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BIRTH OUTCOMES IN PREGNANT WOMEN TREATED WITH ARTEMISININ-BASED COMBINATION THERAPIES AT TEMA GENERAL HOSPITAL

BY

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DECLARATION

I, Patricia Chukwuenwenaiwe Bentil, declare that except for other people's investigations which have been duly acknowledged, this work is the result of my own original research, and that this dissertation, either in whole or in part has not been presented elsewhere for another degree.

…… ……

Patricia Chukwuenwenaiwe Bentil (Mrs.) Date

(Student)

…… ……

Dr. Priscilla Awo Nortey Date

(Supervisor)

DEDICATION

This work is dedicated to The Almighty God and my Family

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First and foremost, my sincerest thanks goes to the Almighty God for the enablement to start and complete this study. It had not been easy, but He made a way.

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LIST OF ACRONYMS

ACTs	–	Artemisinin-based Combination Therapies
AL	–	Artemether - lumefantrine
ANC	–	Ante-natal Clinic
AA	–	Artesunate -Amodiaquine
BMI	–	Body Mass Index
CRF	-	Case report form
DOT	–	Directly Observed Treatment
G6PD	–	Glucose-6-Phosphate Dehydrogenase
Hb	–	Haemoglobin
ITNs	–	Insecticides Treated Nets
IRS	–	Indoor residual spraying
IPTp	-	Intermittent Preventive Treatment during Pregnancy
LGTI	–	Lower Genital Tract Infections
OR; AOR	-	Odds ratio; Adjusted Odds Ratio
SD	–	Standard Deviation
SP	–	Sulphadoxine- pyrimethamine
STIs	-	Sexually Transmitted Infections
TGH	–	Tema General Hospital

OPERATIONAL DEFINITION OF TERMS

Abortion - When pregnancy terminates before 28th weeks.

Birth outcomes - End product of pregnancy (low birth weight, normal birth weight, premature birth and still birth).

Low birth weight - Infant weighing less than 2500g at birth

New mothers - Women who delivered less than 7 days and are still on admission at the study site.

Normal birth weight - Infant weighing from 2500g to 3500g at birth.

Premature birth - Infant born before 37 weeks of pregnancy.

Still birth -Baby born dead after 28 weeks of pregnancy.

ABSTRACT

INTRODUCTION: In the treatment of malaria in pregnant women in Ghana, the treatment regimen for first trimester is different from the treatment regimen for second and third trimesters. Quinine is the recommended treatment regimen in the first trimester of pregnancy but this is not well accepted by both prescribers and patients. This seems to be due to perception of likely unwanted side effects that may lead to spontaneous abortion and its longer treatment duration, (anecdotal evidence)[1]. Hence other antimalarials are being used but there is little evidence on the birth outcomes associated with the use of these antimalarials.

METHOD: This study used a retrospective cohort design to examine birth outcomes in two groups of women who received malaria treatment in all the trimesters of pregnancy at the maternity wing of Tema General Hospital. The first group received artemisinin-based combination therapies in pregnancy, and the second group received any other malaria treatment or no treatment at all during pregnancy. Case Report Forms (CRFs) were used in collecting relevant information from maternal record cards of the new mothers. Clarifications were obtained from the new mothers when needed. There were 72 women in each group. This study was conducted from May - June 2015, when deliveries were highest at the Tema General Hospital.

RESULTS: There was no significant differences (p=0.48, 0.52, 0.70, 0.70) in all the four birth outcomes, normal birth outcome, birth weight of the baby, stillbirth and premature birth in the two groups of new mothers. Increasing number of doses of sulphadoxine-pyrimethamine (SP) was observed to result in favourable birth outcomes. Women who took up to two doses of Intermittent Preventive Treatment during Pregnancy (IPTp) had a

[1] The reference for this statement is from series of verbal discussions with different prescribers in Tema, as there were no documented evidence of spontaneous abortion with quinine use in early pregnancy at the facilities visited.

38% decreased odds of normal birth outcome (AOR 0.62, p=0.34), while those who took up to four doses of IPTp had 120% increased odds of having normal birth outcome.

DISCUSSION/CONCLUSION: This study found that birth outcomes in pregnant women who were treated with ACTs in all trimesters of pregnancy were slightly different from birth outcomes in pregnant women who were not treated with ACTs in all trimesters of pregnancy, but these differences were not statistically significant.

CHAPTER ONE

1.0 Introduction

Malaria is endemic in poor tropical and subtropical areas of the world (Prevention, 2014). In Ghana, according to the recent publication on malaria by WHO (2013), about 100% of malaria is caused by *Plasmodium falciparum*, which can progress from mild to severe if early treatment is not administered to the infected person. Malaria in pregnancy is an important public health problem due to the fact that it is the leading cause of anaemia and death in pregnant women.

There is evidence that the pregnant woman is more vulnerable to malaria, than the non-pregnant woman ("Malaria," 2013). Maternal risk factors for malaria in pregnancy include low maternal age and low parity.

In stable high transmission areas, almost all primigravidae, if unprotected, are likely to be infected in early pregnancy, and about half of these would remain infected by the time of delivery if untreated (Brabin et al., 2008).

Pregnant women, particularly in the second and third trimester of pregnancy are more likely than their non-pregnant counterparts to develop severe malaria often complicated by pulmonary oedema, and hypoglycemia, and so foetal death and premature labour are common (Health, 2010).

The main effects of malaria in pregnancy include maternal anaemia, low birth weight (LBW), preterm delivery and increased infant and maternal mortality.

By convention, research is not carried out in pregnant women because of their vulnerability and the safety of most medicines especially in first trimester cannot be guaranteed, due to the risk of teratogenicity, and so, the intake of medicines should be avoided if possible in the first trimester.

Medicines are given to pregnant women only when the benefit of use outweighs the risk of not using them. But in Ghana due to high illiteracy level among women, most of them self-medicate even before reporting to health facilities, and it is usually difficult for them to be able to tell what medications they had used before visiting these health facilities.

In Ghana, Artemisinin-based Combination Therapies (ACTs), are not recommended in the first trimester of pregnancy as current research is not enough to guarantee their safety. Quinine is the medicine of choice for the treatment of malaria in first trimester of pregnancy. For uncomplicated malaria, oral quinine is used alone for 7 days or in combination with clindamycin for 3 days. In severe malaria quinine injection is used. The recommended treatment protocols for Ghana adequately take care of the *Plasmodium falciparum* malaria which is the most prevalent.

1.1 Problem Statement

Quinine is the recommended drug for the management of malaria in first trimester of pregnancy. A review of the drug use records at the Pharmacy unit of Tema General Hospital showed that only 24 cases of malaria had been treated with oral quinine in the past one year, and 200 vials of intravenous quinine had been issued to the hospital wards for only two months in the year. It is not possible to tell how many of these treatments were administered to the pregnant women and if any at all, in which of the trimesters of pregnancy they were given.

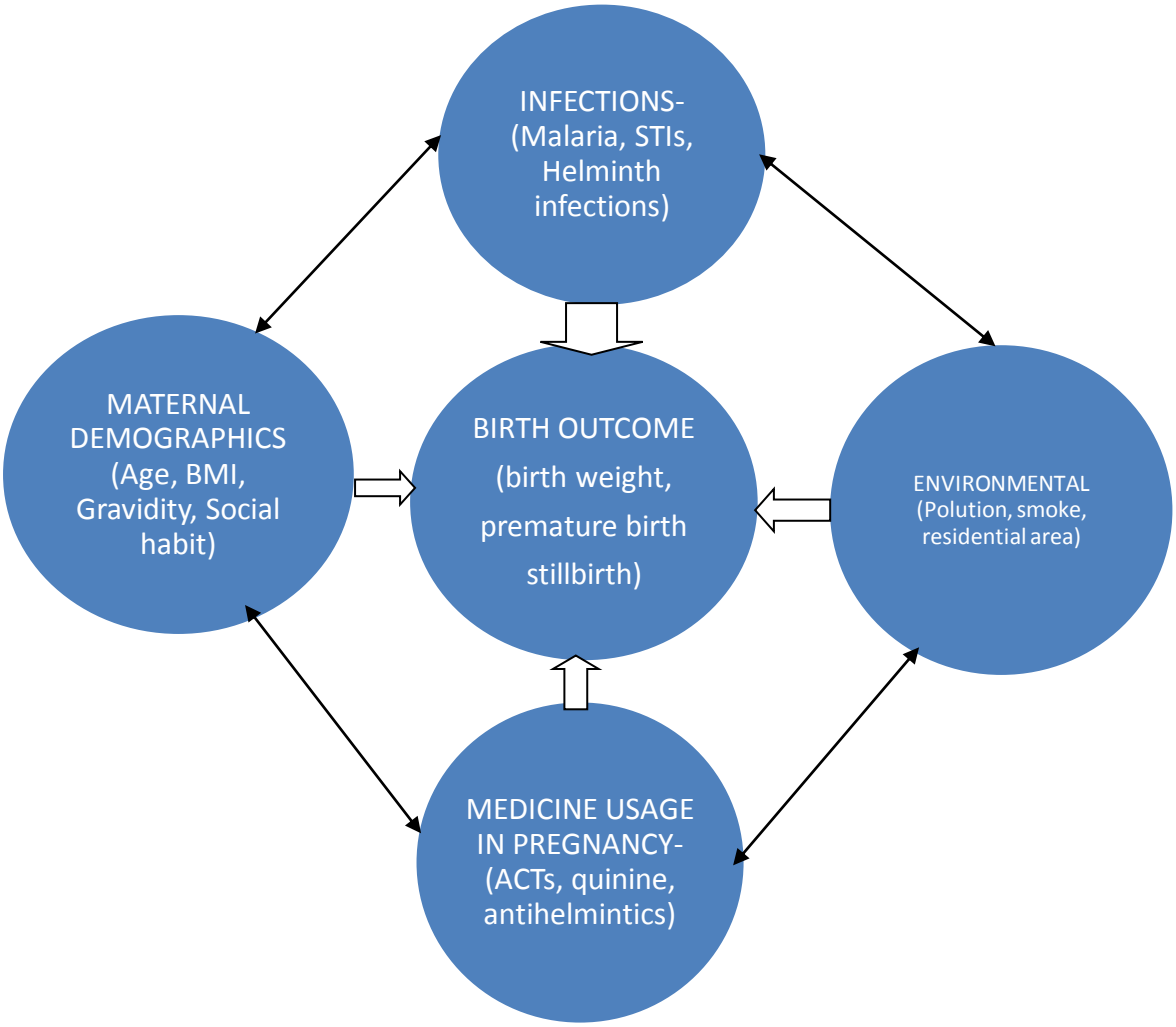
As a follow up on these, some practitioners were interviewed. They claimed that there are adverse outcomes such as bleeding and spontaneous abortion when quinine is used in the first trimester of pregnancy. There is no documented evidence to support this claim.

Despite the fact that ACTs are not recommended in first trimester of pregnancy, instead of using the recommended quinine, ACTs seem to be the preferred choice of treatment in

all trimesters, from discussion with some prescribers at the facility and some other facilities in Tema. The purpose of this study is to examine pregnancy outcome when ACTs are used in all the trimesters of pregnancy instead of quinine or the combination of quinine and clindamycin for the first trimester as recommended by the malaria policy.

Figure 1: Conceptual framework

Birth outcomes and associated factors



From fig. 1 above, it can be seen that abnormal birth outcomes, such as low birth weight, prematurity and stillbirth are caused by various factors, one of these is due to infections when the woman's immunity reduces. Viral, bacteria and protozoan infections are the most common cause of stillbirth (Goldenbrg, McClure, Saleem, & Reddy, 2010).

Maternal age is also a factor for some of these abnormal birth outcomes. Older women from 35-40 years are at increased risk of having premature and LBW babies than younger women (Jolly et al., 2000). Occupation is also a factor – women whose jobs expose them to environmental pollutions like smoke, heavy metals, pesticides etc. are more likely to have premature and LBW babies (Triche & Hossain, 2007a). Women living in highly polluted areas are more likely to develop menstrual disorders and infertility (Triche & Hossain, 2007b).

Level of income is a factor - Women in low income level are more likely to be malnourished during pregnancy, and this could lead to LBW babies (Steketee, 2003). The number of times a woman has been pregnant is another factor. Primigravidae are more likely to suffer from more severe forms of placental malarial which could lead to LBW than in multigravidae (Tako et al., 2005).

Medicines use in pregnancy may lead to unwanted side effects such as cinchonism and hypoglycaemia when quinine is used in the treatment of malaria (Newton et al., 2003). Smoking of cigarette by pregnant women leads to incidence of LBW (Triche & Hossain, 2007b).

The inter-relationship between the variables can be seen from these examples: According to Ovesen et al.(2011), the older the women the more obese they become, and the more likely they could develop diabetes, which is associated with stillbirth (Ovesen et al., 2011). High maternal alcohol consumptions is implicated in premature births and LBW (Nykjaer et al., 2013), and could also be a risk factor for cardiovascular disease in the mother.

1.2 Justification of the Study

This study sought to examine whether birth outcomes in women treated with artemisinin-based combination therapy irrespective of the trimester of pregnancy were similar. Previous studies indicated that birth outcomes were similar in all the women who were treated with ACTs in any of the trimester of pregnancy. The findings of this study will contribute to a collection of evidence that may be used during a review of the current malaria policy which recommends the use of quinine and clindamycin in the first trimester of pregnancy, and ACTs in the second and third trimesters.

1.3 Objectives of the Study

1.3.1 General Objective:

To assess birth outcomes in pregnant women treated with anti-malarials in Tema General Hospital.

1.3.2 Specific Objectives:

1. To determine the type of antimalarials used in treating pregnant women at the Tema General Hospital.
2. To compare the birth weight of babies born to women who were treated with ACTs with those who were not treated with ACTs in the study.
3. To compare the number of premature babies born to women who were treated with ACTs with those who were not treated with ACTs in the study.
4. To compare the number of still births in women who were treated with ACTs with those who were not treated with ACTs in the study.

1.4 Hypotheses

-Null hypothesis: Birth outcome in pregnant women treated with artemisinin based combination therapies, is the same in pregnant women not treated with artemisinin based combination therapies.

-Alternate hypothesis: Birth outcome in pregnant women treated with artemisinin based combination therapies, is not the same as in those pregnant women not treated with artemisinin based combination therapies.

CHAPTER TWO

LITERATURE REVIEW

2.1 Burden of Malaria in Pregnancy

Pregnant women and their unborn babies are vulnerable to malaria. According to a recent study in sub-Saharan Africa between 2000 and 2011, malaria prevalence in pregnant women attending antenatal clinics was 29.5% in East and Southern Africa, and 35.1% in West and Central Africa. The prevalence of placental malaria was 26.5% in East and Southern Africa, and 38% in West and Central Africa (Takem & D'Alessandro, 2013).

In Ghana, malaria caused by *Plasmodium Falciparum* is the most prevalent among pregnant women and it accounts for 28.1% of OPD attendance, 13.7% of admissions and 9.0% of maternal deaths (Health, 2010). In a cross-sectional study among 530 pregnant women in Ghana, the presence of plasmodia infections were assessed by microscopy and Polymerase Chain Reaction (PCR); it was found that 63% of pregnant women harboured malaria parasites. And that with increasing gravidity, infection rates and parasite densities decreased and the proportions of submicroscopic parasitaemia among infected women grew (Mockenhaupt et al., 2000).

2.2 Effects of Malaria in Pregnancy

In reference to the pregnant woman, the effect of malaria infection during pregnancy will depend on the degree of acquired immunity, which in turn depends on the intensity of transmission, the number of previous pregnancies and the presence of other diseases (Health, 2010). Malaria infection is more frequent and severe in primigravidae than in

multigravidae, and its prevalence and intensity increases as gestational age increases (Okafor, Mbah, & Usanga, 2012).

Maternal effects include anaemia, fever, hypoglycaemia, cerebral malaria, pulmonary oedema, puerperal pyrexia and death. In the baby, malaria can result in low birth weight, prematurity, congenital malaria and still birth or neonatal death (Health, 2010).

In the study by Tako et al (2005), they found that placental malaria significantly increases the prevalence of anaemia in women regardless of gravidity or age. In addition, the mean infant birth weight was lower and the percentage of preterm deliveries and low birth weight (LBW) babies were higher in primigravidae and women less than 20 years of age with placental malaria. However, in a multivariate regression model taking relevant covariates into consideration, the major risk factor for preterm deliveries was maternal anaemia. Also, first and second pregnancies were important risk factors for LBW babies (Tako et al., 2005). Malaria through the presence of fever and severe anaemia increased the risk of preterm delivery and stillbirth (Poespoprodjo et al., 2008).

2.3 Prevention and Control of Malaria in Pregnancy

The control of malaria in pregnancy in Ghana depends both on preventing the infection and clearing parasitaemia when the disease occurs. In 2003, Ghana adopted the intervention of using sulphadoxine-pyrimethamine (SP) as Intermittent Preventive Treatment during Pregnancy (IPTp). Three tablets of SP are given monthly from the 16th – 36th week of pregnancy as directly observed treatment (DOT), to the pregnant woman when she attends the antenatal clinic (Health, 2010). Women with either full or partial Glucose -6-Phosphate Dehydrogenase (G6PD) enzyme deficiency, are exempted from using SP (Health, 2010). A recent study by Tutu et al, (2010) showed significant increase

in haemoglobin (Hb) levels of pregnant women who took SP compared to the no SP group (Tutu et al., 2010). Increased number of doses of SP were found to be associated with higher Hb levels in the pregnant women, with no significant adverse reactions. Parasitaemia was more prevalent in the no SP group compared to the SP group (53% vs. 47%). This reduction of maternal anaemia and parasitaemia is in relation to the number of doses of SP taken, thus confirming the beneficial impact of the drug as reported by WHO (Tutu et al., 2010).

Pyrimethamine inhibits dihydrofolate reductase (DHFR) and sulphadoxine inhibits dihydropteroate synthase (DHPS), inhibition of both enzymes prevents synthesis of folic acid in parasites. Because of drug resistance to monotherapies by malarial parasites, this combination is now rarely used outside Africa.

As efficacy reduces, the risk-benefit ratio of use of sulphadoxine-pyrimethamine also reduces, as a result of reports of rare occurrences of severe and fatal adverse events—mainly Stevens-Johnson and Lyell syndromes—as well as even rarer instances of hepatotoxicity and agranulocytosis almost exclusively described after use in chemoprophylaxis in expatriates to the tropics (Cook, 1995). The risk of administering this combination is further raised by the frequency of serious adverse events, mainly skin reactions, noted in patients infected with HIV.

Sulphadoxine-pyrimethamine however continues to be used in many countries in Africa, predominantly because it is a single-dose treatment and cheaper than the alternatives. Other malaria preventive methods in pregnancy include the use of insecticide treated nets.

2.4 Use of Insecticide Treated Nets (ITNs) for Protection in Pregnancy:

Insecticide Treated Nets (ITNs) reduce human-vector contact by physically excluding the vector -mosquitoes, repelling and killing them as they come in contact with the ITNs. Studies have documented their effect in reducing malaria-related illness and death (Phillips-Howard et al., 2003). The chemicals used to treat the ITNs (Pyrethroids like Deltamethrin) are not harmful for pregnant women and are currently used for the impregnation of bed nets (Health, 2010). Since 2003, in Ghana, ITNs are given free to every pregnant woman during her first antenatal visit to the health facility.

The impact of ITNs on malaria in pregnancy was studied in a rural area in western Kenya with intense perennial malaria transmission and the findings were that among women who had been pregnant up to 4 times, ITNs were associated with reductions of 38% in the incidence of malaria parasitaemia and 47% in the incidence of severe malarial anaemia (hemoglobin level < 8 g/dl with parasitaemia) during pregnancy.

The prevalence of placental or maternal malaria was reduced by 35% and the prevalence of low birth weight was reduced by 28% in women who had been pregnant up to four times, but no beneficial impact was observed in women who had been pregnant for five times or more (Ter Kuile et al., 2003). This means that less pregnant women are likely to develop malaria, and are less likely to be treated for malaria in pregnancy if the use of ITNs continues among those with up to four pregnancies.

Indoor residual spraying (IRS) alone or in combination with ITNs is effective in protecting against malaria (Okumu et al., 2013), but IRS is not widely used as ITNs in pregnancy.

2.5. Safety Profile of the Various Anti-Malarials Used in Pregnancy

2.5.1 Quinine

Quinine is considered to be safe during all trimesters of pregnancy, and it is widely recommended as a treatment, although oral quinine is bitter and adverse effects are common and adherence is poor. Newton et al (2003) observed that most of the patients treated with quinine consistently developed cinchonism and had a significantly higher frequency of hypoglycemia (Newton et al., 2003).

In the work of Mcgready et al. (2014) adherence to the 7-day regimen required for maximum cure rates was poor. In the unrealistic setting of supervised administration of quinine in all trials carried out, more than one-third of women had a treatment failure (Mcgready et al., 2014). These incidences of non-compliance to the treatment of quinine could eventually lead to drug resistant malarial cases.

2.5.2 Clindamycin Plus Quinine:

The combination of quinine plus a fixed concentration of clindamycin inhibits growth of quinine-resistant strains, and the antiplasmodial activity observed at quinine concentrations <50 ng/rnl (154 nM) are attributable to clindamycin alone (Seaberg et al., 1984). The combination of these two, clindamycin and quinine have made it possible for treatment duration with quinine to reduce from 7 days to only 3 days.

2.5.3 Artemisinin Based Combination Therapies:

In Ghana, there are five forms of ACTs. These are artesunate-amodiaquine, artemether-lumefantrine, dihydroartemisinin-piperaquine, artemether injection and artesunate

injection. Artemisinin combinations are selectively toxic to malarial parasites and are therefore very effective in the management of malaria. At high doses, artemisinin can be neurotoxic but toxicity has not been found in clinical studies (Meshnick, 2002). Clinically important artemisinins are metabolised to dihydroartemisinin (elimination half-life of about 45 min), in which form they have comparable antimalarial activity to quinine (Kremsner & Krishna, 2004). Artemisinins are generally well tolerated. However, their use in monotherapy is associated with high incidences of recrudescent and must not be used as such.

2.5.4 Artemether – lumefantrine: Effect in Pregnancy

The work of McGready et al (2014), in Thailand, involving 539 pregnant women revealed that artemisinins were well tolerated with no evidence of adverse effects, birth outcomes did not differ significantly to community rates for abortion, stillbirth, congenital abnormality, and mean gestation at delivery.

Reproductive toxicity studies in rats given oral doses of the artemether - lumefantrine combination showed maternal toxicity and increased post-implantation loss at doses ≥ 50 mg/kg (corresponding to approximately 7 mg/kg Artemether). The artemether-lumefantrine combination was not embryotoxic in rats at a dose of 25 mg/kg (corresponding to approximately 3.6 mg/kg Artemether). Following oral administration of the artemether-lumefantrine combination in rabbits, maternal toxicity and increased post-implantation loss were seen at a dose of 175 mg/kg (corresponding to 25 mg/kg Artemether), while the next lowest dose level of 105 mg/kg (corresponding to 15 mg/kg Artemether) was free of treatment-induced effects. Artemisinins are known to be embryotoxic in animals. Reproductive toxicity studies with artemisinin derivatives

demonstrated increased post-implantation loss and teratogenicity (a low incidence of cardiovascular and skeletal malformations) in rats at a dose of 6 mg/kg artesunate and 19.4 mg/kg artemether. In rats, 3 mg/kg artemether was established as the non-toxic dose ("Artemether 20mg/lumefantrine 120mg Dispersible tablets (Novartis Pharma AG), MA069 WHOPAR part 4 12/2011," 2011). This was used in the determination of the safe dosage regimen according to body weight in human.

Three previous studies, by Adam et al. (2009), Manyando et al. (2010), and Mosha et al. (2014) were done assessing Sudanese (62), Zambian (1001), and Tanzanian (2167) pregnant women exposed to ACTs during first trimester. The first two studies, in Sudanese and Zambian women were on small scale, concluded that there were no adverse outcome when ACTs were used in first trimester of pregnancy.

The third study was on large scale and they found that artemether-lumefantrine (AL) exposure in first trimester was associated with reduced risk of miscarriage/stillbirth (OR 1.4; 0.8-2.5) and (OR 0.9; 0.5-1.8) for preterm birth; as opposed to quinine: for miscarriage/stillbirth (OR 2.5; 1.3-5.1) and premature birth (OR 2.6; 1.3-5.3). Congenital anomalies were identified in 4 exposure groups namely AL only (1/164[0.6%]), quinine only (1/70[1.4%]), SP (2/66[3.0%]), and NO-antimalarial exposure group (19/1464[1.3%]).

Mosha et al. (2014) concluded that since artemether-lumefantrine and quinine were used according to their availability rather than to disease severity, it is likely that the effect observed was related to the drug and not to the disease itself.

2.5.5 Artesunate-amodiaquine: effect in pregnancy

There is limited information on the effect of artesunate-amodiaquine in pregnancy. The work of Mcgready & Nosten (2010) found that artesunate-amodiaquine was effective in treating malaria in pregnancy, but there was a 4.5% failure rate, and there was need for more studies to be done with regards to its effects on favourable birth outcomes.

2.5.6 Artesunate and artemether injections: effect in pregnancy

Artesunate and artemether injections have been found to be very safe and effective in the treatment of malaria in the general population. There is limited study on their effect in first trimester of pregnancy, but have been found to be safe in second and third trimester of pregnancies (McGready & Nosten, 2010).

2.5.7 Dihydroartemisinin plus piperaquine: effect in pregnancy

Artemisinins are metabolized into dihydroartemisinin in vivo, and this by product is known to be very effective in clearing parasites load in the human. Artemisinin as monotherapy is usually given twice daily for 5-7 days, but the combination of dihydroartemisinin plus piperaquine has reduced this long duration of treatment to once daily dose for three days. The work of Dellicour, Hall, Chandramohan, & Greenwood (2007) found this combination to be safe for use in the second and third trimesters of pregnancy. However not much is known about the birth outcome of this combination in the first trimester (Dellicour, Hall, Chandramohan, & Greenwood, 2007).

2.6. Other Factors Influencing Outcome of Pregnancy

The birth outcome of normal pregnancy usually is a normal live baby with body weight between 2500g and 3500g in most healthy women irrespective of their geographical location and time of delivery. But then, different factors could influence the delivery of a normal live baby. Some of these factors like environmental factors, maternal factors and neonatal factors are explained below:

2.6.1 Environmental Factors

These include smoking, video display terminals, anaesthetic gases, antineoplastic medicines, and exposures to lead, selenium, and inorganic mercury. Among these, cigarette smoking during pregnancy has been the leading environmental factor for adverse pregnancy outcome. Maternal smoking during pregnancy has been associated with low birth weight (<2500 g). Mothers who smoke during pregnancy are twice as likely to give birth to low-birth weight infants. Similarly, air pollution, pesticide exposure, and stress have also been associated with low birth weight and preterm delivery (Triche & Hossain, 2007).

2.6.2 Maternal Factors

These include socio-demography, genetic makeup and general wellbeing. Pregnant women aged 35-40 years have an odd of 1.41 for delivery before 32 weeks gestation, 1.28 for birth weight below the 5th percentile, and 1.41 for stillbirth as compared to women 18-35 years with reduced odds; Women aged >40 years had higher OR for the same risks (Jolly et al., 2000).

Cardiovascular Disease: A woman with a high lipid profile before conception is predisposed to diabetes and hypertension in pregnancy, which in turn could lead to low gestational age (weight< than 10th percentile for gestational age), pre-term birth (<37 weeks) and low birth weight (weight < 2500g) (Harville, Viikari, & Raitakari, 2011).

Bacterial/Viral Infections: Syphilis, where prevalent, causes most infectious stillbirths, and is the infection most amenable to screening and treatment. Ascending bacterial infection is a common cause of stillbirths, but prevention has proven elusive. Many viral infections cause still births (Goldenbrg, McClure, Saleem, & Reddy, 2010).

HIV Infection: Reduces the woman's resistance to malaria, and may cause malaria treatment to be less effective. It increases risk of malaria-related problems during pregnancy including increased risk of intra-uterine growth restriction, leading to low birth weight. It worsens placental parasitisation in all parities. This is because the HIV infection impairs the ability of the multiparous woman to build up immunity to malaria that comes with increasing parity. Thus malaria infection in the HIV positive multiparous woman is as dangerous as malaria infection in the primigravida. HIV increases risk of preterm labour and risk of maternal anaemia (Health, 2010).

Helminthic Infections: There have been mixed results from studies on the associations of maternal helminth infection and malaria-helminth co-infection on birth outcomes. A group of 696 pregnant women from the Kwale district in Kenya were recruited and tested for malaria and helminth infection at delivery. Birth weight was documented for 664 infants. A total of 42.7% of the mothers were infected with plasmodium falciparum, 30.6% with Schistosoma haematobium, 36.2% with filariasis, 31.5% with hookworm, and 5.9% with Trichuris trichiura; co-infection was present in 46.7%. Low birth weight (weight < 2,500 grams) was present in 15.4% of the offspring (Fairley et al., 2013).

2.7 Summary of literatures reviewed

The information gathered from the literature review – factors affecting a woman's health may consequently affect birth outcome, these are outlined as follows:

The pregnant woman's immunity is reduced in first trimester of pregnancy, and this gives way to infections to set in, including malaria, and is more severe in second trimester of pregnancy, especially in women in their 1-4 pregnancies; and that immunity is restored just before the end of the pregnancy.

Other factors like age, life style (alcohol intake and smoking of cigarette), obesity, worm infestation, viral infection etc. all have negative impact on birth outcomes.

The use of artemisinin-based combination therapies in previous studies was found to be safe even in early pregnancy, and compliance was better.

There is need for more studies to be carried out in early pregnancy in larger populations to further verify the safety of artemisinin-based combination therapies.

This study will use secondary data to examine birth outcomes in all women who were exposed to artemisinin-based combination therapies in all trimester of pregnancy and analyse the result and compare them to see if there are differences at the Tema General Hospital. The outcome of this study will be beneficial in future revision of malarial treatment guideline in pregnancy.

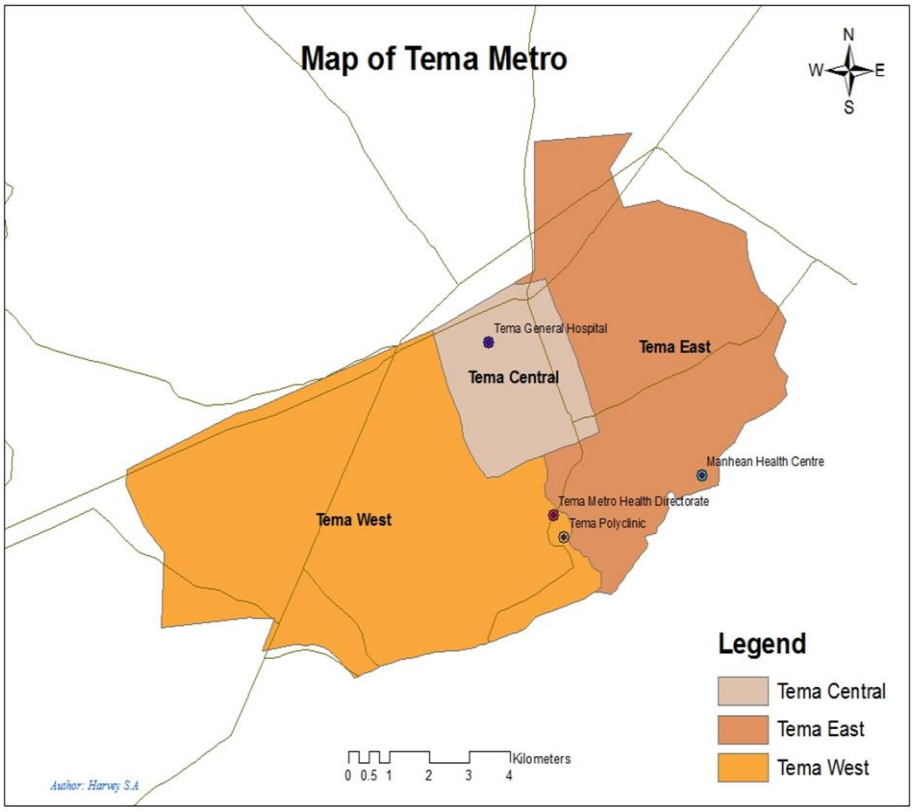
CHAPTER THREE

METHODOLOGY

3.1 Study Design

The design of this study is a retrospective cohort – birth outcome presently, and history of exposures from ANC records with new mothers on admission. The exposure in our study is a rare one (artemisinin based combination therapies in pregnancy using secondary data from maternal record cards at the point when they had just delivered their babies -multiply outcomes- low birth weight, premature birth, stillbirth and normal). This study will use secondary data to analyse birth outcomes in two cohorts of pregnant women treated with artemisinin based combination therapies (cohort one) and pregnant women not treated with artemisinin based combination therapies (cohort two); however there is limited time for follow up of the babies, so only the characteristics at birth on the day of data collection will be used for analysis.

Figure 2: Map of Tema Metropolis



3.2 Study Site

Study was carried out at the lying-in and fourth stage wards of the maternity wing of Tema General Hospital (TGH). The hospital is the district hospital and under Tema Central Sub-metropolis in the Tema Metropolis, which has two other sub-metropolis, Tema West and Tema East, see Figure 2 above.

Tema Metropolis is bounded to the North-East by Ashaiman Municipality, to the North-West by Adentan Municipality, to the West by Ledzokuku-Krowor Municipality, to the South by the Gulf of Guinea and to the East by the Kpone-Katamanso District. The estimated 2012 population of Tema Metropolis was 345,750 (as projected from the 2010 Census), and the population of Tema Central sub-metropolis was 109,909.

Economic activity in Tema is dominated by large industries such as Ghana Ports and Harbours Authority, Cocoa Processing Company, Ghana Textile Printing Company (GTP), Tema Oil Refinery, Unilever, VALCO, Ghacem, Coca cola, Tema Steel, Aluworks, Nestle, Pioneer Food Cannery, Crocodile Machetes etc. In addition, Tema has a free zone area – the main one in the country, with large factories that manufacture goods mainly for export. These companies employ a large workforce, providing livelihood to a large section of the population.

Most of these industries pay the cost of health care for workers and their dependants. With the inception of the National Health Insurance Scheme, these companies are paying premiums to enable their employees and dependants receive free health care services.

Another employment sector comprises small businesses and vocational enterprises (Carpentry, Masonry, Tailoring, Hairdressing, Auto-electrical, Auto-mechanic, Welding, Refrigeration, Air-conditioning, etc.) These engage large numbers of apprentices from within the metropolis as well as from other districts. On completion of their training, most of these young people also set up and continue the cycle of training of other young people. This factor partly accounts for the continuous growth of the population. Most of these self-employed artisans earn sufficient income to be able to cater for their health needs.

There are 5 public health facilities, 4 Quasi-Government health facilities and 58 Private/Industrial health facilities in Tema Metropolis. The low income class of residents in and around Tema frequent the public health facilities whilst the middle and high income class in Tema end up in the private facilities, unless on referral to TGH.

As a public health facility, TGH is well equipped with functioning theatres, neonatal ward with incubators, well stocked Pharmacy unit and diagnostic units. Some of the services offered are Child healthcare, Antenatal/Maternity, Medical, Surgical, Dental,

Rehabilitative, Laboratory/Ultra sound, Chest Clinics etc. This facility is endowed with high caliber Health Professionals especially at the Antenatal/Maternity unit. There are 3 Obstetrician-Gynaecologists, several resident doctors and about 90 midwives. The idea of Focus Antenatal Care originated from one of its Obstetrician-Gynaecologist. The Antenatal Clinic runs on daily basis, with Wednesdays devoted entirely for adolescent care.

Tema General Hospital serves mostly patients from districts outside Tema, like LEKMA, Dodowa, Kpone Katamanso, Ashaiman, and Adenta, due to services rendered under National Health Insurance Scheme. This cashless service delivery at this hospital has caused it to outgrow its capacity due to great influx of patients from the various arears listed above. This is posing great challenge to quality health service delivery at the facility.

In Tema, deliveries are highest from May to August. See Table 2 below. For faster enrolment of study participants, this study was carried out from Wednesday 13th of May to Friday 5th of June 2015 to co-inside with the peak delivery periods.

Table 1: Delivery Trend and Birth Outcomes for the Study Period at TGH, for May – August 2012, 2013 & 2014.

Indicators	2012				2013				2014			
	May	**June**	**July**	**Aug**	**May**	**June**	**July**	**Aug**	**May**	**June**	**July**	**Aug**
Supervised delivery	506	461	396	385	511	675	648	510	870	657	584	500
No of babies	531	478	409	402	533	694	665	525	902	674	608	516
Low birth weight	58	56	66	76	57	46	50	35	74	67	72	64
Stillbirth	15	12	14	19	17	18	18	12	27	27	29	32

Source of Information: Extracted from GHS-DHIMS-2 for TGH
*****Information on prematurity and normal weights were not available

3.3 Variables

3.3.1 Dependent Variables

- Birth Weight
- Premature birth
- Still Birth

3.3.2 Independent Variables

- Demography (age, occupation, income level, alcohol consumption, smoking, BMI, gestational age before delivery, gravidity)
- Malaria in pregnancy
- Other infections (STI, helminth)
- Anti- malarial usage:
    - ACTs
    - Quinine
    - Quinine + clindamycin
    - SP (IPTp)
    - No anti-malarial

3.3.3 Study Population

All new mothers with their babies who attended antenatal clinic at Tema General, from their first ANC visit with the recent pregnancy till delivery at the maternity ward of the hospital.

3.4 Sampling

3.4.1 Pilot Phase for Sample Size Indicator

The design of this study is a retrospective cohort (birth outcome presently, and history of exposures from ANC records with new mothers on admission). There was the need to be sure of what kind of data will be available at the study site. Towards the end of April 2015, a pilot study was carried out with the help of the Matron at the Tema General Hospital. A total of 91 Case Report Forms (CRFs) were completed. Out of these, 17 CRFs were excluded from analysis due to incomplete data (weight, height, and card numbers were omitted), leaving us with only 74 CRFs out of which there were 9 malaria cases treated with artemisinin based combination therapies (ACTs).

After analyzing these, the following information were obtained:

- Mean birth weight (for both cohorts) = 3151g
- Standard deviation (for both cohorts) = 590g
- Mean birth weight of treated cohorts = 3177g
- Standard deviation of treated cohorts = 319g
- Mean birth weight of not treated cohorts = 3148g
- Standard deviation of not treated cohorts = 620g
- Difference in standard deviation of the two cohorts = 301g

3.4.2 Sample Size Calculation

For the purpose of this study, *Sample size calculation in clinical research, the number we need (Patra & Size, 2012)*, was used.

The formula is $n = 2SD^2 (Z\alpha_{/2}+Z_\beta)^2/d^2$;

Where:

- n is the sample size for one group;
- SD is the standard deviation in the birth weight, 590g from above;
- 95% confidence interval and 80% power is assumed, so $Z_{\alpha/2} = 1.96$; $Z_{\beta} = 0.842$;
- d is the effect size between those treated with ACTs and those not treated, 301g from above.

Substituting these in the above formula:

- $n = 2\ (590)^2\ (1.96 + 0.842)^2 / (301)^2 = 60.33$

During the pilot study, the incidence of missing data was 18.68%, multiplying this by 60.33: [18.68/100 x 60.33 = 71.60]; so n is approximately 72.

- For the two groups sample size is 2 x 72 = 144.

This sample size was used for the study.

3.4.3 Data Sources

The following data sources, Maternal Record Book, Ward Register and clarifications from mothers were used to obtain information unto study case report forms (CRFs) at the maternity ward of Tema General Hospital.

3.5 Inclusion Criteria

All new mothers- women who delivered less than 7 days and are still on admission at the study site between 13th May and 5th June 2015

3.6 Exclusion Criteria

Any new mother who received less than two doses of IPTp during pregnancy

Any new mother who had self-administered herbal products during the recent pregnancy

3.7 Data Collection Methods & Tools

A case report form (CRF), sample attached in Appendix A below, was used in collecting information from maternal records card and admission register on the maternity ward of all new mothers and their babies, on admission from days 0-7 after delivery, who had given their informed consent. This information included mother's demographics and all relevant clinical data as contained in the numbered CRFs. In addition, the new mothers were interviewed briefly as some of them had attended antenatal clinics at other facilities before coming to register at TGH, and therefore had more than one maternal record book, where details of earlier treatments administered were recorded. Samples of ACTs were shown to the new mothers to ease recalling of those earlier treatments taken by them. The individual CRFs were fully completed before moving to review the next data sources of the next mother unto new CRFs. A maximum of 15 CRFs were completed in a day.

3.8 Quality Control

Entries on to the CRFs were checked for inconsistencies with the data sources on the ward to eliminate information transfer errors, and double checking of entry of each CRFs were done unto the excel spreadsheet before importing into Stata 13 for analysis. All calculations were cross-checked for accuracy.

3.9 Data Processing and Analysis

Data entry unto excel spreadsheet was done by transferring the coded information from the paper CRF. Every coded answer from the paper CRF entered electronically were double checked for inconsistencies. This was done on daily basis after each CRF had been verified to exclude all possible errors. Confidentiality of information are ensured since

only the identification number of the maternal record book was used, and the laptop password coded.

3.10 Statistical Methods

STATA 13.0 Software was used for data analysis. Numerical variables were summarized into mean and standard deviation. Categorical variables were summarised using cross tabulation to estimate different proportion. The ages were categorized into degrees of tens. The body mass index (BMI) were categorized into underweight (<20), normal BMI (20-25), overweight (25-30), obese (30-40), and very obese (>40). Haemoglobin levels at first and last antenatal visits were categorized into normal (>11.0g/dl), mild anaemia (10.0-10.9g/dl), moderate anaemia (7.0-9.9g/dl), and severe anaemia (<7.0g/dl). The effect of demographic and pregnancy characteristics on primary endpoint of the study were assessed by bivariate analysis. Explanatory variables were included in the multivariate analysis if the variable had p-value < 0.2 in bivariate analysis. Logistic regression model was used to estimate the odds ratio (OR) for the association between binary birth outcomes, birth weight and birth maturity status and medicine exposure. Two sided Chi test p-values were recorded.

3.11 Ethical Consideration

Ethics approval ID No: GHS-ERC: 10/02/15 was obtained from Ghana Health Service (GHS) Ethical Committee before the research was carried out (Appendix A).

Permission was obtained from Tema Metro Health Directorate (TMHD), and also from The Management of Tema General Hospital (Appendix B).

Informed Consent forms (Appendix C) was completed and signed/thumb- printed by each participant before the CRFs (Appendix D) were administered on the day the secondary data were collected from the new mothers.

Confidentiality of information collected was assured.

3.12 Risk and Benefits of this Study

Discomfort of this study was mainly emotional to the women who had a stillbirth or delivered a premature baby. Every effort was made to lessen this discomfort as much as possible by empathizing with them. Participants were reminded that inclusion in the study was voluntary and that they had the right not to respond or withdraw from the study if they so wished.

Participants did not receive any material gift during the study but findings of this study may improve birth outcomes for mothers in the future.

3.13 Declaration of Conflict of Interest:

This study was solely for academic purpose and the researcher has no conflict of interest what so ever in conducting it.

CHAPTER FOUR

RESULTS

Secondary data from the women who had delivered at the Tema General Hospital and had given an informed consent for the data to be collected and their babies observed was used for this study.

4.1 Characteristics of Pregnant Women Sampled for the Study

A total of 144 new mothers were sampled for this study, 72 in each cohort. Table 2 below show their demographics and other characteristics:

The minimum age of women in the study was 17 years and the maximum age was 45 years. Of these, only one of the mothers was 17years old. 4.2% of those who treated with ACTs were underweight, while 2.8% of those who did not treat with ACTs were underweight. 5.6% of the women who treated with ACTs were very obese, as against 4.2% for those women who did not treat with ACTs. 25% of the women who treated with ACTs were primigravidae, while 31.9% of the women who did not treat with ACTs were primigravidae. 23.6% of the women who treated with ACTs have had more than 5 pregnancies, as against 12.5% for whose women who did not treat with ACTs. The mean haemoglobin level at first ANC visit for the women who treated with ACTs was 11.1g/dl, and 10.8g/dl for the women who did not treat with ACTs. At the last ANC visit, the mean haemoglobin level for the women who treated with ACTs was 10.9g/dl, and 10.7g/dl for the women who did not treat with ACTs.

Table 2: **Characteristics of Mothers who participated in the study**

Characteristics	Treated with ACTs N=72		Not treated with ACTs N=72		p-value
	Frequency	%	Frequency	%	
Age group					
17-19	1	1.4	4	5.6	
20-29	36	50.0	36	50.0	
30-39	30	41.7	28	38.9	
40-49	5	6.9	4	5.6	
Mean age (years)	*30.2	**6.5 (28.6-31.7)	*29.1	**6.1 (27.6-30.5)	0.299
Weight					
Mean weight (kg)	*70.7	**16.8 (44-136)	*68.7	**15.9 (45-126)	
BMI					
Under weight	3	4.2	2	2.8	
Normal BMI	20	27.8	24	33.3	
Over weight	19	26.4	24	33.3	
Obese	26	36.1	19	26.4	
Very obese	4	5.6	3	4.2	
Mean BMI	*28.3	**6.3(26.8-29.8)	*27.9	**6.1 (26.5-29.3)	0.72
Gravidity					
Primigravidae	18	25.0	23	31.9	
Secundigravidae	12	16.7	17	23.6	
3 – 4 pregnancies	25	34.7	23	31.9	
≥ 5 pregnancies	17	23.6	9	12.5	
Mean gravidity	*2.6	**1.1 (2.3-2.8)	*2.3	**1.0 (92.0-2.5)	0.08
Other parameters					
Hb (g/dl) 1st ANC	*11.1	**1.3 (10.8-11.4)	*10.8	**1.3 (10.5-11.1)	
Hb (g/dl) last ANC	*10.9	**1.3 (10.6-11.2)	*10.7	**1.5 (10.3-11.0)	

Characteristics	Treated with ACTs N=72		Not treated with ACTs N=72		p-value
	Frequency	%	Frequency	%	
Alcohol consumption	6	8.3	5	6.9	
Smoking cigarette	0	0.0	0	0.0	
STIs in pregnancy	12	16.7	14	19.4	
Helminth infection	33	45.8	27	37.5	
ITN usage	42	58.3	38	52.8	

*Represents data presented in mean, ** represents data presented as Standard Deviation (SD) (95% CI)

4.2 Drug Exposure

It was observed that 32 (22.2%) of the 144 new mothers were exposed to antimalarials in 1st trimester. The 2nd and 3rd trimesters Figures were 31 (21.5%) and 15 (10.4%) respectively (Table 3). Four of the new mothers were given sulphadoxine-pyrimethamine as treatment for malaria. 66 (45.8%) were not exposed to antimalarials.

61 (42.4%) of all new mothers were exposed to antihelminthic, even though only 60 (41.7%) were infected with helminths.

45 (31.3%) of new mothers had only two doses of Intermittent Preventive Treatment during Pregnancy (IPTp) while 25 (17.4%) had at least four doses of IPTp.

All the 144 women were on haematinics. It was mentioned that the women who had less than two doses of IPTp will be excluded in the analysis. This was not done, but rather, we decided to compare the effects of having taken only two doses with the effects of having taken at least four doses.

Table 3: Trimester of Treatment and Antimalarials used in Pregnancy

Trimester				**Antimalarials N=78**
	Artesunate-amodiaquine Frequency (%)	**Artemether-lumefantrine Frequency (%)**	**Quinine Frequency (%)**	**Sulphadoxine-pyrimethamine Frequency (%)**
1st	0 (0.0)	30 (42.9)	0 (0.0)	2 (50.0)
2nd	1 (50.0)	27 (38.6)	2 (100)	1 (25.0)
3rd	1 (50.0)	13 (18.6)	0 (0.0)	1 (25.0)

Tables 4-6 show the birth outcomes and the trimesters of exposures to antimalarials: The result is a row total for each birth outcome in relation to the antimalarial exposure during pregnancy.

Table 4: Birth Outcome in Relation to Antimalarial Exposure Status in First Trimester

Birth outcome	Artesunate-amodiaquine n=0 (%)	Artemether-lumefantrine n=30 (%)	Quinine n=0 (%)	Sulphadoxine-pyrimethamine n=2 (%)
***Abnormal**	0 (0.0)	5 (100.0)	0 (0.0)	0 (0.0)
***Normal**	0 (0.0)	25 (92.6)	0 (0.0)	2 (7.1)
Viability of baby at birth				
Still birth	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)
Live birth	0 (0.0)	29 (93.6)	0 (0.0)	2 (6.5)
Maturity status at birth				
Preterm	0 (0.0)	2 (100.0)	0 (0.0)	0 (0.0)
Full term	0 (0.0)	28 (93.3)	0 (0.0)	2 (6.7)
Birth weight				
Low birth weight	0 (0.0)	4 (100.0)	0 (0.0)	0 (0.0)
Normal birth weight	0 (0.0)	26 (92.9)	0 (0.0)	2 (7.1)

*Abnormal includes stillbirth, premature birth and low birth weight;
*Normal absence of abnormal birth outcome

From Table 4 above: 100% of abnormal birth outcome was due to exposures to ACTs in the first trimester of pregnancy; 92.6% of normal birth outcome was due to exposures to sulphadoxine-pyrimethamine in the first trimester; whilst 7.1% of normal birth outcome was due to exposures to sulphadoxine-pyrimethamine in the first trimester.

Abnormal birth outcomes includes stillbirth, premature birth and low birth weight while normal birth outcome is the absence of these.

Table 5: Birth Outcome in Relation to Antimalarial Exposure Status in Second Trimester

Birth outcome	Artesunate-amodiaquine n=1 (%)	Artemether-lumefantrine n=27 (%)	Quinine n=2 (%)	Sulphadoxine-pyrimethamine n=1 (%)
***Abnormal**	1 (20.0)	4 (80.0)	0 (0.0)	0 (0.0)
***Normal**	0 (0.0)	23 (88.5)	2 (7.7)	1 (3.9)
Viability of baby				
Still birth	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)
Live birth	1 (3.3)	26 (86.7)	2 (6.7)	1 (3.3)
Birth maturity				
preterm	0 (0.0)	2 (100.0)	0 (0.0)	0 (0.0)
Full term	1 (3.5)	25 (86.2)	0 (0.0)	1 (3.5)
Birth weight				
Low birth weight	1 (20.0)	4 (80.0)	0 (0.0)	0 (0.0)
Normal birth weight	0 (0.0)	23 (88.9)	2 (7.7)	1 (3.9)

*Abnormal includes stillbirth, premature birth and low birth weight;
*Normal - absence of abnormal birth outcome

From Table 5 above: 20% of abnormal birth outcome was due to exposures to artesunate-amodiaquine in the second trimester of pregnancy; 80% of abnormal birth outcome was due to exposures to artemether-lumefantrine in the second trimester of pregnancy; 88.5% of normal birth outcome was due to exposures to artemether-lumefantrine in the second trimester of pregnancy; 7.7% of normal birth outcome was due to exposures to quinine in the second trimester of pregnancy; whilst the remaining 3.9% of normal birth outcome was due to exposures to sulphadoxine-pyrimethamine in the second trimester of pregnancy.

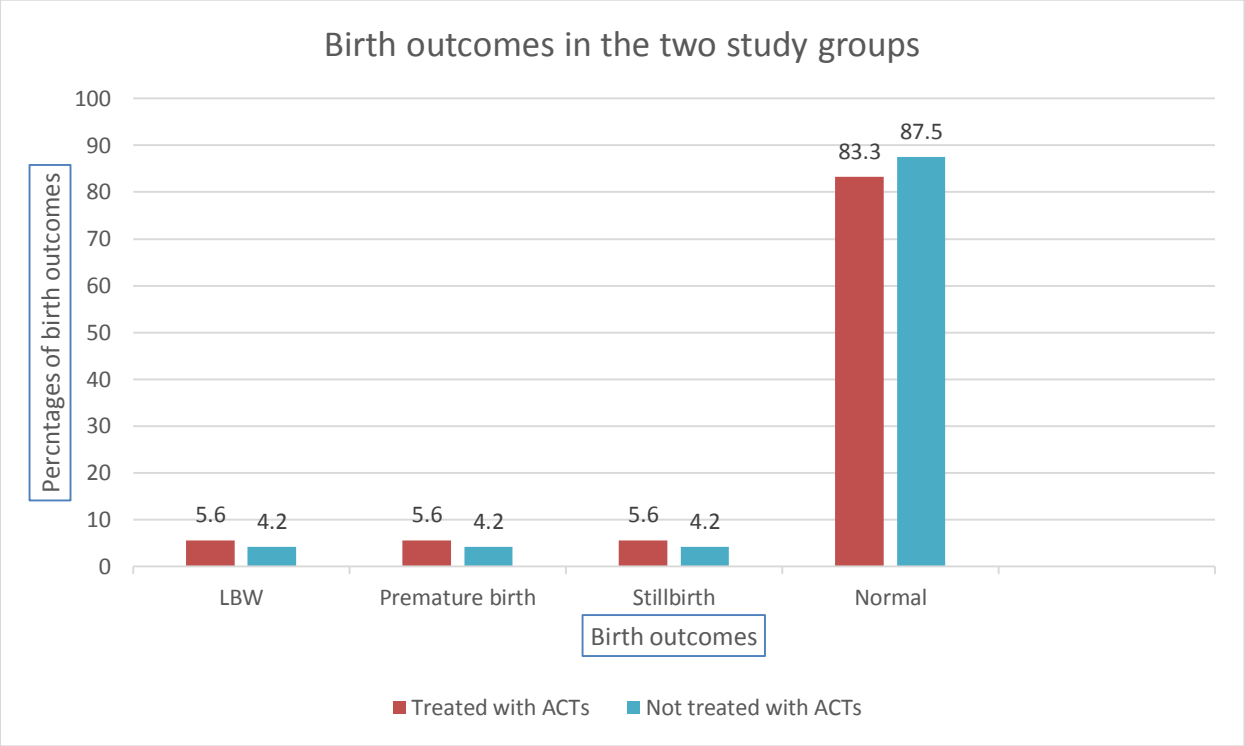
Table 6: Birth Outcome in Relation to Antimalarial Exposure Status in Third Trimester

Birth outcome	Artesunate-amodiaquine n=1 (%)	Artemether-lumefantrine n=13 (%)	Quinine n=0 (%)	Sulphadoxine-pyrimethamine n=1 (%)
***Abnormal**	1 (50.0)	1 (50.0)	0 (0.0)	0 (0.0)
***Normal**	0 (0.0)	12 (92.3)	0 (0.0)	1 (7.7)
Viability				
Still birth	1 (50.0)	1 (50.0)	0 (0.0)	0 (0.0)
Live birth	0 (0.0)	12 (92.3)	0 (0.0)	1 (7.7)
Birth maturity				
Preterm	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Full term	1 (6.7)	13 (86.7)	0 (0.0)	1 (6.7)
Birth weight				
Low birth weight	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)
Normal birth weight	1 (7.1)	12 (85.71)	0 (0.0)	1 (7.1)

*Abnormal includes stillbirth, premature birth and low birth weight;
*Normal- absence of abnormal birth outcome

From Table 6 above: 50% of abnormal birth outcome was due to exposures to artesunate-amodiaquine in the third trimester of pregnancy; 50% of abnormal birth outcome was due to exposures to artemether-lumefantrine in the third trimester of pregnancy. 92.3% of normal birth outcome was due to exposures to artemether-lumefantrine in the third trimester; whilst the remaining 7.7% of normal birth outcome was due to exposures to sulphadoxine-pyrimethamine in the third trimester of pregnancy.

Figure 3: **Birth outcomes in the two study groups:**



In Fig. 3 above, the incidence of low birth weight was 5.6% in women who were treated with ACTs during pregnancy, and only 4.2% in the women who were not treated with ACTs during pregnancy. The incidence of premature birth was 5.6% in women who were treated with ACTs during pregnancy, and only 4.2% in the women who were not treated with ACTs during pregnancy. The incidence of stillbirth was 5.6% in women who were treated with ACTs during pregnancy, and only 4.2% in the women who were not treated with ACTs during pregnancy.

Table 7: Test of Hypothesis that Birth Outcomes in the Two Groups are Similar.

Characteristic	Group	Mean	SD	95% CI	p-Value
Low birth weight	Treated with ACTs	1.90	0.35	1.800-1.900	0.175
	Not treated with ACTs	1.90	0.26	1.900-2.000	
Stillbirth	Treated with ACTs	0.06	0.23	0.001-0.110	0.70
	Not treated with ACTs	0.04	0.20	-0.006-0.089	
Premature birth	Treated with ACTs	0.06	0.23	0.001-0.101	0.70
	Not treated with ACTs	0.04	0.20	-0.006-0.089	
Normal birth outcome	Treated with ACTs	0.83	0.38	0.750-0.920	0.48
	Not treated with ACTs	0.88	0.33	0.800-0.950	

4.3. Testing the Hypothesis of the Study

The null hypothesis of this study was that the birth outcomes in pregnant women who were treated with ACTs is the same in pregnant women who were not treated with ACTs; while the alternate hypothesis is that the birth outcome in pregnant women who were treated with ACTs is not the same as the birth outcome of pregnant women who were not treated with ACTs. From Table 7 above the p-values for the t-test performed with Stata 13 for all the four birth outcomes, low birth weight, stillbirth, premature birth, and normal birth are 0.175, 0.70, 0.70 and 0.48 respectively. These p-values are not statistically significant. This means that the birth outcomes in the two groups of women whether or not they were treated with ACTs in pregnancy are not statistically different from each other. We therefore fail to reject the null hypothesis.

Table 8: Simple Binary Logistic Regression of Normal Birth on Malaria Management and Trimester of Treatment

Characteristics	Frequency (%)	Univariate analysis Crude OR (95% CI)	p-value
Malaria in Pregnancy	78 (54.2)	1.15 (0.5-2.9)	0.77
Trimester of malaria infection			
1st	32 (22.2)	0.85 (0.3-2.8)	0.79
2nd	31 (21.5)	0.82 (0.3-2.7)	0.75
3rd	15 (10.4)	1.03 (0.2- 5.3)	0.98
All trimesters		0.96 (0.6-1.5)	0.87
Not infected	66 (45.8)	1	-
Antimalarial			
Artemisinin based combination therapies	72 (50.0)	0.71 (0.3-1.8)	0.48
Quinine	2 (1.4)	1	-
Sulphadoxine-pyrimethamine	4 (2.8)	1	-
All antimalarials	78 (54.2)	1.11 (0.7-1.7)	0.62
IPTp (Not more than two doses)	45 (31.3)	0.55 (0.2-1.4)	0.22
IPTp (min of four doses)	25 (17.4)	2.19 (0.5-10.1)	0.32
ITN Usage	80 (55.6)	0.93 (0.4-2.4)	0.87

4.4 Normal Birth Outcome and malaria management

123 (85.4%) of the 144 new mothers had normal birth outcome (absence of stillbirth, premature birth and low birth weight). The frequencies for stillbirth (born dead after 28 weeks of gestation), premature birth (born before 37th week of gestation), and low birth weight (LBW, < 2.5kg) were 7 (4.9%), 7 (4.9%) and 7 (4.9%) respectively. In terms of the baby's weight, normal birth weights were 129 (89.6) and low birth weights were 15 (10.4).

Table 8 summarizes normal birth outcome in relation to malarial management:

Women who had malaria in pregnancy and treated have 15% increased odds of normal birth outcome (OR 1.15; 95% C.I 0.5-2.9; p=0.77) compared to women who did not treat for malaria in pregnancy.

Women who had malaria in first trimester and treated are 15% less likely to have normal birth outcome (OR 0.85; 95% C.I 0.3-2.8; p=0.79) compared to women who did not have malaria in pregnancy.

Women who had malaria in third trimester and treated have 3% increased odds of normal birth outcome (OR 1.03; 95% C.I 0.2- 5.3; p=0.98) compared to women who did not treat for malaria.

Women who treated malaria with artemisinin based combination therapies (ACTs) in pregnancy have 29% decreased odds of having normal birth outcome (OR 0.71; 95% C.I 0.3-1.8; p=0.48) compared to women who did not treat for malaria or treated with any other antimalarial.

Women who took at least two doses of intermittent preventive treatment during pregnancy (IPTp) had 45% decreased odds of normal birth outcome (OR 0.55; 95% C.I 0.2- 1.4; p=0.22) compared to women who took at least 4 doses of IPTp.

Women who took at least four doses of IPTp have 119% increased odds of having normal birth outcomes (OR 2.19; 95% C.I 0.5-10.1; p=0.32) compared to women who took at least 2 doses of IPTp.

Pregnant women who slept under Insecticides treated bednets (ITNs) were 7% less likely to have normal birth outcome (OR 0.93; 95% C.I 0.4-2.4; p=0.87) compared to pregnant women who did not sleep under ITNs.

Table 9: Simple Binary and Multivariate Logistic Regression of Stillbirth on Malarial Management and Trimester of Treatment

Characteristics	Frequency (%)	Unadjusted Crude OR (95%CI)	Unadjusted p-value	Adjusted Adjusted OR (95%CI)	Adjusted p-value
Trimester of treatment					
1st	32 (22.2)	0.68 (0.1-6.8)	0.74		
2nd	31 (21.5)	0.70 (0.1-7.0)	0.76		
3rd	15 (10.4)	3.23 (0.5- 1.3)	0.22		
All trimesters		1.33 (0.8-2.7)	0.41		
Not treated	66 (45.8)	1	-		
Antimalarials	78 (54.2)				
Artesunate-amodiaquine	2 (1.4)	0.04(0.002-0.8)	0.03	0.06 (0.003-0.99)	0.05
Artemether-lumefantrine	70 (48.6)	1.28 (0.3-5.9)	0.76		
Quinine	2 (1.4)	1	-		
Sulphadoxine-pyrimethamine	4 (2.8)	1	-		
IPTp, at least 2 doses	45 (31.3)	1.70 (0.4- 7.9)	0.50		
IPTp, at least 4 doses	25 (17.4)	1	-		
ITN Usage	80 (55.6)	1.07 (0.2 –5.0)	0.93		

4.5 Stillbirth Outcome and Malaria Management

From Table 9 above:

Women who had malaria in first trimester and treated have 32% decreased odds of stillbirth (OR 0.86; 95% C.I 0.1-6.8; p=0.74) compared to women who did not treat for malaria in pregnancy.

Women who had malaria in third trimester and treated have 223% increased odds of stillbirth (OR 3.23; 95% C.I 0.5- 21.3; p=0.22) compared to women who did not treat for malaria in pregnancy.

Women who treated with artesunate-amodiaquine in pregnancy had 94% decreased odds of stillbirth (AOR 0.06; 95% C.I 0.003-0.99; p=0.05) compared to women who did not treat for malaria.

Women who treated with artemether-lumefantrine have 28% increased odds of stillbirth (OR 1.28; 95% C.I 0.3-5.9; p=0.76) compared to women who did not treat for malaria.

Women who took at least two doses of IPTp have 70% increased odds of stillbirth (OR 1.7; 95% C.I 0.4-7.9; p=0.50) compared to women who had at least 4 doses of IPTp.

Table 10: Simple Binary and Multiple Logistic Regression of Premature Birth on Malarial Management and Trimester of Treatment

Characteristics	Frequency (%)	Unadjusted OR (95% CI)	Unadjusted p-value	Adjusted OR (95%CI)	Adjusted p-value
Trimester of treatment					
1st	32 (22.2)	1.40 (0.2-8.8)	0.72		
2nd	31 (21.5)	1.45 (0.2-9.1)	0.69		
3rd	15 (10.4)	1	-		
All trimesters		0.90 (0.4-1.9)	0.78		
Not treated	66 (45.8)	1	-		
Antimalarial usage					
Artemether-lumefantrine	70 (48.6)	0.70 (0.2 – 3.2)	0.65		
Artesunate-amodiaquine	2 (1.4)	1	-		
All antimalarials	78 (54.2)	0.98 (0.5 – 1.9)	0.96		
IPTp, at least 2 doses	45 (31.3)	3.12 (0.7 – 14.6)	0.15	2.24 (0.5 – 10.5)	0.31
IPTp, at least 4 doses	25 (17.4)	1	-		
ITN usage	80 (55.6)	1.07 (0.2-5.0)	0.93		

4.6 Premature Birth Outcome and Malaria Management

From Table 10 above:

Pregnant women who had malaria in first trimester and treated had 40% increased odds of premature birth outcome (OR 1.4; 95% C.I 0.2-8.8; p=0.72) compared to the pregnant women who did not treat for malaria.

Pregnant women who had malaria in second trimester and treated had 45% increased odds of premature birth outcome (OR 1.45; 95% C.I 0.2-9.1; p=0.69), compared to pregnant women who did not treat for malaria.

Pregnant women who treated with artemether-lumefantrine had 30% decreased odds of premature birth outcome (OR 0.70; 95% C.I 0.2 – 3.2; p=0.65) compared to pregnant women who did not treat for malaria.

Pregnant women who took at least 2 doses of IPTp have 124% increased odds of premature birth outcome (AOR 2.24; 95% C.I 0.48-10.5; p=0.31) compared to the pregnant women who had at least 4 doses of IPTp.

Table 11: Simple Binary and Multivariate Logistic Regression of Normal Birth on Other Possible Confounders

Characteristics	Frequency (%)	Unadjusted Crude OR (95% CI)	Unadjusted p-value	Adjusted Adjusted OR (95% CI)	Adjusted p-value
Age Group (Years)					
≤19	5 (3.5)	1	-		
20-29	72 (50.0)	1.75 (0.2-17.5)	0.63		
30-39	58 (40.3)	1.20 (0.1-11.9)	0.88		
40-49	9 (6.3)	2.00 (0.1- 41.0)	0.65		
All ages		0.92 (0.5- 1.8)	0.82		
BMI Group					
Under weight	5 (3.5)	1	-		
Normal BMI	44 (30.6)	1.32 (0.1-13.6)	0.82		
Over weight	43 (29.9)	1.29 (0.1- 13.3)	0.83		
Obese	45 (31.3)	2.56 (0.2-28.8)	0.45		
Very Obese	7 (4.9)	0.63 (0.04- 9.7)	0.74		
All BMIs		1.11 (0.7-1.8)	0.68		
Residential area					
Tema west	23 (16.0)	1	-		
Tema east	24 (16.67)	1.05 (0.2-4.8)	0.95		
Tema central	3 (2.1)	1	-		
Outside Tema	94 (65.3)	1.31 (0.4- 4.5)	0.67		
All areas		1.1 (0.8- 1.6)	0.62		
Occupation					
Not employed	16 (11.1)	1	-		
Self-employed	100 (69.4)	0.35 (0.04- 2.8)	0.33		
Formal sector	28 (19.4)	0.40 (0.04- 3.9)	0.43		
All occupations		0.79 (0.3- 1.9)	0.59		

Characteristics	Frequency (%)	Unadjusted Crude OR (95% CI)	Unadjusted p-value	Adjusted Adjusted OR (95% CI)	Adjusted p-value
Income Group GHÇ		1.43 (0.4- 4.7)			
100-500	128 (88.9)	1	-		
501-1000	12 (8.3)	0.87(0.2- 4.2)	0.87		
1001-1500	2 (1.4)	1	-		
1501-2000	1 (0.7)	1	-		
Alcohol	11 (7.6)	0.75 (0.2- 3.7)	0.73		
Gravidity		0.77 (0.5-1.2)	0.24		
Primigravidae	41 (28.5)	1	-		
Secundigravidae	29 (20.1)	0.94 (0.2- 4.5)	0.94		
3-4 Pregnancies	48 (33.3)	0.41 (0.1- 1.4)	0.16	0.42 (0.1- 1.5)	0.18
≥5 Pregnancies	26 (18.1)	0.59 (0.1- 2.6)	0.49		
STI in Pregnancy	26 (36.1)	1.08 (0.3- 3.5)	0.90		
Worm Infestation	60 (83.3)	0.66 (0.3 1.8)	0.40		
Hb (g/dl) at 1st ANC		1.30 (0.8- 2.3)	0.34		
Moderate Anaemia	36 (25.0)	1	-		
Mild Anaemia	35 (24.3)	1.45 (0.4- 5.1)	0.56		
Normal Hb	73 (50.7)	1.72 (0.6- 5.1)	0.33		
Hb (g/dl) at last ANC		1.17 (0.7- 2.0)	0.56		
Severe Anaemia	2 (1.4)	1	-		
Moderate Anaemia	34 (23.6)	0.58 (0.2- 1.6)	0.29		
Mild Anaemia	35 (24.3)	2.93 (0.6- 14.0)	0.18	2.83 (0.6-13.7)	0.20
Normal Hb	73 (50.7)	1	-		

Table 11 summarizes normal birth outcome and other confounders:

Increasing age of women has an 8% decreased odds of normal birth outcome (OR 0.92; 95% C.I 0.5- 1.8; p=0.82). Women in age group 20-29 years are 75% more likely to have normal birth outcomes than women below 20 years (OR 1.75; 95% C.I 0.2-17.5; p=0.63); while women 40-49 years have 100% increased odds of normal birth outcomes (OR 2.0; 95% C.I 0.1- 41.0; p=0.65) than women below 20 years.

Women who are self-employed have 65% decreased odds of having normal birth outcomes (OR 0.35; 95% C.I 0.04- 2.8; p=0.33) than women who were not employed.

Increasing income of women has 43% increased odds of normal birth outcomes (OR 1.43; 95% C.I 0.4- 4.7; p=0.56).

Alcohol consumption by women has 25% decreased odds of normal birth outcomes (OR 0.75; 95% C.I 0.2- 3.7; p=0.73).

As the number of pregnancies increased, the odds of normal birth outcome increased by 23% (OR 0.77; 95% C.I 0.5-1.2; p=0.24). Women with 3-4 pregnancies are 58% less likely to have normal birth outcome (AOR 0.42; 95% C.I 0.1-1.5; p=0.18) than primigravidae.

Women with better haemoglobin levels 1st ANC visit had 30% increased odds of normal birth outcome (OR 1.30; 95% C.I 0.8- 2.3; p=0.34).

Women with better haemoglobin levels at last ANC visit had 17% increased odds of normal birth outcome (OR 1.17; 95% C.I 0.7- 2.0; p=0.56).

Women with moderate anaemia at last ANC visit had 42% decreased odds of normal birth outcome than women with normal HB (AOR 0.58; 95% C.I 0.2-1.6; p=0.29). Women with mild anaemia had 183% increased odds of normal birth than women with moderate anaemia (AOR 2.83; 95% C.I 0.6-13.7; p=0.195).

Table 12: Simple Binary and Multivariate Logistic Regression of Stillbirth with other Possible Confounders

Characteristics		Univariate analysis		Multivariate analysis	
	Frequency (%)	Crude OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Hb (g/dl) at 1st ANC	144 (100.0)	1.32 (0.5- 3.5)	0.58		
Hb (g/dl) at last ANC	144 (100.0)	0.60 (0.3- 1.4)	0.23	0.42 (0.7-14.8)	0.15
Moderate anaemia	34 (23.6)	3.11 (0.7- 14.8)	0.15	6.82 (0.9-50.8)	0.06
BMI Group	144 (100.0)	0.70 (0.3- 1.6)	0.34		
STI in pregnancy	26 (36.1)	0.53 (0.1- 3)	0.47		
Gravidity	144 (100.0)	0.78 (0.4- 1.6)	0.51		
Residential area					
All areas	144 (100.0)	0.74 (0.4- 1.3)	0.32		
Outside Tema	94 (65.3)	0.30 (0.1- 1.4)	0.13	0.18 (0.03- 1.2)	0.07
Age group					
20 to 29 years	72 (50.0)	2.09 (0.4-11.2)	0.39		

Table 12 above is the result obtained by comparing the associations between stillbirth outcome and all other confounding factors.

Women with decreased haemoglobin levels at first ANC visit had 32% increased odds of stillbirth (OR 1.32; 95% C.I 0.5-3.5; p=0.58).

Women with increased haemoglobin level at last ANC visit had 58% decreased odds of stillbirth (AOR 0.42; 95% C.I 0.7-14.8; p=0.15). Pregnant women with moderate anaemia

at last ANC visit had 582% increased odds of stillbirth than women with normal Hb level (AOR 6.82; 95% C.I 0.9-50.8; p=0.06).

Women who had STI during pregnancy and treated had 47% decreased odds of stillbirth (OR 0.53; 95% C.I 0.1- 3; p=0.47).

As the number of pregnancies in a woman increased the odds of stillbirth decreased by 22% (OR 0.78; 95% C.I 0.4- 1.6; p=0.51).

Pregnant women living outside of Tema were 82% less likely to have stillbirth (AOR 0.18; 95% C.I 0.03- 1.2; p=0.07) compared to pregnant women living within Tema.

Increasing age of pregnant women has 109% increased odds of stillbirth (OR 2.09; 95% C.I 0.4-11.2; p=0.39).

Table 13: Simple Binary and Multiple Logistic Regression of Premature Birth with Other Possible Confounders

Characteristics	Frequency (%)	Unadjusted Crude OR (95% CI)	Unadjusted P-value	Adjusted Adjusted OR (95% CI)	Adjusted P-value
Age Group Years					
≤19	5 (3.5	1	-		
20-2	72 (50.0)	0.06 (0.003-1.1)	0.056	0.02 (0.0005-0.9)	0.04
30-39	58 (40.3)	0.30 (0.03-3.3)	0.324	0.11 (0.003-3.9)	0.23
40-49	9 (6.3)	0.5 (0.02-10.3)	0.653	0.26 (0.003-24.0)	0.56
BMI Group					
Under weight	5 (3.5)	1	-		
Normal BMI	44 (30.6)	0.09 (0.005-1.8)	0.12	0.04 (0.008-1.7)	0.09
Over weight	43(29.9)	0.20 (0.01-2.7)	0.22	0.09 (0.004-2.4)	0.15
Obese	45 (31.3)	0.19 (0.01-2.5)	0.21	0.07 (0.002-2.3)	0.14
Very Obese	7 (4.9)	0.67 (0.03-14.0)	0.79	0.13 (0.003-5.2)	0.28
STI	26 (36.1)	1.34 (0.2-11.6)	0.79		
Helminth treatment	60 (83.3)	1.29 (0.6-3.0)	0.56		
Gravidity					
Primigravidae	41 (28.5)	1	-		
Secundigravidae	29 (20.1)	1	-		
3-4 Pregnancies	48 (33.3)	4.65 (0.5-41.6)	0.17	5.04 (0.3-98.1)	0.29
≥5 Pregnancies	26 (18.1)	1.6 (0.1-26.8)	0.74	1.29 (0.03-51.9)	0.89
Occupation					
Not employed	16 (11.1)	1	-		
Self- employed	100 (69.4)	1.72 (0.2-14.9)	0.62		
Formal Sector	28 (19.4)	1	-		

Table 13 above is comparing the association between premature birth outcome and other possible confounders.

Pregnant women between 20 to 29 years were 98% less likely to have premature birth outcome (AOR 0.02; 95% C.I 0.0005- 0.9; p=0.04) compared to pregnant women between 17-19 years.

Pregnant women who had STI in pregnancy and treated are 34% more likely to have premature birth outcome (OR 1.34; 95% C.I 0.2- 11.6; p=0.79) compared to women who did not treat for STI in pregnancy.

Pregnant women who had helminth infection and treated were 29% more likely to have premature birth outcome (OR 1.29; 95% C.I 0.6-3.0; p= 0.56).

Pregnant women in their 3-4 pregnancies had 404% increased odds of premature birth outcome (AOR 5.04; 95% C.I 0.3-98.1; p=0.29), while those in their fifth or more pregnancies had 29% increased odds of premature birth outcome (AOR 1.29; 95% C.I 0.03-51.9; p=0.89) than primigravidae.

Women who were self-employed were 72% more likely to have premature birth outcome (OR 1.72; 95% C.I 0.2- 14.9; p=0.62) than women who were unemployed.

CHAPTER FIVE

DISCUSSION

5.1 Birth outcomes

The use of artemether-lumefantrine for the treatment of malaria in pregnancy was more frequent in all trimesters of pregnancy, than the use of other antimalarials. The differences in the birth outcomes observed between the treated women and those not treated was not statistically significant, after controlling for every known factor that could possibly affect normal birth outcomes. Artemether-lumefantrine was found to be readily available at the facilities were they were prescribed according to the verbal answers from the new mothers who used them during pregnancy. This finding is in line with previous studies reviewed in this work.

It is very clear from this study that the use of quinine in the treatment of malaria in pregnancy was not common, as only 2/78 of pregnant women that had malaria in the study treated with quinine.

The use of artesunate-amodiaquine for the treatment of malaria in pregnancy was also not common in the study as only 2/78 of the women who were treated used it.

The remaining women who were treated in the study used artemether-lumefantrine and sulphadoxine-pyrimethamine. Artemether-lumefantrine was observed to be the drug of choice for prescribers for the management of malaria in pregnancy in all trimesters.

5.2 Doses of Sulphadoxine-pyrimethamine (SP) for Intermittent Preventive Treatment during Pregnancy

Another interesting finding of this study is that increasing doses of sulphadoxine-pyrimethamine (SP) improved favourable birth outcomes. Women who took only two doses of Intermittent Preventive Treatment during Pregnancy (IPTp) had 38% decreased odds of normal birth outcome, while those who took at least four doses of IPTp had 120% increased odds of having normal birth outcome. This supports the work of Tutu et al (2010), which showed significant increase in haemoglobin (Hb) levels of pregnant women who took sulphadoxine-pyrimethamine (SP) compared to the no SP group (Tutu et al., 2010).

It is interesting to note that four pregnant women were given sulphadoxine-pyrimethamine (SP) as monotherapy in treating malaria, two women in the first trimester, and one each in second and third trimesters. This is not a recommended antimalarial for treatment of malaria. Sulphadoxine-pyrimethamine is used for prophylaxis against placental malaria in pregnancy. Interestingly the birth outcomes for the four women were normal.

5.3 Malaria in pregnancy and birth outcomes

Pregnant women who had malaria and treated had 20% increased odds of having normal birth outcomes. Treatment is seen here to be beneficial to the pregnant woman who has malaria. This could imply that any pregnant women with sub-optimal amounts of malaria parasitaemia should be given malarial treatment.

The study showed that pregnant women in the 1st and 2nd trimesters were more prone to having malaria, and had 15% and 18% decreased odds of normal birth outcomes respectively, than women in 3rd trimester who were 3% more likely to have normal birth

outcomes. This is probably due to the reduced immunity in early and mid-pregnancy. This immunity is restored in the third trimester. This finding is in line with that of Okafor et al. (2012).

Women who treated with artemether-lumefantrine are 30% more likely to have stillbirth, and women who had malaria in third trimester were 223% more likely to have stillbirth. During the multivariate analysis it was observed that moderate anaemia was responsible for the stillbirth and not antimalarial usage. This anaemia could be due to the malaria itself. Malaria parasites are known to destroy red blood cells. This finding is similar to that of Mosha et al. (2014).

One unusual finding of this study is that pregnant women who slept under insecticides treated bednets were 8% less likely to have normal birth outcomes. Previous studies have shown that insecticides treated bednets were very beneficial in reducing the incidence of malaria in the vulnerable populations who used them regularly. This could mean that the pregnant women were not sleeping under their insecticides treated bednets consistently.

5.4 Other factors affecting birth outcomes

Pregnant women who were self-employed had 65% decreased odds of normal birth outcome. By self-employment we mean petty traders, hairdressers and seamstresses. This can be explained by the fact that these group formed the low income group, with monthly income ≤ GHÇ500, majority laid between GHÇ 100-200. This income is highly insufficient for the women to cater for themselves and their families. As the income of the women improved, the odds of having normal birth outcomes increased by 43%.

The study also found that as the women increased in age, their odds of having normal birth outcomes decreased by 8%, though women under 20 years old were less likely to have normal birth outcomes. This could be explained by the reason that teenagers are not matured enough for the biological function of carrying pregnancy, let alone having normal birth outcome. The best age group was 20-29 years, with 75% better odds of having normal birth outcomes in comparison to the teenagers.

Increasing BMI has 11% increased odds of normal birth outcomes, though obese women had 160% increased odds of normal birth outcomes. Very obese women are however 37% less likely to have normal birth outcomes. This is due to the fact that very obese women are more likely to have cardiovascular diseases and diabetes which have negative impact on normal birth outcome. This finding is in line with the works of Harville et al., (2011).

Women living outside Tema are 30% more likely to have normal birth outcomes. This was expected as about 89% of the women were living outside Tema, and there were competent staff at the Tema General Hospital to handle every case as they presented at the hospital.

Other Infections like sexually transmitted diseases and helminth infections were found to have negative impact on full gestation of the unborn child. Pregnant women who had STI in pregnancy and treated were 34% more likely to have premature birth outcome and those who had helminth infection and treated were 29% more likely to have premature birth outcome. These findings were also in line with previous works reviewed in this work.

CHAPTER SIX

CONCLUSION AND RECOMMENDATION

6.1 Conclusion

This study found that birth outcomes in pregnant women treated with artemisinin based combination therapies in any of the trimesters of pregnancy were slightly different from the birth outcomes in pregnant women not treated with artemisinin based combination therapies, but these differences were not statistically significant. We are optimistic that Malaria Policy's recommendation for malaria treatment in the first trimester of pregnancy will be reviewed soon after critically analyzing findings of this and other recent researches in these areas.

6.2 Recommendations

1. Ghana National Malaria Programme to review all the work that has been carried out in this area and use the findings to review Treatment Guidelines for Malaria in Pregnancy. This should include the use of artemisinin based combination therapies, especially artemether-lumefantrine in all trimesters of pregnancy. Safety monitoring should still continue at all levels of health service provision after the change is affected.
2. Prescriber's preferences should always be taken into account by Policy Makers before institutionalizing any Treatment Policy.
3. Pregnant women should be encouraged to take the maximum WHO recommended doses of Intermittent Preventive Treatment during Pregnancy as they are truly very beneficial for normal birth outcomes.

4. Sensitization of midwives and other prescribers against the use of sulphadoxine-pyrimethamine for the treatment of malaria in pregnancy should be re-enforced.

6.3 Limitations of Study

Secondary data was used for this study and it was observed that the use of multiple maternal record cards by some of the pregnant women who were health shopping was common, and so need for verbal autopsy in completing CRFs.

Antenatal clinics at the Tema General Hospital (TGH) was started after the 1st trimester of pregnancy by most of the women.

Some of the information on the antimalarial used were recalled by showing the new mothers samples of the various medicines, and cannot be void of bias.

Time constraint for further follow up of the new babies.

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APPENDICES

Appendix A: Clearance from Ghana Health Service Ethics Review Committee.

Appendix B: Approval from Tema General Hospital

Appendix C: Case Report Forms

1. Maternal Record Book No:
2. Age:
3. Weight: Height: BMI:
4. Residential area: a. Tema west b. Tema east c. Tema central d. Outside Tema
5. Occupation: a. Not employed b. Self-employed c. Formal sector
6. Income group (GHC/Month): a. 100- 500 b. 501-1000 c.1001-1500 d. 1501-2000 e. 2001
7. Social habits: a. Smoking: yes or no b. Alcohol consumption: yes or no
8. Gravidity: a. Primigravidae b. Secundigravidae c.3 – 4 pregnancies d. ≥ 5 pregnancies
9. STI in Pregnancy: a. Yes b. No c. If yes which?
10. Worm infestation: a. Yes b. No c. If yes which treatment?
11. Haemoglobin level at first ANC visit:
12. Haemoglobin level at last ANC visit:
13. Malaria in pregnancy: a. Yes b. No c. If yes which trimester?
14. Which malaria treatment was given: a. AA b. AL c. Quinine d. Quinine + Clindamycin e. others…….
15. IPTp in pregnancy: a. IPTp 1 b. IPTp 2 c. IPTp 3 d. IPTp 4 e. IPTp 5 f. None
16. ITN Usage:
17. Baby weight …….
18. Outcome: a. LBW b. Premature birth c. Stillbirth d. Normal

Appendix D: Informed Consent Form

Project: **Birth outcomes in pregnant women treated with artemisinin-based combination therapies at Tema General Hospital.**

This informed consent form has two parts:

- Information sheet (to share information about the study with you); and
- Certificate of consent (for signature should you choose to participate in the study)

You will be given both to keep.

Part 1: Information sheet

Introduction and purpose of the research study

Good morning/afternoon,

My name is _____.

From _____.

Within the Ghanaian health sector, innovations are being sought to improve the ways in which policies on health issues concerning pregnant women are adopted. Previously, enough researches involving pregnant women were not carried out in this population because of fear of causing harm to the unborn child.

A study is being carried out at the maternity unit level to observe new born babies and gather information on the kind of treatments that their mothers received during pregnancy. The findings will inform health policy makers on the need to have a second look at existing policies on maternal prescriptions in Ghana health sector.

Participant selection

You are being invited to participate as a new mother since you are still on admission here, and your experiences will help in this research.

Voluntary participation

Your participation in this study is completely voluntary. As a respondent you are entitled to withdraw yourself from the study at any time without any penalty to you or your baby. Your choice to participate or not will not have any bearing on the treatments you receive from here.

If at any point during the questionnaire/CRF you feel discomfort, you may stop. Should you choose to withdraw, the information you provide will not be used in the study.

Benefits and potential risks of the research study

Policy makers, prescribers at the various levels of the health system and pregnant women will be the main beneficiaries of this study. It is expected that the study findings will feed into ongoing policy dialogues on how to improve maternal and newborn health in Ghana.

No adverse psychological or social risks are expected from this study.

Confidentiality

Any risks to respondents have been further minimized by ensuring anonymity throughout the data collection process. No respondent names will be used anywhere on the questionnaire/CRF, and respondents will be identified in the data analysis through codes only.

Compensation

No incentives will be given for participating in this study, however any incurred expenses will be reimbursed.

Feedback of findings

A series of feedback mechanisms to engage study respondents and other key stakeholders will be conducted, including policy briefs and a final dissemination workshop.

Funding information

This study is self-funded.

This study has been reviewed and approved by the Ghana Health Service Ethical Review Committee.

For further information on this study, or related research project, please contact:

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Hannah Frimpong, Administrator, Ghana Health Service Ethical Review Committee, 0243235225/0507041223

Part 11: Certificate of consent

I have read the foregoing, or it has been read to me. I understand fully the above information. I have had the opportunity to ask questions, and all questions have been answered to my full satisfaction. I consent voluntarily to participate as an informant in this research. I understand that I have the right to withdraw from the study at any time without negative consequence to me in any way.

Signature.

Date _____.

Researcher name _____.

Signature _____.

For further information on this study, or the related project, please contact:

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Hannah Frimpong, Administrator, Ghana Health Service Ethical Review Committee, 0243235225/0507041223