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Maternal and Fetal Outcomes of Monthly Ante-Natal Intermittent Preventive Treatment with Sulphadoxine-Pyrimethamine in Ibadan

Olaolu Olayinka Oni[1, *], Oladapo Olayemi[2], Oluwasomidoyin Bello[2], Olubukola Adesina[2]

[1]Department of Obstetrics and Gynaecology, University College Hospital, Ibadan, Nigeria

[2]Department of Obstetrics and Gynaecology, College of Medicine, University of Ibadan, Ibadan, Nigeria

Email address:

olaoluoni43@yahoo.com (Olaolu Olayinka Oni), oladapo.olayemi@yahoo.com (Oladapo Olayemi), bellodoyin@yahoo.com (Oluwasomidoyin Bello), bukiadewole@yahoo.com (Olubukola Adesina)

[*]Corresponding author

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Abstract: Malaria in pregnancy is associated with many complications therefore the World Health Organization (WHO) in 2012 recommended monthly use of intermittent preventive therapy with sulphadoxine-pyrimethamine (IPTp-SP) to reduce the menace of this disease in malaria endemic region. This study assessed the fetomaternal outcomes of monthly doses of sulphadoxine-pyrimethamine as intermittent preventive treatment (IPTp-SP) in Ibadan. This study was a prospective cohort study. The fetomaternal outcomes of 200 consenting pregnant women on monthly IPTp-SP that completed the study at Adeoyo Maternity Teaching Hospital, Yemetu, Ibadan were analysed. A proforma was used to collect data which included sociodemographic and obstetrics characteristics, prevalence of malaria among the participants and fetomaternal outcomes of the participants. Data obtained were subjected to analysis using statistical package for social sciences (SPSS) for window version 21 and results were presented in appropriate tables, charts and figures. Two hundred participants completed the study and although 11.7% of the participants had malaria parasitaemia at recruitment, only one participant had it at delivery. Most of the participants took 4 doses before delivery. Only 3% of the participants delivered at gestational age less than 34 weeks though 26.5% had preterm delivery. The mean PCV were 30.05±2.60 vs 32.63±3.40 at recruitment and delivery respectively. Only one out of 200 babies and two (1.0%) placental samples tested positive to malaria. The fetal and maternal outcomes of the participants were good following the use of monthly IPTp-SP therefore the uptake of monthly IPTp-SP should be encouraged among pregnant women in malaria endemic area.

Keywords: Malaria, Pregnant, Ibadan, Uptake, IPTp-SP, Fetal Outcomes, Maternal Outcomes

1. Introduction

The menace of malaria in pregnancy can be attributed to its attendant maternal and fetal complications [1]. The maternal complications include anaemia, preterm contraction and labour, renal failure and hypoglycaemia [2]. The complications to the fetus and new born include intra uterine growth restriction IUGR, low birth weight LBW, congenital malaria and placenta parasitization [2-4]. Malaria alone increases the risk of maternal anaemia up to 15%, increases the risk of preterm delivery up to 36%, intrauterine growth restriction up to 70%, low birth weight up to 14% and infant death up to 8% [5]. Therefore, prevention of malaria in pregnancy is one of the important strategies needed to reduce these complications in the malaria endemic countries like Nigeria [6].

According to 2016 World Health Organization (WHO) fact sheet, Sub-Saharan Africa has the highest global malaria burden. Ninety percent of the malaria cases and 92% of malaria deaths occur in this region [7]. The prevalence of malaria in pregnancy in Nigeria ranges between 19.7% to 72.0% according to Salwa et al based on the part of the

country studied and Nigeria is one of the countries with high maternal death due to malaria [8].

Pregnancy is an immunosuppressive state therefore pregnant women with malaria parasitaemia are more prone to complications [9]. However more importantly in pregnancy, there is placenta parasitisation which results from accumulation of infected red blood cells in the intervillous spaces within the placenta, at a much higher concentration than in peripheral circulation [4]. This predisposes the mother to re-infection and fetus to congenital malaria [4, 9].

The World Health Organization (WHO) suggested a three-pronged approach to reduce burden of malaria in pregnancy and one of them was a monthly use of sulfadoxine-pyrimethamine as chemoprophylaxis [10]. The National guideline for prevention of malaria in pregnancy in compliance with WHO guideline has recommended monthly doses of intermittent preventive therapy with sulphadoxine-pyrimethamine (IPTp-SP) after quickening (16 -20 weeks) for all pregnant women including pregnant HIV positive women till deliver [11]. Studies in different regions in Nigeria showed only 10 to 34% of pregnant women received 2 or more doses of IPTp-SP during pregnancy according to report from the National Malaria Elimination Program and ICF International (2016) [12]. Adeoyo Maternity Teaching hospital is one of the hospitals that have adopted this IPTp-SP protocol. Most of their pregnant women benefited from this policy because they were given the IPTp-SP free and as DOTS. It was therefore imperative to assess the maternal and fetal benefits of this guideline in other to encourage other health facilities to adopt it.

2. Materials and Methods

The study was a prospective cohort study of pregnant women receiving care at the antenatal clinic of the Adeoyo Maternity Teaching Hospital, Ibadan in Oyo State, Nigeria between November 2018 to April 2019. The study population consisted of consented pregnant women who booked for antenatal care and followed up till delivery during the period of study. Sample size was calculated using the formula n = Z2pq/d2 yielding a minimum sample of 208 with 10% attrition rate. They were recruited after meeting the inclusion criteria which included consented pregnant women with gestational age ranging from 16weeks to 28weeks and no history of use of sulphadoxine-pyrimethamine in index pregnancy while pregnant women with history of allergy to sulphonamides or pyrimethamines, Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency, chronic medical illnesses or multiple pregnancy were excluded.

The simple random sampling technique was used to select the patients who were followed up till delivery. Physical examination was performed for all the participants. Samples were taken from participants for blood film for malaria parasite at recruitment, during pregnancy as indicated (with complains of malaria symptoms like fever, bitter taste, joint pains and generalized body ache etc) and at delivery. Malaria infestation in participants were diagnosed using blood smears and positive patients were treated with artemisinin combined therapy. However other patients with high temperature but blood film negative for malaria parasite were evaluated and treated for identifiable cause of fever. For the microscopy examination of blood film, staining was done with Giemsa stains and examination of the red blood cells for intracellular malarial parasites [10]. The last normal menstrual period was used to determine the gestational age of the participants and first trimester ultrasound scan for pregnant women who were not sure of their last menstrual period. The IPTp-SP was administered to them as DOTS monthly. Overall, 200 women eventually completed the study and their outcomes were included in the analysis.

Data collected included sociodemographic variables, relevant booking parameters, number of doses of IPTp-SP taken and obstetrics outcomes like birthweight, APGAR score at 5 minute which was an indicator of successful resuscitation of the newborn. Presence of congenital malaria which was confirmed by identifying malaria parasites in the cord blood using microscopy was also reported. Placenta invasion with malaria parasites were also diagnosed and documented with microscopic examination of placental blood though only 193 placenta were released for samples to be taken. Maternal outcomes like anaemia, preterm delivery, fever and maternal parasitaemia were also documented. Also, any participant with temperature of greater than 37.2°C was categorized to have high temperature. Data analysis was done using statistical package for social sciences (IBM SPSS, New York) version 21 and the results were presented in appropriate tables, charts and figures. Ethical approval was obtained from research ethics review committee in Oyo State.

3. Results

The mean age of the participants was 29.91± 5.46years. Majority (59.0%) of the participants were younger than 30years while 41.0% were 30years and above. Most of the participants were married (96.0%). Almost half (49.0%) of the participants had tertiary education while very few had no formal education. Half of the participants were semi-skilled (50%), 28% of them were unemployed while few (7.5%) were professional (Table 1).

Table 1. *Socio-demographic characteristics of participants.*

Variable	Frequency (200)	Percent
Age group (years)	118	59.0
<30		
≥30	82	41.0
Mean ± SD (29.91±5.46)		
Marital status		
Single	8	4.0
Married	192	96.0
Level of Education		
No formal education	1	0.5
Jnr secondary/primary	8	4.0
Secondary	93	46.5
Tertiary	98	49.0
Occupation		
Professionals	15	7.5
Skilled workers	29	14.5
Semi-skilled workers	100	50.0
Unemployed	56	28.0

Most (83.5%) of the participants had between one and three pregnancies before index pregnancy, only 2 (1.0%) of the participants were primigravida. The mean gestational age of the participants was 23.26 ±3.99 weeks at booking which indicates many of the participants booked late as seen in Table 2. The mean weight for the participants was 66.98 ± 11.79kg. Majority of the participants took 4 doses (30.5%) while 45 (20.2%) participants had five doses (Figure 1).

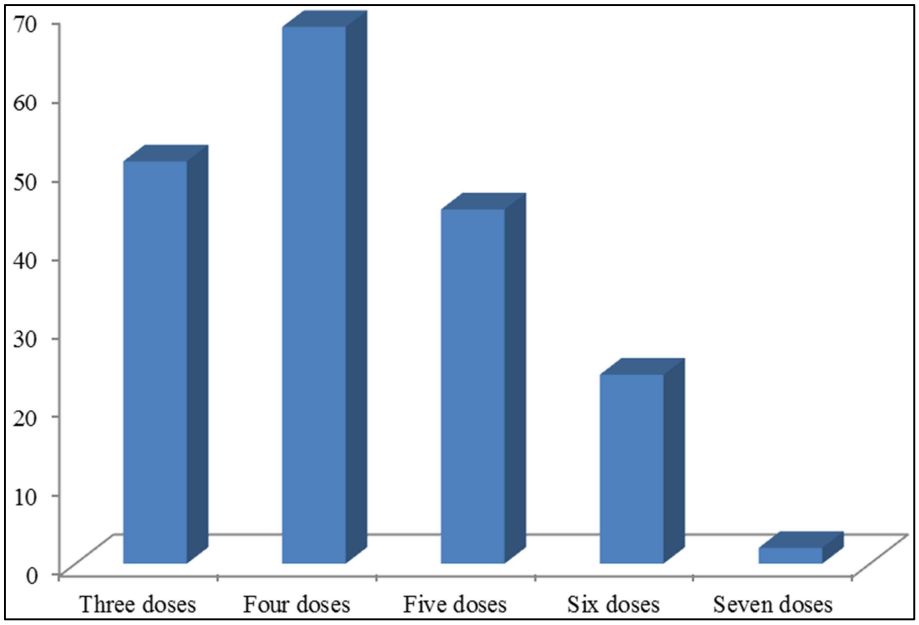

Figure 1. *Maximum number of doses of IPTp-SP taken in pregnancy by the participants.*

Majority, 147 (73.5%) participants gave birth at term and very few participants (3%) gave birth at less than 34 weeks gestation. The mean PCV was 32.63±3.40% at delivery. At recruitment many of the participants (69%) had PCV between 30% and 32% while at delivery, the PCV of just about half of the number of the participants (52.5%) was between 30% and 32%. Twenty-six participants had temperature above normal cut-off (37.2°C) at recruitment out of which 4 participants had temperature greater than 38.0°C while only 13 participants had temperature above the normal cut-off at delivery and none had temperature equal or above 38.0°C. Though 11.7% of the participants tested positive to malaria upon recruitment however only two tested positive for malaria during ante-natal follow up while just one participant tested positive at delivery (Table 3).

Table 2. *Relevant booking parameters of the participants.*

Variables	Frequency (n=200)	Percentage (%)
Gravidity		
None	2	1.0
1-3	167	83.5
≥4	31	15.5
Mean ± SD	2.48±1.49	
Gestational age (weeks)		
16-20	59	29.5
21-25	65	32.5
≥26	76	38.0
Median	24	
Weight (kg)		
<70	130	65.0
70-89	63	31.5
≥90	7	4.5
Mean ± SD	66.98±11.79	
PCV at recruitment (%)		
30-32	138	69.0
≥33	62	31.0
Mean± SD	30.05±2.60	
Temperature at recruitment (°C)		
36.6-37.2	174	87.0
37.3-38	22	11.0
>38	4	2.0

Table 3. *Maternal outcomes.*

Variable	Frequency (n=200)	Percentage (%)
GA at delivery (weeks)		
$28\text{-}33^{+6}$	6	3.0
$34\text{-}36^{+6}$	47	23.5
37-40	129	64.5
>40	18	9.0
Mean±SD	38.00±2.09	
PCV at delivery (%)		
<27	5	2.5
27-29	11	5.5
30-32	105	52.5
≥33	79	39.5
Mean± SD	32.63±3.40	
Temperature at delivery (°C)		
36.6-37.2	187	93.56.5
37.3-37.9	13	6.5
Blood film for MP during antenatal follow up		
Positive	2	0.8
Negative	198	99.2
Mothers'blood film for MP at delivery		
Positive	1	0.5
Negative	199	99.5

Baby's birth weight of the majority (92.5%) of the participants was 2.5kg and above, only few participants 15 (7.5%) had babies who were weighing less than 2.5kg as seen in Table 4. Out of those with low birthweight, three (20%) were less than 1kg while 11 (73.3%) were between 1.6kg and 2.5kg. One hundred and twenty- six (63.0%) participants had the weight of the placenta to be less than 0.7kg. Only two (1.0%) placental samples tested positive to malaria out of 193 samples tested. Just one baby out of 200 babies had malaria parasites and she was treated. About half (53.0%) of the babies had their APGAR score at five minutes to be at least 8 or more. Very few (2.5%) of the participants' babies had neonatal jaundice, 2 (1.0%) babies were admitted to SCBU while also two of the babies were delivered as fresh still born.

Table 4. *Fetal outcomes at delivery.*

Variable	Frequency (n=200)	Percent
Birth weight (Kg)		
<2.5	15	7.5
≥2.5	185	92.5
Mean±SD	3.03±0.59	
Low birth weight (kg)(n=15)		
<1	3	20.0
1.1-1.5	1	6.7
1.6-2.5	11	73.3
Weight of placenta		
<0.7	126	63.0
≥0.7	74	37.0
Mean±SD	0.73±0.51	
Placenta smear for MP (n=193)		
Positive	2	1.0
Negative	191	99.0
Baby's smear for MP (Cord blood)		
Positive	1	0.5
Negative	199	99.5
Apgar scores @ 5 mins		
<8	94	47.0
≥8	106	53.0
Mean±SD	8.45±0.78	
Presence of neonatal jaundice		
Yes	5	2.5
No	195	97.5
Admitted to SCBU		
Yes	2	1.0
No	198	99.0
Stillbirth		
Yes	2	1.0
No	198	99.0

4. Discussion

In assessing the maternal outcomes of monthly doses of IPTp-SP among participants, improved maternal outcomes were noted in this study. Majority of the participants gave birth with mean PCV of 32.63±3.40% which was higher than their average booking PCV. This is surprising because haemodilution and blood loss at delivery ought to have affected the mean PCV at delivery. These findings could have been due to effects of monthly IPTp-SP and regular use of haematinics. None of the mothers had a high grade fever (temperature higher than 38°C) at delivery as compared to the findings at recruitment where 4 participants had high grade fever and they were all among the participants treated for malaria at recruitment. More importantly, majority of the participants had term deliveries. These results are similar to those of Anto et. al, in a study done in Ghana where the authors reported that uptake of higher doses of SP was significantly associated with delivery at term [13] and also Nneka et. al findings in Nsuka where multiple doses of IPTp-SP is associated with reduction in the incidence of anaemia in pregnanc [14]. The effectiveness of monthly IPTp-SP to reduce maternal malaria episodes and improve maternal outcomes is shown in this study.

This study also described the fetal outcomes of monthly doses of IPTp-SP. Most of the babies weighed ≥2.5kg. The study by Anto et. al also showed that majority of the babies weighed above 2.5kg likewise the Filbert et. al study in Tanzania [13, 15]. In the present study, incidence of placenta parasitaemia was very low as only two placenta samples were positive for malaria parasites and very few babies had neonatal jaundice. These findings are also similar to Nneka et. al study in Nsukka and Filbert et. al study in Tanzania [14, 15]. Only two of the babies were delivered as fresh stillborn as a result of labour complications not due to congenital malaria. The reduction in placenta parasitaemia in the study may have been facilitated by the fact that, the last dose for most participants were administered on average within 4 weeks to delivery, clearing existing malaria infections and reducing the susceptibility of the new born to malaria at delivery since the drug provides an extra period of post treatment prophylaxis of 4 to 6weeks [16]. Uptake of multiple doses of SP reduces the prevalence and intensity of placental malaria which is known to contribute significantly to having preterm delivery and low birth weight infants [13-17].

The results provide evidence that the administration of IPTp-SP was effective in reducing malaria infestation from recruitment to delivery by 95% such that only one participant tested positive for malaria infection at delivery against 26 at recruitment. This finding is also comparable with the report from other studies by Filler et al, Agomo et al and Nneka et al [14, 18, 19].

However the study is not without some limitations which include: some of the fetomaternal outcomes assessed in this study could have been affected by some other cofounders especially pregnancy complications or even difficult labour process though patients with pregnancy complications or chronic medical ailments were excluded at recruitments.

5. Conclusion

In conclusion, maternal outcomes and fetal outcomes such as gestational age at delivery, APGAR score, birth weight, PCV at delivery were good among these participants on monthly dose of IPTp-SP. This could be due to incidence of malaria infestation among participants which was very low following the use of monthly IPTp-SP. The study results suggested that successful implementation of the WHO

monthly IPTp-SP strategy will go a long way to improve the birth outcomes of the neonates and the health of pregnant women.

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