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Low Uptake Of Intermittent Preventive Treatment Of Malaria In Hiv-Infected Pregnant Women At An Urban Hospital In Accra, Ghana

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Low Uptake of Intermittent Preventive Treatment of Malaria in HIV-infected Pregnant Women at an Urban Hospital in Accra, Ghana

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By

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Abstract

Objectives: The clinical course and complications of malaria during pregnancy are exacerbated in HIV-positive women. Furthermore, malaria during pregnancy may increase the risk of mother to child transmission (MTCT) of HIV. We assessed the uptake of WHO recommended intermittent preventive treatment (IPT) for malaria and insecticide treated bed nets (ITN) during pregnancy among HIV-negative and HIV-positive pregnant women in a malaria endemic area.

Methods: A cross sectional study of 151 women (96 HIV-negative and 55 HIV-positive) receiving antenatal and HIV care at an urban district hospital in Accra, Ghana from July to August, 2008. The women were interviewed to obtain demographic data and information on the use of IPT and insecticide treated bed nets (ITN) during their current pregnancy. Antenatal care cards were used to verify obstetric history and a record of IPT use.

Results: HIV-positive pregnant women had significantly low uptake of all three doses of WHO recommended IPT compared to HIV-negative pregnant women. Dose 1: 70% and 47% p=0.019, Dose 2: 54.8% and 30.2%, p=0.018. Dose 3: 40% and 9.1% p=<0.002 for HIV negative and HIV positive pregnant women respectively. For ITN use, 43.8% of HIV negative and 36.4% of HIV positive women reported having ITNs at home, p=0.375. Of the women who had nets, 45.2% of HIV negative and 70% HIV positive women reported having slept under a net the previous night, P=0.068.

Conclusion: The low uptake of IPT among HIV-positive pregnant women is of concern in light of emerging evidence that malaria during pregnancy may increase the risk of MTCT of HIV. Comprehensive prevention of MTCT programs should include components aimed at increasing the uptake of IPT among HIV-positive pregnant women.

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Introduction

Malaria is a major global public health problem that places half the world's population at risk and to which approximately 1 million deaths are attributed annually.(1) 90% of these deaths occur in Sub-Saharan Africa and are largely caused by *Plasmodium falciparum*. While the highest burden of disease falls on children under 5 years old, pregnant women and their unborn babies are also very vulnerable to the disease. (2) Approximately 30 million pregnancies occur in malaria endemic areas in Sub Saharan Africa, placing these women and their unborn children at risk. Adverse maternal outcomes include cerebral malaria, maternal anemia, placental malaria and maternal mortality. These are more frequent during epidemics, and in primigravid or immunocompromised women. Fetal and newborn adverse outcomes include intra uterine growth retardation, spontaneous abortion, fetal demise, low birth weight and infant deaths. (3)(4)(5)(6)(7)

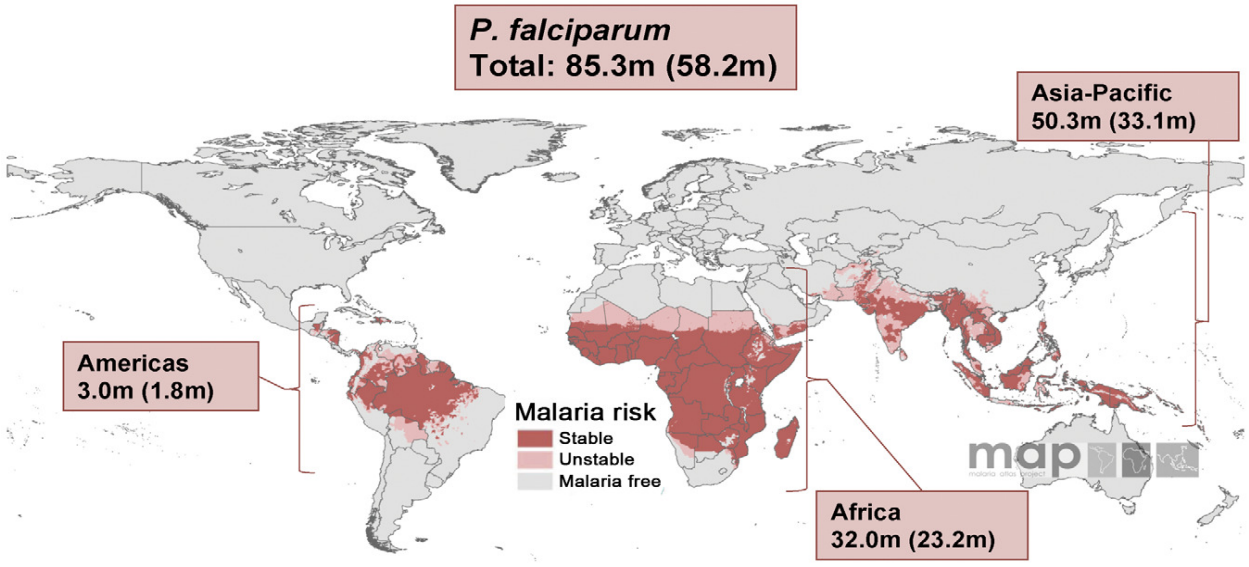


Figure 1. Malaria risk map for P. falciparum and corresponding number of pregnancies in each continent in 2007.(2)

The extent of malaria associated adverse effects is dependent on transmission rates and immunity level of the population.(8) In areas of low or unstable malaria transmission, pregnant women do not develop significant immunity. Thus when they become parasitemic during pregnancy, they are at a high risk of developing severe malaria and serious adverse effects e.g. spontaneous abortion. In areas of high or moderate (stable) malaria transmission, pregnant women develop partial immunity during their subsequent pregnancies that protect them from developing severe malaria. These women are more likely to have asymptomatic parasitemia during pregnancy. However, they are still vulnerable to placental malaria which subsequently leads to adverse fetal outcomes.

The pathogenesis of placental malaria is based on the sequesterization of parasitized red blood cells on the placenta. (1)These infected erythrocytes produce Plasmodium falciparum membrane protein 1(PfEMP1) which adheres to placental chondroitin sulphate A and hylarulonic acid. This accumulation triggers an immune response which alters the placental architecture and compromises maternal-fetal exchange. (2) PfEMP1s are highly variable in structure, and produce a large family of variant surface antigens (VSA) that are expressed of the surface of infected red blood cells. These antigens elicit antibodies which are protective against future infections. This protection is only partial since the VSA vary widely during the course of an infection or during subsequent infections. While primigravid women are at a higher risk of placental malaria, the acquired immunity confers significant immune protection during later pregnancies.

Malaria prevention during pregnancy

Early strategies to prevent the effects of malaria in pregnancy (1950s to Early 1990s) were based on weekly or bi-monthly chemoprophylaxis with chloroquine (CQ) in West African countries and dapsone-pyrimethamine or sulphadoxine-pyrimethamine (SP) in East African countries.(9, 10)These methods were proven to be efficacious but with time, drug resistance coupled with poor compliance led to low efficacy

In 1992, Schultz and others demonstrated that two treatment doses of the anti-malarial drug sulfadoxine pyrimethamine ((1500/75 mg; SP) administered once in the second trimester and once in the third trimester, was efficacious in decreasing placental malaria in an area where persons receive, on average, 50 infective mosquito bites/year. (11) SP is believed to confer a treatment effect by clearing or suppressing asymptomatic placental infections. It is also a slowly eliminated drug, thus possibly maintaining suppressive drug levels and preventing new infections from occurring for several weeks-a prophylactic effect. (12)

SP has been deemed safe for administration during the second and third trimester of pregnancy. Pyrimethamine is in the class of anti-folate drugs that are associated with increased risk of birth defects when taken in the first trimester, but not during the second or third trimester. (13, 14) Other possible side effects associated with SP use include severe cutaneous reactions such as toxic epidermal necrolysis and Stevens-Johnson syndrome. (15) The risk of the cutaneous infections is rare, and not associated with or increased during pregnancy.

WHO policy for malaria prevention during pregnancy in Sub Saharan Africa.

A) Intermittent Preventive Treatment for Malaria (IPT)

Based on this knowledge, WHO recommended Intermittent Preventive treatment (IPT) for malaria in pregnant women (8)This was part of a three pronged approach which included IPT, Insecticide Treated Nets (ITNs) and prompt case management of malaria. IPT involves the administration of a single curative dose of sulfadoxine pyrimethamine (1500/75 mg; SP) at pre-defined intervals after quickening (the mother's recognition of fetal movement, which occurs early during the second trimester) and given at least 1 month apart regardless of whether the woman has parasitemia. At least 2 doses are recommended during the second and third trimesters as part of routine scheduled antenatal clinic visits in areas of stable *P. falciparum* transmission.

The recommended antenatal schedule of four visits, with at least 3 occurring after quickening, offer an opportunity for the delivery of IPT as directly observed therapy during clinic visits. Recent data from Demographic and Health Surveys (DHS) show that, in the majority of countries in sub-Saharan Africa, more than 70% of women attend antenatal clinics at least once during their pregnancy and many attend repeatedly (1)

In 2000, under the auspices of Roll Back Malaria, WHO in consultation with African leaders set a target to provide at least 60% of pregnant women with at least 2 doses of IPT, and insecticide-treated bed nets (ITN) by the year 2010. (16) By 2009, thirty-three countries in the African Region had adopted an IPT policy. (1) The use of IPT has led to an estimated decrease in incidence of: low birth weight 42%, neonatal death 38%, placental malaria 65%, ante-natal parasitemia 26%. (17) At least two doses of IPT with SP has been shown to confer benefit to HIV-negative semi immune pregnant women (12)

Despite the proven effectiveness of IPT, its use in sub-Saharan Africa remains low. (1) Additionally, data on IPT coverage from national surveys remain limited. Estimates of IPT use in sub-Saharan Africa eight years after the Abuja declaration show that only 5 to 44% of pregnant women received at least 2 doses of IPT (18) (19) (20) (21) During 2007-2008, only 9 high burden countries had national survey data on IPT, resulting in only 20% of pregnant women who received 2 or more doses of IPT (1)

Several studies have examined factors associated with IPT coverage. Some studies have found associations with level of education (18) (22) However, no association has been found between IPT use and household wealth, knowledge of malaria, travel times to clinic and number of clinic visits. (18) (20) (22) (23)

B) Insecticide Treated Bed nets (ITN)

As part of the three pronged approach to malaria prevention in pregnancy, WHO also recommends universal coverage with Insecticide treated nets (ITNs) (8)Strategies for achieving this goal include occasional campaigns and continuous distribution to pregnant women during ante-natal visits and to mothers and infants during routine immunization contacts. Coverage with ITNs has been rapidly increasing, with household ITN ownership reaching 31% in high burden countries by the end of 2008.(1)

Studies have demonstrated the efficacy of insecticide treated nets in preventing the adverse effects of malaria in pregnancy. (24) Factors that have been associated with increased ITN use include high knowledge of malaria, (23) greater household wealth, (25) and the use of IPT (18)

C) Prompt malaria case management.

WHO also recommends prompt malaria diagnosis and case management, especially in high risk populations like young children or pregnant women. Malaria diagnosis is based on microscopy or rapid diagnostic testing (RTD), but a significant gap persists on this front. (1) In 2008, only 22% of suspected malaria cases were tested in several high burden African countries that reported data to WHO. The use of RDTs was up to 13% in the reporting countries.

The recommended treatment for uncomplicated malaria is Artemisin based Combination Therapy (ACT). (3) The 5 currently recommended ACTs include Artemether-lumefantrine, Artesunate Amodiaquine, Artesunate-mefloquine, Artesunate- Sulfadoxine pyrimethamine, and dihydroartemisinin piperaquine. The choice of medication is based on its efficacy in the particular area or country of use. By 2009, all 42 African countries in which P. falciparum is endemic had adopted and implemented the use of ACTs for treatment.

Most countries report over 50% treatment rates with 5 countries reporting 100% rates of treatment. However, this is in the context of properly diagnosed malaria, which only occurs in a minority of the total malaria cases. For example in Ghana in 2008, approximately 22% of all outpatient cases were appropriately tested. 75% of those who tested positive for malaria reportedly had access to ACT therapy.

Effect of HIV on Malaria during pregnancy

There are reports that HIV infection potentiates the adverse effects of malaria during pregnancy (26) (27) HIV positive pregnant women have higher rates of malaria infection, and poorer response to anti-malarial treatment. (28) Pregnant women in malaria endemic areas develop immunity against placental malaria in subsequent pregnancies. However, HIV infection impairs

this acquired protection against placental malaria and increases prevalence of placental and clinical malaria in HIV-positive women of all gravidities

Studies examining the effect of HIV on IPT efficacy showed that HIV positive women require at least 3 doses to achieve the same benefit observed in HIV negative women who receive 2 doses. (29) (28) Based on this evidence, WHO recommended 3 courses for HIV-infected pregnant women and for all pregnant women in areas in which the antenatal HIV prevalence exceeds 10% and routine HIV testing is not available World Health Organization (8)

Approximately 1 million pregnancies each year are associated with malaria and HIV co-infection (30)(31).Infection with malaria is associated with higher HIV viral load, which is the single most important risk factor for the transmission of HIV from HIV-infected mother to the child (32) In addition, placental malaria in HIV positive women may alter the placental architecture, increasing the risk of vertical transmission of HIV. (33) There are conflicting reports on the effect of malaria on Mother –To-Child-Transmission (MTCT) of HIV (34) (35)(36) A recent study from Uganda found that placental malaria was associated with increased MTCT, even at low maternal viral loads (37) .

Aims of the study

The effects of malaria in pregnancy, the development and implementation of prevention strategies in Sub Saharan Africa are well known. HIV is known to confer increased vulnerability to malaria during pregnancy. It is crucial to target HIV-positive pregnant women for more effective malaria control, especially in the face of the possible contribution of malaria on MTCT of HIV. Current estimates of IPT coverage are on all pregnant women and to our knowledge, no study has attempted to evaluate IPT coverage in this particularly vulnerable group of HIV –

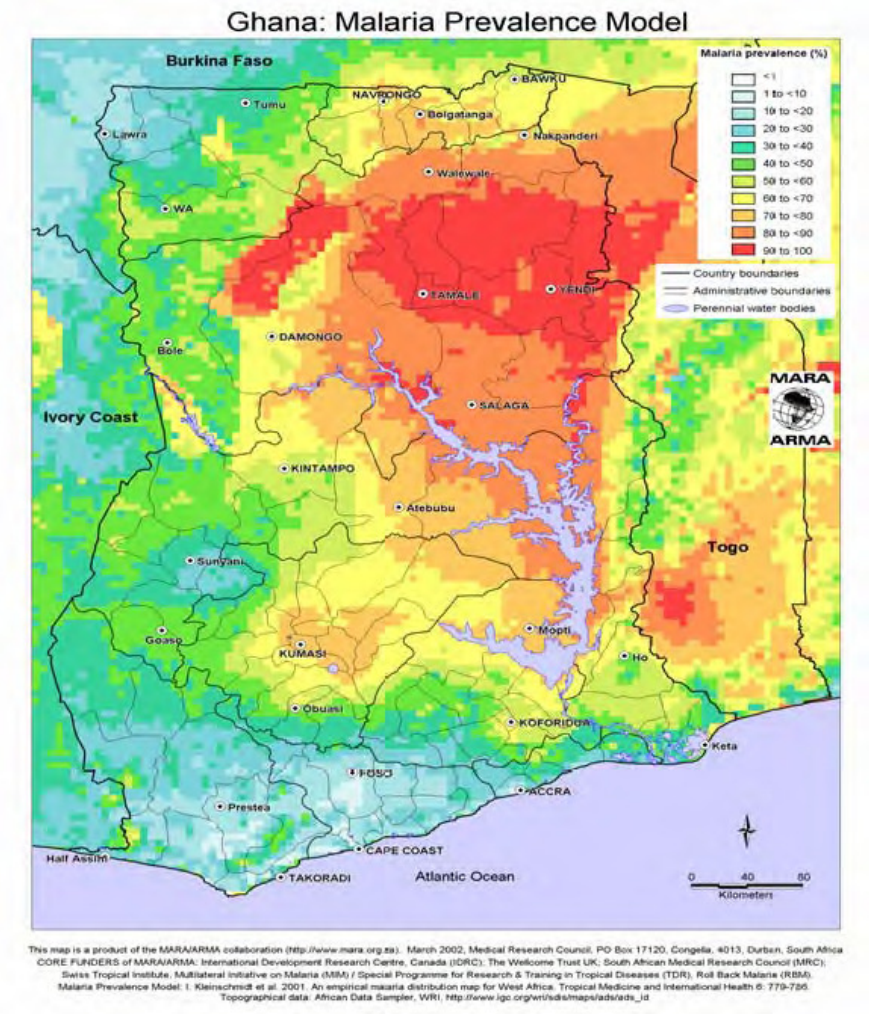
positive women. We therefore designed a pilot study to evaluate the coverage of IPT in pregnant women in Accra Ghana, and to stratify IPT coverage on the basis of HIV serostatus. We also evaluated the uptake of ITN in both groups.

Methods

Study site

The study was conducted at Ridge hospital, a district hospital in the capital city Accra, from July to August 2008. Ridge is a public hospital which is under the administration of the Ghana Health Service (GHS). The Ministry of Health (MOH) and the GHS oversee the public health and clinical care sectors in Ghana.(38) The MOH exercises oversight and overall control of the entire health system, and GHS is responsible for delivery of public health and clinical services. GHS operates at four levels: national, regional, district, and sub-district. There are over 320 hospitals, 760 health centers, and 1120 clinics in the country. Of these facilities, 83% are in the public sector and 9% are faith-based institutions most of which are closely integrated with GHS.

Malaria is hyper-endemic in all parts of the country, and transmission occurs year-round with seasonal variations during the rainy season. According to Ghana Health Service (GHS) health facility data,(39) malaria is the number one cause of morbidity, accounting for about 38% of all outpatient illnesses, 36% of all admissions, and 33% of all deaths in children under five years. Between 3.1 and 3.5 million cases of clinical malaria are reported in public health facilities each year, of which 900,000 cases are in children under five years. Malaria accounts for approximately 14% of outpatient attendance by pregnant women in Ghana, 11% of hospital admissions, and 9% of maternal deaths



This map is a product of the MARA/ARMA collaboration (http://www.mara.org.za). March 2002, Medical Research Council, PO Box 17120, Congella, 4013, Durban, South Africa
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Malaria Prevalence Model: I. Kleinschmidt et al. 2001. An empirical malaria distribution map for West Africa. Tropical Medicine and International Health 6: 779-786.
Topographical data: African Data Sampler, WRI, http://www.igc.org/wri/sdis/maps/ads/ads_id

http://www.mara.org.za/

IPT with SP was adopted as the national policy in 2004, with three doses of SP to be administered to HIV-negative pregnant women starting after quickening (16 weeks or thereafter). The doses are administered at least one month apart with the last dose administered at least one month before delivery. All doses of SP are to be administered under direct observation. HIV-positive pregnant women are expected to receive monthly doses of SP after quickening (with a total of four doses)

In 2006, the National Health Insurance Scheme (NHIS) was implemented. By July 2008, 50% of the population had been enrolled, resulting in increased attendance at health facilities. As a

result, the percentage of women attending ANC clinics four or more times increased from 69% in 2003(40) to 78% in 2008(39) A nationwide health facility survey in 2008 found that IPT is offered in 94% of facilities sampled. Significant gains have been observed in other Malaria intervention indicators. Between the 2003 and 2008 ITN ownership and use, and treatment with ACTs increased significantly. (Table 1) Despite strong ANC attendance and IPT coverage, challenges such as SP stock-outs and lack of enough trained healthcare workers continue to hamper IPT delivery.

The antenatal clinic (ANC) at Ridge Hospital handles approximately 100 pregnant women each clinic day. The prevalence of HIV among pregnant women attending the ANC at Ridge Hospital is 5%. This compares with the national average of 3.6% (41) HIV testing is carried out at the ANC and positive cases are referred to the HIV clinic located in the same hospital for prevention of Mother-To-Child Transmission of HIV (pMTCT) services. The HIV clinic also serves as a referral pMTCT center for pregnant women diagnosed with HIV in other clinics in the area. During the two months of the study, approximately sixty HIV-infected pregnant women attended the clinic for pMTCT care.

INDICATOR	**2003 DHS**	**2006 MICS**	**2008 DHS**
Proportion of households with one or more ITN	3%	19%	33%
Proportion of children under five years old who slept under an ITN the previous night	4%	22%	28%
Proportion of pregnant women who slept under an ITN the previous night	3%	NA	20%
Proportion of women who received two or more doses of IPT during their last pregnancy in the last two years*	0	28%	44%

Proportion of children under five years old with fever in the last two weeks who received treatment with ACTs*	N/A	3%	12%

Table 1: Recent Survey Estimates of Malaria Indicators (38)

DHS: Demographic and Health Survey MICS: Multiple Indicator Cluster Survey

Enrollment and data collection

Pregnant women attending antenatal clinic (ANC) and the HIV clinic at the hospital were invited to participate in the study. After explanation of the study goals and obtaining informed consent, an interviewer administered questionnaire was used to obtain demographic and socio-economic data. Antenatal care cards that pregnant women carry with them and present to clinic throughout their pregnancy were used to verify the obstetric history, record of prior laboratory investigations, history of malaria in pregnancy and a record of IPT use.

Data analysis

IPT coverage

IPT was defined as the administration of a single curative dose of sulfadoxine pyrimethamine ((1500/75 mg; SP) Coverage was defined according to WHO recommendations as follows:

Dose 1: numerator= number of women who received first dose of IPT Denominator= all women who were 16 or over weeks in gestation.

Dose 2: numerator= number of women who received 2nd dose of IPT, Denominator= all women 20 weeks of gestation and over.

Dose 3: numerator= number of women who received 3rd dose of IPT. Denominator= all women 24 weeks of gestation and over.

Statistical analysis

Analyses were performed using SPSS version 17. The student's t test was used to determine the differences in mean age between the two study groups. Pearson chi square was used to determine differences between the two study groups in terms of marital status, education, occupation and gestation. Logistic regressions were used to determine the effect of age, marital status, education, occupation and gestation on IPT uptake and ITN use. Pearson chi square was used to determine the impact of IPT use on ITN use, and vice versa.

Ethics statement/ Ethical considerations

The study protocol was reviewed and approved by the Ethics Committees of the University of Ghana Medical School and Yale University School of Medicine. All participants provided verbal consent (English, translated into Twi, Ga or Ewe)

Results

Baseline characteristics of the study population

151 pregnant women (96 HIV-negative and 55 HIV-positive) participated in the study. The baseline demographic and obstetric characteristics of the women stratified by HIV status are shown in Table 1.

	HIV-positive	**HIV-negative**	
parameter	**n=96**	**n=55**	
Age (years); mean (sd)	29.02 (5.355)	28.60 (5.384)	
≤18 years	2/100 (2.0)	1/55 (1.8)	
19-24	21/100 (21.0)	11/55 (20.0)	
25-34	60/100 (62.0)	33/55 (60.0)	
≥35	17/100 (17.0)	10/55 (18.2)	
Marital status			
Married	91 (94.8)	42 (76.4)	
Single	5 (5.2)	13 (23.6)	P=0.001
Education history			
Illiterate	13 (13.5)	9 (16.4)	
Primary education	5 (5.2)	8 (14.5)	
Junior Secondary (JSS)	47 (49)	32 (58.2)	
Senior Secondary (SSS)	16 (16.7)	5 (9.1)	
Tertiary education	10 (10.4)	0 (0)	
Other (vocational, madrasa)	5 (5.2)	1 (1.8)	P=0.029
Occupation			
unemployed	8 (8.3)	4 (7.3)	
Informal	72 (75)	47 (85.5)	
Formal	16 (16.7)	4 (7.3)	P=0.239
Gestation			
< 16 weeks	16 (16.7)	6 (10.9)	
16-19 weeks	7 (7.3)	6 (10.9)	
20-23 weeks	8 (8.3)	10 (18.2)	
≥ 24 weeks	65 (67.7)	33 (33.7)	P=0.213

There were no significant differences in age, occupation and gestation between the two groups. Most women were employed in the informal sector as market traders, hair dressers or seamstresses. Notably, most women visiting both the general ANC and HIV clinic were at or about 24 weeks gestation. There were significant differences in marital status and education level between the two groups: There were significantly more single women in the HIV-positive group, and HIV-positive women were less likely to have a senior secondary education or above.

IPT coverage

IPT coverage based on gestational age is shown in Figure 1. WHO recommends the first dose of SP after quickening (16 weeks) and subsequent doses are spaced at least 4 weeks apart. For all the women due for their first dose, the IPT coverage was 70% and 47% for HIV-negative and HIV-positive, respectively ($p=0.019$). For the second dose, the coverage was 54.8% and 30.2% for HIV-negative and HIV-positive, respectively ($p=0.018$). For the third dose, the coverage was 40% and 9.1% for HIV-negative and HIV-positive women, respectively ($p<0.002$). HIV-positive pregnant women had lower uptake for each of the recommended doses.

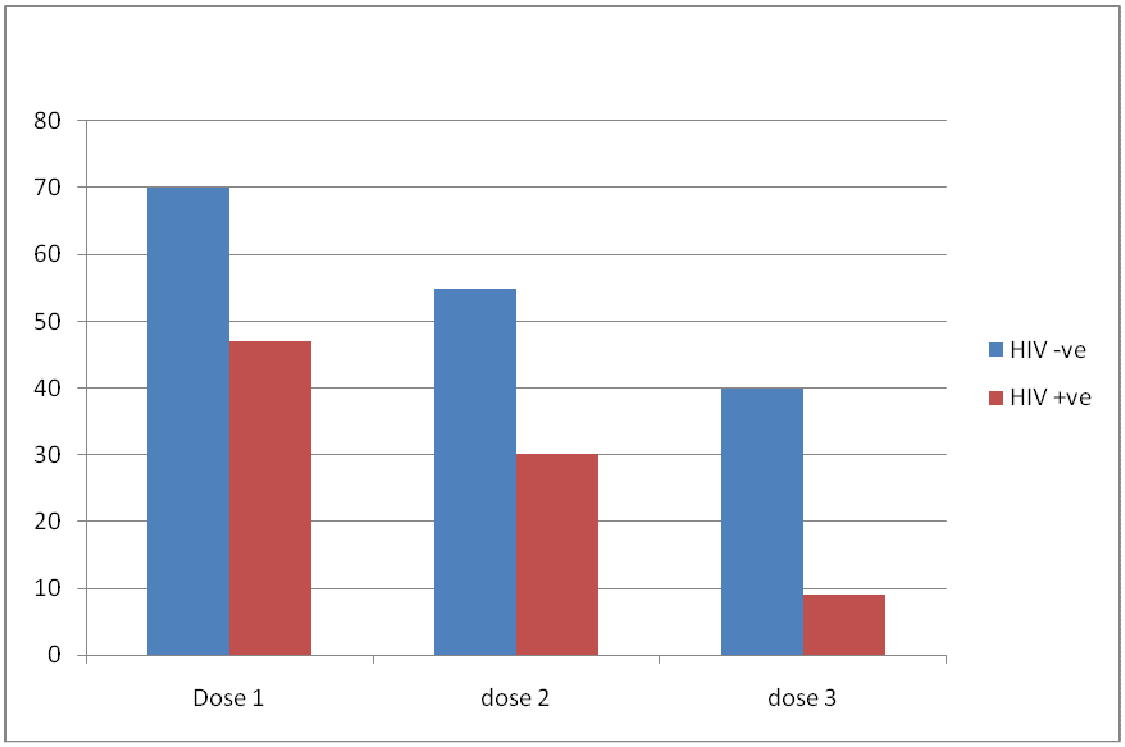

FIG 1: IPT coverage in HIV-negative and HIV-positive pregnant women.

Patterns in IPT administration

We investigated patterns of IPT administration following WHO recommendation of the first dose after quickening (16 weeks) with subsequent doses spaced 1 month apart : 20weeks and 24 weeks for the 2nd and 3rd doses respectively. The percentage of women in the different gestation groups who are on dose 1, 2 and 3 are shown on table 2. For both groups, the majority of women on dose 1, 2 and 3 received it at or above 24 weeks gestation

	Dose 1			Dose 2			Dose 3		
Gest. (wks)	**HIV -**	**HIV +**	**P value**	**HIV -**	**HIV +**	***P value***	**HIV -**	**HIV +**	***P value***
16-19	14.3	0	*0.335*						
20-23	37.5	40	*0.914*	0	10	*0.357*			
≥ 24	80	57.6	*0.019*	61.5	36.4	*0.018*	40	9.1	*0.002*

Table 2: Percentage of women on Dose 1, 2 and 3 of IPT stratified by HIV serostatus and Gestational age.

Predictors of IPT coverage

The effect of individual level variables on IPT coverage was investigated for the entire study population. Using a logistic regression model, none of the following factors were found to be significant predictors of IPT use: Age, (p=0.910) gravidity, (p=0.415) marital status, (p=0.092) occupation, (p=0.761) and education (0.216). In addition, using chi square analysis, ITN use was not found to be a significant predictor of IPT use. (p=0.074)

ITN uptake

We evaluated the prevalence of the use of ITNs among our study population. 43.8% of HIV-negative and 36.4% % HIV-positive women reported having ITNs at home. P=0.375. Of the women who had nets, 45.2% of the HIV negative and 70% of HIV positive women reported having slept under a net the previous night. P=0.068. The reasons given by participants for not using ITN included heat and discomfort sleeping under the net, lack of poles on their beds to hang the net, and waiting to use the net for their newborn.

Predictors of ITN use

We also studied the effect of individual level variables on ITN use by the entire study population using logistic regressions. The following factors were not found to be significant predictors of ITN use: Age, (p=0.987) gravidity, (p= 0.564) marital status, (p=0.934) occupation, (p=0.927) and education (p=0.736). In addition, using chi square analysis, IPT use was not found to be a significant predictor of ITN use. (p=0.074)

Discussion

In this exploratory cross-sectional study, we found that pregnant women receiving antenatal care at an urban hospital in Ghana have IPT coverage below the WHO target to provide at minimum 60% of pregnant women with at least 2 doses of IPT by the year 2010. In addition, HIV positive pregnant women had significantly lower coverage for all IPT doses. While IPT coverage for HIV negative women approached the desired target with 54% of women on at least 2 doses, the coverage for HIV positive women fell below target with 30.2% women on at least two doses.

Our finding of low IPT coverage is consistent with a previous study from a hospital in southern Ghana where 77%, 26%, and 24% of all pregnant women received one dose, at least two doses, and three doses of IPT respectively (42). Studies elsewhere in sub-saharan Africa show consistently low IPT coverage. In Malawi, a study in an urban hospital revealed that 45.1% and 30.6% of pregnant women received one and two doses of IPT, respectively (43). A nationwide survey in Malawi showed that 67.5% and 29.3% of pregnant women received one, and two or more doses of IPT, respectively (National Statistical Office, Malawi 2001). Similar percent coverage was reported in a study in Kenya; 43.4% and 23.7% of pregnant women received one

and two doses, respectively (21).These previous studies, however, did not stratify the women into HIV-negative and HIV-positive categories.

Our findings that HIV-positive women were less likely to receive IPT and to complete the recommended doses are of concern given the fact that HIV infection confers increased susceptibility to malaria in all pregnant women, regardless of their gravidity. (28) This places these women and their unborn children at an increased risk of malaria- associated adverse effects. For this reason alone, HIV-positive pregnant women need to be targeted for better coverage with IPT. Adding to this need are the emerging reports that malaria during pregnancy may increase the risk of MTCT of HIV (37) Preliminary results have not yielded uniform results to support this hypothesis, but the possible contribution of malaria to MTCT of HIV is of major public health concern, and further supports the need to target HIV-positive women for better malaria control.

One of the key factors contributing to the disparity in IPT coverage between HIV-negative and HIV-positive pregnant women in this study was poor coordination between the different levels of service delivery to pregnant women in the hospital. The general ante-natal clinic emphasized malaria control through IPT and ITN use. However, the focus of the HIV clinic for its pregnant women was the provision of antiretroviral agents to prevent MTCT of HIV. The importance of IPT and the possible risk association between malaria and HIV transmission was not emphasized. In addition, some patients attending the HIV clinic were referred from several satellite clinics and in most instances were not aware of the availability of free IPT services at the general ANC.

Weak links between different disease- specific programs have been identified elsewhere as a major cause for poor IPT delivery. (44) Gaps in IPT delivery occur due to lack of coordination between Malaria and HIV control programs with reproductive services. (30) WHO recommends a four visit schedule for the delivery of "focused antenatal care" which would entail a "one stop shop" package of antenatal services that also includes malaria and HIV control. This approach calls for strengthened associations between the above mentioned programs.

Our study findings also indicate late IPT uptake. While WHO recommends Dose 1 administration after quickening (16 weeks), most of the women in our study received their first IPT dose at or after 24 weeks. This was the case for both the HIV-negative and HIV-positive groups, and contributed to low coverage especially for dose 2 and 3. In Tanzania, late ANC attendance, especially in rural areas was identified as a key factor hindering IPT coverage. (45) Most women attending late received one dose or none. Economic, psychosocial and cultural factors contributing to late clinic attendance that were identified in the Tanzania study include: Poverty and inability to pay for travel and ANC services, low decision making capacity on when to attend clinic, superstitions that bar women from exposing their pregnancies especially during the first two trimesters, and shyness/guilt associated with exposing pregnancy that is acquired outside a recognized marriage. For HIV-positive women, the stigma of attending a HIV clinic and thus being identified as suffering from the disease is a significant hindrance.

Of the individual level variables evaluated in this study, none reached statistical significance as predictors of IPT coverage. These include maternal age, gravidity, marital status, occupation and education. It is important to note however, that some factors approached statistical significance, and point to possible individual level factors affecting IPT uptake. Evaluation of marital status showed a trend towards married women having more IPT coverage than single women.

(P=0.092) Additionally, a breakdown of the education levels of our study population indicated that illiterate women tended to have lower IPT coverage, though not statistically important. (p=0.068) (Appendix 1)

Previous studies have identified education as a predictor for better IPT coverage. A study in rural Kenya showed that women with formal education were more likely to have received at least one dose of IPT. (18) Another study from Kampala, Uganda showed that the completion of secondary education or higher predicted the use of IPT during pregnancy. (22) In our study population, HIV-positive women were more likely to be illiterate than their HIV negative counterparts.(p= 0.029) Thus while analyzing for IPT coverage, education is a significant confounding factor. Similarly, HIV- positive women were more likely to be single. (p=0.001) Marital status, to our knowledge, has not been reported as a significant predictor of IPT coverage but is a possible confounding factor in this study.

The use of ITN also approached statistical significance as a factor associated with higher IPT uptake. (P=0.074) In a Kenyan study, Gikandi et al. reported that pregnant women who used ITN were more likely to have received at least one dose of IPT. (OR: 1.68, 1.20–2.36)(18) This finding could reflect either that clinics that offered ITN during regular ANC visits were also more likely to offer IPT. It might also indicate that the women who were educated on malaria prevention were more likely to seek both ITN and IPT. In studies that reported low IPT coverage, pregnant women reported that SP was not offered to them in clinic. (46) Lack of awareness of the availability of IPT contributes to low coverage. (18) This highlights the need for more malaria specific education, both to healthcare workers and patients. Attendance to educational sessions that target malaria prevention and informs patients on the services available at their clinic has been associated with higher IPT use. (23)

There were no significant differences in ITN possession between HIV- negative and HIV-positive women.(p=0,375) However, of the women who had ITN, only 45.2% HIV- negative and 70% HIV- positive women reported using them. (p=0.068) This result highlights the fact that having a bed net in a household does not necessarily mean that it would be used by the pregnant woman. Some of the women reported that they were waiting to use the net for their newborn baby. These women recognized the need to protect their newborns, but had limited knowledge of the risk of malaria during pregnancy and that the ITN would protect both the mother and the baby. In addition, studies indicate that in a household that has both a pregnant woman and a child under 5, the latter is more likely to use the available ITN.(47)

Other women reported lack of a proper means to hang their bed net. This finding could result from several factors that were outlined in the Ethiopian bed net utilization study, (48) which also apply to our patient population: Firstly some household designs are not amenable to bed-net use. I.e., some bed nets are rectangular and require four hanging points, which might be impossible in a house that has a round shape, or is built from material that cannot withstand the constant traction from attached bed nets e.g. mud/ dung houses. There are some nets that only require one attachment directly above the bed/ sleeping space, and these are more amenable to use in such a situation. Secondly, while it is easier to drape a net over a raised bed, some women sleep on a mat on the floor, or share a space that is not easily covered with a net. Economic and hierarchical factors determine who sleeps on a bed, and thus who is more likely to use an ITN. In some families, the parents sleep on the bed, while children sleep on mats on the floor. In others, it might be the women or girls who sleep on the floor. These findings are important, especially to organizations and companies that design insecticide treated bed-nets for use in a population of low social economic means such as ours.

Some women cited the difficulty of using bed-nets during times of high ambient temperatures. This problem is exacerbated for women who live in close quarters.

We evaluated the effect of individual factors such as age, gravidity, marital status, occupation and education on ITN use. None of these factors were significant predictors of ITN use in our population. However, IPT use showed a close to significant association with ITN use as mentioned above. Other studies have identified education (18) and high knowledge of malaria (23) as predictors of ITN use. Our logistic regression analysis was hampered by low sample size, since only 62/151 (41%) women in our total sample reported using ITNs.

Our study indicates that HIV-positive women who had bed nets were more likely to use them, although the result did not achieve statistical significance. ($p=0.068$) To our knowledge, studies that evaluate ITN uptake in pregnant women do not stratify based on HIV serostatus. This is an interesting finding that requires further evaluation and corroboration. It is a positive indication that HIV- positive women in our study population, who are known to be at risk for more severe malaria, were more likely to adhere to malaria prevention strategies that were presented to them.

Conclusion

Our findings suggest the need to intensify the strategies to increase IPT coverage for HIV-positive pregnant women in sub-Saharan Africa. Increasing IPT coverage will not only avert the known malaria-related adverse effects on the mother and the child, but possibly lead to a further reduction in the incidence of MTCT of HIV in the sub-region. There should be a concerted effort to integrate malaria prevention during pregnancy into comprehensive PMTCT programs for HIV-positive women.

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Appendix 1:

Results of Logistic regressions, evaluating which individual level factors predict IPT use.

	B	S.E.	Wald	df	**Sig.**	Exp(B)	95% C.I.for EXP(B)	
							Lower	Upper
Age	.005	.044	.013	1	**.910**	1.005	.922	1.096
Mar	1.877	1.116	2.830	1	**.092**	6.533	.734	58.171
Occup			.547	2	**.761**			
Occup(1)	.392	1.111	.125	1	**.724**	1.481	.168	13.066
Occup(2)	.591	.805	.540	1	**.462**	1.806	.373	8.746
educ			7.057	5	**.216**			
educ(1)	-2.350	1.286	3.341	1	**.068**	.095	.008	1.185
educ(2)	-2.428	1.477	2.702	1	**.100**	.088	.005	1.595
educ(3)	-1.193	1.068	1.248	1	**.264**	.303	.037	2.460
educ(4)	-.771	1.195	.416	1	**.519**	.463	.044	4.815
educ(5)	-.004	1.388	.000	1	**.998**	.996	.066	15.132
Constant	-2.378	1.922	1.530	1	**.216**	.093		

Key: Mar= marital status, single or married

Occup=occupation. 1= informal sector, 2= formal sector

Educ= education. 1=illiterate, 2= primary, 3= Junior secondary, 4= senior secondary, 5= Tertiary