

**PREGNANCY OUTCOMES IN WOMEN WITH  
MALARIA IN AREAS WITH DIFFERENT LEVELS OF  
MALARIA TRANSMISSION IN KENYA**

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## DECLARATION

This thesis is my original work and has not been presented for a degree in any other University.

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## **DEDICATION**

I dedicate this thesis to my parents Mr. and Mrs Dache and all the members of my family for their love, support, and encouragement during this process.

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## **LIST OF ABBREVIATIONS**

<b>DOMC</b>	Division of Malaria Control
<b>GoK</b>	Government of Kenya
<b>Hb</b>	Haemoglobin
<b>HIV</b>	Human Immunodeficiency Virus
<b>HMIS</b>	Health Management Information System
<b>IgG</b>	Immunoglobulin G
<b>IPT</b>	Intermittent Preventive Treatment
<b>ITN</b>	Insecticide Treated Nets
<b>ITROMID</b>	Institute of Tropical Medicine and Infectious Diseases
<b>IUFD</b>	Intrauterine Foetal Death
<b>IUGR</b>	Intrauterine Growth Retardation
<b>KDHS</b>	Kenya Demographic Health Survey
<b>KEMRI</b>	Kenya Medical Research Institute
<b>LBW</b>	Low Birth Weight
<b>MDG</b>	Millennium Development Goals
<b>RBM</b>	Roll Back Malaria
<b>SPSS</b>	Statistical Package for Social Scientists
<b>SVD</b>	Spontaneous Vertex Delivery
<b>WHO</b>	World Health Organisation

## **ABSTRACT**

Pregnant women in malaria prone areas may be subjected to a variety of adverse consequences from malaria infection including: maternal anaemia; premature delivery/miscarriage; low birth weight and perinatal mortality. A retrospective hospital record-based study for Kenya was conducted in Kisumu District (a malaria endemic zone), Kwale District (a malaria endemic zone), Kericho District (a malaria epidemic zone) and Meru South district (a malaria low transmission zone).

The objective of this study was to determine the magnitude of these adverse effects among pregnant women with malaria in selected hospitals in Kenya between January 2006 and October 2007). Inpatient and maternity ward registers for January 2006 to October 2007 were reviewed and malaria cases, mortality, abortions, stillbirths, birth weights, mode of delivery and maternal anaemia cases were recorded.

There were significantly more malaria cases among pregnant women in Kisumu district hospital compared to other hospitals ( $P < 0.0001$ ).

The association between premature deliveries and malaria diagnosis in different areas of malaria transmission was not statistically significant when Kisumu was compared with all the districts ( $P$ -value=0.073). However, when Kisumu is compared with Meru south and Kericho the association was statistically significant ( $P$ -value=0.039). Generally the proportion of women diagnosed to have had malaria who delivered prematurely was higher among women who also had a diagnosis of anaemia except in Msambweni district hospital. In Kericho all the women who had malaria and concurrent anaemia delivered prematurely. In Msambweni district the proportion of premature deliveries was higher among those who had concurrent

anaemia diagnosis (71%). The chances of delivering a low birth weight baby in Kisumu as compared to other hospitals was significant (P-value = 0.03). The likelihood of delivering a low birth weight among women who had malaria and delivered prematurely was significant in Kisumu (OR=5.5, C.I. = 1.2-24.2, p-value = 0.02), Kericho (OR=undefined, P-value=0.009) and Meru south (OR = undefined, P-value = 0.002). Therefore the gestation at delivery and not per-se the malaria diagnosis may influence the birth weight. Therefore malaria may contribute to low birth weight indirectly through premature delivery. Routine hospital data such as birth weight and number of malaria cases can provide information on the level of malaria transmission and trends useful for the health services to target appropriate malaria interventions and to allocate resources to control outbreaks of malaria epidemics.

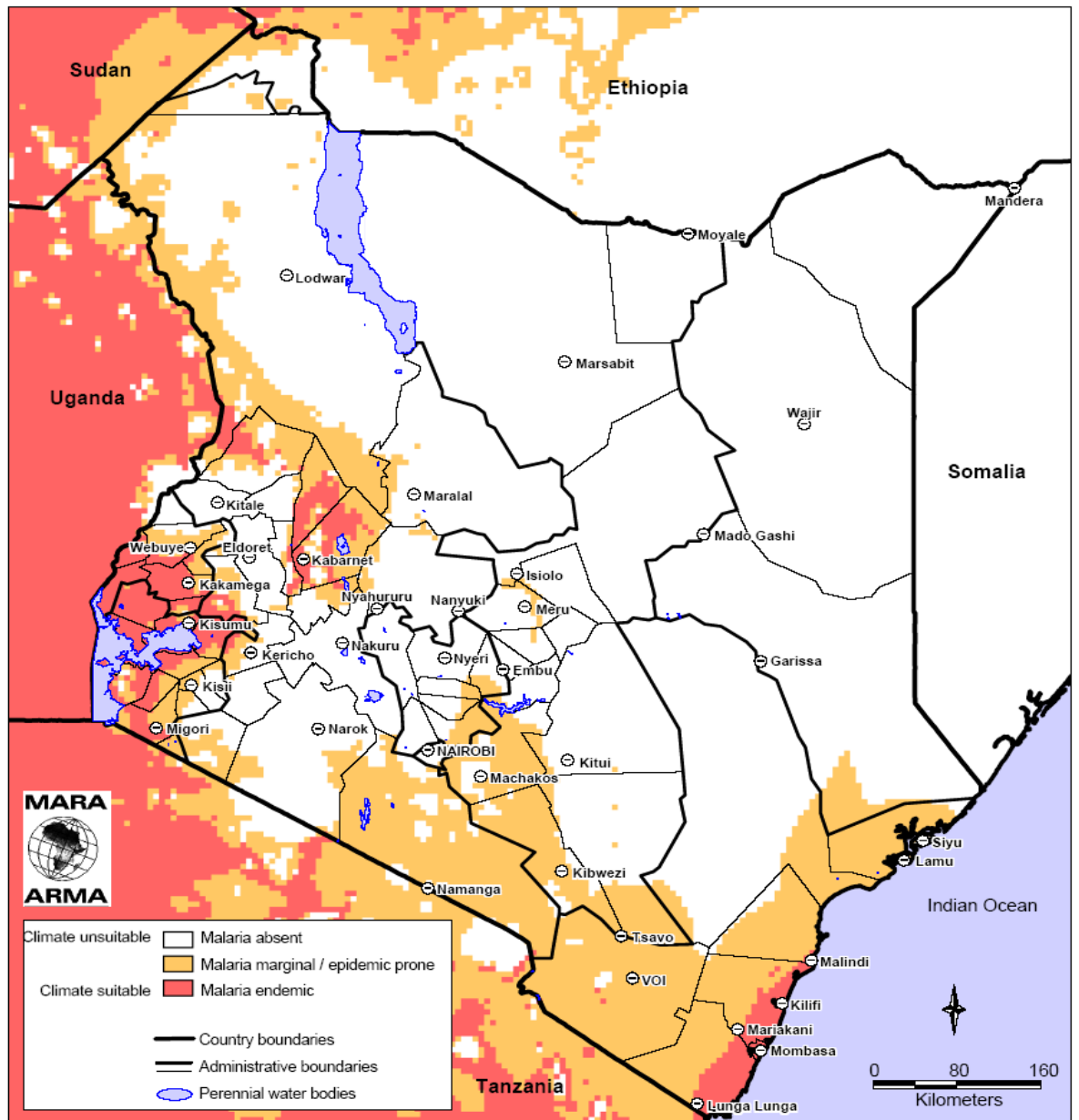
# CHAPTER ONE

## 1.0 INTRODUCTION

### 1.1 Background

Malaria affects approximately 20 million people in Kenya annually; the cumulative human suffering and economic loss caused by malaria is immense (Snow *et al.*, 1998). It is estimated that, annually, 26,000 children under five years of age (72 per day) die from the direct consequence of malaria infection (Snow *et al.*, 1998) and pregnant women suffer severe anaemia and have a high likelihood of delivering infants with low birth weight (Menendez, 1999). Most Kenyan households especially in endemic areas are affected by the financial hardship caused by malaria. It is estimated that a total of 170 million working days are lost each year because of malarial illness, which in turn affects the countries economy, leading to increased poverty (Ministry of Health-Kenya, DOMC, 2007).

The distribution of malaria in Kenya is not uniform, because of geographical differences in altitude, rainfall and humidity. These factors influence transmission patterns, as they determine vector densities and intensity of biting. The country may be divided into four malaria eco-zones: stable malaria (Nyanza, Coast, and Western Provinces) seasonal malaria (Central, Eastern, and North Eastern Provinces), highlands prone to malaria epidemics (mainly Rift Valley Province and some parts of Nyanza Province), and malaria free (Nairobi and some parts of Central Province) (Figure 1).



This map is a product of the MARA/ARMA collaboration (<http://www.mara.org.za>). July 2001, Medical Research Council, PO Box 17120, Congella, 4013, Durban, South Africa  
 CORE FUNDERS of MARA/ARMA: International Development Research Centre, Canada (IDRC); The Wellcome Trust UK; South African Medical Research Council (MRC); Swiss Tropical Institute, Multilateral Initiative on Malaria (MIM) / Special Programme for Research & Training in Tropical Diseases (TDR), Roll Back Malaria (RBM).  
 Malaria distribution model: Craig, M.H. et al. 1999. Parasitology Today 15: 105-111.  
 Topographical data: African Data Sampler, WRI, [http://www.igc.org/wri/sdis/maps/ads/ads\\_idx.htm](http://www.igc.org/wri/sdis/maps/ads/ads_idx.htm).

**Figure 1 Distribution of endemic malaria in Kenya (Courtesy of Mara), 2001.**

Malaria infection during pregnancy is a major public health problem in tropical and subtropical regions of the world. In most endemic areas of Africa, pregnant women are the main adult risk group for malaria. Every year at least 30 million women in malaria prone areas of Africa become pregnant; most of these women live in areas of relatively stable malaria transmission (WHO, 2000). The main burden of malaria infection during pregnancy results from infection with *Plasmodium falciparum*. The impact of the other three human malaria parasites (*P. vivax*, *P. malariae*, and *P. ovale*) is less clear (WHO, 2000).

The symptoms and complications of malaria during pregnancy differ with the intensity of malaria transmission and thus with the level of immunity acquired by the pregnant woman (WHO, 2003). Since malaria transmission intensity may vary within the same country from areas of relatively stable transmission to areas of unstable or epidemic transmission, the clinical picture of malaria infection during pregnancy may likewise range from asymptomatic to severe, life-threatening illness (WHO, 2003). In areas of epidemic or low (unstable) malaria transmission, adult women have not acquired any significant level of immunity and usually become ill when infected with *P. falciparum*. For pregnant women in these areas the risk of developing severe malaria is 2-3 times higher than that for non-pregnant women living in the same area. Maternal death may result either directly from severe malaria or indirectly from malaria-related severe anaemia. In addition, malaria may result in a range of adverse pregnancy outcomes, including low birth weight (LBW), spontaneous abortion, and neonatal death (WHO, 2003).



In areas of high and moderate (stable) malaria transmission, most adult women have developed sufficient immunity that, even during pregnancy, *P. falciparum* infection does not usually result in fever or other clinical symptoms. In these areas, the principal impact of malaria infection is malaria-related anaemia in the mother and the presence of parasites in the placenta. The resulting impairment of foetal nutrition contributes to low birth weight and is a leading cause of poorer infant survival and development (Steketee *et al.*, 2001). In areas of Africa with stable malaria transmission, *P. falciparum* infection during pregnancy is estimated to cause an estimated 75,000 to 200,000 infant deaths each year (Steketee *et al.*, 2001).

## **1.2 Statement of the problem**

Malaria is the leading cause of mortality and morbidity in Kenya, particularly among pregnant women and children under five years of age. Almost 70% of the Kenyan population are at risk of malaria infection and 1.5 million pregnant women are susceptible annually (MOH, Kenya, 2007). Various interventions have over the years been put in place to effectively control malaria in Kenya and have since been facing various challenges such as accessibility and distribution. Few studies have assessed the importance of malaria infection as a cause of LBW in areas of low, epidemic and endemic malaria transmission, where the risk of spontaneous abortion and still birth is very high in women of all parities. There is, therefore, a need to document such findings to provide information on the level of malaria transmission, its magnitude and possible subsequent adverse outcomes among pregnant women useful for the health services to target appropriate malaria interventions especially in pregnancy and allocate resources to control outbreaks of malaria epidemics.

### **1.3 Justification of the Study**

It is estimated that in areas where malaria is endemic, around 19% of infant LBWs are due to malaria and 6% of infant deaths are due to LBW caused by malaria. These estimates imply that around 100,000 infant deaths each year could be due to LBW caused by malaria during pregnancy in areas of malaria endemicity in Africa (Snow *et al.*, 2003).

Despite the toll that malaria exerts on pregnant women and their infants, this was until recently a relatively neglected problem, with less than 5% of pregnant women having access to effective interventions. During the past decade, however, potentially more effective strategies for prevention and control of malaria in pregnancy have been developed and shown to have a remarkable impact on the health of mothers and infants.

In Kenya few studies have been done to quantify the actual outcomes of malaria in pregnancy. Therefore this study endeavoured to investigate on the status of or outcomes of malaria in pregnancy in selected areas in Kenya to enable care providers and policy makers to appropriate intervention strategies and policies.

## **1.4 Hypothesis**

Adverse pregnancy outcomes in women with malaria infection are common in areas with different levels of malaria transmission in Kenya.

## **1.5 Objectives**

### **1.5.1 General Objective**

To determine pregnancy outcomes in women with malaria admitted at Kisumu, Msambweni, Kericho and Meru South district hospitals maternity clinics between January 2006 and October 2007.

### **1.5.2 Specific Objectives**

1.5.2.1 To determine the incidence of malaria among pregnant women admitted at Kisumu, Msambweni, Kericho and Meru South district hospitals.

1.5.2.2 To determine the relationship between malaria in pregnancy, age and parity.

1.5.2.3 To determine the prevalence of low birth weight, still births, preterm deliveries and maternal mortality in pregnant women diagnosed with malaria.

## CHAPTER TWO

### 2.0 LITERATURE REVIEW

#### 2.1 Malaria and Life cycle of *Plasmodium* Species

Malaria is a life-threatening parasitic disease transmitted by *Anopheles* mosquitoes. It was once thought that the disease came from fetid marshes, hence the name malaria, (bad air) (WHO, 2001). In 1880, scientists discovered the real cause of malaria to be a one-cell parasite called *Plasmodium*. Later they discovered that the parasite is transmitted from person to person through the bite of a female *Anopheles* mosquito, which requires blood to develop her eggs (White, 1996).

There are four types of human malaria parasites namely *Plasmodium vivax*, *P. malariae*, *P. ovale* and *P. falciparum*. *P. vivax* and *P. falciparum* are the most prevalent world wide with *P. falciparum* being the most virulent type of malaria infection. *P. falciparum* malaria is most common cause of malaria in sub- Sahara Africa, accounting largely for the extremely high mortality in this region (White, 1996). There are also worrying indications of the spread of *P. falciparum* malaria into new regions of the world and its reappearance in areas where it had been eliminated (WHO, 2001).

The malaria parasite enters the human host when an infected *Anopheles* mosquito takes a blood meal. Inside the human host, the parasite undergoes a series of changes as part of its complex life cycle (Figure 2).

Its various stages allow *Plasmodium* to evade the immune system, infect the liver and red blood cells, and finally develop into a form that is able to infect a mosquito again when it bites an infected person. Inside the mosquito, the parasite matures until it reaches the sexual stage where it can again infect a human host when the mosquito takes her next blood meal, 10 to 14 or more days later (WHO,2006). Malaria symptoms appear about 9 to 14 days after the infectious mosquito bite, although this varies with different *Plasmodium* species. Typically, malaria produces fever, headache, vomiting and other flu-like symptoms. If drugs are not available for treatment or the parasites are resistant to them, the infection can progress rapidly to become life-threatening. Malaria can kill by infecting and destroying red blood cells (anaemia) and by clogging the capillaries that carry blood to the brain (cerebral malaria) or other vital organs (WHO, 2001).

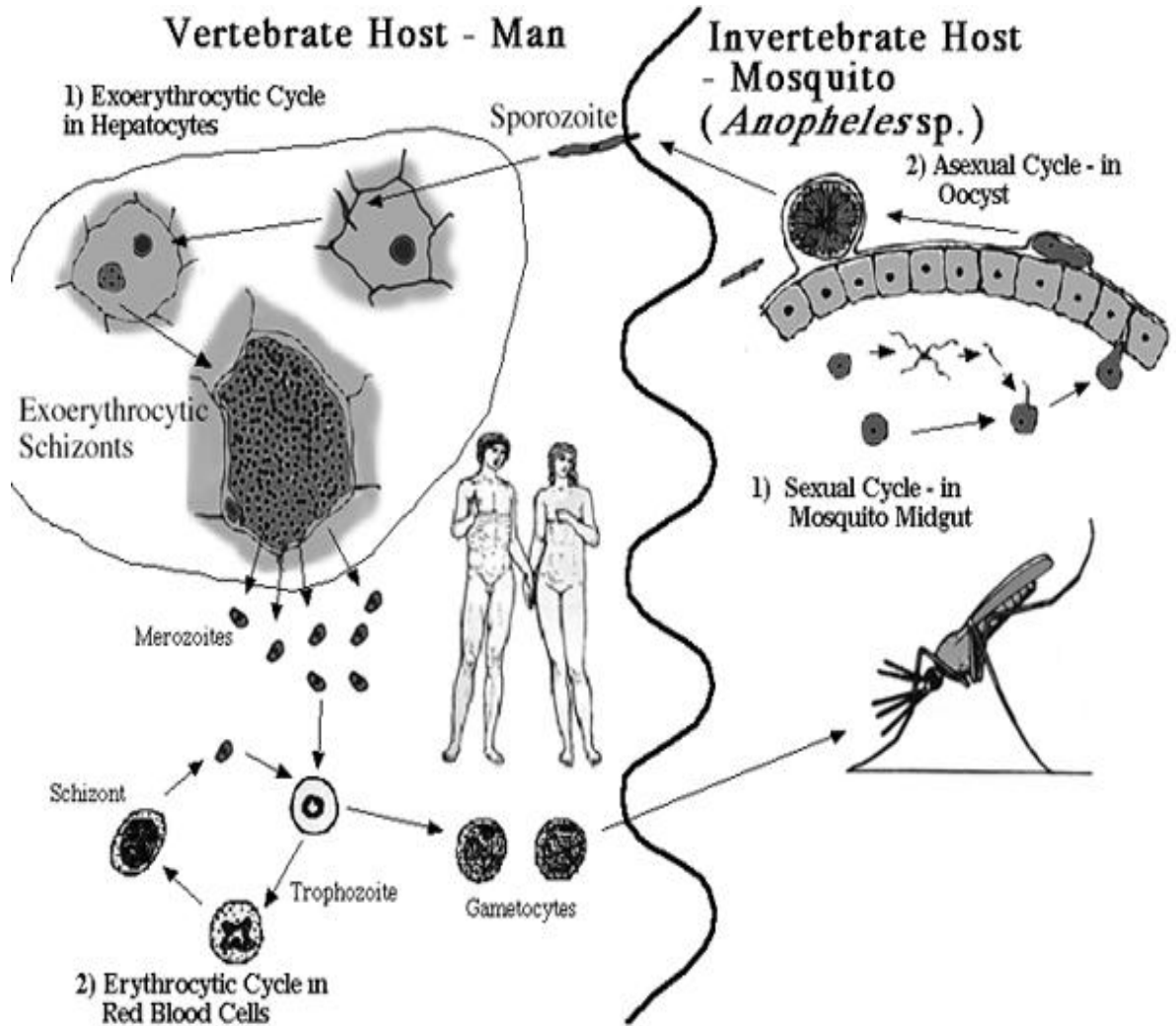


Figure 2 Life cycle of Human Malaria (Courtesy of Parasitological Notes, The Travel Doctor site, 2007)

## **2.2 Prevalence and Burden of Malaria**

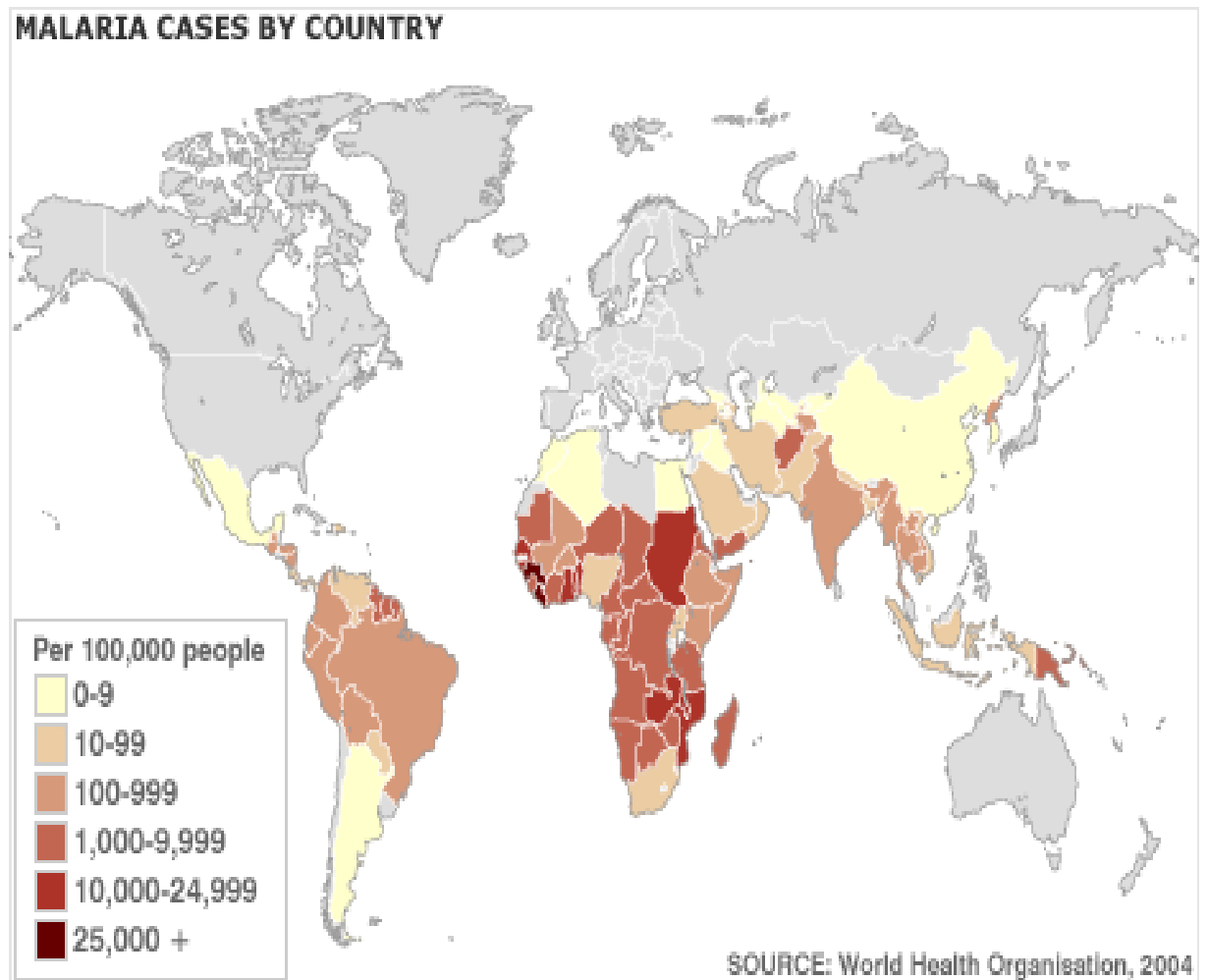
### **2.2.1 Global burden of malaria**

At the end of 2004, 107 countries and territories with approximately 3.2 billion people were at risk of malaria transmission (Figure 3). An estimated 350–500 million clinical malaria episodes occur annually; most of these are caused by infection with *P. falciparum* and *P. vivax* (World Malaria Report, WHO, 2005).

*Falciparum* malaria causes more than 1 million deaths each year (Steketee *et al.*, 2001). It also contributes indirectly to many additional deaths, mainly in young children, through synergy with other infections and illnesses. Patterns of malaria transmission and disease vary markedly between regions and even within individual countries. This diversity results from variations between malaria parasites and mosquito vectors, ecological conditions that affect malaria transmission and socioeconomic factors, such as poverty and access to effective health care and prevention services (WHO, 2005).

Sub-Saharan Africa accounts for about 60% of total malaria cases and more than 80% of malaria deaths worldwide with about 75% of global *falciparum* malaria cases. *P. falciparum* causes the vast majority of infections in this region and about 18% of deaths in children less than 5 years of age. Malaria is also a major cause of anaemia in children and pregnant women resulting in low birth weight, premature birth and infant mortality (World Malaria Report, WHO, 2005)





**Figure 3 Global burden of Malaria (Source, WHO, 2004)**

### **2.2.2 Malaria in Africa**

The various *Plasmodium* species prevalent in Africa include *P. falciparum* accounting for 93% of malaria cases, *P. vivax* or *P. falciparum* /*P. vivax* mixed accounting for 7% of malaria cases with the principal vectors being *A. gambiae*, and *A. funestus*. An estimated proportion of population at risk of malaria is 66% (Hay *et al.*, 2004), estimated contribution to the global burden of clinical malaria cases 59%

(Korenromp, 2004), estimated contribution to the global burden of clinical falciparum malaria cases: 74% (Korenromp, 2004) and estimated contribution to the global malaria mortality burden: 89% (The World Health Report, WHO, 2003).

Africa remains the region that has the greatest burden of malaria cases and deaths in the world. In 2000, malaria was the principal cause of around 18% of deaths of children under 5 years of age in sub-Saharan Africa thus about 803 000 (uncertainty range of 710 000- 896 000) deaths (Rowe *et al.*, 2005). During the 1980's and the early 1990's, malaria mortality in rural Africa increased considerably, probably as a result of increasing resistance to chloroquine (Korenromp *et al.*, 2003; Rowe *et al.*, 2005). Malaria is also a significant indirect cause of death: malaria-related maternal anaemia in pregnancy, LBW and premature delivery are estimated to cause 75,000–200,000 infant deaths per year in sub-Sahara Africa (Ter Kuile *et al.*, 2004). Malaria epidemics result in an estimated 12 million malaria episodes and almost 310,000 deaths per year in Africa (Worrall *et al.*, 2004). In contrast to the endemic countries in sub-Sahara Africa, Egypt and Morocco have only residual malaria transmission and occasional imported cases (World Malaria Report, WHO, 2005). In endemic African countries, malaria accounts for 25–35% of all outpatient visits, 20–45% of hospital admissions and 15–35% of hospital deaths, imposing a great burden on already fragile health-care systems (World Malaria Report, WHO, 2005).

### **2.2.3 Malaria in Kenya**

Approximately 1.5 million women become pregnant in Kenya each year. Majority of these women live in areas of moderate to intense transmission of malaria. Malaria infection poses a risk to the unborn child since it may lead to adverse outcomes such as abortion, stillbirth, congenital infection, LBW, prematurity and intra-uterine growth retardation while in the mother it leads to malaria illnesses and mortality (MOH, Kenya, 2007). Pregnancy related maternal mortality is estimated at 414/100,000(KDHS 2003). Severe anaemia manifests in approximately 6,000 primigravida women (MOH, 1998). Haemorrhage complicating malaria related anaemia during pregnancy contributes significantly to maternal mortality. Approximately 2–15% of severe maternal anaemia, 8-14% LBW, 8-36% to pre-term LBW, 13-70% of intrauterine growth retardation –LBW, and 3 – 8% increased infant mortality are attributable to malaria each year (MOH, 1998).

### **2.2.4 Economic Burden of Malaria**

The world malaria report estimated a decrease in economic growth due to malaria in highly endemic countries whereby more than 1%/year malaria transmission season generally coincides with the planting and/or harvesting season and brief periods of illness exact a high cost on the world's poorest regions (World Malaria Report, WHO, 2005). The estimated global annual cost of malaria in 1995 was US\$ 2 billion for both direct and indirect costs, including loss of labour with a current estimated annual expenditure of US\$ 26 million on malaria prevention and treatment and US\$ 65 spent per malaria fatality worldwide.

The estimated worldwide expenditure on malaria research is only US\$ 58 million, which is one thousandth of the US\$ 56 billion spent globally on health research annually (World Malaria Report, WHO, 2005).

### **2.3 Malaria and Pregnancy**

The pattern of clinical malaria varies with the intensity of transmission. In areas of stable transmission, severe malaria is confined to children aged <5 years and manifests itself mainly as severe anaemia (Snow *et al.*, 1993; Marsh *et al.*, 1995). However in areas of unstable transmission, severe malaria may occur at all ages (White, 1996), and pregnant women of all parities are at higher risk of developing severe malaria than non-pregnant women (Nosten *et al.*, 1991).

In areas where malaria is highly endemic, a protective semi-immunity against *P. falciparum* is acquired during the first 10–15 years of life, and the majority of malaria-related morbidity and mortality happens in young children (WHO, 2003). However, in contrast with low malaria prevalence in adults, pregnant women in endemic areas are highly susceptible to malaria, and both the frequency and the severity of disease are higher in pregnant than non-pregnant women (Brabin, 1983; Korenromp, 2004). In pregnancy, there is a transient depression of cell-mediated immunity that allows foetal allograft retention but also interferes with resistance to various infectious diseases (Meeusen *et al.*, 2001). Cellular immune responses to *P. falciparum* antigens are depressed in pregnant women in comparison with non-pregnant control women (Riley *et al.*, 1989; Fievet *et al.*, 1995). Anti-adhesion antibodies against chondroitin sulphate A-binding parasites are associated with

protection from maternal malaria, but these antibodies develop only over successive pregnancies, accounting for the susceptibility of primigravidae to infection (Duffy and Fried., 1999). Indeed, women in first and second pregnancies are the most affected, with both gravidity and primiparity influencing susceptibility to malaria infection (Bouvier *et al.*, 1997; Cot *et al.*, 1995; Deloron and Maubert, 1995; Mutabingwa *et al.*, 1993). Numerous epidemiological studies have reported a broad range of conditions during pregnancy which are a result of malaria (Salihu *et al.*, 2002; Mockenhaupt *et al.*, 2002; Shulman *et al.*, 2001; Carles *et al.*, 1998; Greenwood *et al.*, 1992). As with peripheral parasitaemia, placental infection is also most frequent and heaviest in primigravidae (McGregor *et al.*, 1983).

Malaria in pregnancy causes maternal anaemia and Low Birth Weight (LBW) (Brabin, 1991). The causes of LBW are multifactorial, but malaria infection is the most important particularly in the primigravidae living in stable malaria-endemic areas (Brabin and Piper, 1997). In stable malaria-endemic areas it has been estimated that about 40% of LBW is attributed to malaria (Brabin and Piper, 1997). Birth weight is one of the most important determinants of infant survival in tropical developing countries (Greenwood *et al.*, 1992). Infants with LBW have rapid growth, which exhausts their iron reserves (Dallman *et al.*, 1980). This leads to iron-deficiency anaemia, which will increase susceptibility to respiratory and gastrointestinal tract infections in infants and increased risk of morbidity and mortality (Kahn, 1991).

## 2.4 Anaemia and Pregnancy

In malaria-endemic countries of Africa, anaemia is very common in pregnant women and in children under five (WHO, 2003). Although anaemia is multifactorial with causative factors including iron deficiency and other nutritional deficiencies, helminth infection, and HIV, however, malaria is clearly an extremely important factor (Murphy and Breman, 2001). Over half of malaria-related deaths are attributed to severe malaria anaemia (which is defined as malaria parasitaemia and a haemoglobin (Hb) concentration less than 50 g/L) (Murphy and Breman, 2001). Several anti-malarial interventions have been shown to prevent anaemia, including insecticide-treated nets, residual spraying, malaria chemoprophylaxis, and, more recently, intermittent presumptive treatment of infants (i.e. anti-malarials co-administered with childhood immunization). Insecticide-treated nets have been shown to decrease all-cause mortality (Crawley, 2004).

The pathogenesis of malaria anaemia remains incompletely understood. Dyserythropoiesis (disordered red cell development, which is, at least in part, due to inflammatory cytokines acting on erythroid precursors), intravascular haemolysis of infected red cells, and destruction of both parasitized and uninfected erythrocytes by splenic macrophages are all important (Roberts *et al.*, 2005; Ekvall, 2003). Interestingly, it has been estimated that ten or more uninfected erythrocytes may be lost for each infected one (Price *et al.*, 2001), presumably because malaria infection alters uninfected erythrocytes. The probable causes of red cell loss include oxidation of band 3 (the anion transporter of the erythrocyte membrane) or membrane lipids,

and deposition of IgG, complement, or immune complexes on the erythrocyte surface (Price *et al.*, 2001).

In pregnancy, anaemia has a significant impact on the health of the foetus as well as that of the mother. Twenty percent of maternal deaths in Africa have been attributed to anaemia (Harrison, 1975). Foetuses are at risk of preterm deliveries, low birth weights, morbidity and perinatal mortality due to the impairment of oxygen delivery to placenta and foetus (Brabin, 1991, WHO, 1991; De Mayer, WHO, 1989). World Health Organization estimates that more than half of pregnant women in the world have a haemoglobin level indicative of anaemia ( $< 11.0\text{g/dL}$ ), the prevalence may however be as high as 56% or 61% in developing countries (WHO, 1994). Women often become anaemic during pregnancy because the demand for iron and other vitamins is increased due to physiological burden of pregnancy. The inability to meet the required level for these substances either as a result of dietary deficiencies or infection gives rise to anaemia (Van de Broek *et al.*, 2000).

Anaemia ranges from mild, moderate to severe and the WHO pegs the haemoglobin level for each of these types of anaemia in pregnancy at  $10.0 - 10.9\text{g/dL}$  (mild anaemia)  $7 - 9.9\text{g/dL}$  (moderate anaemia) and  $< 7\text{g/dL}$  (severe anaemia) (WHO 1989). Prevalence of anaemia can be as high as 61% in developing countries (WHO, 1994) with a high incidence and severity occurring among primigravidae living in malaria endemic areas (Matteli *et al.*, 1994).

## **2.5 Malaria and Low Birth Weight**

### **2.5.1 Pathophysiological process**

Most malaria infections, and the most severe morbidity and mortality, are caused by *P. falciparum*. Most *P. falciparum* infections occur in sub-Saharan Africa, and the *P. falciparum* parasite has been shown to be more common in pregnant than non-pregnant women and to have a substantial adverse effect on pregnancy outcome (causing both prematurity [gestation of <37 weeks] and intrauterine growth retardation [IUGR] (Ismail, 2000). Erythrocytes infected with *P. falciparum* congregate in the maternal placental vascular space, where the parasites replicate. Malaria-infected placentas are frequently observed to carry antibodies, cytokines, and macrophages, which are indicative of an active immune response. This immune response may stimulate early labour, though the precise effect of malaria-parasitized placentas on prematurity is not clear (Ismail, 2000; Sullivan *et al.*, 1999).

The IUGR effect appears to relate to nutrient transport to the foetus. First, a high density of parasites and chronic parasite infection in the placental blood and the associated cellular immune response may result in consumption of glucose and oxygen that would have gone to the foetus. Second, histopathological studies of infected placentas have found thickening of the cytotrophoblastic membranes, which may interfere with nutrient transport (Ismail, 2000; Verhoeff, 2001)). However, the details of these biological processes remain uncertain given that they can be studied only after the placenta has been delivered. Malaria-associated maternal anaemia may



also contribute independently to IUGR (Ismail, 2000; Verhoeff, 2001) most likely through a reduction in oxygen transport to the foetus.

Until recently, the mechanism through which parasite sequestration occurs in the placenta has been unclear. However, recent studies in Kenya and Malawi have identified certain parasite strains i.e. *P. falciparum* that are found at an increased frequency in pregnant women and have suggested that these strains may be selected for due to their ability to adhere to chondroitin sulphate A on the syncytiotrophoblast (Fried and Duffy, 1996; Maubert *et al.*, 1999; Rogerson *et al.*, 1995).

The observations described above relate to malaria contracted during pregnancy among women residing in areas of stable malaria transmission. The adverse effects in unstable areas may be quite different, with the effects of severe malaria, such as febrile episodes and stillbirths, becoming more apparent (Newman *et al.*, 2003).

### **2.5.2 Risk for Low Birth Weight**

Low Birth Weight is the single greatest risk factor for neonatal and infant mortality (McCormick, 1985). Although most of the evidence arises from studies in the developed world, a recent analysis of cross-sectional data on birth weight and survival from five sites in sub-Saharan Africa showed that infant mortality is three times higher for LBW babies than for those of normal weight (Guyatt and Snow, 2001). The effects on neonatal mortality are even more marked, with a LBW baby being nine times more likely to die in the first month of life than a normal-weight (Guyatt and Snow, 2001). The risks for mortality increase steadily as the birth

weight decreases to below the LBW threshold, though the data are limited (USAID and CDC, 1993).

In Malawi, infant death rate per 1,000 live births was 650 for babies with birth weights of less than 1,500g, 276 for babies with birth weights of 1,500g to 1,999 g, 58 for babies with birth weights of 2,000 to 2,499 g, and 24 for babies with normal birth weights (>2,499 g) (USAID and CDC, 1993).

LBW can be due to prematurity or IUGR. Identifying LBW cases caused by prematurity can be difficult, as many women are usually not certain of their gestational age; as a result, very few studies report separately data on LBWs for preterm infants and those for infants with IUGR. It was previously thought that malaria mostly affects IUGR (Brabin, 1991), though recent work has shown malaria to also be important in prematurity (Menendez *et al.*, 2000; Okoko *et al.*, 2002).

LBW is also a well-documented risk factor for poor neuro-sensory, cognitive, and behavioural development, as well as for limited school performance and academic achievement (McCormick *et al.*, 1992; Taylor *et al.*, 2000; Teplin *et al.*, 1991). Most of the studies concerned with these factors have been conducted in developed countries, and many have focused on very LBW (usually less than 1,001g). However, the most vulnerable group appears to be those infants born prematurely, who will be two to four times more likely to experience failure in school than infants of normal birth weight and will need specialist support or educational services (Hack *et al.*, 1995).

## 2.6 Malaria and HIV/AIDS

Malaria and HIV/AIDS mutually reinforce each other and contribute synergistically to morbidity, mortality and burden on health systems (World Malaria Report, 2005). This is especially true in southern Africa, where HIV is highly prevalent and malaria is unstable and therefore affects a relatively large proportion of adults, HIV infection has probably contributed to observed increases in malaria cases during the 1990s (Craig *et al.*, 2004; Korenromp *et al.*, 2005). In Central Africa, where large areas of countries have malaria transmission at high intensity, malaria is likely to be an important contributor to morbidity and mortality in HIV/AIDS patients.

In areas of unstable malaria transmission, HIV infection augments the risk of developing severe and fatal malaria (Grimwade *et al.*, 2003; Grimwade *et al.*, 2004). In areas of stable endemicity, HIV infection among adult men and non-pregnant women increases the incidence of clinical malaria and its severity and case fatality (Whitworth and Hewitt 2004). These effects are most pronounced in HIV/AIDS patients with advanced immunosuppression. Pregnant women who have high rates of both HIV and malaria infection are a particularly vulnerable group. Co-infected pregnant women are at very high risk of anaemia and malarial infection of the placenta, which contributes to poor birth outcomes (Ter Kuile *et al.*, 2004).

Conversely, there is some evidence that malaria may exacerbate HIV infection. Acute malaria episodes temporarily increase viral replication and hence HIV viral load, which may accelerate disease progression and contribute to heterosexual HIV transmission (Kublin *et al.*, 2005). In addition, as an important cause of anaemia,

malaria frequently leads to blood transfusions, which is a potential risk factor for HIV infection.

The increased disease burden resulting from co-infection with HIV and malaria highlights the need for better integration of health services for both diseases. HIV-infected adults should be targeted for free or subsidized distribution of ITNs (WHO, 2006). The recurrent non-malarial fevers in HIV/AIDS patients could cause considerable overuse of anti-malarial drugs under the policy of presumptive anti-malarial treatment of all acute fevers (Nwanyanwu *et al.*, 1997). To reduce costs and the risk of drug resistance, capacity for laboratory diagnosis of febrile disease should be increased in countries with high HIV prevalence and high malaria incidence. Prompt and effective combination treatment is particularly important for HIV-infected individuals who might be prone to treatment failure with conventional anti-malarial drugs (Birku *et al.*, 2002; Kanya *et al.*, 2001). By preventing acute increases in viral load, good coverage of anti-malarial treatment could contribute to limiting HIV disease progression and transmission (Kublin *et al.*, 2005).

# CHAPTER THREE

## 3.0 MATERIALS AND METHODS

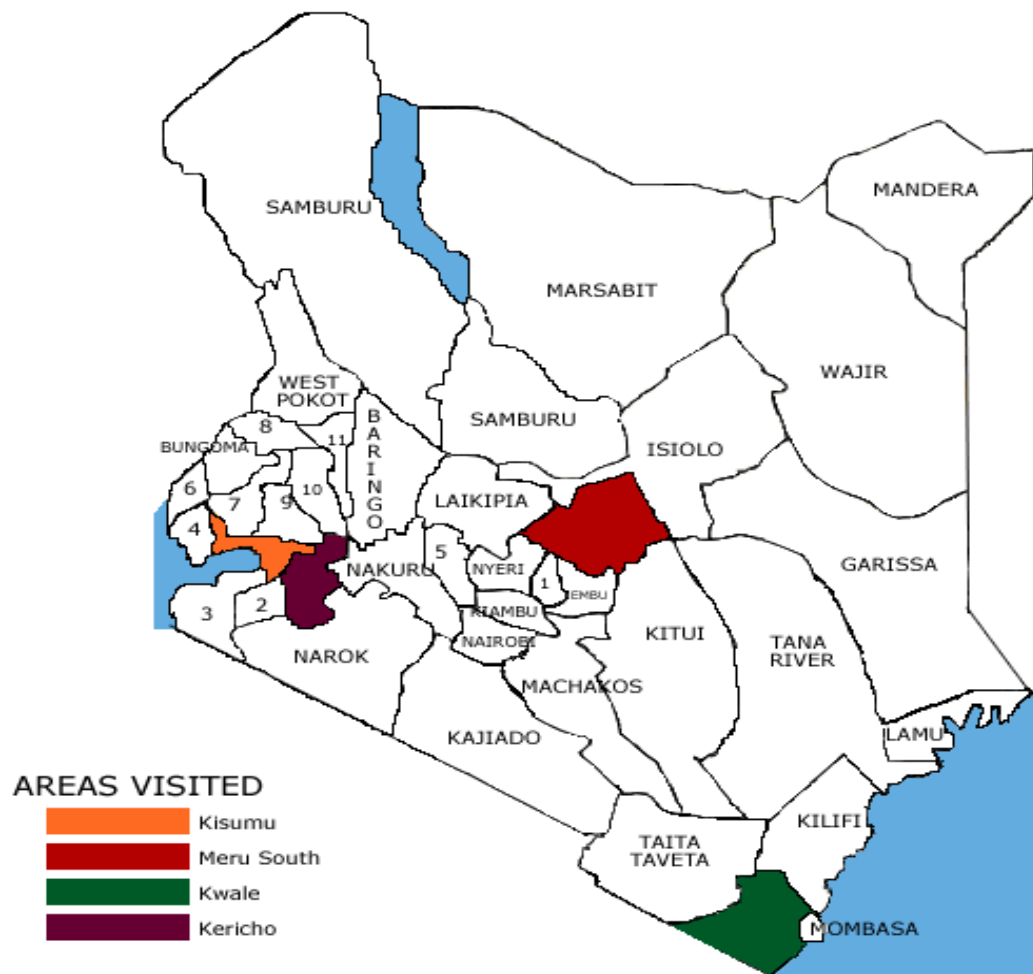


Figure 4 Map of Kenya Showing Study Areas, 2006.

### **3.1 Study Areas**

The study was done in public health facilities in Kisumu, Msambweni, Kericho and Meru South District Hospitals (Fig 4).

#### **Kisumu District**

Kisumu on Longitude 33° 20'E and 35° 20'E and Latitude 0° 20'S and 0° 50'S is one of the districts located in Nyanza Province and covers a total area of 918.5 Km<sup>2</sup> with four administrative divisions, is an area of stable malaria transmission. The divisions are Winam, Maseno Kombewa and Kadibo.

The topography is divided into two zones; Kano Plains and Midland areas. Notable features include scarps, Kano plains and due to the structure on the escarpment, the lowlands are vulnerable to flooding. The district has three major rivers and an 80 Km long shoreline along Lake Victoria with more than 13 beaches.

The mean annual rainfall varies with altitude and proximity to the highlands along Nandi and Tinderet escarpments. The average annual rainfall during the short rains between August-September is 450mm-600mm and in the long rainy season between April and May is 1000mm-1800mm. The mean annual maximum temperature is 25°C to 30°C and minimum temperatures of 9° C to 18° C with a general mean annual temperature of 20 °C to 30 °C.

#### **Kisumu District Hospital**

Kisumu District hospital is situated within the main city centre of Kisumu City, within in Winam division the most densely populated division within the district.

The facility serves as a referral institution for both governmental and private health institutions within and outside the district. The hospital offers an integrated package of essential health care services within its out patient settings and in patient services for various disease conditions. Daily outpatient attendance ranges between 100 and 200 patients. It has eight functional wards with others still under construction to decongest the already existing structures in place. It has a bed capacity of 177 and two baby cots for inpatient services

### **Kericho District**

Kericho, one of the districts located in Rift Valley Province, occupies a total area of 2,110.6 Km<sup>2</sup>. It has seven divisions with Londiani being the largest occupying 532 Km<sup>2</sup> while Chilchila Division occupies 172 Km<sup>2</sup>. The district has an average population density of 238.5 persons per Km<sup>2</sup>.

Kericho is characterised by undulating topography and lies in the Lake Victoria basin. It is well drained with rivers, some which are characterised by rapid falls. It has the highest altitude of 3000m above sea level and lowest of 1800m above sea level. The average annual rainfall is 1800.5 mm, mean annual maximum temperature of 22.3° C and minimum temperature of 10.8° C.

### **Kericho District Hospital**

Kericho district Hospital is situated at the heart of Kericho Town within Kipsigis County Council. The facility serves as a referral institution for both governmental and private health institutions within and outside the district. The hospital provides both inpatient and outpatient services and has a hospital bed capacity of 174.

### **Meru South District**

Meru south is one of the districts located in Eastern Province. To the north it borders Meru Central, Tharaka to the North East, Embu and Mbeere to the south Kirinyaga and Nyeri Districts and to the West is the peak of Mt. Kenya. Total area covered by the district is 1,092.9 Km<sup>2</sup> including 360 Km<sup>2</sup> of Mt. Kenya forest with five administrative divisions namely, Muthambi, Magumoni, Chuka, Mwimbi and Igambang'ombe. The altitude ranges from 400m above sea level to 5200 m at the peak of Mt. Kenya with several ridges and hills. Drainage pattern is characterised by rivers and streams draining into the Indian Ocean through Tana River. The district has a bimodal rainfall pattern with rains falling during months of March to May and October to December with the highest rainfall ranging from 500mm to 2200mm. Average temperatures range from 14°C to 17°C in the highlands to 22°C to 27°C in the lowland areas.

### **Meru South District Hospital**

Meru South District Hospital is situated in Chuka Division, a few kilometres from Chuka Town centre and it serves as a referral hospital for the various health centres, dispensaries, sub district hospitals and other hospitals in the area. It has a total bed capacity of 126 and provides both inpatient and outpatient services.



## **Kwale District**

Kwale, is one of the districts located in South Eastern corner of Kenya in Coast province lying between latitudes 3° 3' and 4° 45' South and Longitudes 38 °31' and 39° 31' East. The district covers 8,260 Km<sup>2</sup> with 62 Km<sup>2</sup> under water, consisting of seven divisions namely Msambweni, Kinango, Matuga, Kubo, Lunga Lunga, Samburu and Kwale and an average population density of 60 persons/ Km<sup>2</sup>.

Kwale has four major topographical features; Coastal plain, Foot Plateau, Coastal Uplands and Nyika Plateau and there are seasonal rivers that form the drainage pattern. In all 92% of the district is characterised as low agricultural potential area.

The climate is Monsoon type i.e. hot dry and cool. There are two rainfall seasons short rains experienced between October and December and long rains between March or April and July precipitation varying in various areas. Average annual temperature is between 24.5°C to 27.5°C.

## **Msambweni District Hospital**

Msambweni District Hospital is situated in Msambweni Division in Kwale District Hospital. It provides both inpatient and out patient services with a bed capacity of 167. It also serves as a research hospital due to various diseases affecting the population in the area.

## **3.2 Study design**

A descriptive retrospective study determining the pregnancy outcomes in women with malaria in Msambweni, Kisumu, Kericho and Meru South District Hospitals from January 2006 to October 2007 was done.

**Case Definition:** A case was defined as a female patient of childbearing age, confirmed or diagnosed to be having malaria infection either clinically or through laboratory tests who sought maternity services in the study hospitals.

### **3.3 Study Instruments**

Data was collected using a structured data abstraction form. The abstraction form was pre-tested at Meru South District Hospital and the necessary adjustments made before embarking on the actual data collection.

### **3.4 Data Collection Methods**

Research authorization was sought and obtained from the Ministry of Science and Technology to permit the carrying out of the study in the hospitals. All maternity files or records from January 2006 to October 2007 were retrieved for review. Records of patients who had been diagnosed with malaria infection while seeking maternity services were separated from the other files and available relevant data entered into the data abstraction forms. All the data abstraction forms were coded and validated daily during data collection.

### **3.5 Research Variables**

Data on the following variables was collected (Appendix 1):

- **Socio-demographic factors:**
  - Age
  - District of residence

- **Medical History:** The variables considered for medical history included history of chronic diseases and other infection like HIV, TB, Anaemia among others
- **Pregnancy factors:**
  - ◆ Parity: number of past deliveries and abortions
  - ◆ Gravidity: total number of pregnancies a subject has had.
  - ◆ Gestation: duration of the pregnancy in weeks
  - ◆ Birth-weight: birth-weights of the newborns. Low birth weight was described as a birth weight of less than 2500g. Above 2500g was termed normal birth weight.
  - ◆ Gestation at birth: duration of the pregnancy at delivery where an abortion or miscarriage was described as delivery of the foetus at less than 28 weeks of gestation, a premature delivery described as delivery of the foetus between a period of 28 weeks and 35 weeks. A term delivery described as delivery of the baby or foetus between a period of 36 weeks and 40 weeks.
  - ◆ Mode of delivery : whether it was a normal delivery i.e. Spontaneous Vertex Delivery or an assisted delivery described as Caesarean Section or Vacuum Extraction

- ◆ Outcome of delivery: status of the foetus at birth. A live birth, a stillbirth described as a birth which the baby is born dead,
- ◆ Inter Uterine Foetal Death described as a case where the foetus dies in the womb during the pregnancy period.
- ◆ Status of the mother: whether the mother was alive or dead after childbirth

- **Clinical variables:**

- ◆ Malaria in pregnancy: whether the patients had been diagnosed with malaria
- ◆ Malaria diagnosis: type of diagnosis of malaria that was done, a clinical diagnosis using signs and symptoms or a laboratory confirmed diagnosis with the use of the various malaria laboratory tests.
- ◆ Maternal anaemia: haemoglobin level of the patient, whether she suffered from anaemia or not. Anaemia described as a blood haemoglobin level of less than 11.0 g/dl
- ◆ Degree of maternal anaemia: Severe anaemia described as a haemoglobin level of less than 7 g/dl, Moderate anaemia described as a haemoglobin of between 7g/dl to 9.9g/dl and mild anaemia as a haemoglobin level of between 10g/dl to 10.9g/dl (WHO,1989)

- ◆ Other diagnosis: any other diagnosis or complications including premature rupture of membrane, ante-partum haemorrhage, maternal distress, foetal distress, obstructed labour, post-partum haemorrhage, retained placenta, pre-eclampsia.

### **3.6 Data Management and Statistical Analysis**

Data from the records were entered into a computer database using Microsoft Excel software and analyzed with Epi Info statistical package. Double entry of data was done to minimize errors. The data was then cleaned and validated before analysis. To ensure confidentiality all personal identifiers were removed. Frequency distributions, univariate and multivariate analysis, measure of central tendency of distribution i.e. mean and measure of variability i.e. range was done and results presented in tables and bar charts. Continuous data were compared by Student T-test. P-value <0.05 was considered significant.

### **3.7 Ethical considerations**

Approval from the University as well as the Ministry of Science and Technology was sought and obtained (Appendix 2). Permission was also sought and obtained from the Medical Officer of Health in the various hospitals. The data accessibility is limited to the chief researcher only, to ensure confidentiality of the participants' information.

## **CHAPTER FOUR**

### **4.0 RESULTS**

The total number of recorded child births during the period of January 2006 and October 2007 in the four hospitals studied was 21,241 (Table 2). Meru south district had the highest number of recorded deliveries (7,771) while Msambweni district had the lowest number of recorded deliveries of 3243. There were 4,818 child births in Kisumu district hospital and 5,409 child births in Kericho district hospital.

#### **4.1 Social demographic and general characteristics of the women**

##### **4.1.1 Mean Age and Range of pregnant women diagnosed to have malaria at the time of delivery at Kisumu, Kericho, Meru South and Msambweni District Hospitals, January 2006 to October 2007.**

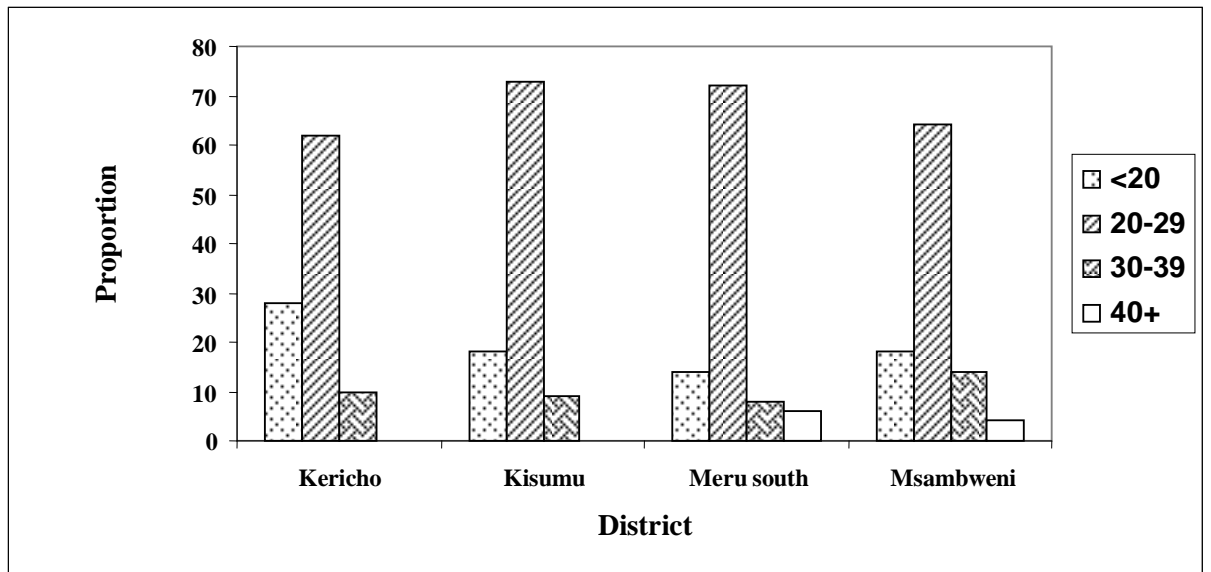
The mean age of women in all the four health facilities was 24 with a range of 14 to 41 years (Table 1). The mean ages were similar in all the health facilities ranging between 23 and 24 years old. Kisumu district had the lowest recorded age of 14 while Meru south district had the highest recorded age of 41 years diagnosed with malaria.

**Table 1 Mean Age and Range Of Participants**

<b>Hospital</b>	<b>Range</b>	<b>Mean</b>
Kisumu	14-39	24
Kericho	16-38	23
Meru south	18-41	24
Msambweni	15-40	23

**4.1.2 Age distribution of pregnant women diagnosed to have malaria at the time of delivery at Kisumu, Kericho, Meru South and Msambweni District hospitals, January 2006 to October 2007.**

In all the health facilities majority of the women delivering diagnosed to have malaria were aged between 20 and 29 years while a small percentage were aged above 40 years (Figure 5). Kericho district had a slightly high population aged below 20 years (28%) while Meru south district had the highest number of those aged 40 years and above (6%).



**Figure 5 : Proportional age distribution per age groups**

#### **4.2 Incidence of malaria among pregnant women at the time of delivery at Kisumu, Kericho, Msambweni and Meru South district hospitals, January 2006 to October 2007.**

The total number of recorded child births conducted during the years 2006 and 2007 in the four hospitals studied was 21,241 (Table 2). Meru South district had the highest number of recorded deliveries (7,771) while Msambweni district had the lowest number of recorded deliveries of 3243. There were 4,818 child births in Kisumu district hospital and 5,409 child births in Kericho district hospital.



**Table 2 Proportion of Women Diagnosed with Malaria**

Hospital	Total number of deliveries	Malaria diagnosis			Incidence of malaria (%)	Odds Ratio	C I*	P-value*
		Clinical (%)	Lab (%)	Total				
Kisumu	4818	45 (50)	45 (50)	90	1.87	3	2.3-4.1	<0.0001
Kericho	5409	17 (44)	22 (56)	39	0.72	0.75	0.5-1.1	0.10
Meru South	7771	21 (58)	15 (42)	36	0.46	0.39	0.3-3.6	<0.0001
Msambweni	3243	15 (54)	13 (46)	28	0.86	0.94	0.6-1.4	0.84
Total	21241	98 (52)	95 (48)	193	0.91			

\* 95% confidence interval

One hundred and ninety three (0.91%) women who gave birth in the four hospitals were diagnosed to have malaria. Forty eight percent (95) of these malaria diagnoses were laboratory confirmed while the rest were based on clinical judgment.

Kisumu District Hospital had the highest proportion of women who delivered at the hospital diagnosed to have malaria (1.87%) which was more than twice the proportion in all the other hospitals (Table 2). Meru south district hospital had the lowest proportion of women with malaria at 0.46%. Malaria diagnosis was positively and significantly associated with diagnosis at Kisumu District Hospital (OR=3, CI=2.3-4.1, P-value <0.0001) and negatively and significantly associated with delivery at Meru South District Hospital (OR=0.39, CI=0.27-0.58, P<0.0001),

when these facilities are compared with the other facilities. Kericho district hospital had the highest proportion of laboratory confirmed malaria diagnosis at 56% (22 cases) while Meru south had the lowest at 42% (15) with 50% (45cases) in Kisumu and 46% (13cases) in Msambweni district hospital.

#### **4.2.1 Number of previous deliveries among pregnant women diagnosed with malaria at Kisumu, Kericho, Meru South and Msambweni District Hospitals, January 2006 to October 2007.**

The number of previous deliveries ranged between zero and ten (Table 3) with most of the women having zero and one to two children in most of the districts.

**Table 3 Distribution of Number Past Deliveries**

<b>District</b>	<b>Frequency of previous deliveries</b>			
	<b>0 (%)</b>	<b>1-2</b>	<b>3 -4</b>	<b>5 and above</b>
Kericho	16 (41)	20 (51)	3 (8)	0 (0)
Kisumu	37 (43)	35 (40)	10 (11)	5 (6)
Meru south	18 (50)	11 (31)	5 (14)	2 (5)
Msambweni	8 (31)	12 (46)	5 (19)	1 (4)

#### 4.2.2 Proportion of pregnant women diagnosed with concurrent malaria and maternal anaemia at the time of delivery at Kisumu, Kericho, Meru South and Msambweni District Hospitals, January 2006 to October 2007.

Kisumu district hospital had the highest proportion of pregnant women who had malaria and anaemia concurrently at 34%. In all the facilities more than one quarter of malaria cases had concurrent anaemia (Fig 6). The likelihood of having anaemia among those who delivered in Kisumu compared to those who delivered in other facilities was not statistically significant (Chi-square=1.18, P-value=0.76). Compared with Kericho and Meru south only the Chi-square = 1.08, P-value=0.58 therefore statistically not significant.

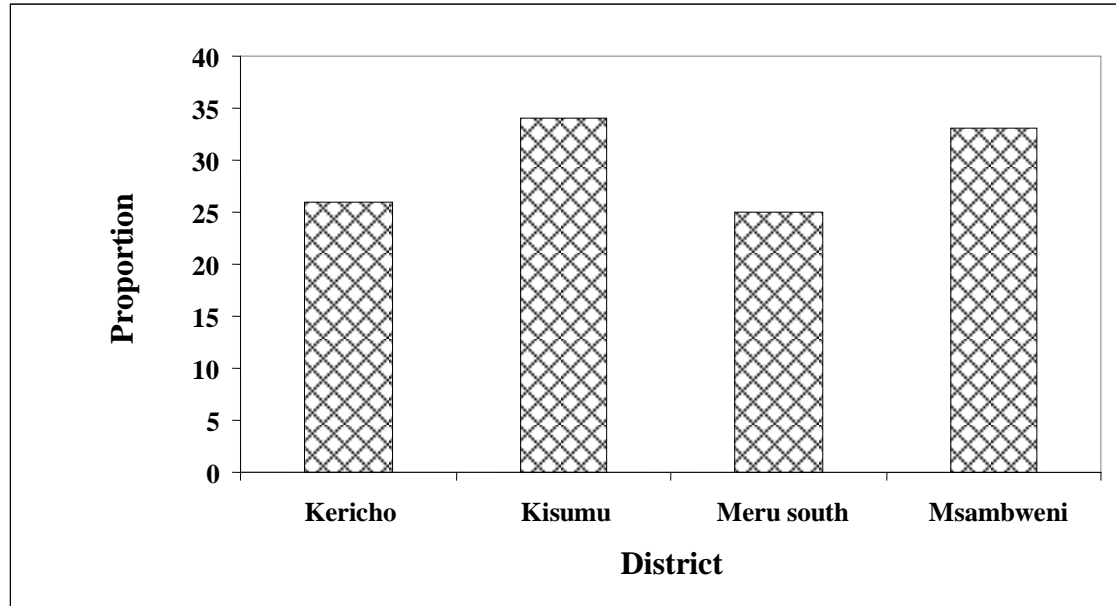


Figure 6 Proportion with concurrent malaria and anaemia

### **4.3 Adverse pregnancy outcomes**

The adverse pregnancy outcomes which were analysed for included: premature delivery, low birth weight, outcome of delivery and maternal anaemia. Stratification was done for all these factors using possible confounding factors which included method of malaria diagnosis (either clinical or laboratory), parity of the woman and number of foetuses. The effect of premature delivery on the outcome of delivery and birth weight was also assessed.

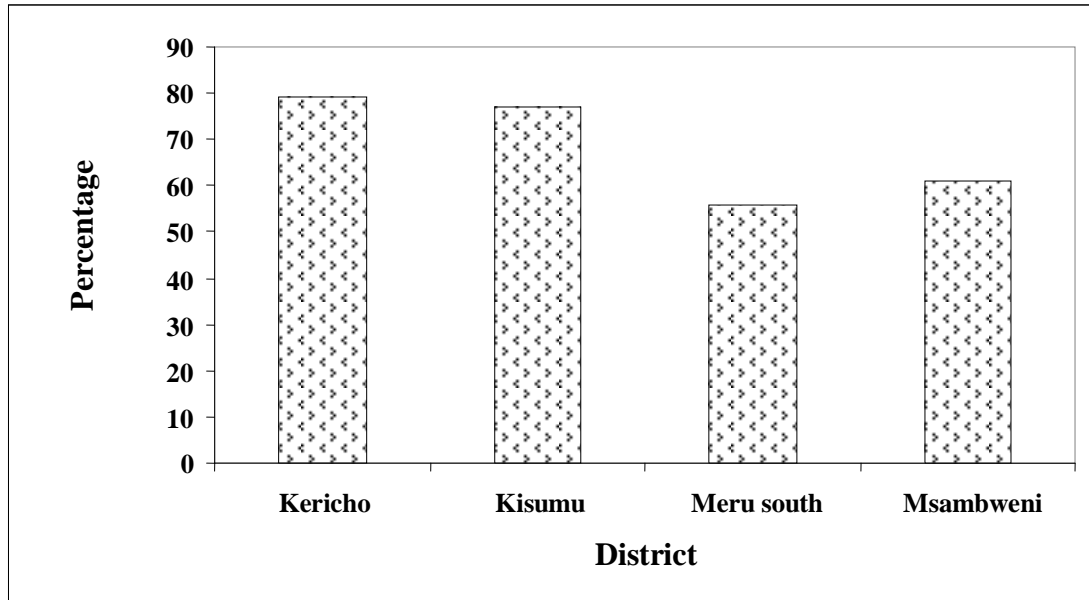
#### **4.3.1 Premature delivery**

**Mean gestation at birth among pregnant women diagnosed with malaria at the time of delivery at Kisumu, Kericho, Meru South and Msambweni District Hospitals, January 2006 to October 2007.**

The mean gestation at birth for pregnant women with malaria in all the districts ranged between 18 and 40 weeks with a mean of 33 weeks (Table 4). Msambweni district had the highest mean gestation at birth (35) while Kisumu and Kericho districts had the lowest (32).

**Table 4 Mean and Range Of Gestation at Delivery**

<b>Hospital</b>	<b>Mean (Weeks)</b>	<b>Range (Weeks)</b>
Kericho	32	26-38
Kisumu	32	18-40
Meru south	34	27-40
Msambweni	35	32-38



**Figure 7 Proportion with Premature Delivery or Miscarriage**

The proportion of participants who had premature delivery or miscarriage was highest in Kericho district hospital at 79% (31). The percentage of participants with premature delivery or miscarriage was 77% (40) in Kisumu, 61% (8) in Msambweni and 56% (20) in Meru South district (Figure 7). The association between prematurity and malaria diagnosis in different areas of malaria transmission was not statistically significant when Kisumu is compared with all the districts (Chi square=6.94, p-value=0.073). However when Kisumu is compared with Meru South and Kericho the association was statistically significant (Chi-square=6.48, p-value=0.039). Miscarriages represented a very small percentage of the deliveries in the facilities ranging between 3 and 12% (many of them may not have been captured since they might not have gone to the maternity wards).

#### 4.3.2 Premature delivery and method of malaria diagnosis among pregnant women diagnosed with malaria at the time of delivery at Kisumu, Kericho, Meru South and Msambweni District Hospitals, January 2006 to October 2007.

The proportion of women with premature delivery or miscarriage was highest among women with laboratory confirmed malaria in all the districts except Kericho district. The proportion of women with premature delivery or miscarriage among laboratory confirmed malaria cases was 89% (24) in Kisumu district, 73% (16) in Kericho, 67% (10) in Meru South and 66% (4) in Msambweni district hospitals (Figure 8). The likelihood of having a premature delivery among those with laboratory confirmed malaria diagnosis at Kisumu is not statistically significant compared to the other facilities.

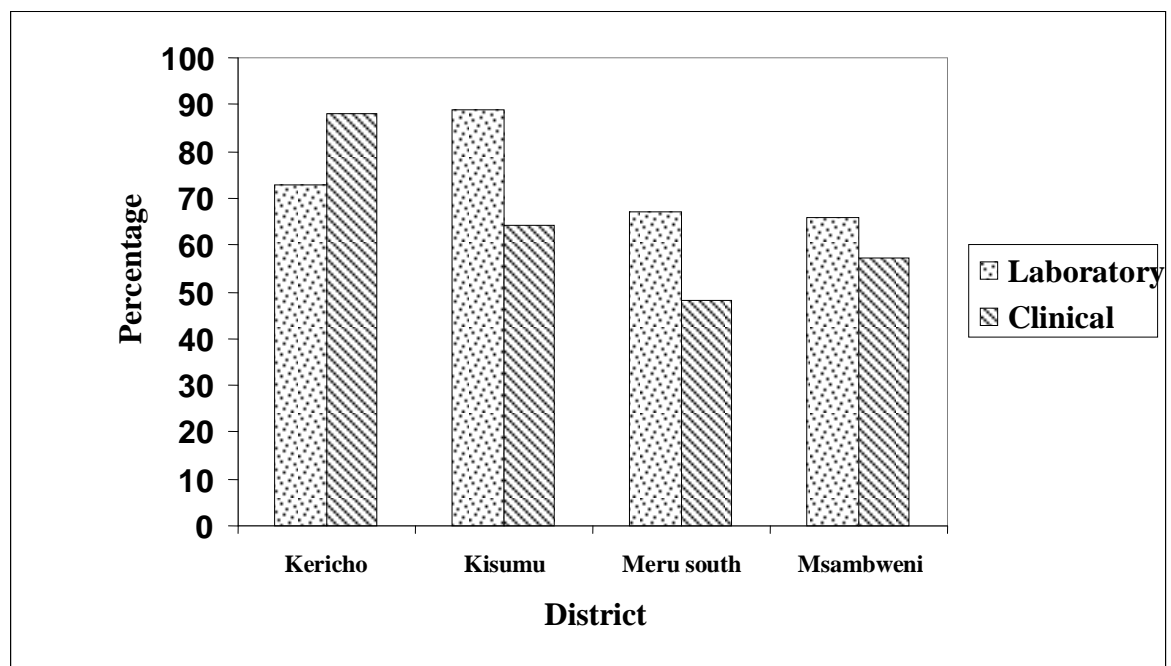


Figure 8 Premature delivery among those with clinical or lab diagnosis

**4.3.3 Maternal anaemia and prematurity among pregnant women diagnosed with malaria at the time of delivery at Kisumu, Kericho, Meru South and Msambweni District Hospitals, January 2006 to October 2007.**

Generally the proportion of women diagnosed to have had malaria who delivered prematurely was higher among women who also had a diagnosis of anaemia except in Msambweni district hospital. In Kericho all the women who had malaria and concurrent anaemia delivered prematurely (Table 5). In Msambweni district the proportion of premature deliveries was higher among those who had concurrent anaemia diagnosis (71%). The likelihood of having premature delivery in women who had malaria and also anaemia was near significant only in Kericho district (Chi-square = 3.38, P-value = 0.06)

**Table 5 Frequency of Premature Deliveries among Pregnant Women with Maternal anaemia**

<b>District</b>	<b>Frequency of Prematurity (%)</b>	<b>OR (C.I)</b>	<b>P-value</b>
Kisumu	14 (87)	3.3 (0.6-17.5)	0.13
Kericho	10 (100)	Undefined*	0.06
Meru south	5 (56)	1.0 (0.2-4.5)	0.6
Msambweni	2 (50)	0.4 (0.03-5.2)	0.46

\*value in one cell = 0

#### 4.3.4 Birth weight among pregnant women diagnosed with malaria at the time of delivery at Kisumu, Kericho, Meru South and Msambweni District Hospitals, January 2006 to October 2007.

The proportion of participants who had recorded low birth weight was highest in Kisumu district hospital at 54% (25). Meru south and Msambweni district hospitals had the lowest proportions of recorded women with low birth weights at 25% (9) for Meru south and 25% (3) for Msambweni. The proportion of low birth weight was 41% (15) in Kericho district hospital (Figure 9). The likelihood of delivering a low birth weight baby in Kisumu as compared to other hospitals was significant (Chi-square = 8.47, p-value = 0.03). When Kisumu is compared with Kericho and Meru South only the Chi-square is =7.19 and the p-value = 0.02

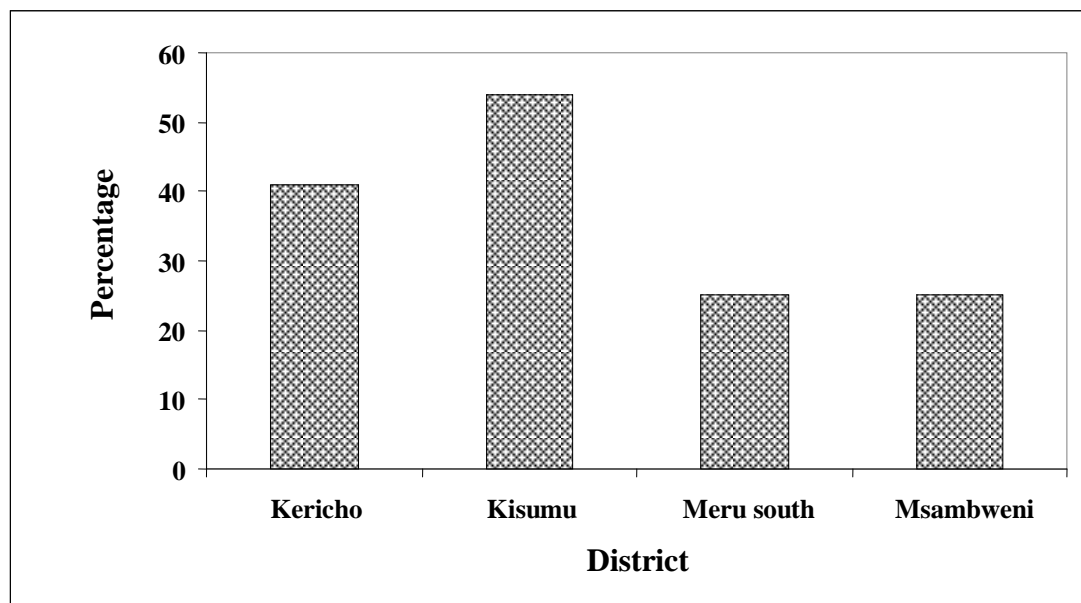


Figure 9 Proportion of Pregnant women with LBW deliveries



#### **4.3.5 Birth Weight and prematurity among pregnant women diagnosed with malaria at the time of delivery at Kisumu, Kericho, Meru South and Msambweni District Hospitals, January 2006 to October 2007.**

The proportion of babies born with standard low birth weight was higher among those who had premature deliveries in all the health facilities (Table 6). The proportion of the low birth weight among those with prematurity was highest in Kisumu district at 65% (22). Kericho district had 51% (15), Meru South 45% (9) and Msambweni 29% (2) low weight among premature deliveries. The likelihood of delivering a low birth weight among women who had malaria and delivered prematurely was significant in Kisumu (OR=5.5, C.I. = 1.2-24.2, p-value = 0.02), Kericho (OR=undefined, p-value=0.009) and Meru South (OR = undefined, P-value = 0.002). Therefore the gestation at delivery and not per-se the malaria diagnosis may influence the birth weight. Therefore malaria may contribute to low birth weight indirectly through pre-mature delivery.

**Table 6 Frequency of LBW among women with Premature Deliveries**

<b>District</b>	<b>Low Birth Weight (%)</b>	<b>OR ( C.I)</b>	<b>p-value</b>
Kericho	15 (51)	Undefined*	0.009
Kisumu	22 (65)	5.5 (1.2-24.2)	0.02
Meru south	9 (45)	Undefined	0.002
Msambweni	2 (29)	1.2 (0.07-19.6)	0.5

\*value in one cell = 0

**4.3.6 Birth weight and maternal anaemia among pregnant women diagnosed with malaria at the time of delivery at Kisumu, Kericho, Meru South and Msambweni District Hospitals, January 2006 to October 2007.**

The proportion of women diagnosed to have malaria who had low birth weight babies was consistently high in women with concurrent maternal anaemia than those who did not have (Table 7). The proportion of women who had Low Birth Weight and had maternal anaemia was highest in Kisumu district (88) and lowest in Meru South district (44%).

**Table 7 Proportion of Pregnant Women with Concurrent Malaria Anaemia and LBW outcome**

District	Frequency of low birth weight	
	Maternal anaemia (%)	No maternal anaemia (%)
	<b>and LBW</b>	
Kericho	7 (79)	8 (29)
Kisumu	14 (88)	11 (37)
Meru south	4 (44)	5 (19)
Msambweni	2 (50)	1 (13)

**4.3.7 Outcome of delivery among pregnant women diagnosed with malaria at the time of delivery at Kisumu, Kericho, Meru South and Msambweni District Hospitals, January 2006 to October 2007.**

Eighty percent of all babies were delivered alive in all the hospitals. Kericho district had the highest proportion of babies delivered alive (87%) while Kisumu district had the highest proportion of babies delivered either as still birth or Intra Uterine Foetal Death (IUFD) (29%) (Table 8). Still birth/IUFD and delivering in Kisumu District Hospital were positively associated though the association was not statistically significant at 95% confidence level.

**Table 8 Outcome of delivery among Pregnant Women with Malaria**

<b>Hospital</b>	<b>Alive (%)</b>	<b>Still birth/IUFD (%)</b>	<b>Odds Ratio</b>	<b>Confidence Interval</b>	<b>P-value*</b>
Kisumu	34 (71)	14 (29)	2.3	0.90-5.9	0.08
Kericho	33 (87)	5 (13)	0.51	0.2-1.6	0.30
Meru south	30 (83)	6 (17)	0.73	0.2-2.2	0.71
Msambweni	10 (84)	2 (16)	0.71	0.1-4.2	0.95

**Table 9 Prematurity and Unfavourable Outcome among pregnant women diagnosed with malaria**

District	Frequency of unfavourable outcome	
	Premature (%)	Term (%)
Kericho	5 (17)	0 (0)
Kisumu	12 (33)	2 (17)
Meru south	6 (30)	0 (0)
Msambweni	1 (14)	1 (25)

The proportion of babies born dead was higher among those premature than those born at term in all the hospitals except Msambweni hospital. The proportion of still births and IUFD among premature deliveries was highest at 33% (12) in Kisumu, and lowest at 14% (1) in Msambweni. The proportion was 30% (6) in Meru South and 17% (5) in Kericho district hospitals (Table 9).

**4.3.8. Mode of delivery among pregnant women diagnosed with malaria at the time of delivery at Kisumu, Kericho, Meru South and Msambweni District Hospitals, January 2006 to October 2007.**

The two methods of delivery in all the four hospitals were spontaneous vertex delivery (SVD) and Caesarean section. Eighty nine percent of the deliveries were by spontaneous vertex delivery in all the facilities.

The proportion of SVDs was 95% (40) in Kisumu, 92% (33) in Kericho, 89% (8) in Msambweni and 78% (28) in Meru South district hospitals (Figure 10). The likelihood of having an SVD in either of the hospitals than others was however not statistically significant.

#### Mode of delivery among the participants

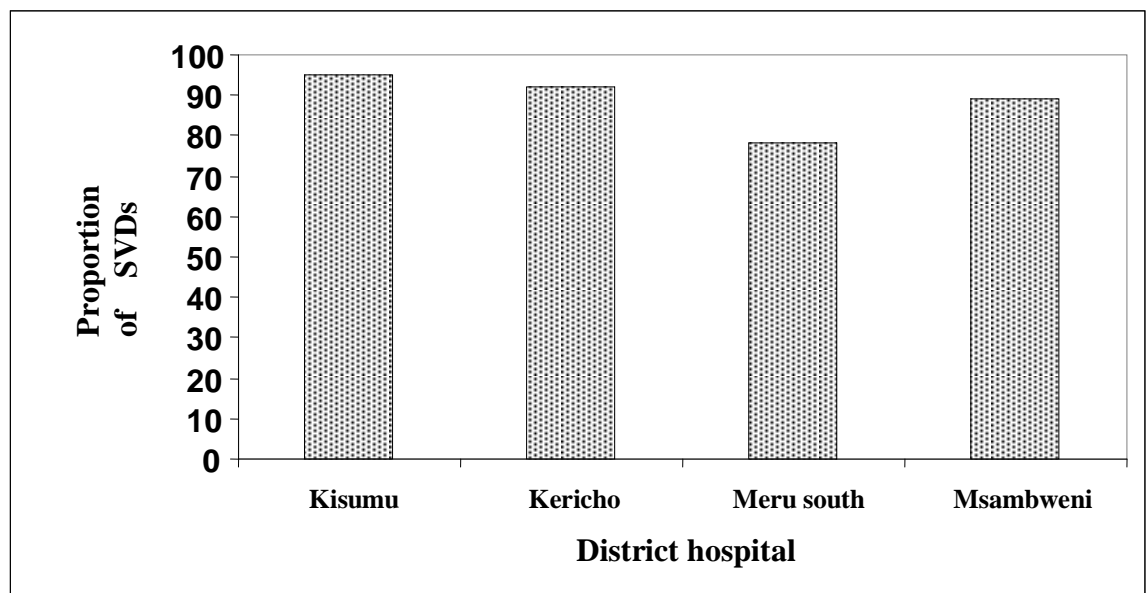


Figure 10 Proportion of Pregnant Women who had SVDs

#### 4.3.9 Other variables

##### 4.3.9.1 Multiple pregnancies

There were only 3 documented cases of twin pregnancy from the four hospitals over the time period. The number of twin pregnancies was two in Kisumu and one in Msambweni district hospitals.

#### **4.3.9.2 Number of foetus and prematurity**

There were only 3 documented twin pregnancies among women diagnosed to have malaria in all the 4 hospitals (2 from Kisumu and 1 from Msambweni). This figure was statistically too small to influence the time of delivery.

#### **4.3.9.3 Complications affecting outcome**

- Chronic illnesses: data on chronic disease especially HIV/AIDS and Tuberculosis was not available
- Pregnancy and labour complication – data on pregnancy related complications including premature rupture of membranes, ante-partum haemorrhage, postpartum haemorrhage, obstructed labour, prolonged labour was not available.

#### **4.3.9.4 Birth weight and number of foetuses**

The numbers were too few to analyse for this variable

## CHAPTER FIVE

### 5.0 DISCUSSION

This study of pregnancy outcomes in women with malaria indicates that adverse pregnancy outcomes are common in women diagnosed with malaria in different areas of malaria transmission. This finding has been demonstrated in other studies undertaken elsewhere especially in most endemic areas of Africa where pregnant women have been found to be the main adult risk group for malaria (WHO, 2000). Kisumu district and Msambweni districts which are areas of malaria endemicity, indicated higher proportion of malaria cases as opposed to Kericho a malaria epidemic prone zone and the least incidence of malaria cases in the malaria low transmission area of Meru South (Table 2).

The mean age of the women seeking maternity services diagnosed with malaria in this study was 24 years of age (Table 1). In all the four district hospitals, the highest proportion of women diagnosed with malaria were between the ages 20 and 29, followed by the age group of less than 20 years of age, 30 to 39 years of age and finally women above the age of 40 years were least diagnosed with malaria (Figure 4). A number of studies conducted in sub-Saharan Africa have reported a significant association between maternal age and malaria infection during pregnancy (Bouyou-Akotet *et al.*, 2003; Rogerson *et al.*, 2000; Steketee *et al.*, 1996; Dicko *et al.*, 2003). In a study conducted in Blantyre, Malawi, after stratifying by gravidity, associations between age and parasite prevalence were stronger than those between gravidity and prevalence after stratifying by age (Rogerson *et al.*, 2000).

Other studies have shown that young women of child-bearing age may be more susceptible than older women to malaria because they are still in the process of acquiring natural immunity to malaria (Dicko *et al.*, 2003; Shi *et al.*, 1995; Oeuvray *et al.*, 2000; Johnson *et al.*, 2004). In Cameroon, age was a major risk factor for placental malaria, with younger first-time mothers more likely to have placental malaria (Tako *et al.*, 2005). Similarly, in Zaire, mothers with malaria parasites in placentas were younger (mean age 24) than mothers with without parasites in placentas (mean age 29) (Anagnos *et al.*, 1986).

The findings of this study are consistent with previous studies since in most of the hospitals, a high proportion of women diagnosed with malaria were carrying their first, second and a lower proportion, third pregnancies. The number of diagnosed malaria cases gradually reduced in women who were in their fourth, fifth and more number of pregnancies (Table 3). Studies carried out in Malawi, Gambia, Kilifi District in Kenya among others indicated that malaria infection rates were most consistently demonstrated to be higher in women in their first and second pregnancies, with lower rates in later pregnancies (McGregor, 1984; Shulman *et al.*, 1996; McGregor *et al.*, 1983). Malaria has been observed to affect primigravidae more than multigravidae in areas of stable transmission (McGregor, 1984).

In the present study, adverse pregnancy outcomes cases including premature delivery, low birth weight, stillbirths, IUFD and maternal anaemia were reported in women diagnosed with malaria in the different malaria transmission areas. The average gestation at delivery for all the women who were diagnosed with malaria was 33 weeks and ranged between 18 to 40 weeks in all the four districts studied



(Table 4). This shows that a high proportion of women who were diagnosed with malaria delivered prematurely with Kisumu and Kericho Districts portraying the lowest mean of gestation at delivery. Premature deliveries were highest in Kericho, followed closely by Kisumu, Msambweni and lastly Meru South District hospital (Figure 6). Pregnant women in malaria-prone areas may experience a variety of consequences from malaria infection including maternal anaemia, high placental parasitaemia, Low Birth Weights from prematurity and intrauterine growth retardation (IUGR), foetal parasite exposure and congenital exposure and infant mortality linked to both preterm LBW and IUGR-LBW (Steketee *et al.*,2001).

Generally, the proportion of women diagnosed to have had malaria who delivered prematurely was higher among women who also had a diagnosis of anaemia excluding Msambweni district hospital. In Kericho all the women who had malaria and concurrent anaemia delivered prematurely. In Msambweni district the proportion of premature deliveries was higher among those who had no concurrent anaemia diagnosis as compared to those who were anaemic (Table 5). Concurrent malaria and anaemia occurred in all the four district hospitals with Kisumu having reported the highest number of cases, followed by Msambweni, Kericho and lastly Meru South District hospital (Figure 6). Anaemia has been shown to be a common consequence of *P.falciparum* infection and infected pregnant women develop clinical anaemia as a result (Steketee *et al.*, 2001). Many other causes of anaemia that occur concurrently in pregnancy have been identified therefore no unique hallmarks of malaria-driven anaemia have been identified making it difficult to evaluate the contribution made to anaemia in pregnancy by malaria (Mattelli *et al.*,

1994). For the foetus, severe maternal anaemia may result in intrauterine growth retardation, still birth, and low birth weight (Hoestermann *et al.*, 1996; MacLeod and Rhode, 1998; Brabin, 1991; Brabin and Piper, 1997).

Cases of low birth weight occurred in all the four district hospitals, the highest number was in Kisumu followed by Kericho and Meru South and Msambweni with the same proportions (Figure 9). Low birth weight was observed in premature deliveries in all the hospitals (Table 6). The proportion of women diagnosed to have malaria who had low birth weight babies was consistently high in women with concurrent maternal anaemia than those who did not have concurrent malaria and anaemia. The proportion of women who had low birth weight and had maternal anaemia was highest in Kisumu district, followed by Kericho, Msambweni and lowest in Meru south district hospital (Table7). Several studies have shown that malaria is the most important cause of Low Birth Weight in stable malaria endemic areas especially among primigravidae (Mc Gregor 1984; Brabin and Piper, 1997). Studies have shown malaria to be a major cause of anaemia in children and pregnant women resulting in low birth weight, premature birth and infant mortality (World Malaria Report, WHO, 2005).

Eighty percent of all babies were delivered alive in all the hospitals. Kericho district had the highest proportion of babies delivered alive while Kisumu district had the highest proportion of babies delivered either as still birth or IUFD among premature deliveries, followed by Meru South, Kericho District Hospital and lowest in Msambweni (Table 8). The proportion of stillbirths and IUFD was higher among babies born premature than those born at term in all the hospitals except

Msambweni hospital (Table 9). Studies have shown malaria in pregnant women to be a major cause of premature birth and infant or neonatal deaths and stillbirths (World Malaria Report, WHO, 2005). Malaria associated maternal anaemia may result in intrauterine growth retardation, still birth, and low birth weight (Hoestermann *et al.*, 1996; MacLeod and Rhode, 1998; Brabin, 1991; Brabin and Piper, 1997).

There were two different methods of diagnosis of malaria that were used by the clinicians, clinical diagnosis using signs and symptoms and laboratory confirmed tests. The highest proportion of women who had premature deliveries were diagnosed of malaria through laboratory confirmed tests, highest proportion portrayed in Kisumu followed by Kericho, Meru South and Msambweni District Hospital though in Kericho the proportion was higher in clinically diagnosed patients as compared to laboratory confirmed diagnosis (Figure 7). However WHO recommends that a clinical diagnosis be made followed by laboratory confirmation test.

Kisumu district hospital had the highest proportion of normal deliveries (SVD), followed by Kericho, Msambweni and Meru South District hospitals. All the four district hospitals in totality had eighty nine percent of the deliveries being normal deliveries, and the rest assisted ones (Caesarean Section) (Figure 10).

## **5.1 Limitations of the Study**

### **Unavailability of data**

The records or maternity files were poorly filled. Data on various variables were inconsistently filled in the records with very vital data missing for example some files had no data on Hb levels or birth weights. Socio-demographic characteristics or patient's history data were unavailable in most of the maternity files. Data on medical history of the patient were unavailable in most files. This could have been due to false responses from the patient or they didn't know if they suffered from any ailment or disease. Lack of antenatal profile tests in the records made it impossible to also find cases of chronic diseases. Secondly, files were missing in the records department and there was no way of tracing them, therefore hindering accessibility to the important information that this study required. Finally, in certain cases of referrals, Babies born before Arrival (BBA) and pregnant women who arrived at the second stage of labour, no information at all on the patient and the baby was made available in the files.

### **Use of Hospital records**

Hospital record based studies have many limitations including not being representative of the disease pattern at the community level due to varying health seeking behaviour by pregnant women of Facility Based Antenatal Care.

The available data was therefore collected, analysed and reported.

## **CHAPTER SIX**

### **6.0 CONCLUSION AND RECOMMENDATIONS**

#### **6.1 Conclusion**

The findings of this study suggest that pregnant women diagnosed with malaria are likely to experience adverse pregnancy outcomes including premature deliveries, Low Birth Weight, maternal anaemia, stillbirths and Intrauterine Foetal Death. The women who live in areas of stable and unstable and low malaria transmission are likely to suffer from malaria or rather at risk of malaria infection. The findings demonstrated that the age group between 14 and 29 are likely to be at risk of malaria this being the age group with the highest number of malaria diagnosed cases compared to the age group 30-42 years of age.

Women with malaria are likely to develop maternal anaemia and therefore likely to deliver prematurely, babies with Low Birth Weights. Also, the same women could experience miscarriages or abortions, stillbirths and Intra Uterine Foetal Death.

Laboratory diagnosed malaria could be the better way of malaria diagnosis as compared to clinical diagnosis though WHO recommends clinical diagnosis confirmed by a laboratory test thereafter.

## 6.2 Recommendations

The following recommendations were made from the present study.

- Identification of a reasonably effective chemo-prophylactic regimen through research for treatment of malaria cases, reduction of incidences and eventual eradication of the disease
- Ensuring that high-risk pregnant women have access to the drug for the prevention of malaria. Access is limited by many factors including low providers' awareness of the regimen, poor health-seeking behaviour of pregnant women who tend not to receive antenatal care and poor availability of drugs.
- There is a need to build the capacity of health providers on IPT since a large number of health professionals in the country may not be familiar with IPT, disseminate related information to providers and the general public, and to integrate the method into clinical practices at all levels of the health care system.
- More specifically, women need to be made aware of the IPT method, and they need to be encouraged to seek facility-based methods of antenatal care rather than home-based care to increase their chances of receiving IPT in pregnancy
- Exploration of future use of IPT by low cadre health workers such as community health extension workers and traditional birth attendants. IPT can also be included as a major component of home-based antenatal care offered by midwives to women who would not attend facility-based antenatal care.

- Determination of the effectiveness of IPT method in various clinical settings, as well as research to determine how best to integrate the method into existing levels of the health care delivery system.
- Active promotion of ways of prevention of malaria through various interventions like IPT and ITN recommended by WHO and Roll Back MALARIA and DOMC, Kenya.
- Upgrading of HMIS at all levels of healthcare system through computerization and ensuring efficient training of the hospital staff in order to ensure provision of accurate quantitative and qualitative data which is essential for identifying major health problems that can be used to evaluate health policies for planning health programmes and the efficient management of health services. Also an upgraded HMIS opens up a continuous dialogue between those who collect and the users of information with the aim of improving health services, disseminates timely information to users including those who work in research and health administration and finally create and maintain a health information database at the district.

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# APPENDICES

## Appendix 1: Data Abstraction Form

### Pregnancy outcomes in women with malaria in areas with different levels of malaria transmission in Kenya

#### Data Abstraction Form

##### Identifiers

1. Identity number \_\_\_\_\_ Year \_\_\_\_\_ Date \_\_\_\_\_  
\_\_\_\_\_
2. District \_\_\_\_\_
3. Hospital \_\_\_\_\_

##### Sociodemographic

Age \_\_\_\_\_

Marital status: Married [ ] Single [ ]

Level of education: None [ ] Primary [ ] Secondary [ ] Tertiary [ ]

##### Illness

Malaria diagnosis: Clinical [ ] Laboratory [ ]

Maternal Anaemia Yes [ ] No [ ]

Degree of Maternal Aneamia: Mild [ ] Moderate [ ] Severe [ ]

##### Pregnancy related

Parity \_\_\_\_\_ gravidity \_\_\_\_\_ Gestation \_\_\_\_\_

Gestation at birth: Term [ ] Preterm [ ] Miscarriage [ ]

Outcome of delivery: Live birth [ ] Still birth [ ] IUFD [ ]

Number of babies: One [ ] Two [ ] Three [ ]

Birth weight \_\_\_\_\_ Normal [ ] LBW [ ]

Status of mother: Alive [ ] Dead [ ]

Other complications \_\_\_\_\_

Mode of delivery: Caesarian section [ ] SVD [ ] Vacuum extraction [ ]

Other illnesses \_\_\_\_\_

## **Appendix 2: Research Authorization Letter**



REPUBLIC OF KENYA

## MINISTRY OF SCIENCE & TECHNOLOGY

Telegrams: "SCIENCE TEC", Nairobi  
Telephone: 02-318581  
E-Mail: [ps@scienceandtechnology.go.ke](mailto:ps@scienceandtechnology.go.ke)

JOGOO HOUSE "B"  
HARAMBEE AVENUE,  
P.O. Box 9583-00200  
NAIROBI

When Replying please quote  
Ref. NO. MoST/13/001/37C 707/2

30<sup>th</sup> October, 2007

Jacqueline J. Dache  
Jomo Kenyatta University  
P.O. BOX 62000  
**NAIROBI**

Dear Madam

### RE: RESEARCH AUTHORIZATION

Following your application for authority to conduct research on "*Pregnancy outcomes in women with malaria associated anaemia in areas with different levels of malaria transmission in Kenya*".

This is to inform you that you have been authorized to research in Kwale Kisumu, Embu and Kericho District hospitals for a period ending 28<sup>th</sup> February, 2008.

You are advised to report the District Commissioner and the Medical Officers of Health of the districts you will visit before embarking on your research project.

On completion, you are expected to submit two copies of your research report to this office.

Yours faithfully,

  
M. O. ONDIEKI  
**FOR: PERMANENT SECRETARY**

CC: The District Commissioner  
Kwale District  
Kisumu District  
Kericho District

The Medical Officers of Health  
Kwale District Hospital  
Kisumu District Hospital  
Kericho District Hospital  
Embu District Hospital