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Antimalarial Prescription Pattern in Pregnant Women in Multicenter in Jos, Nigeria.

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Abstract:-Malaria in pregnancy is a huge burden and the World Health Organization (WHO) has recommended the use of *artemisinin*-combination therapy in its treatment. This study aim to assess the prescription pattern of antimalarial among pregnant women in Jos. Method: The study was conducted at the antenatal clinic of Jos University Teaching Hospital, Bingham University Teaching Hospital and Plateau State Specialist hospital, all in Jos. The study was a descriptive prospective design from 2018 to 2019. All pregnant women who visited the antenatal clinic and were prescribed antimalarial were included in the study. Sample size was 392 and participants were selected using a systemic random sampling method. There were two groups: One being the women who were treated for malaria and the other group was those who had no malaria and used only *sulphadoxine-pyrimethamine* for prophylaxis during this current pregnancy. The data was analyzed as descriptive statistics using Statistical Package for Social Sciences version 23.Results: The antimalarial prescription pattern in pregnancy was assessed and majority of the participants (44.1%) were between 20-29 years (modal age). Most of the participants (24.7%) had tertiary education and (99.2%) were married, 44.1% were Primigravidae while 55.9% were Multigravidae. Our study revealed that *artemether-lumefantrine* (AL) combination was mostly used (55.9%) for the treatment of malaria in pregnancy.Conclusion: An evaluation of the antimalarial drug prescription pattern will promote the availability of the needed medicines for the prophylaxis and treatment of malaria in pregnancy and ultimately enhance rational use and safety of these medicines.

Keywords:- *Antimalarial, Artemether-lumefantrine, prescription pattern, Nigeria.*

I. INTRODUCTION

Malaria is an acute disease caused by species of protozoal genus Plasmodium. The species of Plasmodium include; *P. falciparium, P. vivas, P. malariae, P.ovale*and *P. Knowlesi*. Malaria has been a menace to the human race since ancient times, although man's understanding of the disease has increased, the disease is yet to be eradicated. It is a major global health burden causing high mortality and morbidity in the developing world with an incidence rate of about 247 million per year and just under a million deaths annually; Children living in Africa account for a large proportion of this burden[1]. The World Malaria Report for 2016 showed that malaria continues to be a major public health problem in 97 countries and territories in the tropics and subtropics; approximately 214 million cases of malaria said to be occurring annually and 3.2 billion people are at risk of infection. An estimated 438,000 deaths were attributed to malaria in 2015, the report showed that sub-Saharan Africa accounted for 90% of all malaria deaths[2]. According to the latest report by WHO (2021), there were estimated 229 million cases and 409 000 deaths globally in 2019. Malaria is both preventable and treatable with the global priority being to reduce the disease burden and death in addition to retaining the long-term vision of the eradication of malaria[3]. The number of malaria cases and deaths in this report is more than what was reported in 2016, this calls for more action aimed at prevention and early diagnosis and treatment of malaria so as to reduce malaria burden worldwide.

Some population groups are at a high risk of contracting malaria and developing severe disease, these include; pregnant women, infants, children under five years of age, mobile population, travelers, patients with HIV and AIDS, non-immune migrants, and other immune-

compromised individuals have the highest morbidity and mortality[2].

Malaria in pregnancy is a major, preventable cause of maternal morbidity and poor birth outcomes. Malaria infection during pregnancy can lead to miscarriage, premature delivery, congenital malaria infection and perinatal death amongst others. Treatment with *artemisinin*-based combination therapies (ACTs) and intermittent preventive treatment (IPTp) using *Sulphadoxine-pyrimethamine* have been recommended[3]. Recently, an alternative strategy consisting of intermittent screening and treatment in pregnancy (ISTp) using Rapid Diagnostic Tests (RDT) and treatment with ACT during antenatal care visits have been reported to enjoy better user uptake than the IPTp[4].

This study aim to assess the prescription pattern of antimalarial among pregnant women in Jos, with specific objectives being to determine the type of anti-malarial prescribed, to determine the gestational age of use and to assess the level of compliance with national policy on malarial control as well as the conformity to WHO guidelines on malarial treatment in pregnancy.

II. METHOD

The study was conducted at the antenatal clinic of Jos University Teaching Hospital, Bingham University Teaching Hospital and Plateau State Specialist hospital, all in Jos. The study was a descriptive prospective design from 2018 to 2019.

Inclusion/exclusion criteria: All pregnant women on visit to the antenatal clinic who were prescribed antimalarial according the drug choice of the physician were included in the study, but excluded if they had co-mobidities like typhoid fever. Sample size was 392 calculated using OpenEpi Version 3 with a 20% attrition and participants were selected using a systematic random sampling method by dividing the population size by the proposed sample size and obtaining a set sampling interval. There were two groups: One being the women who were treated for malaria and the other group was those who had no malaria and used only SP for IPT prophylaxis during this current pregnancy. All the women received folic acid tablet 5mg and fersolate 200mg daily as haematinics throughout the study.

Data collection: Some information were extracted from the patient medical case notes and antenatal cards such as: demographic data- age, gravidity,antimalarial drug prescribed, trimester of the pregnancy; reason for the prescription - prophylaxis, or treatment (based on clinical symptoms and/or laboratory investigations). These information was entered into the data collection form and stored in Microsoft excels spreadsheet.

Data analysis: The data was analyzed using Statistical Package for Social Sciences version 23. The descriptive statistics of Mean Age, Occupation, Trimester, Diagnostic Approach,Name of Antimalarial drugs, Distribution of Antimalarial drugs by Trimester, the distribution of Antimalarial drugs by Goal of Therapy (prophylactic or treatment). Ethical Consideration: Approval was obtained from the ethical committees of the three study sites, informed consent was obtained from participants and data was anonimyzed.

III. RESULTS

A total of 392 pregnant women were recruited from one secondary and two tertiary health facilities within Jos metropolis. These include Jos University Teaching Hospital with the most number of participants (71.9%), This was followed by Plateau State Specialist Hospital (19.1%) and then the least was from Bingham University Teaching Hospital (8.9%) respectively (table 1).

Table1: Participants' recruitment by facility

Facility	F	%
Jos University Teaching Hospital (JUTH)	282	71.9
Plateau State Specialist Hospital (PSSH)	75	19.1
Bingham University Teaching Hospital (BUTH)	35	8.9
Total	392	100.0

➢ *Demographic Characteristics of Participants*

Ages of participants range from 17 – 48 years with overall mean age of 29.3±5.7 years. Majority of the participants (44.1%) were between 20-29 years (modal age) with only few (2.0%) as teenagers. Most of the participants (24.7%) had tertiary education with few (3.1%) having no formal education. On marital status, majority of the participants (99.2%) were married and only 0.8% were single. Parity was grouped into Primigravidae and Multigravidae, indicating that 173 participants representing 44.1% were Primigravidae while 219 representing 55.9% were Multigravidae respectively. On Alcohol intake, 3 participants representing 0.8% takes alcohol. On the other hand only 1(0.3%) smokes cigarette on average of 1 stick per day as shown in table 2.

Table 2: Demographic characteristics of participants (n = 392)

Variables	F	%	Mean±Std.Dev
Age group (years) <20	8	2.0	29.3±5.7
20-29	173	44.1	
30-39	148	37.8	
40-49	9	2.3	
Not known	54	13.8	
Education			
No formal education	12	3.1	
Primary	25	6.4	

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Secondary	97	24.7	
Tertiary	145	37.0	
Not known	113	28.8	
Marital status			
Not known	66	16.8	
Married	325	82.9	
Alcohol intake Yes No	3 320	0.8 81.6	
Not specified **Does the woman smoke**	69	17.6	
Yes 1 No 322		0.3 82.1	
Not specified 69		17.6	
Gravidity			
Primigravidae Multigravidae	173 219	44.1 55.9	

Most of the women were housewives by occupation, next were those that were doing their own businesses, with the least being the nurses and the hairdressers (Fig. 1).

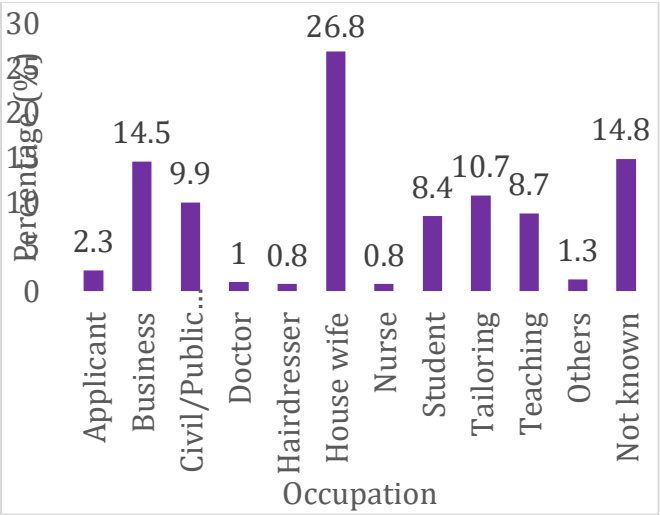

Fig. 1. Occupational distribution

The result showed that 33(8.4%) participants had rapid test diagnosis (RTD), 31(7.9%) had Blood smear while the majority (83.7%) were diagnosed using clinical signs (Fig. 2).

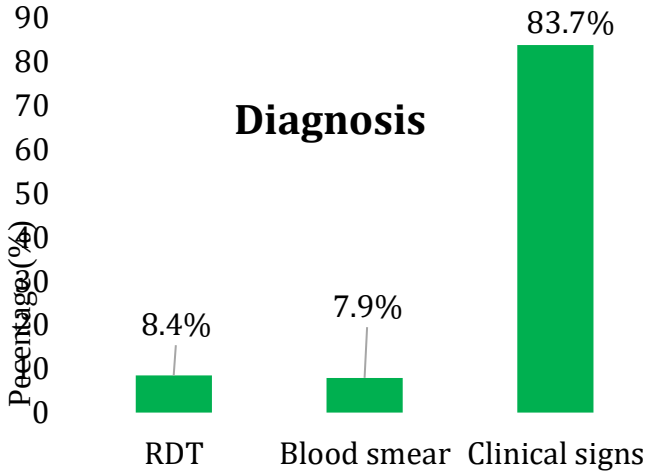

Fig. 2. Method of diagnosis (N = 392)

Of the 392 participants recruited into the study, 51.1% participants took AL alone, 1(0.3%) took AL after the initial treatment with *artesunate*, while 5(1.3%) took Artequick (*dihydroartemisinin& piperaquine)* and AL, Some had artemether injection and then took AL afterwards (2.8). For total AL and SP consumption, 219 (55.9%) used AL in pregnancy apart from routine hematinic while 173(44.1%) used SP (Table 3).

Table 3: Antimalarial prescription pattern

Antimalarial drugs used	**f**	**%**
Artemether/lumefanthrine (AL)	202	51.1
AL and IM *Artesunate*	1	0.3
AL and IM *artemether*	11	2.8
AL and *Artequick® (dihydroartemisinin& piperaquine)*	5	1.3
Sulphadoxine/Pyrimethamine (SP)	173	44.1
Total	392	100.0

Summary of AL and SP prescription pattern

	f	%
AL	219	55.9
SP	173	44.1
Total	392	100.0

Table 4 shows the number of times the pregnant women were exposed to AL during pregnancy. It was discovered that majority (90.0%) were exposed once, while 9.6% and 0.5% were exposed twice and thrice respectively.

Table 4: Number of times exposed to AL during pregnancy (n=219)

Number of times exposed to AL during this pregnancy	F	%
1 (once)	197	90.0
2 (twice)	21	9.6
3 (three times)	1	0.5
Total	219	100.0

The study indicated that 45 participants representing 11.5% experienced severe malaria in pregnancy based on their diagnosis while the rest had uncomplicated malaria (Table 5).

Table 5: Participants' severe malaria in pregnancy status (n = 392)

Experienced severe malaria	F	%
Yes	45	11.5
No	347	88.5
Total	392	100.0

Out of the 165 participants that took AL with records of trimester of use, 8.5%, 34.5% and 57% used it in the 1st, 2nd and 3rd trimester respectively. SP use in 173 participants was 4.4%, 29.2% and 66.4% in the 1st, 2nd and 3rd trimester respectively. In the first trimester, most of the patients (70.0%) took AL while 30% took SP; during the second trimester, 58.8% took AL while 40.2% took SP. Similarly, at the third trimester, 50.8% of the women took AL while 49.2% took SP, but the difference in the intake of the type of antimalarials was not statistically significant (p=0.160), as shown in table 6.

Table 6: Pattern of AL and SP used per Trimester of intake (n=302)

Trimester of use	Antimalarial Drugs used			χ^2	P-value
	AL (n,%)	SP (n,%)	Total (n,%)		
1st Trimester	14(70.0)	6(30.0)	20(100.0)	3.663	0.160
2nd Trimester	57(58.8)	40(41.2)	97(100.0)		
3rd Trimester	94(50.8)	91(49.2)	185(100.0)		
Total	165(54.6)	137(45.4)	302(100.0)		

IV. DISCUSSION

A total of 392 pregnant women were enrolled in this study with the modal age of the participants being 20 - 29 years old. Among the women enrolled, 6.4% had primary, 24.7% had secondary, 37% had tertiary level of education and 3.1% had no formal education. More participants had tertiary education may be because this study was conducted in a place with ready access to many educational facilities. Majority were married women (82.9%). Three (3) of the women, (0.8%) reported intake of alcohol and only one (1) smoke cigarette on the average of one stick per day. Parity: Majority (56%) was multigravidae (Table 2). This study agrees with other studies, which reported that most of their participants were multigravidae[5,6]. This suggests that the women prefer having more than one child in this environment.

In terms of occupation of the women, the housewives were more in number (Fig. 1). Method of diagnosis of malaria was majorly based on clinical signs (Emprical) with 83.7% (Fig. 2), this is similar to the findings in Zambia by Manyando and colleagues [7] in which 82.0% was based on clinical symptoms.

On prescription pattern in table 3, our study revealed that AL was mostly used (55.9%). This is similar to the preliminary study on antimalarial prescription pattern among pregnant women in JUTH, which showed AL use of 59%[8]. A study in Zambia reported that the AL group (87.1%) had received both AL for treatment and SP for IPT prophylaxis[9]. This may be because AL is well tolerated during therapy by pregnant women (with mild adverse events), as reported previously[10].

Majority of the women took AL once (90%) throughout this current pregnancy, while those that took it twice were (9.6%) and the rest took it thrice (Table 4) indicating that most of them had the malaria episode resolved after the AL use and did not need further or repeated treatment. This may be because it contains *artemether* which is fast acting and a long acting *lumefantrine* with a long half-life for elimination and hence good clearance of the malaria parasites, thus making it the preferred first-line ACT in the treatment of malaria in these settings.

There was no complaint of pill burden by any of the participants in this study unlike the report from another study of complaint about the pill burden associated with AL in addition to the fear expressed towards AL being "too strong" to be taken in pregnancy as it may cause miscarriage [11].

For AL (Table 6), 34.5% received the drug in 2nd trimester and 57% in 3rd trimester, which is in line with the WHO/Nigerian national treatment guidelines in pregnancy but a few contrasts with these guidelines, was observed where 8.5% used it in the 1st trimester. A study reported higher use of 33.8% in 1st trimester and 66.2 % in 2nd trimester[5]. Moore and others (2016) also reported 16% exposure to AL in first trimester[6]. Elsewhere, adherence to treatment guidelines for treatment of malaria in pregnancy was reportedly poor as two-thirds of all the treatments (70%) in the first trimester and also about 70% in second and third trimester) were not in line with the guidelines and some (40%) even used the combination of AL along with another antimalarial[12].

According to the WHO, the information on the efficacy, safety and pharmacokinetics of many antimalarial medicines in pregnancy is insufficient especially when used in the first trimester; and because the occurrence of organogenesis is mostly in the first trimester posing a time of greatest concern for possible teratogenicity, even though the nervous system continues to develop throughout pregnancy. Therefore, the World Health Organization has recommended the use of *quinine+ Clindamycin, chloquine* and *proguanil* in the treatment of uncomplicated malaria in pregnancy or the use of ACT as an alternative where the recommended medicines are not available or when they fail[13]. Also, the use of ACT in the first trimester of pregnancy is suggested by WHO when the benefit (for instance to prevent maternal death) outweigh the risk of toxicity to the fetus[14]. Most times, women may not be aware they are pregnant or are unwilling to declare their pregnancy status in the first trimester. This could lead to inadvertent exposure to ACTs, which are the available first-line treatment of malaria in general populations. Consequently, every woman of childbearing age should be asked about the possibility of being pregnant before they are given any antimalarial or any other medicines[7] And when exposed, they should be monitored throughout pregnancy till delivery.

The second group (44.1%) received only SP as IPT prophylaxis (Table 3) during current therapy in accordance to the Nigerian National treatment guideline for the treatment and prevention of malaria in pregnancy[15]. In the SP group (Table 6), 29% of this population received their prophylaxis treatment in 2nd trimester and 66.4% during the 3rd trimester; this is in accordance with the WHO/Nigerian guidelines for prevention of malaria in pregnancy. However 4.4% used SP during the 1st trimester in contrast to the guidelines. One study reported that antimalarial monotherapies of *quinine* and SP were frequently prescribed without consideration to the gestational age of pregnancy, the treatment of pregnant women with fever in line with treatment guideline was poor, and some of the participants prescribed both *quinine* and ACT for malaria prevention in pregnancy, although the majority of them prescribed SP for prophylaxis[16].

These results have implication to safety in pregnancy as this practice of not prescribing according to acceptable treatment guidelines can predispose the pregnant women and their babies to avoidable adverse drug events. Therefore, there is need for advocacy and proper monitoring of adherence to treatment guidelines in the prevention and treatment of malaria in pregnancy.

V. CONCLUSION

The antimalarial prescription pattern in pregnancy was assessed and our study revealed that *artemether-lumefantrine* (AL) combination was mostly used (55.9%) for the treatment of malaria in pregnancy. Majority of the women took AL once (90%) throughout this current pregnancy, while those that took it twice were (9.6%) and the rest took it thrice. *Sulfadoxine-pyrimethamine* was found to be the only drug combination used for prophylaxis. An evaluation of the antimalarial drug prescription pattern will promote proper planning and availability of the needed medicines for the prophylaxis and treatment of malaria in pregnancy and ultimately enhance rational use and safety of these medicines.

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