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MALARIA IN PREGNANCY

IMPACT OF SOCIOECONOMIC INDICATORS

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ATTESTATION

I do hereby attest that I am the sole author of this project/thesis and that its contents are only the result of the readings and research I have done

ETHELBERT ONYEKA UKAEGBU (UNISE10421)

DEDICATION

This work is dedicated to the Almighty God for His Grace, Inspiration, Provision and Guidance in making this Dissertation a huge success in record time

To My Lovely wife and the mother of my children for Her Spiritual, Physical, Moral and Emotional support all through this PhD program

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ABSTRACT

Pregnancy-associated malaria has negative consequences for both mother and baby. Globally, about 125 million pregnancies occurred in endemic areas of malaria transmission in 2007, resulting in average of 83 million live births. Pregnant women in malaria-endemic areas are faced with up to 50 percent higher risk of infection during pregnancy compared with non-gravid women. In areas exposed to high and stable *plasmodium falciparum* transmission, maternal malaria infection is usually asymptomatic but is associated with maternal anaemia. In low transmission or epidemic areas it very often triggers clinical symptoms and severe disease condition. Prevalence of malaria in pregnancy is much higher in girls and women aged 15–19 years and decreases with each subsequent pregnancy. The overall prevalence rate of gestational malaria in this study at Government Regional Hospital, Makeni is 20.4%. Most (77.7%) of the positive cases are from women in their first ANC visit and adolescents are majorly in this category. 136 (44.4%) of the positive cases are adolescents who are also having their first ANC visit. Teenage pregnancy often risks girls health and impediments to their, social, economic and political progress and empowerment of adolescent and young girls in Sierra Leone. All teenage pregnancies irrespective of the outcome have adverse consequences for the adolescents, their parents and the community.

Studies on the impact of socioeconomic factors on gestational malaria have provided mixed results. A cross sectional and systematic review was conducted to evaluate available evidence on the impact of socioeconomic indicators on malaria in pregnancy. The study demonstrated that pregnancy associated malaria are impacted by socioeconomic indicators. The observed association between socioeconomic indicators and *Plasmodium* infection could be due to the effect of socioeconomic status(SES) factors on access and behaviors towards malaria diagnosis, treatment, and prevention measures in Sub-Saharan Africa (SSA). The study also showed that lack of education was a significant predictor of gestational malaria. Education also enhances knowledge, skills, and ability of the individual to access information that promotes health. A summary estimate deduced from the five studies showed that a single US dollar decrease in the monthly income of individuals is associated with a 2% increase in the odds of malaria infection. Higher income also provides better schooling, housing, and nutrition that could enhance malaria prevention. The household wealth index has a directly associated with the capacity of the

pregnant woman to buy and consume nutritious food while occupation determines the disposable income available for the pregnant woman to prevent malaria or to engage in formal health-seeking behavior if malaria occurs.

A summary analysis of 30 studies, which treated wealth index as a categorical variable, showed a 20% reduction in the odds of Plasmodium infection with a single unit increase in socio-economic group or wealth index category of individuals. It is established that peripheral parasitemia may remain below the level of microscopic detection while malaria parasites are harbored by the placenta. Submicroscopic infections during pregnancy were associated with lower mean hemoglobin irrespective of gravidity, and with increased risk of anaemia and also significantly increased risks of Low birth weight (LBW) in prim gravidae.

About 66.7% (1001) of the women attending ANC were using Sulfadoxine-pyrimethamine (SP) while (64.4%) use the Insecticide treated nets which shows that use among pregnant women remains well below the international target for 2010 of 80% coverage. Overall, prevalence of malaria parasitaemia decreased progressively during the antenatal visits, irrespectively of gravidity status, maternal age, marital status or clinic of attendance. Another explanation may be that some of the infections detected in the first weeks of pregnancy were subpatent malaria infections (ie, below the level of detection of microscopy and RDT) present before conception. Because the level of microscopic infections was higher during pregnancy than before pregnancy, it is assumed that some of these pre-pregnancy infections were subpatent and that they eventually became microscopic because of changes in the physiology and immunity of the women during early pregnancy. Malaria prevalence at first antenatal visit can be reduced with interventions that reach all women of childbearing age, such as universal bed net distribution. The challenge of tackling this public health menace however, remains how to access women in the first trimester of pregnancy. Therefore, pre-conceptional strategies against malaria in pregnancy may be of clear interest. A vaccine against VAR2CSA-parasites (Variant Surface antigen 2 CSA) which could elicit protective immunity prior to pregnancy to best protect women during early pregnancy may be proposed as a complementary strategy to those already recommended during pregnancy. Such a vaccine is currently under evaluation (Tuikue & Deloron, 2015).

A Cross-sectional data analysis 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. LBW manifests an intra-uterine growth retardation (IUGR) and preterm delivery,

which are compelling indicators of infant morbidity. A previous analysis showed that a baby is twice as likely to be born with a LBW if the mother has an infected placenta at delivery. Malaria is believed to reduce birth weight through a combination of systemic and local effects. First, malaria may affect birth weight through malaria-induced anemia. Second, malaria may also reduce birth weight through placental infection. These adverse birth outcomes have been extensively associated with *P*. *falciparum* infection during pregnancy. By and large the reduction of newborns birth weight is multifactorial, and it can be related to socioeconomic, nutritional, environmental, and clinic factors during pregnancy in Sub-Saharan Africa.

The social cognitive theory (SCT) used in this dissertation study makes it possible for the readers to understand the essence of using a theoretical model to study and understand health behaviors at personal, behavioral and environmental levels. The SCT model describes the relationships between individuals, their behaviors and the environment and how these interact to define human behaviors. The consideration of these tripartite factors during the design of malaria intervention programs elaborates an all-inclusive package that will deliver the goals and objectives of such interventions. It is pertinent that malaria interventions planners should target low-SES pregnant women to reduce inequalities in the women's health care seeking behavior when there is malaria infection. Furthermore, these low-SES women can be reached through health education sessions during focused Antenatal clinic visits about maternal health and malaria in pregnancy. I also recommend the complimentary use of RDT and microscopy for ANC screening. This is because of submicroscopic cases of malaria infection. Besides the immediate health concerns of pregnancy-associated malaria there are broader public health concerns that need to be considered. Pregnant women are also significant reservoir of gametocytes, suggesting that they may constitute a major source of malaria transmission to the community at large. Beyond the social and public health problem it poses, malaria is also an economic problem. The Ministry of Health should undertake rigorous awareness campaigns to educate mothers on the importance of regular ANC visits and IPT use targeting especially those with lower incomes or less education. However, since the control of malaria in many countries has historically been achieved without such malaria-specific interventions, socioeconomic development could potentially provide an effective and sustainable means of control in malaria-endemic countries especially in Sub-Saharan Africa.

CHAPTER ONE: INTRODUCTION

Malaria scourge remains a major Public Health problem globally, resulting in about half a million deaths annually. Approximately half of the global population live in areas that are at risk of malaria transmission across 91 countries and territories (CDC, 2019). An estimated 228 million cases of malaria occurred globally in 2018, and 405,000 people died, mostly children in Sub Saharan Africa (CDC, 2019). The number of partners and resources in malaria control efforts has tremendously increased within the past decade. The scale-up of malaria interventions has saved millions of lives worldwide and has reduced malaria mortality by 25% from 2010 to 2016, resulting in hopes and plans for elimination and ultimately eradication of malaria (CDC, 2019).

Malaria has a serious impact on the populace resulting in decreased national productivity and loss of man hours. Malaria is a febrile disease and acute infection caused by the protozoa of the genus Plasmodium. Four species commonly known to infect human are Plasmodium malariae, Plasmodium falciparum, Plasmodium vivax and Plasmodium ovale. There is a fifth plasmodium which is an avian specie that infects human, known as Plasmodium knowlesi. Most malaria morbidity and mortality are caused by P.falciparum infection. The malaria parasites are normally transmitted to persons by a bite of female anopheles mosquito when having a blood meal with the introduction of sporozoites. The sporozoites migrate to the hepatocytes of the liver forming merozoites which are released into blood circulation where they infect the erythrocytes (red blood cells). During the asexual reproduction in the blood, the merozoites that infect the red blood cells develop into trophozoites which undergo division to form schizonts. The schizonts finally ruptures the red blood cells and release merozoites, which infect other red cells to repeat the cycle. A subset of the trophozoites exit the asexual cycle and develop into gametocytes. The male gametocytes are called microgametocytes while macrogametocytes are the female gametocytes. This asexual stage leading to the eventual rupture of the red blood cells are responsible for the clinical manifestation of malaria (CDC, 2016). The disease starts with flu-like symptoms that include headache, fever, chills, muscular aches, vomiting, diarrhea, weakness and sweats (Bartoloni and Zammarchi, 2012). In fatal cases, when death occurs, it is mainly

associated with celebral malaria leading to brain damage or damage to vital organs (Bartoloni and Zammarchi, 2012).

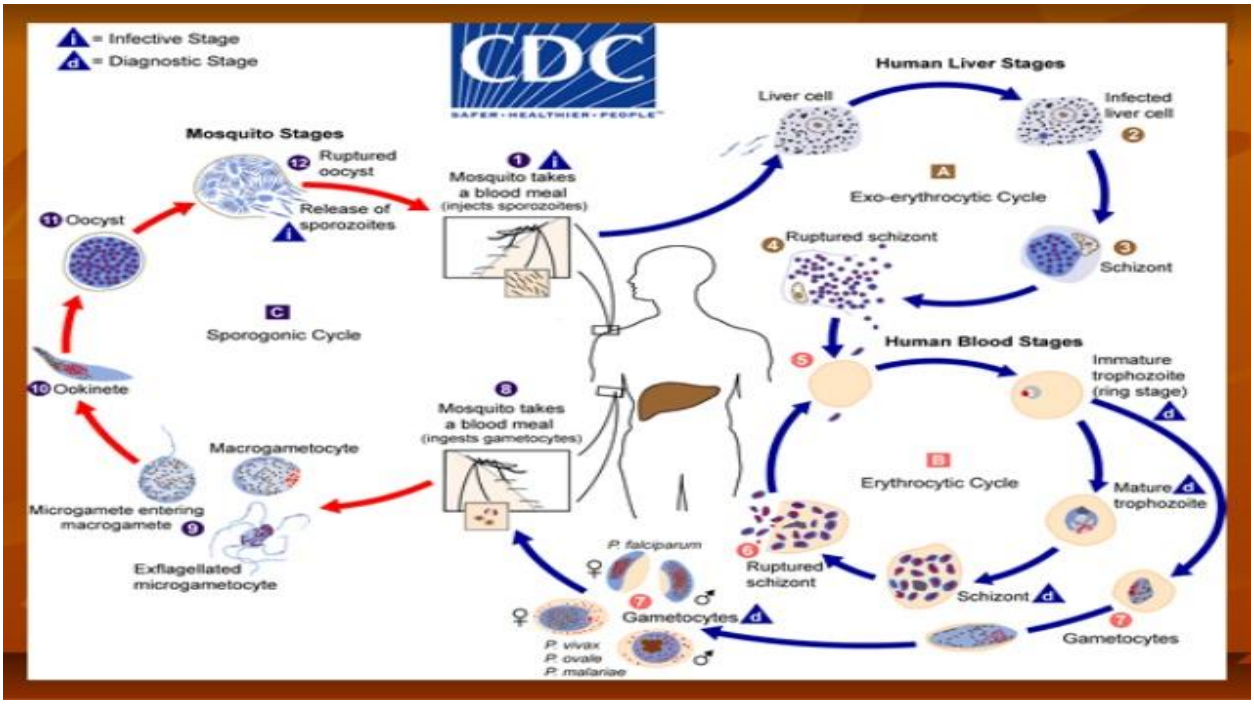

Figure 1: Life Cycle of Malaria Parasite

Malaria occur majorly in poor tropical areas of the world. In many of these affected countries, it is the leading cause of death and illness. The most vulnerable groups in areas with high transmission are the young children who are yet to develop appropriate immunity and pregnant women, whose immunity has decreased as a result of pregnancy (CDC, 2019).

The relationship between malaria disease and poverty is described as a vicious cycle. The debate whether malaria infection is a consequence of or cause for low household socioeconomic status (SES) has been on for years (de Castro and Fisher, 2012). The microeconomic relationship between malaria burden and composite wealth indices is mixed and contradictory (Worrall et al, 2005). Comparatively, individuals in the poorest households had a higher burden of malaria prevalence than those from less-poor households (Vincent et al, 2018).

Pregnant women (primigravidae) are known to be susceptible to malaria and also have higher prevalence and densities of malaria parasitaemia than non-pregnant women from the same population, in malaria transmission areas. The level of risks varies with the age of pregnant

women, reflecting cumulative exposure to malaria over a lifetime, and with parity, as a result of pregnancy-specific immunity acquired after exposure to malaria in previous pregnancies. Maternal malaria immune status determines the consequences of malaria infection during pregnancy. However, infections are associated with fetal growth retardation and maternal anaemia and can also result in pregnancy loss or preterm delivery, acute illness and maternal mortality (Anna et al, 2015).

1.1BACKGROUND

The upsurge in the burden, pathogenesis and clinical sequel of malaria in pregnancy has combinatorial adverse impact on both mother and foetus that further worsened the situation of diagnosis, treatment and prevention. Pregnancy-associated malaria is a main cause of maternal morbidity globally resulting in poor birth outcomes. Pregnant women are more susceptible to malaria infections than their non-gravid peers in malaria endemic areas. Pregnant women are 3 times more likely to suffer severe malaria than their non-pregnant counterparts and have a mortality rate from severe malaria that approaches 50%. Furthermore, malaria parasites sequester and replicate in the placenta. Malaria associated maternal illness and low birth weight is mostly associated with Plasmodium falciparum infection and predominantly occurs in Africa (WHO, 2017). Approximately, 125 million pregnant women globally are exposed to the risks of malaria in pregnancy (MiP) annually, resulting in 200,000 deaths (Mohammed Solail et al, 2015).

According to World Health Organisation (WHO), Sierra Leone is among the seven countries in Sub Saharan Africa where more than a quarter of the population is infected with at any given time. The malaria parasite increases the risk of complication and death during pregnancy and child delivery. It causes approximately four in ten hospital consultations country-wide and contributes to nearly 20% of mortality in children. This negatively affects the nation's productivity as it prevents people from going to work and also children from going to school (UNICEF, 2018).

In Sierra Leone, malaria affect pregnant women disproportionately, with infection posing great risk to the mother and foetus. Malaria infection is endemic in Sierra Leone and pregnant women are liable to increased anaemia, high risk of severe anaemia, low birth weight, foetal loss and

increased infant mortality. The incidence of Plasmodium falciparum infection is more than 85%. In spite of the fact that Sierra Leone has launched many initiatives, namely, Insecticides treated nets and the Intermittent Preventive Treatment of malaria in pregnancy with IPTp-SP (as recommended by WHO), the level of utilization of this cost-effective initiatives is still low. The President Malaria Initiative (PMI) in 2015 launched a six year strategic plan, with an ambitious goal for malaria prevention and control in the member countries. Sierra Leone was eventually selected two years later in 2017, as the PMI focus country in the 2017 fiscal year (FY).

In other to achieve the universal coverage target for IPTp as enshrined in the PMI plan, it becomes necessary to continuously assess the level of its utilization and other covariates, which should be used to guide policy making on the prevention and control of pregnancy-associated malaria.The symptoms and complications of pregnancy-associated malaria vary according to malaria transmission intensity in the given geographical area and the person's level of acquired immunity. In high-transmission places where there is enhanced level of acquired immunity, P,falciparum infection in pregnancy is usually asymptomatic. At this stage, the parasites may be present in the placenta and contribute to maternal anaemia despite the absence of established peripheral malaria parasitaemia (WHO, 2017).

In low-transmission areas where women of reproductive age have limited exposure and hence low acquired immunity to malaria, MiP is associated with an increased risk of severe malaria, anaemia, and possibly spontaneous abortion, stillbirth, low birth weight and prematurity. In such situations, all pregnant women, regardless of the number of times they have been pregnant, are highly prone to malaria infection.

1.2 PROBLEM STATEMENT

Pregnant women whose immune system has been decreased as a result of pregnancy are likely to develop severe malaria than non-gravid women infected at the same area. Malaria leads to the death of about 10,000 pregnant women and 200,000 infants annually (Hartman and Fischer, 2010). Malaria in pregnancy can lead to miscarriages, low birth weight, premature delivery, congenital infection and/or perinatal death (CDC, 2019). Heterogeneous results have been reported in existing literatures by diverse researchers regarding the effect of house structure,

education level, occupation, income, and wealth on malaria. The impact of socioeconomic indicators is critical in the control of MiP and requires further studies. Thus knowing the socioeconomic risk factors of malaria in adults would be relevant in designing strategies for the control of the disease in this population.

Pregnancy-associated malaria is prevalent majorly at the time of first antenatal visit. Consequently, this early malaria infection in pregnancy has been associated with negative health outcome of maternal and foetal wellbeing such as maternal anaemia, low birth weight and intrauterine growth restrictions. During pregnancy, malaria parasitaemia is often asymptomatic, therefore treating only symptomatic women will eventually fail to address majority of infected cases, since asymptomatic infections can have serious health consequences. Moreso, even if all pregnant women are to be screened for malaria, parasitaemia will be mostly undetected because parasites are sequestered in the placenta. As a result of this, given the significant adverse effect of malaria in pregnancy, and the challenge associated with diagnosis as a result of placental malaria, most control efforts are channeled towards preventing malaria and presumptive treatment. There remain substantial gaps in the coverage of core malaria control tools. In 2015, an estimated 43% of the population in Sub-Saharan Africa was not protected by Insecticides treated nets or indoor spraying with insecticides which is the primary method of malaria vector control (WHO, 2015). Despite the fact that Sierra Leone has launched several malaria control initiatives, such as insecticides treated nets and the intermittent preventive treatment of pregnancy associated malaria with IPTp-SP, the level of this cost-effective utilization is still low. Therefore, in order to achieve the universal coverage target for IPTp as stated in the PMI plan, it is necessary to continuously assess the level of utilization of IPTp-SP and its covariates, which should be appropriately used in guiding policy making on the prevention and control of malaria in pregnancy.

1.3 RESEARCH OBJECTIVES

GENERAL OBJECTIVE

To assess the correlation between malaria in pregnancy and socio-economic indicators.

SPECIFIC OBJECTIVES

1) To assess the level of utilization of malaria preventive measures among pregnant women attending ANC at Government Regional Hospital Makeni, Sierra Leone
2) To examine the relationship between family income of pregnant women and risk of malaria infection
3) To determine the association between education of pregnant women and level of compliance to malaria control measures
4) To examine any relationship between employment of pregnant women and incidence of malaria in pregnancy
5) To establish any significant difference between prevalence at first antenatal visit and subsequent visits.
6) To evaluate the association between gestational malaria and reduction of newborn birth weight

1.4 RESEARCH QUESTIONS AND HYPOTHESIS

This study examined the correlation between malaria in pregnancy and socio-economic indicators

Research Question 1: Is there increase in the level of utilization of malaria preventive measures among pregnant women attending ANC at Government Regional Hospital Makeni, Sierra Leone

H_0: There is no increase in the level of utilization of malaria preventive measures among pregnant women attending ANC at Government Regional Hospital Makeni, Sierra Leone.

H_a : There is increase in the level of utilization of malaria preventive measures among pregnant women attending ANC at Government Regional Hospital Makeni, Sierra Leone

Research Question 2: Is there any association between income of pregnant women and incidence of malaria in pregnancy?

H_0 : There is no association between income of pregnant women and incidence of malaria in pregnancy

H_a : There is an association between income of pregnant women and incidence of malaria in pregnancy

Research Question 3: Is there any association between education of pregnant women and utilization of malaria control initiatives

H_0 : There is no association between education of pregnant women and utilization of malaria control initiatives

H_a : There is association between education of pregnant women and utilization of malaria control initiatives

Research Question 4: Is there any relationship between employment of pregnant women and incidence of malaria in pregnancy

H_0 : There is no relationship between employment of pregnant women and incidence of malaria in pregnancy

H_a : There is a relationship between employment of pregnant women and incidence of malaria in pregnancy

Research Question 5: Is there any significant difference between prevalence at first antenatal visit and subsequent visits

H_0 : There is no significant difference between prevalence of malaria at first antenatal visit and subsequent visits

H_a : There is significant difference between prevalence of malaria at first antenatal visit and subsequent visits

Research Question 6: Is there any association between gestational malaria and reduction of newborn weight.

H_0 : There is no association between gestational malaria and reduction of newborn weight.

H_a : There is association between gestational malaria and reduction of newborn weight.

1.5 NATURE OF STUDY

In this study I answered the Research Questions by utilizing a cross-sectional design using both primary and secondary data. A cross-sectional research design was considered appropriate for this study because it enables me to investigate association between exposure to risk factors and the outcome of interest (Levine, 2014). The primary data were from the pregnant women attending ANC on Wednesdays every week at the Government Regional Hospital, located in the Northern Region of Sierra Leone, Bombali District. The secondary data utilized in this study was from the ANC data base.

The study examined the correlation between malaria in pregnancy and socio-economic indicators. For this study, I used all available participants who provided complete data during the routine ANC visits at the Government Regional Hospital Makeni. Employing quantitative method has the advantage in that smaller groups of participants can be used to make inference about larger groups that may be costly to study. In addition, using secondary data is less time consuming and cost-effective.

1.6 DEFINITION OF TERMS

Insecticide treated nets: Bed-nets treated with insecticides used to shield from mosquito bite and prevent malaria

Socioeconomic Status: The social standing or class of an individual or group often measured by a combination of education, income, and occupation (American Psychological Association, 2017).

Antenatal: Period of pregnancy from conception to the onset of labour.

Low birth weight (LBW): Birth weight less than 2.5kg

1.6.1 ASSUMPTIONS

I assumed that the secondary data obtained from the data base of the ANC, Government Regional Hospital were accurately documented and error-free. And also that the data used in this research represents the population pregnant women in the Northern region of Sierra Leone, since the work was done in the regional hospital.

1.6.2 SCOPE AND DELIMITATION

The scope of the research was limited to the Makeni, where the Regional hospital is situated at the Northern Region of Sierra Leone. Hence the results of the study may not be generalizable to the entire country of Sierra Leone, but rather the Northern Region of the country.

1.6.3 LIMITATIONS

The limitations of study may include the use of secondary data where data for the variables in the study were not available. The secondary data collected were collected for additional knowledge in the study and not to answer Research questions.

1.6.4 SIGNIFICANCE

The consequences and risks associated with malaria in pregnancy rely on a myriad of factors. The vulnerability of the pregnant women to malaria is as a result of their immunity impairment compared to non-pregnant women. Consequently, women become susceptible to the disease during pregnancy resulting in higher risks of morbidity and mortality for both the mother and the foetus. A research conducted in the Democratic Republic of Congo showed more malaria infection among pregnant women than non-pregnant women of child-bearing age with 37.2% and 30.4% respectively (Taylor et al, 2011b). A comparative analysis revealed that pregnant women are more attracted to mosquitos than their non-pregnant

counterparts (Lindsay et al, 2000, Ansell et al, 2002). In the Gambian population, Lindsay et al (2000) demonstrated that pregnant women were more attractive to the anopheline vector, Anopheles gambiae mosquitoes than their non-gravid counterparts under an untreated bed net. The same research revealed that the number of mosquitos entering the bed nets each night was 1.7 – 4.5 times higher in the pregnant group than the non-pregnant women. The study further revealed that pregnant women also received higher proportion of bites under the bed nets than their non-pregnant counterparts (70% and 52% respectively). In conclusion the researchers suggested that physiological and behavioral changes associated with pregnancy could be partially responsible. This research clearly reveals that pregnant women are more prone to infection by malaria parasites than other non-gravid women. The vulnerability of pregnant women to malaria is also more important in among women in their first and second pregnancies as a result of inadequate development of pregnancy-specific immune responses against the subpopulation of parasites that sequester the placenta. Hence the women in their first or second pregnancies are more susceptible to the deleterious effects of malaria than multi-gravid women who are more protected. However, this gravidity dependence is a function of the level of acquired immunity received after repeated malaria infections.

The use of ITNs prevents malaria infection and ultimately miscarriages, anaemia, neonatal and maternal deaths attributed to malaria in pregnancy. In this study I assessed the relationship between the use of ITNs and other socioeconomic indicators like family income, education and employment status of the pregnant women. The results will be relevant in similar communities, because malaria is a global malady and can be transmitted to travellers from non-endemic areas (CDC, 2012b). The outcome of this study could be used to promote social change and health seeking behaviors by Public health workers and health in improving that increases uptake of ITN among pregnant women.

1.7 DEFINITION OF VARIABLES

DEPENDENT VARIABLES: Malaria in pregnancy: This is defined as the occurrence of malaria during the period of pregnancy using clinical and laboratory standards as defined by the World Health Organization (WHO, 2000).

INDEPENDENT VARIABLES: Socioeconomic status. These include the pregnant women's data that measure social and economic factors, namely measurement of income level (wealth index), educational level, employment (Rubin et al, 2014, Trusting et al, 2013). Wealth index are categorized as no education, primary, secondary and tertiary. Occupation is categorized as unemployed, self-employed and employed (NMIS).

CHAPTER TWO – LITERATURE REVIEW

2.0 INTRODUCTION

Malaria is a serious Public Health challenge that cause immense mortality and morbidity). It is a major impediment to socioeconomic development ultimately leading to poverty (MCSP, 2015). It is also the leading cause of deaths and illnesses in most of the countries affected by it (Mali et al, 2007). Maternal illness and low birth weight are the outcome of Plasmodium falciparum infection which occurs majorly in Africa (WHO, 2013).In Africa, about 25 million women become pregnant annually. They are all at the risk of developing malaria in pregnancy which may have serious consequences for both the mother and foetus, especially for primigravidae woman (Desai et al, 2007). Malaria in pregnancy may lead to maternal anaemia, spontaneous abortions and poor pregnancy outcomes. The infection is asymptomatic most times; however the parasite may be present in the placenta contributing to maternal anaemia. placental parasitaemia (WHO, 2013). A report by WHO (2013) shows that maternal anaemia and placental parasitaemia can lead to low birth weight, contribute to infant mortality and also increase the risks of severe malaria inducing spontaneous abortion, still birth and prematurity (WHO, 2013).

2.1 LITERATURE SEARCH STRATEGY

I undertook the literature search on published research work by accessing the electronic Selinus university library databases and electronic search engines such as Google Scholar. The words or search terms used included malaria in pregnancy, Malaria among pregnant women in Sierra Leone, malaria preventive measures, Socio-economic impact of malaria in pregnancy and diagnosis/treatment/control of malaria in pregnancy. The literature search was limited to articles published from 2000 to 2020.

2.2 THEORETICAL FOUNDATION

The SEM was the theoretical framework used to undertake this study. The model is a multilevel, interactive approach to investigating health-related behaviours and conditions (McKenzie et al, 2009). It postulates that health-related behaviours and conditions are part of a larger system that can be approached from multiple levels(McKenzie et al, 2009). The five levels of influence in the ecological model are, the Individual level or intrapersonal level, the Intrapersonal level, the Organizational or Institutional level, the Community level and finally the Public policy level (McKenzie et al, 2009). The intrapersonal level seeks to identify individual characteristics that tend to influence behavior such as the person's attitude, knowledge and skills. While the interpersonal level involves processes and groups like family, friends and peers who provide identity and support. The organizational level on the other hand involves churches, stores or community organizations that implement rules, regulations and policies that promote or constraint behaviors. The community level can be social networks that involve community norms. The public policy level involves local, state, and federal agencies that implement policies and laws to regulate or support healthy practices (Winch, 2012).

In understanding health and disease patterns, focusing on the social and physical environments is vital. There are characteristics of the social and physical environment that defines human experience and personal behaviors (Abdulkarim, 2012). Social, economic and political systems shape behaviors of individuals and populations, which influence access to resources necessary to maintain good health (Abdulkarim, 2012). Moreso, SEM focuses attention on the context of behavior when implementing interventions (Panter-Brick et al, 2006). The levels of SEM enables us understand the factors that put people at risk of malaria and help explain the reason for low uptake of ITNs among pregnant women in Northern Sierra Leone. SEM involves the interaction and interdependence between factors and across all levels of health problem where it emphasize on the interactions with the physical and socio-cultural environments (National Institutes of Health, 2005). In SEM, the model may be used to focus attention on the social and physical settings where it examines the interplay between pregnant women and the external factors that shape that define their behaviors (Panter-Brick et al, 2006). This is analyzed through the different levels of SEM. A study conducted by Diala et al (2013) focused on the perception of pregnant women regarding IPTp in malaria prevention and its adherence. In this study, the SEM took into

cognizance the individual, community, societal and environmental contexts of behavior and social change, which involved cultural norms, religious beliefs, tradition and environmental factors (Diala et al, 2013).The study instruments were based on factors may tend to motivate or impede the behavior of pregnant women in treating and preventing malaria at the individual, community and environmental levels. The individual level was related to autonomy and personality, beliefs about malaria, and efficacy of modern treatment.

Women were usually influenced by partner or immediate family. (Diala et al, 2013). The people the women were connected to like the spouse or family member do play a vital role in their access to care. At the community level, interaction of the women involved people outside of the women's family circle. This level of interactions includes neighbors, peers, relatives, friends and other community members. These all are related to culture and norms of the community that play vital roles in influencing the choices and behaviors of pregnant women. For instance, pregnant women may be required to seek care in health facilities with providers who offer traditional medicines. Cultural norms that include the behavior of individuals in the society do play a vital role in the beliefs and actions of pregnant women. As regards the environmental level (environmental and community levels), economic factors, knowledge of malaria in pregnancy, adhering to providers instructions, waiting times, antenatal facilities, and providers attitude play a vital role in adhering to antenatal care services (Diala et al, 2013). The SEM model was used in this research using ITN as the preventive measure for malaria.

Factors at all levels of SEM relate to the health-seeking behaviors of the pregnant women to seek antenatal care where IPTp for malaria treatment when needed. The Family and community support do play a key role in the decision-making of the pregnant women to seek preventive care and treatment. This research utilized SEM to focus on the perception of pregnant women on IPTp and also on the uptake of ITNs among the pregnant women. The individual level relates to the level of education of the pregnant women in association with uptake of ITN. The interpersonal level relates to family income. The organizational level relates to access to antenatal care including availability of IPTp.

2.3**OVERVIEW OF MALARIA IN PREGNANCY**

Long before the discovery of the malaria parasite in 1880 by Alphonse Laveran (Bockarie et al., 1999), pregnant women have been burdened by malaria. However, the association between the two conditions was described only since the early 20th century (Desai et al., 2007). In the first quarter of the 21st century, malaria continues to place approximately 125 million pregnant women at risk each year who live in malaria endemic areas, of whom 32 million live in sub-Saharan Africa (Dellicour et al., 2010).

It is established that pregnant women are susceptible to the adverse effect of malaria. They have a higher tendency to be infected with malaria than non-pregnant women. And once infected, pregnant women have more possibility of experiencing increased severity of the disease as a result of reduced level of immunity. This is caused partly by transient depression of cell-mediated immunity that normally occurs during pregnancy (Griffith et al, 2007). The effects of malaria in pregnancy are triggered by different factors, which include the woman's level of immunity, her gravidity, the trimester of pregnancy, and the presence or absence of co-morbidity (Coll et al, 2008). Apart from the immune suppression associated with malaria in pregnancy, Plasmodium falciparum-infected erythrocytes can accumulate or sequester in the placenta, making it to be unavailable in the peripheral blood and hence undetectable when using malaria detectable techniques. Pregnancy associated malaria is most times asymptomatic. Hence the presence of these undetectable malaria parasites in the placenta often contributes to poor foetal growth, premature labour, low birth weight, maternal anaemia and spontaneous abortion (Amegah, 2013, Rogerson et al, 2018). Therefore malaria in pregnancy predisposes the pregnant women and their babies to adverse outcomes.

Plasmodium falciparum accumulates in many body sites as protein called P.falciparum membrane protein (PfEMPI). This protein has multiple variants and often evades removal by the spleen and immune system because of its tendency to accumulate in many sites inside the body. The unique variant of PfEMPI that mediate placental sequestration is called VAR2CSA, which binds to chondroitin sulphate A (CSA) (Salanti et al, 2004). VAR2CSA is found in females and it is also parity-dependent, so multigravida women have more protective antibodies and relatively more protected from the aftermath of placental malaria infection than the primigravidae women. Salanti et al (2004) also demonstrated that women with high levels of

plasma anti-VAR2CSA IgG antibodies were delivered of babies with adequate birth weight than women with low levels of the plasma antibodies. Women only have the tendency of being exposed to VAR2CSA when they are pregnant. During the first pregnancy, the initial exposure to the infected red cells could generate a fatal outcome to the mother and especially the foetus as a result of lack of requisite immunity. In malaria endemic areas of Sub-saharan Africa, the end-results of pregnancy associated malaria in multigravida women are milder than in areas of lower transmission of malaria. This explains the reason why both primigravidae and multigravida women are susceptible to malaria in pregnancy and the complications associated with it, such as coma, miscarriage, acute lung injury in the mother, and still birth in areas of low malaria transmission (Desai et al, 2004).

2.4 BURDEN OF MALARIA IN PREGNANCY

In Sub-Saharan Africa, approximately 25million pregnant women are at risk of Plasmodium falciparum infection every year. About one in four women have evidence of placental infection at the time of delivery (Meghna et al, 2007). The impact of malaria in pregnancy is also affected by the status of malaria in the community. The major factors which influence the epidemiology of P,falciparum malaria and that which is caused by other species of malaria parasites are, the intensity of transmission and immune response of the infected person. Malaria transmission in an area may be stable or unstable. And immunity is maintained through continued exposure to plasmodium parasites. In stable transmission areas, most infections of malaria are symptomless (Desai et al, 2007). In areas of unstable, non-endemic transmission, adult women without significant level of immunity are more likely to be symptomatic when they are infected, and are also at greater risk of developing severe disease (WHO, 2004). Lower parity, especially first and second pregnancies and younger ages, tend to increase the susceptibility to malaria (Mutabingwa et al, 2005).

The burden of pregnancy associated malaria is evident in Sub-saharan Africa. It is associated with diverse consequences on the pregnant woman, the foetus and the newborn. The adverse effects are LBW, preterm birth, spontaneous abortion, congenital infection and maternal death

(Chinweuba, 2017). Anaemia is shown to be prevalent in primi-gravidae and secondigravidae women than in subsequent pregnancies (Malaria Consortium, 2007; WHO, 2004).

In Sierra Leone, malaria is a major threat to the socioeconomic development of the country with an estimated 7 – 12 days lost days averagely per episode of malaria. It impose substantial burden on individuals, households and the government.

2.5 ECONOMIC IMPACT OF MALARIA IN PREGNANCY

The economic burden of malaria is enormous in Sub-Saharan Africa. In the malaria strategic plan (2005-2010), malaria is defined as "a disease of the poor – it affects the poorest and keeps them poor". Rogerson et al (2018) reported that malaria can be quantified in terms of both financial and non-financial implications. The researchers presented the economic costs as provider costs, the health system costs, User fee and cost to households who access these services. Others are economic impacts like reduced labour productivity of women infected. This economic burden tends to stress the pregnant women further together with their households especially those in the category of low socio-economic status. The associated economic pressure also tends to determine the health-seeking behavior of the pregnant women. They may avoid seeking formal care and consequently patronize the informal sector thereby endangering the lives of the foetus and mother. The treatment of malaria in Sierra Leone is free at the government facilities, but other costs ranging from transportation to indirect costs during ANC have major impact on the households' budget of low SES pregnant women. When there is stock out of free SP or ITNs, pregnant women may be forced to purchase their medications from private pharmacy stores or patient medicine vendors. The cost of treatment of malaria in Africa is between 2 and 25 USD and for monthly preventions is between 15 and 20USD. Hence the total amount spent on malaria as regards prevention, treatment and loss of human productivity can significantly compromise the income of poor households. Pregnant women normally incur both direct and indirect costs in prevention and treatment of malaria. The direct costs include fees, drugs, and transportation. The indirect costs include decreased productivity, adverse effects on the baby (Butto-Menezes et al, 2016).

2.6 IMPACT OF EDUCATION ON MALARIA IN PREGNANCY

Compared to developed countries, maternal mortality and other maternal health indicators are worse during pregnancy in developing countries (WHO, 2015).

Onah and fellow researchers (2006) conducted a study to identify the factors that are associated with the use of maternity services. They reported a high association between educational status of pregnant women and health seeking behaviors. The maternal mortality rate was much higher in women of no education than women with secondary or higher levels of education (Onah et al, 2006). Further findings in this study showed that women with formal education, employment status and low income would not seek antenatal supervision, where there will be exposed to obtaining information on ITN use for prevention of malaria (Onah et al, 2006).

Many interventions on malaria in pregnancy such as the use of preventive measures among pregnant women to reduce the burden of malaria, depends on improved knowledge of the disease and its control, which is also enhanced by increased educational attainment (Dike et al, 2006). However they reported that the educational attainment need not be advanced to have a better knowledge, attitude and perception to malaria (Dike, 2006). Formal education aids in removing some of the cultural ideologies that may lead to misconceptions that affect proper and adequate malaria prevention and treatment. Furthermore, the study showed that people with formal education were more likely to identify mosquito as the vector of malaria. The understanding that mosquito is the cause of malaria was positively associated with perception of environmental management and use of ITNs for prevention of malaria (Dike, 2006). However, some other studies showed no significant relationship (Akaba et al, 2013, Ezire et al, 2015). The findings of Singh, et al, 2013 concluded that the education level of pregnant women was not related to the use of ITNs.

2.7 INCOME IN RELATION WITH MALARIA IN PREGNANCY

Malaria is prevalent in the world's poorest countries as the disease depresses economic growth (Worall et al, 2005). Costs of malaria vary by virtue of socioeconomic status of family households (Uguru et al, 2009). Studies have shown that the direct cost of malaria treatment and

prevention make up to 28 to 34% annual income of poor households and 1-2% of annual income of high income households (Mia et al, 2012).

Malaria leads to low productivity and loss of income, especially since the human and economic costs associated with the declining quality of life, consultations, treatments, hospitalizations and other events related to malaria are highly enormous (Kimbi et al, 2014). A study by Onwuejekwe et al (2004) showed that those within the poorest socioeconomic groups were less likely to own or purchase an ITN and a lower willingness to pay for one. They concluded that the decision to pay for an ITN is propelled by need and higher economic status. Similar report by Worall et al (2005) showed a link between poverty and the use of ITNs. Socioeconomic status (occupation, housing type, rural location) are more directly related to exposure and risk of malaria. Poorer households are less likely to access preventive or curative measures, hence they may be more vulnerable to the adverse effects of malaria. Though there are contrasting findings by Singh et al (2013) which showed the lowest quintile households demonstrated higher rates of ITN use among pregnant women.

2.8 PREVENTION AND CONTROL OF MALARIA

2.8.1 PREVENTION OF PREGNANCY ASSOCIATED MALARIA

Malaria in pregnancy is a major, preventable cause of maternal morbidity and poor birth outcomes. In order to prevent the adverse outcomes of malaria in pregnancy, WHO recommends the use of insecticide treated mosquito nets (ITNs) and Intermittent Preventive Treatment for effective case management of malaria and anaemia in pregnant women (WHO, 2015).

2.8.2 INSECTICIDE TREATED NETS

The Insecticide treated nets repel mosquitoes and other insecticides and hence more effective against malaria prevention than the untreated nets. Therefore if a significant increase in uptake of ITNs is achieved, the chain of infection will be affected via the interruption of the lifecycle of the

mosquitoes. This intervention controls the insect vector of malaria transmission (CDC, 2012). Ankomah et al (2012) reported the outcome of their randomized controlled trials that consistency in the use of ITNs by pregnant women produce favorable infant and maternal outcomes. Singh et al (2013) reported a correlation between the use of ITNs and the decline in the number of stillbirths, improvement in the body weight of babies and a reduction in anaemia associated with pregnant women.

Preventing malaria in pregnancy presents myriads of challenges. The malaria parasitaemia in pregnancy is usually asymptomatic. Therefore treating only symptomatic pregnant women will fail to address the majority of infected cases. In this case, most pregnant women will not show positive test results since the malaria parasites are sequestered in the placenta. Consequently, the focus of most control efforts has been on prevention and presumptive treatment. The two major interventions have been insecticide-treated nets (ITNs) and intermittent preventive treatment in pregnancy (IPTp). World Health organization (2015) reported that intermittent preventive treatment in pregnancy (IPTp) is a highly cost-effective preventive malaria intervention that significantly improves the health of mothers and their newborns in areas of moderate to high malaria transmission.

ITNs are usually distributed at the antenatal clinics with the goal of preventing malaria in pregnancy. ITNs are very effective at preventing malaria when they are correctly used. The major setbacks to ITNs use are supply and distribution. There is a significant correlation between bed net ownership and use by pregnant women. Moreso, insufficient ITN stocks and delays in providing antenatal care until late in pregnancy can prevent pregnant women from receiving the requisite ITNs that would prevent malaria infection. However, not all women effectively use the ITNs they receive the appropriate manner. Regular and proper use of the ITNs by the pregnant women is pivotal in the prevention and control of malaria (Diala, 2013). However, utilization of the ITNs is never equal to ownership of the same. Mbachu et al (2012) demonstrated that ownership and utilization of TTNs were 80.5% and 64.4% respectively. During hot seasons, it is usually uncomfortable for the recipients to use the ITNsas recommended. The ITNs may also not be properly taken care of, and hence develop holes and the insecticide wears off eventually.

In 2017, UNICEF, with UK aid funding from the British people and the Global Fund, helped purchase and distribute more than two million ITNs as part of a national campaign targeting

every household in Sierra Leone. In addition, UNICEF assisted to organise an intensive media campaign to encourage children, pregnant women and lactating mothers to sleep under treated nets every night and visit the hospital if they feel unwell.

Surprisingly, after more than a decade of introduction of ITNs and IPTs, their coverages are still significantly low. In 2018, Desai and colleagues in a study discovered that only 39% of pregnant women habitually slept under ITNs. Unfortunately, the high attendance to antenatal clinic in malaria endemic areas as reported by Van Eijik et al (2013) has not translated to high uptake of ITNs by pregnant women. Hill et al (2013) categorized the barriers associated with the use of ITNs into three distinct groups. They are the perspective of the healthcare providers, the household/social/cultural level and finally the perspective of the pregnant women. The issue of stock-out is considered a major barrier to ITN utilization. Hence not all the pregnant women who attended focused ANC eventually receive the ITNs. The household/social/cultural barriers identified the costs of ITNs as the main setback to ITN use (Aluko & Oluwatosin, 2012).Consequently pregnant women of low SES who couldn't receive free ITNs during mass campaigns may not likely own or use an ITN.

Other malaria control strategies include the application of Indoor Residual Spraying (IRS) and Environmental Management (Mbachu et al, 2012).

Figure 2. Pregnant woman collecting ITN during ANC visit

2.8.3 INTERMITTENT PREVENTIVE TREATMENT IN PREGNANCY

The World Health Organization (WHO, 2015) recommended the use of intermittent preventive treatment of malaria in pregnancy by using sulfadoxine-pyrimethamine (IPTp-SP) inorder to gestational and congenital malaria (Amos et al, 2019). IPTp-SP has become a full therapeutic course antidote for malaria in pregnancy administered as a vital component of antenatal care. Although WHO observed a slow efforts in scaling up IPTp-SP in Sub-Saharan Africa as a result of inadequate knowledge of some health workers. A meta-analysis of seven trials that evaluated the use of IPTp-SP was reviewed by WHO. It revealed that three or more doses of IPTp-SP provoked higher mean birth weight and decrease in low birth weight (LBW) than two doses of IPTp-SP. The estimated relative risk reduction of for LBW was 20%. In addition, the group for 3 doses and more were discovered to have less placental malaria (WHO, 2014). Therefore IPTp-SP is an integral part of WHO's three-thronged approach in the prevention and treatment of pregnancy associated malaria, which also include the use of ITNs and prompt and effective case management. The WHO (2014) recommendation for IPTp-SP states that all possible efforts should be made to increase access to IPTp-SP in all areas with moderate to high malaria

transmission in Africa as part of antennal care services. The recommendation of WHO is a schedule of at least four antenatal visits during pregnancy. IPTp-SP is recommended to start as early as possible in the second trimester at each scheduled antenatal care visit until the time of delivery, provided that the doses are given to the pregnant women one month apart. SP should not be given during the first trimester, however, the last dose of IPTp-SP can be administered up to the time of delivery without safety concerns (WHO, 2014).

IPTp-SP ideally, should be administered as directly observed therapy (DOT) of three tablets sulfadoxine/pyrimethamine (each tablet contains 500mg/25mg SP) given the total required dosage of 1500mg/75mg SP. SP can be given with food or empty stomach. But should not be administered to pregnant women who are receiving cotrimoxazole prophylaxis due to a higher risk of adverse events. As part of WHO recommendation is the administration of folic acid at a dose of 0.4mg daily which may be safely given in conjunction with SP. But folic acid at a daily dose of equal or more than 5mg counteracts the efficacy of SP as an antimalarial when administered together with SP (WHO, 2014). WHO also recommends countries in Sub-Saharan Africa to continue to provide IPTp-SP until data to guide this decision-making is available (WHO, 2014).

2.9 TREATMENT OF MALARIA – GENERAL APPROACH

The treatment should only be initiated after appropriate diagnosis has been established by laboratory investigation. Presumptive treatment should only be adopted in extreme situation like severe disease, impossibility of obtaining prompt laboratory diagnosis and strong clinical suspicion (CDC, 2019). The World Health Organization (2016) recommended between four to eight contacts for pregnant women with their health providers inorder to reinforce communication between them and also to enhance the detection of danger signs and the management of potential health risks. The WHO named the improved interaction between pregnant women and healthcare providers as Focused Antenatal Care (WHO, 2016). Focused Antenatal Care is an integrated procedure that examines the holistic health status of the pregnant woman. This include family planning, Voluntary counseling and testing (VCT), birth

preparedness, prevention of mother-to-child transmission (PMTCT) of HIV, tetanus vaccination, and prevention/early detection and treatment of STIs, UTIs and malaria (WHO, 2012).

The moment diagnosis of malaria has been established, appropriate antimalarial treatment must commence at once. The treatment should be guided by three main factors which are, The species of Plasmodium, The clinical status of the patient and the drug susceptibility of the plasmodium parasites.

a. The Plasmodium species. The determination of the infecting species of Plasmodium for treatment purposes is important for three major reasons. Plasmodium falciparum and P.knowlesi infections can cause rapidly progressive severe clinical manifestations. Second, P.vivax and P.ovale infections also require treatment to take care of the hypnozoite forms that are dormant in the liver and can cause a relapsing infection. Finally, P.falciparum and P.vivax species have different drug resistance patterns in different geographic regions. The urgent initiation of the appropriate therapy is especially critical for P.falciparum and P.knowlesi infections (CDC, 2019).

b. The clinical status of the patient. Patients with malaria disease are categorized into either uncomplicated or severe malaria. Patients with uncomplicated malaria can be effectively treated with oral antimalarial medication. However, patients who have one or more of the following clinical criteria are considered to have manifestations of more severe disease and should be treated aggressively with parenteral antimalarial therapy: impaired consciousness/coma, severe normocytic anaemia (Haemoglobin <7), renal failure, acute respiratory distress syndrome, hypotension, disseminated intravascular coagulation, spontaneous bleeding, acidosis, haemoglobinuria, jaundice, repeated generalized convulsions, and/or parasitaemia >5% (CDC, 2019).

c. The Drug Susceptibility of Plasmodium. The knowledge of the geographic area of the infection is crucial on the likelihood of drug resistance of the infecting parasite and enables the clinician to choose an appropriate drug or drug combination and treatment course. In addition, if a malaria infection occurred despite use of a medicine for chemoprophylaxis, that medicine should not be a part of the treatment regimen. If the diagnosis of malaria is suspected and cannot be confirmed, or if the diagnosis of malaria is confirmed but species determination is not

possible, antimalarial treatment effective against chloroquine-resistant P.falciparum must be initiated immediately (CDC, 2019).

For treatment for uncomplicated malaria, P.falciparum infections acquired in areas without chloroquine-resistant strains, which include Central America west of the Panama Canal, Haiti, The Dominican Republic, and most of the middle East, patients can be treated with oral chloroquine. A chloroquine dose of 600mg base (=1000mg salt) should be given initially, followed by 300mg base (=500mg salt) at 6, 12, 24 and 48hours after the initial dose for a total chloroquine dose of 1500mg base (=2,500 mg salt). Alternatively, hydroxychloroquine may be used at a dose of 620mg base (=800mg salt) by mouth given initially, followed by 310 mg base (= 400 mg salt) by mouth at 6, 24 and 48 hours after the initial dose for a total hydroxychloroquine dose of 1550 mg base (=2000 mg salt). In addition, any of the regimens listed for the treatment of chloroquine-resistant malaria may be used for the treatment of chloroquine-sensitive malaria. Prompt initiation of an effective regimen that readily at hand would be the preferred strategy (CDC, 2019).

P. falciparum acquired in chloroquine-resistant areas, four treatment options are available. The first two treatment options are available. The first two treatment options are atovaquone-proguanil (Malarone) or artemether-lumefantrine (Coartem). These are fixed dose combination medicines that can be used for non-pregnant adult and paediatric patients. Both of these options are very efficacious. Quinine sulphate plus doxycycline, tetracycline, or clindamycin is the next treatment option. For the quinine sulphate combination options, quinine sulphate plus either doxycycline,or tetracycline is generally preferred to quinine sulphate plus clindamycin because there are more data on the efficacy of quinine plus doxycycline or tetracycline. Quinin treatment should continue for 7 days for infections acquired in Southeast Asia and for 3 days for infections acquired in Africa or South America (CDC, 2019). The fourth option, mefloquine, is associated with rare but potentially severe neuropsychiatric reactions when used at treatment doses. The fourth option is recommended when the other options cannot be used (CDC, 2019).

For paediatric patients, the treatment options are the same as for adults except that the dosage is adjusted by patient weight. The paediatric dose should never exceed the recommended adult dose. Pediatric dosing may be difficult due to unavailability of non-capsule forms of quinine. If

unable to provide paediatric doses of quinine, one of the other three options should be considered (CDC,2019).

If using a quinine-based regimen for children less than eight years old, doxycycline and tetracycline are generally not indicated; therefore, quinine can be given alone for a full 7 days regardless of where the infection was acquired or given in combination with clindamycin as recommended above. In rare instances, doxycycline or tetracycline can be used in combination with quinine in children less than eight years old if other treatment options are not available or are not tolerated, and the benefit of adding doxycycline or tetracycline is judged to outweigh the risk. If infections initially attributed to species not identified are subsequently diagnosed as being due to P.vivax or P.ovale, additional treatment with primaquine or tafenoquine should be administered (CDC, 2019).

P.malariae and P.knowlesi. There has not been widespread evidence of chloroquine resisstance in P.malariae and P.knowlesi species; therefore, chloroquine (or hydoxychloroquine) may still be used for both of these infections. In addition, any of the regimens listed above for the treatment of chloroquine-resistant malaria may be used for the treatment of P.malariae and P.knowlesi infections.(CDC, 2019).

P.vivax and P.ovale. Chloroquine (or hydrochloroquine) remains an effective choice for all P..vivax and P.ovale infections except for P.vivax infections acquired in papua New Guinea or Indonasia. The regimens listed for the treatment of P.falciparum are also effective and may be used. In addition to requiring blood stage treatment, infections with P.vivax and P.ovale can relapse due to hypnozoites that remain dormant in the liver. To eradicate the hypnozoites, patients should be treated with either primaquine phosphate or tafenoquine (CDC, 2019).

Severe Malaria. Patients with manifestations of more severe disease should be treated aggressively with parenteral antimalarial therapy regardless of the species of malaria seen on the blood smear. If severe malaria is strongly suspected but a laboratory diagnosis cannot be made at that time, blood should be collected for diagnostic testing as soon as it available and parenteral antimalarial drugs should be started. All patients with severe malaria, regardless of infecting species, should be treated with intravenous (IV) artesunate (CDC, 2019).

Severe malaria can progress rapidly and must be treated as soon as possible. While timely delivery of IV artesunate is anticipated, health-care providers can consider treating the patient with an oral antimalarial while waiting for IV artesunate to arrive. Health-care providers will need to decide the most feasible route to administer the drug for patients unable to tolerate an oral antimalarial. For example, if this intolerance is due to nausea and vomiting, an anti-emetic preceding the antimalarial may help. For comatose patients, a nasogastric tube can be considered (CDC, 2019).

2.9.1 TREATMENT OF MALARIA IN PREGNANCY

For pregnant women diagnosed with uncomplicated malaria caused by P.malariae, P.vivax, P,ovale or Chloroquine-sensitive P.falciparum, prompt treatment with chloroquine (same treatment schedule as with non-pregnant adults) is recommended. Hydroxychloroquine may be given instead as alternative. However, for women in their second or third trimesters, arthamether-lumefantrine is an additional option. For pregnant women diagnosed with uncomplicated malaria caused by chloroquine-resistant P.falciparum infection, women in their second and third trimesters can be treated with arthmether lumefantrine, and for all trimesters, mefloquine or a combination of quinine sulphate and clindamycin is recommended (CDC, 2019).

Furthermore, WHO recommends that all pregnant women in their second or third trimsters who have uncomplicated P.falciparum infection should be treated with artemisinin-based combination therapy. The short-acting but potent artemisimin component (artesunate, arthesunate or dihydroartemisinin) reduces the parasite level substantially during the first 3days of treatment. While the longer-acting partner drug (lumefantrine, piperaquine, amodiaquine or mefloquine) eliminates the remaining malaria parasites thereby preventing recrudescent malaria (Joel Tarning, 2016). The longer-acting partner drug is also responsible for the post-treatment prophylactic effect by preventing new infections while the drug concentration in the blood exceed the minimum inhibitory concentration of the parasites.

CHAPTER THREE: RESEARCH METHOD

3.0 INTRODUCTION.

This study is aimed at assessing the impact of socioeconomic factors on pregnancy associated malaria. This study is carried out at the Government Regional Hospital, Makeni, Sierra Leone. The government of Sierra Leone acknowledges malaria as a health and socioeconomic burden. This is documented in the National Health Sector Strategic Plan (NHSSP 2010-2015), Sierra Leone Health Recovery Plan 2015-2020, National Ebola Strategy for Sierra Leone 2015-2017 and the Basic Package of Essential Health Services 2010 which was revised 2015 (Sierra Leone Malaria Control Strategic Plan, 2015).

Malaria is endemic in Sierra Leone with stable and perennial transmission all the districts. It is presently the leading cause of mortality and morbidity among under five year old children. Although mostly pregnant women and under five children are mostly affected, the entire population are at risk of the disease (SLMCSP, 2015).

In this study, my quest is to unravel any association between socioeconomic variables and malaria in pregnancy. The independent variables are the socioeconomic factors which include income, education, employment status and occupation. The dependent variable is malaria in pregnancy which is established following standard operating procedures at the Government Regional Hospital, Makeni, Sierra Leone.

3.1 COUNTRY PROFILE

Sierra Leone is situated at the west coast of Africa, between latitude 8 30^0 north and longitude 11 – 30^o west. It shares boundaries with Guinea on the North and East and Liberia on the South-East. The Atlantic Ocean forms a beautiful coastline to the South and West of the country.

Sierra Leone covers a total area of 71,740km^2 (27,699 sq.ml) with coastline of 402km. It has a maritime claim of territorial sea equivalent to 200 nautical miles (370.4km; 230.2miles). Sierra

Leones's continental shelf is 200metres in depth. The projected population for 2015 is 6,506,424 with 57.5% of the population living in the rural areas (SLMCSP, 2015).

The country has diverse terrain, ranging from coastline swamps, through inland swamps and rain forest to one of the highest mountains in West Africa, the Bintumani at 2200m. The secondary palm-bush is the main vegetation and it is interspersed with numerous swamps that are mostly cultivated for rice. These swamps provide ideal breeding places for the mosquito vectors of malaria. The coastal line has many mangrove swamps, which provide the breeding sites for anopheles melas mosquitoes, which is another major vectors of malaria apart from anopheles gambiae and anopheles funestus (SLMCSP, 2015).

Sierra Leone has a typical tropical climate with temperature ranging from 21^0C to 32^0C with an average daily temperature of 25^0C. It has two major seasons annually, the rainy season (May to October) and the dry season (November to April). July and August usually is usually associated with heavy rains. There is an average rainfall of about 320cm annually, while the relative humidity is high ranges from 60 to 90%. (SLMCSP, 2015).

Sierra Leone is a democratic state with a presidency, cabinet, parliament and an independent judiciary. The country is divided into 4 administratively, the Northern, Southern, Eastern and Western regions. The western region is where the capital city, Freetown is located. The Regions are further divided inton14 Health Districts and 149 chiefdoms, There are District/City councils made up of district chairman, mayor, councillors, and administrators who administer the districts; while the chiefdoms are governed by locally elected paramount chiefs. Following the recent decentralization, the country has been divided into 19 local councils that have been further subdivided into 392 wards, each headed by an elected councillor (SLMCSP, 2015)).

The population of Sierra Leone is estimated by the Statistics Bureau as 6,507,059 (MOHS projected population, 2015). Freetown is the capital city with an estimated population of 1,066,910, and is the largest city in the nation. It serves as the economic, commercial, educational and cultural centre of the nation. Bo is the second largest city situated in the southern part of Freetown. It has an estimated population of 256, 553 while Kenema is third with a population of about 182, 106. Makeni which is in the Northern region has an estimated population of 128,656. Makeni is the location of the government regional hospital where this

study is conducted (SLMCSP, 2015). Pregnant women from other hospitals in the region are also referred to Makeni hospital for special antenatal care to facilitatea positive pregnancy experience.

Figure 3. Map of Sierra Leone

3.2 SOCIOECONOMIC CONTEXT

Sierra Leone is grouped among the least developed countries. It was ranked 178 out of the 187 countries in the Human Development Index (UNHDI, 2008). The country gross domestic product (GDP) growth was constant at 7% per year for the period 2003-2007. The average national income (GNI) per person was US$220 in 2006 and approximately 48% of the population lives on less than $1 a day (UNDP, 2009). The country's main economic sector

includes mining, agriculture and fishing. Two-thirds of the working population is engaged in subsistence farming.

The decade-long war, low agricultural productivity, low salaries for formal and informal workers, poor investment, high unemployment rate, corruption, failure to better make use of natural resources, poor health status and high fertility and population growth rates are the principal causes of poverty (WHO, 2005).

The country has great untapped potential to participate in the world economy: it has under-utilized fertile lands on which to cultivate and harvest food; unexploited sea; valuable mineral resources; and it has a large natural deep port with which it could import/export goods.

Sierra Leone's manufacturing sector continues to develop and consists mainly of the raw materials processing and light manufacturing for the domestic market. The service sector has been growing as there have been increasing numbers of Nigerian Banks entering the market.

3.3 METHODOLOGY

The study was across-sectional study design coupled with a systematic review which also employed a quantitative method of data collection through the use of questionnaires, interview and secondary data from the hospital ANC. The approval and research in the hospital was a lot easier based on the fact that I work as a Technical volunteer officially posted to Makeni Regional Hospital by the Sierra Leone Ministry of Health and Sanitation. Pregnant women attend the antenatal clinic on Wednesdays at the Government Regional Hospital, Makeni. The goal of the ANC is to ensure a normal pregnancy that will result in a healthy outcome for both the woman and the baby. According to WHO, ANC is the care provided by skilled health-care professionals to pregnant women in order to ensure the best health outcome for both mother and baby during pregnancy. The components of ANC are, risk identification; prevention and management of pregnancy-related diseases; and health education and health promotion. A vital goal of ANC is identification of women at risk for issues that can complicate their pregnancy adversely affect their health. ANC promotes targeted assessment, during which the skilled healthcare provider interviews, examines and tests the pregnant woman to determine her risk of developing pregnancy-associated complications. One example of establishing risk relates to malaria in pregnancy, because malaria's effects on pregnant women are different based on the levels of

transmission and immunity. Preventive treatment include provision of IPTp-SP and ITNs,are given to the pregnant women during their first visit to the ANC after the first trimester. These services are considered free by the government of Sierra Leone in all the hospitals. Apart from the data collected from the ANC database, the pregnant women who have consented are interviewed for more data. The process is made easier since I work in collaboration with the skilled healthcare providers at the ANC. Subsequently, the pregnant women are sent to the laboratory where they are investigated for malaria parasites, among other tests. The tests routinely done are microscopy and rapid diagnostic tests (RDTs).

Figure 4: Map of Sierra Leone showing Makeni

3.4 MALARIA DIAGNOSIS

The MOHS has endorsed parasitological confirmation of malaria to be part of good clinical practice to improve the quality of care of patients. Prior to the institution of treatment, confirmation should be done using microscopy or rapid Diagnostic Tests (RDTs) and prompt and effective treatment with ACTs (SLMCSP 2015).

3.4.1 GENERAL BACKGROUND. An accurate and prompt malaria diagnosis is pivotal for improved malaria control. This is vital in order to restrict antimalarial treatment to those with confirmed diagnosis, and for a cost-effective and rational use of antimalarial drugs (WHO, 2019; Perkins and Bell, 2008). The unavailability of parasite-based diagnostic techniques leaves health care workers with only clinical algorithms to diagnose malaria. However, the non-specific nature of symptom-based malaria diagnosis results in substantial over-diagnosis and overtreatment. Based on the fact that malaria is the most common diagnosis among African febrile children and one of the prevalent in adults, both over-diagnosis and under-diagnosis have substantial public health implications (Ansah et al, 2010. Chandler et al, 2008). Putting into consideration the decreasing malaria transmission as seen in many areas, the relevance of a parasite based diagnosis hereby increases. In high endemic areas a large proportion of the population, including asymptomatic individuals tend to have parasitaemia most of the time. Consequently, the detection of malaria parasites does not necessarily mean that they are responsible for the patient's illness, since they may only reflect a coincidental infection. A correct malaria diagnosis plays an important role in the monitoring of treatment efficacy and to evaluate the impact of interventions, such as distribution of ITN/LLINs (Long-lasting insecticide nets) or IRS (Indoor residual spraying).

3.4.2 MALARIAMICROSCOPY. It was not long after Laveran described the malaria parasite that Romanowsky in Russia developed a method to stain the parasites, which in combination with the development of improved microscopes made it possible to more thoroughly study them (Editorial, 2009). Romanowsky used a mixture of eosin and methylene blue giving the nucleus purple color and the cytoplasm blue coloration. This technique is the basis for the principles presently used by staining methods of malaria parasites, i.e.Giemsa and Field stain. Microscopy allows for the identification and differentiation of malaria species, determination of parasite stages including gametocytes and the quantification of parasite density. Microscopy is still the method of choice for treatment follow up and investigation of malaria treatment failures. Microscopy remains the gold standard against which other diagnostic methods is evaluated CDC, 2019b). Malaria diagnosis using microscopic technique requires examination of both thin and thick smears from the same patient. Preferably capillary blood should be used for the preparation

of blood films since various additives for venous puncture such as EDTA can affect the parasite morphology making it more difficult for speciation. For thick smear preparation, approximately 10 microliter (μL) is applied on a slide, while the thin film requires 5μL blood. Optimal malaria microscopy is performed with microscopes fitted with x10 paired eyepieces and a x100 oil immersion objective (total magnification x1000) (WHO, 1991). About100 or 200 microscopic fields (0.2-0.5 μL) are normally examined before a malaria infection can be excluded (negative result). In remote areas without access to electricity, microscopy can still be performed using mirror which reflects daylight through the specimen into the eyepieces.

3.4.3 Giemsa staining method. Giemsa stain is a classical stain used for malaria microscopy (Barcia, 2007). It consists of commercially available Giemsa powder, glycerol and methanol. The stock solution can be purchased ready prepared and should be mixed with a phosphatase buffer solution of pH 7.2 prior to staining of the blood smears (WHO, 1991). Under field conditions in endemic areas most times ordinary tap water is used and it works generally well, although a pH differing from 7.2 can affect the purple-blue contrast in the specimens. A concentration of 5% or 10% Giemsa solution for 20-30 minutes is used for both thin and thick smears. The staining solution should be prepared fresh prior to use. The slide for thin smear should be dipped in pure methanol to fix the cells. In the thick smear on the other hand, the cells should be lysed making it easier to examine a denser layer. The sensitivity of a thick smear is 15-20 times higher than a thin film but does not allow for speciation (species determination). For the thin smear the malaria parasites are seen within the red cells with the different characteristics of the species in terms of size, granulation and effect on the infected erythrocytes, which generally allows for species identification if the number of parasites is not very low.

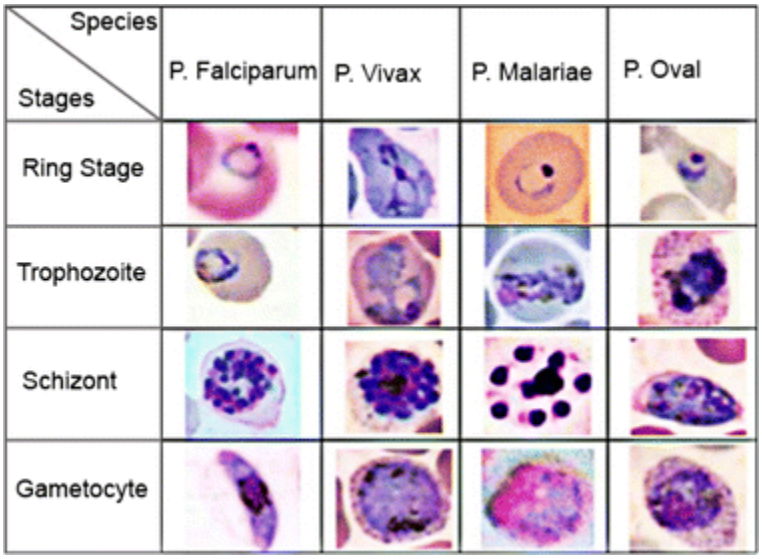

Figure 5: Speciation/stages of malaria parasites

3.4.4 Parasite quantification. There are different methods for quantification of malaria parasites in blood smears. Initially, this was only applicable to P. falciparum infection for estimation of severity of disease and treatment outcome. However, there are recent reports on high malaria parasitaemia also among severe P. knowlesi cases (Singh and Daneshvar, 2013), which probably makes quantification important also for P. knowlesi. The most common technique employed in endemic areas is based on counting parasites in the thick smear against a standard number of white blood cells (WBC). The number of parasites are generally counted against 500 or 200 WBC, then with an estimated 8000 WBC per µL of blood gives a factor of 16 or 40 for calculation of parasites per µL using the simple mathematical formula:(parasites counted / number of WBC counted) x 8000 = parasites per µL (p/µL) In case of very low parasite densities the numbers are often counted in 200 microscopic fields which is equivalent to 0.3-0.5 µL. The numbers are then given as parasites/200 microscopic fields. Another quantification method is to estimate the percentage of infected RBCs in a thin blood smear (Greenwood, 1991, Hommel, 2002). Using this technique the parasite density is reported as % of the RBC infected. The thick smear method has a higher sensitivity and is the first choice in endemic areas. However, it is a herculean task to estimate number of parasites per WBC in high parasitaemias because the density is often underestimated (Bejon, 2006).. Then, estimation of % infected RBCs in a thin smear provide a more accurate result. There are other methods that are semi-quantitative that estimates in pluses (ie+ - ++++) that are still used in some endemic areas. All methods for

estimation of parasite density are associated with potential errors due to varying WBC count and a parasite loss of up to 20% during staining of thick smears (Hommel, 2002, Bejon, 2006, Alves-junior, 2014). Using thin smears there is often an uneven distribution of parasites and if a cell counting ocular is not used, the estimation of RBC per microscopic field can be arbitrary. Parasite quantification provides useful clinical management guidance and is also a useful tool for clinical trials where serial examinations of blood smears are used to determine the parasitological response to anti-malarial treatment.

3.4.5 RAPID DIAGNOSTIC TESTS (RDTs)

Malaria RDTs are based on immunocromatic detection of parasite antigens. The introduction of RDTs for diagnosis of malaria in the early 1990s has had a major impact on fever management in malaria endemic areas. For the first time a health worker in a remote area could rapidly and accurately distinguish between parasitaemic and non-parasitaemic febrile illness (Bell and Peeling, 2006).

Malaria rapid diagnostic tests (RDTs) help in the diagnosis of malaria by detecting evidence of malaria parasites (antigens) in human blood. RDTs enable a reliable detection of malaria infections especial[ly in remote areas that have limited access to good quality microscopy services (WHO, 2019).WHO has also produced a number of guidelines, evaluations and recommendations for the use of RDT, and has also set up standards for the diagnostic performance of RDT with minimum requirement sensitivities of 95% for detection of 100 p/μL (equivalent to 0.002% parasitaemia) and specificities of minimum 90% for P. falciparumcompared with microscopy (Bell and Peeling, 2006, Mouatcho, and Goldring, 2013).

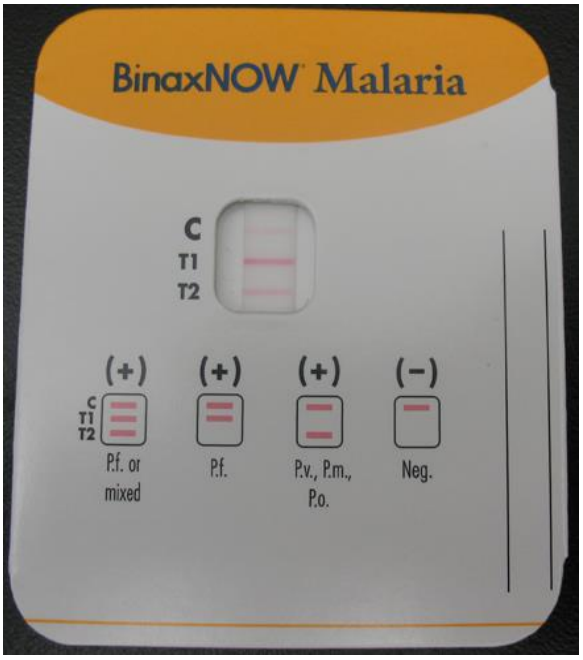

Figure 6: Rapid Diagnostic test for malaria parasites

3.46 HOW MALARIA RDTS WORK

Malaria rapid diagnostic tests (RDTs) assist in the diagnosis of malaria by providing evidence of the presence of malaria parasites in human blood. RDTs are an alternative to diagnosis based on clinical grounds or microscopy, particularly where good quality microscopy services cannot be readily provided (WHO, 2019).

There are variations between products, such as targets and formats, though the principles of the tests are similar. Malaria RDTs detect specific antigens (proteins) produced by malaria parasites in the blood of infected individuals. Some RDTs can detect only one species (*Plasmodium falciparum*) while others detect multiple species (*P. vivax, P. malariae* and *P. ovale*). Blood for the test is commonly obtained from a finger-prick (WHO, 2019).

RDTs are lateral flow immuno-chromatographic antigen-detection tests, which rely on the capture of dye-labeled antibodies to produce a visible band on a strip of nitro-cellulose, often encased in plastic housing, referred to as cassettes. With malaria RDTs, the dye-labeled antibody

first binds to a parasite antigen, and the resultant complex is captured on the strip by a band of bound antibody, forming a visible band at the T - test line of the results window. A control line provides information on the integrity of the antibody-dye conjugate, but does not confirm the ability to detect parasite antigen (WHO, 2019).

3.4.7 MODE OF ACTION OF COMMON MALARIA RDT FORMAT

1. The first step involves mixing the patient's blood with a lysing agent in a test strip or well. This ruptures the red blood cells thereby releasing more parasite protein (antigens),.

2. Dye-labeled antibody, specific for target antigen, is present on the lower end of nitrocellulose strip or in a plastic well provided with the strip. Antibody that is specific for the target antigen, is bound to the strip in a thin line/test line, and either antibody specific for the labeled antibody, or antigen, is bound at the control line.

3. The Blood and buffer, which have been placed on strip or well, are mixed with labeled antibody and are drawn up the strip across the lines of bound antibody

4. If antigen is present, some labeled antibody-antigen complex will be trapped and accumulate on the test line. Excess-labeled antibody is trapped and accumulates on the control line. A visible control line indicates that labeled antibody has traversed the full length of the strip, past the test line, and that at least some free antibody remains conjugated to the dye and that some of the capturing properties of the antibodies remain intact.

5. The intensity of the test band will is a function of the amount of antigen present, at least at low parasite densities (antigen concentration), as this will determine the amount of dye particles which will accumulate on the line. The control band intensity may decrease at higher parasite densities, as much of the labeled antibody will have been captured by the test band before reaching the control (WHO, 2019).

3.5 MOLECULAR METHODS FOR MALARIA DETECTION

The most sensitive methods for malaria diagnosis are based on molecular detection of parasite DNA or RNA. It has been demonstrated that when the malaria incidence in endemic areas decrease in previously more high endemic areas, a large proportion of individuals harboring malaria parasites are asymptomatic with a low parasitaemia, often below the detection limit of both RDT and microscopy. These individuals, however, still constitute a risk for further transmission (Okell, 2012, McMorrow, 2008). Also in places with higher malaria endemicity, low parasitaemias are common among adults and in chronic infections (Okell, 2012).To diagnose these malaria infections, there is a need for molecular methods with high sensitivity (MalERA, 2011, Moonen, 2010).

Conversely, parasite nucleic acids are detected using polymerase chain reaction (PCR). Although this technique is more sensitive than smear microscopy, it remains of limited utility for the diagnosis of acutely ill patients in the standard healthcare setting. Moreover, PCR results are often not available fast enough to be of value in establishing the diagnosis of malaria infection. PCR is most useful for confirmation of the species of malarial parasites after the diagnosis has been established by either smear microscopy or RDT (CDC, 2018).

3.5.1 Species-specific PCR for Diagnosis of Malaria

Plasmodium genomic DNA is extracted from 200ul whole blood using the QIAamp Blood kit (Cat. No 29106; Qiagen inc, Chatsworth, CA) or a similar product that can yield similar concentration of genomic DNA from the same volume of blood. Detection and identification of Plasmodium is done with a Real-time PCR assay as described by Rougemont and colleagues(2004). This is a dual duplex assay that detects both P.falciparum and P,vivax in one reaction, and P.malariae and P.ovale in a parallel reaction, using species-specific TaqMan probes. In cases whereby infection by more than one Plasmodium species is suspected, there is an option to use a conventional nested PCR assay (Snounou et al, 1993) that has an improved resolution of mixed infection compared to the real-time PCR assay (CDC, 2018).

PCR is rated as the most sensitive method for detection of malaria parasites with detection limit between 0,5-10 p/µL (Singh and Daneshvar, 2013; Alemayehu et al, 2013; Proux et al, 2011).Over the years many PCR methods for parasite detection have been published. Snounou and colleagues (1993) established one of the earliest nested PCR methods targeting the 18S ribosomal(r) RNA gene of the four major human Plasmodium species. Rougemont and colleagues (2004) and also Kamau et al (2011) later developed probe based real-time PCRs (qPCR) which is also targeting the 18S rRNA genes. Steenkeste et al.(2009) published a nested PCR method which targets the Cytochrome b (Cyt b) gene in the mitochondrial DNA (Mt-DNA). PCR methods can distinguish between all human Plasmodium species, identify mixed infections and also benefit anti-malarial drug efficacy monitoring, vaccine studies, and screening of vulnerable populations such as pregnant woman (Nosten, 2007)]. The possibility of application of PCR methods on extracted DNA from dried blood spots preserved on filter papers has made them applicable for screening of large series of samples collected in endemic areas (Bereczky, 2005, Hsiang, 2010).

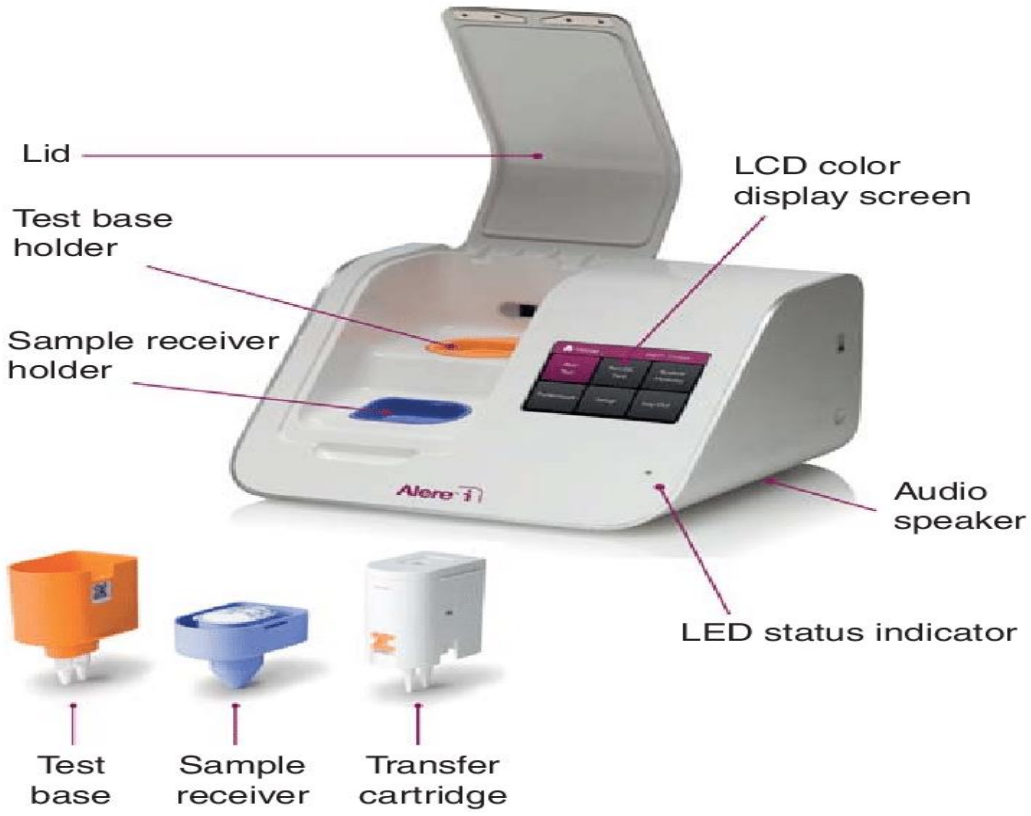

Figure 7: Molecular Diagnostic Platform

3.6 Data collection methods

At enrolment, a questionnaire focused on socio-demographic characteristics, history of fever, and use of insecticides treated nets (ITNs), and intermittent preventive therapy (IPTp).

Information was collected through in-depth interviews with the Medical superintendent of Government Regional Hospital Makeni, Doctors in the maternity wards, Nurses and midwives at the antenatal clinic and staff of pathology department. Separate interviews with the DMO and the consultant pediatrician were arranged to give these senior district level medical officers an opportunity to express their experiences and opinions independently as key decision-makers by virtue of their positions. The interviews with the DMO, as well as FGDs with pregnant women addressed opinions about the rationale and practicability of the IPTp strategy, the availability and usefulness of the national IPTp guidelines.

Smears for malaria were considered negative if no parasites were detected in 100 high power fields. An expert microscopist read 10% random sample of positive and negative slides for quality control. When >=20% of discrepancy in the results was found between the regular microscopists and the expert microscopist when comparing the positive and negative results, all the slides were read again. The rapid diagnostic tests were conducted concurrently and results recorded as either positive or negative after following the standard operating procedure as outlined by the manufacturer.

CHAPTER FOUR: RESULTS

This chapter starts with the results of the descriptive analysis focusing on the socio-demographic characteristics of the study participants. The chapter includes a report of the findings for all six Research Questions and hypotheses. The chapter includes tables and values to illustrate the results.

In sub-Saharan Africa, >50 million pregnant women are exposed to the risk of malaria yearly (Dellicour et al, 2010). The main complications of malaria in pregnancy (MiP) include maternal anemia and low birth weight (LBW), which is associated with higher morbidity and mortality in infancy (Brabin, 1983, Desai et al, 2007).

The prevalence of gestational malaria in this study is 20.4% using the RDT. A comparative analysis was also conducted using peripheral blood microscopy, the positive cases was 10.5%. This could be as a result of the impact of placental sequestration and submicroscopic infection.

The risk of malaria in Sierra Leone is present throughout the country, including urban areas, and the risk is present at all altitudes. The incidence of Plasmodium falciparum Malaria is greater than 85% (IAMAT Sierra Leone, 2019). Although the country has launched several initiatives, such as insecticide treated nets and IPTp-SP use among pregnant women (Gosling et al, 2014,Benneth et al, 2014), the rate of non-use of these cost-effective methods is high and needs further investment to ensure better efficacy of these programs. In 2015, the President's Malaria Initiative (PMI) launched a six-year strategy, setting forth a bold and ambitious goal for malaria prevention and control in member countries. Two years later, in 2017, Sierra Leone was selected as a PMI focus country in the fiscal year (FY) 2017 (PMI , 2017). In order to achieve the target of universal coverage for IPTp stated in the PMI plan, it is necessary to continuously assess the level of utilization of IPTp-SP and its covariates, which should be used to guide policy making on the prevention and control of malaria in pregnancy. This study's objective was therefore to assess the correlation between malaria in pregnancy and socioeconomic indicators.

Disease control strategies in this vulnerable group have focused on athree-pronged approach: intermittent preventive treatment (IPTp) using sulfadoxinepyrimethamine (SP) in the second and third trimester, use of insecticide treated nets (ITNs) provided at antenatal booking, and effective case management of malarial illness and anaemia (WHO/AFRO, 2004). Deployment of these

control strategies is determined by the characteristics of the transmission settings. Effective case management is the primary strategy in areas with low or unstable transmission such as Asia, Latin America and parts of the horn of Africa where most malaria infections eventually result in clinical malaria because of low levels of acquired anti-malarial immunity, whilst in higher or stable transmission areas high levels of acquired immunity in adults means most *P. falciparum* infections remain asymptomatic, yet can have harmful consequences form other and newborn. In these settings, both case management and prevention strategies are used (Bardaji et al., 2008, Menendez et al., 2007, Newman et al., 2003b,Nosten et al., 2004, WHO/AFRO, 2004).

4.1 SOCIO-DEMOGRAPHIC CHARACTERISTICS OF THE PREGNANT WOMEN

Age group	Frequency	Percent
10– 19	405	27.0
20 – 24	465	31.0
25 – 29	418	27.9
30 – 34	122	8.1
35 – 39	81	5.4
40 – 45	9	0.6
Total	1500	100.0

4.2 PREVALENCE OF MALARIA

Malaria Test	Frequency	Percentage
Negative	1,194	79.6%
Positive	306	20.4%
Total	1500	100%

Among pregnant women attending their first ANC visit, 27% were aged between 10 and 19 years and therefore classified as Teenage pregnancies according to the WHO definition. 136 (44.4%)

of the positive cases are adolescents who are also having their first ANC visit. The overall prevalence rate of gestational malaria in this study is 20.4%.

4.3 ADOLESCENT PREGNANCY

The high proportion of adolescent pregnancies (27%) in the study population is in line with Demographic and Health Surveys(DHS) data, indicating that the majority (44.9%) of 19-year-old women had already experienced childbearing. Adolescents were more likely to be diagnosed with malaria and anaemia at their first ANC visit, as reflected by the Odd ratios (ORs) of 2.1 and 1.7, respectively. This might be partially explained by the high number of primipara, who are known to be more susceptible to malaria compared to multipara (Statistics Sierra Leone, 2019), in this group. In the Sierra Leonean setting, pregnant adolescents suffer a whole lot from stigma and social alienation. It is often thought that the lack of social support, rather than physical immaturity, is the major contributing factor for increased maternal deaths in this group (November & Sandall, 2018). This tends to highlight the vulnerability of the adolescent group. It is therefore imperative to explore the possibility setting up a framework for more social support for pregnant adolescents.

Teenage pregnancy is one of the universal problems that affect the lives of adolescent and young girl's. Adolescent pregnancy often risks girls health and cause impediments to their, social, economic and political progress and empowerment of adolescent and young girls in Sierra Leone. All Adolescent pregnancies irrespective of the outcome have adverse consequences for the girls, their parents and the community. At the national level children bearing children has been identified as one of the major causes of obstetric fistula in women and a major determinant of high maternal and child morbidity. Furthermore, the incidence of teenage motherhood is usually higher in rural localities than in urban localities, with Freetown being the city center having the lowest percentage of adolescent mothers. High level of maternal and infant mortality constitutes one of the consequences of teenage pregnancy and mother hood in Sierra Leone (UNFPA, 2011).

The perceptions of the members of the community as per why teenage girls become pregnant cover a wide variety of factors. The three major reasons are: poverty of the parents or the foster parents, the attitude of adolescents towards emulating their peers and lack of control by single parents on the teenagers. Teenage mothers tend to have less access to ante-natal assistance from

medical and health personnel, but more access to traditional birth attendants and community health workers. These findings could be due to the distance or cost of transportation which may negatively affect the already strained purse of the pregnant teenagers. It is certain that all teenage pregnancies, irrespective of the outcome, have adverse consequences for the girls, the parents and the communities. Firstly, the education of the girls is halted prematurely. For many of adolescents, this occurs before the completion of their primary education. The idea of dropping out of the school system destroys their prospects of further educational advancement, and impairs their social, economic and political empowerment in future. Secondly inability to complete their primary or secondary education means considerable financial losses to parents, relatives and guardians who paid for the education of these girls. The negative outcomes of disappointments, frustrations and trauma are not only limited to the girls themselves, but are also experienced by their parents and the communities in which they live. At the national level, teenage childbearing has been identified as one of the main causes of obstetric fistula in women, and a major determinant of high maternal and child morbidity and mortality, which in turn triggers the need for additional investments in health and medical facilities and services. Since many of the teenage mothers are mainly illiterate or semi-illiterate, untrained, unskilled and therefore unemployable, they tend not to make any meaningful contribution to national development. Consequently, they are labeled or considered as liability to the nation, their communities, and their parents. They can rightly be regarded as a potential source of social instability in the country (UNFPA, 2011).

At the international level, Article 1 of The United Nations Convention on the Rights of the Child, which Sierra Leone signed in 1990, defines a child as follows: "A child means every human being below the age of eighteen years unless under the law applicable to the child, majority is attained earlier". At the national level, the 1991 Constitution of Sierra Leone defines the age of majority as 18 years. Hence there are a lot of children bearing children (UNFPA, 2011).

The most important reason for early girl-child marriage is household poverty ravaging the country. Poverty affects the household as a whole, but more importantly the mothers, who are the home managers, and are saddled with responsibility of taking care of the child in many homes. Hence lack of money limits her ability to educate, feed, and provide for the welfare of the children. Consequently, the only option for both mother and daughter is to accept financial support from any man who shows an interest in the daughter, with marital intentions. Fewer

children of teenage mothers, than adult, enjoyed the protection of insecticide treated bed nets. As with the treatment of malaria, the present coverage with insecticide treated bed nets is relatively low (UNFPA, 2011).

Figure 8: Teenage pregnancy

4.4 EFFECTS OF SUBMICROSCOPIC INFECTIONS ON MATERNAL AND INFANT OUTCOMES

A longitudinal cohort study including 1037 pregnant women from Benin evaluated the effect of submicroscopic *P. falciparum* infections on maternal and infant outcomes (Cottrell, 2015). The study was conducted between 2008 and 2011, and the enrolled pregnant women were followed up monthly until the time of delivery. At inclusion, polymerase chain reaction (PCR) and microscopy detected malaria parasites from peripheral blood in 40% and 16% of women, respectively. The proportion of infections declined markedly after two doses of IPTp-SP but rebounded to 34% (by PCR) at delivery. Submicroscopic infections during pregnancy were associated with lower mean haemoglobin irrespective of gravidity, and with increased anaemia risk in primigravidae. Prospectively, submicroscopic infections at inclusion were associated with

significantly increased risks of LBW in primigravidae and premature births in multigravidae. In this study, parasitaemia occurred frequently during pregnancy, but routine microscopic and (histidine-rich protein 2) HRP2-detecting RDTs failed to detect most malaria episodes (WHO, 2015).

4.5 OBJECTIVE

1-To assess the level of utilization of malaria preventive measures among pregnant women attending ANC at Government Regional Hospital Makeni, Sierra Leone

Use of ITN	Frequency	Percent
Yes	966	64.4%
No	534	35.6&
Total	1500	100.0

966 (64.4%) of pregnant women attending ANC use the Insecticide treated nets while 35.6% do not use the ITNs. This shows that use among pregnant women remains well below the international target for 2010 of 80% coverage. Despite free distribution, the use of nets remains low in many places or even tends to decline after free distribution. Insecticide-treated bed nets (ITNs) have also been shown to provide substantial protection against malaria, however the sustainable use of ITNs needs regular retreatment of the insecticide since they lose efficacy after some time (Wakgari et al, 2008).Nearly all experts agree that insecticide treated mosquito nets (ITNs) are a lifesaving intervention, supported by strong evidence from appropriately conducted trials that show ITNs to be very effective at preventing all-cause child mortality and malaria morbidity in children and pregnant women (Lengeler, 2004,Gamble et al, 2009). Under program conditions, ITNs have also been associated with significant decrease in malaria morbidity and all-cause child mortality (Noor et al, 2008, Terlouw et al, 2010, Fegan et al, 2007, Kleinschmidt et al, 2009)

It is also important to note that in areas with high household coverage, ITNs confer protection to individuals not using them through community-level protection from reduced vector densities

(Hawley et al, 2003,Gimnig et al, 2003). A systematic review by Carol et al (2007) also shows that ITNs were associated with some important health benefits for pregnant women and their babies. Women of low gravidity randomised to ITNs delivered fewer LBW babies and were less likely to experience fetal loss (stillbirth or miscarriage). Although the latter was not a primary endpoint in the trials, it is an vital outcome. No significant decrease was observed in pre-term deliveries in the single trial that assessed this outcome. The consistent decrease observed in the miscarriage and stillbirth rates suggests that the effect attributed effect malaria on fetal loss may actually be underestimated in malaria-endemic Africa, where most women remain asymptomatic when infected with P. falciparum.

WHO currently recommends that women in malaria-endemic areas of Africa use both IPTp-SP and ITNs in pregnancy for prevention of malaria. One of the two trials conducted in western Kenya assessed the effect of ITNs and IPTp-SP simultaneously, using a factorial design. This trial showed that ITNs provided benefits in primigravidae when used alone, but it did not demonstrate additional benefits of the combined interventions over either of the single interventions (Njagi, 2002, Njagi et al, 2003). It is also noteworthy that the main benefit of ITNs in women protected by IPTp-SP may thus occur after birth through protection of infants from malaria, since infants ideally share sleeping space with the mother for the first several months to years (ter Kuile et al, 2003).

The result extrapolation from the three cluster-randomised trials to predict the potential impact of programmes that distribute ITNs to individual pregnant women as part of antenatal care should be done with caution. Firstly, the distribution of ITNs as part of antenatal care will leave most women exposed to malaria in the first third or half of pregnancy, when the risk of peripheral malaria parasitaemia is at its peak(Brabin, 1983). By contrast, most women in the cluster-randomised trials became pregnant after ITNs were distributed and were as such protected throughout pregnancy. Secondly, the effect of ITNs in the cluster-randomised trials reflects the combined effects of personal protection (individual barrier protection) and area-wide reductions in malaria transmission (community or mass effect) (Hawley, 2003, Howard et al, 2000, Binka et al, 1998). It is a possibility that the mass killing effect on mosquito populations in areas with a high ITN coverage will result in stronger treatment effects of ITNs than can be achieved with individual nets. It is also likely that the community effect in the cluster-randomised trials may have resulted in a slight underestimation of the magnitude of the effect of ITNs because women

living in control households from adjacent villages not using ITNs will have benefited from the area-wide reductions in vector populations, as has been revealed for effect estimates in young children (Hawley, 2003). Similar considerations from the Thailand-Myanmar border apply to the trial comparing ITNs with untreated nets (Dolan et al,1993). Although, this trial randomised individual women, all trial participants were living in the same densely populated refugee camps and some mass effect by the ITNs cannot be excluded.

Another trial from western Kenya by Njagi and co-researchers is informative in this respect, as it is a trial that compared the effects of ITNs versus no nets using simple randomisation by individual in an area with low ITN coverage (little or no mass effect) (Njagi, 2002,Njagi et al, 2003). This trial and the community-randomised trial by ter Kuile et al. (2002) were conducted simultaneously in contiguous areas with similar malaria transmission at baseline, and similar socioeconomic and educational status and ethnicity of the trial population. The effect estimates were similar between the two trials (in women not randomised to IPTp-SP), which suggests that ITNs may work equally well when provided to individuals as part of antenatal care in the second trimester or when provided to entire communities (D'Alessandro et al, 1996). These observed beneficial effects of ITNs during the first few pregnancies, together with the absence of apparent adverse effect to the developing fetus, the potential beneficial effect on the infant when the net continues to be used after birth (Lengeler, 2004), and the potential for ITNs to reduce malaria transmission through a mass killing effect on mosquito populations, support the current recommendations from WHO to make ITNs available for pregnant women in all regions with stable malaria transmission throughout sub-Saharan Africa, regardless of the degree of malaria transmission intensity. It was discovered that not all those who own nets use them (Dolan et al, 1993) and also the level of utilization is also affected by seasons.

Women aged 10-25 years are largely primi-para and had to receive intense education and care during antenatal care services. This special attention if attributed to this age category may most likely enhance their level of acceptability and usage of ITNs and thereby trigger in a reduction in the incidence of gestational malaria associated with primigravida compared to older women who might not be primipara.

Four randomized trials comparing ITNs with no nets shows significant beneficial effects of ITNs on birth weight and fetal loss in the first few pregnancies in areas with moderate to intense malaria transmission in sub-Saharan Africa. These findings are consistent with a non-randomised

trial in Southern Tanzania, on the effect of socially marketed ITNs conducted in an area with intense perennial malaria transmission (Marchant et al, 2002), and with an excluded randomised controlled trial from The Gambia, which has lower and highly seasonal malaria transmission (D'Alessandro et al, 1996).

4.5.1 Intermittent Preventive Treatment in Pregnancy(IPTp) using Sulfadoxine-pyrimethamine

Intake of SP	Frequency	Percent
Yes	1001	66.7
No	499	33.3
Total	1500	100.0

About 66.7% (1001) of the women attending ANC were using using Sulfadoxine-pyrimethamine (SP) for preventive treatment of malaria in pregnancy while 33.3% (499) of the pregnant women were not taking the malaria preventive treatment. This is far below Roll back malaria target of 80% coverage of less than or equal to 2 doses of IPTp-SP.

Despite one to two decades of implementation of IPTp-SP within national programmes in sub-Saharan African countries, the coverage of this proven intervention for protecting pregnant women is still low (van Eijk et al., 2013). Some of the reasons which have been extensively reported include weak health systems, a lack of reasonably accurate monitoring data, and inadequate use of data for managing programmes at local level (Webster et al., 2013b, Webster et al., 2013a, Hill and Kazembe, 2006, Hill et al., 2013). SP when given as IPTp to asymptomatic parasitaemic pregnant women was associated with a high cure rate and marked increases in the level of haemoglobin concentrations. These findings are consistent with previous findings that revealed IPTp as having a marked beneficial impact on moderate-to-severe anaemia in Mali (Kayentao et al., 2005).More so, despite growing concerns about the impact of SP resistance in eastern and southern Africa, it is established that SP remains effective at clearing existing infections and improving haemoglobin level when provided as IPTp to asymptomatic pregnant women in Mali and Burkina-Faso. SP has many attributes that makes it an excellent candidate for IPTp, and it is therefore likely that it could remain the drug of choice for IPTp in this region

for the foreseeable future. However continued monitoring of SP resistance over the next couple of years in conjunction with monitoring of IPTp-SP effectiveness on birth parameters is essential.

Thus, although much evidence exists on the efficacy of IPTp, there is little evidence on how best to deploy it at programmatic conditions. Hence based on the research findings from a meta-analysis, WHO guidelines now recommend one IPTp-SP dose at each scheduled ANC visit from the second trimester (WHO, 2013). If no dedicated action is taken, this recommendation would face the same coverage issues as before.

4.5.2 Objective 2 -To examine the relationship between income of pregnant women and risk of malaria infection

All (100%) the pregnant women participating in this study are living below $1.90 a day and hence categorized as extreme poverty according to World Bank definition (World Bank, 2019). Consequently, they were categorized into three in terms of their level of income.

4.5.2 Income of Pregnant Women

Income	Frequency	Percent
Poor	500	33.3
Average	834	55.6
Least Poor	166	11.1
Total	1500	100.0

Quantitative assessment of the participants indicate prevalence of poverty which remains widespread in the country (more than half of the population lives in poverty, according to the latest Sierra Leone Integrated Household Survey (SLIHS)) (World Bank, 2019).Based on information about basic needs collected from 15 low-income countries, the **World Bank** defines the extreme **poor** as those living on less than $1.90 a day. The country remains at a “high risk” of debt distress for both the external public debt and also the overall public debt. The current account deficit of the balance of payments is expected to have narrowed to 11.4% of GDP in 2019 helped by the slowdown in imports, which consequently will more than offset the

continued sluggish exports. Until the Ebola outbreak in May 2014, Sierra Leone was seeking to attain the level of middle-income status by 2035, but the country is still bedeviled by post-conflict attributes of high youth unemployment, corruption and weak governance. The country continues to face the issues of enhancing transparency in managing its natural resources and creating fiscal space for development. Problems of poor infrastructure and widespread rural and urban impoverishment persist despite remarkable strides and reforms(World Bank, 2019).

Six studies included in this review reported the nature of the correlation of income status with the occurrence of malaria infection in SSA (Alemu et al, 2011,Gahutu et al, 201, Kibret et al, 2010, Omer et al, 2011,100,109). A high prevalence of *P.falciparum* parasitaemia was seen in preschool children coming from households with low monthly income <5000 Rwanda Francs (equivalent to <5.92 US dollars) compared to those who came from households with average monthly income >5000 Rwanda Francs in Rwanda (Gahutu et al, 2011). Similarly, a study in Cameroon reported increased odds of *Plasmodium* infection in pregnant women with monthly income <28, 000 CFA franc (equivalent to <51.43 US dollars) compared to those with monthly income >28000 CFA franc(Tonga et al, 2013). In the same vain, the prevalence of malaria in Ghana was also higher among pregnant women with a weekly income<200,000 Cedis (equivalent to <20 US dollars) compared to those with a weekly income >200,000 Cedis (Yatich et al, 2009). Furthermore, in Sudan, the odds of *Plasmodium* infection among pregnant women having low income was also found to be two times as likely as the odds of infection in pregnant women with high income (Omer et al, 2011). A study in Ethiopia also found increased odds of *Plasmodium* infection among adults with monthly income <31.25 US dollars compared to those with monthly income >62.5 US dollars (Alemu et al, 2011). However, another study in Ethiopia showcased an increased prevalence of malaria with an increase in annual household income status (Kibret et al, 2010).

A summary estimate based on the five studies showed that a one US dollar decrease in the monthly income of individuals is associated with a 2% increase in the odds of *Plasmodium* infection.

4.5.3 Wealth and malaria

SES (defined in this study by wealth index, occupation and educational level) is closely associated with the income and disposable income or expendable funds for the pregnant woman to seek healthcare needs. The household wealth index has a direct correlation with the capacity of the pregnant woman to purchase and consume nutritious food, while the occupation determines the disposable income (dispensable funds) available for the pregnant woman to prevent malaria or to engage in formal health-seeking behavior if peradventure malaria occurs.

So instead of looking at the independent effect of housing, education, occupation, and income measures on malaria, some studies assessed the combined impact of these factors. The factors included household construction materials (windows, walls, floors, roofs), possession of assets (fridge, car, bicycle, motorbike, television, radio and mobile phone, electricity at home, bed net, animals), water source, type of toilet, education, and occupation of household. Studies converted these different indicators of SES into a single socioeconomic score/wealth index using principal component analysis and treated as a single variable (wealth). Thus, the index provided maximum discrimination in the socioeconomic status of individuals among households.

After determining the weights for each socioeconomic indicator in the index using principal components analysis, the scores in the index were grouped into different socioeconomic categories based on their weights. However, the number and type of socioeconomic indicators used in developing the composite index and number of categories of the socioeconomic factor are different among studies. Many studies grouped the wealth index into five (n = 19)(1 = poorest to 5 = least poor) (Njau et al 2014,Asante et al, 2011,Asante et al, 2013,Brooker et al, 2004, Chaponda et al, 2015,Elmardi et al, 2011,Gosoniu et al, 2012,Graves et al, 2009,Keating et al, 2009, Mathanga et al, 2015,Matthys et al,2006,Pullan et al, 2010, Sezi, 2014, Skarbinski et al, 2012, Somi et al, 2008,Sonko et al,2014 ,Steinhardt, 2013, West et al,2013, Houngbedji et al, 2015) some into four (n = 4) (1 = poorest to 4 = least poor) (Coleman et al, 2010,Ernst et al, 2009,Temu et al, 2012,Yamamoto et al, 2010) and some into three (n = 10)(1 = poor, 2 = average, 3 = least poor) (Mmbando et al, 2011,Clarke et al, 2001 Haji et al, 2016, Homan et al, 2016, Kreuels et al, 2008, Njau et al, 2006, Ronald et al, 2006, Snyman et al, 2015, Wanzirah et al, 2015, Woyessa et al, 2013) categories (i.e. Socioeconomic groups). Many studies also treated the wealth index as a continuous variable(n = 11) (Bousema et al, 2010, De Beaudrap et al, 2011,De Castro and Fisher,2012,Florey et al, 2012, Graves et al, 2009, Kyu et al, 2013, Ronald

et al, 2006, Somi et al, 2007,Somi et al, 2008, West et al, 2013,Winskill et al, 2011). Three of the studies treated wealth both as a categorical and continuous variable (Graves et al, 2009, Somi et al, 2007, West et al, 2013). In summary, 41studies evaluated the relationship between wealth index and the odds of Plasmodium infection. Of the 41studies, 38 were included in the meta-analyses that summarized the relationship between wealth and malaria. A summary analysis of 30 studies, which treated wealth index as a categorical variable, showed a 20% reduction in the odds of Plasmodium infection with one unit increase in socio-economic group or wealth index category of individuals (Mmbando et al, 2011, Njau et al 2006,Asante et al,2011,Brooker et al, 2004,Chaponda, et al, 2015, Charlwood et al, 2001,Clarke et al, 2001, Coleman et al, 2010, Elmardi et al, 2011, Ernst et al, 2009,Gosoniu et al, 2012,,Graves et al, 2009,Haji et al, 2016,Keating et al, 2009, Mathanga et al, 2015, Matthys et al, 2006, Njau et al, 2006,Pullan et al, 2010, Ronald et al,2006, Sezi et al, 2014,Skarbinski et al, 2012, Snyman et al, 2015, Somi et al, 2008,Sonko et al, 2014, Steinhardt et al, 2013, Temu et al, 2012,Wanzirah et al, 2015,West et al, 2013,Woyessa et al, 2013,Yamamoto et al, 2010,Houngbedji et al, 2015).A summary analysis of the eleven studies, which treated wealth index as a continuous variable also showed that the odds of Plasmodium infection decreased by 0.83unit with every one unit increase in the wealth index (Bousema et al, 2010,De Beaudrap et al, 2011, De Castro and Fisher, 2012,Florey et al 2012,Graves et al, 2009,Kyu et al, 2013,Ronald et al, 2006,Somi et al, 2007,Somi et al, 2008,West et al, 2013,Winskill et al, 2011).The remaining two studies, which treated wealth as categorical variable but were not included in the meta-analysis due to lack of sufficient data also showed a trend of lower odds of Plasmodium infection with an increase in the wealth index of individuals(Asante et al, 2013,Gosoniu et al, 2012).Gosoniuet al.(2012) reported significantly lower odds of malaria among individuals who were in the least poor or average socioeconomic category as compared to those in the poorest category. Asanteet al.(2013) also reported a decreased hazard ratio of Plasmodium infection among individuals who were in the group of least poor socioeconomic status as compared to those who were in the poorest socioeconomic group. However, Homanet al.(2016) reported increased prevalence of malaria among individuals with high socioeconomic group as compared to those in the low socioeconomic group. Poverty can also be observed through social indicators like illiteracy level.

4.5.4 Objective 3 -To determine the association between education of pregnant women and level of compliance to malaria control measures

4.5.5 Women Educational Level

Level of Education	Frequency	Percent
No Education	606	40.4
Primary Education	417	27.8
Secondary Education	298	19.9
Tertiary Education	178	11.9
Total	1500	100.0

40.4% (606) of the participants have no formal education. The study also showed that lack of education was a significant predictor of gestational malaria. This agrees with other studies conducted (Afulani, 2015; Gupta et al., 2014; Kim et al., 2018; Mbu et al., 2014; Yusuf et al., 2016). Educational level is associated with the likelihood of seeking appropriate malaria prevention and treatment during pregnancy. Educated women have a tendency of complying with the WHO recommended four to eight ANC visits than less educated women (Afulani, 2015; Gupta et al., 2014; Kim et al., 2018). During the ANC visits, the pregnant women interact with the healthcare workers who advise them on best practices for a successful gestation period. In addition, education was likely to determine the neighborhood where pregnant women reside as well-educated women may not dwell in areas not befitting their status. The general consensus is that with increasing education, most women are most likely to engage in activities that will decrease their risk of contracting Plasmodium infection especially in pregnancy. Axame et al., 2016, reported that level of education significantly influenced ITN ownership ($p=0.003$) and utilization (0.020).

4.5.6Objective 4 -To examine any relationship between employment of pregnant women and incidence of malaria in pregnancy

Employment Status	Frequency	Percent
Employed	330	22.0
Unemployed	1170	78.0
Total	1500	100.0

Employment Status	No of Positives	Percent
Employed	502	33.5
Unemployed	998	66.5
Total	1500	100.0

1170 (78%) of the pregnant women in this study are unemployed and hence may have to depend on their family, husband or boyfriend for sustenance. Moreover, 66.5% of the unemployed women are positive for malaria in pregnancy. This also predicts a positive correlation between employment status and incidence of pregnancy associated malaria.

4.5.7Occupation and malaria

The origin of the disease (malaria) is poorly documented, but archaeological excavations suggest that the expansion of malaria would coincide with the emergence of agriculture/agricultural practices. Retrospective genetic studies demonstrate that malaria has significantly affected humans since the era of agricultural development in Africa and the Near East (Laderman, 2002). Malaria burden also is posited to be linked with the occupation of individuals. Eleven studies assessed if the type of occupation of individuals is associated with the risk of contracting malaria in seven SSA countries. Seven of the studies were cross-sectional (Alemu et al 2011,Amuta et al, 2014, De Castro and Fisher, 2012,Kibret et al, 2010,Gahutu et al, 2011,Kalu et al,2012,Onyido et al, 2011), two were case-control (Ongecha et al,2006, Okebe et al, 2014), and the remaining two were longitudinal in design (Homan et al, 2016, Kreuels et al, 2008). Six of the studies compared the odds or prevalence of malaria between individuals with agricultural related activities

(farmers) and others (traders, civil servants, students, entrepreneurs). A summary analysis based on the six studies (three cross-sectional and three case-control) showed that the odds of *Plasmodium* infection increased among farmers, or children whose parents are farmers than individuals with non-agriculture related occupations. The study by Alemu *et al*. (2014) contributed close to 3/4 of the weight of the summary estimates of the studies that compared the odds of *Plasmodium* infection among farmers, or children with farming parents' versus those with a non-agriculture related occupation.

Another longitudinal study among infants in Ghana also revealed an increased incidence level of malaria among infants with mothers who farmed compared to infants with non-farming mothers (Kreuels et al, 2008). A study in Kenya showed an increased risk of malaria among people with outdoor occupation (Homan et al, 2016). However, De Castro & Fisher (2012) reported lack of significant difference in the prevalence of malaria between farmers and non-farmers in Tanzania(De Castro and Fisher, 2012). As the study by De Castro & Fisher (2012) did not report ORs/RRs estimates or provide raw data on the prevalence/incidence of malaria which was stratified by occupation status, it was excluded from the meta-analysis that estimated the odds of *Plasmodium* infection between farmers and non-farmers. Two other studies in Ethiopia and Nigeria also reported a lack of association between the prevalence of malaria and occupation status (Kibret et al, 2010,Onyido et al, 2011).

A summary analysis of 30 studies, which treated wealth index as a categorical variable, showed a 20% reduction in the odds of *Plasmodium* infection with one unit increase in socioeconomic group or wealth index category of individuals (Mmbando et al, 2011,Njau et al, 2014,Asante et al, 2011,Brooker et al, 2004,Chaponda et al, 2015,Clarke et al, 2001, Coleman et al, 2010,Elmardi et al, 2011, Ernst et al, 2009,Gosoniu et al, 2012,Graves et al, 2009,Haji et al, 2016,Keating et al, Mathanga et al, 2015,Mattys et al,2006,Njau et al, 2006,Pullan et al 2010, Ronald et al, 2006,Sezi 2014,Skarbinski et al, 2012, Snyman et al,2015, Somi et al, 2007,Sonko et al, 2014, Steinhardt et al, 2013, Temu et al, 2012,Wanzirah et al, 2015,West et al, 2013, Woyessa et al, 20 2013,Yamamoto et al, 2010,Houngbedji et al, 2015). A summary analysis of the eleven studies, which treated wealth index as a continuous variable, also showcased that the odds of *Plasmodium* infection decreased by 0.83 unit with every one unit increase in the wealth index (Bousema et al, 2010,De Beaudrap et al, 2011,De Castro and Fisher, 2012,Florey et al, 2012, Graves et al, 2009,Kyu et al, 2013, Ronald et al, 2006,Somi et al, 2007,Somi et al,

2008,West et al, 2013,Winskill et al, 2011). The remaining two studies, which treated wealth as categorical variable but were not included in the meta-analysis due to lack of sufficient data, also showed a trend of lower odds of *Plasmodium* infection with an increase in the wealth index of individuals (Asante et al, 2013,Gosoniu et al 2012). Gosoniu *et al* (2012) reported significantly lower odds of malaria among individuals who were in the least poor or average socioeconomic category as compared to those in the poorest category. Asante *et al*. (2013) also reported a decreased hazard ratio of *Plasmodium* infection among individuals who were in the least poor socioeconomic group as compared to those who were in the poorest socioeconomic group. However, Homan *et al*. (2016) reported increased prevalence of malaria among individuals with high socioeconomic group as compared to those in the low socioeconomic group.

4.5.8 Objective 5 -To establish any significant difference between prevalence at first antenatal visit and subsequent visits.

Most (77.7%) of the positive cases in this work are from women in their first ANC visit at the Government Regional hospital, Makeni and adolescents are majorly in this category.

The research in other places like Mimika shows that approximately two-thirds (64%) of first ANC visit women screened positive for malaria did not report fever, nor was fever suspected by the health worker. In the absence of screening, these women would not have been diagnosed for malaria. The incidence of sub-microscopic and asymptomatic infections has also previously been identified in Papua (Pava et al, 2016, Wylie et al, 2010).The malaria parasite prevalence in 1st visit ANC attendees in Mimika at 18.9% was slightly higher than that reported in 2008 for women at delivery in the same study site (Poespoprodjo, 2008).

By virtue of the fact that women at the first antenatal clinic visit are yet to receive their first dose of sulfadoxine-pyrimethamine for IPTp, malaria infection prevalence at this first visit is most likely to be an indicator of malaria transmission intensity in their community. Preventive strategies against pregnancy associated malaria in sub-Saharan Africa as recommended by the World Health Organization (WHO) are based on insecticide-treated nets (ITNs) and intermittent preventive treatment in pregnancy (IPTp) with sulfadoxine-pyrimethamine. These strategies are usually provided from the second trimester of pregnancy onwards because of the contraindication of sulfadoxine-pyrimethamine during the first trimester and the distribution of

ITNs to pregnant women at their first antenatal care (ANC) visit at approximately 4–5 months of pregnancy (WHO MPACS, 2016). Therefore, pregnant women may be insufficiently or not protected during the first trimester of pregnancy. Previous studies have also corroborated the fact that *Plasmodium falciparum* malaria infection was higher in early than in late pregnancy (Brabin, 1983, Huynh et al, 2015).

Reports from other studies on malaria in the first trimester of pregnancy has shown to be an important risk factor for miscarriage in Southeast Asia (McGready et al, 2012).Furthermore, that women were more likely to be infected with malaria during the first trimester than before pregnancy (21% vs 6.3%).Among the women who were screened for malaria during the first, second, and third month of pregnancy, the prevalence of malaria infection was 16.7%, 9.2%, and 11.2%, respectively presents the risk estimates (odds) of malaria infection throughout the first trimester of pregnancy after adjustment for gravidity. It was also observed that the risk of infection decreased at the end of the first month of pregnancy, it then remained constant until the end of the first trimester. While this trend was observed in multigravidae, the risk of malaria infection seemed to start decreasing only at the end of the first trimester in primigravidae.

This result was found regardless of gravidity that malaria infection was highly incident during the first trimester (incidence rate of 19.7 infections per 100 person-months). The outcome of this research is in accordance with previous publications (Brabin 1983, Walker et al, 2013, Moore et al, 2017), which suggested that malaria occurring at the time of placentation may be responsible for up to 70% of the total exposure to placental infection (Walker et al, 2013).Furthermore, women infected with malaria before conception remained more likely to be infected with malaria during the first trimester of pregnancy. This association may partially be explained by the fact that these women had the same level of exposure to malaria during both periods. Another explanation may be that some of the infections detected in the first weeks of pregnancy were subpatent infections (ie, under level of detection of microscopy and RDT) present before conception. In as much as the proportion of microscopic infections was higher during pregnancy than before pregnancy, it is believed that some of these pre-pregnancy infections were sub-patent and that they became microscopic because of changes in women's immunity and physiology during early pregnancy (Mor and Abrahams,2002. Mor et al, 2011), making women more susceptible to infectious diseases including malaria (Mor and Cardenas, 2010).

Some reports shown, interestingly, the fact that the risk of malaria infection decreased throughout the first trimester in multigravidae. The susceptibility of women to malaria during pregnancy is related to the selection of specific parasites, which have the capacity to sequester within the placenta (Placental malaria). Consequently, with successive pregnancies, a pregnant woman tends to develop increasing level of immunity to these parasites, allowing for a better control of infections (Duffy and Fried, 1999). Variant Surface antigen 2-CSA (VAR2CSA) is the specific variant of *P. falciparum* proteins expressed on the surface of infected erythrocytes (Fried et al, 2006) that allows placenta sequestration. All in all, prevalence of malaria parasitaemia decreased progressively during the antenatal visits, irrespectively of gravidity status, maternal age, marital status or clinic of attendance. Moreso, there was a drop in the number of febrile cases with each subsequent antenatal visit, the third visit having the least number of febrile women with malaria parasites (Accrombessi et al, 2018).

The challenge of tackling this public health menace however, remains how to access women in the first trimester of pregnancy. Therefore, pre-conceptional strategies against malaria in pregnancy may be of clear interest. A vaccine against VAR2CSA-parasites, which could elicit protective immunity prior to pregnancy to best protect women during early pregnancy, may be proposed as a complementary strategy to those already recommended like the use of ITN and IPTp-SP, during pregnancy. Such a vaccine is currently under evaluation (Tuikue & Deloron, 2015).

4.5.9 Objective 6 -To evaluate the association between gestational malaria and reduction of newborn birthweight

The aim of this review was to investigate the impact of malaria during pregnancy on low birth weight (LBW) across all gravidities by collating data from areas in sub-Saharan Africa with various levels of malaria transmission. The present review benefits from a wealth and variety of recently published data on malaria and low birth weight (LBW). Analysis of cross-sectional data on birth weight and survival from five areas in sub-Saharan Africa (SSA) showed that infant mortality is three times higher for LBW babies than for those of normal weight under the same conditions. The effects on neonatal mortality tend to be more pronounced, with a LBW baby

being nine times more likely to die in the first month of life than a normal-weight baby. The risk for mortality steadily increases as the birth weight decreases to below the LBW threshold, though there are still limited data to establish this fact. The risk of placental malaria and its associated morbidity with gravidity have been utilized in the development of a birth weight nomogram (Brabin et al, 1999), where malarious areas and zones of malaria transmission are based on odds ratios for an excess of LBW infants for primigravidae compared with those for multigravidae. Cross-sectional data on the associations between placental malaria infection and birth weight outcome have been collected for all gravidity groups since the late 1940s. A previous analysis showed that a baby is twice as likely to be born with a LBW if the mother has an infected placenta at delivery (Guyatt and Snow, 2001). This research outcome held true both for primigravidae only and for all gravidities. It was based on data from 14 studies from five countries dating from 1948 to 1998, with four of the studies excluding preterm births. Since completion of this analysis, a number of new studies have been published.

Despite the fact that maternal parasitemias have been used routinely to detect malaria during pregnancy, it is well known that peripheral parasitemias may remain below the levels of microscopic detection while parasites are harbored by the placenta (Shulman and Dorman, 2003). Hence, histological examination of the placenta is the most sensitive indicator of maternal infection (Shulman and Dorman, 2003). The examination can show signs of active infection (presence of infected erythrocytes in the intervillous space), past or chronic infection (malarial pigment), or both. This value suggests that approximately half of the LBW cases among those infected with placental malaria are due to malaria (the infected attributable fraction). Given a median prevalence of placental malaria of 26%, the population-attributable fraction (the percentage of all LBW cases due to malaria) is estimated to be 19%. In other words, one-fifth of the LBWs of babies born to mothers in areas where malaria is endemic are due to malarial infection of the placenta while the mother is pregnant. This compares to previous estimates of between 8 and 14% (Steketee et al, 1996). However, the data from an insecticide-treated bed net trial in Kenya has provided vital evidence that a reduction in the rate of malaria transmission can reduce the prevalence of LBW, with even greater reductions expected than those observed, given the anticipated reductions in the control arm through the effects of mass killing of mosquitoes (ter Kuile et al, 2003).

Low birth weight (LBW) reflects an intra-uterine growth retardation (IUGR) and preterm delivery, which are convincing indicators of infant morbidity (Desai et al, 2007, Largerberg et al, 2008, Rogerson et al, 2007, Lawn et al, 2014). LBW has been associated with infant mortality and poor cognitive development, and the occurrence of non-communicable diseases later in life (Lawn et al, 2014,Umbers et al,2011). In fact, LBW due to malaria is associated with up to 100,000 infant deaths each year in endemic countries (Steketee et al,1996,Guyatt et al, 2004). These adverse birth outcomes have been extensively associated with *P. falciparum* infection during pregnancy. Unlike *Plasmodium falciparum*, the *Plasmodium vivax* burden in pregnancy is less well described, and have been reported as having less impact in the newborn (Desai et al, 2007,Nosteen et al, 1999). Though, recent studies have presented the two species as similar threats to the mother and fetus (Mc Gready et al, 2012,Moore et al, 2017). Despite the efforts to reduce malaria the prevalence of these adverse birth outcomes remains high.

Prematurity is one of the adverse effects commonly associated with malaria during pregnancy (Umbers et al, 2011, Cottrell et al, 2015,Stanisic et al, 2015). It usually correlates with infections occurring during the third trimester of pregnancy and contributes to increasing the number of newborns with LBW, which is more likely to be observed in low transmission areas (Desai et al, 2007,Hartman et al, 2010). In MiP, birth weight reduction is the main adverse outcome observed in studies involving *P. falciparum* infections (Desai et al, 2007,Cottrell et al. 2015,Moore et al, 2017,Kalilani et al, 2010). In all these observations, malaria infection during pregnancy represents a critical morbidity that impacts newborns' weight. Some findings in Southeast Asia from Moore *et al*. that show that *P. vivax* infection is associated with small for gestational age (SGA) and *P. falciparum* infection with late preterm, although it could not be correlated with the time of infection (Moore et al, 2017). The reduction of newborns birth weight is multifactorial, and it can be related to socio-economic, environmental, nutritional, and clinic factors during pregnancy in Sub-Saharan Africa. In SSA, *P. falciparum* infections are predominant and, in general, there are several limitations in terms of the health systems that diagnose and treat malaria, and hence summed up with the high rate of co-infection with other diseases, such as HIV and tuberculosis. For pregnant women, the early diagnosis is essential to prevent adverse outcomes, but the number of pregnant women with malaria can be underestimated. Moreso, the reduction of birth weight has different etiologies.

Malaria is thought to reduce birth weight through a combination of systemic and local effects. First, malaria may affect birth weight through malaria-induced anemia or secondly, through placental infection (Bruce-chwatt, 1952). In this case, parasites directly cause a mechanical compromise of placental circulation or indirectly interfere with placental functions and/or induce pathological lesions (Walter et al, 1982, Galbraith et al, 1980). Both malaria-induced anemia and placental malaria are believed to mediate reductions in birth weight primarily through intrauterine growth retardation (IUGR) (Watkinson et al, 1985). This analysis classified newborns as normal birth weight ($\geqslant$2500 g, regardless of gestational age) or LBW (<2500 g). LBW may be due to prematurity, IUGR, or both. LBW babies were further classified as premature-LBW (<2500 g and <37 weeks in gestation) or IUGR-LBW (<2500 g and $\geqslant$37 weeks in gestation), as reported by Steketee et al (1996). Some malaria-infected placentas may present with features that are likened to the condition called massive chronic intervillositis, and these placentas are associated with a significant reduction in birth weight and gestational age (Ordi et al, 1998). The results of this study show that inflammatory infiltration of the intervillous spaces was associated with a reduction in birth weight by close to 0.5 kg, particularly when mononuclear cells were highly increased.

4.6 STUDY IN RELATION TO SOCIAL COGNITIVE THEORY MODEL

Study Results in Relation to the Social Cognitive Theory Model. The social cognitive theory used in this dissertation study makes it possible for the readers to understand the essence of using a theoretical model to study health behaviors at personal, behavioral and environmental levels. The variables in this study expressed these three levels of interaction. The SCT model describes the relationships between individuals, their behaviors and the environment and how these interact to define human behaviors (Nouwen et al., 2009; Omona, 2009; Tiemey et al., 2011). The consideration of these tripartite factors during the design of malaria intervention programs elaborates an inclusive package that will deliver the goals and objectives of such interventions. At personal level, the pregnant woman takes the lead in preventing malaria occurrence. The knowledge of malaria and its prevention methods are critical in applying the preventive measures. Knowledge about malaria has a direct relationship with education and wealth (NMIS, 2015).

The behavioral components of the SCT that were examined in this study are health-seeking behavior towards ANC visit. The WHO (2017b) recommended that the pregnant woman should attend between four to eight ANC sessions during pregnancy. This ANC visit is a platform that encourages interaction with health workers to identify and resolve any impending pregnancy complications like malaria, so as to improve pregnancy outcomes. Pregnant women of higher socioeconomic status, education, and knowledge of the importance of ANC visit were found to attend at least four ANC (Afulani, 2015; Gupta et al., 2014; Kim et al., 2018). The focused ANC session is a means of providing opportunities for the health workers to educate the pregnant women on pregnancy, its outcomes and complications and how to minimize them. The ANC sessions offer opportunities for health workers to update the pregnant woman's knowledge about pregnancy and its best practices. At the environmental level, many factors encourage pregnant women to accept and adhere to formal health-seeking behavior and thereby preventing gestational malaria. Nearest health facility type, region of residence, states of residence and religion are the environmental enablers that interact with personal and behavioral factors of social cognitive theory.

The Ministry of Health and Sanitation implements malaria control programs in all the regions in Sierra Leone. This includes distribution of free LLIN/ITN during focused ante-natal sessions, intermittent preventive therapy during pregnancy, and free anti-malaria medications for effective case management. However, these free medications and medical services are only available in government-owned health facilities. Private health facilities still charge user-fees for medical services rendered to the pregnant women. The occurence of frequent stock-out of anti-malaria medications in public health facilities (Kalanda et al., 2006) and the long delays encountered by pregnant women in such facilities may discourage them from engaging in such formal health-seeking behavior. The low-SES pregnant women may not be able to afford the high cost of medical services in private facilities especially in rural areas. Moreso, the type of nearest health facility plays a critical role in determining the choice of health-seeking behavior available to the pregnant women. Malaria interventions planners should therefore target low-SES pregnant women to reduce inequalities in the women's health care seeking behavior when malaria occurs. Furthermore, these low-SES women should be reached through health education sessions during focused ANC visits about maternal health and malaria in pregnancy.

CHAPTER FIVE: DISCUSSION

Since the first descriptions of the association between malaria and pregnancy in the early 20th century (Desai et al., 2007), malaria continues to be a burden on pregnant women and their offspring. This is in spite of tremendous investments made recently in the fight against malaria through the RBM led initiative to control and eliminate the disease. Among pregnant women living in sub-Saharan Africa, *P. falciparum* malaria remains one of the biggest public health issues aside several major challenges related to its control which requires continued attention to the diagnosis, treatment and prevention of malaria in pregnancy.

This thesis provides further insights into the socioeconomic impact, epidemiology and burden of malaria in pregnancy in an area with intense, highly seasonal malaria, typical for the Sahel region and suggests improvements in the implementation of the intervention putting into considerations the socioeconomic indicators. It highlights the need to scale-up the uptake of the recommended preventive interventions which include the use of ITNs and IPTp regimen using SP, the main drug-based prevention strategy in pregnant women. This discussion chapter is structured around specific objectives based on the main results of this thesis.

Sierra Leone has one of the highest maternal mortality ratios (MMR) in the world according to the latest estimates by the World Health Organization (WHO), but surprisingly little is known about the health status of pregnant women in the Sierra Leonean setting [TMM]. The main findings regarding pregnancy and child birth include high numbers of teenage pregnancies, high rates of anaemia and malaria among pregnant women and a trend of increasing institutional deliveries (SSL,2019).

Malaria infection during pregnancy is a well-known cause of impaired foetal growth due to disturbed development of the placenta, leading to low birth weight (LBW) (Umbers et al, 2011, Guyatt and Snow, 2011, Accrombessi et al, 2018). An infection during the second trimester has the most negative effect on birth weight due to a disturbed development of the placenta (Umbers et al, 2011). In malaria endemic areas such as Sierra Leone, pregnant women are more susceptible to be infected than non-pregnant individuals. This susceptibility reduces in subsequent pregnancies, and therefore primigravid women bear the highest risk. At the same time, it may be challenging to diagnose malaria during pregnancy in areas with high

transmission, since Plasmodium falciparum is often undetectable in blood smears due to sequestration of the parasite in the placenta.

Additionally, in endemic areas, infections are often asymptomatic, leading to chronic infections in pregnant women, which contribute to the development of anaemia and LBW (Fried et al, 2012). Estimates indicate that, in malaria endemic areas like Sierra Leone, 50% of LBW in infants can be attributed to malaria (Dellicour et al, 2010).

Strategies endorsed by the WHO to reduce malaria infections during pregnancy include the wide spread dissemination of bed nets, intermittent preventive treatment with Sulfadoxine/Pyrimethamine (IPTp-SP) and adequate case management of malaria infections in pregnancy. An analysis of existing ANC services in Sierra Leone showed that the lack of essential supplies and infrastructure at service delivery points combined with late first ANC visits is the main hurdle towards the provision of adequate ANC services (MOHS,2017-21,Koroma et al, 2017). During pregnancy, the use of RDTs is preferred over light microscopy due to the possibly diminished peripheral parasite density caused by sequestration of the parasites in the placenta (Koroma et al, 2017).

This study was based on six specific objectives and their corresponding research questions and hypotheses. To assess the level of utilization of malaria preventive measures among pregnant women attending ANC at Government Regional Hospital Makeni, Sierra Leone. The 66.7% of the women attending ANC were using Sulfadoxine-pyrimethamine (SP) for preventive treatment of malaria in pregnancy which is far below Roll back malaria target of 80% coverage. Therefore despite one to two decades of implementation of IPTp-SP within national programmes in sub-Saharan African countries, the coverage of this proven intervention for protecting pregnant women is still low (van Eijk et al., 2013). In the same vain, the level of utilization of ITNs in this study (64.4%) is still below the 80% coverage target of 2010.

5.1 BARRIERS TO UTILIZATION

World Health Organization (2018) identified the Key barriers to pregnant women receiving and using ITNs as women's low knowledge of ITNs, household or cultural constraints such as low social position or economic dependency, high cost and lack of availability of ITNs. These barriers in conformity with the key determinants of ITN use among gravid women assessed

from twenty seven (27) studies: age, marital status, education, employment status, knowledge about malaria/ITNs, and receipt of IPTp. Younger (under 19 years of age) single women were the least likely to use an ITN, same as women with lower education or lower knowledge of malaria or use of ITNs. Intervention studies which targeted these barriers included social marketing campaigns aimed at increasing the level of awareness, and delivery of free or heavily subsidized ITNs through campaigns, antenatal care (ANC) or community-based approaches which aimed to increase access.

Furthermore, among healthcare providers, key barriers to delivering ITNs to pregnant women were provider knowledge, provider attitudes, fees for services, health facility organization, and stock-outs of ITNs.

Implementation in settings with limited resources

The use of ITNs in pregnancy is recommended by all national malaria control programmes in sub-Saharan Africa, but use among pregnant women remains well below the international target for 2010 of 80% coverage, and even further from the 2015 target of universal coverage. The median use of an ITN the previous night among pregnant women across 37 countries for 2009–2011 was 35.3% (range, 5.2%–75.5%), with only 5 countries exceeding 60% by 2015 (Benin, Madagascar, Mali, Rwanda and Tanzania) (World Malaria Report, 2015). ITN use was higher in areas with both a high level of funds disbursement for malaria control and a lower per-head GDP. There have been reports in some places of ITNs being reallocated from routine delivery in ANC clinics to campaign delivery and policy makers have to make difficult decisions to balance costs with the benefits and impact of investments in ITNs. WHO's Malaria Policy Advisory Committee's recommendation is that routine ITN distribution (through ANC and EPI) should continue "before, during, and after" campaigns, and that this recommendation needs to be adopted by both Ministries of Health and donors alike. Future research should focus on improved methods to increase the coverage and use of ITNs among pregnant women especially those of low socioeconomic status.

There is also an urgent need for research to be focused on how best to implement the updated WHO guidelines for IPT-SP in pregnant women, and especially their integration with focused antenatal care through which IPTp-SP is delivered. This strategy requires a continuous identification and quantification of barriers to IPTp-SP high coverage at district and facility levels through operational research and good monitoring methods (Webster et al., 2013b).

Furthermore, in sub-Saharan Africa, preventive strategies against gestational malaria as recommended by the World Health Organization (WHO) are based on insecticide-treated nets (ITNs) and intermittent preventive treatment in pregnancy (IPTp) with sulfadoxine-pyrimethamine. These strategies are usually provided from the second trimester of pregnancy onwards because of the adverse effect or contraindication of sulfadoxine-pyrimethamine during the first trimester and the distribution of ITNs to pregnant women during their first antenatal care (ANC) visit at approximately 4–5 months of pregnancy. Therefore, pregnant women may be insufficiently or not protected during the first trimester of pregnancy (Accrombessi et al, 2018).

5.2 MONITORING OF SP RESISTANCE

There is also increasing level of resistance of malaria parasites to SP. One recent study in Malawi, which included specimens collected from a study site in Blantyre, has shown that greater than 90% of parasites contain markers of drug resistance. More evidence from research conducted in Tanzania suggests that SP may *increase* the risk of malaria. In the presence of the alarming levels of high-grade SP resistance in parts of eastern and southern Africa coupled with some evidences relating to the decreased effectiveness of SP in West Africa, there is a clear need to continue monitoring of SP resistance and to assess its effects on birth parameters. This is especially vital with the recent introduction of seasonal malaria chemoprevention with AQ-SP combination in the Sahel countries. A simple standardized protocol is being developed by the malaria in pregnancy consortium in collaboration with WHO to direct the monitoring of IPTp-SP in Arica.

5.3 TESTING FOR DRUG RESISTANCE

It becomes imperative to perform drug resistance tests in specialized laboratories in order to assess the susceptibility to anti-malarial compounds of parasites collected from specific patients. There are two main laboratory methods that are available: **In vitro tests**: The parasites are grown in culture in the presence of increasing concentrations of drugs; the drug concentration that inhibits parasite growth is used as endpoint. **Molecular characterization**: Molecular markers assessed by PCR or gene sequencing also allow the prediction, to a certain degree, of resistance to some drugs. CDC recommends that all cases of malaria diagnosed in the United States should be evaluated for drug resistance. Specimens from all cases that are diagnosed in the United States

should be sent to the CDC Malaria Laboratory for this drug resistance testing. All specimens submitted for drug resistance testing will first undergo molecular testing by polymerase chain reaction (PCR) for species confirmation. Depending on the species, the age of the specimen, and the previous receipt of anti-malaria regimen, different testing techniques may be employed to assess for the presence of drug resistance. Expanded Laboratory methods for testing for malaria drug resistance include in vitro tests, molecular characterization, determination of drug levels, and animal models. Culturing malaria parasites can be done only for pretreatment specimens that arrive within 72 hours of collection.

Molecular characterization: For some drugs (chloroquine, sulfadoxine-pyrimethamine and similar drugs, atovaquone), molecular markers have been identified that confer resistance. Hence, molecular techniques, such as PCR or gene sequencing can be used to identify these markers in blood taken from malaria-infected patients.

Drug levels**:** When individuals who are presumably taking malaria prophylaxis develop malaria, blood samples can be collected and analyzed for the presence of the drug. The drug is then extracted from the blood and the concentration is determined by the use of high-performance liquid chromatographic methods. Determining the drug level in the blood can help distinguish between drug non-adherence and drug resistance.

5.4 INTERMITTENT SCREENING AND TREATMENT (ISTP) STRATEGY

The adoption of ISTp is believed to reduce the possibility of drug resistance since treatment is only initiated after malaria infection is confirmed. The concept of this strategy is to provide scheduled RDT-based screening as part of focused antenatal care (FANC) and treatment of those with positive results with an effective and long acting artemisinin-based combination therapy (ACT) during the second and third trimesters. Screening periods must be at least one month apart (4-8 weeks) with the aim of treating existing infection and providing post-treatment prophylaxis for up to six weeks (White, 2005).

Although another advantage of this strategy is to reduce the degree of exposure to unnecessary drug pressure in non-infected women, especially in low malaria endemic areas or under seasonal transmission, its success as a viable alternative to IPTp-SP also relies on the use of RDTs and their sensitivity to detect low-level, chronic placental infections. A combined HRP2 and pLDH

based antigen, prequalified by WHO should be recommended (WHO-FIND, 2009), as it has the advantage of increasing the test sensitivity to detect *P. falciparum* infections and other pan-species.

Some studies have evaluated ISTp at ANC as an alternative to IPTp-SP. In this strategy, women are screened for malaria with an RDT at each ANC visit and only women who test positive are treated. This strategy resulted in a higher proportion of maternal infections and clinical malaria during pregnancy compared to IPTp-SP, although it was non-inferior in terms of the proportion of LBW infants. Furthermore, ISTp was found to be less cost-effective than IPTp-SP. So, the evidence reviewed does not support a recommendation for IST as an alternative to IPTp-SP.

5.5 IMPACT OF SOCIOECONOMIC INDICATORS

In trying to establish if there is any association between socioeconomic status and incidence of malaria in pregnancy, the socioeconomic indicators that were evaluated are income, education and employment. Hence the Research Questions 2, 3 and 4 were to examine the correlation between income, education and employment and malaria in pregnancy. Therefore the null hypothesis that there is no correlation between these socioeconomic indicators and gestational malaria is rejected. The alternate hypothesis was found to be true. There was a statistically significant difference in the odds of pregnant women with varying SES and the incidence of malaria during pregnancy.

The study also showed that lack of education was a significant predictor of malaria in pregnancy. This agrees with several other studies conducted (Afulani, 2015; Gupta et al., 2014; Kim et al., 2018; Mbu et al., 2014; Yusuf et al., 2016). Educational level is linked to the likelihood of seeking appropriate malaria prevention and treatment during pregnancy. Educated women have a tendency of complying with the WHO recommended four to eight ANC visits than less educated women (Afulani, 2015; Gupta et al., 2014; Kim et al., 2018). During the ANC visits, the pregnant women have the opportunity to interact with the healthcare workers who enlighten them on best practices for a successful gestation period. In addition, education was likely to determine the kind of environment and accommodation where pregnant women reside as well-educated women may not dwell in places not befitting their status. Other educational levels like primary, secondary and tertiary did not significantly influence the occurrence of malaria in pregnancy after ‘no education’ category.

The Knowledge of malaria and socio-economic upliftment are key factors in adopting the appropriate intervention strategies. Keeping in mind that there is a large number of risk factors that influence vulnerability to malaria including proper knowledge about malaria transmission and prevention, demography and socio-economic status of different population groups.

The current systematic review and meta-analysis suggests that lack of education, low income, poorly constructed houses, and farming are associated with an increased level in prevalence/incidence of *Plasmodium* infection in SSA. Furthermore, the review showed a decreased linear trend of *Plasmodium* infection with an increase in the wealth index, which was measured based on occupation, education, household assets ownership, and quality of the house. A previous review by Tusting *et al*. (2013) also reported lower odds of *Plasmodium* infection among children who belong to households with low SES group as compared to those who belong to high SES households. However, unlike the study which examined the linear trend of decrease in *Plasmodium* infection with an increase in the wealth index/socioeconomic group (continuous or categorical) in different population group, the meta-analysis by Tusting *et al*. (2013)limited the comparison to children in the least poor (richest) and poorest socioeconomic groups. In agreement with this finding another review by Tusting *et al*. (2015)also reported an increased odds of *Plasmodium* infection among individuals living in houses with thatch roof, mud walls, unscreened window, open eaves and lack of ceilings (Tusting et al, 2015).

The observed association between socioeconomic indicators and *Plasmodium* infection may be as a result of the effect of SES factors on access and behaviors towards malaria diagnosis, treatment, and prevention measures in SSA. Socioeconomic status (SES) indicators could affect behavior and practice of individuals to prevent malaria differently. Education is associated with productivity, capital or potential earning, occupational opportunity, and socialization of individuals. Education is also a platform that increases knowledge, skills, and ability of the individual to access information that promotes health (Mbu et al, 2014). Knowledge could lead to a better acceptance and practice of malaria prevention measures. Higher income also provides better housing, schooling, and nutrition that could enhance malaria prevention. Similarly, income level determines the capacity of individuals to buy malaria preventive measures such as insecticide treated nets (ITNs) and indoor residual sprays if it is not freely received. Occupation may affect income level, which in turn affect access to malaria preventive measures.

There are several studies in SSA that have shown an association of mosquito bed net ownership and use with wealth (Macintyre, 2002,Njama et al,2003,Bernard et al, 2009,Noor et al, 2006), occupation (Macintyre et al,2002,Noor et al, 2006), and educational status (Goesch et al, 2006). Another study in Sudan showed an improved use of malaria prevention strategies such asITNs and house spraying with an increase in household wealth (Onwujekwe et al, 2006).

SES may also affect individuals' ability to get diagnosed and appropriately treated for malaria. Educational status could affect the ability to understand written or verbal information about symptoms, treatment, and transmission mechanisms and control/prevention of malaria. This literacy in turn could affect the practice of individuals to get treated for malaria. Financial resource is a factor that could also affect individuals' capability to use available goods and services to treat malaria. For example, the poorest pregnant women may not have sufficient money to cover transportation, consultation with healthcare providers, and payment for drugs in private hospitals when they are ill. As a result, they may tend to shy away from seeking care. A study in Tanzania showed an increased chance of receiving anti-malarial drugs in children who had wealthier families compared to poorer families (Schellenberg et al, 2003).

There is possibility that some SES indicators may also directly affect the occurrence of malaria. Most malaria transmission in Africa occurs due to mosquitoes resting indoors (Huho et al, 2013). The quality of the accommodation therefore determines successful entrance of mosquitoes into the house. A house that is constructed without windows or screens, as is seen in many case scenarios in SSA expose individuals to malaria vectors (Lindsay et al, 2003). A similar study in Gambia found an increased number of indoor residual mosquito vectors in houses made with mud blocks when compared to those with concrete (Kirby et al, 2008). The effect of occupation on malaria incidence can also be direct. Some occupations like agricultural practices may increase contact of individuals with mosquito vectors thereby increasing the risk of *Plasmodium* infection. In addition, when working in forested areas and migratory activities in the highland fringes, individuals will have less access to healthcare facilities thereby increasing the risk of *Plasmodium* infection (Ghebreyesus et al, 2000).

6.0 CONCLUSIONS AND RECOMMENDATIONS

Malaria is a major threat particularly in Sub-Saharan Africa, imposing a heavy human and economic toll. Countries from the sub-Saharan Africa are also called Black Africa. This region is generally subdivided into four sub-regions which are: West Africa, East Africa, Central Africa, and Southern Africa. SSA is made up of 48 countries (including islands) and populated by about 1128 million inhabitants (at the beginning of the 21st century), sub-Saharan Africa is the poorest part of the continent, particularly in the economic field and the most affected by several diseases of the world including malaria.

Malaria has long been a vital topic in the economics literature due to its drag on economic growth. Economic epidemiological models show that individuals tend to increase their protective behavior when malaria is more prevalent in a society. Africa is struggling to defeat malaria for several reasons. Most infections in sub-Saharan Africa are caused by *Plasmodium falciparum*, which is the most serious and dangerous form of the plasmodium disease. It is also in this region that we find the most aggressive species of mosquitoes; transmission rates are therefore much higher than elsewhere around the globe. On the other hand, political and social unrest disrupts malaria control campaigns and often compels large numbers of people to settle in high-risk areas. Donor fatigue is a crucial factor that is negatively affecting the control of malaria. As a symbol of declining malaria aid, the new "America First" budget plans a 44 percent reduction in malaria support from the United States—but the President's Malaria Initiative has been a major actor in this area.

Overall, beyond the social and public health problem it poses, malaria is also an economic problem. As a result, taking action and initiatives against malaria is part of the fight for the sustainability and profitability of companies because this scourge killed 627,000 people in 2012 and malaria causes an annual loss of USD 12 billion as reported by the World Bank. According to WHO, about US$ 100 billion is needed to reach the 2030 malaria targets, with an additional US$ 10 billion to fund research and development for innovations in malaria, including new drugs and insecticides. This investment will deliver a significant return: the outcome will be that nearly 3 billion malaria cases will be averted and more than 10 million lives saved. A malaria-related poverty trap—defined as malaria reinforcing poverty while poverty reduces the ability to deal with malaria—can, in theory, be observed when extreme poverty is initially very high. This point to a possibility of encountering difficulty on the demand side and to situations where malaria

eradication may be out of reach without massive health aid. A health trap may also be the result of a simpler process linked to the scale-up of preventive measures.

We have shown in this research that majority of the women attending ANC became infected with malaria before their first antenatal visit. Hence malaria prevalence at first antenatal visit can be reduced with interventions that reach all women of childbearing age, such as universal bed net distribution. Children born to women with placental infection, but not peripheral malaria are at increased risk of malaria during infancy, even if the mother cleared the infection before delivery. Young women in their first pregnancy are exceptionally vulnerable to placental malaria infection (which causes low birth weights in newborns) because these women have yet to develop the higher levels of immunity that evolve with exposure to malaria over the course of successive pregnancies. For this reason, pregnant girls and women under the age of 20 are at highest risk of malaria infection, and that risk tends to diminish with each subsequent pregnancy. Young women also have less access than older women to life-saving prevention and treatment modalities with young women less likely to use IPTp or ITNs compared with older women. Poor, rural and uneducated populations are mostly affected by malaria, and this also holds true for pregnant women. Since malaria infection occurs more often in the first or second trimester of pregnancy, and women who contract malaria early in their pregnancy disproportionately give birth to low-birth weight babies, it is therefore imperative to reach women in their first trimester with prevention and treatment services. One study, conducted in the Thailand-Myanmar border area, further confirmed the report that women were less likely to contract malaria in the second or third trimester, highlighting the importance of early malaria prevention, possibly even before conception. However, women's choices of anti-malarials during pregnancy are limited because, although the range of available anti-malarial regimens has increased steadily over the past 50 years, relatively few of these drugs have proven effective and safe and in pregnancy, due to the systematic exclusion of pregnant women from clinical trials due to risks, complexities and cost. The most effective anti-malarials (artemisinins) are not recommended in the first trimester of pregnancy, and these drugs or their combinations are currently recommended only for treatment in the second and third trimesters. SP, the current standard of care for IPTp, cannot be used in the first trimester of pregnancy because it is a folate antagonist and thus potentially teratogenic. There is also increasing resistance of malaria parasites to SP which need to be evaluated regularly.

The honeymoon period for malaria control is threatened both by resistance and, in the wake of the recent economic crisis, by so-called donor fatigue, creating a serious risk of a resurgence of malaria, as has occurred repeatedly in the past.

The Ministry of Health should undertake rigorous awareness campaigns to educate mothers on the importance of regular ANC visits and IPT use targeting especially those with lower incomes or less education. There should be a continual free distribution of the ITN at ANCs, health centers, and through campaign strategies by health workers in order to reach out to the entire population. Local government authorities must be interested in supporting strategies that will increase ownership of the ITN among the at-risk population while the continual and consistent utilization is enhanced through education. This could be done by targeting the pregnant mothers and to-be mothers in the district.

However, since malaria control in many countries has historically been achieved without such malaria-specific interventions, socioeconomic development could potentially provide an effective and sustainable means of control in malaria-endemic countries. I also recommend the complimentary use of RDT and microscopy for ANC screening. This is because of submicroscopic cases of malaria infection. Besides the immediate health concerns of pregnancy-associated malaria there are broader public health concerns. We have previously shown pregnant women to be a significant reservoir of gametocytes, suggesting that pregnant women may be a major source of malaria transmission to the community at large (Boudová, 2014).

Bridging the gaps Africa has everything to gain by investing in the fight against malaria. Malaria is already costing the continent's economy USD 12 billion a year in direct losses. The resources needed for malaria elimination are insignificant compared to those required to overcome the disease in case of resurgence, especially given the current resistance to drugs and insecticides.

Also, pregnant women residing in slum areas may have more challenges preventing malaria infection due to overcrowding, lack of water, poor toilet facilities, and lack of appropriate drainage systems. Since the principal goal of malaria prevention and control programmes is to reduce the prevalence of the disease, as well as its economic and social costs, intervention strategies should be sensitive to the financial needs and the socio-cultural conditions of the poor, especially pregnant women residing in slums.

The benefits of investing in the fight against malaria are not only financial: this struggle contributes significantly to education, agriculture, women's empowerment, poverty eradication

and achievement of other Sustainable Development Goals. As such, increasing investment in anti-malaria interventions that target pregnant women while simultaneously addressing the social, cultural and economic factors that heighten susceptibility has the potential to progress our understanding of the disease, and channeling interventions towards the most vulnerable and indigent groups.

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