistance. Mixed-methods approaches, incorporating qualitative interviews, could yield deeper insights into cultural and economic drivers of incomplete adherence and self-medication. Additionally, linking human behavioral data with entomological surveillance may clarify how mosquito transmission dynamics influence the spread of resistant strains.

4.0 CONCLUSION

This study demonstrates that socio-behavioral and clinical factors play a significant role in the occurrence of resistance-related malaria infections in Dutse, northern Nigeria. Treatment difficulty requiring multiple treatment courses emerged as the strongest predictor of resistance-related infections, while completion of the full ACT treatment course and regular use of malaria preventive measures were protective factors. Repeated malaria episodes were also associated with increased likelihood of resistance-related infections, suggesting that frequent infections and repeated exposure to antimalarial drugs may contribute to the selection of resistant parasite strains.

These findings indicate that the emergence and spread of artemisinin resistance should not be viewed solely as a molecular or genetic phenomenon but also as a behavioral, clinical, and health system challenge influenced by treatment adherence, drug use practices, infection frequency, and preventive behavior. Sustaining the effectiveness of artemisinin-based combination therapies in Nigeria will therefore require an integrated malaria control strategy that combines molecular resistance surveillance with interventions aimed at improving treatment adherence, regulating antimalarial drug quality, strengthening clinical management of malaria cases, and expanding preventive measures such as insecticide-treated bed nets and indoor residual spraying.

Overall, integrating socio-behavioral monitoring with resistance surveillance may provide a more comprehensive understanding of resistance dynamics and support more targeted malaria control interventions in high-burden settings. Future malaria resistance surveillance programs should integrate molecular monitoring with patient treatment behavior, drug quality surveillance, and clinical outcome monitoring to effectively contain the spread of antimalarial drug resistance.

5.0 RECOMMENDATIONS

For Public Health and Policy

1. Promote treatment adherence: Intensify health education campaigns to emphasize the importance of completing full ACT regimens.
2. Expand preventive measures: Strengthen community distribution and proper use of insecticide-treated nets, repellents, and indoor spraying.
3. Enhance clinical management: Train healthcare providers in the recognition and management of suspected drug-resistant malaria and institutionalize treatment outcome monitoring in health facilities.
4. Regulate drug quality and access: Enforce stricter controls on informal drug sales and expand access to quality-assured ACTs through formal healthcare channels.
5. Integrate behavioral and molecular surveillance: Combine patient-level behavioral data with genetic resistance monitoring to generate a comprehensive resistance profile.

6. Target vulnerable groups: Prioritize children and young adults for intensified preventive interventions and education campaigns, given their high exposure and risk of repeated infections.

For Future Research

- Conduct multisite studies across diverse ecological zones of Nigeria to assess regional variation in socio-behavioral drivers of resistance.
- Conduct longitudinal studies to better establish causal pathways between treatment practices and resistance emergence.
- Expand molecular analyses to include additional resistance markers such as *pfcr1*, *pfmdr1*, and *plasmepsin 2-3*.
- Apply mixed-methods approaches to capture cultural and socioeconomic determinants of treatment adherence and self-medication.
- Link clinical and behavioral studies with entomological surveillance to better understand how transmission dynamics interact with resistance evolution.

6.0 ACKNOWLEDGMENTS

We gratefully acknowledge the support of the Jigawa State Ministry of Health and the management of Dutse General Hospital, Federal University Dutse Teaching Hospital, and Kudai Primary Health Centre for granting access to their facilities and patients. We thank the healthcare workers who assisted with patient recruitment and data collection. Special appreciation goes to the study participants and their families for their cooperation.

REFERENCES

- Amusan, A., Akinola, O., Akano, K., Hernández-Castañeda, M., Dick, J. K., Sowunmi, A., Hart, G., & Gbotosho, G. (2025). Polymorphisms in Pfk13 domains before and after the introduction of artemisinin-based combination therapy in Southwest Nigeria. *PLOS One*, 20(3), e0316479. <https://doi.org/10.1371/JOURNAL.PONE.0316479>
- Anyasodor, A. E., Ahmed, K. Y., Osuagwu, U. L., Mgbemena, N. C., Kalinna, B. H., Thapa, S., Mahmood, S., & Ross, A. G. (2023a). Delays in seeking treatment for fever in children under five years of age in Nigeria: Evidence from the National Demographic Health Survey. *PLoS ONE*, 18(12) December). <https://doi.org/10.1371/JOURNAL.PONE.0295772>
- Anyasodor, A. E., Ahmed, K. Y., Osuagwu, U. L., Mgbemena, N. C., Kalinna, B. H., Thapa, S., Mahmood, S., & Ross, A. G. (2023b). Delays in seeking treatment for fever in children under five years of age in Nigeria: Evidence from the National Demographic Health Survey. *PLOS ONE*, 18(12), e0295772. <https://doi.org/10.1371/JOURNAL.PONE.0295772><SPAN
- Azmi, W. A., Rizki, A. F. M., Djuardi, Y., Artika, I. M., & Siregar, J. E. (2023). Molecular insights into

- artemisinin resistance in *Plasmodium falciparum*: An updated review. In *Infection, Genetics and Evolution* (Vol. 112). <https://doi.org/10.1016/j.meegid.2023.105460>
- Balogun, J. B., Muhammad, S. S., & Dogara, M. M. (2021). EFFECT OF MALARIA INFECTION ON HEPATIC AND RENAL FUNCTIONS IN PREGNANT WOMEN ATTENDING ANTENATAL CLINIC AT GENERAL HOSPITAL DUTSE, JIGAWA-NIGERIA. *FUDMA JOURNAL OF SCIENCES*, 5(2), 526–530. <https://doi.org/10.33003/FJS-2021-0502-666>
- CDC. (2024). Drug Resistance in the Malaria-Endemic World. *Centers for Disease Control and Prevention*, (7).
- Cox-Singh, J., Davis, T. M. E., Lee, K. S., Shamsul, S. S. G., Matusop, A., Ratnam, S., Rahman, H. A., Conway, D. J., & Singh, B. (2008). *Plasmodium knowlesi* malaria in humans is widely distributed and potentially life threatening. *Clinical Infectious Diseases*, 46(2), 165–171. <https://doi.org/10.1086/524888>
- Dzianach, P. A., Rumisha, S. F., Lubinda, J., Saddler, A., van den Berg, M., Gelaw, Y. A., Harris, J. R., Browne, A. J., Sanna, F., Rozier, J. A., Galatas, B., Anderson, L. F., Vargas-Ruiz, C. A., Cameron, E., Gething, P. W., & Weiss, D. J. (2023). Evaluating COVID-19-Related Disruptions to Effective Malaria Case Management in 2020–2021 and Its Potential Effects on Malaria Burden in Sub-Saharan Africa. *Tropical Medicine and Infectious Disease*, 8(4). <https://doi.org/10.3390/tropicalmed8040216>
- Eastman, R. T., & Fidock, D. A. (2009). Artemisinin-based combination therapies: A vital tool in efforts to eliminate malaria. In *Nature Reviews Microbiology* (Vol. 7, Number 12). <https://doi.org/10.1038/nrmicro2239>
- Jennifer, O. A., & Dogara, M. M. (2016). Prevalence of malaria and risk factors among patients attending Gutse General Hospital, Jigawa State, Nigeria. *International Research Journal of Public and Environmental Health*, Vol , Page - , 2016, 3(11), 270–277. <https://doi.org/10.15739/IRJPEH.16.033>
- Johnston, A., & Holt, D. W. (2013). Substandard drugs: a potential crisis for public health. *British Journal of Clinical Pharmacology*, 78(2), 218. <https://doi.org/10.1111/BCP.12298>
- Ngonghala, C. N., Wairimu, J., Adamski, J., & Desai, H. (n.d.). *The impact of adaptive mosquito behavior and insecticide-treated nets on malaria prevalence*. <https://doi.org/10.1101/2020.05.18.20105916>
- Nsanjabana, C. (2019). Resistance to Artemisinin Combination Therapies (ACTs): Do Not Forget the Partner Drug! *Tropical Medicine and Infectious Disease* 2019, Vol. 4,4(1). <https://doi.org/10.3390/tropicalmed4010026>
- Oladipo, H. J., Tajudeen, Y. A., Oladunjoye, I. O., Yusuff, S. I., Yusuf, R. O., Oluwaseyi, E. M., AbdulBasit, M. O., Adebisi, Y. A., & El-Sherbini, M. S. (2022). Increasing challenges of malaria control in sub-Saharan Africa: Priorities for public health research and

- polycymakers. In *Annals of Medicine and Surgery* (Vol. 81). <https://doi.org/10.1016/j.amsu.2022.104366>
- Sharrow, D., Hug, L., You, D., Alkema, L., Black, R., Cousens, S., Croft, T., Gaigbe-Togbe, V., Gerland, P., Guillot, M., Hill, K., Masquelier, B., Mathers, C., Pedersen, J., Strong, K. L., Suzuki, E., Wakefield, J., & Walker, N. (2022). Global, regional, and national trends in under-5 mortality between 1990 and 2019 with scenario-based projections until 2030: a systematic analysis by the UN Inter-agency Group for Child Mortality Estimation. *The Lancet Global Health*, 10(2), e195–e206. [https://doi.org/10.1016/S2214-109X\(21\)00515-5](https://doi.org/10.1016/S2214-109X(21)00515-5)
- Souza, J. P., Day, L. T., Rezende-Gomes, A. C., Zhang, J., Mori, R., Baguiya, A., Jayaratne, K., Osoti, A., Vogel, J. P., Campbell, O., Mugerwa, K. Y., Lumbiganon, P., Tunçalp, Ö., Cresswell, J., Say, L., Moran, A. C., & Oladapo, O. T. (2024). A global analysis of the determinants of maternal health and transitions in maternal mortality. In *The Lancet Global Health* (Vol. 12, Number 2). [https://doi.org/10.1016/S2214-109X\(23\)00468-0](https://doi.org/10.1016/S2214-109X(23)00468-0)
- van der Pluijm, R. W., Tripura, R., Hoglund, R. M., PyaePhyo, A., Lek, D., ul Islam, A., Anvikar, A. R., Satpathi, P., Satpathi, S., Behera, P. K., Tripura, A., Baidya, S., Onyamboko, M., Chau, N. H., Sovann, Y., Suon, S., Sreng, S., Mao, S., Oun, S., ... Valeche, N. (2020). Triple artemisinin-based combination therapies versus artemisinin-based combination therapies for uncomplicated Plasmodium falciparum malaria: a multicentre, open-label, randomised clinical trial. *The Lancet*, 395(10233), 1345–1360. [https://doi.org/10.1016/S0140-6736\(20\)30552-3](https://doi.org/10.1016/S0140-6736(20)30552-3)
- White, N. J., Pongtavornpinyo, W., Maude, R. J., Saralamba, S., Aguas, R., Stepniewska, K., Lee, S. J., Dondorp, A. M., White, L. J., & Day, N. P. (2009). Hyperparasitaemia and low dosing are an important source of anti-malarial drug resistance. *Malaria Journal*, 8(1), 253. <https://doi.org/10.1186/1475-2875-8-253>
- Winstanley, P., Ward, S., Snow, R., & Breckenridge, A. (2004). Therapy of Falciparum Malaria in Sub-Saharan Africa: from Molecule to Policy. *Clinical Microbiology Reviews*, 17(3), 612. <https://doi.org/10.1128/CMR.17.3.612-637.2004>
- Yang, J., He, Y., Li, Y., Zhang, X., Wong, Y. K., Shen, S., Zhong, T., Zhang, J., Liu, Q., & Wang, J. (2020). Advances in the research on the targets of anti-malaria actions of artemisinin. *Pharmacology and Therapeutics*, 216. <https://doi.org/10.1016/J.PHARMTHERA.2020.107697>
- Zhao, H., Pi, L., Zhao, L., Qin, Y., Zeng, W., Xiang, Z., Yang, Q., Pan, M., Li, X., Zou, C., Chen, X., Zhao, W., Lu, Y., Wu, Y., Duan, M., Wang, X., Li, X., Mazier, D., Huang, Y., & Yang, Z. (2021). First Detection in West Africa of a Mutation That May Contribute to Artemisinin Resistance Plasmodium falciparum. *Frontiers in Genetics*, 12. <https://doi.org/10.3389/fgene.2021.701750>