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Malaria and anemia in pregnancy: A case control study on the effectiveness of intermittent preventive treatment with Sulphadoxine Pyrimethamine against malaria and anemia in Madina

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Malaria is a parasitic infection transmitted through the bites of female Anopheles mosquitoes carrying Plasmodium and is often complicated by anemia. This co-morbidity significantly contributes to maternal and fetal illnesses. Over the years, intermittent preventive treatment with Sulfadoxine-Pyrimethamine (IPTp-SP) has been a key preventive measure against malaria and anemia in pregnant women. Malaria during pregnancy is a considerable public health concern, and IPTp-SP is recommended to address this issue, although concerns about resistance exist. This study aimed to assess the effectiveness of IPTp-SP against malaria and anemia among pregnant women in Madina, Ghana. The research conducted a case-control study involving 174 pregnant women attending antenatal clinics in Madina. Blood samples were collected to assess malaria parasites and hemoglobin levels, and structured questionnaires were used to evaluate knowledge, attitudes, and perceptions. The study found that the use of IPTp-SP was associated with a significantly lower prevalence of malaria ($p<0.05$) and higher mean hemoglobin levels ($p<0.05$) compared to non-users. Most women demonstrated good knowledge and positive attitudes toward IPTp-SP. Despite its effectiveness, improving compliance is necessary to optimize the benefits of IPTp-SP against malaria and anemia during pregnancy in this region.

Key words: Anaemia, haemoglobin, malaria, parasitemia, Sulphadoxine Pyrimethamine.

INTRODUCTION

Malaria, a parasitic infection transmitted through the bites of female Anopheles mosquitoes carrying Plasmodium species, poses a significant global health concern (White et al., 2014). *Plasmodium falciparum*, the predominant cause of malaria in humans in sub-Saharan Africa, is responsible for the majority of malaria-related deaths worldwide (White et al., 2014). Outside of sub-Saharan Africa, Plasmodium vivax is the most prevalent malaria-

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causing agent in regions such as Central and South America, North Africa, and the Middle East (Phillips et al., 2017). The prevalence of malaria is influenced by factors such as altitude, age, and topography, with tropical regions characterized by high rainfall and colder climates posing a greater risk of parasitic infection (Afrane et al., 2014). The life cycle of the *Anopheles* mosquito consists of four stages: eggs, larvae, pupa, and imago (adult stage) (Crans, 2004). While the first three stages occur underwater, the adult mosquito lives outside water for approximately one month, during which it transmits malaria to humans through blood meals (Crans, 2004). This transmission is influenced by climate conditions, including colder temperatures and high rainfall patterns. Certain population groups, such as pregnant women, children under five years old, immunocompromised individuals, and unexposed immigrants, are particularly susceptible to malaria (WHO, 2017). Fortunately, malaria is both preventable and treatable through measures such as intermittent preventive treatment, vaccines, insecticide-treated nets and sprays, and antimalarial drugs (WHO, 2017).

Pregnancy, a nine-month period involving the development of an embryo, consists of three trimesters, with the second trimester being crucial for fetal development and susceptibility to congenital malformations (American College of Obstetricians and Gynecologists, 2017; Celen et al., 2012). Pregnant women require regular monitoring through frequent visits to antenatal clinics, nutritional supplementation, and intermittent preventive treatments, regardless of malaria status (Omics International, 2014; WHO, 2018, 2016). Malaria during pregnancy contributes to maternal and fetal mortality and morbidity, including maternal anemia, low birth weight, and intrauterine growth retardation (Guyatt and Snow, 2004).

P. falciparum is a major causative agent of severe falciparum malaria (Theodore et al., 2023). Poor nutrition and weakened immune systems, such as those in HIV patients, increase the risk of malaria (WHO, 2017; Apte and Katona, 2008). In malaria-endemic areas, where *P. falciparum* infection is intense, over 50 million women experience pregnancy each year, making them more exposed and susceptible to infection (Steketee et al., 2001).

Anemia, characterized by insufficient red blood cells or hemoglobin, is a major complication of malaria and poses risks to both maternal and fetal health (Castro-Gomes et al., 2014; Lane and Vieth, 2014). According to the World Health Organization, there are still cases of increased pregnancy-related malaria due to the non-use of interventions for various reasons, such as low antenatal care attendance, shortage of supplies, poor patient compliance, and resistance to the drug, leading to an increase in malarial incidence (Okell et al., 2017).

Resistance to Sulfadoxine-Pyrimethamine (SP) prophylaxis is increasing due to mutations in humans, particularly in the dihydropteroate synthase and dihydrofolate reductase genes, leading to treatment failure of the SP prophylaxis upon administration (Okell et al., 2017).

Preventing malaria among pregnant women primarily relies on intermittent preventive treatment in pregnancy (IPTp), with SP being the recommended antimalarial drug (WHO, 2017; Ministry of Health, 2005).

SP prevents the use of folinic acid by *Plasmodium* parasites, disrupting their life cycle and reducing parasite oocysts (Aminatou et al., 2010). Adhering to IPTp-SP guidelines, pregnant women should receive a minimum of three doses starting in the second trimester at monthly intervals to reduce peripheral and placental parasitemia, anemia, and associated complications (World Health Organization, 2016). However, despite these interventions, pregnancy-associated malaria remains a significant problem in Ghana, where it contributes to poverty, decreased productivity, and high malaria incidence (WHO, 2017; National Malaria Prevention Control, 2017).

The Ghana National Malaria Control Program aimed for 100% coverage of pregnant women with SP, but the achievement of this objective has been limited, particularly in the Northern, Ashanti, and Southern regions of Ghana (Anto and Boateng, 2017). Non-adherence to IPTp-SP treatment and the emergence of drug resistance pose additional challenges (WHO, 2017; Okell et al., 2017).

The WHO defines anemia in pregnancy as having an hemoglobin level less than 110 g/dL in the first and third trimesters and less than 105 g/dL in the second trimester. Worldwide, anemia affects more than 40% of pregnant women and an estimated 30% of women of childbearing age. South-East Asia and Africa have the highest rates of anemia among pregnant women (48.7 and 46.3%, respectively) (WHO, 2018). Considering the endemic nature of malaria in Ghana and the importance of preventing the disease among pregnant women, further research is imperative to evaluate the impact and effectiveness of SP in reducing malaria and anemia during pregnancy.

Although some studies have explored the efficacy of SP, they have not fully examined its effects on anemia or birth outcomes, making additional research essential (Chalwe et al., 2014; Mikomangwa et al., 2020). By improving the evaluation of IPTp-SP effectiveness, this study aims to contribute to existing knowledge, inform future research, and reduce the health and socio-economic burdens faced by pregnant women and other stakeholders. Therefore, the aim of this study is to investigate the comorbidity between malaria and anemia in pregnancy among women attending two selected antenatal clinics in Accra and to evaluate the contribution of SP in reducing malaria during pregnancy by comparing the hemoglobin levels of pregnant women who take SP with those who do not take the medication.

METHODOLOGY

Study design

A case-control study was conducted in Madina among pregnant women in their second and/or third trimesters attending antenatal care clinics. Study participants were recruited upon informed consent in accordance with the Allied Health Ethical and Protocol Review Committee. The study group comprised 110 pregnant women on IPTp-SP, while the control group included 64 pregnant women who did not take IPTp-SP.

Study site

This study was conducted in the antenatal clinics of two selected hospitals, both in the La-Nkwantanang Municipal Assembly. Pentecost Hospital, Madina, is approximately 2 km away to the south of the University of Professional Studies, and Madina Polyclinic-Kekele is close to the Madina market and two major lorry stations. Both facilities receive attendees from Madina estates, the Madina Zongo communities, Ashaley Botwe, Adjiringanor, Ogbojo, and others.

Data collection methods

Prior to conducting the survey, all investigators at each hospital received similar training. Each questionnaire was independently filled out by two people and subsequently confirmed by a third person. An inspector reviewed each filled questionnaire. Structured questionnaires were given to the participants to obtain information on socio-demographic characteristics, obstetric history, IPTp-SP use, nutritional supplements such as iron and vitamins, medical history such as HIV status, glucose-6-phosphate dehydrogenase (G6PD) deficiency, sickle cell disease, and other complications, including malaria, severe anemia, and helminth infections. The questionnaire also included questions assessing the perceptions of the selected women on malaria and anemia.

Laboratory techniques

Laboratory work was the main research approach in this study. Blood samples were obtained by capillary puncture. Blood films were stained with 10% Giemsa stain for 15 min and examined under a x100 microscope with oil immersion for malaria parasites. A thick film was considered negative if it showed a number of parasites less than 100 per microscopic field. For quality control, 10% of negative samples and 20% of supposed positive samples were obtained and re-examined with different microscopes. The hemoglobin level of pregnant women was measured to the nearest 0.1 g/dl using a Hemocue meter.

Sampling technique and sample size

The sampling of participants was done using both purposive and stratified random sampling techniques. Over a period of two weeks at each facility, a total of 174 pregnant women were sampled from both antenatal clinics according to the ratio of their biweekly attendances.

Inclusion and exclusion criteria

The selection of participants was based on a gestational age of ≥ 13 weeks (second trimester), whether primigravida or multigravida, ≥ 18 years of age, who had attended at least one antenatal care (ANC) session. Participants who were HIV positive, had sickle cell anemia, and had other complications, excluding malaria, such as hemorrhage, sepsis, and helminths infection were not selected.

Ethical concerns

Permission was sought from the hospital administrators, and ethical issues such as written informed consent, privacy, and confidentiality were observed. The purpose and necessity of the research were fully explained to the participants, as well as the risks and benefits. Ethical clearance was obtained from the Allied Health Ethical and Protocol Review Committee of Radford University College with protocol number AHEPR23/02/21.

Reliability and validity of the study tool

This study utilized standard laboratory techniques like Giemsa staining and Hemocue for diagnosing malaria and anemia, respectively. These are well-established methods with high sensitivity and specificity for parasite detection and hemoglobin quantification. The study also used structured questionnaires to assess knowledge and perceptions about malaria in pregnancy. To evaluate the reliability of the knowledge and perception questionnaire, a test-retest assessment was conducted with a subset of participants completing the survey at two different timepoints; a strong correlation between responses at time 1 and time 2 ($r = 0.85$, $p < 0.001$) supports the reliability of this tool.

Data analysis

All data were entered into and analyzed with SPSS version 23. Frequencies and Pearson's Chi-square test were used to compare the relationship between variables. Statistical significance was defined as $p < 0.05$.

RESULTS

Relationship between trimester and gravidity

A total of 174 pregnant women participated in this study, of which 54 were primigravidae and 120 were multigravidae. In the second trimester, there were 22 primigravidae and 44 multigravidae, for a total of 66 women, while the third trimester had 32 primigravidae and 76 multigravidae out of a total of 108 women (Table 1). The results of this study suggest that there is a higher proportion of multigravidae in the third trimester than in the second trimester.

Relationship between species usage and malaria results

A total of 172 participants tested negative for the malaria parasite test. Of this number, 108 had taken SP while 64 had not taken SP. Although the remaining two participants had taken SP, they were positive for the malaria parasite test (Table 2).

Relationship between species usage, hemoglobin levels and malaria infection

Blood samples for hemoglobin estimation were obtained

Table 1. Distribution of pregnant women by trimester and gravidity.

Trimester	Gravidity		Total
	Primigravida	Multigravida	
Second trimester	22	44	66
Third trimester	32	76	108
Total	54	120	174

Table 2. Distribution of pregnant women by SP usage and malaria parasite.

Variable	Malaria parasite		Total
	Negative	Positive	
Yes	108	2	110
No	64	0	64
Total	172	2	174

Table 3. Hb levels of study participants per usage of SP.

Usage of SP	HB Level						Total
	Normal		Low		High		
	Frequency	Percent	Frequency	Percent	Frequency	Percent	
Yes	81	73.6	27	24.6	2	1.8	110
No	43	67.2	21	32.8	0	0.0	64
Total	124	71.2	48	27.6	2	1.2	174

from all participants in both facilities. The majority of the women on SP had normal hemoglobin levels compared to those not on SP (73.6% as against 67.2%). 32.8% of those who had not taken SP, as well as 24.6% of those on SP, had low hemoglobin values, and 1.8% of participants on SP had values above the normal range (Table 3). Two of the samples collected from women on IPTp-SP were positive for malaria, while no positive result was recorded from those not on SP (Figure 1). The general prevalence of malaria in this study was 1.2%.

Relationship between species usage, species dosage, hemoglobin levels and trimester

During the initial prenatal visit, measuring hemoglobin is a common test among pregnant women to assess physical health and anemia. Thus, this study focused on hemoglobin levels during the second and third trimesters (Table 4 and Figure 2).

The hemoglobin levels were also monitored across the various trimesters with respect to the SP dosage taken by the participants (Table 6).

Knowledge and perception of pregnant women on malaria and anemia

Out of 174 participants, 90.8% reported malaria to be caused by bites from infected mosquitoes, with 72.4% reporting that pregnant women, children, and newborns were at the most risk of malaria. 67.2% of the participants knew malaria is dangerous to the mother and transmissible to the fetus. 63.2% agreed that a pregnant woman with malaria is prone to having anemia. On average, 78.8% of pregnant women have sufficient knowledge and a good understanding of malaria and anemia during pregnancy. Apart from the usage of SP that had a significant correlation with the trimester of pregnancy ($\alpha = 0.05$, $p < 0.05$), all other parameters analyzed in this study showed no significant correlation.

DISCUSSION

In Ghana, malaria is the leading cause of disease and death, having an adverse effect on various socio-demographic categories. It adds to the nation's comparatively high maternal mortality rate, which accounts for 11% of all deaths among pregnant women (Wilson et al., 2011). Although anemia is still a serious problem in sub-Saharan Africa, malaria is a major cause of maternal and perinatal morbidity and mortality in these countries (Asa et al., 2008). WHO emphasizes that each pregnant woman should receive IPTp-SP at each ANC visit after quickening, which, in practice, leads to two or

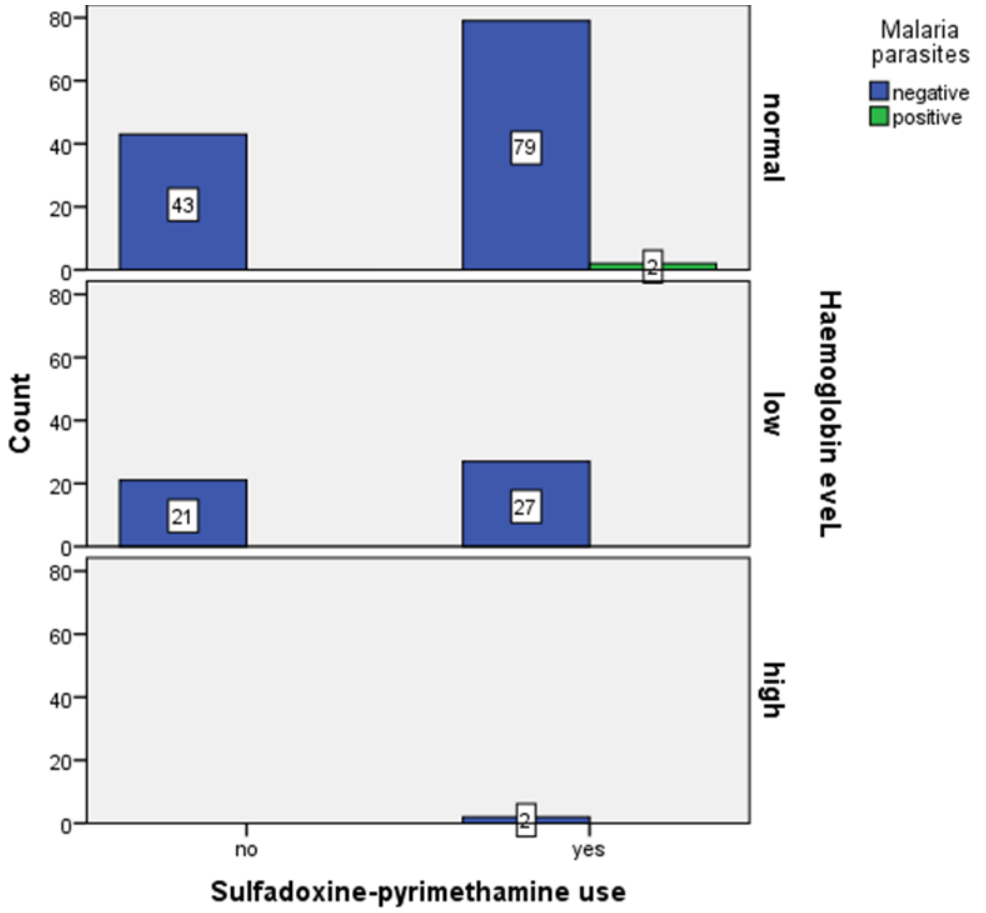

Figure 1. SP usage, Hb level and malaria results among study participants.

Table 4. Cross tabulation between Hb level, SP usage and dosage of SP taken.

HB level			SP dose						Total
			0	1	2	3	4	5	
Normal Hb	SP (Y/N)	Yes	23	28	21	7	1	1	81
		No	20	10	8	5	0	0	43
Low Hb (Anemia)	SP (Y/N)	Yes	6	8	8	5	0	0	27
		No	15	0	3	3	0	0	21
High Hb	SP (Y/N)	Yes	0	0	2	0	0	0	2

three doses during the course of the pregnancy (World Health Organization, 2018). This recommendation is based on reports of beneficial effects of IPTp-SP in preventing maternal malaria and improving pregnancy outcome in studies conducted in Africa (Asa et al., 2008). This study aimed at investigating the comorbidity of malaria and anemia among pregnant women reporting to antenatal clinics of two hospitals in Madina, Accra-Ghana. One hundred and seventy-four (174) expectant mothers who were eligible for SP partook in the study, but only 110/174 had used the drug. A study in Ghana by Ekene et al. (2015) reported low usage among pregnant women. This may be attributed to late and inconsistent visits to ANC clinics. Whereas this study did not collate data on visit frequency, previous reports show late ANC clinic accession and lesser visits lower patronage of

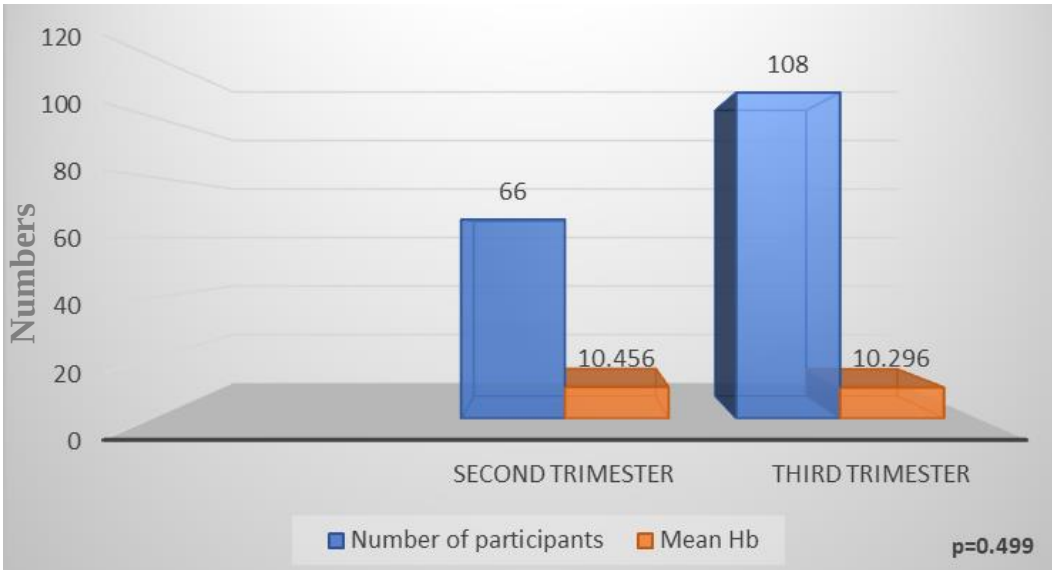

Figure 2. Comparison between Hb across the various trimesters.

Table 5. Cross tabulation between Hb level, SP usage and dosage of SP take.

HB level			Trimester		Total
			Second trimester	Third trimester	
Normal Hb	SP (Y/N)	Yes	23	58	81
		No	23	20	43
Low Hb (anemic)	SP (Y/N)	Yes	6	21	27
		No	13	8	21
High Hb	SP (Y/N)	Yes	1	1	2
Total			66	108	174

IPTp SP (Anchang-Kimbi et al., 2014).

This study revealed that the majority of the study participants who were on SP were in their third trimester (Table 5), and this is similar to the findings of Ekene et al. (2015). Gestation was markedly associated with IPTp use. Although the difference in mean hemoglobin across both trimesters in this study was statistically insignificant, the few studies investigating hemoglobin levels and obstetric outcomes revealed inconsistent results due to significant disparities in study designs, sample sizes, populations, and the time of hemoglobin assessment. In this current study, a large proportion of pregnant women in their third trimester who were taking IPTp-SP had normal hemoglobin levels compared to those who were not taking IPTp-SP; an observation explainable by a longer duration of therapy, thus more doses of SP for compliant mothers by the third trimester. Although two pregnant women in this study had high hemoglobin, increased maternal hemoglobin has not garnered as much concern as anemia due to the likelihood that it may be seen as a sign of adequate nutrition. The efficacy of IPTp-SP in lowering the prevalence of maternal anemia will enhance pregnancy outcomes (Shulman et al., 1999). In this study there was an increase in anemia in pregnant women without SP than pregnant women on SP. The lower rate of anemia in pregnant women on SP and severe anemia observed among pregnant women without SP was consistent with the findings reported earlier in Malawi, where the use of SP was associated with a higher maternal hemoglobin level (Kalilan et al., 2010). Research studies in Nigeria (Asa et al., 2008), Kenya and other regions of Africa, demonstrate that it is effective in reducing the risk of anemia among pregnant women (Steketee et al., 2001; Kayentao et al., 2005). The results from this study demonstrate the effectiveness of SP in reducing the prevalence of malaria and a viable

Table 6. Cross tabulation between Hb level, SP usage, dosage of SP taken and trimester.

Hb level	Trimester	SP dose						Total
		0	1	2	3	4	5	
Normal Hb	Second trimester	17	15	8	6	0	0	46
	Third trimester	26	23	21	6	1	1	78
Low Hb (Anemia)	Second trimester	11	1	4	3	0	0	19
	Third trimester	10	7	7	5	0	0	29
High Hb	Second trimester	0	0	1	0	0	0	1
	Third trimester	0	0	1	0	0	0	1

technique for lowering the risk of anemia.

Conclusion

The study suggests that a significant number of pregnant women in their third trimester, who were taking IPTp-SP, had normal hemoglobin levels compared to those who were not taking IPTp-SP. Although two pregnant women in this study had high hemoglobin levels, increased maternal hemoglobin has not garnered as much concern as anemia due to the likelihood that it may be seen as a sign of adequate nutrition. The efficacy of IPTp-SP in lowering the prevalence of maternal anemia will enhance pregnancy outcomes (Shulman et al., 1999). In this study, there was an increase in anemia in pregnant women without SP than pregnant women on SP. The lower rate of anemia in pregnant women on SP and severe anemia observed among pregnant women without SP was consistent with the findings reported earlier in Malawi, where the use of SP was associated with a higher maternal hemoglobin level (Kalilan et al., 2010). Research studies in Nigeria (Asa et al., 2008), Kenya, and other regions of Africa demonstrate that it is effective in reducing the risk of anemia among pregnant women (Steketee et al., 2001; Kayentao et al., 2005). The results from this study demonstrate the effectiveness of SP in reducing the prevalence of malaria and a viable technique for lowering the risk of anemia.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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