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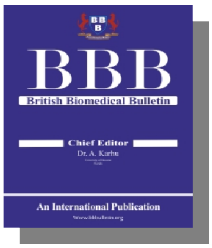


Original

# Prescription Pattern of Antimalarial Drugs in a Teaching Hospital in Nigeria

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A B S T R A C T

**Introduction**
As a response to the anti-malarial drug resistance situation, the World Health Organisation (WHO) recommends that treatment policies for falciparum malaria in all countries experiencing resistance to monotherapies should be combination therapies, preferably those containing an arteminisin derivative (ACT-artemisinin-based combination therapy).

**Methodology**
A retrospective quantitative study was designed to examine case records of patients treated for malaria in a tertiary health hospital in Jos, Northern part of Nigeria between August and December 2012. Questionaires were also distributed to doctors working within the hospital environment. Data on demographic, clinical features of disease, diagnostic procedures and drug administration were collected from the patients' records.

**Results**
Case record files of 130 patients were selected, 80.7% of the patients were prescribed antimalarial drugs. 55.2% of patients admitted for malaria were males, 44.8% were between 21-50 years of age. Fever (35.2%) was the most common presenting symptom, 71.4% of the patients had diagnostic blood slides. Antimalarial drugs were prescribed for malaria and malaria associated with other disease conditions, artemisinin and lumefantrine was the most prescribed antimalarial agent. 44.0% of these drugs were prescribed by trade names, 29.0% were administered orally. The most antimalarial drug prescribed for prevention of malaria in pregnant women was sulfadoxine-pyrimethamine, all the practitioners followed current WHO guidelines , half of the clinicians would prescribe parenteral antimalarial drugs for severe and cerebral malaria, laboratory and clinical assessment were used for malaria diagnosis, 71.4% of the physicians adhered to hospital guidelines.

**Conclusion**
This study indicates the implementation of artemisinin combination therapy in a public health facility; however the success of this new treatment policy would depend on patient adherence to recommendations and provision of ACTs at subsidized costs in Nigeria.



## Introduction

The change in malaria control policy in Nigeria in 2005 in favour of artemisinin-based combination therapy (ACT) became necessary with the prevalence of *Plasmodium falciparum* resistance to chloroquine and sulphadoxine pyrimethamine[1].

Prescription practices have been shown to influence the emergence of resistance to antimalarial drugs[2], thus the success of a new treatment policy would depend on the adherence of health providers and patients to treatment recommendations[3]. This becomes important in order to protect the clinical shelf life of the artemisinin-based combinations since they remain the most valuable drugs currently available for the management of malaria[1].

Informal use of antimalarials could increase the risk of under-dosage, over-dosage or incorrect dosing, treatment failure, the resistance to antimalarial drugs, occurrence of adverse drug reaction and drug interactions which could impact negatively on antimalarial treatment safely[4].

The study focused on evaluating antimalarial drug use on in-patients and prescribing patterns of the physicians within the hospital based on current National policy on malaria treatment. It is hoped that the study would establish goals of providing and promoting pharmaceutical care.

## Materials and Methods

Ethical clearance was obtained from the Ethics and Research Committee of the hospital before the commencement of the study, the study was conducted during the period, August to October 2012. This period is the peak malaria transmission season in this Northern part of Nigeria. The following information was obtained from the case record files: patient's name, age, sex, and date of admission. Other data collected were symptoms, diagnostic test and antimalarial drug prescribed (name, frequency of dosing, route of administration, and duration of therapy) , patient medical history, especially previous use of anti-malarial drugs prior to hospital visit and the percentages of drugs prescribed in generic names, these were entered into data collecting forms. Questionnaires were distributed to physicians working in the hospital.

### Data analysis

Descriptive statistics of frequency and percentage were used for analysis using EPI-info.

## Results

A total of 130 patient medical records were evaluated during the study of prescription pattern and 105 selected. 25 (19.2%) case records were excluded from the study due to incomplete information. The age distribution of the patients were: 1-10 year = 17 (16.2%); 11-20 years = 12 (11.4%), 21-50 years = 47 (44.8) and 29 (27.6%) of the patients above 50 years. Analysis of the prescription collected indicates that; more male 58 (55.2%) than female 47 (44.8%) patients were admitted for malaria treatment.

The presenting symptoms were fever 37 (35.2%), vomiting 17 (16.2%), diarrhea 9 (8.57%), convulsion 12 (11.4%) and other commonest symptoms were anemia, dizziness, loss of appetite and pains 61 (58.1%). Malaria was diagnosed in 61(58.1%) of the patients by microscopic examination of blood films, 30 (28.6%) by clinical signs and symptoms of malaria (Table 1).

Of the 105 patients medical record examined, a total 52 (49.5%) had malaria, 3 (2.9%) were malaria in pregnancy, 1(1.0%) malaria rule out enteritis, 10 (9.5%) malaria in retroviral disease, 3 (2.9%) poorly treated malaria, 5 (4.8%) severe malaria rule out meningitis, 4 (3.8%) resistant malaria, 9 (8.6%) malaria and hypertension, 2 (1.9%) cerebral malaria, 1 (1.0%) malaria and typhoid perforation, 2 (1.9%) malaria in sickle cell disease, 2 (1.9%) severe malaria and 5(4.8%) malaria and hyperglycemia (Table 2).

The most commonly prescribed antimalarial drug was artemisinin-lumefantrine (A+L) (58.1%), followed by dihydro-artemisinin (46.7%), sulphadoxine-pyrimethamine (S+P) (13.3%), quinine (7.6%), artesunate (4.8%), proguanil (2.9%), artemeter (1%) and artequine (1%) as presented in (Fig. 1).

Only (11.8%) of these antimalarial drugs were prescribed by a generic name. Oral administration was the most frequent means of administration (58.5%), followed by intramuscular injection (35.6%) and intravenous administration (5.9%) (Fig. 2). All the medical practitioners 14 (100%) that participated in this study would prescribe ACT for treatment of malaria; 11 (78.6%) of them would prescribe sulphadoxine-pyrimethamine for prevention of malaria for pregnant women. The remaining 6 (42.9%) would prescribe quinine, artemisinin and chloroquine for them (Table 3).

All the physicians 14 (100%) would prescribe antimalarial drug for the treatment of malaria based on current WHO guideline, other reasons for choice of antimalarial drug were antimalarial drug resistance, cost, side effects and adverse drug reaction. Half of the clinicians would prescribe parenteral anti-malarial drug for severe malaria and cerebral malaria while others would prescribe for complicated malaria and problem with oral administration. 9(64.3%) of the practitioners based their treatment on laboratory diagnosis while the remaining 5(35.7%) used both laboratory diagnosis and clinical assessment for their treatment. Almost all the clinicians 10(71.4%) would adhere to hospital guidelines (Table 4).

## Discussion

Advances The most affected age group was 21-50 years, this agrees with other study conducted in Nigeria in which half of the patients were adults[5]. The analysis of our study indicates a higher incidence of malaria infection among the male patients. Malaria is not known to be associated with any sex preference but several studies have reported a higher incidence in male[6]. The higher incidence among the male patients may be a mere reflection of the sex distribution in the study population or an indication of a stronger immunity developed by the female patients[7].

The commonest symptoms were anemia, dizziness, loss of appetite and pains (58.1%). The Presentations of malaria are different at different ages and in areas with different levels of transmission[8]. Fever is a characteristic feature of P. falciparum infection, but about 35.7% of the patients presented this symptom, home medication with antipyretic or antimalarial agents may be responsible for the masking of the fever and such cases may be misdiagnosed when clinical parameters alone are used[7].

Table 1 indicates that most of the prescriptions were based on laboratory investigations while only one fifth was based

on clinical sign and symptoms; this is not surprising because the study center is a tertiary health facility where a more specific diagnosis is required[7]. 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[9]. These disadvantages have favoured the introduction and use of rapid diagnostic tests (RDTs) based on immuno-chromatographic techniques[10]. 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[11]. Several commercially available tests are sensitive, specific, and stable under operational conditions both in Nigeria and elsewhere[12].

The pattern of antimalarial prescriptions is dominated by ACT in our study, the findings from this study are consistent with previous reports that prescribers in tertiary institution tend to adhere more to national treatment guidelines[1]. Since drug resistance had become a major problem with the emergence of resistance of *P. falciparum* to nearly all used antimalarial drugs[13], in response to widespread resistance to older antimalarial drugs, WHO has recommended Artemisinin Combination Therapy (ACTs) as first line therapy for the treatment of uncomplicated malaria[14]. ACT is antimalarial combination therapy with artemisinin derivative as one component of the combination. Artemisinin derivatives have very short half-lives and so their use as monotherapy requires doses over a period of 7 days. Combination of one of these drugs with a longer half- life partner antimalarial drug allows a reduction in the duration of antimalarial treatment while at the same time enhancing efficacy and reducing the likelihood of resistance development[15].

The percentage of antimalarial drugs prescribed in generic name was low; this result correlated with previously studies on generic prescribing which were found to be low in teaching hospitals[16]. This contravenes WHO recommendation in promoting rational use of drugs that drugs should be prescribed in their international non-proprietary names[17]. The oral route was the most prescribed formulation of antimalarials because it is the easiest method of administration; these drugs are completely absorbed by the gastro-intestinal tract[18]. In contrast, the injectable forms were not preferred because they are painful, expensive and needs skill to administer[19].

All the doctors would prescribe ACT for the treatment of malaria; this shows that all the physicians in this hospital follow the current WHO guidelines. This is not in agreement with study conducted by Meremikwu *et al*[5], in which less than a fifth of the primary and secondary health facilities studied used the recommended malaria treatment guidelines[20]. Sulphadoxine pyrimethamine would be prescribed for prophylaxis for pregnant women by more than half of the clinicians. This shows that Sulphadoxine-pyrimethamine prescribed in the study were mainly used for prophylaxis and this is in line with the WHO recommendation and the Nigerian National Antimalarial Guideline and Treatment Policy that sulphadoxine-pyrimethamine should be used as an Intermittent Preventive Therapy (IPT) because of its effectiveness[21]. However some physician would prescribe quinine, artemisinin and chloroquine as prophylactic drugs for these women and this also agrees with research carried out by Okoro *et al*[17], which indicates that Artemisinin derivatives/combinations were prescribed as prophylactic drugs, which is against the national guidelines to be used as prophylactic

agent because they are rapidly acting, it is only recommended as second line agent in the treatment of malaria in pregnancy during the second and third trimester[17]. Quinine can be used as a first line agent in the treatment of malaria and chloroquine might be prescribed by physicians because of its efficacy, safety and cost[22]. Interestly, apart from inexperienced physicians such as medical officers, this study also shows that senior registrar, registrar would also prescribe these drugs for prophylaxis.

The results of our study indicates that all the physicians adhered to current WHO guideline for malaria treatment, the findings from this study are consistent with previous reports that prescribers in tertiary health facilities tend to adhere more to national treatment guidelines than private practitioners[1]. The prescriptions of these antimalarials were based on antimalarial drug resistance, cost, side effects, adverse drug reactions and efficacy of the drugs.

Half of the clinicians would prescribe parenteral antimalarial drug for severe malaria, severe malaria is a medical emergency and may rapidly progress to death without prompt and appropriate treatment[23]. The main objective of the treatment of severe malaria is to prevent the patient from dying; prevention of recrudescence, transmission or emergence of resistance and prevention of disabilities are secondary objectives. The mortality of untreated severe malaria can be 100%, but with antimalarial treatment, the overall mortality falls to 15–20%[24]. As death from severe malaria can occur within hours of admission to hospital or clinic, it is essential that therapeutic concentrations of antimalarial are achieved as soon as possible[24] with intravenous antimalarials. Further, gastrointestinal intolerance and erratic intestinal absorption make the oral route of administration unreliable in these patients[23]. Less than half of the medical practitioners would administer parenteral anti-malarial drug to treat uncomplicated malaria. Uncomplicated malaria is defined as symptomatic malaria without signs of severity or evidence of vital organ dysfunction[25]. Uncomplicated *P. falciparum* infection should be treated according to the sensitivity of the parasite at the area of acquiring the infection. To counter the threat of resistance of *P. falciparum* to monotherapies, and to improve treatment outcome, combinations of antimalarials are now recommended by WHO for the treatment of falciparum malaria[25]. Two or more blood schizontocidal drugs with independent modes of action and thus unrelated biochemical targets in the parasite are used and at present Artemisinin Combinations (ACTs) are the recommended treatments for uncomplicated falciparum malaria[25].

Cerebral malaria would be treated by parenteral antimalarial drug by almost all the physicians, cerebral malaria is the most common complication and cause of death in severe *P. falciparum* infection. In falciparum malaria, 10% of all admissions and 80% of deaths are due to the CNS involvement. On the other hand, CNS manifestations are fairly common in malaria and it could be due to not only severe *P. falciparum* infection, but also high-grade fever and antimalarial drugs[23]. Therefore, it is extremely important to differentiate between these so as to avoid unnecessary anxiety and improper treatment. Parenteral quinine has been traditionally the treatment of choice for cerebral malaria. Artemisinin derivatives have been proved to be equally, if not more, effective in treating cerebral malaria[23].

The current WHO treatment guideline provides evidence-based recommendations for countries on malaria diagnosis and treatment[26]. The guideline places emphasis on testing for malaria with RDTs or microscopy before treating while reaffirming the use of ACTs. However, the findings from our study show that the some of the physicians based

their treatment on both laboratory investigation and clinical assessment.

The results of our study also indicates that some of the clinicians did not comply to the hospital guidelines, Lack of adherence to malaria treatment guidelines was associated with inappropriate prescribing practices in rural Kenya[27]. Clarity of guidelines, strong evidence, adequate funding of guidelines and support by opinion leaders especially professional bodies are some of the factors that positively influence the use of clinical guidelines[5].

## Limitations

The 105 patients selected for this study represents only a fraction of the cases of malaria infection seen in this hospital during the study period , the majority of patients who presented with what was considered as mild degree of malaria infection were always treated and discharged as out- patients. Although August to September is the peak period for malaria, data collection was not done for the whole year. The number of malaria cases in this study centre is relatively small, as there are good access to other health facilitates in the same area.

## Conclusion

The pattern of antimalarial drugs prescription in the study describes good adherence to malaria treatment guidelines, the prescriptions were predominantly Artemisinin Combination Therapy (ACT). Efforts should also be made to decrease inappropriate treatment and delay the emergence of resistance to ACT while enhancing the delivery of ACT for malaria treatment.

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**Table 1.** Patient characteristics and physician's assessment Characteristics

| Description | Number (%) |
|---|---|
| Total number of cases<br>Number of selected cases<br>Number of cases excluded | 130<br>105 (80.8)<br>25 (19.2) |
| **Age (yrs)** | |
| 1-10<br>11-20<br>21-50<br>> 50 | 17 (16.2)<br>12 (11.4)<br>47 (44.8)<br>29 (27.6) |
| **Gender** | |
| Male<br>Female | 58 (55.2)<br>47 (44.8) |
| **Presenting features** | |
| Fever<br>Vomiting<br>Diarrhea<br>Convulsion<br>Others | 37 (35.2)<br>17 (16.2)<br>9 (8.6)<br>12 (11.4)<br>61 (58.1) |
| **Malaria parasite blood slide results** | |
| Positive<br>Negative<br>Clinical assessment | 61 (58.1)<br>14 (13.3)<br>30 (28.6) |

**Table 2.** Clinical indications of antimalarial drugs prescriptions

| No of Patients (%) | Diseases |
|---|---|
| 52 (49.5) | Malaria |
| 3 (2.9) | Malaria in pregnancy |
| 1 (1.0) | Malaria R/O enteritis |
| 10 (9.5) | Malaria in retroviral disease |
| 3 (2.9) | Poorly treated malaria |
| 5 (4.8) | Severe malaria rule out meningitis |
| 4 (3.8) | Resistant malaria |
| 9 (8.7) | Malaria and hypertension |
| 2 (1.9) | Cerebral malaria |
| 1 (1.0) | Malaria and typhoid perforation |
| 2 (1.9) | Malaria in sickle cell disease |
| 2 (1.9) | Severe malaria |
| 5 (4.8) | Malaria and hyperglycemia |

**Table 3.** Antimalarial drug prescription by the doctors

| Rank of the doctors | Number (%) | Antimalarial drug commonly prescribed | Antimalarial drug prescribe for prevention of malaria for pregnant women |
|---|---|---|---|
| Consultant | 6 (42.9) | ACT | S-P |
| Senior registrar | 3 (21.4) | " | Quinine |
| Registrar | 2 (14.3) | " | Artemisinin, S-P |
| Resident doctor | 2 (14.3) | " | S-P |
| Medical officer | 1 (7.1) | " | S-P, chloroquine<br>Quinine |

**Table 4.** Factors governing choice of treatment

| Reasons for the choice of antimalarial drug | Number (%) |
|---|---|
| Current WHO guideline<br>Antimalarial drug resistance<br>Cost<br>Side effects<br>Adverse drug reaction<br>Others | 14 (100%)<br>2 (14.3%)<br>3 (21.4%)<br>2 (14.3%)<br>2 (14.3%)<br>1 (7.1%) |
| Reasons for prescribing parenteral antimalarial drug | Number (%) |
| Severe malaria<br>Uncomplicated malaria<br>Cerebral malaria<br>Problem with oral administration | 7 (50%)<br>6 (42.9%)<br>7 (50%)<br>5 (35.7%) |
| Diagnosis of malaria | Number (%) |
| Laboratory diagnosis<br>Clinical assessment<br>both | 9 (64.3%)<br>-<br>5 (35.7%) |
| Basis of treatment | Number (%) |
| Adherence to hospital guideline<br>Non adherence to hospital guideline | 10 (71.4%)<br>4 (28.6%) |

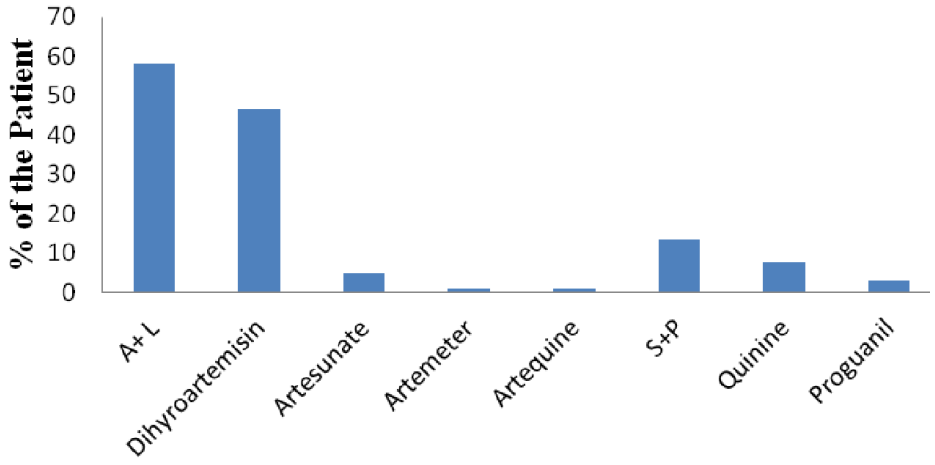


**Figure 1**. Antimalarial drugs used by the patients

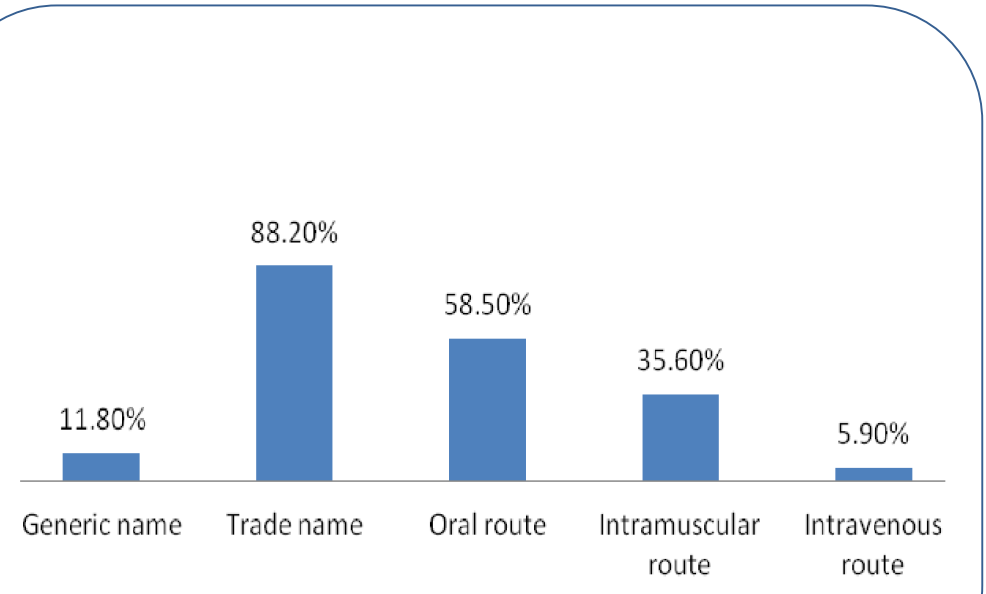


**Figure 2**. Prescription patterns of antimalarial drugs