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Association Between Asymptomatic Malaria Infection and Pregnancy Outcome in Delta State, Nigeria

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Walden University
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Abstract

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by

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MSc., Public Health Parasitology, 2010

BSc., Parasitology and Entomology 1999

Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

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Abstract

Pregnant women are vulnerable due to the pregnancy-induced suppressed immunity in malaria-endemic areas. Asymptomatic malaria in pregnancy (MiP) threatens both the mother, fetus, and neonate via chronic placental malaria which impacts maternal-neonatal exchange. Some studies reported that MiP risk factors vary across locations, however, there are few studies on MiP and pregnancy outcome in Nigeria. The purpose of this study was to investigate the association between asymptomatic placental malaria infection and pregnancy outcome among parturients in Asaba, Delta State, Nigeria. This study was developed with a quantitative methodology that utilized primary and secondary healthcare data from 483 subjects aged 18–49 years from four healthcare facilities between May and July 2021. The Socio-Ecological Model framework was used to explain how parturients can achieve improved pregnancy outcome via the mobilization of multi-levels supports to enhance the compliance of parturients to malaria interventions. Three research questions with three sets of hypotheses were tested with the binomial logistic regression and Chi-square tests. The findings showed a statistically significant association between placental malaria parasitemia by microscopy, intermittent preventive treatment in pregnancy with sulfadoxine-pyrimethamine, use of complementary and alternative medicine, and pregnancy outcome in the study population. The findings of this study could inform malaria control policymaking in Asaba and Delta State on tracking and treating asymptomatic malaria among underserved parturients accessing antenatal services.

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Dedication

This study is dedicated to:

1. The most-high God; my Father, the Lord Jesus Christ, and the Holy Spirit (my counselor and teacher).

2. My mother; Margret Punuka Ajani, whose love and commitment to education has inspired me to keep studying, although she passed on to glory on April 15, 2013, her legacy has brought me this far.

3. All parturients and their neonates in Nigeria who are victims of malaria in pregnancy.

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Chapter 1: Introduction to the Study

Malaria accounts for the highest mortality compared to all other infectious diseases pooled at the global and sub-Saharan Africa (SSA) regional levels. The greatest burden of this vector-borne disease is in the SSA, with Nigeria bearing a 25% burden and ranking highest/first in central Africa bearing 50% of the global burden (Center for Disease Control and Prevention [CDC], 2020; World Health Organization [WHO], 2020).

There is documented evidence in the current literature of the negative impact of malaria pregnancy (MiP). MiP is a public health concern that is impacting huge economic and human resources at various levels of society (WHO, 2020). The United Nation International Children's Emergency Fund (UNICEF) stated that malaria is an urgent public health concern, and all stakeholders should concentrate efforts for the elimination (reduction of the incidence rate of a disease to zero levels in a defined geographical location via thoughtful interventions) and eradication (permanent reduction of the incidence of a particular disease to zero levels at global level via calculated efforts and subsequent interventions are not required) of the disease globally (UNICEF, 2020; WHO, 2016).

Onyemaechi and Malann (2020) reported that parturients are a high-risk group for malaria due to their suppressed immunity by pregnancy. The disease burden of malaria in Nigeria is enormous; among parturients, it accounts for 70% morbidity, 15% anemia, and 5% to 14% prevalence of low birth weight (LBW). An estimated 3.2 million people are at risk of malaria infection. At the global level, several efforts to eradicate the disease failed

to produce the hoped outcome for decades. An estimated 125 million parturients are at risk of malaria infection globally. Researchers have stated that parturients are a reservoir of the *Plasmodium* species via asymptomatic and submicroscopic presentation with placental parasitemia (Onyemaechi & Malann, 2020).

In Nigeria, there is an estimated 3,000 death from malaria resulting in 40% of health expenditures, 50% hospital visits, and up to 50% of hospital admissions annually (Onyemaechi & Malann, 2020). The complications of malaria disease vary based on the level of immunity. In Nigeria, malaria accounts for 70% of morbidity and 11% of mortality among pregnant women and was the reason for 63% of hospital visits in Nigeria in 2018. Parturients are four times as likely to get malaria and two times as likely to die of malaria than their nonpregnant counterparts (Onyemaechi & Malann, 2020). The clinical signs of malaria include fever, chills, loss of consciousness, convulsion, breathlessness, anemia, jaundice, and vital organ dysfunction. (Onyemaechi & Malann, 2020).

Multifaceted factors account for the high malaria burden in Nigeria. Data from the 2015 Nigeria Malaria Indicator Survey (NMIS) and the 2018 Nigeria Demographic and Health Survey (NDHS) revealed that the country is not making noticeable progress in malaria elimination and eradication (National Population Commission [NPC] Nigeria and ICF, 2019; National Malaria Elimination Program [NMEP], National Population Commission [NPopC], National Bureau of Statistics [NBS], and ICF International, 2016). This study may help support a policy design of an appropriately focused intervention that will yield the visible outcome of the anticipated positive social change on MiP prevention

and control strategies. The study outcome may result in the mobilization of a multilevel support system of the socioecological model (SEM) framework for parturients to improve pregnancy outcome via an informed understanding and enhanced utilization of the existing malaria interventions. The Parturients and their neonates could benefit from reduction in the loss of lives and an increased economic resource in the study location and beyond. There could be an increase in malaria interventions uptake via an increased knowledge of effective interventions with cultural acceptance. The findings from this study may result in a reduction in the prevalence of MiP, and the morbidity and mortality associated with the infection via the knowledge from the study could result in better compliance to malaria interventions. There may be an improvement in the health, economic status, investment opportunity, and available income to parturients. Besides, the government may channel the vast resources spent on preventing and controlling malaria into enhancing community well-being.

The findings of this study may inform appropriate strategies for malaria interventions across all levels of society. It could also help the Asaba community in Delta State, Nigeria to recognize their specific risk factors and all the multilevel players (personal, relationship, community, and systems) that have interactions with pregnant women for an improved pregnancy outcome.

The findings from this study could have social change impact via the strengthening of malaria control policy at the system levels, as well as at the personal (individual) and interpersonal (community) level of the SEM theoretical framework. The communication of study findings at the antenatal clinic (ANC) study sites (result

dissemination to subjects and stakeholders) and community town hall meeting could enhance social support from family and community members for parturients protection against mosquito bites and use of existing intervention for the disease control. Other possible positive social change includes the informed understanding and adoption of existing malaria interventions and improved economic resources derived from a malaria free community.

This chapter includes a summary of the selected topic, a preview of research related to the study topic, the background and appropriate literature about the theme of the study. Chapter 1 also includes the independent variables, dependent variables, and other variables for univariate analysis, research questions, and hypotheses. The chapter includes key definitions as well as the purpose of the study, the study's significance, and the theoretical framework. A detailed discussion of the current literature was discussed in Chapter 2.

Background of the Study

Malaria is a significant public health concern in Nigeria; 97% of Nigerians are at risk of this disease, with substantial morbidity and mortality statistics across various age groups (Yaya et al., 2018; WHO, 2020). Malaria impacts parturients and their neonate with complications and mortality. Malaria accounts for a substantial burden on health facilities, depletion of household income, low labor productivity, and national gross domestic product (GDP; WHO, 2019). The implications of asymptomatic malaria among parturients in deterring control efforts and maintaining the parasite cycle have widespread reports (Aguzie, 2018; Bardaji et al., 2017; Omer et al., 2017). Reports have associated

pregnant women with the parasite's reservoir, delaying the extermination of the disease (Aguzie, 2018; Camona-Fonseca & Arango, 2017).

The failure to detect the parasite presence in peripheral and placenta blood through a rapid diagnostic test (RDT) and microscopy, combined with current drug failures due to rapid parasite mutation, necessitate improved research to address this concern, improved testing techniques with cost-efficient strategies are needed to achieve the testing before treatment mandate by the WHO (WHO, 2020). The absence of *P. falciparum* from peripheral circulation by the sequestration in the placenta further complicates treatment and resistance of MiP (Aguzie, 2018; Sungwa et al., 2017; WHO, 2018). According to Sharma and Shukla (2017) the infected red blood cells (iRBCs) by *P. falciparum* causes inflammation, oxidative stress, and apoptosis to the placenta. The iRBCs cross the placenta to evade the host immune responses. These iRBCs darkens and thickens the placenta base impacting maternal and neonates exchange patterns, resulting in intrauterine growth retardation (IUGR), LBW, and other adverse pregnancy outcomes.

Agomo et al. (2016) recommended large scale studies to confirm the low level of mutation in the *P. falciparum* multidrug resistance (*pfmdr) 1* gene on the efficacy of amodiaquine in preventing malaria in pregnancy. These authors reported the need for extensive studies in other locations/places to provide current data on predictors and risk factors for malaria in pregnancy to enable scale-up of malaria control efforts. According to WHO (2017) the benefit of malaria research among pregnant women is critical due to the observed drug failure and parasite resistance among them and their neonates. Malaria

infection is a preventable (based on existing interventions) cause of maternal and neonatal complications, morbidity, and mortality (WHO, 2017). The extensive reports on drug failure warrant further research in various locations to ascertain the mutant strain, mutation threshold (upper limit/level of mutation), and accelerate informed intervention approaches (Aguzie, 2018; WHO, 2019).

In this study, I accessed the placental malaria parasitemia by microscopy (PMPM) disease burden among asymptomatic pregnant women in the target population and its implication on maternal health (maternal anemia status) and neonatal health (baby's birth weight and delivery term). The outcome of this research could improve the understanding of the prevalence of malaria infection among pregnant women and the association between asymptomatic malaria infection, intermittent preventive treatment in pregnancy with sulfadoxine-pyrimethamine (IPTp-SP) compliance, the use of complementary and alternative medicine (CAM), and pregnancy outcomes (maternal anemia, baby's birth weight, and delivery term) in Asaba, Delta State, Nigeria. The use of CAM in this study refers to the use of herbal/plant/traditional medicine by parturients against malaria disease.

I reported the sensitivity of the testing techniques, and this study could contribute to the current understanding of the reasons the efforts of stakeholders for the elimination and eradication of malaria are not yielding the optimal results. This study quantified the disease burden in the target population and location. This population is vulnerable due to their lower immunity and residing in a high burden malaria location. There remains limited documentation for the intended area, population, and study location

(asymptomatic malaria infection and pregnancy outcome, pregnant women, Delta State, Nigeria). The results of the existing literature on malaria infection among pregnant women are heterogeneous, implying region/location specificity, thereby creating a gap for this study to determine the Asaba community specific and result-oriented interventions with adoption strategies, as well as prevailing risk factors of malaria infection. The study findings could determine the efficient interventions and tailored guidance against the risk factors in the study location.

Problem Statement

The malaria problem in Nigeria is life-threatening as 97% of the people are at risk. There are various collaborations (individual, national, and international) to reduce the disease but have not yielded the expected result. Malaria is the second leading cause of death in Africa. The statistics of malaria disease morbidity and mortality are highest in Nigeria (Okeke, 2012). According to Gontie et al. (2020), malaria risk factors in pregnancy to both mother and fetus are enormous. The enumerated risk factors from previous studies on MiP include educational attainments, age, ANC visit, gestational age, parity (the total number of pregnancies beyond 20 weeks), gravidity (the total number of confirmed pregnancies irrespective of the outcome), IPTp-SP compliance, and insecticide treated net (ITN) use (Gontie et al., 2020).

Asymptomatic malaria is deadly, especially among parturients, children, and visitors from nonmalarial areas. This is because it is often undetected, therefore not treated. After 8 to 30 days of infection, the condition begins with flu-like symptoms such as fever, headache, joints and muscular aches, vomiting, diarrhea, chills, and sweats.

Untreated malaria infection can result in brain damage and damage to other vital organs including the liver and kidneys. Pregnant women are among the most impacted by malaria because their previously acquired immunoglobulin (in endemic settings) is reduced during pregnancy (CDC, 2020).

Research indicates that malaria induced-anemia accounts for an estimated 10,000 maternal death in Africa each year (WHO, 2020). The infection of the placental by *P. falciparum* impacts maternal and neonatal exchange patterns causing miscarriages, premature births, imparted fetal growth, development, and death (CDC, 2020).

The WHO via the global technical group set a new goal on malaria eradication for 2030. The goal is aimed at reducing malaria by 90% via its elimination in 35 countries globally (WHO, 2016). The objective of this study was to examine the use of some malaria interventions (IPTp-SP and ITN) and to identify some risk factors (listed in current literature from studies in various locations) that relate to PMPM and pregnancy outcome in the study location.

Purpose of the Study: The purpose of this study was to investigate the association between PMPM, IPTp-SP compliance, the use of CAM, and pregnancy outcome (maternal anemia, baby's birth weight, and delivery term) among asymptomatic pregnant women presenting for delivery. I used quantitative methodology in a cross-sectional study design with deidentified survey questionnaires and secondary data collected from four healthcare facilities in Asaba, Delta State, southern Nigeria. The subject's ITN ownership, ITN frequent use, ANC attendance, gravidae, age group, and educational attainment were determined in a univariate and bivariate analysis among asymptomatic

pregnant women in Delta State, southern Nigeria. My goal for this study was to extend research in the field by generating evidence on the association between asymptomatic malaria infection, IPTp-SP compliance, the use of CAM, and pregnancy outcomes among parturients in the target population.

Research Questions and Hypotheses

Research Question 1 (RQ1): What is the association between PMPM (independent variable 1 [IV_1]), IPTp-SP compliance (independent variable 2 [IV_2]), the use of CAM (independent variable 3 [IV_3]), and maternal anemia (dependent variable [DV]) among pregnant women in Asaba, Delta State, Nigeria.?

Null Hypothesis ($H_0$1): There is no association between PMPM (IV_1), IPTp-SP compliance (IV_2), the use of CAM (IV_3), and maternal anemia (DV) among pregnant women in Asaba, Delta State, Nigeria.

Alternate Hypothesis *($H_1$1))*: There is an association between PMPM (IV_1), IPTp-SP compliance (IV_2), the use of CAM (IV_3), and maternal anemia (DV) among pregnant women in Asaba, Delta State, Nigeria.

Research Question 2 (RQ2): What is the association between PMPM (IV_1), IPTp-SP compliance (IV_2), the use of CAM (IV_3), and baby's birth weight (DV) among pregnant women in Asaba, Delta State, Nigeria?

Null hypothesis ($H_0$2) There is no association between PMPM (IV_1), IPTp-SP compliance (IV_2), the use of CAM (IV_3), and baby's birth weight (DV) among pregnant women in Asaba, Delta State, Nigeria.

Alternate Hypothesis ($H_1$2): There is an association between PMPM (IV_1), IPTp-SP compliance (IV_2), the use of CAM (IV_3), and baby's birth weight (DV) among pregnant women in Asaba, Delta State, Nigeria.

Research Question 3 (RQ3): What is the association between PMPM (IV_1), IPTp-SP compliance (IV_2), the use of CAM (IV_3), and delivery term (DV) among pregnant women in Asaba, Delta State, Nigeria?

Null hypothesis ($H_0$3) There is no association between PMPM (IV_1), IPTp-SP compliance (IV_2), the use of CAM (IV_3), and delivery term (DV) among pregnant women in Asaba, Delta State, Nigeria.

Alternate hypothesis ($H_1$3): There is an association between PMPM (IV_1), IPTp-SP compliance (IV_2), the use of CAM (IV_3), and delivery term (DV) among pregnant women in Asaba, Delta State, Nigeria.

The Socioecological Model (SEM) Framework

The theoretical framework for this study was the SEM. The SEM states that health is affected by the interaction between the features of the individual, the community, and the environment that includes the physical, social, and political elements (Kilanowski, 2017). The CDC has adapted the SEM for various public health endeavors to include the scopes of interpersonal, organizational, community, and policy level factors (CDC, 2020; Kilanowski, 2017).The SEM is a theory-based framework for understanding the multifaceted and interactive effects of personal and environmental factors. Some authors have used the SEM to examine various factors that effect, and influence disease prevalence, prevention, and control and it yielded valid study outcomes

(Bronfenbrenner, 1986; Bronfenbrenner,1989; Bronfenbrenner,1977; Kilanowski, 2017). The SEM is also used in the evaluation of programs and policy to ensure safety in the environment (Kilanowski, 2017).

The SEM recognizes that people's health choices and decisions are rooted within a wide interconnected social and ecological/environmental system that determines the health outcome. Therefore, the SEM was an appropriate framework for this study because I used it to highlight the social and environmental (residential, health knowledge and decisions) risk factors influencing parturients adoption of existing malaria control interventions. Using the SEM, I assumed that there is an association between PMPM (biological and an environmental factor), IPTp-SP compliance (personal level factor/health decision by parturients), the use of CAM (an interpersonal/relationship-based factor) and pregnancy outcome (individual, relationship/interpersonal, community, and structural level factors) among asymptomatic parturients.

Nature of the Study

This study was a quantitative methodology with a cross-sectional study design using binomial logistic regression analysis and the Chi-square test statistics. This quantitative study design was appropriate because the survey questions that I designed were structured to generate nominal data that can be analyzed quantitatively. To achieve the study objectives, I used the SEM theoretical framework, and it was well aligned with the variables outlined in the research questions. The hospital data (healthcare facility-based data) were collected via collaboration with the hospital administration/management as a partner organization. The data collection instrument was a paper-based questionnaire

answered by the literate subjects or administered by me in a face-to-face approach to the subjects who are not literate. This approach could have mitigated missing data and errors. I carried out validation with hospital records of subjects to enhance the study validity.

The hospital data (variables) included the following outcome, predictors, and other variables for univariate and bivariate analysis:

- Pregnancy outcome variables (dependent/outcome variable; DV) were maternal anemia based on the standard hematocrit reader with values of 11 g/dL as normal,10 g/dL to 10.9 g/dL as mild, 7 g/dL to 9.9 g/dL as moderate, and less than 7 g/dL as severe anemia (WHO, 2011). I recoded the normal anemia values as anemia absent (AA) and the mild, moderate, and severe as anemia present (AP); baby's birth weight, above or equals 2.5 kg as normal birth weight (NBW), and below 2.5 kg as LBW, preterm and term delivery as less than or equal to 36 weeks and equal to or greater than 37 weeks, respectively.
- The predictor/independent/exposure variables (IVs) included PMPM (IV_1) as positive (presence) placental malaria parasitemia by microscopy (PPMPM) and negative (absence) placental malaria parasitemia by microscopy (NPMPM); the IPTp-SP (IV_2) as to compliant to three or more doses of IPTp-SP during pregnancy (adequate) and not compliant as none or less than three doses IPTp-SP during pregnancy (inadequate) and use of CAM (IV_3) as 'Yes' or 'No' responses.
- The other variables for univariates and bivariate analysis included the subject's ITN ownership (Yes, or No), ITN frequent use (Yes, or No), ANC attendance (once, twice, more than twice during this pregnancy) gravidae (primigravidae,

secundigravidae, and multigravida), age group (18–25, 26–34, 35–42, and 43–49 years), and educational attainment (none, primary, secondary, tertiary, and above).

I analyzed the data using Statistical Package for Social Sciences (SPSS) version 25. The outcome variable and predictor variables were binary variables. I produced an initial descriptive statistic in tables and with percentages to describe the frequency distribution of the independent and dependent variables. I carried out descriptive statistics to explain the study population and features in relation to the relevant variables. I performed a Chi-square test to estimate the association between the PMPM and each of the enumerated risk factors for this study. I checked the logistic regression and Chi-square assumptions for all the independent variables and determined the multicollinearity assumption using the variance inflation factor (VIF). I determined the model goodness-of-fit using the Hosmer-Lemeshow test statistics. I used the binomial logistic regression analysis (inferential statistics) to investigate the association between PMPM, IPTp-SP compliance, CAM usage, and each of the dependent variables at a *P*-value of ≤ 0.05 as significant. I analyzed RQ1, RQ2, and RQ3 by binomial logistic regression.

Definitions of Terms Used in the Study

I adapted some definitions in accordance with the relevant data collection protocols or recognized scholarly interpretation.

Antenatal Care (ANC): The preventive healthcare information, guidance, testing, and treatments given to pregnant women by healthcare officials to enhance good pregnancy outcomes.

Asymptomatic malaria patients: carriers of the malaria parasite but with no signs of the disease.

Complementary and alternative medicine (CAM): Herbal, plant-based and traditional medicine used by pregnant women against malaria infection.

Intermittent preventive treatment in pregnancy with sulfadoxine-pyrimethamine (IPTp-SP): The preventive antimalarial medicine given to pregnant women at routine hospital visits.

Malaria eradication: permanent reduction of the incidence of a particular disease to zero levels at the global level via calculated efforts and successive interventions are not required.

Malaria elimination: reduction of the incidence rate of a disease to zero levels in a defined geographical area via systematic interventions.

Malaria infection: The presence of Plasmodium parasites in the blood/tissues of infected persons. It requires confirmation by any malaria testing techniques.

Malaria risk factors: The features or exposure that increases the chances of developing malaria infection.

Parturients: The expectant mothers/pregnant women.

Polymerase chain reaction (PCR): Molecular laboratory testing for malaria parasites.

Restriction fragment length polymorphism (RFLP): Another type of molecular testing to determine parasite mutant species/gene.

Assumptions

I assumed that the proposed healthcare data provided via survey questionnaires (primary) and routine hospital (secondary) data are void of random/systematic/instrumental error using appropriate sampling methods. I also assumed that the subjects who gave consent and participated in this study reside in Asaba, Oshimilli South local government area and they all gave honest responses to the survey questions. I informed the subjects that I would provide and analyze the data without their names and contact.

I also assumed that the characteristics of the data that was collected via the survey questionnaire and routine clinic data were the same across the study location (Asaba). As the study sites were randomly selected, there were variability in the samples population with the study city being a state capital with varied human populations cutting across various levels. I also assumed that subjects represented women from all educational levels and residential backgrounds.

Scope and Delimitations

This study was limited to Asaba city in Delta State, southern Nigeria due to the constraints of time and cost. In the selection of the variables for this study, it was discovered that there was a range of interventions and risk factors of MiP. However, those interventions and risk factors have varied outcomes in various locations. It is hoped that the findings of this study would enhance existing efforts for a focused intervention and addressing specific risk factors that will have a significant outcome for an improved pregnancy outcome in the study location and beyond. It is also hoped that the results

would be used to influence future intervention policy formulation, elimination strategies, and maybe generalizable to the rest of the Delta State and possibly Nigeria.

Limitations

One limitation of this study is that a few of the survey questions depends on self-reporting by subjects, therefore, recall and misreporting bias may not be ruled out. The questionnaire was administered in a face-to-face interview for subjects that are not literate by me, while literate subjects filled the questionnaire within few minutes in my presence. This approach has the benefit of mitigating the non-response bias but may not guarantee anonymity and truthfulness in sensitive question especially on the use of herbal/plant medicine during this pregnancy (for concern that the healthcare officials does not support the use of CAM).

Significance of the Study

This study is relevant to public health with respect to the study location (southern Nigeria) which is a malaria endemic country with a high prevalence of *P. falciparum* which is the most problematic with respect to virulence and resistance to anti-malaria drugs; and the population (subjects are immuno-compromised during pregnancy) (Ogola et al., 2018; Ruizendaal et al., 2017).

There is evidence in the reviewed documents of studies on the prevalence of maternal malaria in the study location and other areas but none of the studies determined the association between PMPM, pregnancy outcome and other risk factors (ITN ownership, ITN frequent use, ANC attendance, gravidae, age group, and educational attainment of subjects, as revealed in current literature) across three healthcare facility

levels (primary, secondary, and private). The outcome of this study may provide further evidence concerning the association between the enumerated variables for this study in Asaba, Delta State, Nigeria.

This study may have social change implications by providing needed research that could help policy makers, community leaders, healthcare organizations, pregnant women, and other stakeholders to design informed interventions and preventive approaches, including enhanced social support at various levels to reduce the impact of MiP with improved pregnancy outcome. This study could lend further support in the control of the parasite's resistance to drugs and other interventions. The *P. falciparum* resistance is a longstanding challenge in the elimination and eradication of malarial diseases, and useable information on the predisposing factors (such as use of CAM, ITN frequent use, and the refusal to take IPTp-SP) at various locations is not only needed but will improve control efforts among asymptomatic pregnant women that are discussed as the parasite reservoirs. Current statistics on the impact of the disease on immuno-compromised pregnant subjects are striking. WHO and other researchers have called for urgent surveillance and epidemiological studies to ascertain the disease burden and enumerate risks, and outcome factors to prevent further harm to the affected populations (Agomo et al., 2016; Aguzie, 2018; WHO, 2020).

This study is an epidemiological analysis to determine the association among variables, it could quantify the malaria disease burden among the subjects in the study location and the specific risk factors impacting prevention and control in the study location could be determined. The outcome of the proposed study may prove critical for

the study population and location. Southern Nigeria is in the rain forest zone, and with a hot, wet climate, is home to mosquito species (*Anopheles gambae* and *Anopheles funestus*) (Ogola et al., 2018). They transmit the most virulent strain of the parasite (*P. falciparum*) with a high infectious rate year-round (Ruizendaal et al., 2017). Therefore, this study is meaningful, considering the enumerated social and real-world implications on women, fetuses, neonates, and society at large.

Summary and Transition

In the introduction of this study, A*ssociation between asymptomatic malaria infection and pregnancy outcome in Delta State, Nigeria.* I reiterated the need for epidemiological studies in various locations/regions to reduce MiP based on current documents in the field. I highlighted the problem, importance, and significance of the study in enhancing the existing intervention approaches including the expected social changes that the study findings would have in the malaria endemic community of Asaba. I also outlined the methodology that was used to collect both survey questionnaires data and the secondary data (hospital record). In addition, a discussion of the study's theoretical framework, within a quantitative cross-sectional study design was presented. The anticipated assumptions, limitations, and delimitations to the study and how they may be reduced or mitigated were explained.

In Chapter 2, I presented a literature review that covers the MiP variables and risk factors documented in current literature. I provided details on the search strategy, as well as how the identified gaps could be addressed in this study. Further, I discussed the theoretical orientation (SEM) and how it was synthesized in this study.

Chapter 2: Literature Review

Introduction

Malaria in Nigeria is life threatening. Ninety-seven percent of the citizens in this region are at risk of the disease. There are various levels of collaborations (individual, national and international) to control the disease but has not yielded the expected result. Malaria is the second leading cause of death in Africa. The statistics of malaria disease morbidity and mortality are highest in Nigeria (Okeke 2012). According to Gontie et al. (2020) the documented risk factors of MiP to both mother and the fetus are significant. The enumerated risk factors from previous studies on MiP include educational attainments, age, ANC visit, gestational age, parity, gravidity, and ITN frequent use. Asymptomatic malaria can be deadly, especially among parturients, children, and visitors from nonmalarial areas. This is because it is often undetected, therefore not treated. Pregnant women are among the most impacted by malaria, because the previously acquired immunoglobulin (in endemic settings) is reduced during pregnancy (CDC, 2020).

Research evidence in current literature showed that malaria induced-anemia accounts for an estimated 10,000 maternal birth in Africa each year (WHO, 2020). The infection of the placental by *P. falciparum* impacts maternal and neonatal exchange pattern causing miscarriages, premature births, imparted fetal growth and development and death (WHO, 2020).

The objective of this study was to examine the usage of some malaria interventions (IPTp-SP and ITN) and to identify some risk factors (listed in current

literature from studies in various locations) that relate to placental malaria infection and pregnancy outcome in Asaba, Delta State Nigeria.

The purpose of this research was to investigate the association between PMPM, IPTp-SP compliance, the use of CAM, and pregnancy outcome (maternal anemia, baby's birth weight, and delivery term) among asymptomatic pregnant women presenting for delivery in Asaba, Delta State, Nigeria. In this study, I used a quantitative methodology in a cross-sectional study design with deidentified survey paper-based questionnaires and healthcare routine data collected from four healthcare facilities in Asaba, Delta State, Nigeria. I also determined the subject's ITN ownership, ITN frequent use, gravidae, age, and educational attainments in a univariate and bivariate analysis (with PMPM) among asymptomatic pregnant women. In this study, my goal was to extend research in the field by generating evidence on the prevalence of placental malaria disease burden, and prevailing risk factors in the study population and location.

In this chapter, I described the reviewed literature related to maternal malaria and pregnancy outcomes as well as existing interventions on malaria and their usage/utilization. I examined the gaps in the current knowledge base on maternal malaria parasitemia, use of CAM, and the risk factors related to the usage of malaria interventions by pregnant women. The connection between maternal malaria and malaria transmission based on gravidae and educational attainments of parturients were discussed. Further, this study provided explanation of the background of the study, problem statement, purpose, nature of the study, scope, delimitation, limitations of the study, and the significance of the study in this chapter. A description of the available information on the epidemiology

of malaria and the biology of the malaria vector and parasite were explored. I concluded this chapter by explaining the SEM framework as the foundational model selected for this study.

Literature Search Strategies

I used the Google search engine for this literature review. The keywords searched were *malaria, Plasmodium, peripheral malaria, placenta malaria, parasite-resistance, pregnancy, pregnancy outcome,* and *mosquito* in the databases of Walden University Health Sciences (Medline, ProQuest, Ebscohost, Google Scholar, PubMed, PLoS ONE, Science Direct). The approach used for searching for the relevant literature was premised on current literature related to maternal malaria, pregnancy outcome, and the SEM framework. My focus on the literature search was on current (within the past five years) scholarly peer-reviewed articles on journals, academic books, government, and organization publications. However, a few older articles that are foundational to the study were included.

The inclusion criteria for the documentation were:

1. Research publication dates from 2016 to 2021 (excluding foundational documents).
2. Peer-reviewed journal publications or governmental agency documents.
3. Journal articles that met the target population (parturients in Asaba, Delta State, southern, Nigeria, SSA, Africa).
4. Journal articles that discussed malaria/MiP.

The exclusion criteria were as follows:

1. The literature did not support this study (MiP).

2. The literature did not meet the inclusion criteria.

3. The literature did not comply with the target population and year of publication.

4. The literature did not highlight the theme of this study.

The Socioecological Model (SEM)

I premised this study on the SEM. This model explains that personal health behavior is determined by multilevel factors, including personal level (e.g., age, sex at birth), interpersonal level (e.g., family, community), and system level (e.g., local, state, and national government levels, civil society, NGOs, such as roll back malaria initiative, president malaria initiative, malaria elimination and control group) (Awuah et al., 2018; Kumar et al., 2012). These factors impact a person's decision to engage the health system (Revenson et al., 1991). Wright, (2016) stated that positive social support can strengthen health behavioral change. My goal in this study was to examine how the intersection of these factors is associated with PMPM and pregnancy outcome, specifically, the usage of the malaria interventions recommended by the ANC. Awuah et al. (2018) stated that low socioeconomic status (SES) is strongly associated with using an alternative treatment for malaria (Aikins, 2005; Chuma et al., 2010). Therefore, building on the premise of Awuah and colleagues, it is possible that multilevel factors, such as economic status, gravidae, age, (individual level), social support, use of CAM, (interpersonal level), health insurance, PMPM, ANC attendance, and place of residence (system level), affect PMP and pregnancy outcome.

Application of the Theories in Previous Study Similar to This Study

The SEM is a well-established theoretical framework in global health, international development, and communication (Bronfenbrenner,1999; Bronfenbrenner, 1979; McLeroy et al., 1988; Morris, 1975; UNICEF, 2018). The SEM is at the forefront of communication for development (C4D) programs. It is UNICEF'S major framework for the social and behavioral change communication (SBCC) program (UNICEF, 2018). The integration of multilevel engagement of groups and stakeholders enhances health communication and adoption of interventions (Schiavo et al., 2020; UNICEF, 2018). The SEM has been successfully used in public health both locally and internationally (Schiavo et al., 2020). For example, the UNICEF routine immunization program in Kyrgyzstan to increase uptake of immunization was grounded in the SEM. The SEM is centered on the fact that a person's health behavior and decision is a function of the interaction between the social, individual, structural, and the environment that promotes behavior change (Morris, 1975).

Schiavo et al. (2020) stated that the SEM can be used in both quantitative and qualitative studies. This study was quantitative in nature; hence it was appropriate to use the SEM as a framework. The SEM has the advantage of focusing on a multilevel factor; making it most appropriate in the public health field (Bronfenbrenner, 1999; Bronfenbrenner, 1979; McLeroy et al., 1988). Schiavo et al. (2020) stated that the SEM is beneficial in studies involving low health literacy populations. Robinson (2008), in the literature review study on improving fruit and vegetable consumption by the African Americans with low SES, stated that the SEM framework was appropriate for most

public health studies due to the complex interaction of various factors. The use of the SEM in the study on the factors limiting contraceptive use by adolescents in Nigeria by Ezenwaka et al. (2020) yielded a valid contribution to knowledge.

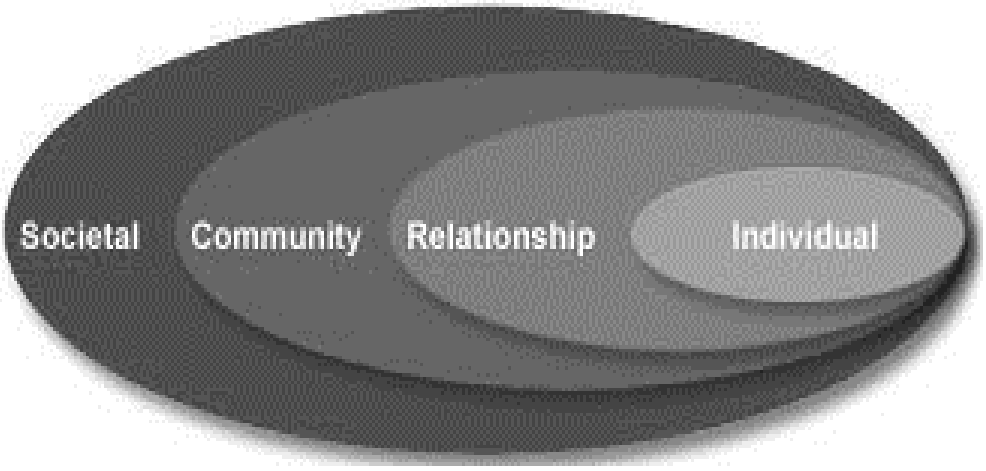
Rationale for the Selection of the SEM framework

Although there is evidence on maternal malaria parasitemia in SSA, no study has determined the association between PMPM, IPTp-SP compliance, use of CAM with pregnancy outcome in Nigeria using primary and hospital routine data across three healthcare facility levels (primary, secondary, and tertiary). This study was used to ascertain some risk factors of placental malaria in the study location and the parturients most at risk based on IPTp-SP compliance, CAM usage, gravidae, ITN ownership, ITN frequent use, and educational attainments.

I enumerated the risk factors for further investigation based on the evidence in the current literature. The study outcome may have social change implications via targeted adjustment at the personal, interpersonal, community, and system level of malaria policies and interventions. The PMPM is an environmental level variable in this model.

Figure 1.

Social-Ecological Model



Source: U.S Center for Disease Control and Prevention, (2020); *https://www.cdc.gov/violenceprevention/overview/social-ecologicalmodel.html*.

The mixed SES of the subjects (pregnant women) implies that their understanding of the utilization of the available intervention is poor, hence the need for proper guidance and support from the ANC staff of the hospital and the malaria stakeholders. This aligned with the relationship and community level of the social support element of the SEM model. Further, the research on determining the association between asymptomatic PMPM, IPTp-SP compliance, use of CAM, and pregnancy outcome among pregnant women in Asaba, Delta State, Nigeria, is a match with the SEM orientation. The SEM is a theoretical framework involving all stakeholders (Bronfenbrenner, 1986; Bronfenbrenner, 1989; Bronfenbrenner, 1977; Kilanowski, 2017). In this study, it involves the government, communities, organizations, malaria control partners, participants, family, friends, and healthcare staff of the ANC.

The observed interactions at the various levels of relationship are an ideal system thinking approach to enhance personal, relationship, community, organizational, and system interaction for goal attainment and social support to parturients. The SEM is a suitable mitigation for the weaknesses/inadequacies of participants (Bronfenbrenner, 1986; Bronfenbrenner, 1989; Bronfenbrenner, 1977; Kilanowski, 2017; Schiavo et al., 2020). In this study, it pertains to health decisions, compliance to IPTp-SP and ITN frequent use, low educational attainments, poor residential location, and housing structures to achieve improved pregnancy outcome Moreover, this study could influence positive social change by mitigating the malaria surge in this group of the immunocompromised persons. Awuah et al.'s (2018) study on the determination of the risk factors of malaria infection seeking behavior among the low SES community in Ghana was grounded in the SEM. It produced valid study findings. The outcome of this research could yield useful information for malaria prevention and elimination programs in Asaba, Delta State, southern Nigeria. The adoption of the SEM framework in this study could achieve effective teamwork in controlling malaria among parturients in the target location. The outcome of this study could be applied to a similar population in other locations in the SSA region.

Literature Review Related to Key Variables and Concepts

Global and National Epidemiology of Malaria

According to the WHO, there were 228 million malaria cases in 2018 compared to 231 million cases in 2017; with 405,000 deaths in 2018 compared to 416,000 in 2017 (WHO, 2019). The economic cost of managing malaria has been rising for years and was

$2.7 million in 2018. The counterpart funding from endemic nations was $900 million, which is 30% of the total funding (CDC, 2020; WHO, 2020). The WHO Africa region bears 93% of cases and 94% of deaths due to malaria worldwide. The *P. falciparum* (mostly in the Africa regions) and P. vivax (mostly in the Americas regions) species are of the highest threat to humans with *P. falciparum* accounting for 99.7% cases in the WHO Africa region, 50% in the WHO South-east Asia, 71% in the Eastern Mediterranean, and 65% in the Western Pacific regions (CDC, 2020; WHO, 2020).

Epidemiology of Maternal Malaria

The WHO, (2020) reported that malaria is a preventable and treatable/curable infectious disease of humans, the causative agent of which is a protozoan parasite *(Plasmodium* species). Both the vector and parasite of malaria have been evolving for decades, and several efforts by scientists and global health bodies to eradicate the disease have not yielded complete success (Talakpo et al., 2019).

Buh et al. (2019) stated that the malaria infection caused by *P. falciparum* infection is the most prevalent in the SSA. It accounts for adverse pregnancy outcomes. Parturients have a higher susceptibility to malaria disease compared to their non-pregnant counterparts. The reinfection, development of a complication, and mortality from malaria disease are common among parturients (Knott, 2016; WHO, 2017). The complications include intrauterine growth retardation (IUGR), preterm delivery, anemia, hypoglycemia oedema, fetal distress, spontaneous abortion, LBW, neonatal mortality and maternal death. While the associated risk factors enumerated in various studies are parturient's age, parity/gravidae, subject's residential location, maternal income level, malaria in

pregnancy awareness, housing structure, IPTp-SP usage, and ANC attendance (Azizi et al., 2018; Buh et al., 2019; WHO, 2018).

The Route and Biology of the Mosquito and Plasmodium Parasite

The Route of Malaria Transmission

The infected *Anopheles* mosquitoes are the vector of the *Plasmodium* species parasite. The parasite can be transmitted via blood transmission, organ transplant, sharing of infected needles/syringes, and neonates can contact congenital malaria via maternal placental (CDC, 2020; WHO, 2020). The transmission intensity of malaria infection is subject to the parasite, vector, human, and environmental factors. The *Anopheles* mosquitoes, after a blood meal, will lay eggs in water, which hatch into larvae and subsequently develops into the adult mosquito. The *A. gambiae* and *A. funestus* prefers clean and clear water for their eggs (WHO, 2020). Further, WHO (2020) stated that the Africa *Anopheles* species prefers the human to animal host hence the high prevalence of the disease in that region. The mosquito lifespan, climatic conditions (pattern of rainfall, temperature, and humidity) are also determinants of malaria transmission.

The Biology of the Plasmodium Parasite

The CDC (2020) reported 176 species of *Plasmodium* species that infect vertebrates, of which 4 (*P. falciparum, P. vivux, P. ovale,* and *P. malariae*) are true parasites of humans. The *P. knowelsi* are sometimes reported to infect humans but its transmission to humans via the mosquito vector without the monkey (intermediate host) is not established. Hence *P. knowelsi* is considered a zoonotic malaria. According to Talakpo et al. (2019), *P. falciparum* and *P. vivax* have the greatest health implication. It

was reported that in 2018, *P. falciparum* accounted for 99.7% of malaria cases in the WHO African region, while P. vivax is the prevalent species in the WHO American region (CDC, 2020; Talakpo et al., 2019).

The life cycle of the *Plasmodium* parasite involves the sexual and asexual forms in a different host. The sexual stage of the parasite occurs in the vector (*Anopheles* species), while the asexual phase takes place in the human host and humans are the intermediate host of the parasite. According to Talakpo et al. (2019), asymptomatic malaria infection can persist in a human host for three to five years and may recrudesce (failure of antimalaria drugs to clear parasite due to parasite resistance to malaria drugs). The persistence of the merozoites and hepatocytes can lead to a relapse of the infection several months or years after the initial infection. The occurrence of relapse is common in *P. falciparum* infection resulting in high parasitemia. The *Plasmodium* species are complex parasites with a complicated lifecycle, which can evade the host immune responses via morphological and antigenic changes. The *Plasmodium* proteins are polymorphic with redundant functions (Talakpo et al., 2019), this parasitic disease accounts for the highest hepatic stage of the life cycle. The hepatocytes multiply and differentiate into the schizonts (made up of the numerous hepatic merozoites). The merozoites invade the red blood cells (RBCs) for the erythrocytic stage. Some merozoites in the RBCs transform into the gametocytes, which are picked up by the mosquito during a blood meal (Talakpo et al., 2019). According to Talakpo et al. (2019), all malaria parasite infections in humans leads to the upsurge of the RBCs (erythrocytes). When the

infection is untreated, it may recrudesce (appearance of malaria parasitemia from residual blood-stage parasite following failed treatment), depending on the *Plasmodium* species.

The Biology of the Plasmodium Parasite in the Vector (Mosquito)

According to the CDC (2020), the global impact of malaria is significant. There are about 400 species, of which 30 are vectors of public health importance (WHO, 2020). The *A. gambiae* and *A. funestus* are the most efficient malaria vectors in the world and are the most prevalent in Africa (Nureye and Assefa, 2020). While the predominant parasite species of malaria is *P. falciparum* (CDC, 2020; WHO, 2020). The malaria parasite is transmitted via the bite of an infected female *Anopheles* mosquito species. *Anopheles* mosquitoes lay their eggs in water, which hatch into larvae, eventually emerging as adult mosquitoes. The female mosquitoes seek a blood meal to nurture their eggs. Each species of *Anopheles* mosquito has its preferred aquatic habitat. For example, some prefer small, shallow collections of freshwaters, such as puddles and hoof prints, which are abundant during the rainy season in tropical countries (WHO, 2020).

The sporogony, or sexual phase of the *Plasmodium* life cycle occurs in the female *Anopheles* mosquito. The male and female gametocytes are picked up from the blood of the human host during the blood meal by the *Anopheles* mosquito. The blood meal is required for the development of their eggs (Onyemaechi and Malann, 2020). According to the CDC (2020), the male and female gametocytes (microgametocytes and macrogametocytes), respectively, are taken by a female *Anopheles* mosquito during a vertebrate blood meal. In the sporogonic cycle (parasite multiplication in the mosquito) and the mosquito's stomach, the fusion of the male and female gametocytes generates the

zygotes that become ookinetes (motile and elongated). The ookinetes invade the midgut wall of the mosquito and develop into the oocysts. The oocysts grow, rupture, and release sporozoites, which make their way to the mosquito's salivary glands for inoculation into a new human host (or other vertebrates host) during a blood meal to continue the malaria life cycle (CDC, 2020).

The Plasmodium Life Cycle in Humans

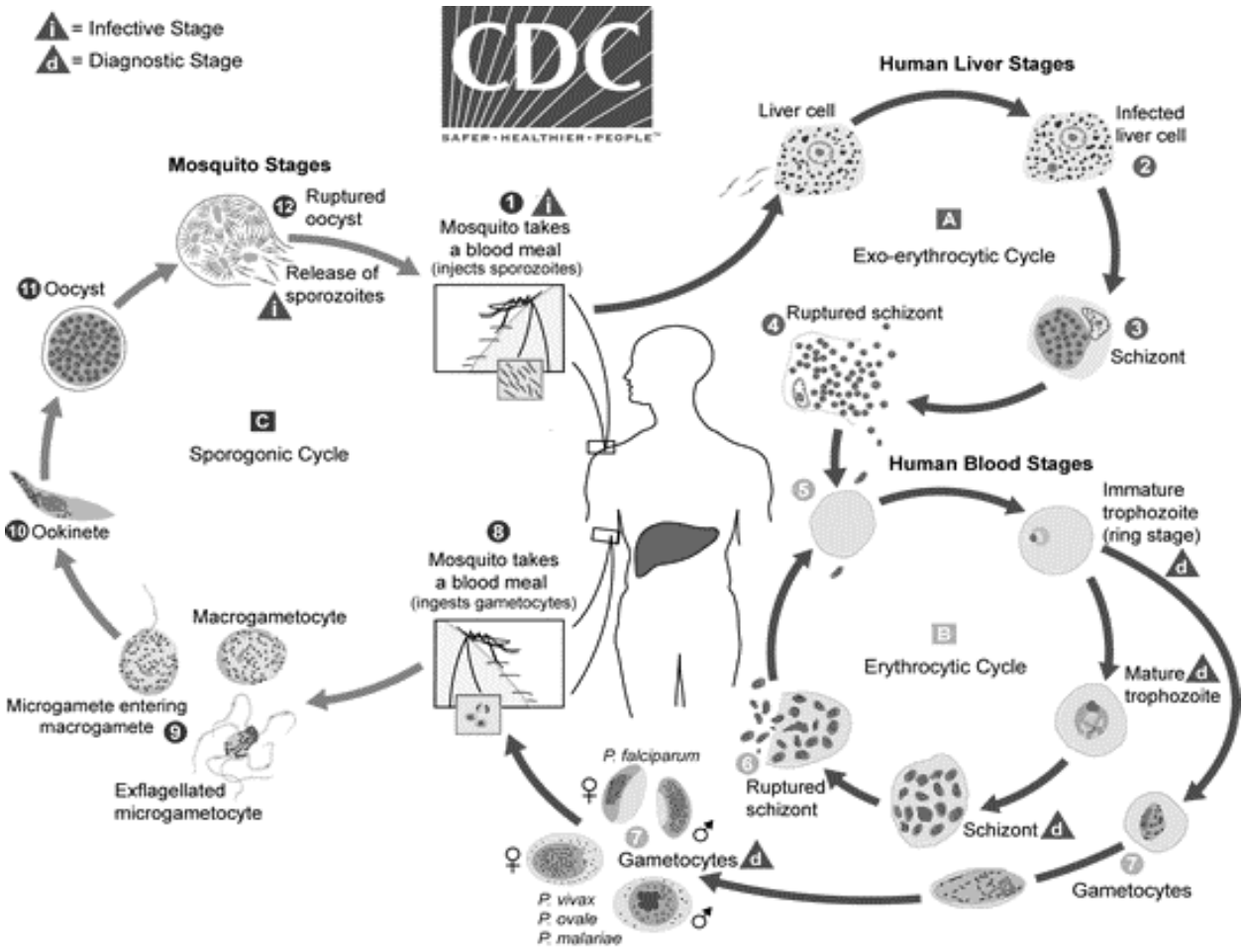
According to Nureye and Assefa (2020), the *Plasmodium* species is a protozoan blood apicomplexan parasite that infects man via the bite of an infected female *Anopheles* mosquito species. The malaria infection by *P. vivax* also occurs throughout Africa but with low infectivity due to the absence of the Duffy gene among the African people. However, this report is controversial and may require further studies to validate (Nureye & Assefa, 2020).

The sexual developmental stage of *Plasmodium* occurs in humans after the inoculation of the sporozoites during blood meal via the bite of an infected female anopheles' mosquito (*A. gambiae and A. funestus*) (CDC, 2020). The sporozoites invade the RBCs and after 30 minutes of blood circulation, enter the liver (hepatocytes); the asexual stage in the human host occurs in the liver (hepatocytes) and the RBCs. These sporozoites migrate to the liver and mature into schizonts that rupture and release the merozoites. These merozoites invade the erythrocytes to undergo the asexual phase of development. The ring stage trophozoites mature into schizonts, which rupture to release the merozoites, of which some become the gametocytes (male and female). The RBSs

ruptures due to the parasites causing fever, chills, and other symptoms of the disease (CDC, 2020; Talakpo et al., 2019).

Figure 2.

Diagram of the Plasmodium Life Cycle



SOURCE: U.S. Centers for Disease Control and Prevention (2020);

http://www.cdc.gov/malaria/about/biology/

Malaria Diagnosis/Testing Techniques

The diagnosis of malaria is via the identification of parasite antibodies from the host blood specimen. The direct diagnostic methods are RDT, microscopy, and molecular

tests, while indirect methods are indirect immunofluorescence antibody (IFA) and ELISA diagnosis (Talakpo et al., 2019). However, the gold standard diagnostic method is light microscopy of stained blood films by giemsa. The light microscopy can detect a malaria infection with 10 to 100 parasite/µl. The professional expertise of the microscopist is a determinant of the sensitivity of this method (Talakpo et al., 2019). The diagnosis of *P. falciparum* in pregnancy includes peripheral and placental blood microscopy, antigen detection tests, polymerase chain reaction (PCR), and placental histology. Placental histology and PCR are the most sensitive in detecting malaria parasitemia (Agomo et al., 2016; Aguzie, 2018; Lufelu et al., 2017).

The rapid diagnostic test (RDT) is an immunochromatographic test used to detect the malaria parasite antigen in the blood specimen. It is void of technical expertise requirements. The WHO recommended the RDT as the first choice of test in high burden areas of malaria infection, but the result should be validated by microscopy. The sensitivity is subject to the selected antigen represented in the test. The RDT for detecting antigens in the blood is immunochromatographic tests to prove the presence of parasite antigens. No electrical equipment, special training, or skills are required to perform these tests. The WHO now recommends RDT as the first choice for malaria diagnosis across the world in all malaria-endemic areas. The sensitivity of the antigen test varies depending on the selected antigens represented in the test. For some RDTs, it is 50 to 100 parasites/µL (Talakpo et al., 2019; WHO, 2020).

PCR is another method in the detection of malaria. This method is more sensitive and more specific than all conventional methods in the detection of malaria. It can detect

below one parasite/µL. PCR test confirms the presence of parasitic nucleic acid. PCR results are often not available as fast enough to be useful in malaria diagnosis in endemic areas. However, this method helps identify *Plasmodium* species after diagnosis by microscopy or RDT test in laboratories that lack microscopic experts. Additionally, PCR is useful for the monitoring of patients receiving antimalaria treatment. Indirect methods are used to demonstrate antibodies to malaria-causing agents. Such methods are used in testing people who have been or might be at risk of malaria, such as blood donors and pregnant women. The method is based on an indirect IFA or an Enzyme-linked Immunosorbent Assay (ELISA) (Talakpo et al., 2019).

Malaria Transmission

Segun et al. (2020) stated that the recent climate changes have adverse consequences on public health in Africa and other tropical regions of the world. Some others, including Talakpo et al. (2019) reported that climate changes favor the spread of vector-borne diseases such as malaria, Zika virus, and dengue fever. This spread is because the parasite life cycle and development in the vector are enhanced in the vector at certain climatic settings. The 18^{o}C to 30^{o}C (65^{o}F to 86^{o}F) temperature with 60% to 90% humidity is favorable to the breeding of the *plasmodium* parasites (Chu & White, 2016). The eggs and larvae stages of the mosquito require water, while the adult needs an appropriate temperature for growth and development. Further, Segun et al. (2020), suggests that malaria transmission is more intense in places where the mosquito lifespan is longer as the parasite has a longer development period inside the mosquito host, and where it prefers to bite humans rather than other animals. The long lifespan and strong

human-biting habit of the African vector species is the principal reason why approximately 90% of the world/global malaria cases are in Africa. The transmission of the malaria parasite also depends on climatic conditions that may affect the number and survival of mosquitoes, such as rainfall patterns, temperature, and humidity. In many places, the transmission is seasonal, with the peak during and just after the rainy season (Segun et al., 2020).

Malaria epidemics can occur when climate and other conditions suddenly favor transmission in areas where people have little or no immunity to malaria. They can also occur when people with low immunity move into areas with intense malaria transmission, for instance, for work or as refugees (Segun et al., 2020). According to WHO (2020), human immunity in malaria infection is another important factor, especially among adults in areas of moderate or intense transmission conditions. Partial immunity is developed over years of exposure, and while it never provides complete protection, it does reduce the risk that malaria infection will cause severe disease. For this reason, most malaria deaths in Africa occur in young children, parturients, and HIV patients. In contrast, in areas with less transmission and low immunity, all age groups are at risk (WHO, 2020). Onyemaechi and Malann (2020) reported that primigravidae show a higher prevalence of malaria than multigravidae and concluded that environmental conditions (temperature, relative humidity, and rainfall) are strongly associated with malaria incidence rate among the gravidae.

Malaria in Pregnancy (Peripheral and Placental Malaria)

Placenta malaria is the presence of the *Plasmodium* parasite in an infected erythrocyte or the parasite pigment/haemozoin in the intervillous spaces of the placenta. The developed asexual forms of the *P. falciparum* sequester in the placenta and evaded the host splenic clearance. Placental malaria infection is mostly asymptomatic, submicroscopic, and undetected by peripheral analysis, thereby complicating treatment (Lufelu et al., 2017).

Ouedraogo et al. (2012) reported that *P. falciparum* malaria infection is mostly asymptomatic in a high burden malaria area and usually yields maternal anemia, placental, and cord blood parasitemia among primigravidae and secundigravidae. Placental malaria does not imply the presence of peripheral malaria. Placental malaria is related to high parasitemia and repeated episodes of the parasites during pregnancy. Ouedraogo et al. (2012) reported a 19.6% prevalence of placental malaria in Burkina Faso and that maternal peripheral blood parasitemia is associated with umbilical cord parasitemia. The identified risk factors are high-density placental and peripheral parasitemia, including primigravidae status. These authors concluded that the low level of umbilical cord parasitemia implied that neonatal infection could be during delivery. Wylie et al. (2020) stated that other effects of malaria in pregnancy include congenital infection and neonatal death. The high vulnerability of pregnant women to *P. falciparum* malaria infection is due to the ability of the iRBCs to sequester in the placental with adverse consequences on pregnancy outcome via the obstruction of maternal and neonatal exchange system. Also, there is evidence of drug failures due to parasite

resistance to anti-malaria medicine. Further, the sequestered parasite in the placenta could be released intermittently into the peripheral blood and cause recurrent maternal infection (Wylie et al., 2020).

Anorue et al. (2020) reported a high prevalence of 65.8% of placental malaria by microscopy in Asaba, Delta State, southern Nigeria, while Achu et al. (2020) gave a prevalence of 8.3% and 17.7% by RDT and microscopy, respectively, of peripheral maternal malaria in the same location. Further, Olukosi and Afolabi (2018) reported a prevalence of 19.5% and 81.4% for peripheral malaria and anemia, respectively, in Lagos, southwest Nigeria. These authors stated that the subjects with anemia are more likely to have malaria infection than those without anemia. Aliyu et al. (2017) reported a prevalence of 22.4% of malaria in their study exploring the predictors of malaria parasitemia and antimalarial resistance forms of Plasmodium isolates in Kaduna State, northern Nigeria. These researchers also reported that significant isolates of *P. falciparum* exhibited multidrug resistance against several antimalarial agents.
Some researchers documented the presence of malaria parasites in the placenta of asymptomatic pregnant women with peripheral parasitemia undetected by microscopy (Omer et al., 2017; Rogerson et al., 2018). There is a gap in current knowledge that this study filled by carrying out a bivariate analysis PMPM with potential risk factors (documented in some literature from other locations).

Omer et al. (2017) reported a high prevalence (58.9%) of placenta malaria with consequences of maternal anemia and LBW of the neonates in their study area (Uganda). These same authors affirmed that positive peripheral malaria at delivery was associated

with LBW among the subject in their study. Moreover, De Beaudrap et al. (2016) reported that in Uganda, that the infants of mothers with malaria-infected placenta are at increased risk of LBW and preterm deliveries compared to babies from mothers with peripheral malaria infection. These authors reported that the time of the disease during pregnancy was a determining factor. Maternal malaria infection in the last 12 weeks to delivery is at increased risk of adverse outcomes for the mother and baby. De Beaudrap et al. (2016) concluded that placenta malaria impacts a baby's growth in the first year of life but that effective malaria treatment early in pregnancy did not yield adverse fetal and neonatal outcomes.

Goyal et al. (2016) stated that 25% of parturients have evidence of placental malaria at delivery in SSA, and in the low malaria setting, gravida is not associated with parasitemia and pregnancy outcome. In Africa, the prevalence of maternal malaria disease (peripheral and placental) is 27.8% based on microscopy. Goyal et al. (2016) stated a need to determine prevalence based on high sensitivity and specificity testing techniques such as PCR and histology. The HIV parturient is at increased risk of malaria infection, while MiP increases the HIV viral load of the subject. Parturient is at increased risk of *P. vivax* and *P. falciparum*. There is no evidence of mixed (more than one specie of the *Plasmodium* parasites) infection, but it decreases with increasing age and parity.

A study by Quakyi et al. (2019) using a cross-sectional hospital-based survey showed that low-density parasitemia is common in high burden malaria areas. Kapisi et al. (2017) stated that a high malaria burden is associated with placental malaria and adverse pregnancy outcome. It was a randomized control trial of IPTp-SP with an

assessment of placental malaria and pregnancy outcomes. These authors reported an association between high malaria burden in pregnancy with primigravidae, lower household, and IPTp-SP usage. LAMB was more sensitive in measuring placental malaria than microscopy and histopathology. Besides, they stated that placental malaria is associated with adverse pregnancy outcomes (Kapisi et al., 2017).

Maternal Malaria and Pregnancy Outcome

Anemia

The definition of anemia varies with the trimester of pregnancy. The value of <11g/dL in the first and last (third) trimester of pregnancy are considered anemic while 10g/dL–10.5g/dL in the second trimester is termed to be anemic (CDC, 1998; Renzo et al., 2015; Rouamba, et al., 2021; Tabrizi & Barjasteh, 2015).

White (2018) reported from their review study that anemia is strongly associated with malaria infection in pregnancy. The risk of anemia increases with increasing pregnancy development. These authors stated that high maternal malaria parasitemia is associated with fetal and neonatal anemia among parturients with asymptomatic malaria infection resulting in adverse maternal and fetal outcomes (White, 2018).

Vasquez et al. (2020) stated that parturient in their first and second trimester is more likely to be infected with the malaria parasites. Also, asymptomatic, and submicroscopic infections relate to adverse pregnancy outcomes. These authors reported that parturients with malaria parasitemia have a two-fold higher risk of anemia than non-pregnant counterparts, and those with maternal malaria has a two-fold higher risk of anemia, which

is associated with maternal morbidity and death, including neonatal death (Vasquez et al., 2020).

Stillbirth and Preterm Deliveries

Moore et al. (2017), in their system and meta-analysis studies, confirmed that MiP is the primary cause of stillbirth among parturients. These authors stated that placental malaria caused by *P. falciparum* has the highest of stillbirth/preterm delivery compared to malaria infection by other species of *Plasmodium*. Besides, the intensity of *P. falciparum* transmission influences stillbirths/miscarriages. Moore et al. (2017) stated that there would be a likely increase in the clinical and adverse pregnancy outcome including stillbirth due to the expected further reduction in acquired immunity among the secundigravida and multigravida as countries attain the elimination and eradication phase of malaria control; hence, more studies on malaria among parturient are required for the optimal protection of this population.

Treatment and Other Interventions on Maternal Malaria

The Drug Treatment of Malaria in Pregnancy

The treatment of malaria has evolved over the years; it dates to the second century in China with a sweet sage wort plant called Qinghai. Later, the Spanish in Peru treated it with the bark of the cinchona tree. The French chemists Pierre Joseph Pelletie and Joseph Bienaime Caventou isolated quinine as the active ingredient against malaria parasite from the Cinchona tree; in 1970, Chinese scientists isolated artemisinin from the Artemisia annua plant, which is still potent today (Talakpo et al., 2019). The WHO recommended the ACT combination therapy against malaria due to the malaria parasite's resistance to

chloroquine, sulfadoxine-pyrimethamine, and amodiaquine (Talakpo et al., 2019; WHO, 2018).

The Use of CAM for Malaria Treatment

The widespread use of CAM by parturients is well documented in the literature (Quakyi et al., 2019). According to WHO, (2013) herbal medicine are products of herbs and plants in the form of liquid, powder, or other formulations. Mothupi (2014) reported from the study on the use of herbal medicine by pregnant women in Kenya that 12% of them use herbal medicine while 20% use it simultaneously with the western medicine (IPTp-SP) they received from the ANC clinic. The author concluded that the ANC officials are unaware of such acts by their patience and recommended the need to train the parturients on the possible interaction effect of such combination. The author further stated that there is a need to determine the association between herbal medicine and pregnancy outcome.

Ogbonnaya et al. (2019) stated that the belief that herbal medicine is safe and effective is widespread among pregnant women in Nigeria. Besides, Nergard et al. (2015) reported that the use of medicinal plants for the treatment of malaria by pregnant women is a growing concern in Mali and other African countries.

The determination of the CAM association with the pregnancy outcome variables for this study is a necessary contribution to the existing knowledge base. There is no current

documentation on the possible association between PMP, CAM, and pregnancy outcome in the study location.

Other Interventions on MiP (ITNs, IRS, and IPTp-SP)

According to Yaya et al. (2018), SSA bears the highest burden of malaria infection. MiP is a key preventable cause of maternal and neonatal morbidity and death with unacceptable statistics. Despite, this evidence, the uptake, and usage of the existing interventions are far below the acceptable threshold in the region. The uptake of malaria intervention remains unsatisfactory and is void of equity in distribution across countries in the SSA (Yaya et al., 2018).

The ITNs and IRS are cost-effective vector control approaches, but the IRS requires extensive coverage to be effective in vector control. The malaria situation in Nigeria requires all stakeholders sincere and urgent attention to accelerate the malaria elimination and eradication plan.

IPTp-SP.

The Nigeria Federal Ministry of Health adopted the use of IPTp-SP in 2005 for malaria prevention and control (Igboeli et al., 2018). The WHO recommended the evaluation and monitoring of IPTp-SP association with pregnancy outcome as an assessment for the continued use of the medicine in pregnancy (Igboeli et al., 2018). Yaya et al. (2018) evaluated the prevalence and pattern of IPTp-SP uptake in some countries in the SSA and concluded that the prevalence is significantly associated with maternal education and family wealth status. Yaya et al. (2018) stated that the barriers to the usage of IPTp-SP include healthcare, economic, individual and community level, late

ANC registration, and poor knowledge. Most countries in Asia and South America are now on malaria elimination; meanwhile, the SSA is far behind with persistent bottlenecks in adopting existing preventive measures. These authors reported low prevalence and usage of IPTp-SP in SSA. They suggested a need to address the policy, structural, and socio-economic status (SES) factors accounting for such outcomes in the SSA region. They recommended the need to identify the potential barriers to the usage of IPTp-SP among parturients in the study location (Yaya et al., 2018).

In a study by Buh et al. (2019) from Sierra Leone, it was found that there was a higher likelihood of IPTp-SP uptake among parturients with higher education, higher parity of greater than four, and adequate ANC visit during pregnancy. These authors concluded that the uptake of IPTp-SP among rural dwellers was higher compared to the urban dwellers. Other authors gave contrary evidence from their studies (Amoakoh-Coleman et al., 2020; Yaya et al., 2018). It implies that there is geographical and locational specificity in the adoption and uptake of interventions.

Amoakoh-Coleman et al. (2020) detailed factors influencing the distribution and uptake of IPTp-SP in the SSA to includes maternal education, the onset of ANC visit, maternal SES, and demographic variables, and health knowledge. Also, the type of healthcare facility (primary, secondary, public, and tertiary), number of ANC attendance and health insurance status influences the uptake of IPTp-SP among parturients (Amoakoh-Coleman et al., 2020).

The WHO recommended that IPTp-SP should be taken monthly from 14 weeks of gestation for a minimum of three doses before delivery. The dosage was reviewed to five

doses or more before delivery due to the extensive wide reports of parasite's resistance to anti-malaria medicine. The observation from various reports in the SSA revealed that the uptake of IPTp-SP is far below expectations (Amoakoh-Coleman et al., 2020).

The review study by Roman et al. (2019) reported a low prevalence of IPTp-SP uptake, and the outcome was attributed to poor implementation approaches, enforcement, leadership, and healthcare problems. These authors suggested that there is a need to ascertain the factors predicting the uptake of IPTp-SP in SSA countries to develop appropriate interventions based on location. Therefore, the existing evidence from studies on the association between IPTp-SP uptake with education and other risk factors in literature is inconsistent. A study by Yaya et al. (2018) yielded an inverse outcome, whereas the study by Buh et al. (2019) reported that higher maternal education is associated with an adequate dosage of IPTp-SP. Yaya et al. (2018) recommended the need to determine the barriers to IPTp-SP uptake in the SSA and that they are region specific. Quakyi et al. (2019) reported a strong association between an increase in IPTp-SP uptake and increased birth weight. An IPTp-SP greater than three doses improve birth weight by 0.165kg. Some studies reported on the effectiveness of the treatment and preventive effect of IPTp-SP on parturients.

Some studies reported that the *Plasmodium* parasite detection difference between microscopy and PCR is significant. For example, Quakyi et al. (2019), reported low uptake of IPTp-SP in Ghana compared to ANC attendance. These authors concluded via their study on plasma level measurement of parturients that the WHO policy on greater than three doses of IPTp-SP is well implemented in their study population. They stated

that malaria infection is particularly threatening in the first and second trimester and before ANC registration; therefore, interventions such as malaria vaccine are necessary. Other studies stated that greater than three doses of IPTp-SP doses improve birth weight compared to the previous two dose regimes (Anchang et al., 2020). Quakyi et al. (2020) recommended a future study to determine the impact of the prolonged use of IPTp-SP on the fetus and neonates.

Igboeli et al.'s (2018) study was to ascertain the prevalence of LBW between the pre- IPTp-SP (2000 to 2004) and post-IPTp-SP (2005 to 2010) for various gravidae in southern Nigeria using retrospective hospital register. The authors reported a slight positive difference in birth weight in the post-IPTp-SP compared to the pre-IPTp-SP, with the primigravidae showing higher prevalence and risk of LBW in both eras. Other risk factors for LBW include maternal smoking status, high blood pressure (HBP)/pre-eclampsia, maternal nutritional status, number of ANC visits, baby's gender, maternal anemia, age, HIV, anemia, and pre-eclampsia being gravidae specific, affecting primigravidae mostly. One outcome of the study by Igboeli et al. (2018) was that there was no reduction in the risk of LBW in the primigravidae when compared with the multigravida despite the policy change in IPTp-SP dosage. The authors concluded that the policy change of IPTp-SP on the prevalence of LBW was not positive in their study area.

Oluwagbemiga et al. (2018) study was in southwestern Nigeria (Oyo state) to ascertain the factors influencing the usage of IPTp-SP in pregnancy. The authors reported that delayed registration for ANC and stock out of IPTp-SP were the observed factors

limiting the use of IPTp-SP medicine. It showed a low usage of IPTp-SP in the study locations. The authors recommended the implementation of the direct observation therapy (DOT) approach in IPTp-SP administration among the ANC subjects.

Anchang et al. (2020) accessed the coverage and effects of IPTp-SP 3-dose to 2-dose regimen on placental malaria parasitemia and LBW in Cameroun via a cross-sectional study design. The authors concluded that IPTp-SP of three or more doses was ineffective in preventing placental malaria. However, IPTp-SP was associated with increased birth weight and hemoglobin levels.

Insecticide Treated Net (ITN)

Sidiki et al. (2020) stated that hindrances to ITN usage by parturient include sweating inside the nets. These authors stated that sleeping and waking up time by parturients are associated with malaria parasitemia. The use of ITN during pregnancy is associated with maternal malaria parasitemia compared to non ITN users.

Dionne-Odom et al. (2017) stated that the factors associated with ITN usage among owners include age, higher education, and wealth level (maternal and paternal), use of family planning, having children under 5 years in the home, and the non-usage has an association with polygamy.

Ezire et al. (2015) reported from their study in Nigeria that there is high knowledge and intention to use the ITN with 64.6% population having ITN while only 19.2% sleep under the ITN. The authors stated that the knowledge of the risk of malaria and the benefits of using the ITN does not translate into the use of the ITN by parturients.

Anikwe et al. (2020) also reported that the use of ITN in Nigeria is far below the recommended standard.

Resistance of Malaria Parasite to IPTp-SP, IRS, and ITN

Toure et al. (2019) in their study on predictors of malaria infection in pregnancy in Guinea, reported that maternal resistance to anti-malaria drugs was a predictive factor for both peripheral and placenta parasitemia. They found that rural dwellers are at increased risk of malaria compared to urban dwellers. Odonga et al. (2016) in their investigation on the impact of placental malaria infection on pregnancy outcome, compared IPTp-SP two-dose compliance pregnant women with the non-compliance ones and reported that there was no difference in birth weight between IPTp-SP two-dose compliance as compared to the non-compliance. The above observation could be attributed to parasite resistance to anti-malarial drugs or inadequate doses of the IPTp-SP medicine by parturient or impact of other risk factors of MiP.

Several authors, (Ngondi et al., 2017; Odonga et al., 2016; Ruizendaal et al., 2017) reported the frequency of molecular markers of IPTp-SP resistance in malaria parasites. Ngondi et al. (2017) showed in their study in Tanzania, that the *dihydropteroate synthetase* (*dhps) 581* parasite gene was common at one health facility but infrequent in all the others, signifying that there is geographic micro-heterogeneity in mutant distribution. These authors suggested that more studies at various locations are required to understand the effect of the *dhps 581* mutant on the continued suitability of IPTp-SP. Therefore, proper surveillance involves the addition of many locations.

The study by Ruizendaal et al. (2017) was able to ascertain the prevalence of IPTp-SP resistance mutation of *P. falciparum* in pregnant women and the public from Nanoro, Burkina Faso. These authors determined the relationship of IPTp-SP dosing with mutations. The result revealed that the occurrence of the triple *dihydrofolate reductase* (*dhfr)* gene mutation was high and significantly higher among the public and during delivery than at ANC enrollment. The quintuple mutations (high resistance strain) were established for the first time in Burkina Faso in that same study. Although IPTp-SP did not significantly affect the occurrence of any of the variations, a high transmission season was linked with increased mutation frequency in delivery samples. The results of these studies raised concerns about the efficacy and continued use of IPTp-SP subsequently.

A study by Achu et al. (2020) revealed the existence of various mutant strains in their study location, indicating IPTp- SP resistance progression. These authors reiterated that the subsequent appearance of mutation at various codons is expected, which will compromise the sustained effectiveness of IPTp-SP in the study area. Further, they suggested that routine surveillance and epidemiological monitoring of mutant strains and IPTp-SP efficacy is necessary for appropriate interventions. Also, additional studies are required to determine the reason for the variability in the outcome from PCR and restriction fragment length polymorphism (RFLP) in parasite detection in their study. Consequently, research on existing malarial parasite resistant strains, and drug combinations to address MiP was recommended.

Based on the current knowledge, there is a need for expanded epidemiological and surveillance studies in various locations to determine the association between

asymptomatic placental malaria infection with pregnancy outcome, including the univariate analysis of potential risk factors, which could support tailored and result-oriented interventions.

The WHO (2017) recommended that regions with reports of Plasmodium falciparum histidine-rich protein 2 and 3 amino acid (*pfhrp2/3*) deletions should carry out extrapolative reference investigations among malaria cases to access the prevalence of *pfhrp2/3* deletions that are triggering false-negative RDT results, to determine if the existing threshold for RDT (>5%) pfhrp*2* deletions causing false-negative RDT results) is due for change (De Beaudrap et al., 2016).

Rogerson et al. (2018) stated that RDT malaria testing techniques are low in detecting the parasite in pregnancy while the PCR is useful in detecting low parasite density. These authors reported that the ongoing clinical vaccine trial is based on *variant surface antigen 2-chondroitin sulphate A (VAR2CSA)* and suggested that sequence variation be further explored to ensure a successful outcome. The authors suggested that comprehensive studies with pregnant women to monitor the trend and pattern of transmission across various geographical zones are required.

In their multicenter study, Bardaji et al. (2016) showed that the molecular diagnostic method was more sensitive in revealing submicroscopic infection than microscopy, and Achu et al. (2020) corroborated this outcome. Bardaji et al. (2016) concluded that *P. vivax* was associated with anemia, impacting fetal health significantly in their study area.

Gravidae.

Reports by researchers finding that the primigravidae (first pregnancy) are highly susceptible to malaria infection compared to the secundigravidae and multigravida (second and subsequent pregnancies) (Omer et al., 2017) remains controversial based on the evidence in the consulted literature (Anorue et al., 2020); still, Olukosi and Afolabi (2018) stated that malaria infection was detected more in the third trimester of subjects and primigravida. A study in Asaba, Delta State by Achu et al. (2020) was longitudinal, monitoring the effect of IPTp-SP on *P. falciparum* mutant strain using peripheral blood. These authors stated that the primigravidae showed a higher prevalence of malaria parasite compared to the multigravida. Anorue et al. (2020) reported that the multigravida (women who have been pregnant more than twice) were more impacted by placental malaria compared to the primigravidae (women in their first pregnancy) and secundigravidae (women in their second pregnancy). Moreover, Dogara et al. (2017) noted that the multigravida had a higher prevalence than the secundigravidae and primigravidae in Dutse, Jigawa State, Nigeria.

Based on the reviewed articles, there is a gap in the current knowledge on risk factors of MiP, and further study is required at various locations. The risk factors seem to be region/location specific. The inconsistent trends warrant additional investigation to understand the risk factors responsible for MiP in this study location. The suggestions in the cited materials indicate an ongoing real-world threat of malaria and the resistance of the *Plasmodium* parasite to anti-malaria medicine among pregnant women. The identified problem is meaningful, and further study is needed. Identifying the association between

asymptomatic PMPM, IPTp-SP compliance, the use of CAM and pregnancy outcome in this study could enhance the previous efforts in managing and controlling malaria infection in pregnancy in the study location and beyond (Feleke et al., 2020; Rogerson et al., 2018). Additionally, the systematic review study by Kakuru et al. (2019) on the assessment of available evidence on the influence of *P. falciparum* and IPTp-SP during pregnancy and subsequent life of the babies reported that the reviewed documents showed heterogeneous results. The authors suggested that further studies are required on the subjects (parturient) to confirm malaria in pregnancy and the impact of IPTp-SP while adjusting for malaria transmission intensity.

Summary and Conclusions

The global campaign for malaria elimination and eradication has not yielded expected outcomes due to vector resistance to insecticides, parasites resistance to anti-malaria medicine, including economic, and administrative issues (WHO, 2020). The WHO, the CDC and several researchers stated that malaria is both preventable and treatable despite the nagging hindrances in achieving elimination. Some countries have achieved eradication (Argentina, Paraguay, Sri Lanka, and Uzbekistan). In contrast, others have achieved elimination (Azerbaijan, Costa Rica, and Turkey) and are in the process of eradication via the use of existing interventions despite their limitations. It implies that the existing interventions/tools are sufficient to eliminate and eradicate malaria (Shretta et al., 2017).

The findings from the reviewed research are largely inconclusive, creating a gap for the further investigation determined in this study. The existing studies did not

determine an association between PMPM, IPTp-SP compliance, the use of CAM and pregnancy outcome across various healthcare facility levels. Besides, the univariate and bivariate analysis of ITN ownership, ITN frequent use, gravidae, ANC attendance, age group, and education attainment of subjects were accessed to determine the prevailing risk factors in Asaba, Delta State, southern Nigeria.

Moreover, current reports revealed that malaria predictors and risk factors vary across various regions in SSA, and the sensitivity of the current malaria testing techniques is a vital concern in the elimination and eradication plan (Omer et al., 2017; Rogerson et al., 2018). The widespread variability/geographical specificity of study outcome on malaria in pregnancy warrants epidemiological studies in various locations to ascertain the continued usefulness and utilization of the existing interventions (e.g., IRS, ITN, IPTp-SP, and case managements) which are region/location specific.

I observed from the reviewed studies that various researchers from other location used cross-sectional study designs with the quantitative method and hospital data to investigate MiP and the findings were a useful contribution to existing knowledge with positive social change (Achu et al., 2020; Anchang et al., 2020; Anorue et al., 2020; Omer et al., 2017; Rogerson et al., 2018; Quakyi et al., 2019).

In this chapter, a discussion of the current evidence on MiP was presented, while the next chapter highlighted the methodology, a description of the study population, sample size calculation and ethical concerns.

Chapter 3: Research Method

Research Design and Rationale

I structured this cross-sectional study design with a quantitative methodology to determine the association between PMPM, IPTp-SP compliance, the use of CAM, and pregnancy outcome among asymptomatic pregnant women in Asaba, Delta State, Nigeria. A univariates analysis of subject's ITN ownership and ITN frequent use, ANC attendance, gravidae, age groups, educational attainment, and PMPM was investigated. I selected Primary, secondary, and private healthcare facilities randomly from the existing healthcare facilities in Asaba, the capital of Delta State for this study. A cross-sectional study is an observational study that involves the analysis of data collected from a population, or a representative subset, at one specific point in time. Cross-sectional studies are useful for testing hypotheses, establishing the odds ratio, and relative risk for developing a disease based on someone's exposure status to a risk factor (Szklo & Nieto, 2019). Cross-sectional studies are ideal because it involves a large sample size, and many risk factors/covariates can be tested simultaneously. Cross-sectional studies are cost and time-efficient compared to case-control and cohort studies (Creswell & Creswell, 2018), and it reveals the trend, pattern, and prevalence of the exposure and outcome variables. However, cross-sectional studies are limited with respects to the temporal association between exposure and outcome because it is void of the time elements (data collection is

limited to a single point in time (single dimension; Creswell & Creswell, 2018; Rudestam & Newton, 2014).

A study by Omer et al. (2017) was a hospital-based study involving parturients presenting for delivery. The authors ascertained PMPM in association with pregnancy outcome in Blue Nile State, Sudan. The highlighted risk factors from the study were maternal young age, primigravidae, secundigravidae, non-registration at ANC, non-usage of ITN, and maternal anemia. These authors stated that there is no association between education and residential location of parturients with placental malaria. They concluded that there was a high prevalence of placental malaria in the study area were due to the non-utilization of malaria interventions. These authors reported adverse pregnancy outcomes with respect to maternal anemia and LBW. In addition, Kang et al. (2016), in a study used retrospective hospital data for the analysis of malaria cases in Malawi. The authors stated that hospital data were sufficient for the observed trend for gender and age. Ozofor and Onos (2017) in their study used retrospective hospital data on malaria cases for 6 years. The enumerated studies yielded valid results to the clinical studies.

The research questions for this study are restated below:

RQ1: What is the association between PMPM (independent variable 1 [IV_1]), IPTp-SP compliance (independent variable 2 [IV_2]), the use of CAM (independent variable 3 [IV_3]), and maternal anemia (dependent variable [DV]) among pregnant women in Asaba, Delta State, Nigeria.?

$H_0$1: There is no association between PMPM (IV_1), IPTp-SP compliance (IV_2), the use of CAM (IV_3), and maternal anemia (DV) among pregnant women in Asaba, Delta State, Nigeria.

$H_1$1: There is an association between PMPM (IV_1), IPTp-SP compliance (IV_2), the use of CAM (IV_3), and maternal anemia (DV) among pregnant women in Asaba, Delta State, Nigeria.

RQ2: What is the association between PMPM (IV_1), IPTp-SP compliance (IV_2), the use of CAM (IV_3), and baby's birth weight (DV) among pregnant women in Asaba, Delta State, Nigeria?

$H_0$2 There is no association between PMPM (IV_1), IPTp-SP compliance (IV_2), the use of CAM (IV_3), and baby's birth weight (DV) among pregnant women in Asaba, Delta State, Nigeria.

$H_1$2: There is an association between PMPM (IV_1), IPTp-SP compliance (IV_2), the use of CAM (IV_3), and baby's birth weight (DV) among pregnant women in Asaba, Delta State, Nigeria.

RQ3: What is the association between PMPM (IV_1), IPTp-SP compliance (IV_2), the use of CAM (IV_3), and delivery term (DV) among pregnant women in Asaba, Delta State, Nigeria?

$H_0$3 There is no association between PMPM (IV_1), IPTp-SP compliance (IV_2), the use of CAM (IV_3), and delivery term (DV) among pregnant women in Asaba, Delta State, Nigeria.

$H_1$3: There is an association between PMPM (IV_1), IPTp-SP compliance (IV_2), the use of CAM (IV_3), and delivery term (DV) among pregnant women in Asaba, Delta State, Nigeria.

The variables in this study were collected from parturients in the last trimester during the ANC and when presenting for delivery, who met the inclusion criteria and consented. The outcome (maternal anemia, baby's birth weight, and delivery term), predictors (PMPM, IPTp-SP compliance, the use of CAM), and other risk variables for univariates analysis (ITN ownership, ITN frequent use, ANC attendance, gravidae, age group, and educational attainment) were obtained via a survey questionnaire and validated with the hospital data. I distributed the consent form to subjects in their last trimester during the ANC and I also collected the consent form from consented parturients during their subsequent ANC visit and gave them the questionnaire to fill. I administered the questionnaires to consented subjects who cannot read at a safe distance void of overhearing by others.

The study took place consecutively at the four randomly selected healthcare facilities with high ANC statistics. It is necessary to obtain these variables by survey because some (ITN ownership, ITN frequent use and use of CAM) are not routine ANC hospital data. Further, the malaria parasitemia (peripheral) is only determined for sick parturients by the healthcare facilities in Delta State. The asymptomatic subjects are not tested. Therefore, the comprehensive collection of these variables by coded structured questionnaire (survey) via collaboration with the partner organization will maintain ethical concern of subject's privacy. However, the hospital case file number of subjects

were inscribed on the questionnaire of consented subjects for validation with hospital records. I secured the collected questionnaires in a locked drawer with limited access in my home during the data collection process to ensure confidentiality. The use of pretested structured questionnaire for data collection including validation with hospital records makes this study unique unlike other studies documented in current literature in the study location, Asaba, Delta State, southern, Nigeria and other areas.

The purpose of this study was to investigate the association between PMPM, IPTp-SP compliance, the use of CAM and pregnancy outcome (maternal anemia, baby's birth weight, and delivery term) among asymptomatic pregnant women attending ANC and presenting for delivery. I utilized quantitative methodology in a cross-sectional study design with deidentified survey questionnaires and secondary routine hospital data collected from four healthcare facilities in Asaba, Delta State, Nigeria for this study. The subject's ITN ownership, ITN frequent use, ANC attendance, gravidae, age groups, and educational attainment were also determined in a univariate and bivariate analysis among asymptomatic pregnant women in Asaba, Delta State, Nigeria. Therefore, my aim in this study was to extend research in the field by generating evidence on the disease burden and the significant risk factors of PMPM among asymptomatic pregnant women in the target population.

In this chapter, I have described the research design and rationale. The research questions and hypotheses were restated in this chapter, and it was followed by the description of the study variables. The methodology that I presented in this study included discussion about the target population, detailed procedure for data collection and

validation, subject recruitment strategies, sampling, and sample size calculation with the G*Power3 software including the use of Slovin's formula (used to calculate sample size necessary to achieve a certain confidence interval when sampling a population with limited information about the population 's behavior). However, a larger sample size than was obtained from the sample size calculated from the Gpower3 software and the Slovin sample size formular because the larger the sample size, the more confident a researcher can be that the outcome/result of the study reflects the population. Large sample size implies smaller confidence interval (Cochran, 1977; Frankfort-Nachmias & Nachmias, 2008). I explained the data collection instrument used in this study (the survey questionnaire as primary data and routine hospital data as secondary). Furthermore, I discussed the threat to validity and reliability, including how to mitigate them. In the instrumentation and operationalizing of the constructs section, I discussed how the instrument (survey questionnaire) was developed, the evidence, and possible threats to internal and external validity. I concluded this chapter with a detailed discussion of the ethical concerns and the informed consent protocols in the study.

Methodology

Study Population and Location

Delta State is an oil, commerce, and agriculturally relevant State in Nigeria. It is in the south-south geopolitical zone with a human population of 4,112,445 (males: 2,069,309; females: 2,043,136) and according to the National Population Commission & National Bureau of Statistics. (n. d), it was projected to 5,663,362 (males: 2,888,315, females: 2,775,047) in 2016. Asaba is the capital city and is in the northern part of Delta

State. Delta State covers a landmass of 18,000 km (6,970 square miles), with about 60% land. It is bounded in the north and west by Edo States and in the east by Anambra, Imo, and River States, while on the southern part is the Bight of Benin encompassing 160km coastline. Delta State is low lying and void of hills (National Population Commission & National Bureau of Statistics, n. d).

Study City/Area (Asaba)

The study sites for this research were four healthcare centers (primary, secondary, and private healthcare facilities) in Asaba. Asaba is the administrative capital of Delta State and is composed of people of different cultural and socioeconomic backgrounds from within and outside Nigeria. It is located at the northern end of the state and has an estimated population of 150,032 (2006 census) and is projected to 181,571 in 2012 at a growth rate of 3% (National Population Commission, n. d). It has an estimated area of 762 square kilometers. The city of Asaba is located at the western edge of the River Niger. The Niger Bridge links Asaba to Onitsha in Anambra State. Asaba maintains an average tropical temperature of 32°C during the dry season and an average rainfall of 2,700 mm during the rainy season, and the city falls within the tropical rain forest region of Nigeria with two major seasons: rainy and dry, with intermittent of harmattan weather. The people are engaged in farming, fishing, commerce, industry, and public and civil service jobs. The sandy beaches of the river are good sites and grounds for recreation and tourism. Travelers from other neighboring States and Regions are attracted to the city,

which is an essential factor in the transmission of infectious diseases including malaria (City Population, n. d)

The language of the indigenous Asaba people is the Ibo language, but its function as the state capital attracted a multitribal population with diverse languages such as Urhobo, Itsekiri, Isoko, Ijaw, Hausa, Yoruba, Fulani, and other minority tribes. Hence the general/common language is the low-grade English language popularly known as Delta pidgin English (Wikipedia, 2020). The Google Map showing Asaba, Delta State is presented as Figure 3.

Figure 3.

Google Map Showing Asaba, Delta State, Southern Nigeria

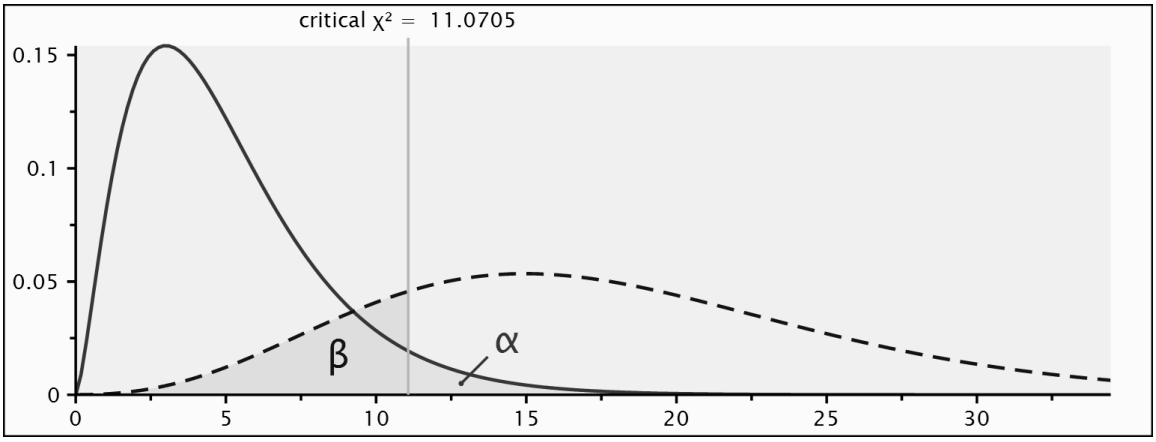
Sampling Approaches (Sample Size and Power Calculation)

Power analysis is used to determine the suitable sample size required to detect an anticipated effect (small, medium, or large) for a study. The effect size measures the strength of the relationship/association between variables, which gives information on the practical meaningfulness of the relationship among variables (Maher et al. 2013). Conducting a power analysis prior to a research study enhances the probability of obtaining a valid, reliable, and accurate statistically significant result (Rudestam & Newton, 2014). I determined the sample size using the G*Power3 software to calculate the minimum sample size based on a medium effect size of 0.3, α of 0.05, power of 0.80 and degree of freedom (df) of five (the df is a function of the number of column and rows

of the DVs and IVs). The output gave a total sample size of 143 for the study as shown in the figure 4 from the G*Power3 software output below.

Figure 4

*Output of the G*Power3 Software Calculation for the Sample Size for This Study*



The Target Population and Sample Size

The Slovin formula (used to calculate sample size necessary to achieve a certain confidence interval when sampling a population with limited information about the population‘s behavior) was used to determine the required sample size as well. The Slovin formular gives researchers the desired accuracy when working with a population that is too large to be sampled in a study (Cochran, 1977). The target population for this study was made up of parturients between the ages of 18–49 years, and who reside in Asaba, Oshimili South local government area, Delta State, Nigeria. The estimated female population in Asaba, Oshimili South local government for 2020 was projected at a 3% growth rate as 110,171 of which 26,441 were females of reproductive age (24% of female population) and the population of parturients was 1,322 (5% of reproductive-age women;

National Population Commission, n. d). The figures above were used with a margin error value of 0.05 and N as 1,322 (with Slovin's formula: $n = N/ (1+[N\{e\}^2])$ to arrive at an adequate sample size for this study of 307. So, adjusting for a 10% response rate gave a sample size of 338.

The Study Duration, Inclusion, and Exclusion Criteria

The study duration: The data collection period was 10 weeks from May 6 to July 7, 2021.

The inclusion criteria: The inclusion criteria involved asymptomatic pregnant women attending ANC and presenting for delivery in the four randomly selected healthcare facilities for the study. Every patient that qualifies as a subject, and who has consented to participate in the study with an auxiliary temperature of $\leq 37.5^{o}C$, absence of fever, chills, and headache in the last 24 hours were recruited for this study.

The exclusion criteria: The exclusion criteria were that any pregnant woman who does not want to participate, or did not sign the informed consent, ill or admitted to the intensive care unit or nonpregnant women and parturient does not reside in the study area. Parturients younger than 18 years or older than 49 years were not recruited.

The Recruitment and Data Collection Approaches

The Recruitment of Subjects

The knowledge and clarification of the study was relayed to the healthcare staff at the ANC, labor ward, and laboratory units of the four randomly selected healthcare facilities in a focused health group discussion by me. The focused group discussion helped to inform and train the hospital staff (partner organization) of this study. The

awareness and training are necessary due to the collaboration in the data collection. The data was collected as primary (survey questionnaires) and secondary (hospital record) data. The primary data included the use of CAM, educational attainments, employment status, ethnicity, residential location, age, phone ownership, usage, internet access, ANC attendance, parity, gravidae, ITN ownership, ITN frequent use, IPTp-SP compliance, and the secondary variables are placental malaria parasitemia (PMP) by RDT and microscopy, maternal anemia, baby's birth weight, delivery term, maternal, and neonatal outcome.

The Data Collection

This study instrument was a survey questionnaire with validation using the hospital records. The creation of the questionnaire was guided by the NMIS questionnaire pattern as most of the survey questions were framed/patterned after the NMIS questions which have already been validated and standardized (NMEP; NPopC), National Bureau of Statistics [NBS], and ICF International, 2016). The information from current literature and discussions with knowledgeable researchers (my committee) on MiP and clinical research guided me in developing the questionnaire instrument.

The questionnaire was worded in a low-grade English language to enhance subjects' understanding irrespective of their SES and educational attainments. The use of low-grade English language to word the questionnaire was necessary because the ANC subjects have mixed socioeconomic status and educational attainments. The consistency of the questionnaire was maintained via a pretesting/pilot testing on 20 subjects, who were in their third trimester and attending ANC in a different healthcare facility (not

selected for this study) in the study location (Asaba). I distributed the consent and subsequently the survey to qualified (based on inclusion and exclusion criteria) and consented subjects.

The details of the pregnancy outcome variable were validated via the hospital records because most of the required data are part of the healthcare routine data. At the same time, the variables that were not contained in the hospital records (ITN frequent use, and the use of CAM variables) were not validated; however, the questions were in low grade English Language and the subjects were assured that their responses will not be used against them now or in the future. The questionnaire was then used to collect information from the subjects on residential location, gravidae, age, educational attainments, ITN ownership, ITN frequent use, and use of CAM.

While at delivery, a laboratory test for PMP by RDT and microscopy was carried out by the health facility laboratory scientists for all qualified and consented subjects as part of their routine care at no costs to the subjects. Each subject laboratory specimen was labelled with their assigned unique code/ID and hospital case file number on the subject's questionnaire. The laboratory analysis was validated by a second senior technician/parasitologist, the outcome of the laboratory test was recorded in the subject's hospital file and the test outcome was communicated to the subjects by the hospital management. The positive cases for malaria were treated with artesunate SP, while positive anemic cases were treated with folic acid and iron supplements according to WHO standards at no cost to the subjects by the healthcare facility. The data were validated, de-identified, and information linking the data to the subjects (hospital case file

numbers) was removed permanently before the data was analyzed and subsequently published.

The PMP Via Microscopy

Placental blood (2mL) was collected (within one hour of delivery) from the maternal side intervillous space of the placenta using a sterile disposable lancet and stored in an Ethylene Diamine Tetracetic Acid (EDTA) anticoagulant bottle labelled with the subject's code/ID (hospital file number) and sent to the laboratory. Blood smears were prepared on a grease-free, clean glass slide at 15mm apart on both ends of the glass slide for the thick and thin smears on the same glass slides with a spreader slide and allowed to air dry before staining with 10% Giemsa at pH 7.2 for 10 minutes and examined under the ×100 oil immersion objective lens of a light microscope (Chessbrough, 2006). High-power magnifications were used to detect the presence of parasites on thick film, while thin films were used to determine the parasite species from positive thick films. The staining and blood film examination was based on the WHO guidelines (WHO, 2010). Also, the parasite density was ascertained with the plus system (Cheesbrough, 2006), which involves the counting of parasites number per high power field and evaluated according (+ [1–10 parasites per 100 high power fields], ++ [>10 parasites per 100 high power fields], +++ [1–10 parasites in one high power field], and ++++ [>10 parasites in one high power field]). If no parasites were observed in 100 fields, the sample was considered negative. The *Plasmodium* species attributes were used

to identify the species of *Plasmodium* encountered (Chessbrough, 2006; WHO, 2010; WHO, 2015).

The PMP Via RDT Testing

The malaria *P. falciparum* test cassette was detached from the foil pouch and placed on a dry surface. Each test cassette was labeled with the subject's code/ID number. A drop of the blood sample was placed on the test cassette, and three drops of diluents added immediately and allowed to run for 10 minutes. The presence of a purple color band in the result window of the test cassette guides the result interpretation. The purple color band on the test reaction zone and the control reaction zone in the result window means the sample was positive whereas a purple color band on the control reaction zone in the result window was interpreted as a negative result (WHO, 2010; WHO, 2020).

The Laboratory Determination of Maternal Anemia

The packed cell volume (PCV) analysis was used for the determination of hemoglobin level. Venous blood samples were used to determine hemoglobin level of the subjects. Capillary tube labelled for each subject code was filled with blood to about two-third of the length of the tube, and one end of the tube was sealed with plasticine. This was centrifuged with hematocrit centrifuge at 5000 revolutions per minute for five minutes. The packed cell volume of the sample was read with a standard Hawksley micro-hematocrit reader. The maternal anemia based on the standard hematocrit reader value of 11 g/dL as normal, 10 g/dL to 10.9 g/dL as mild, 7 g/dL to 9.9 g/dL as moderate, and less than 7 g/dL as severe anemia (WHO, 2011). These values were recoded as

anemia absent (AA) and anemia present (AP). The normal value determined at the third trimester were recoded as AA and the mild, moderate, and severe anemia as (AP).

Data analysis (logistic regression).

The data was analyzed using the SPSS version 25. The data was sorted and checked before computer data entry. The outcome and predictor variables were binary and categorical variables. I produced an initial descriptive statistic in tables and charts with percentages to describe the frequency distribution of the sociodemographic variables/characteristics of the independent variables. Descriptive statistics were carried out to explain the study population in relation to relevant variables. A Chi-square test was performed to ascertain the association between PMPM and each of the selected risk variables (ITN ownership, ITN frequent use, ANC attendance, gravidae, Age groups and educational attainment). The Chi-square assumption were accessed for all categorical independent variables and multicollinearity using the variance inflation factor (VIF) or correlation estimates. The model goodness of fit was determined using the Hosmer-Lemeshow test. The inferential statistics includes binomial logistic regression analysis to investigate the association between PMPM, IPTp-SP, CAM, and each of the DVs at a *P*-value of ≤ 0.05. The RQ 1, RQ 2, and RQ 3 were analyzed by binomial logistic regression. A univariate analysis was done to explain the study population in relation to selected risk variables. The *P*-value determined at 0.05 was the basis for the acceptance or rejection of the null hypothesis. (Frankfort –Nachmias & Nachmias, 2008). The use of binomial logistics regression and Chi-square test aligned with the research question and the restrictive assumptions of linear regression were not required in logistic regression. It

was a robust statistical analysis (Creswell & Creswell, 2018; Rudestam & Newton, 2014). Binomial logistic test is suitable because it could ascertain the level and significance of the variables (Forthofer, & Lee, 2014; Kanyangarara et al., 2016; Sichande et al., 2014). Besides, the study outcome and predictor variables were binary and dichotomous. (Hidalgo & Goodman, 2013). The Chi-square analysis was selected because of its popular application in finding the association between a categorical or dichotomous dependent and independent variables (Creswell & Creswell, 2018; Rudestam & Newton, 2014).

Instrumentation and Operationalization of Construct (Instruments to Measure

The Questionnaire

The questionnaire was partitioned with the same sequence of items for each participant. I avoided paraphrasing/rewording the questions or providing expressive information, interpretation, or explanations to the subjects. The aim was to ensure that the differences in response to questions were due to real difference among subjects. (Frankfort-Nachmias & Nachmias, 2015; Rudestam & Newton, 2014). The subjects were assigned specific code/ID number (for identification) which were used to match all data collected. Information on all the variables were recorded in the questionnaire. This study questionnaire is attached as Appendix A.

Evidence for Reliability and Validity of Instruments

Reliability refers to the function of a test to produce a consistent/same result, when used to measure the same thing, at different times, while validity measures what it proposes to measure. The use of probability sampling and sampling formula in this study

ensured standardized effect size and representativeness. Besides, the questionnaire items were carefully worded to avoid misleading, intimidating, or double-barred questions (Frankfort–Nachmias & Nachmias, 2015; Rudestam & Newton, 2014). Moreover, the pilot test and adjustment of the questionnaire based on the outcome enhanced the reliability and validity of the study.

Mitigating Threat to Internal and External Validity

The chosen design of the study incorporated some methodological strengths, however, some threats to validity exist in this study. The self-reported nature of some variables may have introduced recall bias, which may lead to inaccurate data provided by the participants. Social desirability may have affected the accuracy of reporting of the sociodemographic, SES, ITN frequent use, and use of CAM especially due to the lack of anonymity in the data collection approach. However, the subjects were informed in the consent form that the information they gave will not be used against them now or later and nobody will refer to it against them personally.

The study is a cross-sectional design, and the findings can only be extrapolated in the context of time to the setting of the survey, and a population with similar features. The external validity could be threatened if any inference is made, or findings extrapolated to other population/settings/past/future situations (Creswell & Creswell, 2008). Other possible sources of threat to the internal validity of the study could be through the processes of sample selection, data collection, and instrumentation (Creswell & Creswell, 2008). Also, the random sampling in health facility selection could prevent possible threat to internal validity. The selection of participants with likely extreme score

could also be a threat to internal validity (Creswell & Creswell, 2008). Possible threats to construct validity could be due to inadequate or wrong definitions and measurement of research variables (Creswell & Creswell, 2008). The independent variables and other risk variables were explained based on the SEM (Champion & Skinner, 2008). Chi-square, and binomial logistic regression were properly applied, to avoid threat to construct validity.

The Measurement of Variables

The required hospital data (variables) include the following outcome, predictors, and risk variables for univariate analysis:

- Pregnancy outcome variables (dependent/outcome variable; DV) including maternal anemia based on the standard hematocrit reader categorized as mild, moderate, and severe anemia. The maternal anemia based on the standard hematocrit reader include 11 g/dL as normal,10 g/dL to 10.9 g/dL as mild, 7 g/dL to 9.9 g/dL as moderate, and less than 7 g/dL as severe anemia (WHO, 2011). These values were recoded as anemia absent (AA) and anemia present (AP).The normal anemia value at delivery were recoded as AA and the mild, moderate, and severe anemia as AP. It was recoded as anemia absent (AA) and anemia present (AA); baby's birth weight, above or equals 2.5 kg as normal birth weight (NBW), and below 2.5 kg as low birth weight (LBW), preterm and term delivery as less than or equal to 36 weeks and equal to or greater than 37 weeks, respectively.
- Predictor variables; The independent/exposure variables (IVs) including maternal placental malaria parasitemia (IV_1) as positive (presence) placental malaria

parasitemia (PPMP) and negative (absence) placental malaria parasitemia (NPMP); the IPTp-SP (IV_2) as to compliant to three or more doses of IPTp-SP during pregnancy (adequate) and not compliant as none or less than three doses IPTp-SP during pregnancy (inadequate) and use of CAM (IV_3) as Yes, No responses.

- Other variables for univariates analysis include the subject's ITN ownership (Yes, No), ITN frequent use (Yes, No), ANC attendance, gravidae (primigravidae, secundigravidae, and multigravida), age groups, and educational attainment (none, primary, secondary, tertiary and, above). Table 1, showing the measurement and coding of the variables is attached.

Table 1

The Variables, Response Code and Measurement Type used in This Study

Variable	Response Code	Measurement
Dependent/outcome		
Maternal anemia		Dichotomous/Nominal
AA	0	
AP	1	
Baby's birth weight		Dichotomous/Nominal
NBW	0	
LBW	1	
Delivery term		Dichotomous/Nominal
TD	0	
Preterm	1	
Independent/Predictor		
PMPRDT		Dichotomous/Nominal
NPMPRDT	0	
PPMPRDT	1	
PMPM		Dichotomous/Nominal
NPMPM	0	
PPMPM	1	
IPTp-SP compliance		Dichotomous/Nominal

Adequate	0	
Inadequate	1	
CAM		Dichotomous/Nominal
No	0	
Yes	1	
Risk variables		
ITNs ownership		Dichotomous/Nominal
No	0	
Yes	1	
ITNs use		Dichotomous/Nominal
No	0	
Yes	1	
Gravidae		Ordinal/Nominal
Primigravidae	1	
Secundigravidae	2	
Multigravida	3	
Age group (years).		Ordinal/Nominal
18–25	1	
26–34	2	
35–42	3	
43–49	4	

Educational attainment		Ordinal/Nominal
None	0	
Primary	1	
Secondary	2	
Tertiary	3	

Ethical Consideration

Approval from the institutional review board (IRB) from Walden University, the Delta State Ministry of Health, the data sites, and the subject's confidentiality requirement were maintained as only the de-identified data were analyzed and published. The validation of some variables with the hospital file were done by me. Moreover, this study is void of exploitation of subjects because the outcome of the study for maternal malaria and anemia at the individual level were explained in simple terms to the hospital management to relay to their patients. The positive malaria parasitemia cases were informed and treated with artesunate SP based on WHO guidelines and counselled to seek early malaria treatment for their neonates when unwell. Moreover, the healthcare system was advised to adjust their interventions and care to mitigate the adverse outcome of MiP on their patients based on the study outcome and recommendation.

The consents form would indicate that a participant was at liberty to exit the study at any point during the study. The process to leave the study was simply by informing the

researcher. Any subject who wishes to withdraw from the study was not swayed, coaxed, or pressured to continue.

Informed Consent

The subjects were given complete information about the study at individual levels. The formal consent in writing or thumb printed before the administration of the questionnaire were secured. I provided each subject with standardized introductory information about the study as contained in the questionnaire, after which the subjects were expected to either give or not give consent. The information, which was provided in the low-grade English language for the understanding of the subjects, included research purpose, the source of organizational and monetary support for the study, and the estimated duration (15 minutes) in filling the questionnaire.

After delivery of the baby and placenta, 2 mL of blood was taken from the placenta by the healthcare laboratory scientist for RDT and microscopy analysis to determine the maternal malaria parasitemia status. Also, the hospital record of subjects for maternal anemia test analysis was recorded in each subject's questionnaire. As

detailed by Creswell and Creswell (2018) a consent form was developed and used to produce information on the following:

- Explain the identity of the investigator and the supportive academic organization.
- Guarantee of confidentiality concerning the subject's information.
- Explain the aim of the study.
- Assess the level of subjects' commitment.
- Explain the advantages of the study to subjects.
- Ask permission to contact each subject for follow-up questions by the researcher; and
- Give the women the freedom to participate or withdraw from the study at any time, simply by informing the researcher.
- Each participant either sign or thumbprint on the consent form as a mark of consent.

Limitations, Challenges, and Barriers of the Study

This study was a cross-sectional design; therefore, causality cannot be ascertained, since all samples were taken at delivery. The impact of past infection on maternal, fetus, and neonatal outcomes cannot be determined. Also, the bias arising from self-reporting of demographic and socioeconomic status variables are envisaged in this study; consequently, the mitigation through validation with hospital records was appropriate. The information bias from self-reporting of survey data was mitigated by adequate training of the subjects before the data collection, pretesting of the questionnaire, and validation with hospital records and phone calls. Further, some factors

that could impact fetal outcome, such as maternal nutritional status, child spacing, genetic influences, other infectious diseases, smoking and wrong use of alcohol were not investigated in this study (Kapisi et al., 2017).

Strength of the Study

An essential strength of the study was the use of binomial logistic regressions for the statistical analysis because it is robust in identifying confounders and it is less restrictive for assumptions (Feleke et al., 2020). Also, the use of a pretested structured questionnaire was to ensure appropriate baseline understanding of the survey questions. And lastly, the selection of four health care facilities (primary, secondary, and private health care facilities; comprising two public and two private healthcare facilities) in the state could afford better comparison of study outcomes based on the level of care and location. All the consulted study in Nigeria used data from a single healthcare facility in their study.

Pilot Testing

The questionnaire was pilot tested among 20 respondents with same population features as the study population. The pretest was done in different healthcare facility that was not used for actual data collection. The aim of the pilot test was to ensure baseline understanding of the survey question by subjects during the actual data collection. The result of the pilot test was not reported in this study but was discussed with my committee and the required change(s) in the survey question (framing) was applied accordingly.

Summary and Transition

This cross-sectional quantitative research study used hospital based primary and secondary data from four healthcare facilities in Nigerian to determine the association and the risk factors for PMPM and pregnancy outcomes in the studied population. The data validation was with hospital records (secondary data). The predictor variables and outcome variables, as well as the selected risk factors variables, were discussed with their respective coding for statistical analyses. All statistical analyses were conducted with SPSS version 25, and I reported the details of the results and the analysis of the findings in Chapter 4. I presented the descriptive statistics of the study variables in tables. Specifically, the inferential statistics was carried out through binomial logistic regression models and the calculation of odds ratios, I tested the six null hypotheses in this study. Subsequently, I discussed the results of each of the three research questions and explained the relationships between the independent variables with the study outcome.

Chapter 4: Results.

Introduction

In the previous chapter, I detailed the study methodology. I provided a summary of the purpose, a restatement of the research questions and hypotheses, description of the sampling procedures, and data collection process. I designed this study to investigate the association between asymptomatic malaria infection and pregnancy outcome among pregnant women using quantitative methodology with a cross-sectional design and the risk factors related to placental malaria were analyzed. The findings could provide a basis for a review of policies and interventions at policy, service delivery, and community levels to increase the uptake of the recommended measures/interventions for the prevention of MiP. I developed three RQs and three sets of hypotheses for this study, the RQs are as follows:

RQ1: What is the association between PMPM (independent variable 1 [IV_1]), IPTp-SP compliance (independent variable 2 [IV_2]), the use of CAM (independent variable 3 [IV_3]), and maternal anemia (dependent variable [DV]) among pregnant women in Asaba, Delta State, Nigeria.?

$H_0$1: There is no association between PMPM (IV_1), IPTp-SP compliance (IV_2), the use of CAM (IV_3), and maternal anemia (DV) among pregnant women in Asaba, Delta State, Nigeria.

$H_1$1: There is an association between PMPM (IV_1), IPTp-SP compliance (IV_2), the use of CAM (IV_3), and maternal anemia (DV) among pregnant women in Asaba, Delta State, Nigeria.

RQ2: What is the association between PMPM (IV_1), IPTp-SP compliance (IV_2), the use of CAM (IV_3), and baby's birth weight (DV) among pregnant women in Asaba, Delta State, Nigeria?

$H_0$2 There is no association between PMPM (IV_1), IPTp-SP compliance (IV_2), the use of CAM (IV_3), and baby's birth weight (DV) among pregnant women in Asaba, Delta State, Nigeria.

$H_1$2: There is an association between PMPM (IV_1), IPTp-SP compliance (IV_2), the use of CAM (IV_3), and baby's birth weight (DV) among pregnant women in Asaba, Delta State, Nigeria.

RQ3: What is the association between PMPM (IV_1), IPTp-SP compliance (IV_2), the use of CAM (IV_3), and delivery term (DV) among pregnant women in Asaba, Delta State, Nigeria?

$H_0$3 There is no association between PMPM (IV_1), IPTp-SP compliance (IV_2), the use of CAM (IV_3), and delivery term (DV) among pregnant women in Asaba, Delta State, Nigeria.

$H_1$3: There is an association between PMPM (IV_1), IPTp-SP compliance (IV_2), the use of CAM (IV_3), and delivery term (DV) among pregnant women in Asaba, Delta State, Nigeria.

In this chapter, I provided a summary of the study purpose and research questions. In addition to the introduction, there were three sections in this chapter: data collection, results, and summary. The data collection discussed in chapter 4 described the data collection timeframe and a description of the sample. In the results section, I described

the data cleaning and coding process, provided the descriptive statistics of the demographic/sociodemographic data, placental malaria parasitemia and obstetrics data, the malaria intervention variables, and evaluates the statistical assumptions of the statistical tests performed to answer the research questions. The statistical analysis findings were organized by the research questions. The results of the univariate descriptive statistics, Chi-square (bivariate) statistical analysis of the enumerated risk factors (ITN ownership, ITN frequent use, ANC attendance, gravidae, age groups, and educational attainment), and the placental malaria parasitemia by microscopy (PMPM) variable were presented as well. Finally, in the chapter 4 summary, I gave a collation of the outcome of the analysis from the research questions and transitions to chapter 5.

The pilot test was done on May 5, 2021, on 20 subjects in another health care facility in Asaba that was not listed for the study. The focus of the pilot testing was to establish baseline understanding of the survey questions among the parturients. The result of the pilot test did not impact the data collection procedure. I stated in the proposal that the pilot study aimed to ensure baseline understanding of the questions by the subjects and that I will discuss the outcome with my committee. If needed, I will reframe the questionnaire questions to ensure that all the subjects understand the questions. However, it was discovered after the pilot testing that there was controversy in deciding on the Question 7 of section B in the questionnaire: What is your residential location? Is your area a rural or urban location*?* it was difficult to decide which area was rural/urban because the recruitment criteria stated that the subject resides in Asaba and Asaba is the capital city of the State. Hence, I removed the Question 7 of section B. The pilot study

did not impact this study as there was no change in the data collection, instrumentation, or analysis process.

The data preparation process comprises of three phases viz: the data preparation phase, the preliminary analysis phase, and the primary analysis phase.

Data Preparation

All the subjects who were enrolled in an ANC in the selected healthcare facilities that met the inclusion criteria and consented were recruited into the study. The laboratory and obstetrics data of each subject were matched with the hospital file number of subjects on the survey questionnaires, and I transcribed them into the survey questionnaires and subsequently, the data were carefully entered into the Excel spread sheet version 2013 and checked for error and missing values and corrected via validation with the hospital records. A total of 496 data were collected from the 500 questionnaires that were distributed. But after sieving out missing and incomplete data, I had 483 data points fit for the analysis. Thereafter, the data were opened in SPSS version 25 software package for further analysis as stated in the methodology outlined in Chapter 3.

Preliminary Analysis

In this phase, some of the variables were recoded as proposed, and new variables were computed such as with the PCV values, which were converted to the hemoglobin (Hb) values by dividing by three (Abbott Point of Care Inc., 2016; Koperska, 2018), and thereafter recoded as anemia absent (AA) meaning no anemia, and anemia present (AP) meaning the presence of mild, moderate, and severe anemia. The IPTp-SP compliance variable was recoded into 0 as adequate and 1 as inadequate from the four compliance

levels of zero, once, twice, and more than twice with the inadequate group comprising of the zero, once, and twice while the adequate group is made up of more than twice compliance. According to Aguzie, (2018), the WHO recommended four or more doses before delivery in the malaria high burden region. So, in the preliminary analysis phase, tests of parametric assumptions were performed to determine if there were violations of the logistic regression and Chi-square analysis and if so, what other alternative analyses should be conducted.

Primary Analysis

In the primary analysis phase, I performed statistical tests that answered the research questions of the study. In this study, descriptive statistics performed on the variables revealed no data errors. However, I observed a few missing/incomplete variables which lead to the reduction of the total data from 496 to 483 (after sieving out the missing/incomplete variables). The response rate for this study was 99.2%.

The following is a list of codes and definitions used in this study:

PMP	Placental malaria parasitemia
PMPM	Placental malaria parasitemia by microscopy
RDT	Rapid diagnostic test.
PPMP	Positive placental malaria parasitemia
NPMP	Negative placental malaria parasitemia
AA	Anemia absent
AP	Anemia present

BW	Birth weight
NBW	Normal birth weight.
LBW	Low birth weight
GAD	Gestational age at delivery
N	Population
M	Mean
MD	Mean deviation
SD	Standard deviation
CI	Confidence interval
R^2	Negelkerke pseudo
H-L	Hosmer-Lemeshow test

I conducted preliminary analyses to evaluate the assumptions of the logistic regression. The assumptions of the logistic regression are linearity (for continuous variables), multicollinearity, and absence of high correlation among the IVs (Pallant, 2016; Tabachnick & Fidell, 2012). There was no violation in the assumption of linearity because the IVs were all binary and categorical variables. The outcome of the correlation analysis among the IVs showed that there was no high correlation among the IVs as the values were below the threshold of plus/minus 0.70/0.80 as shown in Tables 2 and 3 below. The result of the collinearity diagnostics in Table 4, showed that the VIF values are below the threshold of 10. They are less than five, which is best. This implies that the

IVs are not highly correlated with each other and there is no violation of the multicollinearity assumption as well.

Table 2.

The Result of the Correlation Analysis to Access the Correlation among the Binary Independent Variables

Pearson Correlation			PMPM	IPTp-SP	CAM use	ITN s ownership	ITNs use
	PMPM	Correlation coefficient	1.000	0.042	0.015	-0.055	0.031
		P-value	-	0.362	0.744	0.228	0.491
		N	483	483	483	483	483
	IPTp-SP	Correlation coefficient	0.042	1.000	0.031	0.030	0.097*
		P-value	0.362	-	0.503	0.509	0.032
		N	483	483	483	483	483
	CAM use	Correlation coefficient	0.015	0.031	1.000	-0.054	0.008
		P-value	0.744	0.503	-	0.235	0.860
		N	483	483	483	483	483
	ITN s ownership	Correlation coefficient	-0.055	0.030	0.054	1.000	0.475**
		P-value	0.228	0.509	0.235	-	0.000
		N	483	483	483	483	483
	ITNs use	Correlation coefficient	0.031	0.097*	0.008	0.475**	1.000
		P-value	0.491	0.032	0.860	0.000	-
		N	483	483	483	483	483

Note: Perfect correlation denoted with plus/minus 0.70/0.80

**Correlation is significant at the 0.01 level (*P*-value).

*Correlation is significant at the 0.05 level (*P*-value)

This table shows that the correlation among the binary independent/predictor variables used in this study were within the acceptable threshold.

Table 3.

The Result of the Correlation Analysis to Access the Correlation among the Categorical Independent Variables

Spearman's Rho		Correlations			
		Age group	Educational attainment	Gravidae	ANC attendance
Age group	Correlation coefficient	1.000	0.175**	0.400**	0.051
	P-value	-	0.000	0.000	0.264
	N	483	483	483	483
Educational attainment	Correlation coefficient	0.175**	1.000	0.105*	0.061
	P-value	0.000	-	0.021	0.180
	N	483	483	483	483
Gravidae	Correlation coefficient	0.400**	0.105*	1.000	0.062
	P-value	0.000	0.021	-	0.173
	N	483	483	483	483
ANC attendance	Correlation coefficient	0.051	0.061	0.062	1.000
	P-value	0.264	0.180	0.173	-
	N	483	483	483	483

Note: Perfect correlation denoted with plus/minus 0.70/0.80

**Correlation is significant at the 0.01 level (2-tailed).

*Correlation is significant at the 0.05 level (2-tailed)

This table shows the correlation among the categorical independent/predictor variables used in this study were within the acceptable threshold.

Table 4.

The Result of the Tolerance and VIF

IVs	Tolerance	VIF

PMPM	0.991	1.009
IPTp-SP compliance	0.988	1.012
CAM use now	0.995	1.005
ITNs ownership	0.766	1.305
ITNs frequent usage	0.764	1.309

The Primary Analysis Phase

The Descriptive and the Analytic Statistics of the Findings

The descriptive statistics explains the details of the demographic/sociodemographic, placental malaria parasitemia/obstetrics, and the malaria intervention variables. I presented the details in Tables 5, 6, and 7, respectively. There were 483 research participants in the study with a response rate of 99.2%. The minimum and maximum age of the subjects that participated in this study were 18 years and 48 years, respectively with a mean age of 28.09 years and standard deviation (SD) of 5.472. About twenty-six percent (25.9%) were between the ages of 18–25 years. Sixty percent of the subjects were between the ages of 26–34 years, 12.8% were between the ages of 35–42 years, and 1.2% were between the ages of 43–49 years. Most (93.6%) of the subjects were married, and only 6.4% were unmarried. Less than two percent (1.9%) had no form of formal education, 2.1% had a primary education, 44.9% had a secondary education, and 51.1% had a tertiary education. Of all the subjects, 57.6% owned ITNs but only 26.3% reported sleeping under it frequently. While 44.3% obtained it from the ANC, 10.1% purchased it. Furthermore, 77.0% of the study population had attended the

ANC more than twice before delivery. The descriptive statistics on gravidae are 20.1% (n = 97), 34.4% (n = 166), and 45.5% (n = 220) for primigravidae, secundigravidae, and multigravida, respectively. The descriptive statistics on the use of CAM showed that 17.6% of the subjects in this study use CAM during this pregnancy. Also, only 15.3% had three or more doses of the IPTp-SP. The mean value of hemoglobin (in g/dL) was 11.02 and the SD value of hemoglobin (in g/dL) was 0.911. The univariate analysis of major variables in this study using frequency table were presented below in Tables 5, 6, and 7.

Table 5.

The Descriptive Statistics of the Demographic and Sociodemographic Variables of Subjects in this Study.

Variable	Frequency (N)	Percentage (%)
Age group (years)		
18–25	125	25.9
26–34	290	60.0
35–42	62	12.8
43–49	6	1.2
Marital status		
Married	452	93.6
Unmarried	31	6.4
Educational attainment		
None	9	1.9

Primary	10	2.1
Secondary	217	44.9
Tertiary	247	51.1
Employment status		
Unemployed	134	27.7
Employed	349	72.3
Mobile phone ownership		
No	23	4.8
Yes	460	95.2
Internet access		
No	176	36.4
Yes	307	63.6
Access to WhatsApp		
No	179	37.1
Yes	304	62.9
Access to Facebook		
No	188	38.9
Yes	295	61.1

Table 6.

The Descriptive Statistics of the Placental Malaria Parasitemia and the Obstetrics Variables in this Study.

Variable	Frequency (N)	Percentage (%)
Maternal anemia		
AA	282	58.4
AP	201	41.6
Baby's birth weight (kg)		
NBW	421	87.2
LBW	62	12.8
Delivery Term/Gestational Age at Delivery		
TD	434	89.9
Preterm	49	10.1
PMPRDT		
NPMPRDT	454	94.0
PPMPRDT	29	6.0
PMPM		
NPMPM	218	45.1
PPMPM	265	54.9
Gravidae		
Primigravidae	97	20.1
Secundigravidae	166	34.4
Multigravida	220	45.5

Table 7.

The Descriptive Statistics of the Malaria Intervention Variables in this Study.

Variable	Frequency (N)	Percentage (%)
IPTp-SP compliance		
Adequate	74	15.3
Inadequate	409	84.7
CAM		
No	398	82.4
Yes	85	17.6
ITN ownership		
No	205	47.4
Yes	278	57.6
ITN frequent use		
No	356	73.7
Yes	127	26.3

The result of the Chi-square analysis (bivariate analysis).

The results of the Chi-square analysis are itemized below and summarized in Table 8.

1. The Chi-square analysis between PMPM and the ownership of ITN revealed that there is no statistically significant association between PMPM and the ownership of ITNs.

$\chi 2$ (1.458, df = 1, P = 0.227).

2. The Chi-square analysis between PMPM and the usage of ITN on frequent bases revealed that there is no statistically significant association between PMPM and the usage of ITNs on frequent bases.

$\chi 2$ (0.46, df = 1, *P* = 0.490)

3. The Chi-square analysis between PMPM and ANC attendance revealed that the association tend towards significance.

$\chi 2$ (5.949, df = 2, *P* = 0.051).

4. The Chi-square analysis between PMPM and gravidae revealed that there is no statistically significant association between PMPM and gravidae.

$\chi 2$ (3.848, df = 2, *P* = 0.146).

5. The Chi-square analysis between PMPM and Age groups revealed that there is no statistically significant association between PMPM and Age groups.

$\chi 2$ (2.582, df = 3, *P* = 0.461).

6. The Chi-square analysis between PMPM and educational attainment revealed that there is a statistically significant association between PMPM and educational attainment.

$\chi 2$ (12.852, df = 2, *P* = 0.020).

Table 8.

The Summary Results from the Chi-square Analysis.

		PMPM		
IVs	N	Pearson $\chi 2$	df	*P*-value
INTs Ownership	483	1.458[a]	1	0.227
INTs Freq. Usage	483	0.476[a]	1	0.490
ANC attendance	483	5.949[a]	2	0.051

Gravidae	483	3.848[a]	2	0.146
Age groups	483	2.582	3	0.461
Educational attainment	483	9.785[a]	3	0.020

Note:

The Prevalence of Placental Malaria, LBW, and Preterm Deliveries in the Study

The prevalence of placental malaria by microscopy and RDT in this study was 54.9% and 6.0% respectively. The prevalence of PMPM was highest among the secundigravida (60.8%), followed by the primigravida (53.6%) and lowest among the multigravida (50.9%) in this study population. Maternal anemia was 41.6%, with 28.6% having mild anemia and 13.3% having moderate anemia; there were no cases of severe anemia in this study. LBW was 12.8%, and preterm delivery was 10.1%. Moreover, only *P. falciparum* specie were identified in this study. There were 49.9% of mild (+) parasitemia cases, while only 5.0% were moderate (+ +) by microscopy. The mild cases were also positive by the RDT. There was no severe (+ + +), and hyper (> + + +) parasitemia malaria cases in this study. The vast difference in prevalence between microscopy (49.9%) and RDT (6.0%) was attributed to the high false-negative by RDT testing techniques.

The Prevalence of Placental Malaria, LBW, and Preterm Deliveries Across the Three Healthcare Facilities in this Study

The prevalence of placental malaria by microscopy in the primary, secondary, and private healthcare facilities were 44.3%, 33%, and 64.5%, respectively. The LBW across the primary, secondary, and private were 21.4%, 9.7%, and 11.9%. Preterm deliveries yielded a prevalence of 21.4%, 6.8%, and 8.7% across the three facility levels. Finally, 60.0%, 63.1%, and 30.6% were anemic across the primary, secondary, and private healthcare facilities. These statistics are presented in Table 9 below.

Table 9.

The Prevalence of Placental Malaria, LBW, and Preterm Deliveries across the three Healthcare Facilities Levels in this Study.

	Prevalence (%)			
Health facility level	PMPM	LBW	Preterm	Anemia
Primary facility	44.3	21.4	21.4	60.0
Secondary (Government) facility	33	9.7	6.8	63.1
Private facility	64.5	11.9	8.7	30.6

Logistic Regression Analysis in Relation to RQ1

The result of the logistic regression analysis to determine the association between PMPM (IV_1), IPTp-SP compliance (IV_2), the use of CAM (IV_3), and maternal anemia (DV) among pregnant women in the study population showed a statistically significant effect on maternal anemia based on the *P*-value in the model indicated in Table 10; χ 2

(3) = 14.562, *P = 0*.002. The model explained 4.0% (Negelkerke's R^2) of the variances in maternal anemia and correctly classified 58.4% of cases. The performance of the PMPM was statistically significant (odd ratio of 0.584, CI: 0.403–0.847, *P* = 0.005). The subjects with PPMPM were 0.584 times as likely (58.4% more likely) to exhibit maternal anemia than the subjects with NPMPM. Also, the use of CAM (odd ratio = 1.631, CI: 1.014–2.625, *P* = 0.044) was associated with an increase in the likelihood of exhibiting maternal anemia in this model. However, the IPTp-SP compliance variable was not statistically significant (odd ratio = 1.426, CI: 0.842–2.415, *P = 0*.186). The Hosmer-Lemeshow test was not significant with a *P*-value of 0.640, implying that the model has a good fit. Subsequent on the above, I rejected the null hypotheses and accepted the alternate hypotheses in respect to RQ1.

Table 10.

The Omnibus Test of Model Coefficients for Research Question 1 Analysis.

Step 1		Chi-square	Df	*P*-value
	Step	14.562	3	0.002
	Block	14.562	3	0.002
	Model	14.562	3	0.002

Note: This table shows the statistical significance of the model explored in RQ 1.

Table 11.

The Variables in the Equation for Research Question 1 Analysis.

B	S.E	Wald	Df	*P*-value	Exp(*B*)

-.339	0.092	13.455	1	0.000	0.713

Table 12.

The Result of the Logistic Regression Analysis for the Individual Performance of the Variables in the Equation for Research Question 1 Analysis.

							95% CI	
		B	S.E	Wald	Df	*P*-value	Odd ratio	LCI	UCI
Step 1[a]	PMPM	-0.538	0.190	8.058	1	0.005	0.584	0.403	0.847
	IPTp-SP compliance	0.355	0.269	1.747	1	0.186	1.426	0.842	2.415
	CAM use	0.489	0.234	4.068	1	0.044	1.631	1.014	2.625
	Constant	-0.493	0.266	3.431	1	0.064	0.611		

Variable (s) entered on step 1: PMPM, IPTp-SP compliance, CAM use. This table shows the statistical significance of each variable being explored in RQ1.

Table 13.

The Hosmer-Lemeshow Test for Research Question 1 Analysis.

Step 1	Chi-square statistics	Df	*P*-value
	2.528	4	0.640

Logistic Regression Analysis in Relation to RQ2

The result of the logistic regression analysis of the association between PMPM (IV_1), IPTp-SP compliance (IV_2), the use of CAM (IV_3), and baby's birth weight (DV) among pregnant women in the study population showed a statistically significant effect

on baby's birth weight based on the *P*-value in the model indicated in Table 14, $\chi 2$ (3) = 35.822, *P* = *0*.000. The model explained 13.4% (Negelkerke's R^2) of the variances in baby's birth weight and correctly classified 87.2% of cases. The performance of the PMPM was statistically significant (odd ratio = 0.171, CI: 0.082–0.357, *P* = 0.000), the subjects with PPMPM were 0.171 times as likely (17.1% more likely) to deliver LBW babies than the subjects with NPMPM. Also, the use of CAM (odd ratio = 2.212, CI: 1.174–4.168, *P* = 0.014) was associated with an increase in the likelihood of delivering LBW babies in this model. However, the IPTp-SP compliance variable was not statistically significant (odd ratio = 1.139, CI: 0.504–2.578, *P* = 0.744). The Hosmer-Lemeshow test was not significant with a *P*-value of 0.985, implying that the model has a good fit. Based on the stated result, I rejected the null hypotheses and accepted the alternate hypotheses in respect to RQ2.

Table 14.

The Omnibus Test of Model Coefficients for Research Question 2 Analysis.

Step 1		Chi-square	Df	*P*-value
	Step	35.822	3	0.000
	Block	35.822	3	0.000
	Model	35.822	3	0.000

Note: This table shows the statistical significance of the model explored in RQ 2.

Table 15.

The Variables in the Equation for Research Question 2 Analysis.

B	S.E	Wald	Df	*P*-value	Exp(*B*)
-1.915	0.136	198.288	1	0.000	0.147

Table 16.

The Result of the Logistic Regression Analysis for the Individual Performance of the Variables in the Equation for Research Question 2 Analysis.

								95% CI	
		B	S.E	Wald	Df	*P*-value	Odd ratio	LCI	UCI
Step 1[a]	PMPM	-1.766	0.375	22.126	1	0.000	0.171	0.082	0.357
	IPTp-SP compliance	0.130	0.417	0.098	1	0.754	1.139	0.504	2.578
	CAM use	0.794	0.323	6.036	1	0.014	2.212	1.174	4.166
	Constant	-1.671	0.401	17.362	1	0.000	0.188		

Variable (s) entered on step 1: PMPM, IPTp-SP compliance, CAM use. This table shows the statistical significance of each variable being explored in RQ2.

Table 17.

The Hosmer-Lemeshow Test for Research Question 2 Analysis.

Step 1	Chi-square	Df	*P*-value
	0.364	4	0.985

Logistic Regression Analysis in Relation to RQ3

The result of the logistic regression analysis of the association between PMPM (IV_1), IPTp-SP compliance (IV_2), the use of CAM (IV_3), and delivery term (DV) among pregnant women in the study population revealed a statistically significant effect on delivery term based on the *P*-value in the model indicated in Table 18; $\chi 2$ (3) = 16.330, *P = 0*.001. The model explained 7.0% (Negelkerke's R^2) of the variances in the delivery term and correctly classified 89.9% of cases. The performance of the PMPM was statistically significant (odd ratio = 0.365, CI: 0.185–0.722, *P* = 0.004), the subjects with PPMPM were 0.364 times as likely (36.4% more likely) to deliver preterm babies than the subjects with NPMPM. However, the IPTp-SP compliance and use of CAM variables were not statistically significant with the following details: odd ratio = 2.847, CI: 0.855–9.481, *P* = 0.088; odd ratio = 1.782, CI: 0.890–3.568, *P = 0*.103 respectively. The Hosmer-Lemeshow test was not significant with a *P*-value of 0.666, implying that the model has a good fit. Therefore, I rejected the null hypotheses and accepted the alternate hypotheses in respect to RQ3.

Table 18.

The Omnibus Test of Model Coefficients for Research Question 3 Analysis.

Step 1		Chi-square	Df	*P*-value
	Step	16.330	3	0.001
	Block	16.330	3	0.001
	Model	16.330	3	0.001

Note: This table shows the statistical significance of the model explored in RQ 3.

Table 19.

The Variables in the Equation for Research Question 3 Analysis.

		B	S.E	Wald	Df	*P*-value	Exp(*B*)
Step 0	Constant	-2.181	0.151	209.478	1	0.000	0.113

Table 20.

The Result of the Logistic Regression Analysis for the Individual Performance of the Variables in the Equation for Research Question 3 Analysis.

								95% CI	
		B	S.E	Wald	Df	*P*-value	Odd ratio	LCI	UCI
Step 1[a]	PMPM	-1.008	0.348	8.400	1	0.004	0.365	0.185	0.722
	IPTp-SP compliance	1.046	0.614	2.906	1	0.088	2.847	0.855	9.481
	CAM use	0.578	0.354	2.658	1	0.103	1.782	0.890	3.568
	Constant	-2.884	0.606	22.628	1	0.000	0.056		

a. Variable (s) entered on step 1: PMPM, IPTp-SP compliance, CAM usage. This table shows the statistical significance of each variable being explored in RQ3.

Table 21.

The Hosmer-Lemeshow Test for Research Question 3 Analysis.

Step 1	Chi-square	Df	*P*-value
	2.379	4	0.666

Controlling for Confounders in this Study Analysis

The Result of Controlling for Confounders Relative to RQ1 in the Logistic Regression Model.

Finally, I used the backward elimination stepwise method in the SPSS to build the final model for this study based on the RQs. In building the final model based on the RQ1 (maternal anemia as DV, the IVs were PMPM, IPTp-SP, and use of CAM) and the enumerated risk factors (ITN ownership, ITN frequent use, ANC attendance, gravidae, age groups, and educational attainment) were entered into the SPSS for logistic regression model with the backward elimination stepwise method. The output from the model showed that PMPM, use of CAM, ITN ownership, ITN frequent use, and ANC attendance showed statistically significant association with the outcome (maternal anemia), hence these variables were used with the DV (maternal anemia) to run the final model with the enter method of the binary logistic regression, χ 2 (5) = 74.922, P = 0.000. This model explained 22.0% (Negelkerke's R^2) of the variances in the maternal anemia and correctly classified 78.5% of cases. The subjects with PPMPM were 0.135 times as likely (13.5% more likely) to be anemic (exhibit maternal anemia) than the subjects with NPMPM. The performance of each variable is presented in Table 24 below. The Hosmer-Lemeshow test was not significant with a *P*-value of 0.818, implying that the model has a good fit.

Table 22.

The Omnibus Test of Model Coefficients for Research Question 1 Final Model Analysis.

Step 1		Chi-square	Df	*P*-value
	Step	74.922	5	0.000
	Block	74.922	5	0.000
	Model	74.922	5	0.000

Note: This table shows the statistical significance of the model explored in RQ 1 final model.

Table 23.

The Variables in the Equation for Research Question 1 Final Model.

		B	S.E	Wald	Df	*P*-value	Exp(*B*)
Step 0	Constant	-1.245	0.109	129.928	1	0.000	0.288

Table 24.

The Result for Controlling for Confounding for Research Question 1 Final Model. Analysis.

								95% CI	
		B	S.E	Wald	Df	*P*-value	Odd ratio	LCI	**UCI**
Step 1[a]	PMPM	-2.002	0.298	45.086	1	0.000	0.135	0.075	0.242
	CAM use	0.654	0.292	5.019	1	0.025	1.923	1.085	3.408
	ITNs ownership	0.697	0.271	6.639	1	0.010	2.008	1.182	3.413

	ITNs frequent use	-0.752	0.309	5.940	1	0.015	0.471	0.257	0.863
	ANC attendance	-0.400	0.193	4.314	1	0.038	0.670	0.460	0.978
	Constant	0.113	0.557	0.041	1	0.839	1.120		

[a] Variable (s) entered on step 1: PMPM, CAM usage, ITNs ownership, ITNs frequent use, and ANC attendance. This table shows the statistical significance of each variable being explored in RQ 1 final model.

Table 25.

The Hosmer-Lemeshow Test for Research Question 1 Final Model.

Step 1	Chi-square	Df	*P*-value
	4.413	8	0.818

The result of controlling for confounders relative to RQ2 in the logistic regression model.

Also, in building the final model based on the RQ2 (baby's birth weight as DV, IVs were PMPM, IPTp-SP, and use of CAM) and the enumerated risk factors (ITNs ownership, ITNs frequent use, ANC attendance, gravidae, age groups, and educational attainment) were entered into the SPSS for logistic regression model with the backward elimination stepwise method. The output from the model showed that PMPM, use of CAM, and gravidae were statistically significantly associated with the outcome (baby's birth weight), hence these variables were used with the DV (baby's birth weight) to run

the final model with the enter method of the binary logistic regression. $\chi 2$ (3), 41.297, *P* = *0*.000. The model explained 15.3% (Negelkerke's R^2) of the variances in the baby's birth weight and correctly classified 87.2% of cases. The subjects with PPMPM were 0.174 times as likely (17.4% more likely) to deliver LBW babies than the subjects with NPMPM. The performance of each variable is presented in Table 28 below. The Hosmer-Lemeshow test was significant with a *P*-value of 0.013, implying that the model does not have a good fit.

Table 26.

The Omnibus Test of Model Coefficients for Research Question 2 Final Model Analysis.

Step 1		Chi-square	Df	*P*-value
	Step	41.297	3	0.000
	Block	41.297	3	0.000
	Model	41.297	3	0.000

Note: This table shows the statistical significance of the model explored in RQ 2 final model.

Table 27.

The Variables in the Equation for Research Question 2 Final Model Analysis.

B	S.E	Wald	Df	*P*-value	Exp(*B*)
-1.915	0.136	198.285	1	0.000	0.147

Table 28.

The Result for Controlling for Confounding for Research Question 2 Final Model.

							95% CI:	
	B	S.E	Wald	Df	*P*-value	Odd ratio	LCI	UCI
PMPM	-1.746	0.376	21.552	1	0.000	0.174	0.083	0.365
CAM use	0.693	0.330	4.424	1	0.035	2.000	1.048	3.815
Gravidae	-0.434	0.184	5.575	1	0.018	0.648	0.452	0.929
Constant	-0.606	0.428	2.006	1	0.157	0.545		

[a] Variable (s) entered on step 1: PMPM, CAM use, and gravidae. This table shows the statistical significance of each variable being explored in RQ 2 final model.

Table 29.

The Hosmer-Lemeshow Test for Research Question 2 Final Model.

Step 1	Chi-square	Df	*P*-value
	16.049	6	0.013

The result of controlling for confounders relative to RQ3 in the logistic regression model.

In creating the final model based on the RQ3 (delivery term as DV), the IVs were PMPM, IPTp-SP, and use of CAM) and the enumerated risk factors (ITNs ownership, ITNs frequent use, ANC attendance, gravidae, age groups, and educational attainment) were entered into the SPSS for logistic regression model with the backward elimination stepwise method. The result showed that PMPM, age groups, gravidae, ANC attendance, and ITN frequent use hah a statistically significant association with the outcome (delivery term), hence these variables were used with the DV (delivery term) to run the

final model with the enter method of the binary logistic regression, χ 2 (5) = 36.966, *P* = *0*.000. The model explained 15.3% (Negelkerke's R^2) of the variances in the delivery term and correctly classified 90.1% of cases. The subjects with PPMPM were 0.378 times as likely (37.8% more likely) to deliver preterm babies than the subjects with NPMPM. The performance of each variable is presented in Table 32 below. The Hosmer-Lemeshow test was not significant with a *P*-value of 0.896, implying that the model has a good fit.

Table 30.

The Omnibus Test of Model Coefficients for Research Question 3 Final Model Analysis.

Step 1		Chi-square	Df	*P*-value
	Step	36.966	5	0.000
	Block	36.966	5	0.000
	Model	36.966	5	0.000

Note: This table shows the statistical significance of the model explored in RQ 3 final model.

Table 31.

The Variables in the Equation for Research Question 3 Final Model.

B	S.E	Wald	Df	*P*-value	Exp(*B*)
-2.181	0.151	209.478	1	0.000	0.113

Table 32.

The Result for Controlling for Confounding for Research Question 3 Final Model.

							95% CI:	
	B	S.E	Wald	Df	*P*-value	Odd ratio	LCI	UCI
PMPM	-0.973	0.357	7.417	1	0.006	0.378	0.188	0.761
Age groups	0.559	0.253	4.862	1	0.027	1.748	1.064	2.873
Gravidae	-0.651	0.222	8.628	1	0.003	0.521	0.338	0.805
ITN frequent use	-0.884	0.437	4.096	1	0.043	0.413	0.176	0.972
ANC attendance	-0.774	0.222	12.161	1	0.000	0.461	0.299	0.713
Constant	0.654	0.735	0.791	1	0.374	1.923		

[a] Variable (s) entered on step 1: PMPM, age groups, gravidae, ITNs frequent use, and ANC attendance. This table shows the statistical significance of each variable being explored in RQ3 final model.

Table 33.

The Hosmer-Lemeshow Test for Research Question 3 Final Model.

Step 1	Chi-square	Df	*P*-value
	3.540	8	0.896

Summary and Transition

The results from the analysis of the combination of primary (Government) and secondary (Government and public) clinical data from four healthcare facilities in Asaba, Delta State, Nigeria were presented. Using the sample size n = 483 and critical level of significance, $P \leq 0.05$; Chi-Square and binomial logistic regression were the two statistical tests used to derive the results.

The RQ1 investigated whether there is an association between PMPM, IPTp-SP compliance, the use of CAM, and maternal anemia among pregnant women in Asaba, Delta State, Nigeria. The result showed that subjects with PPMPM were 58.4% more likely to exhibit maternal anemia than the subjects with NPMPM. The data also showed that the use of CAM was associated with an increase in the likelihood of exhibiting maternal anemia in the study population.

The RQ2 investigated whether there is an association between PMPM, IPTp-SP compliance, the use of CAM, and baby's birth weight among pregnant women in Asaba, Delta State, Nigeria. The result showed that subjects with PPMPM were 17.1% more likely to deliver LBW babies than the subjects with NPMPM. And the use of CAM by parturients was associated with an increase in the likelihood of delivering LBW babies in the study population.

The RQ3 investigated whether there is an association between PMPM, IPTp-SP compliance, the use of CAM, and delivery term among pregnant women in Asaba, Delta State, Nigeria. The study findings showed that subjects with PPMPM were 36.4% more likely to deliver preterm babies than the subjects with NPMPM.

Also, the identified risk factors associated with maternal anemia were ITN ownership, ITN frequent use, and ANC attendance, while the only risk factors associated with baby's birth weight was gravidae. Besides, age groups, gravidae, ITN frequent use and ANC attendance were the risk factors associated with delivery term.

In this chapter, I discuss the data collection and preparation processes and I explain the representativeness of the sample to the population. I also discussed the use of the binomial logistic regression statistical tests that was performed and the reason for the use in this study. I reported the results from the analytical tests performed in line with the research questions and their hypotheses. In the next and final chapter, the interpretation of the results was discussed. The limitations of this study, recommendations for policy and program as well as gaps for future study, and positive social change implications were also discussed.

Chapter 5: Discussion, Conclusion, and Recommendation

Introduction

Malaria is a longstanding public health problem of global significance, and many efforts have been made to eliminate and eradicate the disease. Most malaria-endemic regions of the world, especially in the SSA and Nigeria, are among the low-income countries. The malaria control programs have not yielded the expected outcome, being compounded by poverty and low human resources (CDC, 2020; Onyemaechi & Malann, 2020; WHO, 2020). About 47 of 54 countries in the SSA are malaria endemic and are still in the malaria control programs with persistent low statistics of intervention implementations (WHO, 2020). Malaria infection is a critical public health problem in

Nigeria and the SSA in general despite the available interventions such as the IPTp-SP, ITNs, and treatment regime to prevent *P. falciparum* infection in pregnancy (Yaya et al., 2018; Braun et al., 2015). An estimated 25–30 million of the 125,000,000 parturients at risk of malaria globally are in the SSA. There is evidence in current documents of an estimated 75,000 to 200,000 neonatal mortalities, 900,000 LBW babies, and 10,000 maternal mortalities in the SSA region annually due to malaria disease (CDC, 2020; Onyemaechi & Malann, 2020; WHO, 2020). As a result, several studies have been conducted to determine the risk factors accounting for the high prevalence of malaria morbidity and mortality among parturients and their infants in various regions.

The purpose of this cross-sectional study design with a quantitative methodology was to investigate the association between asymptomatic malaria infection and pregnancy outcome among pregnant women in Asaba, Delta State, Nigeria. I addressed a research gap concerning the variability of malaria risk factors as well as the existence of few evidence of MiP among parturients and pregnancy outcome, in Asaba, Delta State, Nigeria. My specific objective was to ascertain disease prevalence, the prevailing risk factors for this location, the compliance levels of intervention use, and the intervention that gives successful outcome in the study area. The evidence in current documents have not determined the association between PMPM and pregnancy outcome in the study location. The current evidence of similar studies in various locations revealed that the risk factors are location specific (Aguzie, 2018). The compliance and success of existing intervention have regional/location specificity (CDC, 2020; WHO, 2020).

I used a combination of primary (survey questionnaires) and secondary (routine healthcare facility) data to answer the three RQs for this study. In this chapter, I interpreted the findings, discuss the limitations of the study, made recommendations for future research, suggested implications for social change, and summation.

Interpretation of Findings

The findings of this cross-sectional study design using a quantitative research methodology aligned with most of the previous studies conducted on MiP. However, some results differed.

The RQ1 was used to investigate whether there is an association between PMPM, IPTp-SP compliance, the use of CAM, and maternal anemia among pregnant women in Asaba, Delta State, Nigeria. The result of the analysis of RQ1 indicated that PMPM, IPTp-SP compliance, and CAM have statistically significant association with maternal anemia at delivery based on the *P*-value in the model as shown in Table 10. The result of the analysis of RQ1 indicated that subjects with PPMPM were 58.4% more likely to exhibit maternal anemia than the subjects with NPMPM. The data also showed that the use of CAM was associated with an increase in the likelihood of exhibiting maternal anemia in the study population.

I used the RQ2 to investigate whether there is an association between PMPM, IPTp-SP compliance, the use of CAM, and baby's birth weight among pregnant women in Asaba, Delta State, Nigeria. The PMPM, IPTp-SP compliance, CAM use were statistically significantly associated with baby's birth weight based on the *P*-value of the model as shown in Table 14. The data showed that subjects with PPMPM were 17.1%

more likely to deliver LBW babies than the subjects with NPMPM. And the use of CAM by parturients was associated with an increase in the likelihood of delivering LBW babies in the study population.

I used the RQ3 to investigate whether there is an association between PMPM, IPTp-SP compliance, the use of CAM, and delivery term among pregnant women in Asaba, Delta State, Nigeria. The result showed a statistically significant association between PMPM, IPTp-SP compliance, CAM, and delivery term in this study as observed in the analysis of the RQ3 based on the *P*-value in the model indicated in Table 18. The result demonstrated that subjects with PPMPM were 36.4% more likely to deliver preterm babies than the subjects with NPMPM.

The expanded models involving the risk factors of malaria revealed that maternal anemia has a statistically significant association with PMPM, use of CAM, ITN ownership, ITN frequent use, and ANC attendance. The identified risk factors associated with maternal anemia were ITN ownership, ITN frequent use, and ANC attendance. The baby's birth weight showed a statistically significant association with PMPM, CAM use and gravidae. The only risk factors associated with baby's birth weight was gravidae. While the delivery term demonstrated a statistically significant association with PMPM, age groups, gravidae, ITN frequent use and ANC attendance. Therefore, age groups, gravidae, ITN frequent use and ANC attendance were the risk factors associated with delivery term.

Malaria Prevalence Among the Study Population

The confirmation and identification of the parasite by the thick and thin slide microscopy showed 100% of *P. falciparum* in the data. Buh et al. (2019) and Ouedraogo et al. (2012) reported similar results in their various studies. The result of this study is aligned with a study conducted by Omer et al. (2021) and several other studies carried out in the SSA regions (Lufelu et al., 2017; Omer et al., 2017; Onyemaechi & Malann, 2020). This agrees with the documented evidence that 25 million parturients are at risk of malaria infection by *P. falciparum* in the SSA (Balami et al., 2021; WHO, 2020, CDC, 2020). Furthermore, this agrees with the study by Omer et al. (2017) in Uganda, who also reported the identification of only *P. falciparum*. Besides, Anorue et al. (2020) and Achu et al. (2020) in their studies in Asaba also reported only *P. falciparum* species.

Prevalence Across the Healthcare Facility Levels

The prevalence of placental malaria by microscopy in the primary, secondary, and private healthcare facilities were 44.3%, 33.0%, and 64.5%, respectively. The prevalence of LBW across the primary, secondary, and private facilities were 21.4%, 9.7%, and 11.9%. Preterm deliveries yielded a prevalence of 21.4%, 6.8%, and 8.7% across the three facility levels. Finally, 60.0%, 63.1%, and 31.0% were the observed prevalence for anemia across the primary, secondary, and private healthcare facilities.

Prevalence of Major Variables in this Study

The prevalence of placental malaria by microscopy and RDT in this study were 54.9% and 6.0% respectively. The wide difference in prevalence between microscopy and RTD malaria testing techniques in this study was due to the observed large false

negative result by the RDT. The prevalence of placental malaria was highest among the secundigravida (61.0%), followed by the primigravida (54.0%) and lowest among the multigravida (51.0%) in the study population. Maternal anemia was 41.6%, LBW was 12.8%, and preterm delivery was 10.1%. The result of the PMPM showed that only *P. falciparum* specie were identified in this study. In addition, the prevalence of the use of CAM in this study was 17.6%, IPTp-SP adequate compliance was 15.3%. While the prevalence of the ITN ownership and ITN frequent use were 57.6% and 26.3%, respectively.

The result of 54.9% prevalence of placental malaria parasitemia by microscopy in this study lend its support to the concept of asymptomatic malaria infections and its impact on maternal and neonatal health (Omer et al., 2017; Onyemaechi & Malann, 2020; Odorizzi et al., 2016). Malaria parasite asymptomatic state in a high burden malaria area have implication in maintaining the parasite circle and delaying the malaria elimination and eradication program (Berzosa et al., 2018; Katrack, et al., 2018). Although malaria infection in the SSA (a high burden malaria region) is mostly asymptomatic due to the acquired immunity via repeated exposures, it is still highly associated with maternal anemia, still birth, LBW babies, preterm deliveries, maternal and neonatal complications, and death (Aguzie, 2018; Balami et al. 2021; Bardaji et al., 2017; Omer et al., 2017). The observed high prevalence of mild (+) parasitemia in this study aligns with the report by Quakyi et al. (2019) that low density parasitemia is common in high burden malaria regions. The high prevalence of placental malaria parasitemia in this study could be explained by the report by Kapisi et al. (2017) that high burden malaria relates to

placental malaria parasitemia. Furthermore, Anorue et al. (2020) reported a higher prevalence (65.8%) by microscopy from their study in a tertiary healthcare facility in Asaba, Delta State, Nigeria, while Omer et al. (2017) reported 58.9% of placental malaria by microscopy in Uganda.

Maternal Anemia Among the Study Population

The prevalence of maternal anemia in this study was 41.6%. Rouamba et al. (2021) reported similar prevalence of anemia (35.9% and 46.6%) with data collected in 2013/2014 and 2017 in Burkina Faso. Although Olukosi and Afolabi (2018) in their study in Lagos, Nigeria had higher results of 81.4% prevalence of anemia. According to Desai et al. (2007), malaria infection is highly associated with anemia and poor pregnancy outcome at all levels of pregnancy, while White, (2018) reiterated that malaria infection is associated with maternal anemia. These authors stated that *P. falciparum* is directly linked with maternal death in a low transmission setting while in a high transmission setting, it is an indirect cause of mortality via maternal anemia. The present study also revealed a strong association between placental malaria, maternal anemia, preterm deliveries, and LBW. Omer et al. (2021) reported that placental malaria impacted the immune response that may change the hemoglobin level of the parturients and the neonates birth weight. Therefore, a successful pregnancy outcome is dependent on the placental. The analysis of the data in this study showed a strong association between maternal anemia and placental malaria. The prevalence of maternal anemia in this study is higher among subjects with PPMP than in the subjects with NPMP as shown in the results outlined in Chapter 4. There is a statistically significant association between

malaria infection and maternal anemia in pregnancy by various authors across different locations in the SSA (Olukosi & Afolabi, 2018; Rouamba et al. 2021; White, 2018). Nevertheless, several studies reiterated that the cause of anemia is multifactorial (Rouamba et al., 2021; Renzo et al., 2015; Tabrizi & Barjasteh, 2015); worm infestation, nutritional deficiency, poverty, low SES, and poor nutrition have been widely reported in connection with anemia (Ononga et al., 2014; Haider et al., 2013).

The reported prevalence of 17.6% of the use of CAM aligns with the report by Ogbonnaya et al. (2019) that there is widespread belief among parturients in Nigeria that the use of CAM is safe. Nergard et al. (2015) also reported on the increasing use of CAM by parturients in Mali and other African countries.

The low IPTp-SP compliance has been reported in the SSA (Amoakoh-Coleman et al., 2020; Roman et al., 2019). The use of ITN on frequent bases was below the expected standard (Aniekwe et al., 2020; Ezire et al., 2015).

The Credibility of the Testing Techniques (RDT and Microscopy)

Contrary to the outcome of the study by Mfuh et al. (2019), who reported that the RDTs was more sensitive than microscopy, the reverse was the finding in this study. These authors stated that age-specific detection of the *Plasmodium* species was like that of the PCR tests. However, they reported a high false positive result by RDTs compared to microscopy and they reiterated that a positive malaria parasite by microscopy is trustworthy; nevertheless, a negative result does not exclude the presence of the parasite (Mfuh et al., 2019). This implies that the prevalence reported in this study may not be

less but rather higher with the PCR testing techniques, except for the possible minor impact of the limitations of the microscopists with respect to expertise.

Berzosa et al. (2018) concluded that the RDTs are limited, and that microscopy should be used for prevalence studies. This gives credence to the use of microscopy for the confirmation of the malaria parasitemia and specie identification in this study. Zakama et al. (2020) stated that RDTs are effective in diagnosing malaria in non-pregnant subjects. These authors reiterated that RDTs are less efficient in diagnosing placental malaria (Briggs et al., 2019). Vasquez et al. (2018) reported that a newer version of the RDT (HS–RDT) has higher sensitivity in testing placental parasitemia than the routine RDTs (HRP–2) currently available, which were used in this study. Metoh et al. (2020) concluded from their comparative study between RDTs and microscopy test for malaria parasite that microscopy showed a superior sensitivity compared to RDT methods of malaria diagnosis. These authors stated that microscopy is more reliable than RDTs in detecting malaria parasitemia in a high burden malaria area and further recommended the use of the alternatives to the PFHRP2RDTs for placental malaria diagnosis because the HRP2RDT series perform poorly in detecting placental malaria parasitemia. This could explain the poor performance of the RDT in this study. Berzosa et al. (2018) stated that the sensitivity of the RDTs is affected by low parasite densities and that between 100 parasite/µl, the RDTs performance is decreased. This is in line with the observation in this study, there are 49.9% of mild (+) parasitemia cases by microscopy, and all the moderate (+ +) (5%) in this study were positive by the RDT,

However, there was no severe (+ + +), and hyper parasitemia (> + + +) malaria cases in this study.

Placental Malaria Parasitemia and IPTp-SP Compliance

I observed that there was no statistically significant association between compliance to IPTp-SP and placental malaria infection in this study. This could be explained by the fact that the compliance level observed in this study was below the current recommendation of four or more doses before delivery starting from the 4th month of pregnancy. Only 2.6% purchased the IPTp-SP that they used; others depended on its availability in the healthcare facility which was low across the three healthcare facility levels.

The Study Result in Relation to the Socioecological Model Framework

The SEM describes the relationship between the individual, interpersonal (family, friends, and community), and system/structural levels. The SEM is valuable for the review, design, implementation, and evaluation of a comprehensive malaria control program. The factors influencing malaria control are multifactorial and the SEM is a good match for designing a sustainable malaria program. At the individual level, the parturients should use the existing malaria interventions to reduce their exposure and impact of the disease to them and their neonates. So, the sensitization of parturients to utilize the existing malaria interventions to reduce the prevalence of the disease should be encouraged. At the interpersonal level (household, family, and community) involves the influences of the social support system. Training focused on the interpersonal connections of parturients to reduce their vulnerability to malaria infection will enhance a

positive pregnancy outcome. Appropriate information to family, friends and community members could scale up the use of malaria interventions by parturients. In fact, malaria elimination and eradication require community mobilization and involvement. And finally at the system level of the SEM, policies and programs on malaria control should focus on the various supports and connections of parturients to enhance pregnancy outcome. The use of the SEM in this study has highlighted the importance of the multiple levels of engagement to enhance maternal and neonatal improved pregnancy outcome.

Limitation of the Study

The limitation of the study is the absence of a molecular testing/analysis (via the PCR or histology) of the placental parasitemia of the malaria parasite, which is attributable to financial constrain. These techniques have improved sensitivity, specificity, and can quantify parasitemia (with respect to the PCR) (Mfuh et al., 2019). In addition, the use of hospital routine data of placental malaria by RDTs and microscopy, implies that misdiagnosis cannot be ruled out with respect to errors in reading by the microscopist, accurate staining of slides, or misidentification of the parasite species. Therefore, I was not in control of the quality of these secondary data. Furthermore, the survey questionnaires were based on self-reporting, hence, re-call and information bias could not be ruled out and the quality of the collected data may not be in the desired/required standard. In addition, I observed about 2.6% of missing and incomplete data and after all efforts to complete them were explored without success, they were removed from the data used in the final analysis and this could impact the internal

validity of the study. Also, the result of this study was limited to the Asaba city in Delta State, Nigeria. Hence, it cannot be generalized to Delta State or Nigeria.

Recommendations

This study resulted in some interesting findings that can contribute to the current body of knowledge in MiP research. There is need for further study using the PCR or histology techniques which has a lower limit of detection of the *P. falciparum* of about 0.0001 parasite/µl as well as detecting mixed infections but microscopy cannot detect mixed infection (Berzosa, et al., 2018). Besides, the result of the RDT analysis in this study calls for further investigation because the RDTs are meant to detect the antigens of plasmodium species and not the parasites; implying it should have a sensitivity advantage over the thick film microscopy because it should (by design) pick parasitemia below the threshold of microscopy (Mfuh, et al., 2018). Therefore, an enhanced/improved testing techniques is required to ascertain the false negative (due to threshold limit) by microscopy.

An adequate sensitization of parturients on the need to take the recommended doses of the IPTp-SP is urgently required. Further, policy could be reviewed at the local, state, and national government levels to focus on tracking and treating asymptomatic malaria cases via the inclusion of routine malaria testing for parturients during the ANC in the study location. I also recommend that further studies should be carried out to determine the components/active ingredients of the CAM used by pregnant women against malaria in the study location. And a cohort study on the comparism of the long-time impact of IPTp-SP and CAM on pregnancy outcome is recommended.

Implication for Positive Social Change

The result of this study has provided information on the prevalence of placental malaria infection in Asaba, Delta State, Nigeria, which is necessary to guide institutions and stakeholders in malaria control programs. The healthcare facilities that provided the data should be sensitized on the study's outcome for enhanced care of the parturients subsequently. The statistics from this study on the utilization of existing malaria interventions are far below the expected target for elimination and eradication of this aged-long infection. There is need for a renewed and concerted efforts on parturients via the identified multiple levels of influences highlighted in the SEM (individuals, interpersonal, community, and system levels) on the need to use the ITNs, IPTp-SP, laboratory testing, and prompt treatment of malaria cases. The health education message should be clear that parturients are not sick of malaria does not exclude the fact that they could be carriers of the parasite, and their babies could be impacted. Besides, parturients may become sick subsequently via recrudesce.

The results of this study could affect positive social change at the individual, interpersonal, community, and system levels of the SEM. The study results showed that asymptomatic parturients have a high prevalence of malaria infection. The use of the ITN and IPTp-SP malaria interventions by subjects in this study were far below the expected threshold. Therefore, strategies such as health education at the ANC, community levels and disseminating this study results to the Delta State Ministry of Health and other malaria control stakeholders could enhance the use of the ITNs and IPTp-SP by parturients in this location and beyond. Further, the findings from this study could have a

social change impact via the communication of study findings at the ANC study sites (result dissemination to subjects and stakeholders) and community town hall meeting could enhance social support from family and community members for parturients protection against mosquito bites and enhance the use of the existing interventions for the disease control.

Moreover, on the individual level, the communication of the findings of this study at the ANC, prenatal clinics, and social media blogs/professional website could lead to social change via the increase in the adoption of malaria interventions by parturients. This could reduce the morbidity and mortality due to MiP, yield improved pregnancy outcomes, and improved economic resources available to parturients in the study location and beyond. Further, policy on malaria elimination and eradication could be expanded at the local, state and, national government levels to focus on tracking and treating asymptomatic malaria cases among parturients via the inclusion of routine malaria testing for parturients during the ANC. So, expanding the current malaria control strategy of testing and treating only sick subjects to accommodate asymptomatic parturients in the testing and subsequent treatments when needed could reduce the present burden of MiP in this location. Also, strengthening the use of the ITN and IPTp-SP among subjects via adequate dissemination of this study findings could reduce MiP and yield improved pregnancy outcomes in this location. In addition, health education discouraging the use of CAM by parturients should be incorporated into the ANC services by the healthcare management.

Conclusion

The high prevalence of placental malaria in this study could be attributed to the low utilization of the existing interventions (ITNs, IPTp-SP compliance) and it resulted in adverse pregnancy outcome (maternal anemia, LBW, and preterm deliveries) as reported in the result section. In this chapter, an overview of the research study, along with interpretations of the results of data analyses in view of the stated hypotheses, the alignment between the findings of the current study and previous research results reported in current literature are provided. In addition, public health recommendations were made based on the findings of the current study along with suggestions for future research as pertains to the statement of the problem that was addressed in this study. Incorporating the findings of this study to the existing body of evidence could guide the malaria control stakeholders to expand interventions to track and treat asymptomatic malaria infection in pregnancy.

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Appendix A: The Questionnaire

Introduction: Good Morning/Afternoon/Evening Madam, my name is Sally Obi. I am a researcher and doctoral student from Walden University. I am here to invite you to answer some questions on a study on prevention of malaria among pregnant women. You might recall that the nurse gave you a consent form in the past. You have a choice of whether you would like to answer these questions or not. Your responses will only be used for research purposes and is aimed at supporting the health of women in Delta state and Nigeria. I assure you that all your responses will be treated as confidential and will not be discussed with any other person. This interview would last for about 15 minutes. Your participation is voluntary, and you can decide to stop the interview at any time if you do not want to continue. Would you like to volunteer to answer the questions for the study? Yes/No.

Subject's code/ID number:	
Section A: pregnancy outcome variables from laboratory and delivery units of healthcare.	
Question	Response
1. Record PMP by RDT from the Laboratory.	PPMP (1) NPMP(0)
2. Record PMP by microscopy from the Laboratory.	PPMP (1) NPMP(0)
3. What is plasmodium specie present	Write it here……..
4.What is the maternal anemia status?	Just write down the value from the laboratory result…… It will be coded as: AA (0) AP (1)
5.What is the maternal delivery term?	Write down the value from the hospital file…….. It will be coded as: Preterm (≤36 weeks) (0) Term (≥37 weeks) (1)
6.What is the baby's weight	Write down the value from the hospital file …… It will be coded as:

	NBW (2.5kg and above) (0) LBW (< 2.5kg) (1)
7. What is the maternal outcome	Alive = 1 Dead = 0
8. What is the neonatal outcome	Alive = 1 Dead = 0
Section B: Demographic variables	
1. what is the month and year of your birth?	Write it down……
2. How old were you in your last birthday?	Write it down……..
3. How old are you now?	18-25 years (1) 26–34 years (2) 35–42 years (3) 43-49 years (4)
4. Are you married to the man you are living with now?	Yes (1) No (0)
5. What is your marital status	Married (5), Widowed (4), Separated (3), Divorced (2) Never married (1), Others specify……..
6. Name the area you live?	Interbau to Okpanam road (1) Ime-ogbe (2) Bonsac (3) Oduke (4) Jarret/Cable (5) Infant Jesus Area (6) Behind Specialist Hospital (7) Across Koko (8) Across Submit (9) DLA (10) Others Specify (11)
7. Have you ever attended school?	Yes (1) No (0)
8. What is your highest level of educational qualification?	No formal Education (1) Primary Education (2) Secondary Education (3) Tertiary education (4)
9. Are you currently employed?	(self-employment or paid employment with income) Yes (1) No (0)
11. Do you own a mobile phone?	Yes (1)

	No (0)
19. Does your phone have internet access?	Yes (1) No(0)
12. How often do you access the internet with your phone?	Daily (4) Weekly (3) Monthly (1) None (0)
13. Do you have WhatsApp in your phone?	Yes (1) No (0)
14. Do you have Facebook in your phone?	Yes (1) No (0)
15. What materials are used for the roof of the house where you live?	Thatched/ Palm leave (1) Wood/plank/Tarpaulin/Plastics (2) Zinc/Metal/Ceramic Tiles/Asbestos Sheet (3) Other (Specify)…….. 0
16. Do you have mosquito net screening on your house windows and doors?	Yes (1) No (0)
17. What is your ethnic group?	Ibo, Urhobo, Itsekiri, Isoko, Ijaw, Hausa, Yoruba, Others……. (Tick the one that applies)
18. How many children do you have that you gave birth to?	None (0) One (1) Two (2) More than two (3)
19. How many of your children are staying with you?	None (0) One (1) Two (2) More than two (3)
20. Do you have children that are not staying with you?	Yes (1) No (0)
21. How many of your children are not staying with you?	None (0) One (1) Two (2) More than two (3)
22. How many times have you been pregnant?	Once (1) Twice (2) More than two (3)
23. How many ANC did you attend during this pregnancy?	None (0) One (1) Two (2) More than two (3)
Section C: malaria intervention variables	

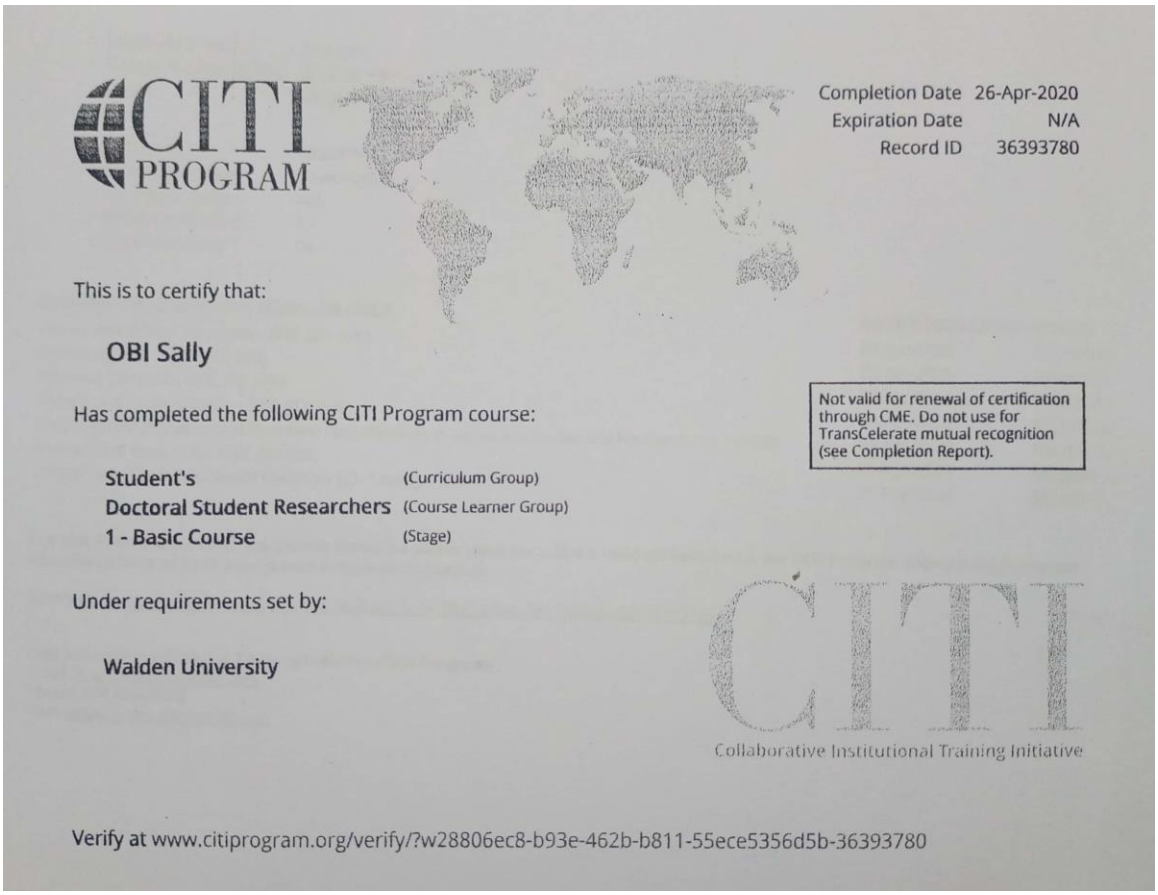
1. Have you taken IPTp-SP during this pregnancy? (Show the sample of a dose of SP)	Yes (2) No (0) Not sure(1)
2. How many doses IPTp-SP doses did you take during this pregnancy?	None (0) One(1) Two(2) More than two(3)
3. Where did you get the IPTp-SP that you took during this pregnancy?	None (0) ANC clinic (1) Purchased(2)
4. Do you have insecticide treated net (ITN) against mosquito for your own use?	Yes (1) No (0)
5. Where did you get the net?	ANC (1) Purchased (0)
6. Did you sleep under a treated mosquito net (ITN) last night?	Yes (1) No (0)
7. Do you sleep under a treated mosquito net (ITN) all the time?	Yes (1) No (0)
Section D: other variables.	
8. Do you take herbal/ plant/native/traditional medicine for malaria?	Yes (1) No (0)
9. How often do you take herbal/plant/native medicine?	None (0) Once (1) Twice (2) More than twice (3)
10. Did you take herbal/plant/native medicine during this pregnancy for malaria?	Yes (1) No (0)

Thank you for your responses to the survey questions. Can I use your responses for my research study as stated in the consent form, Yes / No.

Definition of terms:

PMP: Placental malaria parasitemia.
RDT: Rapid diagnostic test.
PPMP: Positive Placental malaria parasitemia.
NPMP: Negative Placental malaria parasitemia.
AA: Anemia absent.
AP: Anemia present.
NBW: Normal birth weight.
LBW: Low birth weight.

Appendix B: Citi Training Certification



CITI PROGRAM

Completion Date 26-Apr-2020
Expiration Date N/A
Record ID 36393780

This is to certify that:

OBI Sally

Has completed the following CITI Program course:

Not valid for renewal of certification through CME. Do not use for TransCelerate mutual recognition (see Completion Report).

Student's (Curriculum Group)
Doctoral Student Researchers (Course Learner Group)
1 - Basic Course (Stage)

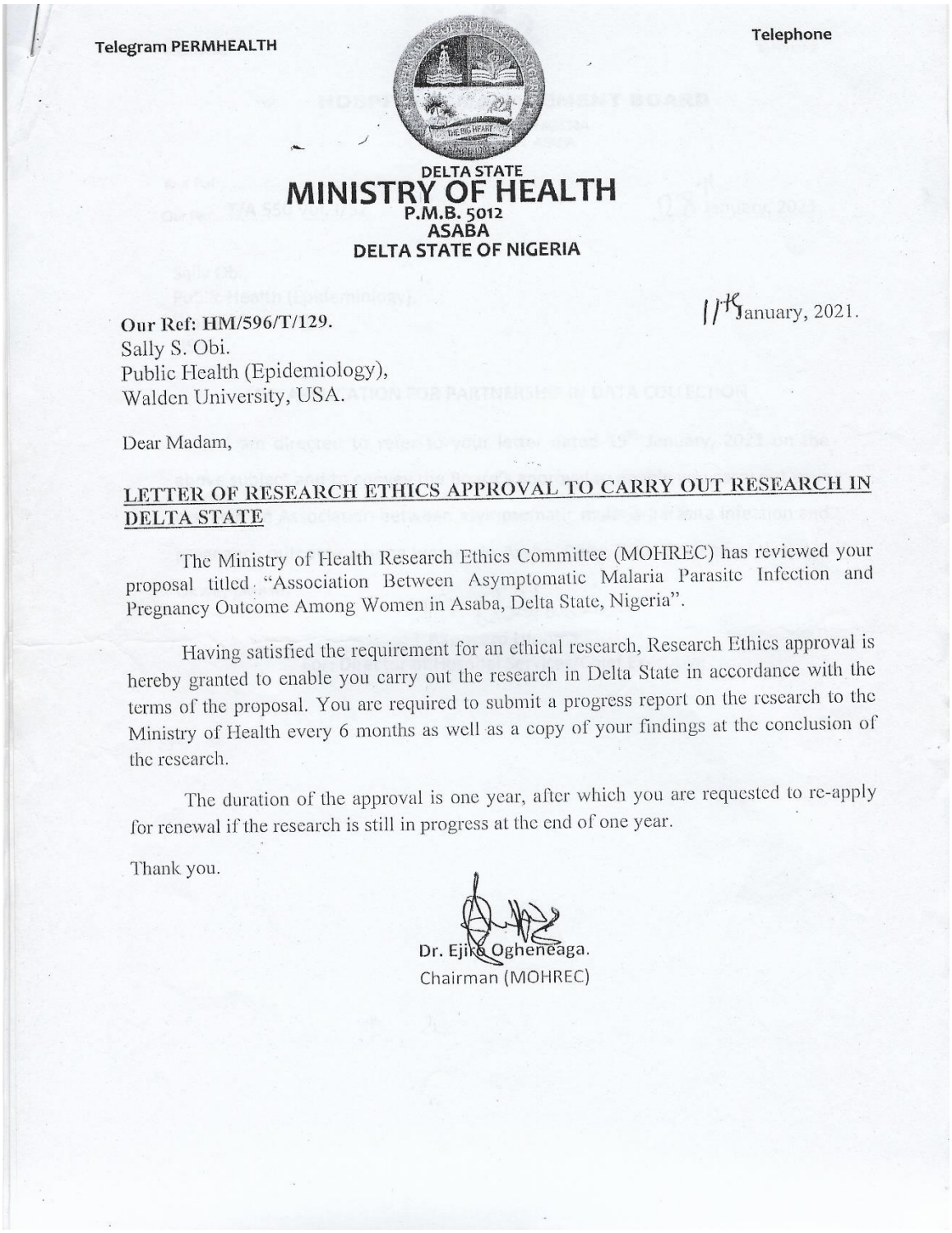
Under requirements set by:

Walden University

CITI
Collaborative Institutional Training Initiative

Verify at www.citiprogram.org/verify/?w28806ec8-b93e-462b-b811-55ece5356d5b-36393780

Appendix C: Approval Letter for Research from Delta State Ministry of Health.



Telegram PERMHEALTH

Telephone

DELTA STATE
MINISTRY OF HEALTH
P.M.B. 5012
ASABA
DELTA STATE OF NIGERIA

11th January, 2021.

Our Ref: HM/596/T/129.
Sally S. Obi.
Public Health (Epidemiology),
Walden University, USA.

Dear Madam,

LETTER OF RESEARCH ETHICS APPROVAL TO CARRY OUT RESEARCH IN DELTA STATE

The Ministry of Health Research Ethics Committee (MOHREC) has reviewed your proposal titled "Association Between Asymptomatic Malaria Parasite Infection and Pregnancy Outcome Among Women in Asaba, Delta State, Nigeria".

Having satisfied the requirement for an ethical research, Research Ethics approval is hereby granted to enable you carry out the research in Delta State in accordance with the terms of the proposal. You are required to submit a progress report on the research to the Ministry of Health every 6 months as well as a copy of your findings at the conclusion of the research.

The duration of the approval is one year, after which you are requested to re-apply for renewal if the research is still in progress at the end of one year.

Thank you.

Dr. Ejiro Ogheneaga.
Chairman (MOHREC)