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**Research Article**

# EFFECTIVENESS OF INTERMITTENT PREVENTIVE TREATMENT IN PREGNANCY WITH SULPHADOXINE-PYRIMETHAMINE AGAINST MALARIA IN NORTHERN NIGERIA

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**ABSTRACT**

Malaria in pregnancy remains a major public health concern, in spite of the adoption of WHO recommended intermittent preventive treatment (IPTp) with sulphadoxine-pyrimethamine (SP) for its control in Nigeria. We conducted a cross –sectional study of 108 consenting pregnant women attending antenatal clinic at Bingham University Teaching Hospital in Jos, Nigeria between August–December 2017. Malaria infection was detected by microscopy and haemoglobin was measured and anaemia was defined as haemoglobin lower than 11 g/dL. A total of 79 (73.1%) IPTp users and 29 (26.9%) non-IPTp users were recruited. A total of 11.1% of IPTp users had malaria compared with 25.0% of non-IPTp users ($P < 0.01$). A total of 16.7% of non-IPTp users were anemic compared with 1.9% of IPTp users ($P < 0.01$). After controlling for other variables the effect of IPTp-SP remained statistically significant ($P<0.01$). Conclusion: These results suggest that Intermittent Preventive Treatment with Sulphadoxine-Pyrimethamine is useful in preventing malaria and anaemia among pregnant women in Nigeria.



## INTRODUCTION

Malaria affects approximately 50 million women per year in malaria-endemic areas because malaria an immense public health problem in pregnancy [1] . Pregnant women, especially primigravidae and secundigravidae, are particularly vulnerable to malaria than non-pregnant women from the same area [2]. Among pregnant women especially primigravidae living in holoendemic areas or perennially exposed to malaria, malaria is a major contributory cause of anemia, in sub-Saharan Africa [3]. Complication of maternal malaria such as anaemias put pregnant women at greater risk of other morbidities including placental abruption, placenta previa, premature labor, and maternal death [4].

Intermittent preventive treatment in pregnancy (IPTp) with the drug sulfadoxine-pyrimethamine (SP) is recommended by the World Health Organization to reduce the burden of malaria and improve birth outcomes; this is extensively chosen as malaria control in most African countries [5]. The provision of SP at each scheduled focused antenatal-care visit in the second and third trimesters has recently been updated and recommended by WHO [3, 6, 7]. IPTp-SP has been shown to reduce malaria episodes, malaria-related anemia, and incidence of low birth weight [8,9]. Importantly, IPTp-SP is attractive because of its single-dose therapy of IPTp-SP makes it attractive for simple administration and good compliance [10].

Studies have shown that resistance to SP is increasing in West Africa and thus the effectiveness of IPTp-SP has been doubtful [11, 12]. In addition, in 36% of children and approximately 30% of pregnant women in central Ghana SP treatment failure has been detected [13]. Assessment of possible association between IPTp-SP use and decreased prevalence of maternal malaria and malaria associated anemia despite increased resistance may provide information on its effectiveness in controlling malaria and anemia in pregnancy. Therefore, in this study, the effectiveness of IPTp-SP in preventing maternal malaria and malaria-associated anemia and other contributory factors among pregnant women attending antenatal clinic (ANC) at Bingham University Teaching Hospital was assessed.

## MATERIALS AND METHODS

### *Study Area*

The study area has been described by Builders [14]. Briefly , the study was carried out in Northern part of Nigeria, in this area Research has shown that in there is marked difference

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between the high transmission rate (the short wet season) and low transmission rate (the long dry season). The variations in occurrence are due to rainfall, altitude and temperature. High rainfall is associated with high incidence malaria while places with high altitude and low temperature tend to be associated with lower rates of transmission [15]. Therefore this area was selected because of the highest peak malaria transmission is between the month of August and December.

### *Study Population*

The study population comprised all consenting pregnant women attending antenatal care unit of Bingham University Teaching Hospital between August and December 2017. Excluded from the survey were pregnant women who refused to give consent to the study and those who gave a history of allergy to sulfonamide-containing drugs and pregnant women.

### *Ethical Clearance*

Ethical approval was sought from the Bingham hospital's research ethics committee. Sample collection, processing, and analysis were carried out as required by the committee.

### *Study Design*

A cross-sectional design was used, the participants were randomly selected. The sample site (hospital) was purposefully selected because in this hospital, antenatal clinic is functional and the IPTp-SP policy is implemented.

### *Data Collection*

One hundred and nine (109) pregnant women were into the study. Some health and obstetric pieces of information such as gestation, gravidity, parity, and SP intake were obtained from the Antenatal Clinic (ANC) booklets of respondents; other information was collected using a structured questionnaire administered by trained research assistants. Three milliliters (3 mL) of venous blood was collected from the median cubital or cephalic veins of the arm of pregnant women into labeled vacutainers, containing Ethelene Diamine TetraAcetic Acid (EDTA). Thick blood films were prepared on labeled microscope slides, Giemsa-stained and observed by a trained and licensed microbiologist for malaria diagnosis. if one or more parasites are present, this was denoted as positive and negative if none is seen after observing 100 high power fields. Haemoglobin (Hb) level was determined using the SYSMEX KX – 21 haematology analyser (Sysmex Corporation, Kobe, Japan) was used to determine Haemoglobin (Hb) level recorded and sickling status was determined by the sodium metabisulphite method as described by Cheesbrough [13].

### *Statistical Analysis*

Data were entered into SPSS statistical software version 22.0 for Windows and analyzed. Frequencies and percentage were used to compare relationships between variables. 2-tailed test of significance was done by bivariate analysis using Pearson correlation coefficient.

## RESULTS

### *General Characteristics of Respondents*

In this result, 79 (83.2%) of the pregnant women received Sulphadoxine-Pyrimethamine, they were in the age range of 14 years to more than 31 years. There were highly significant correlation between IPTp-SP users and non IPTp-SP users in terms of age, gestation, gravidity and parity as indicated in table 1.

**Table 1** Health and obstetric information of participants

| Variables | IPTp-SP users | Non IPTp-SP users |
|---|---|---|
| Age | | |
| 14-20 | 3 (2.8%) | 1(0.9%) |
| 21-30 | 41 (38%) | 19 (17.6) |
| > 31 | 35 (32.4) | 9(8.3) |
| Gestation | | |
| Second | 58 (79.6%) | 14 (13%) |
| Third | 28 (53.7%) | 8 (7.4%) |
| Gravidity | | |
| Primigravidae | 21 (9.4%) | 8 (7.5%) |
| Secundigravidae | 19 (17.6%) | 4( 3.7%) |
| Multigravidae | 45 (41.7%) | 11 (10.2%) |
| Parity | | |
| 0 | 20 (18.5%) | 9 (8.3%) |
| 1 | 15 (13.9%) | 5 (4.6%) |
| 2 | 24 (22.2%) | 2 (1.9%) |
| >-3 | 24 (22.2%) | 9 (8.3%) |

**. Correlation is significant at the 0.01 level (2-ailed).

### *Effect of IPTp-SP on laboratory tests*

Table 2 indicates effect of IPTp-SP on laboratory tests. There was highly significant correlation between IPTp-SP users and non IPTp-SP users based on malaria test, anaemia test, Sickling test, HIV test, stool and urine test.

**Table 2** Effect of IPTp-SP on laboratory tests

| Tests | IPTp-SP users | Non IPTp-SP users |
|---|---|---|
| Malaria | | |
| Positive | 22 (20.4%) | 3 (2.8%) |
| Negative | 66 (61.1%) | 19 (17.6%) |
| Anaemia | | |
| Haemoglobin g/dL (Mean) | 12.9 | 11.9 |
| % | 86 (79.6) | 20 (20.4) |
| Positive | 0 | 2 (1.9%) |
| Negative | 86(79.6%) | 20 (18.5%) |
| Sickling | | |
| Positive | 3 (2.8%) | 5 (2.8%) |
| Negative | 83 (75) | 17 (17.6) |
| HIV | | |
| Positive | 2 | 2 (1.9%) |
| Negative | 84(77.8%) | 20 (18.5%) |
| Stool | | |
| Positive | 3 (2.8%) | 3 (2.8%) |
| Negative | 83 (76.9%) | 19 (17.6%) |
| Urine | | |
| Positive | 12 (11.1%) | 12 (11.1%) |
| Negative | 74 (68.5%) | 10 (9.3%) |

**. Correlation is significant at the 0.01 level (2-tailed).

***Effect of IPTp-SP on peripheral parasitaemia***

There was no significant correlation between IPTp-SP users and non IPTp-SP users in terms of parasite density as illustrated in table 3.

**Table 3** Effect of IPTp-SP on peripheral parasitaemia

| Variables | One dose | Two doses |
|---|---|---|
| Parasite density | | |
| + | 5 (4.6%) | 2 (1.9%) |
| ++ | 5 (4.6%) | 10 (9.3%) |

***Effect of IPTp-SP dosage on other parameters***

Table 4 shows correlation between IPTp-SP dosage and other parameters. There was no significant correlation between IPTp-SP and non IPTp-SP users based on IPTp-SP dosage on anaemia, HIV, stool and urine infection.

**Table 4** Effect of IPTp-SP dosage on other parameters

| Variables | One dose | Two doses |
|---|---|---|
| Haemoglobin g/dL (Mean) | 11.6 | 14.8 |
| % | 68 (63) | 18 (16.7) |
| Sickling Positive | 3(2.8%) | 5 (4.6%) |
| HIV Positive | 1 (0.9%) | 1 (0.9%) |
| Stool infection Positive | 1 (0.9%) | 2 (1.9%) |
| Urine infection Positive | 6 (5.6%) | 6 (5.6%) |

## DISCUSSION

Pregnant women are the main adult group at risk of malaria and are four times more likely to suffer malaria than other adults. Every year an estimated 30 million women living in Africa's malaria endemic countries become pregnant [16]. Pregnancy reduces a woman's immunity to malaria, making her more likely to become infected and affected [16]. Pregnant women's increased vulnerability to malaria can have devastating consequences for both the women and their unborn children. The problems that malaria infections cause during pregnancy differ depending on the type of malaria transmission area [17].

Out of one hundred and eight consented pregnant women who participated in this study, only seventy nine (79) had used IPTp. Late first ANC clinic enrolments and fewer visits have been reported to limit IPTp- SP usage [18]. IPTp-SP users were highly significantly (P = 0.01) older than nonusers, this indicates that usage of IPTp is dependent on age.

Researchers have shown the beneficial effects of IPTp-SP in preventing maternal malaria and improving pregnancy outcome in studies conducted in Africa [9, 20]. In this study there was a strong correlation between IPTp usage and gestation (P=0.01), this might be because the women were already conversant with the routine procedures at the ANC. Therefore, they reported early and regularly and secondly pregnant women at the third trimester are expected to have had several ANC visits during which the IPTp intervention should have been administered [18]. The result of this study is in agreement with survey conducted by Nwaefuna *et al*., 2015 in which more women with pregnancy experience were IPTp users [21].

Pregnant women in primigravidae from malaria-endemic communities with different levels of transmission have high prevalence of malaria infections [22], also placental infection is associated with the presence of malaria parasites in the peripheral blood of clinically symptomatic pregnant women [23]. Thus, there was high significant correlation between IPTp usage and gravity. Studies have shown that pregnant women, especially primigravidae and secundigravidae, are more susceptible to malaria infections [24], additionally reports had indicated that malaria infections were most common among primigravidae and secundigravidae, suggesting that any measure to protect pregnant women against malaria should be prioritized to first and second pregnancies [22]. A simple explanation is that pregnancy is associated with a decrease in immunity; this is more pronounced in primigravidae than in multigravidae [24].

Increasing parity is reflected in the acquisition of antibodies specific for parasite variant antigens expressed on the surface of infected erythrocytes, as a result of the decreasing susceptibility to pregnancy-associated malaria [24, 25]. A high significant correlation between IPTp usage and parity was observed in this study. This finding supports the survey which shows that prevalence of malaria infections is parity-related and primigravidae was the most at-risk group during pregnancy [22, 26].

Malaria prevention consists of a chemoprophylaxis which involves protection of women with intermittent preventive treatment during pregnancy [27, 28]. The prevalence or rate of malaria was lower in pregnant women who had used IPTp than those who did not use IPTp . The lower prevalence may be partly caused by the high ANC attendance rate with high usage of IPTp which may as a result of steady supply including accessibility and adherence of SP in this health facility and women's positive attitudes towards the use the drug during pregnancy [29,30]. This explains the strong correlation between IPTp usage and *P.falciparum* infection.

Maternal anaemia is multifactorial caused poor nutrition, intestinal parasites, and socioeconomic. Status [10, 21] . The lower rate of anemia was observed among pregnant women using IPTp) this is consistent with many findings reported earlier in many countries, which indicates that IPTp is effective in reducing the risk of anemia among pregnant women [9, 10]. Since IPTp-SP was highly effective in reducing maternal malaria-associated anemia in pregnancy [10, 21, 29], therefore this explains the high correlation between the IPTp usage and anaemia.

The interactions between HIV and malaria during pregnancy are complex. The prevalence and density of malaria parasites are higher in pregnant women who are also HIV positive as demonstrated by many researchers [31, 32] . Many studies have also shown that HIV alters the patterns of malaria during pregnancy so that women of all gravidities are at the same level of risk, therefore a strong correlation between the IPTp usage and HIV was observed in our study. This explains the

requirement of at least 3 doses of SP for HIV-positive women as the current recommended preventive therapy for malaria during pregnancy [5].

Conditions such as helminth infections, HIV, and sickle cell disease may contribute to the incidence of anemia among populations in sub-Saharan Africa [30] and research has shown that malaria is the only contributory factor for anemia and severe anemia among pregnant women, this supports the high correlation between the IPTp usage and sickling, stool and urine infection.

In areas of malaria endemicity, the rapid spread of *P. falciparum* parasites that are resistant to SP poses a major threat to the prevention of malaria in pregnancy [33, 34]. SP resistance is mediated through mutations at the genes encoding *P. falciparum* dihydrofolate dihydrofolate reductase (*Pfdhfr*) and dihydropteroate synthase (*Pfdhps*)[35, 36]. In this study patients who received two doses of SP had higher parasite density than those who received one dose. The treatment failures as well as rise in the prevalence of molecular markers of SP resistance have been reported in recent studies [10, 21]. The finding of our study is consistent with research conducted by Braun *et al*., 2015 in which infection prevalence was actually higher in women having taken two as compared to one dose of SP [37]. Survey carried out by Mpogoro *et al*., 2014, indicated that the receipt of ≥ three doses of IPTp-SP was not associated with reduction of peripheral malaria; therefore there was no significant association between parasite density and dosage of IPTp- SP [30].

Since maternal anaemia is associated with malaria and maternal anaemia is associated with many contributory factors such as HIV and other infections [ 21, 10], there was no significant correlation between the IPTp-SP dosage and other parameters because the correlation between parasite density and IPTp-SP dosage was not significant.

***Limitation***

The study was cross-sectional in nature therefore the data did not include follow-up, this limited us from collecting data on placental malaria, congenital and perinatal mortality, and birth weight. However many studies have been conducted on the useful effect of IPTp-SP in the reduction of low birth weight, neonatal mortality and placental malaria [8, 10, 19, 21]. This survey did not represent the wider population in Northern Nigeria; however this hospital was selected for this study because it has enormous ANC clinic attendants [38]. Other limiting factors were inability to assess the number of ANC visits, the timing of these visits and lack of data on effect of IPTp uptake in relation to ANC attendance.

## CONCLUSION

IPTp-SP is useful in the prevention of pregnancy associated malaria, maternal anaemia and other contributing factors. Effort is needed to increase the uptake of optimal doses of IPTp-SP in order reduce SP resistance and the use of ITNs and effective case management, as recommended by the WHO should be encouraged in this malaria –endemic area.

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