The efficacy of sulphadoxine-pyrimethamine in the prevention of peripheral malarial parasitaemia among antenatal attendees at the Ahmadu Bello University Teaching Hospital, Shika-Zaria

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ABSTRACT

Objective: To determine the efficacy of Sulphadoxine-Pyrimethamine (IPT) in the prevention of peripheral malarial parasitaemia among antenatal attendees at the Ahmadu Bello University Teaching Hospital, Shika-Zaria.

Methodology: It was a Cohort study in which women in their index pregnancy, not more than Para 2 between 16 and 24 weeks of pregnancy were recruited. A total of one hundred and eleven participants who fulfilled the inclusion criteria were followed up till 36 weeks of gestation. All participants took Sulphadoxine Pyrimethamine (3 tablets) at booking after assessment and they all had the second dose after four to six weeks. **Results:** At booking 16 (14.4%) of the participants had Malaria Parasites; this figure reduced significantly to 1 (3.6%) at 36 weeks. There was also marked improvement in the packed cell volume.

Conclusion: This study has shown that the use of two treatment doses of Sulphadoxine-Pyrimethamine for the prevention of malaria is associated with a significantly lower prevalence of peripheral malarial parasitaemia, clinical malaria in pregnancy, maternal anaemia, and a high mean packed cell volume.

Keywords: Malaria in antenatal attendees, Prevention, Sulphadoxine-pyrimethamine, ABUTH

Introduction

Malaria continues to be a major health problem in areas of high endemicity like the sub Saharan African countries, causing severe disease in pregnant women and children.[1-3]It is of public health importance in Africa because of the climatic factors, poor environmental sanitation and cultural habits which favour transmission all year round. [4]

Globally, the statistics on malaria are depressing and are getting worse as malaria is still being transmitted in over 100 countries in the tropics and subtropics with over 2 billion people (40% of the world population) permanently at the risk of infection. [4] It is estimated that 90% of the annual 500 million cases of malaria occur in sub Saharan Africa, where 80% of the estimated 1.5-3.0 million annual deaths are attributed to malaria.[5]

Malaria in pregnancy has a high mortality of up to 40% and in Nigeria, malaria

contributes directly or indirectly to 11% of all maternal deaths.[6]

Women who have lived in endemic areas without protection from malaria will have acquired partial immunity from recurrent malaria parasitaemia by the time they are old enough to become pregnant; this is like any other adult indigenous to these endemic areas.[7] Acquired immunity to malaria is grossly undermined by pregnancy probably due to the known alterations in the immune response in the pregnant state (decline in immunity) leading to increased parasitaemia and clinical malaria. [7-10] It remains an established fact that the frequency and severity of malaria is greater in the pregnant than in the non-pregnant state [7, 10] and also that the complications of malaria attack is more likely to result in the pregnant than in the non-pregnant state.[11] It is of importance to note that multigravidae and older women are better protected than primigravidae and younger women in the same endemic area because they have already achieved higher levels of immunity through more past episodes of repeated malaria parasitaemia[7] and of recent, distinct antibodies called anti-adhesive antibodies have been identified in pregnant women in endemic areas mainly in multigravidae but lacking in primigravidae, this lack could explain the increased malaria susceptibility in primigravidae.[7]

The breakdown of immunity against malaria and its associated risk of severe maternal anaemia and adverse effects to the fetus is more marked in the first pregnancies and such tendency decreases with increasing parity.[7-10, 12-15] Maternal mortalities from severe malaria related anaemia in pregnancy in adolescent primigravidae have been reported.[16]

Most immune pregnant women remain asymptomatic even in the presence of parasitaemia, although febrile episodes may occur and in such cases they are usually mild. Nevertheless, high grade fever may occur and lead to pregnancy interruption by causing mid-trimester abortion or preterm labour. [4, 7, 17] Again in areas of endemic malaria, there is an increased risk of maternal anaemia, intrauterine growth restriction (IUGR), and delivery of low birth weight babies, fetal distress, intrauterine fetal death (IUFD), and stillbirth [7,14, 17] which altogether results in increased maternal and perinatal morbidity and mortality.

Previous studies have shown that regular antenatal chemoprophylaxis prevents malaria attack and associated complications

like spontaneous abortion, preterm delivery, intrauterine growth restriction (IUGR) and delivery of low birth weight babies.[7, 13, 18-25] Presently, there is overwhelming evidence indicating the lack of prophylactic effect of weekly Pyrimethamine for chemoprophylaxis against malaria in pregnancy, particularly falciparum malaria in certain endemic areas such as Southwestern Nigeria. [7, 18] Intermittent Preventive Treatment (IPT) involves making available to pregnant women at least two preventive treatment doses of an effective antimalarial drug during the antenatal period. This approach has been shown to be safe, inexpensive and effective. [26-28] The aim of this study was to determine the efficacy of Sulphadoxine-Pyrimethamine (Intermitent Preventive Treatment) in the prevention of peripheral malarial parasitaemia among Antenatal attendees at the Ahmadu Bello University Teaching Hospital, Shika-Zaria. Specifically, this study looked at the prevalence of malaria parasitaemia in peripheral blood smear at booking in the target group and determined the effect of Intermittent Preventive Treatment (IPT) on malaria parasitaemia in the peripheral blood smear of the subjects.

Methodology

It was a Cohort study in which women in their index pregnancy, not more than Para 2 between 16 and 24 weeks of pregnancy were recruited. A total of one hundred and eleven participants who fulfilled the inclusion criteria were followed up till 36 weeks of gestation. All participants who gave their consent took the same batch of Sulphadoxine Pyrimethamine (3 tablets) at booking after assessment under direct observation and they all had the second dose after four to six weeks. Data was collected using a structured questionnaire.

Women that were excluded from the study include those with sickle cell anaemia patients, HIV positive patients, previous adverse reaction (hypersensitivity) to Sulphonamides, those who booked elsewhere, those who previously took S-P combination before booking and those who did not give their consent. Those who took full doses of other anti-malarials were also excluded.

Participants who developed malaria during the study period were treated with Arthemisinin/ Lumefantrine combinations.

All participants continued with their antenatal visits and on each occasion they

were asked of symptoms attributable to malaria as well as other symptoms. They were examined for anaemia and blood pressure measurements were also done as well as symphysiofundal height measurement amongst others. They received haematinics (Fersolate 200mg twice daily and Folic acid 5mg daily) and they were dewormed with two Tablets of Mebendazole. Participants were given insecticide treated nets (ITNs) and encouraged to sleep under it.

Case Definition of Malaria:

In this study, this was defined as the participants who develop fever, headaches, joint pains, nausea/vomiting in the absence of other causes of the above symptoms with or without peripheral malarial parasitaemia.

Laboratory Investigations:

Haemoglobin concentration of the participants was checked at the point of recruitment, according to the routine antenatal care practice, and at 36 weeks in line with the study objectives. Thick and thin blood film for malaria parasite was done as well as parasite count. Specie identification was carried out using standard Giemsa staining. All these were done at the beginning of the study to exclude asymptomatic malaria parasitaemia and repeated at 36 weeks, also in line with the study objectives.

Statistical Analysis:

Information obtained at the end of the study was analyzed using SPSS 17.0 statistical software. Frequency tables were made and results tested for significance using the Student t-test and Chi Square (X^2), with level of significance (α) set at ≤ 0.05.

Results

The antenatal clinic of the ABU Teaching Hospital Shika – Zaria books at least thirty to forty patients weekly. During the period of the study a total of 120 participants were initially recruited and out of these, 111 who fulfilled the inclusion criteria were finally used for the study (5 declined and 4 were lost to follow up) All participants were followed up till 36 weeks of gestation. Forty point five percent of the participants were between the ages of 20-24 years and 35.1% were between 25-29 years as shown in Figure 1.

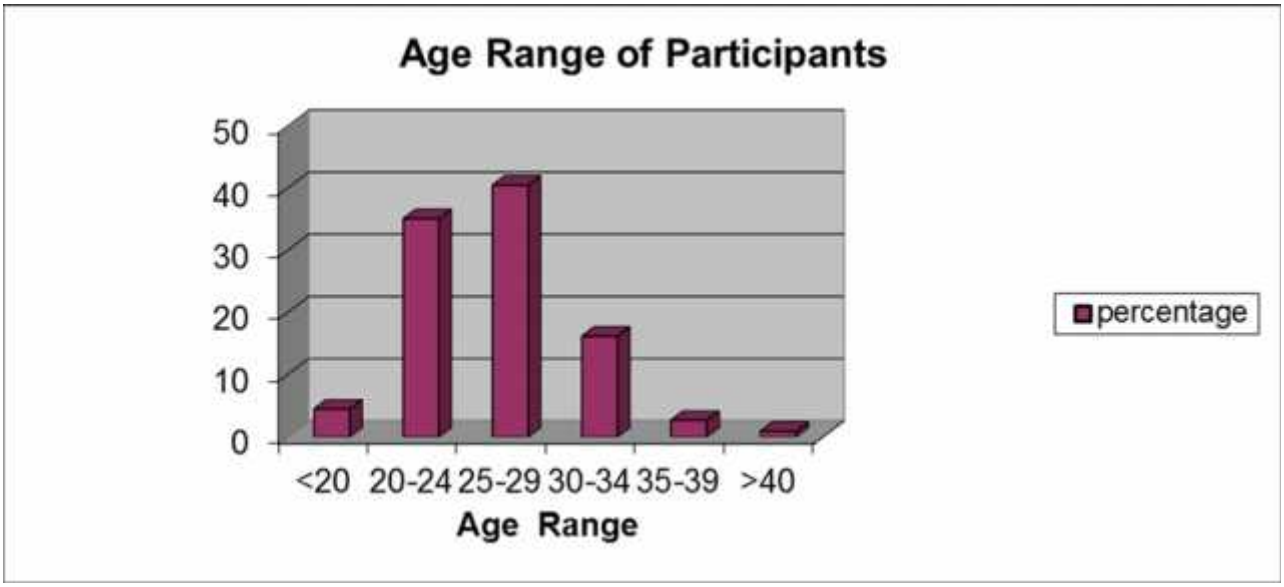

Figure 1: Age Distribution of Participants

Table 1 shows the socio-demographic profile of the participants. Sixty five percent of the participants were of zero parity, 50% had secondary school education and 45.9% were married to civil servants. Ninety five point four percent of the participants booked between 20 and 24 weeks.

At booking 16 (14.4%) of the participants had MPs; this figure reduced significantly to 1 (3.6%) at 36 weeks as shown in figure 2.

Table 1: Socio-demographic profile of Participants:

		FREQUENCY	(%)
A	**Parity :**		
	0	**72**	**(64.8)**
	1	**28**	**(25.2)**
	2	**11**	**(10.0)**
B	**Educational Level**		
	Primary	**8**	**(7.2)**
	Secondary	**56**	**(50.5)**
	Tertiary	**47**	**(42.3)**
C	**Husband's Occupation**		
	Civil servant	**51**	**(45.9)**
	Skilled	**15**	**(13.5)**
	Unskilled	**2**	**(1.8)**
	Student	**4**	**(3.6)**
	Unemployed	**1**	**(0.9)**
	Others	**38**	**(34.2)**
D	**G/A at Booking**		
	<20 weeks	**2**	**(1.8)**
	20- 24 weeks	**106**	**(95.5)**
	>24 weeks	**3**	**(2.7)**

Of the 16 participants who had parasitaemia, 15 had MPs of one plus and 1 had MPs of two pluses. At 36 weeks the only participant who had parasitaemia had MPs of one plus. All participants took Sulphadoxine Pyrimethamine (3 tablets) at booking after assessment and they all had the second dose after four to six weeks. Participants continued their normal Antenatal care. Only 11.7% of the participants took some form of antimalarial before booking and of these 10.8% took Chloroquine while only one participant 0.9% took Artemisinin/Lumefantrine combination.

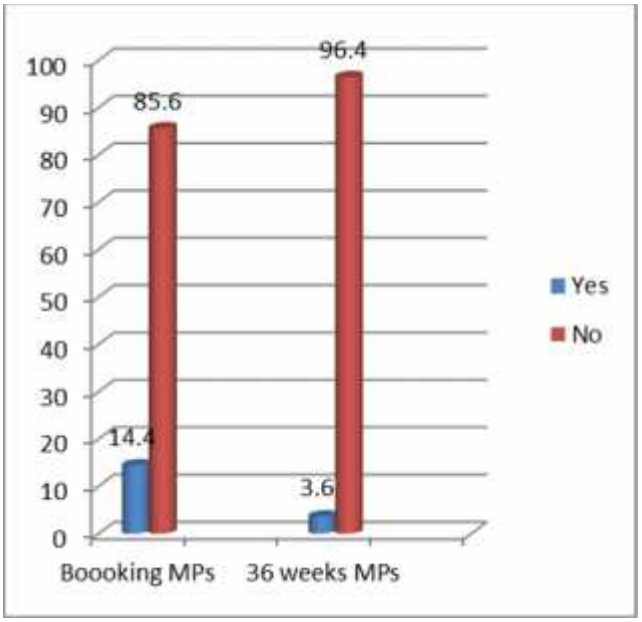

Figure 2: Peripheral Malaria Parasitaemia at Booking and at 36 weeks

Table 2: Symptomatic Malaria among Participants at First Visit Relevant History

Symptoms	Frequency (%)
Headache/ Fever	4 (3.6)
Dizziness/weakness	1 (0.9)
Joint pains	1 (0.9)
None	105 (94.6)
Signs	
Febrile	4 (3.6)
Palor	1 (3.6)
None	106 (95.5)

Figure 3 shows that 55% of the participants had a Packed cell volume of above 34% at booking, and this increased significantly to 79.3 % at 36 weeks. Forty one percent had a Packed cell volume of 29% -33% at booking and this number reduced to 18.9% at 36 weeks. During the first visit after the first dose of SulphadoxinePyrimethamine four patients (3.6%) complained of headache/fever, one complained of dizziness/weakness (0.9%) and another had joint pains (0.9%); among them four were febrile (0.9%) one was mildly pale, (0.9%) as shown in Table 4. These patients were treated with Athermisinin/ Lumefantrine combinations and they took the next dose of SulphadoxinePyrimethamine subsequently.

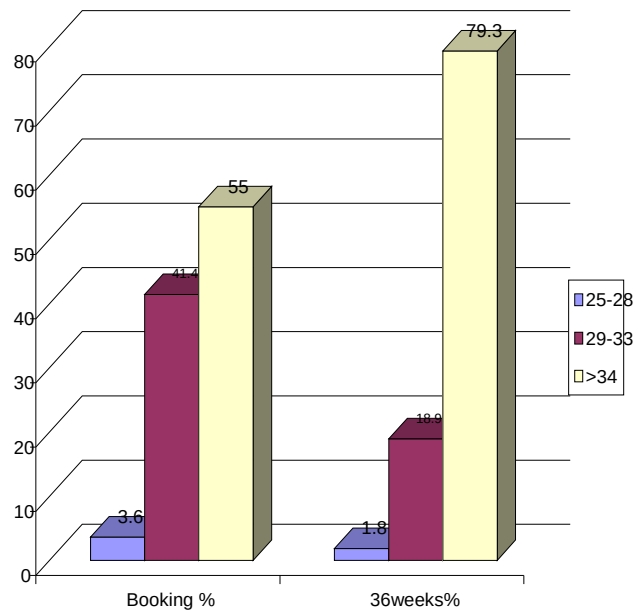

Figure 3: PCV at Booking and at 36 weeks

Table 3: Relationship between ITNs& Booking Mps Booking MPs

	Yes	No	Total
ITN Yes	10	61	71
No	6	34	40
Total	16	95	111

Pearson's Chi Square(X^2) = 0.017; df = 1; p-value = 0.895

Table 4: Relationship Between Type of Residence & Booking Mps Booking MPs

	Yes	No	Total
Slum/Squatter	11	54	65
Others	5	41	46
Total	16	95	111

Pearson's Chi Square(X^2) = 0.800; df = 1; p-value = 0.371

No other participant had symptoms or physical signs suggestive of malaria till 36 weeks. Sixty one of the participants who had ITNs in their houses did not have peripheral malarial parasitaemia at booking as compared to 34 who did not have ITNs; this is shown in Table 3. The p value was 0.895 and this was not found to be statistically significant. Table 4 shows that more participants lived in Squatter/ Slum (65) and a higher number of such people had malarial parasitaemia at booking (11) than those who lived in other types of residence (5). The p value was 0.371 and this relationship was also not statistically significant.

Of the 61 participants who had a Packed cell volume of above 34%, 51 did not have MPs at booking compared to only 10 who had MPs; this relationship was not statistically significant (p value was 0.599) as shown in Table 5. Table 6 shows that 88 of the participants who had a Packed cell volume of more than 34% did not have MPs at 36 weeks, p value was <0.001, and this was statistically significant. The average number of clinic visits by participants was six.

Table 5: Relationship between PCV and Mps at Booking Booking MPs

		Yes	No	Total
PCV	25-28	1	3	4
	29-33	5	41	46
	>34	10	51	61
Total		16	95	111

Pearson's Chi Square(X^2) = 0.026; df = 1; p-value = 0.599

Table 6: Relationship between PCV & Mps at 36 weeks Mps at 36 weeks

		Yes	No	Total
PCV	25-28	1	1	2
	29-33	3	18	21
	>34	0	88	88
Total		4	107	111

Pearson's Chi Square (X^2) = 22.582; df = 2; p-value < 0.001

Discussion

This study was conducted among pregnant women of low parity in a tertiary hospital in the Northern part of Nigeria in order to determine the efficacy of Sulphadoxine Pyrimethamine (S-P) in the prevention of peripheral malarial parasitaemia among antenatal attendees.

The finding support previous studies that have consistently shown S-P combinations to be extremely effective in the prevention of malaria in pregnancy. These studies have shown that the use of S-P combinations is associated with a very low prevalence of peripheral and placental malarial parasitaemia, malaria related anaemia and delivery of low birth weight babies. [20, 29,30] Although most authors worked using 2 to 3 treatment doses of S-P, a few of them have shown that even women who booked late and received only one treatment dose of S-P on evaluation following the first dose of S-P showed a significant benefit from this intervention. [20]

In this study, the participants had two treatment doses of S-P and they were found to have a very low incidence (3.6%) of peripheral parasitaemia at 36 weeks. This figure is slightly lower than 5.3% reported by Shulman et al among low parity women in Kenya [20]Ojo T. O in Ile-Ife, Nigeria (6.6%) [31] and also Challis et al (6.3%) in Mozambique.[32] This differences may be due to the smaller sample size in this study and the later end point of the study which was 36 weeks and not 34 weeks as was in the Ile-Ife study.

The 96.4% of the pregnant women in this study who did not have peripheral malaria parasitaemia at 36 weeks are most likely to have reduced incidence of placental malaria parasitaemia and low birth babies if followed to delivery.

Maternal anaemia with its attendant complications remains a major challenge to the Obstetrician practicing in this environment, and malaria is a major cause. In this study it was found out that the use of two treatment doses of S-P was associated with a significant increase in the mean Packed Cell Volume at 36 weeks (33.9± SD3.00 and 36.1± SD 2.7) this result is consistent with the findings of other investigators. [20, 33, 34]

This study also shows that there is a low incidence of clinical malaria among the participants as shown in Table II. (The participants were booked and on haematinics; most were educated and employed.) Those who developed clinical malaria were treated promptly and they continued with the study.

The following were some limitations of this study. The use of a control group was not possible in this study due to ethical reasons. A comparison with another drug used for antimalarial prophylaxis in pregnancy like Pyrimethamine alone will have been ideal but it will be unethical to administer such drug to patients in the light of current evidence in favour of Sulphadoxine-Pyrimethamine and also this will go contrary to the recommendation of the National Guideline on Malaria in pregnancy. Giving a placebo will also be unethical because this will be withholding the benefits of Sulphadoxine Pyrimethamine in the patients attending antenatal care in this centre.

Conclusion

In conclusion, this study has shown that the use of two treatment doses of S-P for the prevention of malaria is associated with a significantly lower prevalence of peripheral malarial parasitaemia, clinical malaria in pregnancy and maternal anaemia, and a high mean Packed Cell Volume in pregnant women as their pregnancy advanced.

It is therefore recommended that Sulphadoxine Pyrimethamine be made widely available in all health centers in the country and provided free of charge to all pregnant women because of it proven efficiency in the prevention of malaria in pregnancy and its sequelae.[35]

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