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Incidence of malaria infection and adherence to antimalarial treatment guidelines at Bingham University Teaching Hospital, Jos, Nigeria

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Abstract
The development of antimalarial resistance has been a foremost barrier to malaria control. The aim of this study was to investigate the incidence of malaria infection and adherence to Antimalarial Treatment Guidelines (ATG) at Bingham University Teaching Hospital (BhUTH), Jos, Nigeria. A descriptive cross-sectional study was carried out to assess malaria infection diagnosis, antimalarials prescription pattern and adherence to the ATG by physicians over a two-year period. The study extracted data from 570 prescriptions of different patients and 227 patient files. The demographics of the patients was also obtained. Analyses were carried out using Statistical Package for the Social Sciences (SPSS). The study revealed that of the 227 patients treated for malaria, 65 % (n=148) underwent laboratory investigations before treatment while 35 % (n=79) were treated empirically. Artemether-Lumefantrine was the most prescribed antimalarial for treatment of uncomplicated malaria while parenteral Arteether and Sulfadoxine/Pyrimethamine (SP) was the mainstay for treating severe malaria. This study also revealed that physicians placed patients on antimalarials without confirmatory test indicating poor adherence to the ATG. Adherence to ATG has the potential to limit resistance to antimalarial drugs and should therefore be discouraged.

Keywords: Malaria; Guidelines; Antimalarial; Artemisinin-based combination; Artemeter-Lumefantrine

INTRODUCTION

Malaria remains a major public health concern globally, especially in sub-Saharan Africa. The management of malaria and adherence to treatment guidelines are crucial for reducing morbidity and mortality rates associated with the disease [1,2]. Clinical practice guidelines are declarations with suggestions aimed at improving patient care. They are created using evidence that has been carefully considered, thoroughly analyzed, and evaluated for both their advantages and disadvantages relative to other treatment plans [3]. The best available research should be translated into clinical practice according to these recommendations for improved patient outcomes. Clinical practice guidelines are also essential to providing patient-centred care [3].

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They are instructions or concepts that indicate existing or upcoming norms of policy for assisting healthcare professionals in patient care decisions including diagnosis, therapy, or related clinical conditions. They are created using carefully thought-out statements that include suggestions, tactics, or data to help patients and healthcare professionals decide on the best course of action for a certain condition [4].

The application of such recommendations has demonstrated the effectiveness of guideline-driven care in altering the procedure and result of professional patient care [5]. By drawing attention to inefficient, risky, and wasteful practices, the successful application of clinical practice standards has been linked to improved patient care. Evidence-based recommendations assist patients by raising the standard of treatment they get, which boosts their health outcomes and quality of life. Researchers, healthcare professionals, and healthcare systems all gain from it. These recommendations reduce inconsistency in care and simplify clinical choices. By implementing treatment recommendations that encourage clinically good procedures and discourage ineffective ones, patient morbidity and death can also be considerably decreased [6].

The importance of malaria surveillance as a continuous and systematic collection of malaria-related data, analyzing and interpreting such and seeking ways of utilizing them in planning, implementation and evaluation of public health practice is the way forward in tackling malaria especially in the Sub-Saharan region of West Africa [7]. In 2013, a study was carried out in Anambra State where it was observed that less than 50 % of patients were sent for laboratory examination before they were treated. The level of confidence in presumptive clinical diagnosis was considered to be unrealistic especially with evidence of high levels of inaccuracy leading to wastage of antimalarial administered in such cases [8]. The compliance and challenges in implementing the revised National Malaria Control Guidelines in public health facilities in Cross River State of Nigeria were looked into by a group of researchers in June 2022. According to the researchers, there was lack of adherence to the National guidelines in the case management of uncomplicated malaria such as the prescription and administration of parental drugs especially intramuscular artemether to patients instead of the recommended oral ACT [9]. A group of researchers in Ogun State observed that there was a significant difference between private and public healthcare workers in their adherence to national malaria diagnosis and treatment guidelines. While those in the public facilities were attributed to have about 60% compliance rate, this was not so in the private facilities where the adherence rate was about 27%. The availability of the antimalarials within the facilities and drug promotion by manufacturers were factors attributed to differences experienced. These researchers also observed that presumptive diagnosis for malaria was as high as 95% in private facilities compared to 23% in public facilities [10]. Another group of researchers reported poor compliance by physicians to national malaria treatment guidelines with regards to confirmation of the parasites before the commencement of treatment in febrile illnesses. In about 94% of the children below five years of age that were sampled, antimalarials were prescribed out of which 91 % were ACT combinations. Among those sent for laboratory confirmation, only 49% were positive indicating that some of those that had been given a prescription for malaria did not need it [11]. Poor adherence to ATG often results in antimalarial resistance as such the continual monitoring of adherence to ATG is vital in malaria endemic regions. This research aimed at studying the level of adherence to anti-malarial treatment guidelines in Bingham

University Teaching Hospital (BhUTH), Jos, Plateau State with the specific objectives of determining the cases that were diagnosed based on laboratory investigations and/or clinical manifestations; the anti-malarial drugs used in the treatment of malaria cases within a two-year period and assessing the level of compliance of the physicians to the National Treatment Guidelines. The process of obtaining data on the incidence of malaria and the antimalarial treatment being utilized serves as a step towards the right direction in the collation of data that can be referenced in taking vital decisions in the health sector that can aid in the curbing of malaria.

EXPERIMENTAL METHODS

The study area was Bingham University Teaching Hospital (BhUTH), Jos located in Jos North within Jos Metropolis of Plateau State, North- Central Nigeria.

A two-year retrospective study of patients with malaria infection that reported to the institution were investigated. Ethical clearance was obtained from the Institutional Health Research Ethical Committee of BhUTH before the collection of the data. Data collected were treated with utmost confidentiality. The study was carried out utilizing a Data Extraction form that captured relevant information such as age, gender, diagnosis, laboratory investigations, results, co-morbidities, and drugs used in the course of treatment from patient's files and prescriptions. Version 24 Statistical Package for Social Sciences (SPSS) software was used to generate descriptive statistics (proportion, means) in response to the study objectives. A total of 384 patients was calculated as sample size. All patients whose antimalarial prescriptions were accessed within the time frame and patient files with information on laboratory screening for malaria served as inclusion criteria.

RESULTS

Demographic characteristics of the patients. Demographic data of 570 patients was analyzed., out of which 57.9 % were within ages of 0 – 17 years and 42.1% being older than 17 years. There were more male patients (51.2 %; n=292) than female patients (48.8 %; n=278).

Co-Morbidities in patient treated for malaria. The patients' files accessed showed 63.7% (n=145) had no co-morbidities while 36.3% (n=82) had either one co-morbidity or a combination of more than one (Table 2). Anaemia was the most prevalent co-morbidity with 16.3% (n=37) of the patients having malaria followed by enteric fever in 5.3% (n=12). Gastroenteritis occurred in 4.4% (n=10); 3.9% (n=9) had Peptic ulcer disease (PUD); Malnutrition was diagnosed in 3.1% (n=7); 1.8 % (n=4) had Urinary Tract Infection (UTI) while 1.3% (n=3) of the patients were diagnosed with both anaemia and gastroenteritis alongside malaria infection. The other dual co-morbidities accounted for less than 0.5 %.

Adherence to guidelines in the diagnosis of malaria. The number of patients who underwent a confirmatory laboratory test for malaria was 65% (n=148) as presented in Table 3. The remaining 35% (n=79) of the patients did not undergo any laboratory test for diagnosis but were rather diagnosed based on their presenting signs and symptoms. This therefore, constitutes a deviation from guidelines recommendation which upholds diagnosis-based treatment for all patients with suspected malaria. Among the patients who underwent a confirmatory test, 74.8 % (n=111) tested positive for malaria while 25.2% (n=3) tested negative. Among those who tested positive, 74.9% (n=83) were classified as uncomplicated malaria while 25.1% (n=28) were classified as severe malaria according to the WHO classification of malaria.

Antimalarial prescription pattern. The prescription of antimalarial during the period of study stood at 565 as shown in Table 4. Out of these, 80.2% (n=453) were Artemisinin Combination Therapies (ACT), 14.7% (n=83) were monotherapies while 5.1% (n=29) were Non-ACT Combinations. Overall, the pattern of prescription shows that Artemether-Lumefantrine (77.4%; n=351) was the most prescribed ACT in the hospital followed by Dihydroartemisinin-Piperaquine (DP) (4.4%; n=20) and then Artesunate-Sulfadoxine/Pyrimethamine (2 %; n=9) for the treatment of uncomplicated malaria. Parenteral Arteether & Sulfadoxine/Pyrimethamine (16.1%; n=73) was the only combination therapy for treatment of severe malaria while SP (n=29) was the only Non-ACT Combination used for Intermittent Preventive Therapy of Malaria in Pregnancy (IPTP).

The most frequently used monotherapy in the hospital was Parenteral Arteether (65.1%; n=54) for the treatment of severe malaria. This was followed by parenteral Quinine (14.4%; n=12) which was mainly used for treatment of malaria in pregnancy. Also, Proguanil (20.5%; n=17) was used in the treatment of malaria in sickle-cell disease (SCD) patients both children and adults.

Table 1: Demographic characteristics of patients

Characteristic		Frequency (n)	Percentage (%)
Age (years)	0-5	206	36.1
	6-17	124	21.8
	18-25	86	15.1
	≥26	154	27.0
	Total	**570**	**100**
Gender	Female	278	48.8
	Male	292	51.2
	Total	**570**	**100**

Table 2: Co–morbidities with malaria in Bingham University Teaching Hospital

Co – morbidity	Frequency (n)	Percentage (%)
Anemia	37	16.3
Enteric fever	12	5.3
Gastroenteritis	10	4.4
PUD	9	3.9
Malnutrition	7	3.1
UTI	4	1.8
Anemia + Gastroenteritis	3	1.3
Anemia + PUD	1	0.4
None	145	63.7
Total	227	100

Table 3: Proportion of patients tested for malaria

Variables		Frequency (n)	Percentage (%)
Laboratory tests	Test Ordered	148	65
	Test Not Ordered	79	35
Result of laboratory tests	Tested Positive	111	74.8
	Tested Negative	37	25.2
Type of malaria	Uncomplicated	83	74.9
	Severe	28	25.1

Table 4: Drugs used in the treatment of malaria in BhUTH

Drug category	Drugs	Frequency (n)	Percentage (%)
Artemisinin Combination Therapy (ACT)	Artemeter – Lumefantrine	351	77.4
	Dihydroartemesinin – Piperaquine	20	4.4
	Artesunate - Sulfadoxine/Pyrimethamine (SP)	9	2.0
	Arteether Injection/SP	73	16.1
	Total	**453**	**100**
Non-ACT Combination	Sulfadoxine - Pyrimethamine (SP)	29	100
Monotherapy	Arteether Injection	54	65.1
	Quinine	12	14.4
	Proguanil	17	20.5
	Chloroquine	0	0.0
	Amodiaquine	0	0.0
	Total	**83**	**100**

DISCUSSION

The analysis carried out, revealed that majority of patients treated for malaria at the teaching hospital within the study period were aged 0 – 5 years accounting for over one third of the total patients treated for malaria infection at the facility (n=570). Slightly more than 50% of surveyed patient files and prescriptions were that of children between ages 0–17 years which is far greater than the findings in two hospitals in the eastern part of Nigeria which accounted for just 26% of surveyed patients that fell within this age group [9]. This finding proves that in Nigeria just as it has been reported in the rest of Sub-Saharan Africa, children below the age of five years are the most vulnerable group to malaria infection [8,9,12].

For this study, adherence was measured in terms of parasitological diagnosis of malaria and treatment with an appropriate or recommended drug. Non-adherent treatment on the other hand, was measured in terms of inconsistency in confirmatory diagnosis of malaria and prescribing of antimalarials which are not recommended. Hence, malaria case management in this hospital was characterized by sub-optimal adherence to the treatment guidelines majorly in terms of confirmatory diagnosis before treatment. Out of the 227 patients file assessed, two-thirds of the patients underwent a confirmatory test for malaria while the rest were diagnosed clinically based on the patient's presenting symptoms. This is a deviation from WHO guidelines recommendation which upholds diagnosis-based treatment for all patients with suspected malaria. WHO recommends that, there should be a confirmatory Parasitological Laboratory test before Treatment. Parasitological confirmation is essential as the result informs the clinician's decision on whether or not to prescribe an antimalarial [12].

The inability to correctly diagnose and treat non – malarial fever contributes to the decision to treat all or most fever as malaria [6]. The study also showed that 35% of malaria cases were diagnosed presumptively based on presenting symptoms majorly fever. This deviates from the National Antimalarial Treatment Policy which states that a parasitological diagnosis is required in all suspected cases of malaria before initiating treatment. The only condition where presumptive treatment is permissible is in an area where either supplies or trained personnel are not available [13]. In Nigeria it has been demonstrated that such practice has its potential risks, for instance, children who are treated presumptively without confirmatory tests could be exposed to unnecessary adverse – drug reaction such as gastrointestinal disturbances, hepatotoxicity and neurotoxicity which may be associated with ACTs [14].

Multi – drug resistant *Plasmodium falciparum* malaria continues to spread

throughout the world and has led WHO to recommend combination therapy as first – line treatment majorly the artemisinin-based compounds as standards due to the proven effectiveness and lack of resistant case reports [9,15] among the anti-malarial drug prescribed, Artemisinin combination therapy accounted for highest number of prescriptions. This included Artemether–Lumefantrine, Dihydroartemisinin–Piperaquine, Artesunate/sulfadoxine + Pyrimethamine (ASP) and Arteether injection/SP (ASP). This is a reflection that the hospital adhered specifically with the recommendations of the WHO Antimalarial Treatment Guideline (ATG) published first in 2006. This study's results are in concordance to a study carried out in Abuja, Nigeria which revealed an increase in the prescription of ACTs following the WHO recommendations [16]. The Study also showed Artemether – Lumefantrine accounted for 62.1% of the total antimalarial prescriptions.

In this study, it was also observed that Dihydroartemisinin – Piperaquine was mainly used as second-line drug in cases of relapse or treatment failure on treatment of uncomplicated malaria with Artemether – Lumefantrine. This is also in accordance with the specifications proposed by the Federal Ministry of Health [14]. It was also observed that intra-muscular (IM) arteether alone or IM arteether administered daily for ~~3~~ three days then followed by a full dose of Sulfadoxine/Pyrimethamine (SP) which was the mainstay for the treatment of severe malaria in the hospital. This procedure was not in line with the proposed use of IM or IV Artesunate, (IV Quinine or IV Artemether) in the treatment of severe malaria after which an oral ACT is used for the complete eradication of the parasite [17]. Clinical studies are yet to show the effectiveness and safety of this combination in the treatment of un-complicated or severe malaria. However, there would be a need for clinical researches to be carried out to prove the hypothesis.

Arteether is an ethyl ether derivative of artemisinin that is oil soluble, has a long elimination half-life (>20 hours) and is more stable than the other artemisinin compounds [18,19]. High doses of arteether have caused damage in animal studies, but there is less evidence that these effects are seen in humans [16,20]. It is a substitute for quinine because of drug safety issues seen with quinine [21,22]. Hence this could be the reason for the use of the parenteral antimalarial drug (arteether) in the treatment of severe malaria as opposed to that recommended in the WHO treatment guidelines for malaria [7].

This study also showed that in 3 % of cases (n=17), Proguanil was administered with Folic acid in patients who have sickle cell disease, for prophylaxis of malaria infection in this group and this is in line with the recommendation proposed by the Federal Ministry of Health [14]. It was also observed that Sulfadoxine and Pyrimethamine combination was administered as a prophylactic agent against malaria in pregnant women attending the ante – natal clinic. This is also in line with the specifications of the World Health Organization (WHO) for Intermittent Preventive Treatment in Pregnancy (IPTP) [19,20]. In 14.4 % (n=12) of cases, Quinine was used. This occurred mainly in the treatment of malaria in pregnant women, though WHO recommends combination with Clindamycin for a more effective therapy in all trimesters of pregnancy. It was also observed that Artemether-lumefantrine was used for malaria therapy in the second and third trimesters of pregnancy and this conforms to a study that showed similar efficacy and safety with for the treatment of uncomplicated malaria in the second and third trimesters of pregnancy [23].

Conclusion. This study revealed a high degree in the prescription of Artemisinin–Based Combination Therapy (ACT). Nevertheless,

physicians did not adhere strictly to the guideline. Some of the cases treated were done based on clinical presentation as opposed to the parasitological/confirmatory diagnosis. It was also observed that treatment pattern in the hospital were not in conformation to the WHO guidelines.

Malaria is still considered a global health problem, the morbidity and mortality burden of malaria could be reduced by strengthening prevention, improving malaria diagnosis, using correct therapy based on artemisinin combination and adopting strategies aimed at preventing drug resistance.

The policy of Malaria treatment in Nigeria should not be limited only to change in the guidelines, but also include continuous drug utilization studies sponsored by Federal Ministry of Health to ensure rational prescription of these drugs and the implementation of the guideline. Also, efforts should be geared towards the prevention and vector control measures and the complete eradication of malaria in Nigeria.

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