ORIGINAL ARTICLE

Plasmodium falciparum parasitaemia among booked parturients who received two doses of sulfadoxine-pyrimethamine (SP) for intermittent preventive treatment in pregnancy (IPTp) in a tertiary health facility Southeast Nigeria

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ABSTRACT

Background: Malaria is preventable but has contributed significantly to maternal morbidity and mortality in our environment. Malaria parasitaemia during pregnancy is mostly asymptomatic, untreated but with complications. **Aim:** A follow-up study aimed at determining plasmodium falciparum parasitaemia and associated complications among booked parturient who had intermittent preventive treatment with sulfadoxine-pyrimethamine (SP) compared with another study among unbooked parturients who did not take SP for intermittent preventive treatment in pregnancy (IPTp). **Materials and Methods:** This study was conducted in the labour ward complex of Federal Teaching Hospital, Abakaliki from March to May 2012. Five hundred booked parturients at term that received two doses of SP were consecutively recruited. A structured data collection sheet was administered to each parturient. Thick and thin blood films were prepared for quantification and speciation of parasitaemia, respectively. The haemoglobin concentration and birth weights were determined. Analysis was done with the Statistical Package for the Social Sciences (SPSS) software with level of significance at *P* value < 0.05. **Results:** The prevalence of malaria parasitaemia in the study was 59.6%. The mean age of parturients was 28.7 (5.5). The highest prevalence of malaria parasitaemia, 92% was found among the parturients aged ≤19 years. The association between age and parasitaemia was significant (x^2 = 16.496, *P* = 0.000). The median parity was 1.0 (3.0). The highest prevalence of asymptomatic parasitaemia, 65.5% was noted among the nulliparous parturients. The association between parity and parasitaemia was significant (x^2 = 11.551, *P* = 0.003). Majority of the parturients were of high social class. Those of the lowest social class (class 5) had the highest prevalence (80%) of parasitaemia. The association between social class and parasitaemia was significant (x^2 = 9.131, *P* = 0.003). Prevalence of anaemia in the study was 14%. The non-parasitaemic and parasitaemic parturients had mean haemoglobin concentrations of 12.7 g/dl and 10.4 g/dl, respectively. There was significant association between haemoglobin concentration and parasitaemia (x^2 = 39.143, *P* = 0.000). The prevalence of low birth weight was 3.0%. The relationship between birth weight and parasitaemia was significant (x^2 = 2.535, *P* = 0.000). **Conclusion:** The was reduction in asymptomatic malaria parasitaemia compared to parturients who had no SP though the prevalence was still high showing possibly increasing resistance to SP but the treatment was still very effective in reducing anaemia and low birth weight associated with malaria in pregnancy.

Key words: Intermittent preventive treatment, malaria, Nigeria, sulfadoxine-pyrimethamine

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INTRODUCTION

Malaria is a parasitic disease of humans especially in the sub-Saharan Africa, where about 90% of death due to malaria occur.[1] The term malaria originated from the medieval Italian; 'mala aria' which means 'bad air' and the disease was formerly called ague or marsh fever due to its association with swamp and marsh land.[2] Malaria

is a vector borne disease caused by the parasite of the genus *Plasmodium.* It is transmitted by the bite of an infected female anopheles mosquito. Four species are responsible for malaria infestation*, Plasmodium falciparum, Plasmodium malariae, Plasmodium ovale and Plasmodium vivax. Plasmodium falciparum* is the commonest in Africa and responsible for up to 98% of cases in Nigeria and is associated with severe morbidity and mortality.[3,4] *Plasmodium malariae* and *ovale* are responsible for 2% of cases while *Plasmodium vivax* is not found among indigenous Nigerians.[4]

Pregnant women and children are specifically susceptible to malaria in endemic regions due to low immunity.[1] The burden of the disease is enormous in malaria endemic countries like ours. Each year, approximately 50 million women living in malaria endemic areas throughout the world become pregnant, of which more than half live in tropical Africa with intense transmission of *Plasmodium falciparum*.[5] An estimate of 10,000 of these women and 200,000 of their infants die as a result of malaria infection. Malaria in pregnancy is an important cause of anaemia, miscarriages, intrauterine growth restriction, low birth weight, still birth and other pregnancy-related complication.[3] These complications are made worst in tropical Africa by poverty, poor nutrition, limited access to health care, human immunodeficiency virus (HIV) and micronutrient imbalance (vitamin A, Zinc, Iron and Folate). In Nigeria, malaria accounts for 60% of outpatients consultations and 11% of maternal mortality is due to malaria in pregnancy.[3,4] Seventy percent of pregnant women in Nigeria suffer malaria with maternal and fetal complications.[3] The problem is compounded by high level of resistance to first- and second-line antimalarial drugs as shown by the drug therapeutic efficacy trial conducted in the six geopolitical zones of the country which showed resistance ranging from 23-96%.[4]

Intermittent preventive treatment of malaria in pregnancy is the administration of curative dose of effective antimalaria at least twice to all pregnant women whether or not they are infected with malaria parasites. This is aimed at treating and preventing malaria episodes in pregnant women. A small number of Randomized Controlled Trials and prospective studies in Kenya[6,7] and Malawi[8,9] demonstrated the efficacy and cost-effectiveness of the use of sulfadoxine-pyrimethamine (SP) in pregnancy in preventing anaemia and low birth weight in the 1990s. Following this the World Health Organisation (WHO) recommended the use of at least 2 doses of intermittent preventive treatment with SP in areas of medium and high transmission of malaria parasites. This is because in malaria endemic areas, malaria in pregnancy is usually asymptomatic, undetected and untreated.[10-12] Many countries in sub-Saharan Africa had introduced intermittent preventive treatment with SP into their malaria program with different levels of coverage. The problem with compliance was overcome with the use of Directly Observed Treatment (DOT) in the antenatal clinics.

There are varying reports from different countries on the effectiveness of intermittent treatment with SP. Newman RD *et al.* reported that plasmodium falciparum malaria in pregnancy poses a great risk to both the woman and her neonate through anaemia, low birth weight and is responsible for up to 35% of preventable low birth weight in malaria endemic areas.[13] They reported that this adverse effect was reduced by intermittent preventive treatment with SP which is available, cheap, acceptable and easily administered.[13] Others reported that intermittent preventive treatment with SP was effective in reducing both placental malaria and low birth weight in nulliparous and primiparous pregnant women.[14,15] In Ghana, there was a report of substantial decline in placental malaria and maternal anaemia with associated increase in birth weight after the implementation of intermittent preventive treatment in pregnancy with sulfadoxine-pyrimethamine.[16] Large case control studies had demonstrated the favorable safety profile of SP and no increased teratogenesis when administered in the second and third trimesters.[17] Some authors had suggested additional preventive measures to supplement SP therapy, especially in the first trimester when malaria is deleterious for the woman and her offspring and safety of SP cannot be guaranteed.[16,18]

Though some resent studies had demonstrated reduction in low birth weight and placental malaria with failure in adherence to direct observed treatment scheme and strong dose effect,[19,20] others had reported the spread of resistance to SP which pose a great public health problem.[21,22] This resistance is as a result of point mutations in the dihydrofolate reductase (pfdhfr) and dihydropteroate synthase (pfdhps).[22] Although these triple and quadruple mutations were frequent, there was no evidence of correlation between these genotypes and lack of efficacy of SP in the context of intermittent preventive treatment in pregnancy.[21] This however, suggests the obvious that SP will soon be compromised in Africa.[21]

This study was aimed at evaluating the effectiveness of intermittent preventive treatment of malaria during pregnancy with SP in reducing peripheral malaria parasitaemia, maternal anaemia and low birth weight among booked parturients in the Federal Teaching Hospital Abakaliki, Southeast Nigeria.

MATERIALS AND METHODS

This was a prospective cross-sectional study conducted in the labour ward complex of the Federal Teaching Hospital, Abakaliki, Ebonyi state, Nigeria over a 3 month period from March to May 2012. The state is made up of 13 local government areas, one urban, one semi-urban and some

rural areas. It occupies a land mass of 5932 km^2 and has the population of 2.1 million people as was reported in 2006 by the National Population Commission. About 75% of the population are rural dwellers with subsistence farming as their major occupation.[23] Malaria transmission is endemic in the state.

The Federal Teaching Hospital is located in Abakaliki the capital city of the state. This is the major tertiary hospital in the state. The study population included all booked women presenting in labour at term within the study period who received two doses of SP for intermittent preventive treatment of malaria in pregnancy. The exclusion criteria were those who refused consent, symptomatic (fever, chills, rigor, nausea, vomiting, headache), preterm labour, HIV in pregnancy, antepartum haemorrhage, hypertension in pregnancy, twin delivery. A structured data sheet was administered to the women by the authors after explaining the purpose of the study and obtaining informed consent which was later re-confirmed in the postnatal ward after delivery. Information obtained included age, parity, gestational age and social class. The social class was calculated using the protocol of social classification by Olusanya, Okpere and Ezimokhai from the husband's occupation and the woman's level of education.[24]

Peripheral blood was collected from the antecubital vein via an aseptic procedure and used to prepare two thick and two thin films on pre-labeled glass slides for each parturient. The thick film was for malaria parasite identification while the thin film was for identification *Plasmodium species.* The thick blood films were allowed to air dry at room temperature and thereafter were stained with 5% Giemsa stain for 20 minutes, then rinsed with water, allowed to air dry and microscopic examination done under oil immersion at 100× magnification. The presence of 1-10 parasites/100 thick film fields (0.25 µL of blood) or more was regarded as positive. We employed the WHO semi-quantitative method of parasite density estimation which is done by visualizing a 100-field perimeter, equivalent to 0.25 µL of blood which is the method adopted in our hospital. The thin blood films were allowed to air dry and were then fixed with absolute methanol for 1 minute after which they were stained with Giemsa stain for 20 minutes, then rinsed with water and allowed to air dry before microscopic examination was done to identify the *Plasmodium species.* The haemoglobin estimation was done using the hemocue system (hemocue AB, Angel-holm Sweden) which consist of a pre-calibrated, portable, battery or main operated photometer. No dilution was required as blood was run by capillary action directly into a corvette containing sodium nitrite and sodium azide that convert the haemoglobin to azidemet haemoglobin. The absorbance is then measured at a wave length of 565 and 880 Nm. This is reliable as high level of bilirubin, lipids or white blood cells do not affect measurements.[25] Anaemia was determined using the WHO standard of haemoglobin concentration less than 11.0 g/dl. The neonates were weighed with an electronic weighing machine and the birth weight recorded. The samples were prepared, read and analyzed by each of two experienced laboratory scientists dedicated to the study to ensure quality control. The research and ethics committee of the Federal Teaching Hospital approved the study protocol. Those diagnosed with asyptomatic malaria parasitaemia were managed according to the Obstetrics and Gynaecology departmental protocol. Asymptomatic malaria parasitaemia is the identification of malaria parasite in the blood film of a parturient that had no symptoms of malaria infestation.

The minimum sample size of 362 women for the study was computed using 38%[11] successful prevention from analysis of similar studies in sub-Saharan Africa using the formula proposed by Daniel, Lwanga and Lameshow.[27,28] This was increased to 434 women to control for attrition. The coded data was fed into the computer using Statistical Package for the Social Sciences (SPSS) programme (2010) version 20 and analysis done. A *p*-value less than 0.05 was considered significant.

RESULTS

A total of 500 booked parturients at term that received 2 doses of intermittent preventive treatment of malaria with SP were consecutively recruited into the study. The mean age was 28.7 (5.5) years and ranged between 17-39 years. The median parity was 1.0 (3.0) and ranged between 0-5. Majority of the parturients were of high social class. The parturients within the age-group 20-29 years were the majority 279/500 (55.8%) [Table 1]. The prevalence of

Table 1: Socio-demographic characteristics of parturients

Variable	Number (500)	%
Age (years)		
≤ 19	12	2.4
20-29	279	55.8
30-39	209	41.8
≥ 40	—	—
Parity		
0	165	33.0
1-4	298	59.6
≥ 5	37	7.4
Social class		
1	234	46.8
2	76	15.2
3	99	19.8
4	81	16.2
5	10	2.0
Birth weight (kg)		
≥ 3.0	352	70.4
2.5-2.9	133	26.6
1.5-2.4	14	2.8
≤ 1.5	1	0.2

asymptomatic malaria parasitaemia in the study was 298/500 (59.6%). The highest prevalence of asymptomatic malaria parasitaemia 11/12 (92%) was found among the parturients who were ≤ 19 years. The association between age of parturients and asymptomatic malaria parasitaemia was statistically significant (x^2 = 16.496, *P* = 0.000).

One hundred and eight (65.5%) of the 165 nulliparous parturients had asymptomatic malaria parasitaemia while 177/298 (59.4%) of the parturients of para 1-4 had asymptomatic malaria parasitaemia. Thirty-five percent (13/37) of the grandmultiparous parturients were parasitaemic. The association between parity and asymptomatic malaria parasitaemia was statistically significant (x^2 = 11.551, *P* = 0.003). Majority of the parturients of social class 5 (8/10 (80%) were parasitaemic. A significant percentage of social class 4 (51/81 (63.0%), social class 3 (61/99 (61.6%), 75% of social class 2 and social class 1 (121/234 (51.7%) had asymptomatic malaria parasitaemia. The association between social class and asymptomatic malaria parasitaemia was statistically significant (x^2 = 9.131, *P* = 0.003) [Table 2].

When the variables were controlled by using logistic regression, only social class was the variable shown to be statistically significant as explanatory to asymptomatic malaria parasitaemia [Table 3].

Among the parasitaemic parturients, 291/298 (97.7%) had one plus (+) of parasite density while 7/298 (2.3%) had parasite density of two plusses (++). No parturient had parasite density of three plusses (+++) [Figure 1].

The prevalence of anaemia in the study using the WHO standard of haemoglobin concentration 11.0g/dl was 70/500 (14%). The mean haemoglobin concentration for non-parasitaemic parturients was 12.7 g/dl while that of parasitaemic parturients was 10.4 g/dl. All the parturients with two plusses (++) of parasite density had anaemia.

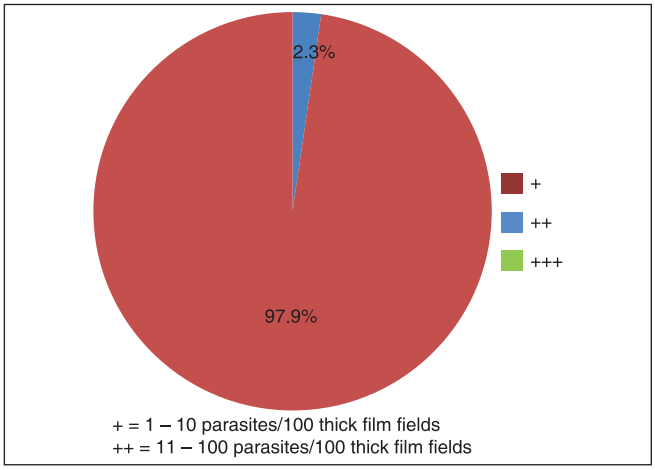

Figure 1: Parasite density of parasitemic parturients

No parturient however had haemoglobin concentration less than 8.0 g/dl. The association between malaria parasitaemia and anaemia was statistically significant (x^2 = 39.143, *P* = 0.000) [Tables 4 and 5].

When the variables were controlled by using multivariate logistic regression, malaria parasitaemia and age were the statistically significant variables explanatory for anaemia in the study [Table 6].

Five hundred babies were delivered during the study period. The mean birth weight was 3.2 (0.8) kg and ranged between 1.4–5.4 kg. The prevalence of low birth

Table 2: Socio-demographic characteristics and Asymptomatic malaria parasitemia

Variable	Parasitemic		Non-parasitemic		x^2	*P* value
	Number	%	Number	%		
Age (years)						
≤ 19	11	92.0	1	8.0	16.496	0.000
20-29	180	64.5	99	35.5		
30-39	107	51.2	102	48.8		
≥ 40	—	—				
Parity						
0	108	65.5	57	34.5	11.551	0.003
1-4	177	59.4	121	40.6		
≥ 5	13	35.1	24	64.9		
Social class						
1	121	51.7	113	48.3	9.131	0.003
2	57	75.0	19	25.0		
3	61	61.6	38	38.4		
4	51	63.0	30	37.0		
5	8	80.0	2	20.0		
Birth weight (kg)						
≥ 3.0	200	56.8	152	43.2	2.535	0.000
2.5-2.9	83	62.4	50	37.6		
1.5-2.4	14	100	—			
≤ 1.5	1	100	—			

Table 3: Logistic regression analysis of contributory factors to asymptomatic malaria parasitemia

Variable	Odds ratio	95% CI	*P* value
Age	1.422	0.500-1.703	0.4973
Parity	0.659	0.190-1.083	0.7735
Social class	0.309	0.110-0.836	0.0053

CI – confidence interval

Table 4: Parasite density and maternal hemoglobin concentration

Parasite density	number (500)	hemoglobin concentration(g/dl)				x^2	*P* value
		min	max	mean	std		
Absent	202	10.0	16.2	12.7	1.25	39.143	0.000
+	291	8.6	15.0	12.0	1.57		
++	7	8.5	13.7	10.4	1.69		

Min – Minimum; Max – Maximum; Std – Standard deviation

weight in the study was 15/500 (3.0%). Three hundred and fifty two neonates weighed 3.0 kg and above. All the low birth weight neonates were deliveries of parasitaemic parturients. The relationship between birth weight and asymptomatic malaria parasitaemia was statistically significant ($x^2 = 2.535$, $P = 0.000$) [Tables 1 and 2]. When the variables of age, parity, social class, haemoglobin concentration and malaria parasitaemia were controlled by using multivariate logistic regression, only haemoglobin concentration and malaria parasitaemia were shown to be statistically significant as explanatory variables to low birth weight in the study [Table 7].

DISCUSSION

The prevalence of asymptomatic malaria parasitaemia was still high (59.6%) in the study. This was however lower than 77.6%[28] prevalence reported among unbooked parturients who did not receive intermittent preventive treatment with SP in the same center. It was much higher than 16%[29] prevalence that was reported in Abakaliki in the year 2007. This may be as a result of increasing resistance to SP. The doses of SP for intermittent preventive treatment of malaria in pregnancy were prescribed and taken concurrently with high dose of folate which may reduce the efficacy of SP. Recurrent infestation between and after the doses of SP may also account for the high prevalence due to high intensity of malaria transmission in our area. The highest prevalence (92%) of asymptomatic malaria parasitaemia was found among the parturients aged 19 years or less. The association between maternal age and asymptomatic malaria parasitemia was statistically significant. This compares with other studies in Nigeria which reported maternal age less than 20 years as a significant risk factor.[30] The highest prevalence of asymptomatic malaria parasitaemia among parity groups was found among the nulliparous parturients who had 65.5% prevalence. This compares with previous studies which associated malaria parasitaemia with low parity.[31,32] The association between parity and asymptomatic malaria parasitemia was statistically significant. This may be due to acquisition of parity specific immunity which decreases susceptibility as parity increases.[32] Among the social classes, the highest prevalence of 80% asymptomatic malaria parasitemia was found among the parturients of the lowest social class (class 5) while the least prevalence of 51.7% was found among social class 1. The association was significant. This may be due to the fact that parturients of low social class are predominantly uneducated, rural subsistent farmers dwelling in dirty and bushy environment where mosquitoes breed more. They may not afford correct treatment for malaria as well as not use other preventive measures like insecticide treated nets. Multivariate logistic regression of the factors also showed social class as the only significant factor for malaria parasitaemia in this study.

Table 5: Maternal hemoglobin concentration

Hemoglobin concentration	Number (500)	(%)
≥ 11.0g/dl	430	86
8-10.99g/dl	70	14
6-7.99g/dl	—	—
≤ 6g/dl	—	—

Table 6: Logistic regression analysis of contributory factors to anemia

Variable	Odds ratio	95% CI	*P* value
MP	0.703	0.230-2.153	0.000
Parity	0.901	0.807-1.006	0.065
Age	0.627	0.348-1.338	0.001
SC	0.710	0.461-1.453	0.400

MP – Malaria parasitemia; CI – Confidence interval; SC – Social class

Table 7: Logistic regression analysis of contributory factors to low birth weight

Variable	Odds ratio	95% CI	*P* value
Age	0.656	0.726-2.779	0.512
Parity	0.521	0.160-1.500	0.219
Social class	1.000	0.500-1.323	0.392
HbC	0.596	0.052-0.202	0.000
MP	0.991	0.475-1.409	0.001

CI – Confidence interval; HbC – Hemoglobin concentration; MP – Malaria parasitemia

The prevalence of anaemia in the study was 14%. This was low compared with the report of 46.8%[33] prevalence in a previous study in the center among unbooked parturients who did not receive intermittent preventive treatment with SP. This was also very low compared with the reports of 59.6%[34] and 71%[10] prevalence from Calabar and Lagos, respectively among women who had not received intermittent preventive treatment with SP. This shows that SP may still be effective in preventing anaemia in pregnancy due to malaria. The mean haemoglobin concentration for non-parasitaemic parturients was higher than that of the parasitaemic parturients. Haemoglobin concentration also decreased with increased parasite density. The association of anaemia with parasitaemia was significant. Logistic regression of the factors showed malaria parasitaemia and age as significant factors for anaemia.

The prevalence of low birth weight in the study was 3.0%. This was low compared with 21.1%[35] reported in a study in the center among unbooked parturients who did not receive intermittent preventive treatment with SP. This was also lower than the 19%[36] prevalence reported in previous studies from sub-Saharan Africa. This shows that SP may still be effective in reducing low birth weight associated with malaria in pregnancy when used for intermittent preventive treatment. Low birth weight is an important contributor to high neonatal and infant morbidity and mortality in malaria endemic areas

like ours. Only haemoglobin concentration (anaemia) and malaria parasitaemia were significant factors for low birth weight after multivariate logistic regression of the factors.

CONCLUSION

The study demonstrated reduction in asymptomatic malaria parasitaemia when compared with those that did not receive intermittent preventive treatment in pregnancy (IPTp), though the prevalence was still high showing possibly increasing resistance to SP but the treatment was still very effective in reducing anaemia and low birth weight associated with malaria in pregnanmcy.

A larger and community-based study is required in the future which may be more representative of the entire population.

The use of SP for intermittent preventive treatment of malaria in pregnancy is still required until other more effective ways of preventing malaria in pregnancy are discovered.

LIMITATIONS

This may not be the true representation of the entire population as the study was carried out in a tertiary referral hospital located in the urban area.

Calculation of the absolute parasite density (ring forms) would have been better than the semi-quantitative method of parasite density estimation used in the study.

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