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Current Trends In Antimalarial Drug Resistance In Nigeria: A Mini Review

Rita Ayanbolade Olowe[1]*, Otutu Olawumi[2], Ajayi Yewande O .[3] and Olowe O. Adekunle[2]

[1]Research Ethics Unit, UNIOSUN Teaching Hospital UTH, Osogbo, Osun State, Nigeria
[2]Department of Medical Microbiology and Parasitology.. College of Health Sciences, P.M.B. 4000. Ogbomoso, Oyo State
[3]National Agency for Food and drug administration and control (NAFDAC), Nigeria

Corresponding Author: olowerita@gmail.com

ABSTRACT

The study aimed to review the current trend in antimalarial drug resistance in Nigeria. Methods: We developed and conducted an exhaustive search strategy on PubMed, online Search Engines, and Google Scholar to find scientific articles reporting antimalarial drug resistance in Nigeria. The highest global malaria burden is in Nigeria, a nation with significant antimalarial drug resistance. This paper examines the most recent advancements, challenges, and prospects for addressing the urgent issue of antimalarial drug resistance in Nigeria. The primary objective of this work is to investigate the emergence and spread of resistance to antimalarial drugs, specifically artemisinin-based combination therapies (ACTs). Furthermore, it examines the factors that lead to this resistance, including medication pressure, vector resistance, and health system issues. According to the research, practical measures to address malaria medicine resistance include public health education campaigns, robust monitoring and surveillance systems, and regular reassessment of drug policy.

Moreover, the report explores prospective areas of concentration for future research, such as developing novel antimalarial medications, exploring alternative treatment modalities, and strengthening collaborations on an international level. According to the findings of this review, policymakers, healthcare professionals, researchers, and communities in Nigeria must collaborate in a comprehensive and empirically supported approach to address the issue of antimalarial drug resistance. In order to maintain the efficacy of antimalarial drugs and prevent the development of resistance, urgent action is necessary to address malaria in Nigeria and globally.

Keywords: Antimalarial drug resistance, *Plasmodium falciparum*, artemisinin-based combination therapies, malaria control, Nigeria

INTRODUCTION

The extensive impact of malaria on Nigeria's health, economic development, and social well-being underscores its status as a significant public health issue in the nation. Nigeria carries a disproportionate share of the burden of the disease's incidence and fatalities worldwide. The global malaria prevalence in 2020 was expected to be 61 million individuals, with Nigeria accounting for 27% of these cases (World Health Organisation, 2021). Malaria is strongly associated with significant morbidity and mortality rates in the country, particularly among pregnant women and children under the age of five (National Malaria Elimination Programme, 2021). The high incidence of malaria in Nigeria has a detrimental effect on healthcare expenses, productivity, and socioeconomic progress (Alonso et al., 2019).

Effective antimalarial drugs are crucial for treating and preventing malaria, and their use is indispensable for the country's efforts to manage and eliminate the illness. However, the persistence and dissemination of antimalarial drug resistance pose a significant threat to these strategies. Recognising the high occurrence of drug-

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resistant malaria parasites in Nigeria has led to the adoption of artemisinin-based combination therapies (ACTs) as the first treatment option for early disease cases (Oyibo et al., 2021). Antimicrobial resistance can be stopped by taking proactive steps and monitoring things, even with antimicrobial chemotherapeutic therapies (ACTs) (Ajayi et al., 2020).

This article aims to provide a comprehensive overview of the current trends and challenges related to antimalarial drug resistance in Nigeria. By compiling data from published literature and elucidating the patterns of resistance to commonly used antimalarial drugs (ACTs), this review will analyse the impact of drug resistance on the country's efforts to control and eliminate malaria. This review aims to provide guidance for future research in the field and to inform evidence-based approaches for reducing antimalarial drug resistance by critically addressing these problems. Academics, healthcare professionals, and policymakers in Nigeria and other countries can significantly benefit from the conclusions of this study in their efforts to eliminate malaria.

EPIDEMIOLOGICAL OVERVIEW OF MALARIA IN NIGERIA

As of 2020, Nigeria accounted for 27% of the total malaria cases worldwide, establishing itself as a significant contributor to the global malaria burden (World Health Organisation, 2021). Despite significant variations in frequency throughout different regions of Nigeria, malaria is a persistent disease. Adebayo et al. (2021) identified rainfall, temperature, humidity, and the number of vectors as factors influencing transmission patterns. Due to the high prevalence of malaria vectors in the southern and central regions of the country, these areas experience the highest transmission rates (Akinola et al., 2019). Malaria is a persistent issue throughout the year in many regions, with its peak occurring between the rainy months of April and October (National Malaria Elimination Programme, 2021).

Malaria disproportionately affects children under the age of five and pregnant women in Nigeria. Based on projections from the World Health Organisation, 21.8 million children under the age of five contracted malaria in 2020, accounting for 36% of all cases in this age group globally (2021). Primary risks associated with malaria during pregnancy include maternal anaemia, low birth weight, and heightened mortality (Anto et al., 2019). To reduce the high malaria burden in these vulnerable communities, it is imperative to implement targeted therapies and strengthen health services.

The predominant etiological agent of malaria in Nigeria is the Plasmodium falciparum parasite, which is found in over 95% of cases (National Malaria Elimination Programme, 2021). The virulent form of the malaria parasite, P. falciparum, is associated with malaria complications such as cerebral malaria and severe anaemia (Kwenti, 2018). According to a study by Oyibo et al. (2021), P. falciparum is more likely than other Plasmodium species to develop antimalarial drug resistance. This poses a significant challenge for malaria control and eradication initiatives in Nigeria.

Although less prevalent than P. falciparum, Nigeria also harbours additional Plasmodium species, such as P. ovale and P. malariae (Morakinyo et al., 2018). The consequences of malaria induced by these species are generally less severe and present with comparatively milder symptoms. Their presence in Nigeria underscores the need to implement dependable diagnostic methods and treatment protocols tailored to each unique species of malaria to control all instances of the illness efficiently.

The distributions of Plasmodium species in different regions of Nigeria exhibit variations, with Plasmodium falciparum being the predominant species. While the extent of endemicity may differ among the

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different geographic zones of the country, systematic study indicates that P. falciparum is consistently prevalent in all regions (Nmadu et al., 2015). A comprehensive understanding of the distribution patterns of Plasmodium species in Nigeria is crucial for monitoring the emergence and dissemination of drug-resistant parasites and devising specific strategies to manage malaria.

Historical Perspective on Antimalarial Drug Resistance in Nigeria

The 4-aminoquinoline chloroquine was previously considered the benchmark for malaria treatment in Nigeria due to its high efficacy, proven safety, and low cost. The rapid proliferation of Plasmodium falciparum parasites resistant to chloroquine significantly impeded malaria control efforts throughout the 1980s and 1990s (Oguche et al., 2014). The initial documentation of treatment failures and reduced parasite clearance rates occurred during research undertaken in Nigeria during the late 1980s, resulting in the first observations of chloroquine resistance (Sowunmi et al., 1990). Mortality and morbidity rates from malaria increased simultaneously with the development of chloroquine resistance, which made the drug ineffective (Muhammad et al., 2017).

In response to the growing frequency of chloroquine resistance, the Nigerian government launched a study of malaria treatment options. In 2005, the Federal Ministry of Health recommended that the National Malaria Control Programme (NMCP) discontinue chloroquine as the first treatment for patients with uncomplicated malaria. This policy shift was prompted by the World Health Organisation (WHO) recommendations and clinical studies, which advocated for the use of artemisinin-based combination therapies (ACTs) as the first treatment for uncomplicated P. falciparum malaria in areas where chloroquine is not practical.

The Federal Ministry of Health selected artemisinin-based combination therapies (ACTs) as the primary treatment for uncomplicated malaria in Nigeria 2005 following the identification of widespread chloroquine resistance. Antimicrobial chemotherapeutic combinations (ACTs) contain an artemisinin derivative that works quickly and a complementary drug, like lumefantrine or amodiaquine, that works for a longer or shorter time. The idea behind this combination is to use artemisinins' ability to kill parasites quickly and companion medicine's ability to work for a longer time to stop recurrence and slow the development of resistance (Eastman & Fidock, 2009).

Ajayi et al. (2013) identified artemether-lumefantrine (AL) and artesunate-amodiaquine (ASAQ) as the two most often used combination therapies (ACTs) in Nigeria. Antiretroviral therapy (ACTs) made treatment much more effective in Nigeria; they were better than chloroquine at curing people and quickly getting rid of parasites (Falade et al., 2005). Nevertheless, in a country with a large population and diverse healthcare systems, ensuring the availability, affordability, and proper use of ACTs has been challenging (Onwujekwe et al., 2009).

In order to facilitate the execution of anti-malaria therapies, the Nigerian government has initiated several programmes, such as the National Malaria Strategic Plan (NMSP) and the Roll Back Malaria (RBM) effort (National Malaria Elimination Programme, 2021). The objectives of these programs were to enhance the accessibility to quality-assured ACTs, enhance diagnostic skills, and promote adherence to treatment guidelines. Nevertheless, the transition to ACTs encountered several challenges, including insufficient resources, inadequate supply chain management, and the presence of substandard and counterfeit drugs (Kaur et al., 2015).

Continuous monitoring of the efficacy of artemisinin-based combination treatments

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(ACTs) and early detection of resistance are not just important, they are crucial. These drugs remain the foundation of malaria treatment in Nigeria, and to maintain their efficacy in the face of parasite resistance, it is essential to closely observe the situation, make necessary policy modifications, and conduct proactive research, as was done in the past with chloroquine resistance.

CURRENT TRENDS IN ANTIMALARIAL DRUG RESISTANCE

Artemisinin Resistance

In malaria-endemic regions, such as Nigeria, a notable concern is the development of artemisinin resistance, characterised by the delayed elimination of parasites after treatment with artemisinin-based combination therapies (ACTs). Contemporary studies have indicated the presence of artemisinin-resistant Plasmodium falciparum parasites in Nigerian patients who received artemisinin-converting tablets (ACTs), as demonstrated by extended periods of parasite clearance (Ajayi et al., 2020; Oguche et al., 2014). On the third day after receiving artemether-lumefantrine (AL) medication, 5.2% of patients experienced ongoing parasitemia, above the 10% threshold the World Health Organisation (WHO) set for suspected artemisinin resistance in 2011. These results are derived from the research conducted by Ajayi et al. (2020). To identify and control the dissemination of resistance, these results emphasise the requirement of heightened consciousness and consistent surveillance of the effectiveness of artemisinin in Nigeria.

The discovery of molecular markers associated with artemisinin resistance has significantly enhanced our understanding of the genetic foundation of resistance and the optimisation of resistance surveillance. An investigation conducted by Ariey et al. (2014) revealed a correlation between specific mutations in the propeller domain of the kelch13 (k13) gene and a delay in parasite clearance. This finding establishes the gene as a reliable genetic indicator for artemisinin resistance. Although uncommon, studies conducted in Nigeria have demonstrated that isolates of P. falciparum do indeed include k13 mutations (Oyebola et al., 2018; Talundzic et al., 2019). A minority of the isolates (3.2%) exhibited k13 alterations, as reported by Oyebola et al. (2018). These modifications, primarily non-synonymous ones, are associated with developing resistance to artemisinin in southeast Asian bacteria. Although rare in Nigeria, tracking the growth of artemisinin resistance indicators and applying this knowledge to shape policy responses necessitates continuous genetic surveillance of k13 mutations.

Figure 1A. Below shows structures of artemisinin (ART) and other clinically viable derivatives. (B) Synthetic trioxane and tetraoxane ART analogs.

Partner Drug Resistance

For an artemisinin combination therapy (ACT) to be successful, both the artemisinin and the companion drugs, often long-acting compounds that eradicate residual parasites and prevent subsequent infection, are essential. When it comes to ACT companion drugs in Nigeria, the most common ones are Artemisinin-Lumenfantrine (AL) and amodiaquine (artesunate-amodiaquine, ASAQ). The emergence of resistance to these companion drugs in recent years has prompted concerns concerning the long-term effectiveness of antiretroviral therapies (ACTs) (Ajayi et al., 2020; Oyibo et al., 2021). According to a study by Ajayi et al. (2020), 18.9% of the P. falciparum isolates from Nigeria had lumefantrine IC50 values higher than the resistance threshold. This suggests a reduced susceptibility to the treatment. Oyibo et al. (2021) and Sowunmi et al. (2017) reported that treatment failure rates of amodiaquine in some Nigerian populations vary from 7.4% to 12.5%.

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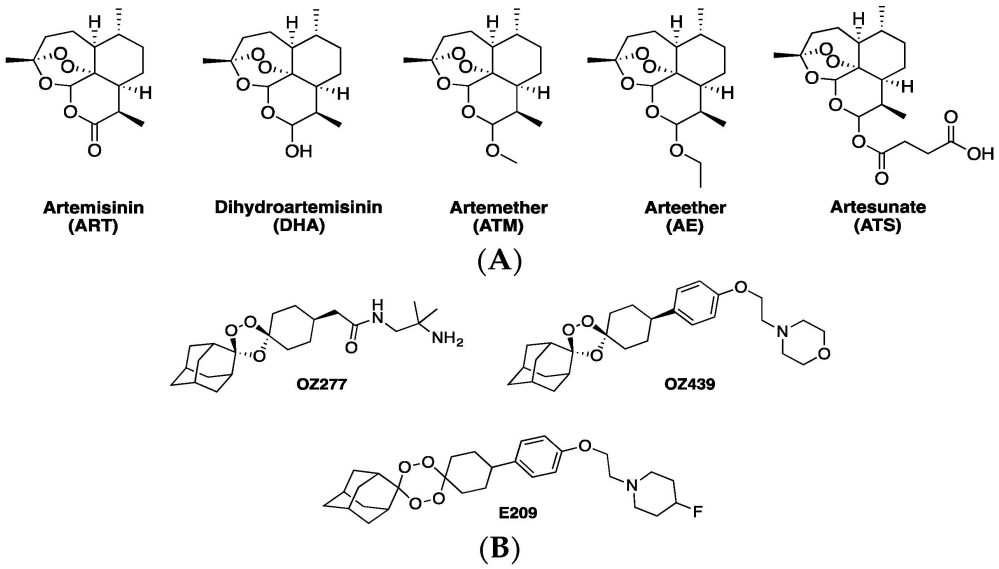

Figure 1: (**A**) Structures of artemisinin (ART) and other clinically viable derivatives. (**B**) Synthetic trioxane and tetraoxane ART analogs

Partner drug resistance has a substantial impact on the overall effectiveness of antiretroviral therapy (ACT) in Nigeria. The artemisinin component rapidly eliminates the majority of the parasites, while the companion medication efficiently eliminates the remaining ones and prevents their resurgence (Eastman and Fidock, 2009). Parasites that acquire resistance to drugs administered in combination with other therapies are more prone to elude treatment, require more time to be eliminated from the body, and ultimately reproduce more disease-resistant parasites (Oyibo et al., 2021). However, there is hope. It is imperative to consistently assess the effectiveness of companion medications using in vitro and vivo studies to overcome this challenge. So that ACTs can still work even when malaria parasites become resistant, Okombo and Ochieng (2019) suggest making and using new drugs that work in different ways with ACTs.

Sulfadoxine-Pyrimethamine Resistance

In order to safeguard pregnant women in regions with high transmission rates against malaria and its adverse consequences, the World Health Organisation (2014) proposes the use of intermittent preventative therapy in pregnancy (IPTp). Sulfadoxine-pyrimethamine (SP) is a crucial component of this approach. The development of resistance to SP in P. falciparum poses a challenge to the effectiveness of IPTp-SP in Nigeria and other African countries (Chauvin et al., 2015). The studies conducted by Iwalokun et al. (2018) and Olapeju et al. (2018) revealed that P. falciparum isolates originating from Nigeria exhibit notable quantities of SP resistance markers. These markers include the quintuple mutant haplotype, which comprises the dhfr triple mutant and dhps double mutant. It was found by Iwalokun et al. (2018) that these resistance signs make IPTp-SP less effective at lowering maternal anaemia, placental malaria, and low birth weight.

Given the extensive resistance to SP, there is an urgent requirement for novel strategies to prevent malaria during pregnancy in Nigeria. An alternative approach is to screen pregnant women for malaria using rapid diagnostic tests (RDTs) and provide treatment for positive cases with a powerful antimalarial medication. Periodic screening and treatment in pregnancy (ISTp) is the term used to

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describe this approach (Tagbor et al., 2015). Using dihydroartemisinin-piperaquine (DP) instead of SP in treating IPTp has shown promise in real-world studies (Kakuru et al., 2016). However, more meticulously planned studies are necessary to evaluate the effectiveness and safety of these different methods in the Nigerian context. To protect pregnant women from malaria in the age of SP resistance, a comprehensive approach should emphasise improving prenatal care services, expanding access to prompt diagnosis and treatment, and promoting insecticide-treated nets (ITNs). Figure 2: Pharmaceuticals employed as agents in typical ART combination therapy (ACT). Prime prospects for ACT utilisation include ATM-LF, DHA-PPQ, ATS-MQ, and ATS-AQ.

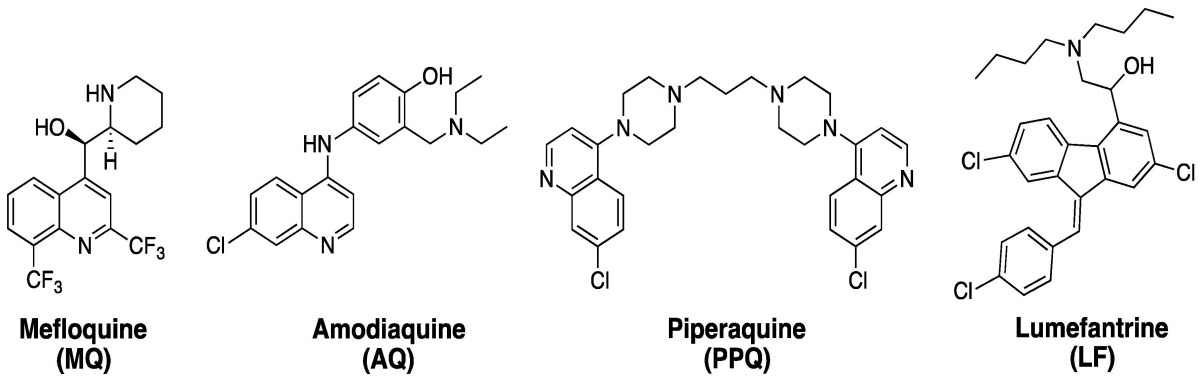

Figure 2: Common ART combination therapies (ACT) partner drugs. The most widely used ACTs are ATM-LF, DHA-PPQ, ATS-MQ, and ATS-AQ.

Heller, L.E.; Roepe, P.D. Artemisinin-Based Antimalarial Drug Therapy: Molecular Pharmacology and Evolving Resistance. *Trop. Med. Infect. Dis.* **2019**, *4*, 89. https://doi.org/10.3390/tropicalmed4020089

FACTORS CONTRIBUTING TO ANTIMALARIA DRUG RESISTANCE

Drug Pressure

An essential factor contributing to the emergence and proliferation of drug resistance in Nigeria is the prolonged and widespread usage of certain antimalarial drugs by a large number of individuals. Overusing some antimalarial drugs causes a lot of selection pressure within the Plasmodium parasite population, making it easier for strains resistant to these drugs to live and reproduce (White, 2004). The extensive history of overusing chloroquine in Nigeria, as well as the overuse of sulfadoxine-pyrimethamine (SP) and artemisinin-based combination therapies (ACTs), are the leading causes of the emergence and growth of drug resistance there (Oguche et al., 2014; Oyibo et al., 2021). In their study, Oyeyemi et al. (2019) found that self-medication, taking too little of the drug, and not following treatment instructions are all examples of inappropriate antimalarial use that make the drug pressure problem worse and speed up the development of resistance.

The proliferation of substandard or counterfeit antimalarial drugs in Nigerian marketplaces is an additional significant factor contributing to drug resistance. Substandard drugs refer to genuine pharmaceuticals that do not meet quality requirements due to inadequate production methods. In contrast, counterfeit drugs are intentionally and illegally mislabeled in terms of identification and origin (World Health Organisation, 2017). In their study, Kaur et al. (2015) found that sub-therapeutic doses resulting from low-quality antimalarials can facilitate the identification of resistant parasites. This phenomenon

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arises due to the often inadequate concentrations of the active component. According to research by Kaur et al. (2015), 9.3% of antimalarial drugs in Nigeria have a quality issue, with a significant portion being counterfeit or of poor quality. Pharmaceutical interventions for malaria that depend on these inferior drugs are inefficacious and exacerbate the emergence of drug resistance.

Vector Resistance

Insecticide resistance in malaria vectors, particularly in Anopheles mosquitoes, is a significant barrier to malaria control interventions and indirectly contributes to developing antimalarial drug resistance. By the widespread use of insecticide-treated mosquitoes (ITNs) and indoor residual spraying (IRS), mosquito populations in Nigeria have developed resistance to insecticides (Awolola et al., 2018). Insufficient success in mosquito population suppression through vector control programs due to pesticide resistance can lead to the ongoing or even exacerbated transmission of malaria parasites, including drug-resistant strains (Hemingway et al., 2016). The continuous exposure of the parasite population to antimalarial drugs facilitates the proliferation and dissemination of drug resistance. Multiple research (Awolola et al., 2018; Okorie et al., 2015) have reported significant resistance to widely used pesticides in Anopheles mosquitoes in Nigeria. This underscores the significance of implementing efficient strategies to control pesticide resistance.

An effective approach to managing vectors that optimises the use of existing resources is integrated vector management (IVM) (World Health Organisation, 2012). However, several problems may indirectly lead to the spread of drug resistance to antimalarials. This makes it harder to implement effective IVM strategies in Nigeria. These challenges include insufficient financial resources, a deficiency in entomological monitoring capacities, and disagreement among stakeholders (Chanda et al., 2015). The involvement and cooperation of these stakeholders are crucial in the fight against insecticide resistance. Failure to properly execute and monitor vector control programmes can lead to uncontrolled spread of malaria, especially drug-resistant strains. Another problem with IVM algorithms is that they rely too much on a small group of pesticides for vector control, which increases the chance of insecticide resistance (Hemingway et al., 2016). Nigeria needs to improve its integrated vector management (IVM) skills to stop the spread of malaria and lessen the effects of drug resistance. This can only be done by doing more research, surveillance, and working with different groups.

Health System Challenges

The escalating prevalence of antimalarial drug resistance in Nigeria is a pressing issue that demands immediate attention. This trend can be linked, in part, to the inadequate diagnostic systems and monitoring procedures within the country's healthcare system. Accurate malaria diagnoses are pivotal in preventing the unnecessary use of antimalarial medications, which may specifically target the parasite population, and in providing effective treatment for malaria (World Health Organisation, 2015). However, in Nigeria, particularly in remote and isolated areas, the availability and use of reliable diagnostic methods such as microscopy and rapid diagnostic tests (RDTs) are consistently limited (Oyibo et al., 2017). This situation can lead to individuals mistakenly identifying fevers as malaria, resulting in the improper use of antimalarial drugs and the emergence of parasites that exhibit resistance to them. Inadequate surveillance methods impede the timely detection and monitoring of medication resistance, making it challenging to carry out targeted therapies and modify treatment programs (Mbachu et al., 2020). To optimize

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the effectiveness of antimalarial medications while mitigating the proliferation of resistance, it is urgent to enhance diagnostic instruments and monitoring systems.

For Nigeria to effectively address the issue of malaria medicine resistance, it is imperative that it promptly initiates efforts to enhance its healthcare system. A well-functioning health system is the only means to attain access to quality-assured antimalarial drugs, practise rational drug use, and implement effective actions to prevent malaria (World Health Organisation, 2018). Despite the challenges of insufficient funding, staffing shortages, and inadequate supply chain management that afflict Nigeria's healthcare industry (Onwujekwe et al., 2020), there is potential for progress. The presence of these problems could lead to a lack of antimalarial drugs, the spread of fake or low-quality drugs, and the improper use of antimalarials, all of which would help drug resistance grow and spread. However, with strategic investments in health funding, workforce development, supply chain management, and the implementation of quality assurance systems for antimalarial drugs, Nigeria can strengthen its health infrastructure. Notwithstanding the significant issue of antimalarial drug resistance in Nigeria, the country has the potential to achieve progress in the prevention, diagnosis, and treatment of malaria if its healthcare system is effectively managed.

STRATEGIES FOR MITIGATING ANTIMALARIA DRUG RESISTANCE

Drug Policy Reassessment

For Nigeria to mitigate the impact of drug resistance, it is imperative to periodically evaluate its national antimalarial drug policies and implement any required modifications. The Nigerian National Malaria Elimination Programme (NMEP) plays a crucial role in this, coordinating the monitoring and assessment of antimalarial drug effectiveness and revising treatment guidelines. Due to the potential for the development and dissemination of malaria-resistant parasites, it is imperative to consistently assess the effectiveness of existing therapeutic approaches and make necessary adjustments based on available evidence (World Health Organisation, 2018). Periodic therapeutic efficacy studies (TES) are essential for assessing the effectiveness of first- and second-line antimalarial drugs against Plasmodium falciparum (World Health Organisation, 2009). The data acquired from these studies and other pertinent information help the decision-making process for amending the national antimalarial drug policies in Nigeria, ensuring the use of the most effective and safe drugs for malaria treatment.

To mitigate the high incidence of antimalarial drug resistance in Nigeria, it is imperative to investigate several therapeutic alternatives, encompassing combination medications. Because resistance is always showing up to the first-line artemisinin-based combination therapies (ACTs), we must quickly evaluate new drug regimens that can treat malaria effectively while lowering the risk of resistance developing (Ouji et al., 2018). As part of this effort, new combination therapies are being used to get the most out of existing drugs, and the potential of new antimalarial compounds like synthetic endoperoxides and aminoquinolines is being looked into (Okell et al., 2018). Triple antimicrobial combinations (ACTs), made up of an artemisinin derivative and two partner drugs that work in different ways, have shown promise in improving treatments and lowering the risk of resistance (van der Pluijm et al., 2020). An alternative method to decelerate the emergence and dissemination of resistance is the implementation of MFTs, which stands for multiple first-line therapies. This refers to the simultaneous deployment of several ACTs in a population (Boni et al., 2008). Due to the short shelf life of current first-line antimalarial drugs (ACTs), Nigeria

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could increase its supply of effective antimalarial drugs by looking into and analysing alternative treatments and combination therapies.

Surveillance and Monitoring

An essential measure to decrease antimalarial drug resistance in Nigeria is establishing dependable monitoring systems to monitor the efficacy of therapy and the trends of resistance. Continuous and systematic collection, analysis, and interpretation of data on antimalarial drug therapy efficacy and resistance is crucial for detecting changes in medicine sensitivity and informing timely policy responses. Surveillance is used to describe this procedure (World Health Organisation, 2018). The National Malaria Elimination Programme (NMEP) established a surveillance system to evaluate the efficacy of antimalarial medications in Nigeria in 2021, which includes conducting Treatment Efficacy Studies (TES) and gathering information on treatment failures and adverse events. However, this approach might benefit from further refinement to encompass a broader range of areas and enable speedier data reporting from all regions of the country. In order to do this, it is necessary to offer healthcare providers education on the proper protocols for gathering and presenting data uniformly.

Additionally, electronic data management systems can facilitate the rapid analysis and dissemination of surveillance data (Nkumama et al., 2017). To effectively monitor the progress and dissemination of drug resistance against malaria, Nigeria should allocate resources to establish dependable monitoring systems. This would enable the government to adapt its drug strategy and measures accordingly.

An essential complement to the traditional methods of monitoring the efficacy of antimalarial medications in Nigeria is the implementation of genetic surveillance for resistance genes. In molecular surveillance, advanced lab methods like DNA sequencing and polymerase chain reaction (PCR) are used to find and describe genetic changes in Plasmodium falciparum parasites that make them resistant to drugs (Ishengoma et al., 2019). In contrast to clinical efficacy analysis, this approach has several advantages, including the potential to identify novel resistance indicators, monitor resistance patterns over different periods and geographical locations, and detect resistance before it manifests clinically (Nsanzabana et al., 2018). Research by Oboh et al. (2018) and Oyebola et al. (2021) showed that molecular surveillance could find signs of resistance to artemisinin and medicines used with it in Nigeria. In this study, plasmepsin 2-3 gene amplifications were used to find bacteria resistant to piperaquine and kelch13 (K13) gene changes were used to find bacteria resistant to artemisinin. The existing system for monitoring antimalarial drug resistance in Nigeria can be enhanced by including molecular surveillance. Implementing this will enable Nigeria to enhance its ability to identify and describe resistance early, hence facilitating the development of focused interventions and monitoring of global resistance trends.

Public Health Education

An essential measure in decreasing the level of drug resistance in Nigeria is to enhance public knowledge on the proper use of antimalarial medications. The World Health Organisation (2018) states that public health education programmes aim to increase knowledge, cultivate favourable attitudes, and encourage healthy behaviours regarding the prevention, diagnosis, and treatment of malaria infections. To reduce malaria drug resistance, effective public education programmes should stress the importance of only using antimalarial drugs that have been quality-checked, sticking to treatment plans exactly, and not getting sick from taking too many pills (Talisuna et al., 2012). This can be achieved through various means of

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communication, including health lectures, town hall meetings, and school-based programmes; interpersonal communication, such as counselling provided by healthcare professionals; and community-based interventions, such as radio, television, and print media (World Health Organisation, 2018). In Nigeria, it is necessary to implement focused and culturally suitable educational programs to enhance awareness and comprehension of antimalarial drug resistance. Studies have shown that the general population generally has a limited degree of knowledge on this topic (Umar et al., 2021). By increasing public awareness about the risks of malaria and promoting informed decision-making about the use of these medications, Nigerians can contribute to the continued effectiveness of antimalarial treatments. Community involvement is crucial in these initiatives, as it fosters a sense of collective responsibility and support in combating drug resistance.

In order to mitigate the high incidence of antimalarial drug resistance in Nigeria, it is imperative for public health educators to emphasise the significance of completing treatment regimens. As per the World Health Organisation (2015), a significant contributing element to the emergence and dissemination of malaria resistance is inadequate treatment, which refers to the premature cessation of antimalarial drugs by patients. This phenomenon, in turn, enables the survival and reproduction of resistant parasites. Studies conducted by Anyanwu et al. (2017) and Oyekale (2017) have established a correlation between non-compliance with recommended antimalarial medication regimens in Nigeria and factors such as poverty, limited educational achievement, and misunderstandings about malaria treatment. To address this issue, public health education initiatives should prioritise encouraging individuals to adhere to their treatment regimens, which include strictly following the prescribed courses of antimalarial medication, even if their symptoms improve prematurely (World Health Organisation, 2018). Medical practitioners, as key stakeholders, should provide guidance to patients, pharmaceutical packaging should have unambiguous and straightforward instructions, and community-based programs should be implemented to promote understanding and compliance with treatment (Anyanwu et al., 2017). The use of directly observed therapy (DOT) has been empirically demonstrated to improve medication adherence and treatment outcomes. This entails patients ingesting their medication while under the supervision of a healthcare practitioner or a qualified community volunteer (Aung et al., 2015). The role of healthcare professionals in patient education and support is crucial, as they can provide the necessary guidance and information to ensure responsible medication use and mitigate the risk of resistance development.

FUTURE DIRECTIONS AND RESEARCH PRIORITIES

A primary research objective in the fight against antimalarial drug resistance in Nigeria and globally is the development of novel antimalarial chemicals. The emergence and spread of Plasmodium falciparum parasites that are resistant to artemisinin-based combination therapies (ACTs) have emphasised the urgent requirement for new medications with distinct mechanisms of action to treat malaria without developing resistance (Hooft van Huijsduijnen et al., 2020). Several intriguing chemicals are now under investigation. New synthetic endoperoxides like OZ439 and artefenomel are among the substances. So are aminoquinolines like ferroquine and cipargamin, and DSM265 and MMV390048 are inhibitors of important parasite enzymes (Hooft van Huijsduijnen et al., 2020; Phillips et al., 2017). The efficacy of these compounds against malaria has been demonstrated through preclinical and early clinical studies. Furthermore, certain

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compounds have shown potential against artemisinin-resistant parasites (Phyo et al., 2016; White et al., 2016). In order to expedite the development of novel antimalarial medications, Nigeria and other countries affected by malaria must increase their investment in research and development (R&D) and bolster their capabilities in drug discovery and clinical trials (Maxmen, 2016).

To mitigate the rise of antimalarial drug resistance in Nigeria, it is imperative to research prospective alternative therapeutic approaches. Furthermore, it is imperative to not only create novel pharmaceuticals but also to enhance the efficacy of existing antimalarial drugs and explore alternative treatment approaches that can impede the emergence of resistance (Huijben & Paaijmans, 2018). Combining an artemisinin derivative with two companion drugs that have distinct modes of action is a highly promising strategy. The technical term for this method is triple artemisinin-based combination therapies (TACTs) (van der Pluijm et al., 2020). Evidence from clinical trials has shown that TACTs, compared to standard ACTs, enhance treatment effectiveness and reduce the risk of resistance formation (van der Pluijm et al., 2020). Another potential approach to decrease the chances of recurrence and ensure complete elimination of the parasite is prolonged artemisinin regimens, which involve a lengthier duration of artemisinin therapy (Ashley et al., 2014). In order to enhance the efficiency of antimalarial drug administration and reduce the selection pressure for resistance, continuous research is being conducted on the application of molecular diagnostic techniques to inform treatment choices and track the emergence of resistance (Nsanzabana et al., 2018).

It is imperative to advance research on antimalarial drug resistance and establish effective strategies to reduce it in Nigeria and other countries by enhancing regional and global partnerships. Collaboration among researchers, policymakers, healthcare practitioners, and communities is vital to addressing the global issue of drug resistance (Talisuna et al., 2012). According to a study by Ajayi et al. (2020), collaboration between Nigeria and other West African nations can improve the monitoring and response to antimalarial drug resistance by exchanging information, resources, and proven methods. Ajayi et al. (2020) emphasise that these collaborations can facilitate the alignment of regional drug policies and treatment guidelines, which is essential for the consistent and evidence-based management of malaria cases. Collaborations among pharmaceutical corporations, research institutes, and funding organisations on an international scale can significantly support Nigeria in medication development, clinical trials, and resistance monitoring (Maxmen, 2016). The World Wide Antimalarial Resistance Network (WWARN) is a global collaborative platform that collects, analyses, and shares data that can significantly serve researchers and policymakers in Nigeria and other malaria-affected countries (World et al., 2021). By strengthening regional and international collaborations and optimising global knowledge and resources, Nigeria can advance its research agenda on antimalarial drug resistance and contribute to the global effort to eliminate malaria.

CONCLUSION

Antimalarial drug resistance is a significant issue in Nigeria, and this study has presented the most recent advancements, challenges, and remedies to address this problem effectively. The development and dissemination of resistance to artemisinin-based combination therapies (ACTs) and other antimalarial drugs pose a threat to ongoing efforts to control and eliminate malaria. This review has identified several significant factors, including drug pressure, vector resistance, and health system complexities, contributing to the emergence

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of resistance. The review stressed that the best way to deal with these problems is through a comprehensive and evidence-based strategy that includes vital monitoring and surveillance systems, public health education programmes to teach people how to use antimalarial drugs properly, and regular reevaluations of drug policy. The conclusions of this research further underline the need for such a strategy to decrease resistance to antimalarial drugs. This has far-reaching implications for Nigeria's policies and practices in controlling malaria.

For the issue of antimalarial drug resistance to be effectively addressed, it is imperative that communities, researchers, healthcare professionals, and politicians in Nigeria collaborate promptly. This collective effort is crucial in the battle against malaria. It is recommended that the Nigerian government give priority to implementing evidence-based strategies for monitoring and responding to antimalarial drug resistance through the National Malaria Elimination Programme (NMEP). Implementing public health education and provider training can contribute to promoting the responsible use of antimalarial drugs, allocating resources to research and development of innovative compounds, and establishing a national surveillance system to assess the effectiveness of antimalarial drugs. In order to intensify the fight against resistance to antimalarial drugs, the government should promote regional and international collaborations to leverage resources and expertise from all parts of the globe. The business sector, including research institutes and pharmaceutical companies, has crucial mandates in facilitating capacity building for resistance surveillance and response, as well as developing innovative drugs and diagnostic tools. The implementation of public health education campaigns, prompt diagnosis and treatment of malaria, and strict adherence to treatment regimens are crucial measures that communities and individuals can adopt to address the issue of antimalarial drug resistance.

A comprehensive approach is required to address the complex issue of the emergence and spread of resistance to antimalarial medications. This analysis highlighted the need to reassess drug policy, public health education, research and development, regional and international collaborations, monitoring and surveillance, and the overall status of antimalarial drug resistance in Nigeria. In order to optimise the use of existing antimalarial treatments, limit the development of resistance in parasites to new drugs, and sustain the long-term battle against malaria, Nigeria should adopt a comprehensive and evidence-based strategy. Furthermore, the effort to combat antimalarial drug resistance can be more effectively integrated by all stakeholders by adopting a comprehensive approach encompassing communities, researchers, healthcare practitioners, and legislators. In order to accomplish its long-term goal of reducing malaria rates and enhancing the health of its population, all stakeholders engaged in Nigeria's battle against malaria must unite and maintain their dedication. Effective reduction of antimalarial drug resistance can only be achieved under such circumstances.

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