Malaria Treatment Services in Nigeria: A Review

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SUMMARY

Malaria remains a major Public Health problem in Nigeria and causes death and illness in children and adults, especially pregnant women. Malaria case management remains a vital component of the malaria control strategies. This entails early diagnosis and prompt treatment with effective antimalarial medicines. The objectives of this review is to enable health professionals to understand the magnitude of malaria treatment services in Nigeria, to improve knowledge for rational malaria management within different health system contexts with a view to improving access to malaria treatment. The review therefore looks at the following areas: clinical disease and epidemiology; the burden of malaria in Nigeria; objectives of treatment; antimalarial treatment policy; malaria diagnosis, treatment strategies/ National responses; treatment sources. The review concludes that for improved malaria treatment services in Nigeria, there is an urgent need to develop adequate strategies that will ensure better access to medicines by getting evidence-based and effective medicines to the people who need them, whether by reducing their costs, promoting equity in access, improving their distribution, increasing their efficacy and acceptability, or slowing down the development of antimicrobial resistance.

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INTRODUCTION

Clinical disease and epidemiology

Malaria is caused by infection of red blood cells with protozoan parasites of the genus *Plasmodium*. The parasites are inoculated into the human host by a feeding female anopheline mosquito. The four *Plasmodium* species that infect humans are *P. falciparum, P. vivax, P. ovale* and *P. malariae*.[1] The first symptoms of malaria are nonspecific and similar to the symptoms of a minor systemic viral illness. They comprise: headache, lassitude, fatigue, abdominal discomfort, and muscle and joint aches, usually followed by fever, chills, perspiration, anorexia, vomiting and worsening malaise. Malaria is, therefore, frequently over-diagnosed on the basis of symptoms alone, especially in endemic areas like Nigeria, because of this non-specificity of symptomatology.[2] If treatment is not delayed and effective treatment is given, there is full rapid recovery. However, if ineffective treatment is given or treatment delayed, this can progress to severe malaria especially in children manifesting as coma (cerebral malaria), metabolic acidosis, severe anaemia, hypoglycaemia, acute renal failure or acute pulmonary oedema. In high-transmission settings, infected but asymptomatic persons constitute an important part of the infectious reservoir. Even though treated cases (mainly children) have higher densities of gametocytes, and infectivity is positively related to gametocyte density, children constitute only a proportion of the infective reservoir.[3]

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The burden of malaria in Nigeria

In Nigeria, the burden of malaria is well documented and has been shown to be a big contributor to the economic burden of disease in communities where it is endemic and is responsible for annual economic loss of 132 billion Naira.[4-6] It is estimated that 300,000 deaths occurring each year, 60% of outpatient visits and 30% hospitalizations are all attributable to malaria.[7,8] In addition, at least 50% of the population has at least one episode of malaria annually resulting in high productivity losses while children that are aged less than 5 years have 2 to 4 attacks annually.[5] The disease is particularly virulent among pregnant women and children under 5 years of age, due to their low levels of immunity. A strong correlation between malaria and poverty has also long been recognized. Not only does malaria thrive in poverty but it also impedes economic growth and keeps households in poverty.[9] Hence the poor bear a disproportionate burden of the disease.[10] Malaria case management therefore remains a vital component of the malaria control strategies. This entails early diagnosis and prompt treatment with effective antimalarial medicines.

Objectives of treatment

The objective of treating uncomplicated malaria is to cure the infection as rapidly as possible. Cure is defined as the elimination from the body of the parasites that caused the illness. This prevents progression to severe disease, and additional morbidity associated with treatment failure. In treatment

evaluations, it is necessary to follow patients for sufficient time to appropriately assess cures. The duration of post-treatment follow-up is based on the elimination half-life of the antimalarial medicine being evaluated. The current recommended duration of follow-up is a minimum of 28 days for all antimalarial medicines, while it is extended for longer periods of time depending on elimination half-life (42 days for combinations with mefloquine and piperaquine).[1] When possible, blood or plasma levels of the antimalarial should also be measured in prospective assessments so that drug resistance can be distinguished from treatment failures due to inadequate drug exposure. The public health goal of treatment is to reduce transmission of the infection to others, i.e.to reduce the infectious reservoir and to prevent the emergence and spread of resistance to antimalarial medicines. The adverse effects, profile and tolerability of antimalarial medicines, and the speed of therapeutic response are also important considerations.[1]

Treatment with antimalarias lead to reduction of malaria transmission by two mechanisms[11]

1. reduction of gametocytes by eliminating the asexual blood stages from which gametocytes derive. The faster the clearance of asexual blood parasites the greater the effect on reducing infectivity. The potent anti-infective properties of artemisinins are, therefore, partly due to their rapid parasite clearance action. In *P. vivax, P. malariae* and *P. ovale*, gametocytes have a short developmental period (2–3 days) and mature gametocytes are short-lived.
2. lowering parasite infectivity through either a direct effect on gametocytes (gametocytocidal effect) or on the parasite developmental stages in the mosquito (sporonticidal effect) Artemisinins are the most potent gametocytocidal drugs among those currently being used to treat an asexual blood infection.[12,13]

Antimalarial treatment policy

In high-transmission settings re-infection is inevitable, but the cure of malaria (i.e. prevention of recrudescence) is important; it benefits both the patient, by reducing anaemia, and the community, by reducing the parasite reservoir and slowing the emergence and spread of resistance. The WHO malaria treatment guidelines recommend that antimalarial treatment policy should be changed at treatment failure rates considerably lower than those recommended previously.[1] This major change reflects the availability of highly effective drugs and the recognition both of the consequences of drug resistance, in terms of morbidity and mortality, as well as the importance of high-cure rates in malaria control. It is now recommended that a change of first-line treatment should be initiated if the total failure proportion exceeds 10%. However, it is acknowledged that a decision to change may be influenced by a number of other factors; these include: the prevalence and geographical distribution of reported treatment failures; health service provider and/or patient dissatisfaction with the treatment; the political and economical context; and the availability of affordable alternatives to the commonly used treatment.[1]

Nigeria National Antimalarial Treatment Policy[5]:

This is a set of recommendations and regulations concerning antimalarial drugs and their utilization in the country. This policy is continuously evaluated, reviewed and updated whenever appropriate by the national malaria control programme. The goal of the antimalarial treatment policy is to use the available resources efficiently to maximize the reduction in mortality and morbidity due to malaria. The purpose of antimalarial treatment policy is to: provide rapid and long lasting cure; reduce morbidity, including malaria related anaemia; prevent the progression of uncomplicated malaria into severe and potentially fatal disease; reduce the unfavourable effects of malaria in pregnancy through intermittent preventive treatment and minimize the likelihood and rate of development of drug resistance. The policy contains information on decision on whether a sick patient requires antimalarial treatment or not; recommended treatment for uncomplicated and severe malaria; chemoprophylaxis for various at risk groups; criteria for review of antimalarial treatment policy and regulation and deployment of antimalarial medicines. The policy also states the relationship between the various health care levels in the country and their management capabilities of malaria as shown in figure 1.

Figure 1: various health care levels in the country and their management capabilities of malaria

Health care level	Cadre of staff	Expected management capabilities
Level III		
Teaching Hospitals, Specialist Hospitals, FMCs and some Private Hospitals	Specialist Physician or Highly skilled Senior Physician	Intensive care for severe disease
Level II		
General Hospitals, Comprehensive Health Centres, Cottage Hospital and Private Hospitals	Medical officers, General Practitioners, Nurses and Community Health Officers	In-patient care Basic laboratory support for confirming diagnosis and monitoring. Assessing complications
Level I		
Health Centre with or without laboratory facility. Dispensaries, Health posts and community based providers.	Community Health Extension Workers, Village Health Workers, Patent Medicine Vendors	Syndromic approach focusing on disease identification, initiation of appropriate treatment and urgent referral of severe malaria

Diagnosis of malaria

Prompt and accurate diagnosis of malaria is part of effective disease management and the diagnostic approaches most commonly used are based on the symptoms and signs of the disease, microscopic diagnosis, molecular diagnosis and serology. All these methods have their disadvantages[14-16] for example, microscopic diagnosis is time-consuming and labour-intensive and in many malaria-endemic areas like Nigeria, there is lack of trained microscopists and reliable equipment.The syndromic approach is largely unreliable because the symptoms of malaria are very non-specific and leads frequently to incorrect diagnoses and unnecessary use of antimalarial drugs. It also results in additional expenses and increases the risk of selecting for drug-resistant parasites. Molecular diagnosis is expensive and requires a specialized laboratory, while serological diagnosis does not detect current infection but rather measures past experience. These disadvantages have favoured the introduction and use of rapid diagnostic tests (RDTs) based on immunochromatographic techniques.[16] In general, RDTs for malaria diagnosis uses immunochromatographic methods to detect *Plasmodium*-specific antigens in a finger prick blood sample and can be performed in approximately 15 minutes by individuals with minimal training.[16,17] They save the cost and time wasted on presumptive treatment particularly with the high cost artemisinin-combination therapy (ACTs) which is now the recommended first line treatment for malaria.[18] Several commercially available tests are sensitive, specific, and stable under operational conditions both in Nigeria and elsewhere. [2, 19-21]

Treatment strategies/ National responses

Prompt and proper treatment services that are equitable and pro-poor are needed in malaria endemic countries in order to mitigate the impact of the disease on the poor. A strong health system provides for effective delivery of proper treatment services to its citizens.[22] However in many developing countries, access to prompt and proper health services remain a major problem. Nigeria like many other sub-Saharan African countries is bedeviled with the problem of low level of access to proper treatment especially of common illnesses like malaria.[23] This is due mainly to the general poor state of the health system, high cost of health services, lopsided distribution of health facilities in favor of the urban areas and gross underfunding of the health sector resulting in lack of subsidies and exemptions to the poor. Concerns over the burden of malaria led to the development of several global control strategies and targets such as those under the millennium development goals (MDG) and Roll Back Malaria (RBM) which were set in order to encourage malaria-endemic communities to control the disease. Heads of state of African countries made a commitment, in April 2000 at Abuja, Nigeria, to ensure that at least 60% of those suffering from malaria have prompt access to affordable and appropriate treatment within 24 hours of the onset of symptoms. One of the key strategies endorsed by the Abuja meeting was to take actions to ensure that by 2005 at least 60% of those suffering from malaria have prompt access to appropriate and affordable treatment and are able to initiate treatment within 24 hours of the onset of symptoms. This was termed effective management of malaria nearer the home and was thus adopted as another strategy to combat malaria.[24] However, achieving high levels of access to effective malaria treatment remains a challenge for malaria control programs. This challenge was made worse by the increasing resistance to existing antimalarial medicines that has led governments to change their treatment policy. Based on this the Nigerian government changed its first line drug to the more expensive arthemisinin based combination therapy (ACT) and recommended that all fevers be treated presumptively with ACTs where confirmation cannot be made.[5] This was also in line with WHO recommendation for endemic countries where the availability and use of laboratories are limited. However the current WHO treatment guideline provide evidence-based recommendations for countries on malaria diagnosis and treatment.[25] The guideline places emphasis on testing for malaria with RDTs or microscopy before treating while reaffirming the use of ACTs. ACT is cost effective in almost all settings where there is drug-resistance primarily due to the fact that future expensive episodes of malaria, or in the worst case hospital admissions, are avoided by intervening early. Translating policy into practice and ensuring that ACT reaches the majority of children and vulnerable adults with malaria has, however, proved very challenging.[26] In addition, ACTs are expensive and it is therefore important to save them from drug resistance by ensuring rational use.

The World Health Organization (WHO) advises presumptive diagnosis as the basis for first-line treatment of uncomplicated malaria in places where a parasitological test is not possible. This policy allows uncomplicated malarial illnesses to be treated by village health workers, shopkeepers, or relatives in the home, and thus minimizes delays in treatment, especially for those living a long way from formal health facilities. Home-based treatment is a simple and effective initiative that is revolutionizing the treatment of malaria in Nigeria. and Africa, putting essential drugs and know-how into the hands of those who most need them - mothers and community based caregivers. However given the costs of newer treatments (ACTs), greater emphasis has to be placed on improving the quality of malaria treatment services. Furthermore, intermittent preventive treatment for prevention of malaria in pregnancy (IPTp) is a key component of malaria control strategy in Nigeria and sulfadoxine-pyrimethamine (SP) is the drug of choice. Despite the evidence of the effectiveness of IPTp strategy using SP in reducing the adverse effects of malaria during pregnancy the uptake and coverage in Nigeria is low.

A cross-sectional study carried out between July and August 2007 among 209 pregnant women in a rural Local Government Area of Ekiti State, Nigeria showed that IPTp use among pregnant women was very low and there was poor adherence to the directly observed therapy (DOT) scheme.[27] The authors suggested that concerted effort should be made to increase awareness of IPTp among the public especially women of child bearing age and that health workers should also be trained and monitored to ensure adherence.

Malaria treatment sources

Different factors affect the source of reception of malaria treatment services especially perceived severity ranging from simple fever or uncomplicated malaria to severe or complicated malaria.[28] Uncomplicated presentations are more likely managed at home initially, while cases with convulsions or severe malaria are more likely to seek care from a health care practitioner. Multiple care-seeking events and switching between types of providers is also common.[29]

Patients in Nigeria access treatment for malaria in a diverse range of outlets in the public and private sectors. The public sector consists of primary health centres (PHC), secondary and tertiary hospitals while the private sector is large and heterogeneous consisting of a wide range of providers both registered and unregistered such as private hospitals, pharmacies, patent medicine dealers and traditional healers with patent medicine dealers accounting for more than half of all providers.[30] However, there is a possibility that the poor and rural dwellers do not have access to appropriate treatment due to the limited number of trained providers and inequities in the distribution of these providers in favour of the urban areas.[23] A study in Anambra state, Nigeria showed that the most preferred source of provision of malaria treatment services for the respondents was public hospitals followed by training of mothers, treatment in Primary healthcare centres, traditional healers and patent medicine dealers were the least preferred strategies for improving malaria treatment. Some of the preferences differed by socio-economic status and by a lesser extent, the geographic location of the respondents.[31] Another study in Anambra state, Nigeria[32], showed that urban–rural geographic differentials exist in access to malaria treatment services, increasing the vulnerability of the rural dwellers to consuming inappropriate treatment which is likely to worsen their disease burden. For instance, the pattern of drug use that was found in this study has equity implications for appropriate treatment of malaria in Anambra state and even Nigeria because the two main failing drugs were used more by rural dwellers. Also, the low-level providers with low quality of services were also significantly and predominantly used more by the rural dwellers. These findings infer that the rural dwellers received lowest quality of treatment from all ramifications and current efforts in Nigeria to provide malaria treatment services do not address geographic inequities in service delivery. It was therefore suggested that there should be re-invigoration of public facilities for appropriate diagnosis and treatment of malaria, in addition to improving the financial and geographic accessibility of such facilities.

The primary healthcare is the entry point into the Nigerian healthcare sector and is aimed at providing healthcare services to the grass root, however use of primary health facilities as the first resort for malaria management is low. It is estimated that only about 20% of malaria episodes are treated in the health centres.[33] In order to cope with deficiencies in the performance of formal health services especially in the rural areas where malaria is most endemic, communities have resorted to self-medication through the unregulated private and informal sector.[33] However, Most times they are required at these facilities to distinguish between antimalarials and choose which one they want.[35] Presently there are more than two hundred brands of ACTs in the Nigerian market, which can be bought over the counter[30] and community members usually do not have appropriate information on over-the-counter medicines, hence this has led to widespread ineffective treatment of fevers.[36] The private sector is also poorly regulated hence the administration of anti-malarials is often erratic.[37] In both urban and rural areas the first source of treatment is usually from the patent medicine dealers (PMDs).[38] Previous studies have substantiated the critical role of these PMDs in malaria treatment, indicating that they serve as the first point of contact for care in more than half of the cases in rural Nigeria.[23,28,39] They are readily available and their services apparently cheaper on the short run due to nonpayment of consultation fees and transport costs.[40, 41] However, concerns are being raised about their adherence to treatment guidelines, the appropriateness and quality of drugs that they provide as they usually do not have any formal training.[42] An in-depth study of PMDs in three Nigerian states revealed that relatively few of them were aware of the new government policy on antimalarial drugs, Sulfadoxine-pyrimethamine was the most common drug they stocked, followed by Chloroquine with ACTs being the least in stock and Monotherapy artesunate drugs were also common.[28]

Generally malaria treatment services and practices are still inadequate in both the public and private sector. From the demand side, cost is a major barrier to effective treatment.[35] Access to ACTs, is still constrained by cost as they cost much more than the previously used antimalarials, with a dose averaging about 504 naira ($4).[28] The high cost of ACTs often result in patients opting for a cheaper alternative or not buying the full regimen.[43] This is further compounded by lack of financial risk protection in Nigeria especially for the informal sector where the most poor belong. This means that even the poor pay out of pocket to receive treatment each time they have malaria which could be several times a year. From the supply side the lack of adherence to treatment guideline and poor prescribing practices of providers are major constraints to proper treatment.[28] Other factors that influence provider treatment practices in other African settings include client expectations, expected profit margins, pharmaceutical company promotions, and local regulation.[44]

Several initiatives have been put in place over the years to improve access to proper malaria treatment, including training of community health workers and role model mothers (RMM) in treatment of febrile children with ACT. These community-based agents are trained to assist in administering drugs for fever as the availability of effective anti-malarial drugs at home is one way to ensure prompt access to treatment.[8] Studies have also shown the feasibility of this method.[33] Some states in Nigeria have also abolished user fees for children under five and for pregnant women in public health facilities, in an effort to improve access to effective treatment. However, the policy also does not make any provision for the different socio-economic groups as there are many people outside of the target groups of pregnant women and children under five years at risk of incurring catastrophic costs due to malaria.

With the newly introduced high cost ACT, and the new WHO treatment guidelines, a policy option to improve diagnosis and prescribing pattern in private sectors will be to train PMDs in the appropriate use of RDTs and ACTs. It is likely to decrease inappropriate treatment and delay the emergence of resistance to ACT while enhancing the delivery of ACT for malaria treatment

CONCLUSIONS AND RECOMMENDATIONS

Antimalarial medicines have an important role to play in reducing malaria transmission and in curtailing the spread of drug resistant parasites. Early cure of blood infections, such as by providing good access to diagnosis and treatment will, in itself, be effective in lowering malaria transmission. The success of a new treatment policy would depend on the adherence of health providers and patients to the recommendations. The bottlenecks and beauracracy that discourages individuals from assessing treatment in public hospitals should be addressed by the management of those institutions because it has been documented that public hospitals were ranked and rated the most preferred choice for the improvement of malaria treatment services in both the higher socio-economic status group and rural areas.

Within the context of increasing antimalarial costs and or decreasing malaria transmission, the importance of limiting antimalarial treatment to only those confirmed as having malaria parasites becomes paramount. Provision of RDT kits and ACTs at subsidized costs will go a long way in improving malaria treatment services in Nigeria. RDTs offer the possibility for accurate and accessible detection of malaria parasites, and have an important role in limiting malaria over-diagnosis and over-treatment. Indigenous plantations for cultivating active ingredients and local manufacturing of ACTs is further expected to lower the costs of the drugs and increase its utilization and lower the incidence and impact of malaria. There is also an urgent need to develop adequate strategies that ensure better access to medicines by getting evidence-based and effective medicines to the people who need them, whether by reducing their costs, promoting research and development, improving their distribution, increasing their efficacy and acceptability, or slowing down the development of antimicrobial resistance.

Considering that the quality of care received by patients is poor, the government must, as a matter of priority and importance, provide continuous training for lower level health cadres and informal providers to improve the level of care they provide. Thus urgent interventions should be developed and implemented so as to remedy this inequity. This may include the training of drug sellers that bound in the rural areas. There is evidence that shopkeepers, if properly trained, can improve their targeting of antimalarials in Nigeria[45] Training of mothers should be encouraged but home management will not work if the quality of services of PMDs and pharmacy shops where drugs for home management are purchased are not improved. Therefore, there is the need for a holistic improvement of malaria treatment services

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