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EFFECTIVENESS OF INTERMITTENT PREVENTIVE TREATMENT WITH SULPHADOXINE-PYRIMETHAMINE AND INSECTICIDE TREATED NETS ON THE PREVENTION OF MALARIA IN PREGNANCY IN NON-MALARIAL ENDEMIC AREA IN KENYA

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ABSTRACT

***Background*: Malaria prevention strategies have significantly reduced the prevalence of malaria in pregnant women in several studies done in malaria endemic regions.**
***Objective*: To determine the effectiveness of Intermittent preventive treatment with sulphadoxine-pyrimethamine and Insecticide treated nets on the prevention of malaria in pregnancy in a non-malaria endemic area.**
***Design*: Comparative study.**
***Setting*: Kapsabet District Hospital in Nandi County.**
***Subjects*: One hundred and fourty three non-randomised pregnant women were followed through the Antenatal clinic before 28 weeks gestation until delivery and compared with records of 600 pregnant women (non-intervention arm), who attended ANC and delivered at the hospital.**
***Results*: The incidence of malaria infection in pregnancy was 21% in the non-intervention group compared with 8% in the intervention group, (p-value 0.000). The incidence of low birth weight was 12.5% in the non-intervention group compared with 5.6% in the intervention group (p-value 0.018); with a reduction of low birth weight by 50% in the intervention group. The incidence of Still births was 6% in the non-intervention group and 1.4% in the intervention group (p-value 0.025). There were two (0.3%) cases of maternal mortality in the non-intervention group and no mortality in the intervention group which was statistically not significant but clinically significant.**
***Conclusion*: The use of intermittent preventive treatment with sulphadoxine-pyrimethamine and Insecticide Treated Nets is effective in prevention of malaria in pregnancy in non-malaria endemic region and is associated with reduction of adverse pregnancy outcome. There is therefore a need of up scaling the use of sulphadoxine-pyrimethamine during pregnancy, and availing subsidised long lasting insecticide treated bed nets to pregnant women countrywide.**

INTRODUCTION

In Africa it is estimated that twenty five million pregnant women are at risk of malaria infection during the antenatal period (1-3). Malaria is a febrile illness caused by the *plasmodium falciparum ,vivax, ovale* and *malaria.* The *plasmodium falciparum* contributes up to 98% of malaria cases. In moderate to high transmissions areas the point prevalence of malaria infection in pregnancy (peripheral or placental) in all gravidae is estimated at 27.8% (4). The pregnant woman is most at risk especially in the second trimester due to the tendency of the malaria parasite hiding in the placental bed (5,6) . Pregnancy associated malaria results in several adverse outcomes which are; maternal anaemia, low birth weight (Lbwt), preterm deliveries and congenital malaria, perinatal and maternal death. Maternal death attributable to malaria from direct and indirect causes in low / high transmission areas is between 93-320 / 100,000 live births are findings from studies done in high endemic areas such as Mozambique and Gambia (7,8). In malaria endemic regions, malaria contributes to 70% of Intra Uterine Growth Restriction (IUGR) and 36% of

preterm deliveries, sever anaemia 26% (9,10), 20% of Low birth weight (<2500g) (4, 11). In high transmission areas of Africa, malaria induced Lbwt is estimated to be responsible for between 62,000-363,000 infant deaths every year which translates to 3-17 deaths per 1,000 live births (12). In malaria endemic region transmissions are common throughout the year (perennial). In Kenya there are two regions; around Lake Victoria and along the coast (13). While in non-malaria endemic regions there is limited transmission throughout the year but potential for epidemic outbreaks such as the highland districts of Kenya (13). World health organization (WHO) recommends a three-pronged approach to the prevention and management of malaria in pregnancy, which are: Two doses of sulphadoxine –pyrimethamine (SP) during pregnancy, Use of insecticide treated nets (ITNs) and Case management (14).

Meta-analysis of intervention trials suggest that successful prevention of malaria infections decrease the risk of maternal anaemia by 38%, Lbwt by 43%, and perinatal mortality by 27% (1). Intermittent preventive treatment with SP (IPT-SP) was found to reduce the prevalence of maternal parasitaemia to 10.4% in a study done in Nigeria (15). In other countries in Africa it was found out that use of ITNs in pregnancy was beneficial to maternal and foetal outcome but is not significant on the reduction of the prevalence of malaria (16). The Government of Kenya (GOK) policy on prevention and management of malaria in pregnancy is: To ensure that all pregnant women living in malaria areas will have access to two SP doses at 16-27 weeks and 28-36 weeks, to increase access to ITNs amongst people at risk especially young children and pregnant women, and Effective community based communication to encourage prompt treatment of fever (14). The GOK targets by 2006 were: To have 60% of pregnant women receiving two SP in second and third trimester (23). There are variations among African countries (Kenya included), as follows, 33-93% for one dose and 24-68% for the two or more doses (1). Another target was to have 80% of fever or anaemia cases to be appropriately managed at ANC services and to achieve over 60% of pregnant women to sleep under treated nets during their confinement. By December 2006, 50% of pregnant women were using ITNs (14,17).

Studies at malaria-endemic regions of Kisumu and Kilifi had demonstrated significant reduction in incidence of anaemia among pregnant women following administration of IPT-SP. There is also strong evidence to suggest decreased incidence of LBwt following IPT-SP (18). The study in Bondo demonstrated that IPT-SP is effective in controlling maternal anaemia in areas of high transmissions especially among primigravidae, however the use of ITNs alone showed a substantial protective effect against anaemia in primigravidae (19).

Evidence from studies in Siaya, Kenya, confirms findings from Gambia that ITNs may confer some protection against malaria infection among pregnant women (20). Evidence from other areas in Africa is less conclusive, but areas of epidemic risk in South East Asia have shown significant protection against anaemia and low birth weight through the use of ITNs by pregnant women (21).

GOK implemented the IPT-SP policy in the year 1998 and currently the coverage is 33-93% in malaria prone areas (22). ITNs access was equally improved in the year2004 / 2005 by provision of subsidised treated nets to children and pregnant women through ANC and in the year 2006 there was distribution of ten million free ITNs to vulnerable groups in malaria prone districts (23). Therefore a larger proportion of pregnant women are on IPT-SP and more than half of them sleep under treated nets in most of malaria prone districts. The study was conducted in Central Nandi district where IPT-SP coverage was 88.5% for both first and second doses. The current national malaria guidelines on prevention of malaria during pregnancy recommends IPT-SP and ITN for all pregnant women in malaria endemic and non-malarial endemic regions. However, the effect of this in non- malaria endemic regions has not been objectively evaluated. This study aims to determine the effectiveness of the interventions. Understanding the effectiveness and dynamics of the interventions on malaria during pregnancy in this region will help to revise malaria preventive approaches during pregnancy.

Other studies have shown that in Africa 11.4% (100,000) of all infant deaths in endemic areas is caused by malaria associated Lbwt (24), the effect of Lbwt is greatest in infants born to primigravida contributing to 17.6% of neonatal deaths and 9.8% of infant deaths (25). Nine hospital based studies showed that placental malaria was associated with twice the risk for stillbirth (26). More recent reports from both malaria endemic and non-endemic areas show higher prevalence of congenital malaria ranging from 8% to 33%, these were detected by use of PCR (27,28). The Abuja declaration of April 2000 at the Africa head of states summit on `Roll Back Malaria`(RBM) recognised the disease and its economic burden that malaria places on hundreds of people and the barriers it contributes to development and alleviation of poverty (27). There is little information on the effectiveness of the intervention on Malaria prevention in pregnancy in the non-endemic areas. The objective of the study was to determine the effectiveness of Intermittent preventive treatment with sulphadoxine-pyrimethamine and Insecticide treated nets on the prevention of malaria in pregnancy in a non-malaria endemic area. The study participants were fully informed about the study before being requested to participate. An informed consent was obtained from all the participants recruited into the

study. Approval was obtained from Kenyatta National Hospital / University of Nairobi Ethics and Research Committee. Permission was sort for and granted by the hospital medical superintendent to conduct the study.

MATERIALS AND METHODS

Study Design: This was pre and post IPT/ITN/IRS Intervention comparison study, where a group of pregnant women who received IPT and used ITNs were followed through the antenatal clinic until they delivered and compared with records of other group of women who attended ANC and delivered at the hospital before the implementation of intervention strategies.

Study population: Pregnant women attending antenatal care (ANC) at Kapsabet District Hospital. The average attendance is 300 mothers daily. With a population of 18,000 pregnant women annually.

Study Duration. The study was conducted between February and August 2010.

Study Area: The study was conducted at Kapsabet district hospital, in Nandi County, it has a catchment population of 364,000. The hospital has 4500 deliveries each year with an estimated 40% home deliveries. The high malaria transmissions season is February to August annually.

Inclusion criteria: Consenting pregnant women who presented to ANC in the first and second trimester before 28 and weeks of pregnancy. Exclusion criteria, decline to provide informed consent, clients commencing ANC after 28 weeks of pregnancy clients known to be allergic to SP.

Sampling procedure: Mothers attending antenatal clinic (ANC), who consented to the study and met the inclusion criteria were recruited consecutively until the desired sample size was reached, the consenting mothers were then followed antenatal till delivery

Sample size: The minimum sample size was calculated using the formula for comparative studies, 143 women were recruited into the study for the intervention group and 600 for the non-intervention group was the number of pregnant women who delivered within the study period.

Study tools and procedure: Three research assistants who were qualified nurses were recruited and trained on the study. The questionnaire was pretested before the commencement of the study, recruitment of the clients was done sequentially till the desired sample size was reached. Recruitment of study participants was carried out after meeting the eligibility criteria. The questionnaire was administered to the study participants by the research assistants and the principal investigator. Part A of the questionnaire was administered at recruitment and during administration of the second dose of SP which was at the ANC and was directly observed (DOTS). Recruited woman were advised to seek treatment at the District hospital or nearby health facility should they fall sick. Documentation of malaria infection were based on those who were diagnosed with clinical malaria and put on anti-malarial drugs and those who tested positive for malarial parasites. Women were advised to deliver at the District hospital, and if they did deliver elsewhere then they were to report to the ANC within one week of delivery. Study participants attended ANC routinely and at delivery. Part B: of the questionnaire was administered and data collection form filled. Records and files of 600 pregnant women who attended and delivered at the hospital were reviewed and data on those diagnosed with malaria, birth weights, still births, and maternal mortality from malaria was documented on non-intervention data collection form. Some of the records were found not to have complete entries. The challenges during the data collection included mothers willingness to give details of their residential environment, irregular antenatal care visits, these were addressed by informing the mothers that the study will benefit the community.

Data analysis: Data were checked and cleaned before entering into software programme for social science research (SPSS version 16). Analysis was done using SPSS and excel. Chi-square and student t-test were used to test the relationships between the use and non-use of treated nets and malaria infection, malaria infection and pregnancy outcome

Study limitations: The use of ITNs was assessed through self reporting and the consistency of ITN use could not be verified. Use of ITNs is affected by the type of housing which were not similar for all the participants.

RESULTS

There were 143 who used the ITN/ITP and 600 hundred were non-users.

Table 1
Socio-demographic characteristics of the study participants.

Characteristic		STUDY GROUPS Non- Intervention (%)	Intervention (%)	Total (%)	P- Value
	<15	4 (0.76)	0 (0)	4 (0.5)	
	15-24	357 (59.5)	73 (51)	430 (57.9)	
	25-34	192 (32)	61 (42.7)	253 (34.1)	
	35-44	44 (6.3)	9 (7.3)	53 (7.1)	
	45+	3 (0.5)	0 (0)	3 (0.4)	
Age (yrs)	Total	600 (100)	143 (100)	743 (100)	0.13
	0	357 (59.5)	83 (58)	440 (59)	
	1	141 (23.5)	30 (21)	171 (23)	
	2	72 (12)	21 (14.7)	93 (12.5)	
	3+	30 (5)	9 (6.5)	39 (5.5)	
Parity	Total	600 (100)	143 (100)	743 (100)	0.11
	1	274 (45.2)	0 (0)	274 (37.2)	
	2	278 (46.3)	65 (45.6)	343 (45.8)	
	3+	48 (8.0)	78 (54.4)	126 (17)	
ANC Visits	Total	600 (100)	143 (100)	743 (100)	0.001

Table 1 shows the mean age for the non-intervention group to be 24 years, while for the intervention group was 25 years. The study participants were of parity 0 (59.5% in the non- intervention and 58% in the intervention group). Participants in the non-intervention group had less ANC visits, 45.2% had one visit, 46.3% had two visits and only 8% had more than two visits, compared with the intervention group where most of the participants had more than two visits (54.4%)

Figure 1
Gestation at administration of first dose of SP (Intervention group)

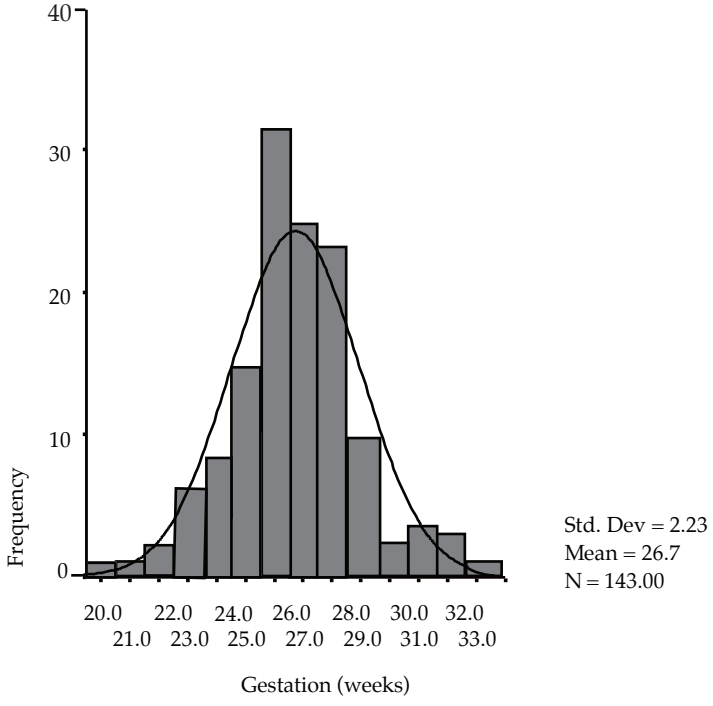

Figure 1, Shows that the mean gestational age at administration of first SP dose was at 26 weeks which was within the WHO recommended period (16-27 weeks).

Figure 2
Gestation at administration of second dose of SP. (Intervention group)

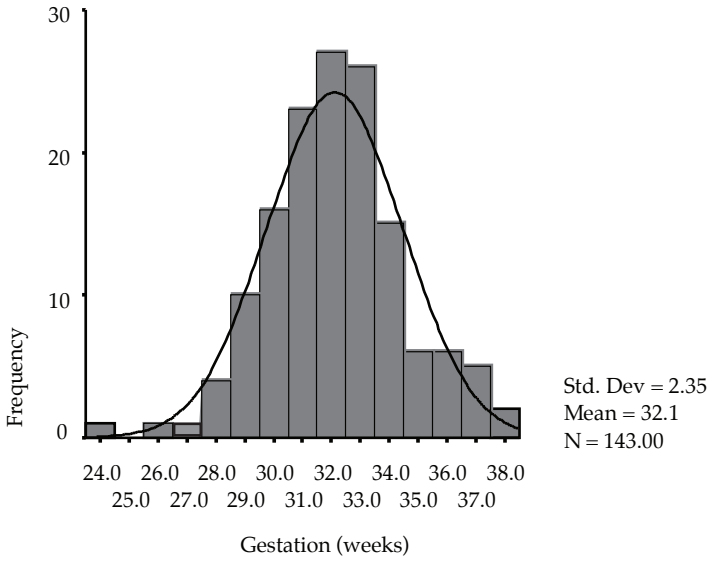

Figure 2, shows that the mean gestational age at administration of second SP dose was at 32 weeks, this is within the WHO recommended period (28-36 weeks).

Figure 3
Methods of malaria prevention. (Intervention group)

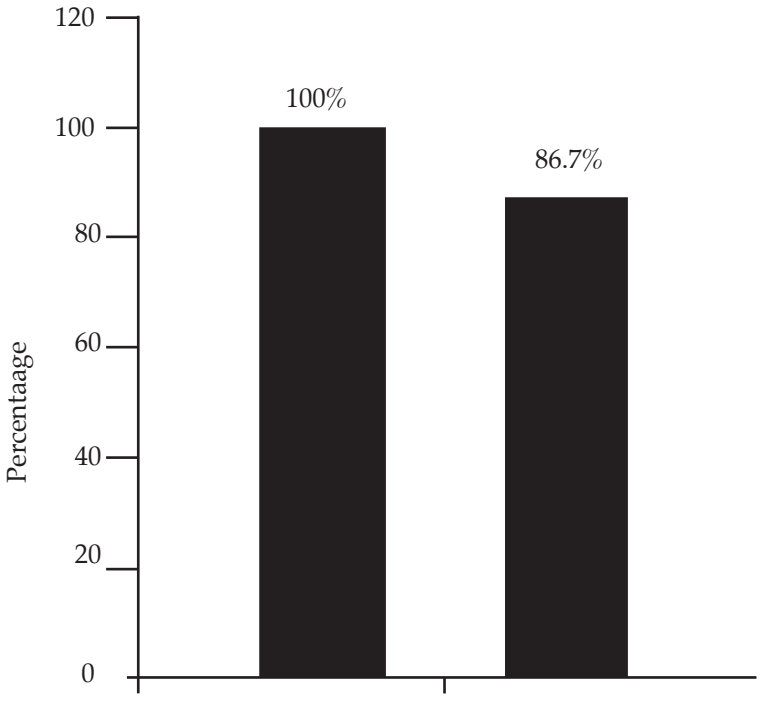

Figure 3, shows malaria protection methods used by the prospective study group (n=143). All the study subjects used IPT (100%) and 87 % used IPT and ITNs.

Table 2
Comparison of pregnancy outcomes between the Non- intervention and the Intervention group

Pregnancy out come	Non- Intervention (n=600)	Intervention IPT/ITNS (n=143)	P-value	Odds Ratio Confidence	95% Interval
Malaria infection in pregnancy	126(21%)	11(8%)	0.000	0.024	1.7-6.1
Low birth weight	75(12.5%)	8(5.6%)	0.018	0.027	1.1-5.1
Still births	36(6%)	2(1.4%)	0.025	0.014	1.2-16.7
Maternal mortality	2(0.3%)	0(0%)	0.489	----	0.78-.84

OR = Odds Ratio, CI = Confidence Interval

Table 2 shows that, the prevalence of malaria was 21% in the non-intervention group compared with 8% in the intervention group.Twelve point five percent had low birth weight in the non-intervention group compared with 5.6% in the intervention group. Still births was more prevalent in the non-intervention group (6%) compared with intervention group (1.4%). There were two (0.3%) cases of maternal mortality in non-intervention group, and no maternal death in the intervention group. The mortality was not attributable to the malaria infection, but due to obstetric haemorrhage.

Table 3
Correlation of Malaria in pregnancy and Low Birth Weight

	Low Birth Weight(n=83)			
	Non- Intervention group (n=75)	Intervention group (n=8)	Total	P- value
Malaria infection in pregnancy.	46(61%)	0 (0%)	46(100%)	
No malaria infection in pregnancy.	29(39%)	8(100 %)	37(100%)	
Total	75(100%)	8(100%)	83(100%)	0.001

Table 3, shows that 61% of the women in the non-intervention group who had malaria infection during pregnancy also delivered low birth weight babies compared to 0% in the intervention group. Thirty nine pecent of the women in the non-intervention group who had no malaria infection in pregnancy also had low birth weight babies compared to 8% in the intervention group.

DISCUSSION

This study found that the incidence of malaria infection in pregnancy was 21% in the non-intervention group compared to 8% in the intervention group, (p=0.000), this is comparable to the study done by Stekette *et al* where the point prevalence of malaria infection without interventions was 25% (4) and Falade *et al* who found that the incidence of malaria infection with IPT-SP intervention was 10% (28). The incidence of low birth weight was 12.5% in the non-intervention group compared to 5.6% in the intervention group (p-value 0.018), this represented reduction of low birth weight by 50%, which is comparable to the findings of Duffy *et al*, who showed that preventive interventions reduced low birth weight by 43% (1). In this study 61% of the women in the non-intervention group who had malaria infection during pregnancy also delivered low birth weight babies compared to 0% in the intervention group. Thirty nine pecent of the women in the non-intervention group who had no malaria infection in pregnancy also had low birth weight babies compared with 8% in the intervention group (p=0.001 Table 3). There is a significant difference in low birth weight between the two groups among those who had no malaria infection during pregnancy which could be attributed to better antenatal care in the intervention group for other causes of low birth weight.

The incidence of Still births was 6% in the non-

intervention group and 1.4% in the intervention group (p=0.025, Table 2). This represented a reduction in perinatal mortality by 66% which is a much better outcome compared to results obtained from meta-analysis of intervention trials where perinatal mortality was reduced by 27% (1). There were two (0.3%) cases of maternal mortality in the non-intervention group and no mortality in the intervention group.

There was no difference in age and parity distributions between the two study groups. Most of the study participants had a mean age of between 24-25 years (60%) in the non-intervention group and (51%) in the intervention group. Larger proportions of participants (59%) in both groups were primigravida which is also the group more susceptible to malaria in pregnancy (Table 1). Participants in the intervention group had more ANC visits, more than two visits (78%) compared with (8%) in the non- intervention group (p=0.001, Table 1). The difference in ANC visits could be attributed to counselling and follow up during antenatal care in the intervention group.

In this study the use of intermittent preventive treatment SP and insecticide treated nets was associated with favourable pregnancy outcome (p<0.05, Figure 4). Other factors which could have contributed to the favourable change is health promotion education on the vector control activities, improved awareness on the signs and symptoms and early treatment of malaria which accompanied social mobilisation during the implementation of the interventions in the year 2002. IPT/ITN policy is indeed good, but cost implications especially on sustainability of ITN provision and development of resistance to SP might be challenging in the near future. The on going trials of malaria vaccine in Kenya is a much more promising intervention.

LIMITATIONS OF THE STUDY

The use of ITNs was assessed through self reporting and it was yes or no answer, but the consistency of ITN use could not be verified. Use of ITNs is affected by the type of residential house which were not the same.

In conclusion, the use of Intermittent preventive treatment with sulphadoxine-pyrimethamine and Insecticide treated nets is effective in prevention of malaria in pregnancy in non-malaria endemic region and is associated with reduction of adverse pregnancy outcomes. There is therefore a strong need to make the long lasting insecticide treated bed nets available for use by the pregnant women.

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