MALARIA IN PREGNANCY, EVALUATION OF UPTAKE OF INTERMITTENT PRESUMPTIVE TREATMENT AND INSECTICIDE TREATED NETS IN KIBITI RUFIJI

By

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CERTIFICATION

The undersigned certifies that he has read and hereby recommend for acceptance by the Muhimbili University of Health and Allied Sciences a dissertation entitled **Malaria in Pregnancy: Evaluation of Uptake of Intermittent Presumptive Treatment and Insecticide Treated Nets in Kibiti Rufiji,** in fulfilment of the requirements for the degree of Mater of Public Health of the Muhimbili University of Health and Allied Sciences.



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DEDICATION

Dedication to my beloved family and my wife **Francisca C. Mbele.** I say thank you for the tolerance you displayed during my studies.

ABSTRACT

A cross sectional household survey was conducted in Kibiti Rufiji. The study intended to evaluate the uptake of Intermittent Presumptive Treatment in pregnancy (IPTp) and Insecticide Treated Nets (ITNs). Previous studies have shown that there is an increase of Sulfadoxine-Pyrimethamine resistance to plasmodium species and also studies explain that the impairment of the immune system is greatest observed in immunosuppresed women and this could explain the increased susceptibility to malaria seen in pregnant women with HIV infection.

Another factor contributing and promote malaria transmission in Africa is social-economic dynamic. A household survey was conducted in June-July, 2007 using structured questionnaire to collect quantitative information from randomly selected households. Households were selected using EPI random walk method; respondents were mothers who delivered within two years. Findings from this study will help to put forward recommendations to policy makers, implementers and users of these malaria control strategies on how to maximize utilization of services or looking for new malaria control strategies during pregnancy.

In this study the proportion of women who received at least one dose of SP for IPT during their last pregnancies was found to be (95.0%) this could be due to awareness and availability of SP tablets in MCH-clinics. Not surprisingly, use of SP for IPT during pregnancy was more common in recent years, corresponding to efforts to scale up IPT.

The figure is somehow above that of the Abuja target of (60%) coverage to be achieved by the year 2005. The relatively high proportion of women who received at least one dose of SP for IPT in this study implies its acceptance by women. Late presentation at antenatal clinics reduces the women's chances to receive the appropriate number of SP doses for IPT.

Findings from this study indicate that (78.0%) of women who received at least one dose of SP for IPT had made more than two antenatal clinic visits. This could be due to the fact that the district has been complying with Focused Antenatal Care program that was being provided as antenatal package to improve antenatal clinic attendance seeking for antenatal care, provide chances for provision of SP tablets for IPT. The proportion of women who received the second dose of SP tablets for IPT was found to be higher (57.0%) with more antenatal visits.

Women are made to take SP in clinic in the presence of health workers so as to improve adherence of women to SP regimen. This is only possible if drugs for IPT are adequate and water supply is regularly maintained.

The reason for 6 women out of 11 women which 50% who did not receive SP tablets for IPT was that health workers forgot to give SP tablets while 5 women about 50% mentioned poor supply of water as a barrier to Directly Observed Treatment practice. So Source of water are not in the vicinity of health facilities, moreover fetching, boiling and

storing of boiled water is cumbersome and time consuming. When the stored water becomes insufficient, procedure such as delivery and sterilization of equipment is given priority. This forced the health workers to postpone SP dose schedule without informing the pregnant women.

Majority of women seemed to have fairly good knowledge of malaria control strategy using ITNs. Findings indicate that more than three quarters 89% of women are sleeping under ITNs while only 11% of women are not sleeping under the nets, however the reasons for not sleeping under ITNs were not asked. It is obvious that malaria poses a threat to a woman during pregnancy; hence its prevention is crucial. Women were asked to mention where they obtained their bed nets, women mentioned the various sources, this study shows that majority of women 80% obtained their bed nets through the voucher system, 15% bought their bed nets from the normal shops and (5%) mentioned other sources like, being given by their relative. All women (100%) who were sleeping under the mosquito nets said that bed nets were treated with NGAO and even the re-treatment were done by using NGAO.

Ministry of Health must specifically target the availability and quality of nets that can suit the local situation. The popularization of treated nets should be accompanied by insecticide monitoring activities to provide evidence base for changing insecticide use. The study shows that 64% of women who did not receive SP tablets for IPT had low

birth weight babies while women 8% who received Sp tablets for IPT during their last pregnancy had low birth weight babies.

This explaining that use of SP tablets for IPT is protective against low birth weight, this shows the value of full course of SP tablets for IPT in preventing low birth weight, but lament that there are currently no safe drug to use for IPT in the first trimester and an additional challenge is that many women register for ANC too late. The results from this study show that majority 62% of women are sleeping under mosquito nets the birth weight of their babies ranged from 2.5 to 3.5kg and 40.0% of those who are not sleeping under mosquito nets birth weight of their babies also ranged from 2.5 to 3.5kg this indicates that the use of ITNs is protective, however in this study the result is not statistically significant, but this insignificance could be contributed by a small sample size.

Therefore priority should be placed on developing ANC-based programmes that include both IPT and ITNs, along with other essential antenatal intervention, such as HIV. Study indicates that 67% of women who received SP tablets for IPT had pre-term deliveries while those who did not receive SP tablets for IPT has shown only 11%. This shows that IPT could influence the birth outcome. All 220 (100%) respondents had no fetal loss. Result from this study shows that the use of ITNs have direct impact on low birth weight. Perhaps the major problem is re-treatment of nets since it is only regularly treated nets that give a protective effect; also the study discovered that treated nets have

a protective effective on preterm delivery may be this could be due reduction of malaria episodes, therefore women should be encouraged to use long-lasting insecticidal nets and at the same time MoH should improve accessibility of ITNs.

The use of IPT significantly reduces the risk of severe maternal anemia (3.0%) against (82.0%) $p<0.05$. It is likely that this impact is because SP reduces or eliminates the parasite biomass thus resolves the anemia and allows secondary erythropoesis to continue.

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ACRONYMS

ALU	Artmether Lumefantrine
ANC	Antenatal Care Clinic
CI	Confidence Interval
DU	Delivery Unit
DHFR	Dihydrofolate Reductase
DHPS	Dihydropteroate Synthetase
FANC	Focus Antenatal Care
HIV	Human Immunodefiency Virus
IPTp	Intermittent Presumptive Treatment in pregnancy
ITN	Insecticide Treated Nets
IgG	Immunoglobulin G
LWB	Low Birth Weight
MoH	Ministry of Health
msp	Merozoite Surface Protein
NMCP	National Malaria Control Program
PCR	Polymerase Chain Reaction
RBM	Roll Back Malaria
RR	Risk Ratio
SP	Sulfadoxine-Pyrimethamine
VSA	Variant Surface Antigen
WHO	World Health Organization

CHAPTER ONE

1.0 INTRODUCTION

1.1 Global Overview

Malaria is the major public health problem in the world and kills more people than any other communicable disease except tuberculosis (afrol News, 2007). Its prevalence worldwide is estimated to be in the order of 300- 500 million clinical cases each year. About 80% of malaria cases occur in Africa (WHO, 2003).The worldwide mortality due to malaria is estimated to be over one Million deaths each year, about 90% of all malaria death occurs in sub-Saharan Africa. *Plasmodium falciparum*, the most virulent of the four human malaria parasites species and is the main specie found in sub-Saharan Africa. The most wide spread malaria vector in Africa is *Anopheles gambiae* complex and due to its inherent characteristics it is the most difficult vector to control (WHO, 2003).

1.2 Transmission of Malaria

There are four species of plasmodium causing Malaria; *Plamosmodium falciparum, Plasmodium ovale, Plasmodium malariae and Plasmodium vivax.* Among those, *Plasmodium falciparum* accounts for majority of the infection and is fatal. Increased risk of disease is linked with changes in global climatic conditions, agriculture and irrigation projects, mining activities, migration, drug resistance, insecticide resistance and road

construction. All these factors promote high level of malaria endemicity has impact on control measures (Ijumba *et al.*2002)

The population groups most vulnerable to malaria are children under five years of age and pregnant women gravida one and two due suppress immunity. Also the social-economic dynamic prevailing in Africa promotes malaria transmission.

1.3 Malaria Situation in Tanzania

Malaria is endemic in almost all parts of Tanzania and ranks number one is terms of mortality and morbidity. *Plasmodium falciparum* malaria accounts for over 30% of the national disease burden with estimated number of malaria cases ranging between 14 and 18 million and between 100,000 and 250,000 deaths per year, (MoH, 2002).

1.4 Burden of Malaria in Pregnancy

Malaria infection during pregnancy is a major public health problem in tropical and subtropical regions including Tanzania. In most endemic areas of the world, pregnant women are the main adult risk group for malaria (WHO, 2003).The population at risk of adverse consequence of malaria in pregnancy include, women with low parity (Gravida one and two) and women with co-infection with immunodefiency virus (Steketee *et al,* 1996). *Plasmodium falciparum* infection carries high morbidity for fetus and the mother especially during the first and second pregnancies. It causes about 3%-15% of severe anaemia in pregnant women and up to 10,000 malaria related deaths per year.

It accounts for about 30% of preventable low birth weight in newborns and contributes 3%-8% of infant mortality which is about 75,000 deaths per year (WHO, 2000), and up to 60% maternal malaria cases and spontaneous abortions are reported (Irshad, 2002). In Tanzania, malaria accounts for 20% of all maternal deaths each year (MOH, 2002). Complications due to *Plasmodium falciparum* malaria in pregnancy being more severe the mortality is doubled (13%) compared to non-pregnant women (6.5%). Acute pulmonary oedema and hypoglycemia are common complications in pregnancy, jaundice and altered level of consciousness may also occur (Kakkilaya, 2002), congenital transmission of malaria may occur, though uncommon, affecting 0.8% of all infants born in Dar es Salaam (Mwaikambo and Mclarty, 1985). During pregnancy malaria tends to be more atypical in presentation. This could be due to hormonal, immunological, and hematological changes of pregnancy. Parasitemia tends to be 10 times higher as a result; the complications from *Plasmodium falciparum malaria* are more common in pregnant compared to non-pregnant women (Kakkilaya, 2002).

Malaria during pregnancy can be controlled and reduced with appropriate low cost interventions such as use of Insecticide Treated Nets (ITNs) and appropriate chemoprophylaxis, (JHPIEGO, 2002). Case management is less effective as a preventive strategy particularly in endemic areas because so many cases are asymptomatic, however appropriate malaria case management is important thus reducing uncomplicated malaria advancing to complicated malaria and reduces in case fatality rates, (Monica, 2000).

1.5 Strategies for controlling Malaria in pregnancy

In the past, across sub-Saharan Africa, administration of chloroquine chemoprophylaxis during pregnancy was common, but little was known about its impact on *Plasmodium falciparum* infection during pregnancy. Therefore, cross- sectional studies in antenatal care clinics (ANCs) and delivery units (DUs) were conducted in Koupéla District, Burkina Faso. Chloroquine chemoprophylaxis was reported by 69% of 597 pregnant women at ANCs and by 93% of 853 women in DUs. *Plasmodium falciparum* peripheral parasitemia was identified in 29% of women at both ANCs and DUs. Placental parasitemia was identified in 22% of delivering women and was strongly associated with low birth weight (LBW) and prematurity. In multivariate analysis, use of chemoprophylaxis was not associated with a reduction in the prevalence of placental parasitemia, LBW, or prematurity (Sodiomon *et al.*,2003).

Despite the high reported chloroquine chemoprophylaxis coverage, peripheral and placental malaria rates remain high and are associated with known adverse outcomes during pregnancy, including maternal anemia, prematurity, and LBW. In a cross-sectional, year-round study among 839 delivering women in Agogo, Ghana, *P. falciparum* was screened for in both, peripheral and placental blood samples, and associations with maternal anaemia, low birth weight (LBW) and preterm delivery were analyzed.

Study indicated that in peripheral blood, *P. falciparum* was observed in 19%, 34%, and 53% by microscopy, HRP2 test, and PCR, respectively. For placental samples, these figures were 35%, 41%, and 59%. Irrespective of diagnostic tool, *P. falciparum*

infection increased the risk of anaemia. Positive peripheral blood results of microscopy and PCR were not associated with LBW or PD. In contrast, the HRP2 test performed well in identifying women at increased risk of poor pregnancy outcome, particularly in case of a negative peripheral blood film. Adjusting for age, parity, and antenatal visits, placental HRP2 was the only marker of infection associated with LBW in addition to anaemia. Likewise, HRP2 in peripheral blood of seemingly aparasitaemic women was associated with preterm deliveries and anaemia.

Study concludes that peripheral blood film microscopy not only underestimates placental malaria. In this highly endemic setting, it also fails to identify malaria as a cause of foetal impairment. Sub-microscopic infections detected by a HRP2 test in seemingly aparasitaemic women increase the risks of anaemia and preterm deliveries. These findings indicate that the burden of malaria in pregnancy may be even larger than thought and accentuate the need for effective anti-malarial interventions in pregnancy (Mockenhaupt *et al.,* 2006). Alternative prevention strategies, such as use of insecticide treated mosquito nets and intermittent preventive treatment with more-effective antimalarials is needed (Sodiomon *et al.* 2003*).*

Years later Intermittent Presumptive Treatment in pregnancy (IPTp) involves providing all pregnant women at least two preventive treatments of an effective anti-malarial drug. This approach has been shown to be safe, inexpensive and effective. One study in Malawi evaluating IPTp showed a decline in placental infection (32% to 23%) and in the number of low birth weight babies (23% to 10%) (Scott *et al.,* 2006).

Research outputs indicate that IPT and the use of Insecticide-treated nets (ITNs) decrease both the number of malaria cases and malaria death rates in pregnant women and their children (Menendez *et al.,* 2007). A study in an area of high malaria transmission in Kenya has shown that women protected by ITNs every night during their first four pregnancies produce 25% fewer underweight or premature babies. In addition, ITNs use benefits the infant who sleeps under the net with the mother by decreasing exposure to malaria infection.

Health education programmes, social marketing and lobbying to reduce the prices of ITNs and re-treatments are helping to encourage the use of ITNs by pregnant women. The roll back malaria (RBM) movement promotes the use of insecticide-treated bed nets (ITNs) and intermittent presumptive treatment (IPT) of malaria infection as preventive measures against the adverse effects of malaria among pregnant women in Africa. Intermittent Presumptive Treatment (IPT) in pregnancy involves giving a curative treatment dose of an effective antimalarial drug at predefined intervals during pregnancy (World Malaria Report, 2005).

IPT in pregnancy was first introduced in areas of high malaria transmission as a measure to reduce the adverse impact of *Plasmodium falciparum* malaria in pregnancy. Because of IPTp's positive impact, some researchers extended its use in infancy (IPTi) to reduce morbidity and mortality in the first year of life.

Sulfadoxine-Pyrimethamine (SP) was the first line drug for treatment of uncomplicated malaria, it has now changed to Artmether Lumefantrine (ALU) but SP still used for IPTp despite its high resistance this could be explained by the fact that women adhere to the drug regimens. IPT by SP remains the better regimen as found in many countries due its easiness of administration.

Research has recognized that ACTs have two serious limitations; first because of embryo-toxicity, they should not be used to treat pregnant women during the first and the second trimester, since they do not kill the hypnozoite stage (Medicine for Malaria Venture, 2006).

Intermittent preventive treatment of malaria during pregnancy (IPTp) is a key intervention in the national strategy for malaria control in Tanzania. The National Malaria Control Program Sulfadoxine Pyrimethamine (SP), which was the first line drug for treatment of uncomplicated malaria, also recommended to be administered in the second (20 weeks) and third (30 weeks) trimesters of pregnancy during antenatal care (ANC) visits.

The IPTp control strategy uses the platform of Focused Antenatal Care (FANC), a comprehensive antenatal care approach for pregnant women that provides services in early detection and management of diseases including malaria, counseling on health

promotion and preparedness, complication readiness, and individualized birth planning. The new guidelines include the practice of Intermittent Presumptive Treatment (IPT) using the anti-malarial drug Sulfadoxine Pyrimethamine (SP), is effective intervention that prevents and controls the effects of malaria on mother and their unborn children. The FANC program recommends that all pregnant women be given two doses of SP during the second and third trimester, regardless of whether or not they show signs of malaria. This approach is helping to ensure that more women are protected from contacting the disease during pregnancy.

1.6 New strategies for malaria Control

The emergence and spread of drug resistant malaria represents a considerable challenge to controlling malaria. To date, malaria control has relied heavily on a comparatively small number of chemically related drugs, belonging to either the quinoline or the antifolate groups. Only recently, the artemisinin derivatives have been used but mostly in south East Asia. Experience has shown that resistance eventually curtails the life-span of antimalarial drugs (Davis *et al.*, 2005).

Controlling resistance is key to ensuring that the investment put into developing new antimalarial drugs are not wasted. Current efforts focus on research into new compounds with novel mechanisms of action, and on measures to prevent or delay resistance when

drugs are introduced. Drug discovery and development are long, risky and costly ventures (Davis *et al.*, 2005).

Antimalarial drug development has traditionally been slow but now various private and public institutions are at work to discover and develop new compounds. Today, the antimalarial development pipeline is looking reasonably healthy. Most development relies on the quinoline, antifolate and artemisinin compounds. There is a pressing need to have effective, easy to use, affordable drugs that will last a long time.

Drug combinations that have independent modes of action are seen as a way of enhancing efficacy while ensuring mutual protection against resistance. Most research work has focused on the use of artesunate combined with currently used standard drugs, namely mefloquine, amodiaquine, sulfadoxine/pyrimethamine, and chloroquine. There is clear evidence that combinations improve efficacy without increasing toxicity.

However, the absolute cure rates that are achieved by combinations vary widely and depend on the level of resistance of the standard drug. From these studies, further work is underway to produce fixed dose combinations that will be packaged in blister packs (Olliaro *et al.*, 2004).

1.7 Preventing Placental Pathology

In a high-transmission setting infections are acquired every few days or weeks throughout life. Mortality is high in childhood, but by the time of adulthood and pregnancy, infections are largely asymptomatic—although they are often still patent (this requires a total burden of greater than 100 million parasites) (White., 2005). Thus, immunity prevents life-threatening parasite burdens, and suppresses the pro-inflammatory response (which causes illness), but it does not prevent infection. In pregnancy this immune control is impaired in the placenta, which acts as a "privileged site" for parasite multiplication. The aim of using IPT in pregnancy is to reduce or eliminate the adverse effects of malaria on maternal anaemia and birth weight, and, in addition, in a low-transmission setting, to prevent severe malaria in the mother.

How malaria produces intrauterine growth retardation is still unresolved, but in *P. falciparum* malaria, retardation tends to be greatest in the first pregnancy, and often occurs without maternal illness. The greater the placental parasite burden, the greater is the reduction in birth weight. "Placental malaria" histological evidence of placental accumulation of parasitized erythrocytes or malaria pigment deposition has often been used as an endpoint in intervention studies, although the quantitative relationship between placental malaria and reduction in birth weight remains poorly characterized (White.2005).

1.8 Sulfadoxine Pyrimethamine (SP) sensitivity

On the basis of the rapid selection for mutant Plasmodium falciparum parasites resistant to these antifolate drugs and the precipitous decline in efficacy of Sulfadoxine-pyrimethamine after it was introduced in South America and Southeast Asia, experts predicted that sulfadoxine-pyrimethamine would have useful therapeutic life of only about five years in Africa and might fail even more quickly because of higher rates of transmission of malaria and of use of the drug (Nzila *et al.,* 2000).

SP resistance is associated with mutations in the dihydrofolate reductase (*pfdhfr*) and dihydropteroate synthase (*pfdhps*) genes. Pyrimethamine is a selective, competitive inhibitor of dihydrofolate reductase and earlier in the folate pathway sulfa drugs inhibit dihydropteroate synthase. Several point mutations are connected toantifolate drug resistance. The quintuple mutation (triple *pfdhfr*: I51, R59, N108 and double *pfdhps*: G437, E540) is discussed as a relevant molecular marker of SP treatment failure. Atovaquone-proguanil is a relatively new antimalarial drug that inhibits mitochondrial electron transport. Point mutations in the *cytb* codon 268 are associated with resistance to this combination (Mirjam *et al,* 2007) Study to investigate the overall efficacy of Sulfadoxine-pyrimethamine (SP) treatment and the corresponding transmission potential for patients infected with SP-resistant Plasmodium *falciparum* showed mathematical model of the in-host dynamics of *P. falciparum* infections was used to simulate

infections with parasites having different numbers of mutations in the *dhfr* and *dhps* genes and their responses to SP treatment. The treatment outcome and transmission potential of each simulated infection following SP treatment was assessed by tracking asexual parasite density and the number of days with sufficient mature gametocytes to give a >95% probability of infecting a mosquito.

The results show treatment failure only occurring in patients infected with parasites having two mutations in dihydrofolate reductase (DHFR) combined with at least two mutations in dihydropteroate synthetase (DHPS) or with parasites having a triple mutation in DHFR.

Highly mutated parasites (three mutations in each gene) caused the highest clinical failure rate, while moderately mutated parasites (three mutations in DHFR plus one mutation in DHPS) produced a high rate of asymptomatic parasitological failure following SP treatment. This high rate of asymptomatic recrudescence caused the transmission potential of infections with moderately resistant parasites to exceed that of highly resistant parasites. The model output suggests that infection dynamics following SP treatment and the overall transmission potential is inherently linked.

The combination of prolonged asymptomatic parasitaemia and increased transmission potential allows parasites having three mutations in DHFR, but fewer mutations in DHPS, to expand largely unnoticed (Michelle *et al.*, 2006).

1.9 Problem Statement

Without a better understanding of the pharmacodynamic effects of IPT, it will be difficult to make rational improvements in this promising approach to malaria prevention. The most parsimonious explanation for its effectiveness is that IPT provides antimalarial prophylaxis that, if sufficiently lengthy and effective, is beneficial both to the pregnant woman and the infant. But how lengthy and how effective?

Systematic surveillance for resistant malaria shows high level of resistance of plasmodium falciparum to sulfadoxine-pyrimethamine (SP) across eastern and southern parts of Africa. The study assessed in vivo SP efficacy after two years of use as an interim first-line drug in Tanzania, and determined rates of treatment failures obtained after 14 and 28 days of follow-up. The study was conducted in the Ipinda, Mlimba and Mkuranga health facilities in Tanzania.

Children aged 6-59 months presenting with raised temperature associated exclusively with Plasmodium falciparum (1,000-100,000 parasites per μl) were treated with standard dose of SP (Mugittu *et al.,* 2005).

In Ghana, SP failure was recently observed in 28% of treated children; the (dhfr) triple mutation (Ile51+Arg59+Asn108) increased the risk of treatment failure 10-fold. Moreover, pregnancy may influence the value of resistance makers because, due to specific ligand expression, *P.falciparum* sequesters in the placenta intervillous space.

The absence of microscopically visible parasites in peripheral blood despite placental parasitemia is one common consequence. Although the sensitivity of Polymerase Chain Reaction (PCR) in detecting placental infection in peripheral blood approaches 100%, it is unclear whether circulating parasite genotypes in pregnant women represent the actual parasite population or only part of it.

Extensive discordance between placental peripheral polymorphic merozoite surface protein (msp) genotypes has been reported, but rather homogeneous parasite populations have been reported as well. So far, it is unknown whether and what extent the value of SP resistant typing. In Ghana, the *P.falciparum dhfr* triple mutation is highly predictive for SP treatment failure in children, whereas *dhps* alleles are not (and were thus not assessed here).

In the present study, the differential effect depending on the *dhrf* alleles of plasma pyrimethamine on parasite density is suggestive of resistance. One major advantage of SP in IPTp lies in its single dose administration, but resistance is anticipated to spread and intensify. Here, it has been shown that 93% and > 50% of the women harbored parasites with the *dhfr* core mutation Asn 108 and the high resistance triple mutation, respectively.

HIV infection increases the risk of malaria infection in pregnant women. Antibodies to variant surface antigens (VSA) on infected erythrocytes might protect against malaria in pregnancy. They postulated that HIV-induced impairment of humoral immunity to VSA mediates the increased susceptibility to malaria. They compared serum concentrations of antibodies to VSA by flow cytometry or agglutination, and to merozoite proteins AMA-1 and MSP119 by ELISA, in 298 pregnant Malawian women, and related the findings to malaria and HIV infection, CD4-positive T-cell count, and HIV-1 viral load. Concentrations of IgG to placental type VSA were lower in HIV-infected women than in HIV-uninfected women, among women with malaria and those without malaria.

The impairment was greatest in first pregnancy. Agglutinating antibodies to placental VSA were present in a lower proportion of HIV-infected than HIV-uninfected women 58 (35.1%) against 50 (53.8%). The degree of antibody binding by flow cytometry was correlated with CD4-positive T-cell count and inversely with HIV-1 viral load.

Concentrations of antibodies to AMA-1 were lower in HIV infection but were not correlated with CD4-positive T-cell count or viral load. Responses to MSP119 were little affected by HIV infection. In multivariate analyses, HIV was negatively associated with amount of antibody to both VSA and AMA-1but not MSP119. HIV infection impairs antimalarial immunity, especially responses to placental type VSA. The impairment is greatest in the most immunosuppressed women and could explain the increased susceptibility to malaria seen in pregnant women with HIV infection (Mount *et al.*, 2004*)*.

Malaria prevention is particularly challenging in HIV infected women, who might constitute up to 40% of antenatal population in southern Africa.

HIV infected pregnant women are more likely to fail antimalarial treatment and require three or more doses of IPTp with sulfadoxine-Pyrimethamine to obtain the same effect achieved with two doses in HIV-uninfected women (Menendez *et al,*2007*)*.

Therefore, since mid 2006 SP was replaced by Artmesinin based combination (Artmether and Lumefantrine-ALU) as a first line drug for treatment of malaria as national policy and this change was done because of increasing resistance to SP. The aim of this study is to evaluate the IPTp uptake and perform a current situational analysis IPTp in Kibiti ward. The outcome of this study will indicate the true status of IPTp and ITNs use by pregnant women.

1.9.1 Rationale

According to National Malaria Control Program (NMCP) guidelines Sulfadoxine Pyrimethamine (SP) is recommended for IPTp in two doses. Now with increasing SP resistance it becomes necessary to evaluate the impact of this strategy. With the prevailing HIV epidemic, malaria in pregnancy becomes worst and therefore how IPTp is providing protection in HIV positive mothers remains largely unknown in Tanzania. The other strategy is use of ITNs in pregnancy is presently implemented as a voucher system.

It is important to evaluate how many mothers in rural area have this option and have adopt this strategy given the economic constrains. Provide insight in the prevailing situation the result will indicate the uptake rates of IPTp and ITNs thus providing National Malaria Control Program (NMCP) the basis for developing appropriate policy for these strategies.

1.9.2 Broad Objective

To evaluate Intermittent Presumptive Treatment (IPT) and Insecticide Treated Nets (ITNs) uptake by mothers in Kibiti Rufiji.

1.9.3 Specific Objectives

(1) To determine the proportion of women who completed IPT dose schedule

(2) To determine the proportion of women who are using ITNs

(3) To determine prevalence of low birth weight in relation to use of IPTp and ITNs.

(4) To determine prevalence of fetal loss in relation to use of IPTp and ITNs.

(5) To determine prevalence of anaemia during pregnancy in relation to use of IPTp and ITNs

CHAPTER TWO

2.0 Review of Literature

Currently, the recommended intervention strategies for preventing malaria during pregnancies are Intermittent Preventive Treatment (IPT) with sulfadoxine-pyrimethamine and Insecticide-Treated Bed nets (World Health Organization, 2004). However, in many African countries, the coverage of such interventions varies from modest to extremely low (Holtz *et al.,* 2004and Guyatt *et al.,* 2004). Although reports repeatedly mention the need to focus on behavioural aspects to better reach pregnant women, little has been done to actually promote such studies.

Furthermore, though the intervention studies mention "vulnerable groups", "utilization of health-care services", "delay", or "beliefs" as important factors for effective prevention and treatment all wordings which should immediately call social scientists on stage behavioural and other social science research going beyond simplistic knowledge, attitudes, and practices studies is largely absent. Fortunately, interest in social science studies on malaria in pregnancy is slowly awakening. Antenatal clinics provide an avenue for interventions that promote maternal and infant health. Timely antenatal attendance is the key for delivering the prevention package to pregnant women. About 40% of pregnant women from Africa present for the first time to antenatal clinics in the second trimester of pregnancy, and 25% come for the first time in third trimester. This means that at least the first dose of SP for IPT could be given in time to most pregnant women (WHO, 2003). Studies conducted in Malawi indicate that the proportion of

women receiving at least one dose of SP for IPT during pregnancy is relatively high 67%-92.7%, where the proportion of those receiving the second dose is much lower 29%-39% (Rogerson *et al.*, 2000 and Timothy *et al.*, 2004). In Kenya the uptake of SP in pregnant women at ANC was reported to be 23.7% for two doses of SP and 43.4% for one SP dose (Van Eijk *et al.*, 2004). There is clear evidence that the resistance of *Plasmodium falciparum* to sulfadoxine-pyrimethamine has increased in Malawi over the past 10 years. According to (Plowe *et al.*, 2005) resistance to sulfadoxine-pyrimethamine was absent in Malawi in 1990.The level of cumulative RI-RII-RIII parasitological failure probably reached a peak in Ndirande in 1999. Similar failure rates with chloroquine in six sites in Malawi led to a policy change in 1993 (Khoromana *et a.l*, 1986). *Plasmodium falciparum* resistance to sulfadoxine/pyrimethamine SP is due to mutations in the dihydrofolate reductase (*dhfr*) and dihydropteroate synthetase (*dhps*) genes. Large-scale screening of the prevalence of these mutations could facilitate the surveillance of the level of SP resistance *in vivo*. The prevalence of mutations in *dhfr* and *dhps* in relation to S/P efficacy was studied in four sites of differing endemicity in Sudan, Mozambique, and Tanzania. The sites we reorganized in order of increasing resistance and a significant increase in the prevalence of triple mutations in codons c51, c59, and c108 of *dhfr* was observed. A similar trend was observed when *dhfr* genotypes were combined with c437 of *dhps*. Since the differences in SP resistance between the sites were minor, but nevertheless revealed major differences in *dhfr* genotype prevalence, the role of *dhfr* as a general molecular marker seems debatable. The differences may reflect variation in the duration and magnitude of SP usage (or other

antifolate drugs) between the sites. Thus, triple *dhfr* mutations may prove suitable only as a general guideline for detecting emerging S/P resistance in areas where SP has been introduced recently. However, changes in susceptibility within the same area with moderate levels of resistance may be possible by longitudinal surveillance of a subset of *dhfr/dhps* mutations that has been associated with SP resistance *in vivo* in a defined location (Alifrangis *et al.* , 2003).While community knowledge about the malaria–mosquito link can be considered fundamental in determining the use of insecticide-treated bed nets, prompt and effective treatment depends on illness recognition. However, malaria-related symptoms can be easily confused with pregnancy-related symptoms. No publication was found that explores the way pregnant women distinguish malaria signs from general malaise and other common symptoms (e.g., nausea, vomiting, weakness, etc.) during pregnancy. Furthermore, it is necessary to determine whether pregnant women's susceptibility to anaemia is commonly known, and if people realize the link between anaemia during pregnancy and malaria (Ribera *et al.,* 2007).

Without a better understanding of the pharmacodynamic effects of IPT, it will be difficult to make rational improvements in this promising approach to malaria prevention. The most parsimonious explanation for its effectiveness is that IPT provides antimalarial prophylaxis that, if sufficiently lengthy and effective, is beneficial both to the pregnant woman and the infant. But how lengthy and how effective? (White, 2005).

Control of malaria in pregnancy through prevention or treatment may save lives of mothers and babies. Selection of drugs for treatment of infected pregnant women, or for prevention in exposed populations is problematic owing to resistance to established drugs and lack of pregnancy-specific safety and pharmacological data for new drugs. Encouragingly, a number of new drugs and combinations of drugs hold promise for effective treatment, but adequate data on their safety in pregnancy is currently lacking.

Our principal challenges are to decide which drugs to develop for use in malaria treatment and prevention in pregnancy and to develop mechanisms to rapidly and comprehensively evaluate their safety. Prevention of malaria in pregnancy by vaccination may also become possible, but targets must be closely defined, and strategies developed to test candidates against meaningful end points (Rogerson *et al.*, 2006).

The problem with malaria models, even one as advanced and comprehensive as this new model, is that they are still a vast oversimplification of a very complex system. The characterizations of immunity, population antimalarial pharmacokinetics and pharmacodynamics, and the epidemiology of malaria transmission in current models is all insufficient. In addition, geographical, behavioural, and biological heterogeneities are not accounted for adequately.

Modellers should be encouraged to describe clearly the limitations of their predictions. We really do not know whether the results of sensitivity analyses and the conclusions

basedon these simplifications can be extrapolated to the "real world". In this particular case, we are not even very sure how IPT "works". (White, 2006). Descriptive cross-sectional analysis of *P. falciparum* prevalence in pregnant women at first antenatal visit and of women at delivery who had received two sulphadoxine-pyrimethamine treatments for malaria has protective effect. HIV status was assessed in 621 women who attended antenatal care and for delivery at two rural hospitals in southern Malawi in 1993-94. Information was collected on maternal age, parity and gestational age.

Prevalence of *P. falciparum* was measured at first antenatal visit and delivery. Women were given two routine treatment doses of sulphadoxine-pyrimethamine (SP), at first antenatal visit and between 28 and 34 weeks gestation, conforming to Malawi government policy on antimalarial control during pregnancy.

Prevalence of HIV infection was 25.6% and all infections were HIV type-1. In primigravidae malaria prevalence at recruitment was 56.3% in HIV-infected and 36.5% in HIV-uninfected women. The corresponding figures for multigravidae were 23.8% and 11.0%, respectively. HIV-infected primigravida had increased malaria prevalence at all gestational ages. Peak parasite prevalence occurred earlier in gestation in HIV-infected primigravidae (16-19 weeks if HIV-infected; 20-23 weeks if HIV-uninfected). The relative risk for parasitaemia in HIV-infected compared to HIV-uninfected women was significantly increased in three of five parity groups, including the two highest ones (parity>3), indicating that parity-specific immunity to malaria was impaired.

Malaria prevalence at delivery remained high in HIV-infected women despite prior routine treatment with sulphadoxine-pyrimethamine in pregnancy. There was no significant difference in parasite prevalence at delivery between women who did or did not use sulphadoxine-pyrimethamine.

Thus the Malawi study concludes that HIV infection is associated with a significant increase in malaria prevalence in pregnant women of all parities with the effect apparent from early in gestation. Two treatment doses of sulphadoxine-pyrimethamine were inadequate to clear parasitaemia in many women by the time of delivery and this occurred independently of HIV status and despite high sensitivity to SP in this area.

Therefore there is a need to undertake longitudinal studies to determine the incidence of *P. falciparum* infection in HIV-infected and uninfected pregnant women and to reassess the frequency and timing of sulphadoxine-pyrimethamine treatment doses in these women. Late pregnancy re-infections with *P. falciparum* probably explain the high parasite prevalence at delivery following Sulphadoxine-pyrimethamine treatment at 28-34 weeks gestation (Verhoeff *et al.*, 1999).

CHAPTER THREE

3.0 METHODOLOGY

3.1 Description of the study area

The Rufiji District situated about 178 kilometers south of Dar-es-Salaam, andis one of the six Districts of the Coast Region. Rufiji District located in the southof the Region, has six Divisions with 19 wards divided into 94 registered villageswith 385 hamlets. Its vegetation is mainly formed of tropical forests and grassland. The district has hot weather throughout the year and two rainy seasons, short rains (October to December) and long rains (February to May). A prominent feature in the District is the Rufiji River with its large flood plain and delta.

Rufiji District is home to several ethnic groups in the Ndengereko (who according to oral tradition, are original inhabitants of the area) other group includes Matumbi, Nyagatwa (concentrated in the delta area), Ngindo, Pogoro and Makonde. The majority of people in Rufiji are subsistence farmers; major crops include cassava, maize, rice, millet, sesame, coconut, and cashew nuts. Fruits such as mangoes, oranges, pineapples, papaya and jack fruits are also grow.

Kibiti is one ward among the nineteen wards of Rufiji Distict. It has two health facilities one dispensary owned by Swedish church and one health center owned by government. Both facilities provide antenatal services and serve four villages, Kibiti A, Kibiti B, Mtawanya and Kinyanya. The population in Kibiti is 29,187 with 6,168 households.

3.2 Study design

This was a cross-sectional house hold survey. Structured questionnaires were by trained Research assistants.

3.3 Study population

The study population consisted of women delivered within two years.

3.4 Sample size

The sample size is calculated using the formula,

$$n = \frac{Z^2 P (100-P)}{E^2}$$

Where;

n = the required minimum sample size

Z = is the standard normal deviation corresponding to 95% confidence interval = 1.96

P = is the proportional of women who received SP for IPT taken 29% (MoH, 2002)

E = is the margin of error on P estimated to be 6%.

Hence;

$$n = \frac{1.96^2 * 29 (100-29)}{6^2}$$

$$n = \frac{7,909.8544}{36}$$

$$n = 219.718$$

Therefore the required minimum sample size was 220.

3.5 Sampling method

Method used was the EPI random walk; we went to a central location within the community which was the market. Selection of direction was done at random by spinning a bottle, then we moved in a straight line in that direction, and then we counted all houses that we passed until we reached the of the village. Then, one of these numbered houses was picked at random to form the starting point for the survey. The research team was lead by a local guide, who was familiar with the area and the population.

3.6 Criteria for enrolment:

To be enrolled in the study the subject must meet the following criteria:

1. Women who had delivered within two years.
2. Must be Kibiti resident.

3.7 Recruitment and training of research assistant

Two research assistants were recruited and trained for two days consequently in order to build the capacity for good data collection.

3.8 Data collection tool

A structured questionnaire in Swahili language was used to collect the information from respondents and it had five parts. Part one dealt with demographic characteristics of the respondent. Part two covered uptake of IPTp and ITNs. Part three to five covered low birth weight, fetal loss and anemia during pregnancy in relation to use of IPTp and ITNs.

3.8.1 Data collection procedure

The interview team (Research assistants, local guide and Principal investigator visited the households. Interviews with the respondents were carried out at their homes after introduction, going through the eligibility criteria and informed consent obtained. Respondents were interviewed privately and the answers were recorded on questionnaire.

3.9 Pre-testing of the research instrument

The questionnaire was pre-tested in Kibiti before to find out whether the questions were clear and arranged logically. After pre-testing modification of questionnaire was done before embarking on the actual field.

3.10 Data handling and analysis

Data were collected and recorded by using questionnaires. Data collection tools were reviewed by a team supervisor at the end of each day for accuracy and completeness. Any problems identified were addressed by the study team prior to the next day of data collection. The analysis was done in Epi-Info.

3.11 Quality assurance

Procedures for quality assurance were maintained throughout the study. Team supervisor reviewed the data collected daily to identify missing be addressed before returning to the field the next day.

3.12 Dissemination of outputs

Issues identified in the community will first be disseminated back to the community through the Information, Education and Communication Materials (IEC messages). Regular weekly meetings with the stakeholders another forum for transmitting study outputs to the community. At national level, participation of the investigators in meetings and working groups will facilitate transmission of the study outputs at this level. We are planning to circulate the project report to all stakeholders. A plan for the dissemination of the overall study results will be developed in collaboration with the stakeholders especially the Tanzania Ministry of Health. In general the results will be disseminated to the participating district and other appropriate bodies within the Tanzanian MOH. Results will also be submitted to peer-reviewed scientific journals and presented at national and international meetings.

3.13 Ethical consideration

The nature of this study was thoroughly explained and defined to eligible participants by researcher. In particular participants were informed that research has an academic requirement for the Masters Degree in Public Health. Participants were assured that the responses will be kept confidential and the names will not appear in any of the document.

3.14 Consent

As per local norms that fulfill the inclusion criteria was asked for their informed written consent agreeing to participate in the study. The consent form was translated from English into Swahili and back translated to ensure that accuracy of content and information that could level of literacy is maintained. Consent forms were ready loudly in Swahili by trained team members to the participant, details about the trial was explained. Information regarding maintenance of confidentiality of data will also be explained. Opportunity for asking and answering questions were also part of this consent process. Participants were asked to sign a consent form (or place a ink finger print or an 'X') in the appropriate place on the form.

3.15 Limitation of the study

Limitation of time has influenced in data collection.

3.16 Definition of terms

Primigravida: a pregnant woman who is having her first pregnancy

Secondgravida: a pregnant woman carrying her second pregnancy

Multigravidae: pregnant women who had three or more pregnancy

First trimester: pregnancy below twelve (12) weeks gestation

Second trimester: pregnancy between 13 and 24 weeks of gestation

Third trimester: pregnancy between 25 and 36 of weeks of gestation

Preterm delivery: delivery before time below 37 weeks of pregnancy

Full term delivery: delivery at actual time 37-40 weeks of pregnancy

Post term delivery: delivery after time above 40 weeks of pregnancy

NGAO: Insecticide used to treat bed nets

MTUHA: One of health information management system useful in collection of information from health facilities

Abuja target: Malaria conference done in Abuja Nigeria to improve IPT coverage 60% to be achieved by 2005

CHAPTER FOUR

RESULTS

A total of 220 women in 216 households were interviewed. This was 100% of the estimated sample size; all the interviewed women had children less than two years of age. The social demographic characteristics of these women are shown in table 1.

Majority of women, about 40% visited the antenatal clinic three times. Perhaps this explains the essence of Focus Antenatal Care. Because of antenatal clinic visits are reasonably high intervention such as IPTp can be implemented.

Table 1: Demographic characteristics of the study population

Variables	Number of women (n=220)	Percent
Age group (years)		
- 19	39	17.8%
20-24	72	32.9%
25-29	51	23.3%
30-34	21	9.3%
35 Above	36	16.2%
Unknown	1	0.5%
Marital status		
Married	151	68.6%
Not married	69	31.4%
Gravidity		
Primigravida	72	32.7%
Secondgravida	46	20.9%
Multigravidae	102	46.4%
Education level		
No formal education	2	0.9%
Primary education	80	36.7%
Secondary education	127	58.3%
Above secondary	11	4.1%

Table 2: Frequency of antenatal clinic attendance

Frequency of Clinic attendance	Number of women (n=220)	Percent
1	10	4.6%
2	25	11.4%
3	87	39.7%
4	68	31.1%
5	17	7.4%
More than 5	13	1.4%
Total	**220**	**100%**

Utilization of IPT at antenatal clinic

The proportion of women who had received SP tablets for IPT was acceptably high. Of the 220 women interviewed 209 (95%) had received SP tablets. However it important to show the proportion of women who received one dose of SP only since this will have much less impact (p=0.0063)

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Table 3: Number of SP doses that women received

	No IPTp	One dose of IPTp	Two doses of IPTp	
Antenatal visits		**No. (%)**	**No. (%)**	**Total**
Up to 2	11 (5%)	18 (8.6%)	21(10.1%)	39
More than 2	0(0%)	51(24.4%)	119 (56.9%)	170
Total	**11(5%)**	**69(33.0%)**	**140 (67.0%)**	**220**

Table 3 shows that MCH cards of majority of women had received two recommended doses of IPT (63.0%) while (31.0%) had received only one dose of during pregnancy. In addition, 57% of pregnant women who received two doses of SP for IPT had made more than two antenatal clinic visits compared to 10.0% who had one or two antenatal visits. The likelihood of getting two doses of SP for IPT are significantly high, when women visit antenatal clinic more than twice (p=0.0063). It was of interest to know whether the women actually swallowed SP tablets under Directly Observed Therapy. The questionnaire elicited if they had swallowed SP tablets in the clinic or were given SP tablets to swallow at home. Seventy seven percent (162) of them had swallowed SP tablets at the antenatal clinic, while 23% (47) of them took SP tablets to swallow at home. Women who took SP tablets to swallow at home were asked to give reasons for

not doing that. Table 4 shows reasons given by women for not swallowing the SP tablets at antenatal clinic.

Table 4: Reasons for not swallowing SP in the clinic

Reasons	Responses (N=47)	Percent
Didn't want to share cups	13	27.7%
Can not take drug on empty Stomach	34	72.3

From the above, in order to increase compliance perhaps there may be room for information sharing. If women could be informed to bring their own cups and light snack the Directly Observed Therapy could be further increased to achieve a maximum compliance.

The questionnaire attempted to delineate what factors could be barriers for the uptake of IPTp. This is important because in order to increase coverage, it is important to understand possible barriers. Eleven mothers responded to the question why they had not taken SP tablets for IPT. About 50% said that Health workers did not give them SP

either they had forgotten or SP tablets were out of stock while a similar proportion said that there was unsafe water hence they could not swallow SP tablets for IPT in the clinic.

Use Insecticide Treated Nets (ITNs)

An additional control strategy is the use of ITNs during pregnancy; an attempt was made to determine the proportional of women who were using treated nets. The response distributions are summarized in the Table 5.

Table 5: Distribution of users and non-users of ITNs

ITN use	Number of women (n=220)	Percent
Yes	195	88.6%
No	25	11.4%
Total	**220**	**100%**

Table 5 indicates that majority of women (89.0%) were sleeping under mosquito nets while (11.0%) were not sleeping under the treated nets during their last pregnancy. The effectiveness of ITNs depends on the fact that nets are regularly treated. Additional questions were asked to establish if the nets were treated or remained untreated. About (50.0%) of the ITNs were acquired in the past 6 months and the other (50.0%) acquired more than one year. The implication of this is that nets acquired more than one year will most unlikely be retreated thus losing their preventive potential. Rufiji district has a pilot

project on access of ITNs through the voucher system. Women were asked from where they got their bed nets. The major source mentioned by (80.0%) was through the voucher system followed by purchase from the shop.

Table 6: Distribution of various sources of acquiring bed nets

Source of bed net	Number of women (n=195)	Percent
Bought from the shop	30	15.4%
Voucher system	156	80.0%
Other sources	9	4.6%
Total	**195**	**100%**

The voucher system gives a subsidized net plus insecticide. This treatment will last for 6 months only and then the owner has to re-treat at market prices. Re-treatment remains the problem.

Low birth weight in relation to use of IPT and ITNs

From the MCH cards the birth weight was noted in relation to the use of SP tablets for IPTp and ITNs.

Table 7: Birth weight in relation to IPT user and non- users.

IPTp use	Birth weight under 2.5 (%)	2.5 and above (%)	Total
Yes	16 (7.7%)	193 (92.3%)	209
No	7 (63.6%)	4 (36.4%)	11
Total	**23**	**197**	**220**

The relationship between low birth weight and use of IPT is important mother who used IPT, their children were less likely to have low birth weight babies (p=0.023). Therefore the use of IPT is protective against low birth weight.

Table 8: Birth weight in relation to use and non-use of ITNs

ITN use	Birth weight in kg under 2.5	(%)	2.5 and above	(%)	Total
Yes	24	(10.9%)	171	(87.7%)	195
No	8	(32.0%)	17	(68.0%)	25
Total	**32**		**188**		**220**

Low birth weight and ITNs use was not significant since (p=0.35). The use of ITNs did not have a direct impact on low birth weight. Perhaps the major problem is re-treatment of nets since it is only regularly treated nets that give protective effect.

Fetal loss in relation to the use of IPT and ITNs

Fetal loss is also one of the complications of malaria in pregnancy. This study attempted to show proportion o women that had fetal loss and its association with use of IPTp and ITNs.

All the 220 women interviewed none had reported fetal loss. There were (29) women with preterm deliveries but they delivered live babies. May be the association between fetal loss and IPTp in this study is study is insignificant since there was no fetal loss among mothers who had not use IPT, but this could be because of there were small in number.

Table 9: Outcome of pregnancies for ITNs users and non-users ITN

Outcome	Responses Yes (%)	No (%)	Total
Preterm	24 (12.3%)	16 (64.0%)	40
Full term	168 (86.2%)	9 (36%)	177
Post term	3 (1.5%)	0 (0%)	3
Total	**195**	**25**	**220**

Table 8 show the outcome of pregnancies of women who used ITNs during their last pregnancies against non-users of ITNs, 64.0% of women who are not sleeping under Mosquito nets had preterm deliveries compared to users of ITNs (12.0%). This comparison was found significant (p- value<0.05). ITNs use had less likelihood of

preterm deliveries. Treated nets have a protective effect; mothers will suffer less number of malaria episodes and thus reduce the potential of preterm deliveries.

Anemia in pregnancy

In high in high malaria endemic areas maternal anemia is the most important clinical complication. This study explored the prevalence of anemia and its association with control strategies, which are IPT and ITNs use.

Table 10: IPT use by hemoglobin status

	Hemoglobin status				
IPT use	**Normal (%)**	**Mild anemia (%)**	**moderate (%)**	**severe anemia (%)**	**Total**
Yes	43 (20.6%)	121 (57.9%)	39 (18.7%)	6 (2.8%)	209
No	1 (9.1%)	1 (9.1%)	0 (0%)	9 (81.8%)	11
Total	**44**	**122**	**39**	**15**	**220**

The above table shows that use of IPT is significantly reduces the risk of severe maternal anemia (3.0% against (82.0%) $p<0.05$. It is likely that this impact is because SP reduces or eliminates the parasite biomass thus resolves the anemia and allows secondary erythropoesis to continue.

Table 11: ITNs use by hemoglobin status

ITN use	Hemoglobin status Normal (%)	Mild anemia (%)	Moderate (%)	Severe anemia (%)	Total
Yes	37 (19.0%)	91 (46.7%)	59 (30.3%)	8 (4.0%)	195
No	4 (16.0%)	5 (20.0%)	3 (12.0%)	13 (52.0%)	25
Total	**41**	**96**	**62**	**21**	**220**

Table 11 shows hemoglobin status for women who used ITNs during their last pregnancy and non-users of ITNs. 52.0% reported to have severe anemia during their last pregnancies, while users of ITNs (4.0%) reported to have severe anemia during their last pregnancies ,therefore the study shows ITNs use could contribute in reducing anemia during pregnancy (p=0.0009).

CHAPTER FIVE

DISCUSSION

This study was conducted in Kibiti ward in Rufiji District which is a rural setting. Malaria during pregnancy and maternal mortality is undoubtedly an important public health problem as in many other districts in the country. In recent years, the corner stone for malaria prevention during pregnancy has been the provision of IPTp using SP Directly Observed Therapy at antenatal clinics together with the use of ITNs by pregnant women. The aim of this study was to evaluate ongoing control strategies aimed at reducing the burden of malaria in pregnancy.

IPT Uptake

A relatively high proportion of women received at least one or two doses of SP for IPTp during their last pregnancies. This uptake had a significant impact on maternal health, then hemoglobin status improved and for the new born there was significant improvement in birth weight. Similar findings were reported from Malawi (Leavens, 2002). Further, this level of IPTp coverage is above that of Abuja target of (60%) by year 2005. These results indicate that there is adequate awareness and acceptance of this strategy by the community. However, the coverage can still increase if antenatal clinic is made more user friendly in terms of supply of drinking water and education. These results are based on a recall cross-sectional household survey. Ideally there should have been a controlled area for comparison or similar pre-intervention data for comparison. Unfortunately this ideal design was not possible and remains a major limitation of the

study. On the other hand, the survey did not attempt to unearth the impact indicators like status of anemia, low birth weight, fetal loss etc. Perhaps this data in addition to the regular collection of the MTUHA data by Ministry of Health (MoH) will enable evidence based decision to be taken.

One of the major concerns of IPTp is using SP. Parasite resistance to SP (Mirjam *et al.*, 2006) is high and increasing. Currently there is no antimalarial that can replace SP for IPTp. Regular impact surveys are thus pertinent because it is important to establish impact trend and resistance data for decision makers.

Insecticide Treated Nets (ITNs) coverage

Majority of women had fairly good knowledge of malaria control strategy using ITNs. Findings indicated that more than three quarters (89.0%) of women were sleeping under ITNs while only (11.0%), were not using ITNs. The ITNs strategy for preventing malaria in pregnancy is for individual personal protection it is thus important, that every pregnant women acquires and uses ITNs. In contrast to these ITNs coverage in a community is important because higher the coverage in a community makes ITNs a Public Health strategy as against individual protection. Because of this concept perhaps our data did not show a significant impact on low birth weight since malaria transmission remains stable because of low community coverage.

As individual protection to the user's preterm delivery was significantly reduced due to perhaps reduction in malaria episodes by at the pre-partum period. Similar findings were reported by (Marchesin *et al.,* 2004). The issue of retreatment of ITNs remains a major Public Health hurdle.

This survey did not directly elicit or measured a proxy marker for re-treatment. To do this would have been desirable but due to constrain of time we attempted to establish this indirectly and this may give rather rough estimates at re-treatment.

Health indicators

The study showed that women who did not receive SP tablets for IPTp had significantly higher low birth weight than women who received SP tablets for IPTp during their last pregnancy. Receiving two doses had a higher reduction of low birth weight. A part from low birth weight, the use of IPTp and ITNs also showed a positive impact on preterm delivery, on fetal loss and no resolution of anemia. These combined parameters are important indicators of maternal and new born mortality. Strategies to improve these parameters will have a significant impact on maternal and new born health.

CHAPTER SIX

CONCLUSIONS

i) The study has shown that uptake of SP tablets for IPT in women attending antenatal a clinic is high (95.0%). Uptake of the second dose of SP tablets for IPT also is high (57.0%).

ii) The more the times pregnant woman attends antenatal clinic the likelihood of getting a second dose of SP tablets for IPT is high.

iii) Irregular supply of water to health facilities, refusal of sharing cups and belief that that taking SP on empty stomach among women was dangerous, were found to be the barrier in the Directly Observed Therapy practice of IPT using SP.

iv) Use of ITNs is 89.0% and majority the acquired their bed nets by voucher system (80.0%) and all bed nets were treated and re-treated by NGAO.

v) IPT is protective against low birth weight; this shows the value of full course of SP tablets in preventing low birth weight.

RECOMMENDATIONS

i) Monitoring of SP resistance in pregnancy when used as IPTp drug.

ii) Research for alternative antimalarials for use in IPTp

iii) Improve accessibility of ITNs to pregnant women.

iv) Women should be encouraged to use long-lasting insecticidal nets.

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