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Antimalarial Drugs Utilization, Adherence to Malaria Treatment Guideline and Awareness of the Guideline among the Health Providers

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Abstract

Background: Prompt and appropriate administration of effective antimalarial drug is paramount in the prognosis and treatment of severe malaria. Artesunate injection has been chosen over quinine injection as first line drug for severe malaria treatment following evidences of lower mortality, proven efficacy, ease of use and safety profile. Adherence to this policy will lead to more effective treatments.

Objective: The aims of this study were to audit antimalarial drug utilization in management of severe malaria, assess the adherence to severe malaria treatment guidelines and assess the levels of awareness of the 2015 severe malaria guidelines among health practitioners.

Methods: The study was carried out in two secondary hospitals in two phases using two methods. The first method is a retrospective survey using a structured data collection form to collect data on drug use from severe malaria patients' folders. Second method was a cross sectional prospective study, using validated questionnaires to assess the medical practitioners' drug of choice for severe malaria treatment and their awareness of the new treatment guidelines.

Results: A total of 563 folders of participants were audited, almost half of the patients (48.5%) were 1-5 years, 33 doctors and 17 hospital pharmacists participated. The prevalence of severe malaria was 0.8%, the most prescribed initial and follow up treatment was injection artesunate (84.2%) and oral artemether-lumefantrine (73.7%) respectively. The most common antibiotic and infusion used were ceftriaxone (74.2%) and dextrose saline (65.5%) respectively. About 78.8% of the doctors possessed and implemented the new treatment guideline (NTG) while 72.7% of the doctors were aware of the NTG, 70.6% of the pharmacists were not aware. Age (P-value=0.0004) and facility (P-value=0.0001) of the prescribers were significantly associated with the doctors' choice of medication for each patient.

Conclusion: Parenteral artesunate is the most prescribed medication for severe malaria treatment. The healthcare providers in these facilities were adherent to the new treatment guideline for severe malaria with doctors being more aware of the guideline than the pharmacist.

Keywords: Severe malaria treatment guideline; Malaria; Adherence; Artesunate injection; Nigeria

Introduction

Severe malaria is a life-threatening medical emergency, requiring in-patient care with prompt and effective treatment to avert immediate death due to multiple organ dysfunctions. In most cases it is acute, with signs of organ dysfunction and/or high level of parasitaemia and is associated with high mortality [1]. Symptoms of severe malaria include generalized convulsions, severe normocytic anemia, hypoglycemia, metabolic acidosis with respiratory distress, fluid and electrolyte disturbances, acute renal failure, acute pulmonary edema and adult respiratory distress syndrome (ARDS), circulatory collapse, shock, septicemia (algid malaria), abdominal bleeding, jaundice, hemaglobinuria, high fever and hyperparasitemia [2].

In Nigeria, malaria remains one of the most important health problems, accounting for 25% of infant mortality, 30% of under5 mortality and 11% of maternal mortality [3]. Between 2000 and 2010, at least 50% of the population had one episode of malaria per year, while children below 5 years had two to four attacks. A review of hospital records in tertiary facilities in western Nigeria indicated that 11.3% of hospital admissions were due to severe malaria with 89% being children less than 5 years of age [4].

For nearly 400 years intravenous quinine, usually formulated as a dihydrochloride salt, has been the principal drug used to treat severe *falciparum* malaria. A loading dose of 20 mg/kg is recommended to reduce the time needed to reach effective concentrations in the blood. Despite its long history of

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efficacy, quinine has significant limitations [5]. It has been observed that even with prompt administration of quinine; case fatality rates in severe malaria often exceed 20%, especially, in areas of South East Asia [6]. Slow, constant intravenous infusion is the preferred route for giving quinine; a process that is not always achievable. Quinine can also be given by deep intramuscular injection into the anterior thigh, however intragluteal injection should be avoided because of the risk of sciatic nerve damage, and the absorption is slow and uncertain. A few studies have shown good efficacy and tolerability for rectal administration of quinine, without the problems of the intramuscular route or the complexity of intravenous administration [7]. Adverse effects resulting from quinine therapy are cinchonism which often occurs at conventional dose regimens, tinnitus, deafness, dizziness, and vomiting. Hypoglycaemia is a less common, but more serious, adverse effect. Some people are allergic to quinine and develop skin rashes and edema, even with small doses. Toxic levels of quinine can occur following rapid intravenous administration and can result in heart rhythm disturbances, blindness, coma, and even death; hence the recommendation for routine cardiac monitoring during parenteral treatment [6]. Quinine has a narrow therapeutic ratio, causing hyper insulinaemic hypoglycaemia (more frequent and severe in pregnancy) and prolongs the QTc interval when given parenterally, particularly if infused too rapidly. Intramuscular quinine is effective, but can cause local toxicity as well as hypoglycaemia in patients who may not have intravenous access [8]. Especially, in Southeast Asia there is evidence of increasing quinine resistance so that artemisinins (mainly artesunate) are now increasingly used as first line treatments for severe malaria in many areas [9]. In accordance with the WHO policy of antimalarial drug usage in severe malaria treatment, quinine still remains the drug of choice in children when artesunate (AS) products are not available, although it suffers from certain drawbacks [10].

Artesunate (AS) is a semisynthetic derivative of artemisinin whose water solubility facilitates absorption and provides an advantage over artemether (AM) because it can be formulated as oral, rectal, intramuscular, and intravenous preparations. Artesunate is rapidly hydrolyzed to dihydroartemisinin, which is the most active schizonticidal metabolite. Injectable administration of AS results in a more rapid systemic availability of AS compared with intramuscular artemether and quinine. This pharmacokinetic advantage may provide a clinical advantage in the treatment of severe malaria [11]. Rectal AS has been shown to be absorbed rapidly, with a considerable inter-individual variability. Artesunate is highly effective against multidrug-resistant *falciparum* malaria and severe malaria in Vietnam, Thailand, China, and Myanmar; however, only limited studies have been carried out in Africa [12].

Recent studies showed that intravenous AS is associated with lower mortality, proven efficacy, ease of use and excellent safety profile in the treatment of severe malaria. The two key studies are SEAQUAMAT (South-East Asian Quinine Artesunate Malaria Trial) that was conducted in four South-East Asian countries with over 1461 patients (including 202 children) [13] and AQUAMAT (Artesunate versus Quinine in the treatment of severe malaria in African children) that was undertaken in 11 centers in 9 African countries and conducted with over 5400 children [14]. These studies revealed a relative reduction in morbidity and mortality of 34.7 and 22.5% respectively in AS recipients. In addition, intravenous AS was found to offers a number of advantages over quinine in terms of not requiring rate-controlled infusion or cardiac monitoring and had better efficacy in the treatment of severe and complicated childhood malaria [15-17].

These results led World Health Organization to revise the severe malaria treatment guidelines, recommending injectable artesunate as the first-line treatment for severe malaria followed by a complete course of an effective artemisinin-based combination therapy (ACT) as soon as the patient can take oral medications [15]. As a result of this change, an additional 195,000 deaths could be averted every year in Africa (Injectable Artesunate Stakeholders' Meeting Report, 2012). Following the new WHO guidelines, the National Guidelines for Diagnosis and Treatment of Malaria of the Federal Republic of Nigeria changed the national policy for the treatment of severe malaria in both children and adults from intravenous quinine to injectable AS in 2015 [2].

Despite the current WHO guideline, artemether and quinine still remain acceptable alternatives where parenteral AS is not available. However, this policy change requires a number of clinical and operational adaptations, as quinine has been the treatment of choice for many decades. In addition, research has shown that medical practitioners follow various patterns when it comes to the prescription of various drugs for ailments [18]. Proven clinical effectiveness was seen as the most important criterion considered by medical practitioners from both private and public health facilities when prescribing while majority of medical practitioners rely on multiple sources of drug information in prescribing [18-20]. In 2015, Nigeria adopted AS as firstline drug for treatment of severe malaria with quinine and artemether as second line treatment. Currently, there are no data on the use of artesunate injection for the treatment of severe malaria according to recommended treatment guideline in Enugu State, Nigeria. Hence, the aims of this study were to audit antimalarial drug utilization in management of severe malaria, assess the adherence to severe malaria treatment guidelines and to assess the levels of awareness of this 2015 severe malaria guideline among health practitioners.

Research Methodology

Study design

The study employed two designs; retrospective and cross-sectional design.

Study setting

The study was carried out in Enugu State, using two secondary hospitals namely: Bishop Shanahan Hospital Nsukka (BSH), and District Hospital Nsukka (DHN). The two hospitals receive referrals from surrounding health care centers and

private hospitals. Bishop Shanahan hospital is a missionary hospital with different units/wards (out-patient, children, male, female, antenatal, immunization) with about 120 bed spaces and a medical staff strength of over 70 staff. District hospital is a government owned hospital with about 80 bed spaces. In addition to outpatient and inpatient services, it offers immunization, antenatal and maternity services. It has staff strength of over 90 staff. These locations were selected because they have data dated as far back as 2015 relating to the utilization of the appropriate drug for the treatment of severe malaria. The areas where these selected hospitals are located are endemic for malaria infection with high prevalence during the rainy season.

Patient population/sampling

The population size included all available case files in the archives of the selected hospital, while the sample size was all malaria files that where specific for severe malaria.

Ethical considerations

Ethical approval for this study wassought from the Ethics Review Board of University of Nigeria Teaching Hospital (UNTH) Enugu State, Nigeria. The procedure did not involve blood sampling.

Data collection

All the files containing diagnosis of malaria were assessed and those with severe malaria were included in the study while those of uncomplicated malaria were excluded. The patient files were sorted out based on the presence of *P. falciparum* asexual parasitemia and one or more of the following manifestations in the absence of any other identifiable cause: impaired consciousness, metabolic acidosis, hypoglycemia, severe anemia, renal impairment, jaundice, pulmonary edema, significant bleeding, shock and hyperparasitemia [21].

Data collection instruments

A data collection form was developed and used to collect the information for the retrospective part of this study. The form was divided into four sections. Section one was the demographic section of the patients; section two captured the medications prescribed (antimalarials, antibiotics and analgesics); section three captured the supportive treatments given while the fourth section was on the pill burden and the number of drugs prescribed in generics. The data was collected from 2016 to 2019.

Also, properly constructed questionnaire for the hospital pharmacists and the medical doctors was used in the cross-sectional part of this study to assess the prevalence of the use of artesunate injection in severe malaria among medical practitioners in accordance with the National Treatment Guideline. The questionnaire for the pharmacists was divided into two sections: section A captured the demographics of the hospital pharmacists while section B assessed the knowledge of the hospital pharmacist of the new treatment guideline. The questionnaire of the medical doctors was divided into two sections: section A made up the demographics of the medical doctors, section B comprised of two sub sections which captured clinical manifestations used in diagnosis of severe malaria and preferred treatment for severe malaria and the practice of the medical doctors on the management of severe malaria.

Data analysis

The data obtained were coded into excel sheet and subsequently analyzed with Statistical Package for Social Sciences (SPSS) version 20. Descriptive statistics of demographic and clinical variables were conducted and represented as frequencies, percentage, means, standard deviation and range. A proportional comparison (chi- square) test and mean difference (T-test) were carried out. P-value <0.05 was taken as significant and it was set at 95% confidence interval.

Results

Participants' demographic characteristics

Table 1 shows the demographic characteristics of the patients. Out of the 563 participants whose folders were assessed in the retrospective part of the study; about half were female patients (51.0%) and children under 5 years (48.5%).

Table 1 Patients' demographic characteristics.

Variables	Frequency (%)
Gender	
Male	276 (49.0)
Female	287 (51.0)
Age	
Undefined age	15 (2.7)
5 years and below	**273 (48.5)**
6-18 years	107 (19.0)
19-30 years	64 (11.4)
31-59 years	61 (10.8)
60 years and above	43 (7.6)
Site	
Bishop Shanahan hospital	**396 (70.3)**
District hospital Nsukka	167 (29.7)
Year of study	
2016	137 (24.3)
2017	129 (22.9)
2018	**188 (33.4)**

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2019	109 (19.4)

Majority of the doctors were males (66.7%) while majority of the pharmacist population were females (58.8%). The majority of the doctors and pharmacists who participated in the study were of the rank of Medical Officers (97.0%) and Principal Pharmacist (64.7%) respectively. More than half of the Doctors (60.6%) were aged 31 to 40 years while more than half of the pharmacists (58.8%) were of younger age (20-30 years) **(Table 2).**

Table 2 Demographic characteristics of doctors and pharmacists.

Variables	Frequency (%)	
	Doctors	Pharmacist
Gender		
Male	**22 (66.7)**	7 (41.2)
Female	11 (33.3)	**10 (58.8)**
Marital status		
Single	8 (24.2)	7 (41.2)
Married	**25 (75.8)**	**10 (58.8)**
Rank (Pharmacist/Doctors)		
Principal Pharmacist		**11 (64.7)**
Senior Pharmacist/Medical officers	**32 (97.0)**	4 (23.5)
Assistant chief pharmacist		1 (5.9)
Chief pharmacist/Consultant	1 (3.0)	1 (5.9)
Age		
20-30years	7 (21.2)	10 (58.8)
31-40years	**20 (60.6)**	4 (23.5)
41-50years	6 (18.2)	3 (17.6)
Year of Practice		
1-10years	**25 (75.8)**	**13 (76.5)**
11-20years	8 (24.2)	4 (23.5)

Drugs used in treatment of severe malaria

Table 3 shows the frequency distribution of drugs as prescribed for patients with severe malaria. All the patients diagnosed of severe malaria received either parenteral artesunate (84.2%) or intramuscular artemether (15.8%) as initial anti-malarial medication; none received quinine injection. However, artemether-lumefantrine (73.7%) was the most frequently prescribed follow up anti-malarial drug. More than two-thirds of the patients (74.2%) were given intravenous ceftriaxone antibiotics with IM paracetamol being the most common analgesic used.

Table 3 Drugs used in treatment of severe malaria in the study hospitals.

Drugs used	Frequency (%) N=563
Initial Antimalarial	
IV artesunate	396 (70.3)
IM artesunate	78 (13.9)
IM artemether	89 (15.8)
Follow Up Antimalarial	
Artemether-lumefantrine	415 (73.7)
Artesunate-amodiaquine	148 (26.3)
Antibiotics	
IV ciprofloxacin	31 (5.5)
IV ceftriaxone	422 (74.9)
IV Augmentin	50 (8.8)
IV flagyl	12 (2.13)
IV cefuroxime	10 (1.7)
IV ampiclox	38 (6.7)
Analgesics	
IM paracetamol	508 (90.2)
Syrup paracetamol	23 (4.0)
IM diclofenac	14 (2.4)
IM diclofenac + IM paracetamol	18 (3.2)
Infusions	
No infusions	93 (16.51)
Dextrose saline	369 (65.54)
Dextrose water	81 (14.38)
Ringer lactate	20 (3.55)
Blood Transfusion	
Yes	379 (67.3)
No	184 (32.7)

Patients' pill burden and generically prescribed drugs

About 75% of the patients were prescribed at least 4 medications and above concurrently, with less than half (46.5%) being generic drugs. The assessment of each patient prescription showed that 71.4% had one or more drugs written in branded form while only 28.6% were written in generic form.

Assessment of medical doctors' and hospital pharmacists' awareness of treatment guideline for severe malaria

Table 4 contains results of doctors' awareness of treatment guideline for severe malaria, the majority of the doctors (78.8%) reported that their facilities have a recommended guideline for treatment of severe malaria. About 73% of the doctors correctly stated that IV/IM artesunate was the first line treatment for severe malaria. Nevertheless, majority of them (60.6%) erroneously thought that IV quinine was the second line treatment for severe malaria instead of IM artemether. Surprisingly, approximately 79% agreed that they rarely use laboratory findings in the diagnosis of severe malaria and rely almost always on clinical presentations. Greater than two-thirds of the pharmacists (70.6%) were not aware of the recommended first and second line treatment of severe malaria. Most pharmacists (82.4%) do not know if their facility had a drug formulary or not and if they adhere to the National Malaria Treatment Guideline **(Table 5)**.

Table 4 Assessment of medical doctors' awareness of treatment guideline for severe malaria.

S. No	Questions	Responses	Frequency (%)
1	Does your hospital possess any recommended guideline for treatment of severe malaria?	No	7 (21.2)
		Yes	**26 (78.8)**
2	What is the first line treatment guideline for severe malaria?	IV/IM Artesunate	**24 (72.7)**
		IM artemether	3 (9.1)
		IV quinine	4 (12.1)
		ACT	2 (6.1)
4	Is the prescribed dose according to guideline?	No	5 (15.2)
		Yes	**28 (84.8)**
5	What is the second line treatment guideline for severe malaria?	IV artesunate	**5 (15.2)**
		IM artemether	2 (6.1)
		IV quinine	**20 (60.6)**
		ACT	6 (18.2)
6	What supportive medication(s) is/are used for severe malaria?	Analgesics	3 (9.1)
		Hematinics	4 (12.1)
		Antibiotics	7 (21.2)
		*	3 (9.1)
		**	5 (15.2)
		***	**11 (33.3)**
7	How often is laboratory findings used in diagnosis?	Rarely	**26 (78.8)**
		Always	7 (21.2)
8	How often is/are clinical finding(s) used?	Rarely	7 (21.2)
		Always	**26 (78.8)**

*- Vitamin C + Multivitamins + Analgesics
**- Analgesics + Hematinic + Antibiotics
***- Multivitamins + Analgesics + Hematinic + Antibiotics

Table 5 Assessment of hospital Pharmacists' awareness of treatment guideline for severe malaria.

S. No	Questions	Responses	Frequency (%)
1	What is the first line treatment of severe malaria according to the guideline?	Not aware	12 (70.6)
		IV/IM artesunate + oral ACT	3 (17.6)
		IM artemether + oral ACT	1 (5.9)

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		IV quinine + oral ACT	1 (5.9)
2	What is the second line treatment of severe malaria according to the guideline?	Not aware	12 (70.6)
		IV/IM artesunate + oral ACT	1 (5.9)
		IM artemether + oral ACT	1 (5.9)
		IV quinine + oral ACT	3 (17.6)
3	What is the third line treatment of severe malaria according to the guideline?	Not aware	16 (94.1)
		IM artemether + oral ACT	1 (5.9)
4	Does your hospital possess a formulary?	No	14 (82.4)
		Yes	3 (17.6)
5	Does your hospital follow the National Antimalarial Treatment Guideline?	No answer	14 (82.4)
		No	3 (17.6)
6	What is the most prescribed antimalarial drug for the treatment of severe malaria in the hospital?	No answer	1 (5.9)
		IV/IM artesunate	8 (47.1)
		IM artemether	2 (11.8)
		IV quinine	3 (17.6)
		α-βarteether injection	3 (17.6)
7	What is/are the most available antimalarial in your hospital?	Artemether-lumefantrine tab	4 (23.5)
		Artesunate injection	2 (11.8)
		*	3 (17.6)
		**	2 (11.8)
		***	6 (35.3)

*- Quinine Inj + Artemether-Lumefantrine Tab + Artesunate Inj
** - Artemetherinj + *
*** - A-Barteetherinj + Artesunate-Mefloquine Tab + **

Association of anti-malarials prescribed and patients' demographics data

The inferential analysis done showed the age of the patient (p-value=0.004) and site of study (p-value=0.0001) were significantly associated with the initial anti-malarial medication prescribed for patients with severe malaria. Majority of the patients of all ages received IV artesunate followed by IM artemether. There was no significant association between patients' demographic characteristics and follow up anti-malarial drugs prescribed **(Table 6)**.

Table 6 Association of anti-malarials prescribed and patient's demographics data.

Variables	Initial antimalarial					Follow-up antimalarial			
	IV ATS (%)	IM ATS (%)	IM ATM (%)	Total (%)	p value	ATM-LFT (%)	ATS-AMO (%)	Total (%)	p value
Age									
≤ 5 years	33	6.7	8.7	48.5		35.5	13	48.5	
6-18 years	14.9	1.8	2.3	19		15.3	3.7	19	
19-30 years	9.1	1.8	0.5	11.4	**0.004***	8.7	2.7	11.4	0.119
31-59 years	6.6	2.1	2.1	10.8		7.6	3.2	10.8	
≥60 years	4.1	1.4	2.1	7.6		4.4	3.2	7.6	
Gender									

Male	32.9	7.6	8.5	49	0.239	36.1	13	49	0.932
Female	37.5	6.2	7.3	51		37.7	13.3	51	
Site of study									
Bishop Shanahan hospital Nsukka	70.3	0	0	70.3	**0.000***	52.2	18.1	70.3	0.66
District hospital Nsukka	0	13.9	15.8	29.7		21.5	8.2	29.7	
Year of study									
2015	17.1	3	4.3	24.3	0.263	19.2	5.2	24.3	0.068
2016	16	3.9	3	22.9		17.1	5.9	22.9	
2017	22	5.2	6.2	33.4		25	8.3	33.4	
2018	15.3	1.8	2.3	19.4		12.4	6.9	19.4	

*Significant at p< 0.05
ATS=Artesunate; ATM=Artemeter; LFT=Lumefantrine; AMO=Amodiaquine

Association of drug of choice and medical doctors ' and pharmacists ' demographic characteristics

Table 7 shows that marital status (p=0.002) was significantly associated with doctors' choice of drug for the treatment of severe malaria. There was no association between drug of choice and pharmacists' demographic characteristics **(Table 8)**. When the association of patients ' age and supportive medications prescribed for management of severe malaria was done, it showed that patients' age was significantly associated with the choice of antibiotics (p-value=0.0001), analgesic (p-value=0.0001), infusion (p-value=0.0001), and blood transfusion (p-value=0.0001) to be prescribed for a patient. The Association between diagnostic method and Doctors' demographic data revealed that there was no significant association found between diagnostic method used and Doctors' demographic characteristics (gender, marital status, age, rank, and years of practice).

Table 7 Association of drug of choice and medical doctor's demographic characteristics.

Variables	IV/IM ATS (%)	IM ATM (%)	IV quinine (%)	ACT (%)	Total (%)	p value
Gender						
Male	51.5	6.1	3	6.1	66.7	0.23
Female	21.2	3	9.1	0	33.3	
Marital status						
Single	9.1	3	12.1	0	24.2	0.002*
Married	63.6	6.1	0	6.1	75.8	
Rank						
Medical officer	69.7	9.1	12.1	6.1	97	0.943
Consultant	3	0	0	0	3	
Age						
20-30 years	15.2	3	3	0	21.2	0.763
31-40 years	42.4	6.1	9.1	3	60.6	
41-50 years	15.2	0	0	3	18.2	
Year of practice						
1-10 years	51.5	6.1	12.1	6.1	75.8	0.499
11-20 years	21.2	3	0	0	24.2	

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*Significant at p <0.05
ATS – Artesunate; ATM - Artemether

Table 8 Association between drug of choice and pharmacists' demographic characteristics.

Variables	IV/IM ATS (%)	IM ATM (%)	Ivquinine (%)	ACT (%)	Total (%)	p value
Gender						
Male	11.8	17.6	5.9	5.9	41.2	0.951
Female	17.6	17.6	11.8	11.8	58.8	
Marital status						
Single	11.8	17.6	5.9	5.9	41.2	0.951
Married	17.6	17.6	11.8	11.8	58.8	
Rank						
Pharmacist	17.6	17.6	17.6	11.8	64.7	0.741
Senior. Pharmacist	11.8	5.9	0	5.9	23.5	
Ass. chief pharmacist	0	5.9	0	0	5.9	
Chief pharmacist	0	5.9	0	0	5.9	
Age						
20-30 years	11.8	5.9	11.8	11.8	41.2	0.243
31-40 years	17.6	11.8	5.9	5.9	41.2	
41-50 years	0	17.6	0	0	17.6	
Year of practice						
1-10 years	17.6	23.5	17.6	17.6	76.5	0.499
11-20 years	11.8	11.8	0	0	23.5	
*Significant at p < 0.05						

Discussion

The present study aimed to evaluate the drug utilization pattern in the treatment of severe malaria between 2016-2019 in two secondary hospitals in Nsukka, Enugu State. The study also assessed the conformity of practitioners to the new malaria treatment guideline and explored patients' demographic variables associated with prescriber's choice of drug. The key findings revealed that parenteral artesunate was the most frequently prescribed anti-malarial drug for the initial treatment of severe malaria. The artemisinin-combination therapy [artemether-lumefantrine (AL) or artesunate-amodiaquine (AAQ)] was prescribed as follow-up treatment for all patients treated of severe malaria. None of the patient received parenteral quinine. The initial choice of antimalarial was associated with patients' age and the specific facility. Nevertheless, more than two third of the doctors and less than one third of pharmacists assessed were aware of the new malaria treatment guideline.

About half the proportions of the patients were females and aged 5 years or less. This supports the claim that children below five years are more vulnerable to malarial attack than other older age range (WHO, 2015). The majority of the medical folders with patients diagnosed of severe malaria were obtained from the Faith-based hospital, Bishop Shanahan hospital, while one third of them were from the government facility. This observation suggests that the community have more confident that they will receive prompt and better medical services from faith-based hospital than in public/ government hospital, since severe malaria is a medical emergency that needs urgent attention it justifies the choice of the hospital by the community.

The findings of the current study fully comply with the stipulated protocol for the treatment of severe malaria in Nigeria. All the patients assessed in these facilities received either parenteral artesunate or intramuscular artemether as initial treatment of severe malaria and a full course of ACT in compliance to the standard treatment guidelines. These findings are similar to those previously reported in other African countries. For instance, a cohort study among 1,191 patients with severe malaria conducted in 8 public health facilities in Ghana and Uganda showed that 93 percent of the patients received initial treatment with artesunate, while 32.5% received follow-up oral ACT [22]. However, this present report differs from the report from Swaziland after adopting

AS injection over quinine for treatment of severe malaria. A study by Dlamini et al. revealed that 11%, 44% and 45% of the patients diagnosed of severe malaria between 2011-2015 received artemether lumefantrine (AL), quinine injection and AL plus quinine respectively [23]. The superior compliance to standard treatment guideline reported in the present study could be because of improved availability, affordability and access to the recommended parenteral AS in most health facilities in Nigeria.

More than two-thirds of the patients were concomitantly given intravenous ceftriaxone in the course of management of severe malaria. Ceftriaxone is a second-generation cephalosporin; hence its use is recommended mostly when other antibiotic must have proved ineffective to avoid exposure to resistance development. The use of ceftriaxone in the management of severe malaria in the study site may not be in accordance with the practice of good antibiotic stewardship. However, the use may be necessitated by the fact that some patients may have been on other antibiotic during self medication or even from a referral hospital. Another factor could be the need to arrest a particular life-threatening presentation by the patient arising from severe bacterial infection.

In terms of analgesic use, expectedly, almost all the patients received paracetamol for pain relief. More than half of them were placed on the intramuscular preparation which made it the most commonly prescribed dosage form. It was also observed that supportive medication like intravenous fluids was also common with majority of the patients receiving intravenous dextrose saline. Very few patients were transfused with blood indicating that severe malaria induced anemia was not very common in the study population. Patients' pill burden and practice of generic prescription were also evaluated from the medical folders. Findings revealed that more than two third of the patients were prescribed at least 4-5 medications concurrently, while more than half were not prescribed by their generic names. The pill burden is within acceptable limit but the prescribers did not conform to the generic prescription guideline.

An assessment of the association between anti-malarials prescribed and patients' demographic characteristics revealed that the initial choice of antimalarial for management of severe malaria was significantly associated with patients' age ($p=0.004$) and the facility ($p=0.000$). Intravenous artesunate was the preferred choice of initial therapy in patients across all ages except patients aged 19 to 30 years where intramuscular artemether was preferred. The type of anti-malarial stock often varies from one facility to another. A study has shown that patients, drug company representatives, and practitioners' experience influence hospital stocks of anti-malarials [24]. In this study, Bishop Shanahan hospital, a faith-based facility prescribed mainly intravenous artesunate, while district hospital, a government-owned facility preferred intramuscular artesunate or artemether to other available options. This disparity in practice seen could be the result of a difference in update training, drug availability, and awareness of the new malaria treatment guidelines among practitioners in the two facilities. For the follow up treatment, artemether-lumefantrine and artesunate-amodiaquine were used. There was no association between patients' demographic characteristics and follow up anti-malarial drugs prescribed.

A higher proportion of doctors compared to pharmacists were aware of the new malaria treatment guideline in Nigeria. This finding was somewhat different from the outcome of a related study in Malawi. In the Malawian study, more than 96 percent of the healthcare practitioners (doctors, nurses, and pharmacists) were aware of the treatment guideline for severe malaria [25]. However, in the current study, the doctors may have fared better in this regard considering that they are the primary point of call for all patients that visit the hospital. They are directly involved in patients' diagnosis and prescription of medications for the treatment of various disease states including malaria. However, pharmacists as custodians of drugs should be guided by the prescribed National treatment guidelines in determining drugs to be recommended for inclusion to the hospital formulary and the ones to be stocked in pharmacy. Therefore, the findings of this study emphasized the need for training of healthcare practitioners especially hospital pharmacists and overall public awareness campaign centered on malaria treatment protocols as approved by the country's health policy makers, in tandem with international best practices.

The implication of this study is that the recommendation of artesunate use as first-line drug in the treatment in the treatment of severe malaria is being upheld by the physicians practicing in secondary hospitals in the study area. This adherence/compliance will result in good therapeutic outcome in the management of severe malaria in this area with a reduction in its complication and mortality rate.

This study has some inherent limitations which were taken into consideration during analysis and interpretation of results. First, the study sampled few hospitals (two) which may not be the exact representation of what is obtained in other facilities. Secondly, the study did not make adjustment for the periods of observation of industrial action by the District Hospital Nsukka; these periods may be responsible for false low prevalence of severe malaria recorded in this study.

Conclusion

Parenteral artesunate was mostly preferred and prescribed anti-malarial medication for patients diagnosed of severe malaria in the study facilities. All patients received parenteral artesunate or artemether (as alternative to artesunate) as first line treatment followed by a complete 3-days course of ACT and none received quinine. The doctors in these facilities are compliant with the standard treatment guideline with regard to the use of artesunate in the treatment of severe malaria. With respect to the treatment guidelines, medical doctors were more informed than the Pharmacists; thus, Pharmacists are encouraged to be more concerned in treatment guidelines and policy by attending conferences, workshops and continuing education trainings that will keep them abreast of current issues.

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Conflicts of Interest

Authors declare that there are no competing interests among them in this study

References

1. White NJ, Pukrittayakamee S, Hien TT, Faiz MA, Mokuolu OA (2014) Malaria. Lancet 383:723-735.
2. Federal Ministry of Health (FMOH, 2015). http://www.severemalaria.org/site/mmvsmo/files/content. Accessed May 31, 2019.
3. Edelu BO, Ndu IK, Igbokwe OO, Iloh ON (2018) Severe falciparum malaria in children in Enugu, South East Nigeria. Niger J Clin Pract 21:1349-1355.
4. Adesoro O, Shumba C, Kpamor J, Achan J, Kivumbi H et al, (2016) Health worker perspectives on the possible use of intramuscular artesunate for the treatment of severe malaria at lower-level health facilities in settings with poor access to referral facilities in Nigeria: A qualitative study. BMC Health Serv Res 16:566-576.
5. Qigui L, Peter W (2010) Artesunate: The Best Drug in the Treatment of Severe and Complicated Malaria. Pharmaceuticals 3:2322-2332.
6. The Artemether Quinine Meta-analysis Study Group (2001) A meta-analysis using individual patient data of trials comparing artemether with quinine in the treatment of severe falciparum malaria. Trans R Soc Trop Med Hyg 95:637-650.
7. Barennes H, Kailou D, Pussard E, Munjakazi JM (2001) Intrarectal administration of quinine: an early treatment for severe malaria in children? Sante 11:145-153.
8. Woodrow CJ, Haynes RK, Krishna S (2005) Artemisinins. J Postgrad Med 81:71-78.
9. Jones KL, Donegan S, Lalloo DG (2007) Artesunate versus quinine for treating severe malaria. Cochrane Database Syst Rev 17: CD005967.
10. WHO (2011) Guidelines for treatment of malaria. (2nd edn). Geneva.
11. Li Q, Milhous WK, Weina P (2007) Artemisinins in Malaria Therapy, (1st edn), Nova Science Publishers Inc: New York, NY, USA.
12. Pasvol G (2006) The treatment of complicated and severe malaria. British Med Bulle 75: 29-47.
13. Dondorp AM, Nosten F, Stepniewska K, Day N, White N (2005) Artesunate versus quinine for treatment of severe malaria: A randomised trial. Lancet 366:717-725.
14. Dondorp A, Fanello C, Hendriksen I, Gomes E, Seni A, et al. (2010) Artesunate versus quinine in the treatment of severe falciparum malaria in African children (AQUAMAT): An open-label, randomised trial. Lancet 376:1647-1657.
15. WHO (2013) Management of severe malaria. A practical handbook. Geneva: World Health Organization.
16. Maka DE, Chiabi A, Obadeyi B, Mah E, Nguefack S, et al. (2016) Economic evaluation of artesunate and three quinine regimens in the treatment of severe malaria in children at the Ebolowa Regional Hospital-Cameroon: A cost analysis. Malaria J 15(1): 1-15.
17. Byakika KP, Nyakato P, Lamorde M (2018) Assessment of parasite clearance following treatment of severe malaria with intravenous artesunate in Ugandan children enrolled in a randomized controlled clinical trial. Malaria J 17(1): 400.
18. Kamuhabwa AAR, Kisoma S (2015) Factors Influencing Prescribing Practices of Medical Practitioners in Public and Private Health Facilities in Dar-es-Salaam. Tanzania 14:2107-2113.
19. Schumock GT, Walton SM, Park HY, Nutescu EA, Blackburn JC, et al. (2004) Factors that influence prescribing decisions. Ann Pharmacother 38: 557-556.
20. Davies NM, Gunnell D, Thomas KH, Metcalfe C, Windmeijer F, et al. (2013) Physicians prescribing preferences were a potential instrument for patients' actual prescriptions of antidepressants. J Clini Epidemio 66(12):1386-1396.
21. WHO (2015) Guidelines for the treatment of malaria, 2015. Guidelines For The Treatment of Malaria: 71-88.
22. Ampadu HH, Asante KP, Bosomprah S, Akakpo S, Hugo P (2019) Prescribing patterns and compliance with World Health Organization recommendations for the management of severe malaria: A modified cohort event monitoring study in public health facilities in Ghana and Uganda. Malaria J 18(1).
23. Dlamini SV, Kosgei R J, Mkhonta N, Zulu Z, Makadzange K, et al. (2018) Case management of malaria in Swaziland, 2011–2015: on track for elimination? Public Health Action 8(1):S3-S7.
24. Mangham JL, Hanson K, Mbacham W, Onwujekwe O, Wiseman V (2014) What determines providers stated preference for the treatment of uncomplicated malaria? Soc Sci Med 104:98-106.
25. Kalilani PLV, Lungu D, Coghlan R (2011) Knowledge and malaria treatment practices using artemisinin combination therapy (ACT) in Malawi: Survey of health professionals. Malaria. J. 10.