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Pregnancy Outcome of Women Treated with *Artemether-lumefantrine* for Uncomplicated Malaria in Jos, Nigeria

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Abstract:-
Background: Malaria is a burden to human race. In areas with high malaria transmission, young children and pregnant women are particularly vulnerable to malaria infection and death. The global burden of malaria and that of poverty mirrors each other and malaria is well thought out to be both a cause and consequence of poverty; with fifty eight percent of malaria cases occurring in the poorest 20% of the world's population and those who are least likely to have access to treatment. The World Health Organization recommends the use of Artemisinin-based combinations (ACTs) that includes *artemeter-lumefantrine* for the treatment of malaria in pregnancy, of which safety data is limited, hence the need for their post-market surveillance. The overall aim of this study is to assess the safety profile of *artemeter-lumefantrine* use among pregnant women and their newborn.

Method: This was a Multi-Centre prospective cohort study of antimalarials in pregnant women in their second and third trimester of pregnancy. There were two cohorts of ACT arm and the SP arm and a total sample size of 392.Results:Pregnancy outcome: The study revealed that most of the participants (68.1%) had term deliveries (live birth). But, 11(2.8%) had post term delivery, 2(1.3%) had abortion while 6(1.5%) had miscarriage, 12(3.1%), while 40(10.2%) had Preterm birth. There was no significant association between pregnancy outcomes and antimalarial drugs used. Conclusion:The pregnancy outcome following the use of *artemether-lumefantrine* and that of *sulphadoxine-pyrimethamine* include live birth and stillbirth at term, premature delivery, post term deliveries,miscarriage and longer duration of labour. Abortion occurred only in the AL group and neonatal death only in the SP group. There is need for continuous post-market surveillance of these antimalarials among pregnant women.

Keywords:- *Pregnancy outcome, antimalarial, artemether-lumefantrine, uncomplicated malaria.*

I. INTRODUCTION

Malaria has been a menace to the human race since antiquity. In areas with high malaria transmission, young children and pregnant women are particularly vulnerable to malaria infection and death [1]. The maps of the global burden of malaria and that of poverty is a reflection of each other and malaria is well thought out to be both a cause and consequence of poverty; with fifty eight percent of malaria cases occurring in the poorest 20% of the world's population and those who are least likely to have access to treatment [2-3]. It is reported that six countries - Nigeria, the Democratic Republic of Congo, Burkina Faso, Mozambique, Cote d'Ivoire and Mali - account for 60%, of malaria deaths worldwide in 2010 [2].

Summary of complications of malaria in pregnancy are miscarriage, premature delivery and intrauterine growth retardation. Others are Intrauterine death, Stillbirth, and Low birth weight. Again, fetal or perinatal death, and Maternalanaemia can occur [4-5]. Complications of post term pregnancy or prolonged gestation include fetal macrosoma, placental insufficiency, meconium aspiration[6].

Among the ACTs recommended by the World Health Organization for the treatment of malaria in pregnancy include*Artemether-Lumefantrine*[7].*Lumefantrine*is of the aryl-amino alcohol class of antimalarial drugs, itis active against all human forms of malaria including resistant strains of *P.falciparum*[7].*Lumefantrine*with long half-life provides a longer period of suppressive post-treatment prophylaxis against relapses and new infections [1]. An advantage of this ACT is that *lumefantrine* is not available as a monotherapy and has never been used alone for the treatment of malaria and the absorption of *lumefantrine* is enhanced by co- administration with fat [1].

Pregnant women are usually excluded from initial clinical trials of medicines, which will include the pregnant women, who may now need such medicines for treatment, prophylaxis or diagnosis of diseases [8-9]. Adverse drug reactions documented for this combination in adults include

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headache, anorexia, dizziness, asthenia, arthralgia, myalgia, and skin rash as a delayed reaction[11-12].

To our knowledge, there is paucity of safety data on the usage of *artemisisin*-combination therapies in pregnancy and this has been collaborated by some researchers who have used different study designs [13-19]. The compulsory non-inclusion of pregnant women in clinical trials generally, and that of the pioneering studies of *artemisinins* and *artemisinin*-combination therapies in particular may have accounted to the current limited data on their safety in pregnancy. Even the available limited data on safety have little record of the impact of *artemether-lumefantrine* on gestational age at delivery and duration of labour.

There are documentations of embrayo lethality and development abnormalities in animal studies [20-21], and on pregnant mice exposed to *artemether-lumefantrine* reported prolongation of the gestation period and a reduction in uterine contractions during labour[22]. Risk of maternal and pregnancy complications as well as in the new born increases from 39 weeks gestation, and are more in the "late term" pregnancy of 40-42 weeks gestation [23-24]. Impending post term pregnancy occurrence happens when pregnancy is > 40 weeks gestation [25]. Therefore prolonged gestation beyond 40 weeks should be prevented where possible if medicines are found to cause this.

Thus, studying the impact of *artemether-lumefantrine* on gestation age at delivery using a cohort observational study design is apt; and possible subsequent recommendation(s) based on the knowledge gained from the study may be helpful in our environment and globally in other settings. Countries in Sub-Saharan Africa (including Nigeria), Asia and South America have changed to *artemisinin*therapy as first and second line treatment for malaria, thus there is a great need for post-marketing surveillance or pharmacovigilance to ascertain the safety of these drugs in pregnant women who may be exposed to malaria treatment with *artemether-lumefantrine*combination. Pregnancy outcome documentation obtained from meticulous follow up of all pregnant women treated with *artemisinin*compounds as well as subsequent development in their new born is encouraged.

Most safety data on antimalarials in pregnancy come from spontaneous or passive reporting of adverse events. Many developing countries have adopted post-market safety systems that rely exclusively on passive surveillance, but this strategy is said to have failed for malaria due, in part, to low level of spontaneous or passive reporting of adverse drug reactions (ADRs) to ACTs from malaria endemic countries [26]. Therefore, there is great need for active pharmacovigilance as used in this study, which is preferable when compared to spontaneous reporting. There is lack of Centres and resources for routine pharmacovigilance in many countries in sub-Saharan Africa and where they exist, there is little research or surveillance. The presence of pharmacovigilance Centre and personnel with adequate skills in addition to the practice of active surveillance of adverse drug events in our study site will help in the detection and assessment of the safety of *artemisinin*-combination therapy among pregnant women. The overall aim of the study was to assess the safety profile of *artemether-lumefantrine* among cohort of pregnant women and the specific objective was to identify the pregnancy outcomes.

II. METHOD

The Study design was a Multi-Centre prospective cohort study of antimalarials in pregnant women. The study settings were Jos University Teaching Hospital (JUTH), Plateau State Specialist hospital (PSSH) and Bingham University Teaching Hospital(BUTH), all in Nigeria.Pregnant women in their second or third trimester and their newborn were studied. There were two cohorts: ACT arm and the SP arm.Pregnant women in 2nd and 3rd trimester who consent to participate were included while **w**omen with comorbidities and those who received antimalarials outside study sites were excluded from the study.Sample sizewas calculated with OpenEpi, Version 3, to be 392 with 20% attrition.Statistical analysis: Data was analyzed using Statistical Package for Social Sciences (IBM SPSS Statistics) version 23.0**.** Analytic methods weredescriptive analytic method where frequencies, mean and standard deviation were generated for socio-demographic characteristics of participants and clinical variables where applicableand predictive analytical method to test for any statistical significant relationship using chi-square statistic, fishers exact test and t-test. P-value ≤ 0.05 were considered statistically significant.Ethical approvals were obtained from the three site institutional ethical committee, written informed consent was obtained from the participants and **d**ata was anonymized before analysis (confidentiality).

III. RESULTS

Participants were recruited from Jos University Teaching Hospital (71.9%), Plateau State Specialist Hospital (19.1%) and Bingham University Teaching Hospital (8.9%) (Table 1).

Table 1: Participants' recruitment by facility

Facility	F	%
JUTH	282	71.9
PSSH	75	19.1
BINGHAM	35	8.9
Total	392	100.0

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Fig. 1: Occupational distribution

Ages of participants range from 17 – 48 years with overall mean age of 29.3±5.7 years. Ages were further classified into <20 years, 20-29 years, 30-39 years and 40-49 years. Majority of the participants (44.1%) were between 20-29 years (modal age) with only few (2.0%) as teenagers (Table 4). Most of the participants (24.7%) had tertiary education with few (3.1%) having no formal education. On marital status, the study revealed that majority of the participants (99.2%) was married. Only 0.8% was single and 5(1.3%) women were twins (Table 2)

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

Age group (years)	**F**	**%**	**Mean±Std.Dev**
<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	
Secondary	97	24.7	
Tertiary	145	37.0	
Not known	113	28.8	
Marital status			
Not known	66	16.8	
Married	325	82.9	
Single	1	0.3	

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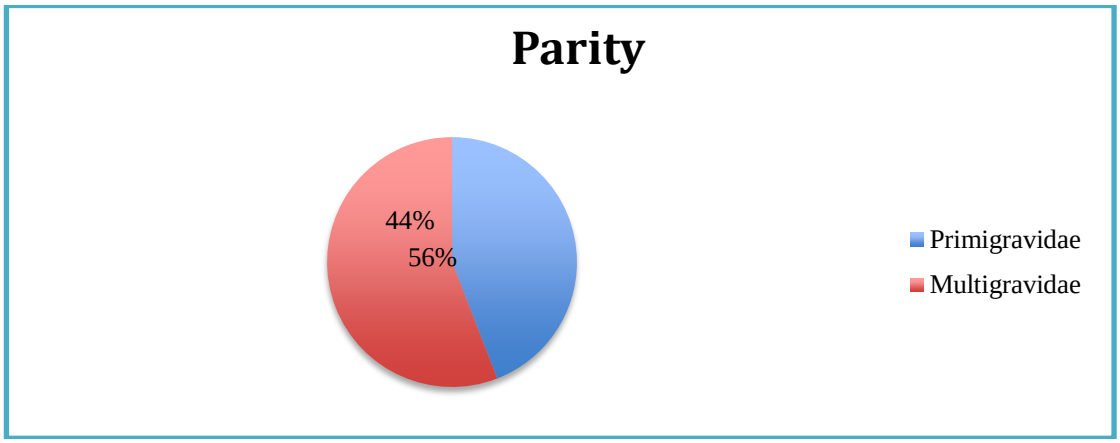

Fig. 2: Parity Overall mean parity was approximately 3±2.

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 (Figure 3).

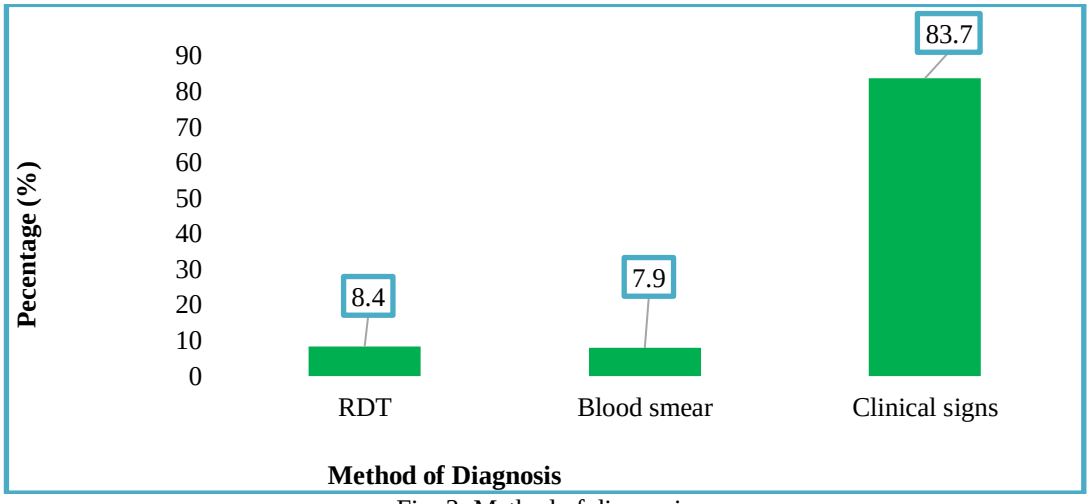

Fig. 3: Method of diagnosis
N = 392

Table 3 shows the number of times participants were exposed to AL during pregnancy. From the results majority (90.0%) were exposed once, while 9.6% and 0.5% were exposed twice and thrice respectively.

Table 3: Number of times exposed to AL during pregnancy

Frequency of exposure 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**

IV. PATTERN OF AL AND SP USED PER TRIMESTER

Out of the participants that took AL, 8.5%, 34.5% and 57% used it in the 1st, 2nd and 3rd trimester respectively while SP use was 4.4%, 29.2% and 66.4% in the 1st, 2nd and 3rd trimester respectively.

Table 4: Pattern of AL and SP used per Trimester of Intake (n=302)

Trimester of use	Antimalarial Drugs used		
	AL	SP	Total
1st Trimester	14(70.0)	6(30.0)	20(100.0)
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)

- **Pregnancy outcome:** The study revealed that most of the participants (68.1%) had term deliveries (live birth). But, 11(2.8%) had post term delivery, 2(1.3%) had abortion while 6(1.5%) had miscarriage, 12(3.1%), while 40(10.2%) had Preterm birth (Table 5). There was no significant association between pregnancy outcomes and antimalarial drugs used (Table 6).

Table 5: Pregnancy outcome (n=392)

Pregnancy outcome	f	%
At term delivery (Live birth)	267	68.1
At term delivery (Still birth)	12	3.1
Post term delivery	11	2.8
Had Abortion	2	0.5
Had miscarriage	6	1.5
Had preterm birth	40	10.2
Not known (Lost to follow up)	54	13.8

Table 6: Type of Antimalarial drugs used and pregnancy outcome

Type of Antimalarial drugs used and pregnancy outcome (n=392)

Pregnancy outcomes	Type of antimalarial drugs used f(%)			p-value
	AL + SP(219)	SP Alone(173)	Total(392)	
Had abortion	2(0.9)	0(0.0)	2(0.5)	0.102[f]
Had miscarriage	5(2.3)	1(0.6)	6(1.5)	
Had preterm birth	15(6.8)	25(14.5)	40(10.2)	
At term delivery (Live birth)	151(68.9)	116(67.1)	267(68.1)	
Post term	7(3.2)	4(2.3)	11(2.8)	
Not known	33(15.1)	21(12.1)	54(13.8)	

f = Fisher's exact test (CI= 0.072-0.132)

Relationship between Types of Antimalarial Used and Delivery Outcomes: Relationship between Antimalarial drugs prescribed and duration of labour revealed that 22 participants have duration of labour greater than 24 hours out of which 54.5% were in the AL group and 45.5% in the SP group. The difference was not statistically significant (χ^2 = 4.221, p=0.377) as seen in table 7.

Table 7: Relationship between Antimalarial Drugs used and Duration of Labour (n=392)

Duration of labour	Antimalarial Drugs used			χ^2	P-value
	AL	SP	Total		
0hrs.	7(87.5)	1(12.5)	8(100.0)	4.221	0.377
<12hrs.	136(54.4)	114(45.6)	250(100.0)		
12-24hrs.	31(53.4)	27(46.6)	58(100.0)		
>24hrs.	12(54.5)	10(45.5)	22(100.0)		

There was no statistical association between Gestational age (weeks) using last menstrual period (LMP) as at the time of intake of drugs and the type of Antimalarial drugs taken (χ^2 = 8.049, p=0.347). There was a week non-significant, but positive correlation between gestational age (weeks) of pregnancy and duration of labour (hour) (r = 0.024, p = 0.690). This implies that the intake of antimalarials as gestational age increases, causes duration of labour to partially increase (Table 8).

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Table 8: Relationship between Duration of Labor and the Gestational Age of Pregnancy at which they took the Antimalarial (n=392)

	Gestational age (wks.) using LMP - Trimester				χ^2	p-value
Duration of labor	**<37 weeks**	**37 - 41weeks**	**>41weeks**	**Total**		
0 hrs.	1(16.7)	4(66.7)	1(16.7)	6(100.0)	8.049	0.347
<12 hrs.	13(5.8)	178(79.1)	34(15.1)	225(100.0)		
12- 24 hrs.	1(2.0)	41(82.0)	8(16.0)	50(100.0)		
> 24 hrs.	4(18.2)	14(63.6)	4(18.2)	22(100.0)		
Not known	56(63.7)	31(34.1)	2(2.2)	89(100.0)		
Correlation						
Duration of labour versus Gestational age	r	p				
	0.024	0.690				

Duration of labour was also not significant with Number of times exposed to Antimalarial drugs (χ^2 = 12.681, p=0.148) as reported in table 9.

Table 9: Relationship between Duration of Labor and the Number of Times they took Antimalarial (n=392)

	Number of times exposed to Antimalarial Drugs				χ^2	p-value
Duration of labor	**1**	**2**	**3**	**Total**		
0 hrs.	7(87.5)	1(12.5)	0(0.0)	8(100.0)	12.681	0.148
<12 hrs.	232(92.8)	17(6.8)	1(0.4)	250(100.0)		
12- 24 hrs.	57(98.3)	1(1.7)	0(0.0)	58(100.)		
> 24 hrs.	20(90.9)	2(9.1)	0(0.0)	22(100.0)		
Not known	54(100.0)	0(0.0)	0(0.0)	54(100.0)		

The study revealed that gestational age at which they took the antimalarial does not affect the mode of delivery (χ^2 = 1.608, p=0.941) as seen in table 12.

Table 12: Relationship between Mode of Delivery and the Gestational Age at which they took the Antimalarial (n=392)

	Mode of delivery						p-value
Gestational age at first intake of drugs using LMP	**Not known**	**SVD**	**C/S**	**SVD (with Episiotomy)**	**Total**	**X^2**	
<37 weeks	0(0.0)	11(64.7)	5(29.4)	1(5.9)	17(100.0)	1.608	0.941
37 - 41weeks	77(25.4)	157(51.8)	47(15.5)	22(7.3)	303(100.0)		
>41weeks	27(37.5)	31(43.1)	9(12.5)	5(6.9)	72(100.0)		

In table 13,Majority of the participants was exposed to Antimalarial drugs once. Out of which more than half (55.7%) had Spontaneous Vagina Delivery (SVD), (20.5%) had Caesarian section (C/S) and (9.4%) had SVD with episiotomy respectively. Out of 39 participants who were exposed to Antimalarial drugs twice, 48.7% had SVD while 2.6% had C/S. This difference was not statistically significant (χ^2 = 11.357, p=0.077).

Table 13: Relationship between Mode of Delivery and the Number of Times they took the Antimalarial (N=392)

	Mode of delivery					χ^2	p-value
Number of times exposed to Antimalarial Drugs	**Not known**	**SVD**	**C/S**	**SVD (with Episiotomy)**	**Total**		
1	51(14.5)	196(55.7)	72(20.5)	33(9.4)	352(100.0)	11.357	0.077
2	19(48.7)	19(48.7)	1(2.6)	0(0.0)	39(100.0)		
3	0(0.0)	1(100.0)	0(0.0)	0(0.0)	1(100.0)		

Most of the participants who took AL (63.5%) had Spontaneous Vaginal Delivery (SVD) and among those who took SP was 53.2%. The difference was statistically significant (χ^2 = 12.120, p = 0.007) and recorded (Table 14).

Tables 14: Relationship between Type of Antimalarial Used and Mode of Delivery (n = 392)

Variable	**Use of Anti-malarial drugs**			χ^2	p-value
Mode of delivery	**AL (n=219)**	**SP (n=173)**	**Total (n=392)**		
SVD	139(63.5)	92(53.2)	231(58.9)	12.120	0.007
Caesarian section (C/S)	37(16.9)	37(21.4)	74(18.9)		
SVD with Episiotomy	10(4.6)	23(13.3)	33(8.4)		
Not known	33(15.1)	21(12.1)	54(13.8)		

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Gestational age at delivery were categorized according to WHO standard into Pre-term (<37 weeks), Term (37-41 weeks) and >41 weeks as Post term [27]. Majority of the participants who took AL (71.7%) had gestational age between 37-41 weeks. Similarly, majority of those who took SP had gestational age between 37-41 weeks (7.05%). Participants who took AL had average gestational age of 38.1±8 weeks while participant who took SP had average gestational age of 38.2±3.3 weeks respectively (Table 15). Overall average gestational age at delivery was 38.1±4.2 weeks. There was no statistical association between antimalarial drug used and gestational age at delivery (p = 0.415).

Tables 15: Relationship between Type of Antimalarial Used and Gestational Age at Delivery (n = 392)

Variables	**Use of Anti-malarial drugs**			**□²**	**p-value**
Gestational age at delivery	**AL (n=219)**	**SP (n=173)**	**Total (n=392)**		
Preterm (28-<37 weeks)	22(10.0)	26(15.0)	48(12.2)	2.850	0.415
Term (37 - 41weeks)	157(71.1)	122(70.5)	279(71.2)		
Post term (>41weeks)	7(3.2)	4(2.3)	11(2.8)		

Majority of the participants (65.9%) had normal delivery at 37-41 weeks gestational age at delivery compared to gestational age <37weeks (52.1%) and >41weeks (63.6%) respectively. This difference was statistically significant (χ^2 = 244.544, p=0.001) meaning there is a statistically significant relationship between the gestational age at delivery and the mode of delivery (Table 16).

Table 16: Relationship between Mode of Delivery and Gestational Age at Delivery (n=392)

	Mode of delivery					**χ^2**	**p-value**
Gestational age at delivery (Weeks)	**Not known**	**SVD**	**C/S**	**SVD With Episiotomy**	**Total**		
< 37	9(18.8)	25(52.1)	11(22.9)	3(6.3)	48(100.0)	244.544	0.001
37-41	7(2.5)	184(65.9)	58(20.8)	30(10.8)	279(100.0)		
> 41	0(0.0)	7(63.6)	4(36.4)	0(0.0)	11(100.0)		
Not known	54(100.0)	0(0.0)	0(0.0)	0(0.0)	54(100.0)		

V. 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%) and in terms of occupation, the housewives were more in number. 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 multigravidea. This study agrees with other studies, which reported that most of their participants were multigravidea[28-29], and the method of diagnosis of malaria was majorly based on clinical signs (Empirical) with 83.7%, this is similar to the findings in Zambia by Manyando et al. [14], in which 82.0% was based on clinical symptoms.

On prescription pattern, our study revealed that AL was mostly used (55.9%). Antimalarial prescription pattern and the adverse drug reactions during therapy among the pregnant women have previously been reported [12, 30].

Pregnancy outcome is known as the final result of fertilization event and the types of pregnancy outcome include live birth (full term or preterm birth), stillbirth, spontaneous abortion and induced abortion[31]. Of the 392 women, abortion of pregnancy (≤12 weeks gestation) occurred in 2 (0.5%) all of which were in the AL group. This is different from the result of another study which showed occurrence of abortion to be AL = 7(1.4%), and 8 (1.6%) in the SP group [4]. Miscarriage: Miscarriage (late abortion occurred after first trimester exposure (13 to ≤28 weeks) was in 6 (1.5%) participants with 5 in the AL group and 1 in the SP group. The risk of miscarriage in the ACT group in another study was not statistically significant when compared with *quinine*, but authors recommended that there was a need for confirmatory studies to rule out a smaller than three-fold increase in risk [32].

Stillbirth at term occurred in 12 and in equal numbers in the two groups (AL =6; SP=6). Unlike in a study where it occurred mostly in their SP group AL = 9, SP = 13 [4], and 1 stillbirth in the SP group[33].Stillbirth in AL group was possibly related to consanguinity (Marriage to a close relation like cousins) in a study [34]. However, none of the stillbirth observed in this current study was associated with consanguinity.

Forty (40, 10.2%) had preterm delivery (SP = 25; AL=15). This is similar to the report from a study where preterm delivery was AL = 71(14.1%), SP = 90 (17.4%) indicating that the rates of premature delivery was more in their SP group[4]. Full term delivery (Live births) was similar in both groups and majority of the women (267, 68.1%) had term live deliveries. This similarity has also been reported elsewhere in which case AL was 395(78.4%) and 377(73.1%) for SP group [4].

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Post term delivery took place in 11 women, in the AL group (7) while 4 was in the SP group. Similarly, Wannang and Odesanya [22], showed a prolongation of the gestation period thereby increasing gestational age at delivery in pregnant Mice exposed to AL. Even though the AL group had malaria in pregnancy, malaria is said not to be a risk for post-datism[6, 23, 25]. The risk of maternal and pregnancy complications and in the newborn increases from 39 weeks gestation [23-24], therefore, post term delivery is not desired so as to prevent complications that may arise. The complications of post term pregnancy or prolonged gestation include fetal macrosoma which was also observed in this study and this may lead to childhood obesity, and metabolic syndrome as they grow, while for the mother: Uterine rupture, genital tract laceration and excessive bleeding after delivery [6].

Unknown (Lost to follow up) pregnancy outcome was in 54 (13.8%); AL = 33; SP =21 participants, this is slightly different from what was observed in another study showing AL = 22 (4.4%), SP = (5.4%) 28 [4]. This may be because addresses and contacts of participants in this study were more traceable, hence reducing loss to follow up than is obtainable in Jos.

The overall early neonatal death (death ≤ 7 days post-delivery) was 2, both occurring in the SP group and none in the AL group. Though this difference was not statistically significant (0.506 ^{f}), it can be considered clinically significant as it involves death and its attendant trauma on the family. Although in 2010, Manyando and colleagues [4] reported that early neonatal death was similar (2.3%) in both their AL and SP groups. A different study showed that the total infant mortality rate was 38 per 1,000 live-born singletons; significantly more infant deaths occurred in the *artesunate*, 6.7% (8/120) than AL 0.9% (1/117) group, p¼0.036 [34]. It is worthy of note that perinatal mortality includes both stillbirth and early neonatal death.

Relationship between Antimalarial drugs used and Duration of Labour: Relationship between antimalarial drugs used and duration of labour revealed that most participants had normal duration of labour (Within 24 hours). Again, most participants who had longer duration of labour (>24 hours) were in the AL group. Likewise, Wannang and Odesanya [22], showed a reduction in acetylcholine-mediated uterine contractions during labour thereby increasing the duration of labour in pregnant Mice exposed to AL.

Relationship between types of antimalarials used and mode of delivery:Most of the participants who took AL (63.5%) had Spontaneous Vaginal Delivery (SVD) without episiotomy and in those who took SP was 53.2%. This difference was statistically significant (p = 0.007), (Table 21). While SVD with episiotomy was in 8.4% of the participants was 33 out of which AL =10, SP = 23.

Gestational age at delivery was categorized according to the reported WHO standard into Pre-term (28 - <37 weeks), Term (37-41 weeks) and (>41 weeks) as Post term [27]. The overall mean gestational age at delivery was 38.1±4.2 weeks. Majority of the participants who took AL (71.7%) had gestational age between 37-41 weeks (average gestational age of 38.1weeks for AL). Majority of those who took SP (70.5%) had gestational age between 37-41 weeks (average gestational age of 38.2±3.3 weeks for SP), and another study reported a mean gestational age at delivery to be: AL = 39.0 weeks, SP = 38.9 weeks and this is comparable [4].

Further breakdown of the type of antimalarial used in pregnancy and the gestational age at delivery revealed that for <28 weeks, AL = 7(3.2), SP = 1(0.6%); 28 to <37 weeks was AL = 7(3.2%), SP = 11(6.4%); 37 to 41 weeks was AL = 157(71.1%), SP = 122(70.5%); >41 weeks was AL= 7(3.2%), SP = 4(2.3%). While the unknown were AL = 33(15.1%) and SP = 21(12.1%). This was also similar to the account from another study which showed that ≤28 weeks AL = 5(1.1%), SP = 2(0.4%); >28 to <37 weeks AL = 58(12.4%), SP = 85(18.2%); >37 weeks AL = 385(82.6%), SP = 358(76.7%); AL = 18(3.9%), SP = 22(4.7%) were unknown [4].

The overall early neonatal death (death ≤ 7 days post-delivery) was 2, both occurring in the SP group and none in the AL group. Though this difference was not statistically significant (0.506 ^{f}), it can be considered clinically significant as it involves death and its attendant trauma on the family. Although in 2010, Manyando and colleagues [4], reported that early neonatal death was similar (2.3%) in both their AL and SP groups. A different study showed that the total infant mortality rate was 38 per 1,000 live-born singletons; significantly more infant deaths occurred in the *artesunate*, 6.7% (8/120) than AL 0.9% (1/117) group, p¼0.036 [34]. It is worthy of note that perinatal mortality includes both stillbirth and early neonatal death.

VI. CONCLUSION

The pregnancy outcome following the use of *artemether-lumefantrine* and that of *sulphadoxine-pyrimethamine* include live birth, still birth at term, premature deliverypost term deliveries, miscarriage and longer duration of labour. Abortion occurred only in the AL group and neonatal death only in the SP group. There is need for more surveillance in the use of these antimalarials among pregnant women.

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