HYPERTENSIVE DISORDERS OF PREGNANCY AMONG PREGNANT WOMEN WITH MALARIA ATTENDING ANTENANTAL CLINIC AT ABIA STATE UNIVERSITY TEACHING HOSPITAL (ABSUTH), ABA, ABIA STATE.

BY

OFFIAH, ANULIKA JESSICA (B.Sc)

REG.NO.: 20144919388

A THESIS SUBMITTED TO THE POSTGRADUATE SCHOOL,

FEDERAL UNIVERSITY OF TECHNOLOGY OWERRI,

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IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE AWARD OF THE DEGREE OF MASTER OF PUBLIC HEALTH (MPH) DEGREE IN EPIDEMIOLOGY AND DISEASE CONTROL

SEPTEMBER, 2021

CERTIFICATION

This is to certify that this work **"Comparative Study of Restricted Activities Days in Hypertension Induced Stroke Versus Non-Hypertension Induced Stroke: The Role Of Demographic Factors, Lifestyles And Compliance With Treatment Regimen" was carried out by Amaechi Ifeanyichukwu Paul (Reg. No: 20144919338)** in partial fulfilment for the award of Master's Degree in Public Health (Epidemiology and Disease Control option), in Department of Public Health, Federal University of Technology, Owerri.

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DEDICATION

This research work is dedicated to my loving mother of blessed memory, Mrs. Nnenna Offiah. Mommy, you remain evergreen in my heart.

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DEFINITION OF TERMS

MALARIA: Disease that causes fever and shaking of the body caused by the bite of a female anopheles mosquito mostly in tropical regions.

PREGNANCY: The state of being pregnant. Many women experience vomiting, dizziness, body weakness, nausea during pregnancy. A pregnancy test is done to confirm if a woman is pregnant.

ANTENATAL: This relates to the medical care given to pregnant women which involves antenatal care/classes/screening. It teaches pregnant women what to expect during pregnancy as well as how to take care of themselves during and after pregnancy.

MORTALITY RATE: The death rate due to malaria infection.

MORBIDITY RATE: The rate of incapacitation as a result of malaria infection.

PRIMIGRAVIDAE: This is a woman who is pregnant for the first time.

PARITY: This is the number of times a woman has given birth.

PROTEINURIA: This is when there is a large amount of protein (≥300mg/d) in a pregnant woman's urine.

MULTIPAROUS: When a woman has given birth more than once.

ABSTRACT

This study on the Hypertensive disorders of pregnancy among pregnant women attending Abia State University Teaching Hospital, Aba (ABSUTH) was carried out between March and April, 2018. The general aim of the study was to determine the influence of malaria on hypertensive disorders of pregnancy (HDP) among pregnant women attending ante-natal clinic at ABSUTH, Aba. The study design used in this research was a hospital-based cross-sectional study. This study design involved analyzing data from a population at one specific time. A total of sixty (60) pregnant women was drawn from a total population of seventy-one (71) pregnant women using the Taro Yammane sample size formula. The respondents were first tested for malaria using the rapid diagnostic test (RDT) kits, and those who tested positive for malaria were included in the daily study population and were given identification numbers to avoid counting an individual twice. The Taro Yammane sample size formula was applied to get the sample size for each day. Random sampling technique (Balloting) was used in selecting participants for the study after determining the study population for each day. A structured questionnaire with reliability coefficient of 0.88 was used to determine the socio-obstetric characteristics of the pregnant women, malaria parasite density was determined by microscopy, blood pressure of the women was determined using a Mercury sphygmomanometer and urinalysis was carried out using Macherey-Nagel medi test combi-9 test strips. The data on socio-obstetric history of the pregnant women focused on three variables; maternal age, parity, and trimester. There was a significant relationship between HDPs and malaria parasite density among the pregnant women ($X^2 = 10.40$, P-Value = 0.034, df = 4). The result on the influence of maternal age on HDPs among the pregnant women with malaria showed a significant influence. Age ≤18 ($X^2 = 4.788$, P-Value = 0.309) and also among pregnant women between 26-44 years ($X^2 = 8.607$, P-Value = 0.071), on the contrary, there was no significant influence of maternal age on HDPs among pregnant women with malaria, aged 19-25 years ($X^2 = 0.617$, P-Value = 0.962) and among ≥45 year old pregnant women ($X^2 = 0.000$, P-Value = 1.000). The result on the influence of trimester on HDPs among the women with malaria showed a significant influence across the three trimesters ($X^2 = 11.00$, P-Value = 0.022, df =4). Also, the results showed a significant influence of parity on HDPs among the women ($X^2 =3.81$, P-Value = 0.432, df = 4). The study has shown that malaria affects the blood pressure of pregnant women which might cause hypertensive disorders during pregnancy. It is therefore, necessary that pregnant women be enlightened on the importance of early ante-natal visits and the need for pregnant women to protect themselves against malaria.

Key Words: Malaria Parasite Density, Hypertensive Disorders of Pregnancy, Trimester, Maternal Age, Parity.

CHAPTER ONE

INTRODUCTION

1.1 Background Information

Malaria prevention and control still remains a challenge in Africa, where malaria is endemic in 45 African countries including Nigeria, and about 588 million people being at risk (WHO, 2008).

Malaria is caused by the parasite plasmodium which can be spread to humans through the bite of an infected mosquito. Of the five types of plasmodium (*P. falciparium, P.ovale, P. malaria, P. vivax and P. knowlesi*), the plasmodium *falciparium* is the deadliest and affects the lives of almost 40 per cent of the world's population (Omang, Ndep, Offiong, Otu and Onyejose, 2020).

In 2017, Nigeria accounted for the greatest malaria burden worldwide, (25%), (WHO, 2008). In 2019, six African countries accounted for 50% of all malaria cases globally: Nigeria (23%), the Democratic Republic of Congo (11%), United Republic of Tanzania (5%), Burkina Faso (4%), Mozambique (4%), Niger (4%), (WHO, 2020). In malaria-endemic countries, such as Nigeria, "About 50% of Nigerian population have at least one episode of malaria each year with nearly 110 million clinical cases and an estimated 300,000 deaths per year" (WHO, 2013; Federal Ministry of Health, 2011). Mortality is very high in people that are not

sufficiently protected by an acquired immunity such as young children especially below five years, pregnant women and migrants from regions where malaria is not found (WHO, 2013).About 10,000 women and 200,000 babies die annually because of malaria in pregnancy (Omang, Ndep, Offiong, Otu and Onyejose, 2020). Out of 72% of pregnant women, that suffers malaria, 50% of these pregnant women carry malaria parasite in their placenta without noticing it, which makes them, three(3) times more likely to suffer from other severe diseases (Goshyu and Yitayew, 2019; Omer, Idress, Adam, Abdelrahim, Nouredein, Abdelrazig, Elhassan and Sulaiman, 2017; Fana, Bunza, Anka, Imam and Nataala, 2015).

Pregnancy, which can be referred to as gestation, is the time in which one or more offspring grows inside a woman (NICHD, 2013). Childbirth typically occurs around 40 weeks from the start of the last menstrual period (LMP) (NICHD, 2013; Abman, 2011). In normal pregnancies, there are significant changes in cardiovascular functions which occur to meet the metabolic needs of both the mother and foetus (August and Lindheimer, 1995; Lindheimer and Katz, 1992). Examples of these changes, include an approximate of 40% to 50% increase in maternal cardiac output and blood volume, whereas, arterial blood pressure (BP) and total peripheral resistance tends to decrease (August and Lindheimer, 1995; Lindheimer and Katz, 1992). However, these significant hemodynamic changes that normally occur in pregnancy, do not express themselves in women who develop hypertensive disorders in pregnancy (HDP)

Hypertensive disorders in pregnancy (HDP) an umbrella term for high blood pressure (HBP) disorders which includes; preexisting and gestational hypertension, preeclampsia, and eclampsia, complicate up to 10% of pregnancies, and represent a significant cause of maternal and perinatal morbidity and mortality (Braunthal and Brateau, 2019). In Nigeria, it is estimated that 5-10% of pregnancies are complicated by HDPs (Emuveyan, 1995; Itam and Ekabule, 2002; Myers and Baxer, 2002; Audu and Ekele, 2002; Omole-Ohonsi and Shehu, 2001; Hayman, 2003; Salako, Aimakhu, Odukogbe, Olayemi and Adedapo, 2004), and this results in more admissions in the antenatal period than any other disorder (Myers and Baxer, 2002). HDPs are associated with significant elevations in total peripheral resistance, proteinuria, enhanced responsiveness to angiotensin II, elevated blood pressure, marked reductions in renal blood flow and glomerular filtration rate (August and Lindheimer, 1995; Lindheimer and Katz, 1992 and Mammaro et al, 2009). Various studies have reported potential links between malaria and hypertension in pregnancy (Ndao, Dumont, Fievet, Doucoure, Gaye and Lehesran, 2009; Duffy, 2006; Muehlenbachs, Mutabingwa, Edmonds, Fried and Duffy, 2006; Etyang, Smeeth, Kennedy, Cruickshank and Scott, 2016). Similar studies have shown that placental malaria has similar pathophysiological mechanisms with HDPs such as preeclampsia. These mechanisms includes placental ischemia, endothelial dysfunction, and production of pro-inflammatory cytokines (Challier

and Uzan, 2003; Benyo et al, 2001; Sibai, 2003; Sibai, Dekker and Kupferminc, 2005; Brabin and Johnson, 2005).

Pregnant women with these conditions experience a higher incidence of intra-uterine growth restriction (IUGR), maternal morbidity, (Brabin and Johnson, 2005), placental abruption, preterm labor, low birth weights (LBW), perinatal death, fetal loss, super-imposed preeclampsia (Jain, 1997; Sibai, 2002) and gestational diabetes (Hedderson and Ferrara, 2008).

There is a paucity of information on the possible link between malaria and the occurrence of hypertension, among pregnant women residing in Aba. Therefore, this study will provide additional knowledge to the existing studies, and will inform for future research in similar studies.

Aba's vegetation is a typical rainforest area. It is an urban town with much open drainage, puddles, inefficient and inadequate waste disposal system with huge refuse litters, found in strategic areas of the town. The environment is ideal for the breeding of mosquitoes and transmission of malaria.

For the purpose of this study, the focus is on gestational hypertension and preeclampsia as the HDP. The independent variables are malaria and socio-obstetric characteristics including maternal age, parity and trimester.

The study was guided by the following questions:

I. What is the distribution of malaria parasite density among the pregnant women attending clinic at ABSUTH, Aba?

II. What is the prevalence of hypertensive disorders among the pregnant women with malaria attending antenatal clinic at ABSUTH, Aba?

III. What is the relationship between hypertensive disorders of pregnancy and malaria parasite density among the pregnant women attending antenatal clinic at ABSUTH, Aba?

IV. What is the influence of maternal age on hypertensive disorders of pregnancy among women with malaria attending antenatal clinic at ABSUTH, Aba?

V. What is the influence of trimester on hypertensive disorders of pregnancy among women with malaria attending antenatal clinic at ABSUTH, Aba?

VI. What is the influence of parity on hypertensive disorders of pregnancy among women with malaria attending antenatal clinic at ABSUTH, Aba?

1.2 Problem Statement

Malaria is one of the most severe global public health problems worldwide, particularly in Africa, where Nigeria has the greatest number of malaria cases (Dawaki et al, 2016).Malarial infection during pregnancy is a major cause of low birth weight babies and maternal anemia. Moreover malaria is considered to be an indirect cause of maternal death while hypertension during pregnancy is also major

cause of maternal death principally due to eclampsia in West Africa. Malaria and hypertension are prevalent in Nigeria. People still die from malaria and hypertension in Aba. The environment, Aba offers, is ideal for the breeding of mosquito vectors and provides ideal transmission conditions. Pregnant women residing in Aba are adversely affected by both malaria and hypertensive disorders during pregnancy but the possible link between malaria and hypertensive disorders of pregnancy has not been sufficiently established through research, hence this study. Variables in this study are malaria, maternal age, trimester, parity, preeclampsia and gestational hypertension.

1.3. Objectives of Study

The overall objective of this study is to determine the Hypertensive Disorders among Pregnant Women with Malaria attending Abia State University Teaching Hospital, Aba (ABSUTH).

In order to achieve the general objective of this study, the following are the specific objectives of this study:

i. To determine the distribution of malaria parasite density among the pregnant women attending clinic at ABSUTH, Aba.
ii. To determine the prevalence of hypertensive disorders among the pregnant women with malaria attending antenatal clinic at ABSUTH, Aba

iii. To determine the relationship between hypertensive disorders of pregnancy and malaria parasite density among pregnant women attending antenatal clinic at ABSUTH, Aba.

iv. To determine the influence of maternal age on the hypertensive disorders of pregnant women with malaria attending antenatal clinic at ABSUTH, Aba.

v. To determine the influence of trimester on the hypertensive disorders of pregnant women with malaria attending antenatal clinic at ABSUTH, Aba.

vi. To determine the influence of parity on the hypertensive disorders of pregnant women with malaria attending antenatal clinic at ABSUTH, Aba.

1.4 Hypotheses of Study

The following hypotheses guided the study:

i. H_0: There is no significant relationship between hypertensive disorders of pregnancy and malaria density among pregnant women attending antenatal clinic at ABSUTH, Aba.

   HΛ: There is a significant relationship between hypertensive disorders of pregnancy and malaria density among pregnant women attending antenatal clinic at ABSUTH, Aba

ii. H_0: There is no significant influence of maternal age on hypertensive disorders in pregnant women with malaria, attending antenatal clinic at ABSUTH, Aba.

HΛ: There is a significant influence of maternal age on hypertensive disorders in pregnant women with malaria, attending antenatal clinic at ABSUTH, Aba.

iii. H_0: There is no significant influence of trimester on hypertensive disorders in pregnant women with malaria, attending antenatal clinic at ABSUTH, Aba

HΛ: There is a significant influence of trimester on hypertensive disorders in pregnant women with malaria, attending antenatal clinic at ABSUTH, Aba

iv. H_0: There is no significant influence of parity on hypertensive disorders in pregnant women with malaria, attending antenatal clinic at ABSUTH, Aba.

HΛ: There is no significant influence of parity on hypertensive disorders in pregnant women with malaria, attending antenatal clinic at ABSUTH, Aba.

1.5. Justification of Study

The findings from this will be of immense benefit to obstetricians and other trained and certified Traditional Birth Attendants (TBAs) while counseling their pregnant mother patients by prescribing medication for control of malaria and hypertensive disorders of pregnancy. The Federal and State Ministries of Health will find this

study very useful because it assist them on how to provide adequate interventions on the prevention of malaria in pregnancy (MiP) and hypertensive disorders of pregnancy (HDP). Furthermore, the Local Government Health Departments will use the findings from this study as key tool in their bid to prevent maternal death related to malaria and hypertensive disorders of pregnancy.

The findings from this study will bridge gap between insufficient research on malaria and hypertensive disorders of pregnancy among pregnant women in Aba.

Finally findings from this study will enable Public Health experts to establish Non-Governmental Organizations (NGOs)/Public Health Initiatives (PHIs) on the prevention of Malaria and hypertensive disorders of pregnancy.

1.6 Scope of Study

The aim of this study is to determine the influence of malaria on the blood pressure levels of pregnant women who have malaria in Aba South. The presence of open drainages, inefficient waste disposal methods and flood-prone areas in Aba provides the ideal environment for the breeding and transmission conditions for mosquitoes and malaria parasitemia, this situation could possibly contribute to the occurrence of hypertensive disorders among pregnant women. This study was limited to pregnant women had malaria and no previous history of hypertension. The independent variables in this study are malaria and socio-obstetric

characteristics including maternal age, parity and trimester while the dependent variables are the blood pressure levels of the pregnant women.

CHAPTER TWO

LITERATURE REVIEW

This chapter captures the reviewed literature and is presented under the following subheadings:

2.1 Conceptual Framework

2.1.1 Blood Pressure in Pregnancy

Blood pressure is the medical term that describes the pressure of the blood in the circulatory system, often measured for diagnosis since it is closely related to the force and rate of the heartbeat and the diameter and elasticity of the arterial walls. According to the American Heart Association (2014) Blood pressure measures how hard the blood is pushing against the walls of the arteries. In the body, the arteries carry blood away from the heart. As blood travels through the arteries, it presses against the walls of the arteries.

When the heart beats, it pumps blood, oxygen, hormones and nutrients which circulate round the body to provide the energy which the body needs for its daily activities. As the blood flows, it pushes against the walls of the blood vessels specifically the large arteries. The process of blood circulation is achieved under

pressure. Blood pressure is simply the pressure in the large arteries of systemic-circulation.

Blood pressure is usually expressed in terms of the systolic pressure (maximum during one heart beat) over diastolic pressure (minimum in between two heartbeats) and is measured in millimeters of mercury (mmHg), above the surrounding atmospheric pressure. Blood pressure check is one of the routine screenings which is done during antenatal visits. Normal blood pressure reading is at 120mmHg for systolic and 80mmHg for diastolic. This is abbreviated as 120/80mmHg.

Ogedegbe, Gbenga, Pickering, Thomas, (2010) stated that Blood pressure is measured with a clinical manometer which is regarded as the gold standard. More recently, automated sphygmomanometer is now commonly used. Blood pressure that is low due to a disease state is called hypotension, and blood pressure that is consistently high is hypertension. As earlier stated, during pregnancy, a woman's blood pressure falls during the first and second trimester. BP is at its lowest in mid-pregnancy and starts to rise gradually again from 24 weeks of pregnancy.

However, it is a thing of concern for a pregnant woman to have a BP reading which is ≥140mmHg for systolic and ≥110mmHg for diastolic. This indicates high blood pressure or hypertension in pregnancy.

2.1.2 Hypertensive Disorders of Pregnancies

According to Baldisseri (2020) Hypertension is defined as systolic blood pressure (SBP) greater than or equal to 140 mm Hg or a diastolic blood pressure (DBP) greater than or equal to 90 mm Hg or an increase of at least 30 mm Hg in the SBP and an increase of at least 15 mm Hg in DBP.

Hypertension diseases are frequently occurring diseases experienced by pregnant women due to changes in their cardiovascular system. These changes could be brought about by diverse factors including infectious diseases such as malaria infection in pregnancy, although information to support this occurrence is limited.

Previous studies have shown that pregnancies complicated by hypertension diseases are associated with increased risk of adverse fetal, neonatal and maternal outcomes, including preterm birth, IUGR, perinatal death, acute renal or hepatic failure, ante partum hemorrhage, postpartum hemorrhage and maternal death. (Yucesoy et al, 2005: Lugobe et al, 2020: Bridwell et al, 2019) Hypertension diseases during pregnancy are preeclampsia, gestational hypertension/pregnancy-induced hypertension and eclampsia with blood pressure is ≥110mmHg.

2.1.3. Types of Hypertensive Disorders of Pregnancy

Hypertensive disorders of pregnancy include: Pregnancy – Induced Hypertension, Essential Hypertension, Chronic Hypertension, Preeclampsia, and Eclampsia.

Baldisseri (2020) further Classified and defined the classes of Hypertensive Disorders as follows:

(i) Chronic Hypertension: This is when a woman has pre-existing high blood pressure or hypertension before getting pregnant. A woman can also be considered to be chronic hypertensive if she develops high blood pressure in the first 20 weeks of pregnancy.

(ii) Gestational Hypertension: This is high Blood Pressure that develops after 20 weeks of pregnancy without the presence of proteins in urine or any organ damage.

Gestational Hypertension occurs without proteinuria and usually manifests as diastolic hypertension that resolves 1 to 2 months after delivery. Recurrent gestational is frequent with subsequent pregnancies, as is the development of chronic hypertension.

According to Woelkers, Barton, Dadelszen and Sibai (2015) gestational hypertension is a clinical diagnosis defined by the new onset of hypertension (systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg) at ≥20 weeks of gestation in the absence of proteinuria or new signs of end-organ dysfunction. The blood pressure readings should be documented on at least 2 occasions at least 4 to 6 hours apart. Furthermore, Woelker, *et al.*(2013); Sibai, (2003) diagnosed that gestational hypertension is severe when systolic blood

pressure is ≥160 mmHg and/or diastolic blood pressure is ≥110 mmHg on two consecutive blood pressure measurements at least 4 to 6 hours apart.

(iii) Essential hypertension: This is the presence of underlying pre-partum hypertension, whether diagnosed or undiagnosed, and may be unmasked at time during the pregnancy.

(iv.) Eclampsia: According to Cunningham, Leveno, Bloom, Spong and Dashe (2014) Eclampsia is the onset of seizures (convulsions) in a woman with pre-eclampsia. Its usual onset is after 20 weeks of pregnancy. Eclampsia, like pre-eclampsia, tends to occur more commonly in first pregnancies and young mothers where it is thought that novel exposure to paternal antigens is involved. Furthermore, women with pre-existing vascular diseases (hypertension, diabetes, and nephropathy) or thrombophilic diseases such as the antiphospholipid syndrome are at higher risk to develop preeclampsia and eclampsia. According to Chaiworapongsa, Chaemsaithong, Yeo and Romeo (2014) having a large placenta (multiple gestation, hydratid formmole) also predisposes women to eclampsia. In addition, there is a genetic component: a woman whose mother or sister had the condition is at higher risk than otherwise. Women who have experienced eclampsia are at increased risk for pre-eclampsia/eclampsia in a later pregnancy.

(v) Preeclampsia: According to Eil and, Elosha; Nzerue, Chike, Faulkner, Marquetta, (2012) Preeclampsia is a disorder of pregnancy characterized by the

onset of high blood pressure and often a significant amount of protein in the urine Preeclampsia occurs when there is high blood pressure and protein in urine during pregnancy. This condition usually occurs after 20 weeks of pregnancy and sometimes it occurs earlier as screened by (Al-Jameil; Aziz Khan; Fareed Khan; Tabassum, (2014) There is also an indication of organ (kidney or liver) damage.

Preeclampsia is a multisystem disease that usually occurs most commonly after the 20^{th} week of pregnancy but can also present up to 1 week after delivery with no prior evidence of intra-partum preeclampsia. Patients with chronic preexisting may develop of superimposed preeclampsia with the onset of proteinuria after the 20^{th} gestation week.

In severe disease there may be red blood cell breakdown, low blood platelet count, impaired liver function, kidney dysfunction, swelling, shortness of breath due to fluid in the lungs, or visual disturbances as identified by Al-Jameil; Aziz Khan; Fareed Khan; Tabassum, (2014) Preeclampsia (PE) increases the risk of poor outcomes for both the mother and the baby. If left untreated, it may result in seizures at which point it is known as eclampsia.

WHO, (2011) stated risk factors for PE include obesity, prior hypertension, older age, and diabetes mellitus It is also more frequent in a woman's first pregnancy and if she is carrying twins.

(vi) Mild Preeclampsia: Mild preeclampsia is defined as systolic blood pressure (SBP) greater than or equal to 140 mm Hg or diastolic (DBP) greater than or equal to 90 mm Hg and proteinuria greater or equal to 0.3 g in 24 hours without evidence of end- organ damage.

Mild preeclamspia occurs in 75% cases in United State is severe in the remaining 25% Risks factors include: Preeclampsia with prior pregnancy, Multi fetal pregnancy, Chronic hypertension, Pre-gestational diabetes mellitus, Obesity Maternal age- 35 years or older; Africa race, Antiphospholipid syndrome, Vascular and connective tissue diseases Baldisseri, (2020).

(vii) Chronic hypertension with superimposed preeclampsia: This is another variation of chronic hypertension which occur when a woman has high blood pressure before she becomes pregnant and also the presence of protein in her urine.

(viii) Mild hypertension: Diastolic blood pressure of 90–99mmHg, Systolic blood pressure 140–149mmHg.

(ix) Moderate hypertension: Diastolic blood pressure of 100–109 mmHg, Systolic blood pressure 150–159 mmHg.

(x) Severe Hypertension: Diastolic blood pressure is ≥160mmHg and the Systolic

2.1.4. Epidemiology of Hypertensive Disorders of Pregnancy

According to National High Blood pressure Education program (2000) preexisting hypertension complicates about 3% of all pregnancies and about 6% pregnant women are diagnosed with gestational hypertension. The incidence of preeclampsia in the United States and in 3 – 4 % of all pregnancies worldwide. The highest frequency occurs in primigravidas and the second highest group is among older multiparous women who have morbidity and mortality rates associated with the preeclamptic state. Incidence is higher in those with preexisting or renal vascular disease. According to (Ibrahim and Damasceno, 2012) demographic and lifestyle changes including urbanization contribute substantially to the burden of hypertension in low – medium countries (LMICs)but examining special factors to or more prevalent in LMIC settings might reveal new patho-physiological mechanism that could help to control the disease.

2.1.5. Prognosis of Hypertensive Disorders of Pregnancy

Baldisseri (2020) further suggested that there is an increased recurrence rate of preeclampsia of up to 65% in subsequent pregnancies, particularly in women who had early onset and severe preeclamspia. The incidence is significantly lower (5 – 7%) in women who had mild preeclampsia with their first pregnancy.

The report of the National High Blood pressure Education program (2000) stated that studies have indicated that preeclampsia is predictive of future cardiovascular and cerebrovascular disease, including hypertension, ischemic heart disease, stroke and severe preclampsia, gestational hypertension, or preclampsia with onset as a multipara.

2.1.6 Implications of Malaria-Induced Hypertensive Disorders of Pregnancy

There is approximately one maternal death due to preeclampsia-eclampsia per 100,000 live births, with a case-fatality rate of 6.4 deaths per 10,000 cases (Livingston, Livingston, Ramsey, Mabie, Sibai, 2003; Mackay, Berg, Atrash,2001). According to (Heard, Dekker, Chan, Jacobs, Vreeburg and Priest, 2004). The outcome of hypertension in pregnancy is, not surprisingly, affected by multiple factors. These embrace (but are not limited to) gestational age at onset, severity of disease, and the presence of comorbid conditions including diabetes mellitus, renal disease, thrombophilia, or pre-existing hypertension. Adverse outcomes related to hypertensive of pregnancy can be divided into short-term versus long-term complications. While short-term complications can be further sub-grouped into maternal and fetal complications, long-term outcomes are mainly maternal.

2.1.7. Short-Term Complications of Hypertensive Disorders of Pregnancy

(i) Mother

Outcomes for pregnancy complicated by hypertension range from uneventful pregnancy in women with chronic, controlled hypertension to death in cases of preeclampsia-eclampsia. The major adverse outcomes include central nervous system (CNS) injuries such as seizures (eclampsia), hemorrhagic and ischemic strokes, hepatic damage ranging from transaminase elevation, the so-called "HELLP syndrome" (hemolysis, elevated liver enzymes, and low platelets),hepatic failure, renal dysfunction (spanning the gamut from a trivial reduction in glomerular filtration rate and minimal proteinuria to reversible acute renal failure or so-called acute tubular necrosis to even irreversible renal failure secondary to renal cortical necrosis) as well as increased frequency of caesarean delivery, preterm delivery, and abruption of placenta (Lindheimer, 2000 ; Mackay, Berg, Atrash, 2001 ; Heard, Dekker, Chan, Jacobs, Vreeburg, Priest, 2004).

(ii) Child

As described by Lindheimer, (2000); Hauth, Ewell, and Morris (2000) the effects of chronic, controlled hypertension in pregnancy on the fetus are minimal. However, preeclampsia-eclampsia can lead to higher frequency of induced labor, fetal growth restriction, neonatal respiratory difficulties, and increased frequency

admission to neonatal intensive care unit. Hypertensive disorders of pregnancy, even in its more severe forms, causes only minimal increased risk for perinatal or fetal death.

2.1.8 Long-Term Complications of Hypertensive Disorders of Pregnancy

Though hypertension in pregnancy, preeclampsia is usually thought of as a short-term problem that resolves itself with delivery, it still carries significant risk for remote complications. Those infants born small and premature may experience prolonged stays in neonatal intensive care units and often face developmental delays. Remote outcomes include the risk of preeclampsia in subsequent pregnancies and several long-term maternal health risks as described below:

(i) Risk of recurrence

Barton and Sibai, (2008) stated the risk of recurrent preeclampsia in subsequent pregnancies varies with the severity and time of onset of the acute episode. According to Sibai, Mercer, and Sarinoglu (1991) it is estimated that women with severe, early preeclampsia during their first pregnancy will have a high risk of recurrent preeclampsia in their subsequent pregnancies (25–65%); Sibai, El-Nazer, Gonzalez-Ruiz,1986).

On the other hand, for milder forms of preeclampsia the risk of recurrent episode is still elevated, though to a lesser degree (5–7%) in comparison to women who

remained normal during their first pregnancy (1%) Sibai, Sarinoglu, Mercer,(1992); Mostello, Kallogjeri, Tungsiripat and Leet, (2008); Campbell, MacGillivray and Carr-Hill, (1985). While Bellamy, Casas, Hingorani and Williams, (2007) stated that the recurrence risk of preeclampsia is lower when the first pregnancy was a twin as compared to a singleton pregnancy.

(ii) Cardiovascular complications

According to Bellamy, Casas, Hingorani and Williams, (2007).the association between preeclampsia and cardiovascular diseases is both well described and well documented. Women with history of preeclampsia are at significantly increased risk to develop hypertension, ischemic heart disease, stroke, type II diabetes, and venous thrombo-embolism in comparison with women without history of the disease.

Furthermore, Bellamy, Casas, Hingorani and Williams, (2007).Factors linked to increased risk of long-term cardiovascular diseases are early onset preeclampsia, recurrent preeclampsia, severe preeclampsia, gestational hypertension, or preeclampsia with onset as a multipara.

According to Dane, Batmaz, ozkal, Bakar, and Dane (2014) parity has a significant effect on uterine artery Doppler findings in the first trimester of pregnancy. And that in the group of parous women the mean level of resistance index (RI) had a higher predictive value for miscarriage, early pregnancy induced hypertension

(PIH).

(ii) Cancer

Aagaard-Tillery, Stoddard Holmgren and Dalton (2006); Vatten et al (2002), stated that multiple observational studies evaluated the possible association between hypertension in pregnancy and cancer risk. Overall, women with preeclampsia were found to be at reduced risk or had no excess risk of cancer when followed by extended periods postpartum. While Vatten, Romundstad,Mogren, Stenlund and Högberg, (2002); Cohn, Cirillo,Christianson, Van Den Berg, Siiteri, (2001) confirmed that a recent systematic review found no significant association between preeclampsia and risk of cancer. This "protective" effect of preeclampsia may be explained, at least in part, by the possible role of the immune system in the disease pathogenesis. Women with responsive immune systems may be more vulnerable to develop preeclampsia but enjoy some protection from malignancy.

2.1.7 Prevention, Management and Control of Hypertensive Disorders of Pregnancy

2.1.7.1 Prevention of Hypertensive Disorders of Pregnancy

According to WHO (2011); Henderson, Whitlock, O'Connor… and Rowland (2014) recommendations for prevention include use of aspirin in those at high risk,

calcium supplementation in areas with low intake, and treatment of prior hypertension with medications.

Furthermore, Smith, Lowe, Fullerton….. And Felker-Kantor(2013); McDonald Lutsiv, Dzaja; and Duley (2012) recommended that the use of intravenous or intramuscular magnesium sulphate improves outcomes in those with eclampsia and is generally safe. The most commonly used agents of treatment of blood pressure 160/110mmHg are labetalol, nifedipine and hydralazine. Most commonly used agents for treatment of blood pressures of 149 to 159/90 to 105 mmHg are Methyldopa, Labetalol and Nifedipine.

2.1.7.2 Management of Hypertensive Disorders of Pregnancy

The first principle of treatment of hypertension in pregnancy is to correctly diagnose the category and severity of the hypertension.

(i) Gestational Hypertension

Gestational hypertension is elevated blood pressure, which develops after 20 weeks of gestation in a previously normotensive woman, though without proteinuria. It complicates 6% of all pregnancies. These women are at high risk for developing preeclampsia that can occur at any time including the first postpartum week and need close monitoring. Approximately 15—45% will eventually develop

preeclampsia according to Davis *et al*, 2007; Barton, O'Brien, Bergauer, Jacques, Sibai, (2001).

(ii) Preeclampsia

Close monitoring to recognize fetal distress while receiving treatment is essential. Early onset preeclampsia (less than thirty-four weeks) requires careful use of antihypertensive medications, bed rest, and in-hospital monitoring of both mother and fetus. This approach may help delay delivery and thus improve fetal outcome. Often these patients are intra-vascularly depleted and are more susceptible to precipitous, drug-induced drops in blood pressure. If signs of other fetal or maternal distress are noted, delivery is the definitive treatment. Concerns about hypotension and decreased utero-placental blood flow are central to the treatment of the preeclamptic patient, since placental ischemia is the focal point of preeclampsia pathophysiology.

Furthermore, lowering of BP does not reverse the primary process. The ultimate goal of antihypertensive therapy is to reduce the main risks to the mother, which include placental abruption, accelerated hypertension requiring hospitalization, and target organ-damage including cerebrovascular and cardiovascular complications.

One must be cognizant of the risk for target organ damage is increased, when a sudden change in blood pressure occurs in previously normotensive women. As is true in all dynamic clinical settings, individualization of care is often the rule. In most instances, delivery of preeclamptics is indicated after 37 weeks of gestation or when fetal lung maturity has been confirmed.

2.1.8 Malaria in Pregnancy

The concept malaria in pregnancy is also referred to as Pregnancy - associated malaria and is defined by Shiel. (2020) as a specific syndrome that occurs only in pregnant women and that is characterized by the accumulation in the placenta of red blood cells containing the malarial parasite. Malaria in Pregnancy- causes low birth weight and maternal anemia. Therefore, it is associated with substantial rates of morbidity (disease) and mortality (death) for both the mother and baby

According to Conroy, McDonald and Kain, (2012) globally, 125 million women are at risk and in Sub-Saharan Africa, where over 90% of the world's malaria-related deaths occur,

WHO, (2009) stated that 25 million pregnant women are currently at risk for malaria, accounting for 10,000maternal and 200,000 neonatal deaths per year. Ismail, Ordi, Menendez…. and Alonso (2000); Matangila, Lufuluabo, Ibalanky…

and Geertruyden, (2014) confirmed that 2000 neonatal deaths per year occur due to pregnancy associated malaria.

According to Takem and Alessandro, (2013) in the Sub – Saharan regions in which malaria parasitemia is of high transmission and endemicity, sub-clinical malarial infection is common. Schantz-Dunn and Nour, (2000); Brabin, (1983) stated that fetal complications result from high placental plasmodia burden (in high-transmission regions) and maternal anemia manifesting as still birth, intrauterine growth restriction, low-birth-weight neonates and neonatal and newborn death.

Srivastava, (2010) stated that pregnancy in malaria (PIM), (pregnancy associated malaria (PAM) is caused primarily by infection with *Plasmodium falciparum*. While Perlmann; Troye-Bloomberg, (2000) reported that the most dangerous of the four species of malaria-causing parasites that infect humans. Furthermore, Perlmann; Troye-Bloomberg, (2000) hypothesized that the majority of sequelae in pregnancy results from 2 main factors: the immuno-compromised state of pregnancy and placental sequestration of infected erythrocytes. As discussed previously, adults who live in malaria-endemic regions generally have some acquired immunity to malaria infection as a result of immunoglobulin production during prior infections in childhood. This immunity diminishes significantly in pregnancy, particularly in primigravidas.

A recent study of 300 women delivering in rural Ghana showed higher rates of anemia, clinical malaria, and placental burden of infection among primigravidas compared with multigravidas .The study also noted that babies born to mothers with placental malaria infection were more than twice as likely to be underweight at birth Ofori, Ansah Agyepong …and Akanmori, (2009).

According to Desai,Kuile, Nosten …and Newman(2007) splenic sequestration of malaria infected erythrocytes leads to folic acid deficiency and microcytic anaemia in adults. In pregnant women, additional sequestration of malaria infected erythrocytes occurs in the placenta. Pregnant women therefore suffer disproportionately from severe anemia as a result of infection. Furthermore, Desai *et al* stated that in Africa, it has been estimated that malaria is responsible for 25% of severe anemia during pregnancy (defined as hemoglobin less than 7 gm/dl). According to Monif and Baker, (2004) women with severe anemia are at higher risk for morbidities such as congestive heart failure, fetal demise, and mortality associated with hemorrhage at the time of delivery. Interestingly, the greatest degree of placental infestation is seen in women who have the highest level of immunity, leading to milder maternal symptoms and a disproportionate increase in fetal complications. It could be hypothesized, therefore, that although primigravidas may develop the clinical symptoms of malaria, women with higher

immunity may not demonstrate symptoms, will not receive treatment, and will build a higher placental parasite burden.

Monif and Baker, (2004) further reported that fetal complications result from this placental inflammation, as well as maternal anemia, and manifest as stillbirth, intrauterine growth restriction, and low-birth-weight neonates. Low-birth-weight neonates, in turn, are at higher risk for neonatal and newborn death. Congenital malaria is a relatively rare complication in areas with endemic malaria; however, newborn parasitemia may present 2 to 3 months after delivery when maternal antibodies wear off. It is also thought that infected erythrocytes collected in the placenta stimulate pancreatic β- cell production of insulin, leading to hyper-insulinemia and hypoglycaemia during infection. This contributes to the severity of disease during pregnancy. Other maternal effects of malarial infection result from the "stickiness" of the infected erythrocytes that become trapped in small vessels, resulting in cerebral malaria, renal failure, and thrombocytopenia.

2.1.8.1. Immune Response to Malaria in Pregnancy

According to Ricket, Staalsoe, Koram and Akanmori (2003) women develop increasing resistance to malaria infection over successive pregnancies. This pattern of parity specific resistance has been associated with the acquisition of antibodies to the surface of placental parasitized erythrocytes. Early in the pregnancies,

women generally lack antibodies that react with the surface of placental binding parasitized erythrocytes, which suggests these express novel surface variants.

However, by the second trimester (~20 weeks) many primigravid women possess antibodies that react to laboratory adapted chondroitin sulphate A (CSA) binding lines, suggesting they have been exposed to placental adherent parasitized erythrocytes. Consistent with this interpretation, the blood circulation opens up to the placenta about 10 weeks into pregnancy; and biochemical evidence demonstrates that low sulphate chondriotin proteoglycans sulphate are present in the placenta and intervillous blood spaces by the end of the first trimester and can support parasitized erythrocytes binding in vitro (Agbor-Enoh, Achur, Leke, and Gowda, 2003).

Brabin, (1996) stated that binding phenotype suggests that most placental parasites do not undergo a full cycle of replication in the placenta but circulate and sequester during the later developmental stages. Therefore, women are susceptible to placental infections early in pregnancy, beginning at approximately 10-12 weeks.

During this first exposure, women begin to develop antibodies to placental binding isolates the peak prevalence of puerperal blood parasitaemia in pregnant women occurs at the beginning of the second trimester (between 13 and 20 weeks gestation). Monocytes and macrophages are commonly seen in infected placenta. They frequently contain malaria haemozoin pigment.

Duffy, Mantel, Doubia, and Doumbo, (2006) described that after parasites and monocytes clearance, free malaria parasites or fibrin deposits still persist in the placental infections and could be classified into four: no infection, acute, chronic and past infection. This grade of classification is based on the presence or absence of malarial pigment in the placental blood spaces. These grades are believed to reflect a natural progression of infection and immunity. The presence of parasitized erythrocytes and minimal pigment in macrophages but not in fibrin causes acute infections. Chronic infections are characterized by erythrocytes parasitized and pigment deposits in monocytes and fibrin. While past infections have pigment deposits but no erythrocytes parasitized. The presence of malaria pigment in monocytes intervillous space is associated with poor pregnancy outcomes. Therefore, monocytes play a role in both malaria complications and resolution of infection.

Beeson, Mhango, Dzinjalamala, and Molyneux (2000) stated that both primigravid and multigravid women have adhesion-blocking antibodies effective against sulphate A binding isolates. However, chondroitin, the major difference between primigravid and multigravid women is the timing at which these antibodies are first detected during pregnancy. Thus antibody response may be rapidly boosted upon re-exposure to placental isolates in multigravida women. It has been proposed that this may be a factor in improved pregnancy outcome in multigravid women. Specific surface of CSA antibodies to the binding parasites usually

develop during pregnancy. These antibodies are low or absent in children or men. Therefore non-immune IgG/IgM which facilitates immune evasion is of low affinity. They could be displaced once specific antibodies develop against the CSA ligand in multigravid women as described by Elliott, Brennan and Beeson, (2005).

2.1.8.2 Complications of Malaria during Pregnancy

According to Luxemburger, McGreedy, Kham and Nosten (2001) over the years, researchers have come to discover the fact that malaria has a disked effect, especially on pregnant women. Malaria in pregnancy is an obstetric, social and medical problem requiring multidisciplinary and multidimensional solution. Pregnant women constitute the main adult risk group for malaria and 80% of deaths due to malaria in Africa occur in pregnant women. Malaria during pregnancy reduces birth weight. In this case, newborn babies who normally weigh

Between 2.5kg and 3.2kg (approximately 7.5ibs) now measures less as a result of the malarious condition of the mother during pregnancy. This, in the long run could lead to premature death of the neonate if not properly taken care of, this is regarded as the major determinant of infant mortality

Malaria also causes severe anemia in pregnant women, especially in primigravidae. For these reasons, it's generally advocated that women living in a malaria endemic area should be given chemoprophylaxis during pregnancy even when they are

partial immune. Malaria and pregnancy are matronly aggravating conditions. The physiological changes due to malaria have a synergistic effect on the course of each other, thus making life difficult for the mother, the child and the treating physician. In pregnant women, especially in Abia State, the morbidity due to malaria include anemia, fever illness, hypoglycemia, cerebral, malaria, pulmonary edema, puerperal sepsis and mortality, in cases of severity. The effect of malaria along-side those earlier discussed in the new-born includes premature birth, Intra Uterine Growth Retardation (IUGR), malaria illness and mortality.

According to Thadhani, Maynard, Glssock, Brass and Lam (2019) Proteinuria is one of the cardinal features of preclampsia, a common and potentially severe complication of pregnancy. Protein in pregnancy can also indicate primary renal disease or renal disease secondary to systemic disorders, such as diabetes or primary hypertension. As further stated by Thadhani, Maynard, Glssock, Brass and Lam (2019) this complication is such that 20 to 25 percent of women chronic hypertension, diabetes, and chronic kidney disease develop superposed preclampsia

2.1.9 Prevention and Control of Malaria in Pregnancy

2.1.9.1 WHO Guidance for Prevention and Treatment of Malaria in Pregnancy.

WHO recommends a three-pronged approach to malaria in pregnancy (MIP) which

Includes,(i) Intermittent preventive treatment (IPTp); (ii) Insecticide-treated nets (ITNs) and (iii) Prompt and effective case management. WHOs guidance for each prong is summarized below.

(i) **Intermittent Preventive Treatment in pregnancy (IPTp):** In areas of moderate-to-high malaria transmission, IPTp with sulfadoxine-pyrimethamine(SP) is recommended for all pregnant women at each scheduled antenatal care visit. WHO recommends a schedule of four antenatal care visits. The first IPTp-SP dose should be administered as early as possible during the 2ndtrimester of gestation.

Each SP dose should be given at least 1 month apart; the last dose of IPTp with SP can be administered up to the time of delivery, without safety concerns. IPTp should ideally be administered as directly observed therapy (DOT). SP can be given either on an empty stomach or with food. Folic acid at a daily dose equal or above 5 mg should not be given together with SP as this counteracts its efficacy as an anti-malarial.

WHO recommends daily iron and folic acid supplementation in pregnant women at the dose of 30-60 mg of elemental iron and 0.4 mg of folic acid, to reduce the risk of low birth weight infants, maternal anemia and iron deficiency at term. SP should not be administered to women receiving Cotrimoxazole prophylaxis.

(i) Insecticide-treated nets (ITNs)

ITNs should be provided to women as early in the pregnancy as possible, at the ANC clinic or through other sources in the public or private sectors. The WHO global malaria program recommends distribution of ITNs, more specifically long lasting insecticides nets (LLINs), to achieve full coverage of populations at risk of malaria. The best opportunity for rapidly scaling up malaria prevention is free or highly subsidized distribution of LLINs through existing public health services (both routine and campaigns).

2.1.10 Control of Malaria during Pregnancy

Chloroquine prophylaxis is generally recommended in highly endemic areas like Abia State, most especially for pregnant women and children. None or semi immunes travelling to endemic areas may also be advised to take prophylaxis for the period they are there. There are a number of candidate vaccines against malaria and some field trials are taking place, but until there is a safe and effective vaccine, the primary approach taken is that of control.

In most places where malaria is endemic, the control objectives are to minimize vector-human contact and to treat malaria disease promptly. Reducing breeding sites of mosquitoes, screening of door and windows, use of mosquitoes nets and insecticide sprays, and prompt treatment of malaria episodes can reduce the impact

of malaria. However, people's ability to comply with interventions and to treat sickness is affected by their acceptance of the interventions, their understanding of the nature of the illness and the relationship between vector and infection, as well as other social, economic and cultural factors. For instance, poor households may not have the cash to provide chemoprophylaxis for pregnant women or to purchase bed nets for all household members, even if they accept these interruptions in theory.

2.1.11 Possible Mechanisms for Malaria-Induced Hypertensive Disorders of Pregnancy

(i) Angiogenesis

Blood pressure changes induced by infectious and parasitic diseases such as malaria can result from inflammation caused by the disease. During plasmodial invasion of the red blood cells (RBC), the parasites adhere in the deep endothelia of vital organs such as placenta, brain, adipose tissues, liver and spleen. This is referred to as sequestration. This aids infected RBCs to evade splenic clearance.

The accumulation of high concentrations of toxic parasite components at sites of sequestration triggers a strong activation of the natural host defense mechanism resulting in increased production of leukocytes (B and T lymphocytes).

Sequestration of P. falciparum in infected RBCs change the morphology of the RBCs in order to facilitate the survival of these parasites but this leads to hypoxia and tissue perfusion in the host.

According to Gallego-Delagado and Rodriguez, (2014)recent studies have suggested that peptide hormones of the renin-angiotensin - aldosterone-system (RAAS) play a major role in the pathogenesis of malaria. The liver creates and releases a protein called angiotensinogen, this is broken down by renin which is an enzyme produced in the kidney to form angiotensin I (ang I), ang I is further metabolized to produce angiotensin II (ang II) by the action of angiotensin-converting enzyme (ACE). Ang II is a peptide hormone which is a vasoconstrictor that brings about subsequent increase in blood pressure, in other words, it is a blood pressure regulator and it is also involved in fluid (water and salt) balance.

(Crackower, Saro, Oudit & Penninger, 2002) stated that another enzyme which determines the secretion and concentration of ang II is angiotensin-converting enzyme II (ACE 2), this converts ang II to ang (1-7).

This is a polymorphism associated with less ACE 2 protein that results in higher Ang II concentration, which could be a risk factor for hypertensive disorders during pregnancy. Ang II contributes in modulating adaptive immunity by acting directly on lymphocytes. In response to malaria parasite multiplication in the body, inflammatory molecules are produced in large amounts to combat the invading

antigens, this result in an increased production of white blood cells (lymphocytes). These lymphocytes (B and T) possess angiotensin type 1a receptors (AT1aR). When Ang II binds to lymphocytes via the receptors, there is a proliferation of splenic lymphocytes. This process alters the pathogenesis of malaria parasites which explains the protective effect that increased production of Ang II has on erythrocytes by decreasing erythrocytic invasion by *Plasmodium*.

This association although beneficial in decreasing the severity of malaria infection is a risk factor for increased blood pressure because there will be a direct elevated secretion of Ang II which is a vasoconstriction agent. Increased and sustained activities of vasoconstriction agents narrows the body & smaller blood vessels (arterioles) causing the blood to exert much pressure against the vessel walls and forcing the heart to work harder in order to maintain the pressure. This condition is a key predisposing factor for increased blood pressure which causes hypertensive disorders in pregnant women.

(ii) Oxidative Stress

Oxidative stress is the imbalance between the productions of free radicals (pro-oxidants) and antioxidant molecules which is as a result of excessive production reactive oxygen species (ROS) and reactive nitrogen species (RNS). Oxidative stress can be caused by diverse conditions, one of which is infectious diseases such as malaria infection. During erythrocytic invasion by Plasmodium parasites, the

natural host defense mechanism is activated with involvement of phagocytes (macrophages and neutrophils). This leads to the generation of large amounts of ROS and RNS which creates an imbalance between formation of oxidizing species and the activities of antioxidants. This process triggers Oxidative stress.

Oxidative stress is associated with an increase in production of free radicals such as superoxide anion, hydrogen peroxide, hydroxyl radical and a decreased nitric oxide (NO) synthesis and a reduction in antioxidant bioavailability. A decrease in NO synthesis and reduction in bioavailability of antioxidants play a major role in the maintenance of vascular/endothelial function.

According Rafieian-Kopaei and Baradaran (2013), ROS are mediators of vasoconstriction which is induced by ang II, endothelin –I and urotensin -II. Nitric oxide is released by the endothelium and causes vascular relaxation or dilation. Nitric oxide is rapidly degraded by the oxygen-derived free radical superoxide anion. Superoxide anion acts as a vasoconstrictor and is a major determinant of nitric oxide (NO) biosynthesis and bioavailability. Therefore, an increased production of ROS which are mediators of vasoconstriction and a decrease in the bioavailability of NO, a major vasodilator leads to loss of endothelial function which causes vascular lesions responsible for vascular permeability. Vascular permeability results in endothelial dysfunction which is a major phenomenon in hypertension diseases. Increased oxidative stress and decreased NO bioavailability

is associated with hemodynamic changes responsible for hypertensive disorders during pregnancy

(iii) Cyto-adherence

Physiological conditions during pregnancy render women immune-compromised to infectious diseases such as malaria, particularly, the primigravid as when compared to non-pregnant women. Cyto-adherence is an established stage in the pathogenesis of malaria which confers on malaria parasite the unique ability to adhere to the vascular endothelium (capillary and post capillary venular endothelium. This ability promotes the survival of Plasmodium parasite within its host.

The adhesion of these parasites to the vascular endothelium of several organs such as the heart causes blood flow impairments which can result to the heart working under increased pressure to enable blood circulation in humans. This condition is an enabling factor for developing increased blood pressure, increased maternal heart rate, these can contribute to hypertension diseases during pregnancy.

(iv) Hyper-coagulation

According to Kelton, Keystone, Moore and Jensen (1983) Hyper – coagulation is a state of excessive blood clotting. Blood coagulation is influenced by *P. falciparum* parasite through various mechanisms, one of which is inflammatory response of

the host resulting in excessive generation of inflammation cells. Also, infected RBCs adhere to deeper tissue capillary endothelium leading to extensive damage of the endothelial cells. This further activates blood coagulation and widespread consumption of platelets which are primary factors in blood clotting.

Platelets are activated as early as 24 hours after plasmodial infection. An increased number of circulating platelets may have an early protective role in limiting parasitic burden, but continued activation of platelets and release of platelet-derived immune mediators may have adverse inflammatory outcomes.

Sometimes, these excessive blood clots and most of the products released during host- parasite interaction, which includes platelets, fibrin, parasite proteins, either deposit in or travel to arteries and veins of vital organs such as the heart, brain, liver, adipose tissues, where it results in the obstruction of free circulation of blood, thereby exerting much pressure on organs such as the heart while circulating blood in humans. This condition elevates heart rate, blood pressure and causes endothelial dysfunction. These are an important factor that contributes to developing hypertensive disorders during pregnancy.

2.2 Theoretical Framework

2.2.1 Malaria – Hypertension Hypothesis

The Malaria – Hypertension Hypothesis postulated by Pages and Liles (2013) is applicable in this study 'Hypertensive Disorders among Pregnant Women with malaria in Abia State University Teaching Hospital, Aba, Abia State. According to Page and Liles (2013) the inflammatory pathways activated by malaria infection are similar to those of other diseases. The Malaria – Hypertension Hypothesis postulates that malaria contributes to the burden of hypertension through inflammation which provides the momentum for study and control malaria. In this hypothesis most treatment for infection is based on eliminating the pathogens/parasites by modulating the inflammatory responses that might result in adverse vascular consequence afterwards. Eliminating these inflammatory pathways and their consequences would open the way for trials of adjunctive therapy such as stains or specific cytokine antagonist as a result of infection.

The Malaria – Hypertension as further postulated by Etyang, Smeeth, Cruikshank and Scott states that malaria and high blood pressure are wide spread in low income and middle – income countries, and that malaria is known to cause low birth weight and inflammation. They also postulated that inflammations are so associated with the development of arterial stiffness and high blood pressure in developed countries. Thurston and Daily (2012); explained that the link between

inflammatory conditions and hypertension may be related to disturbances in the levels of endothelial – based growth factors. Angiopoitein – 2 (Ang – 2) is a multimeric ligand of the the Tie 2 receptor, part of a vascular – specific tyrosine kinase signing pathway that is essential for vessel development and stability. Ang – 2 is predominantly secreted by endothelial cell and some muscle in many inflammatory and angiogenic states.

The malaria – hypertension hypothesis is further supported by (Nwokocha, Bafor, Ajayi and Ebeigbe, 2020) in which it was stated that evidence suggest that the link between malaria infection and high blood pressure involves interaction between malaria parasites and erythrocytes, the inflammation process, effects of the infection during pregnancy; effects on renal and vascular function.

The mechanism for the malaria – Hypertension association as stated by (Nwokocha, Bafor, Ajayi and Ebeigbe (2020) include two key mediators: endothelial dysfunction (reduced NO) and increased angiotensin – converting enzyme activity/angiotensin II levels.

The theory of malaria and hypertension in pregnancy is further supported by Ndao *et al.* (2009) in which they stated that malaria is also associated with hypertensive disorders of pregnancy such as gestational hypertension and preeclampsia in young primigravid women.

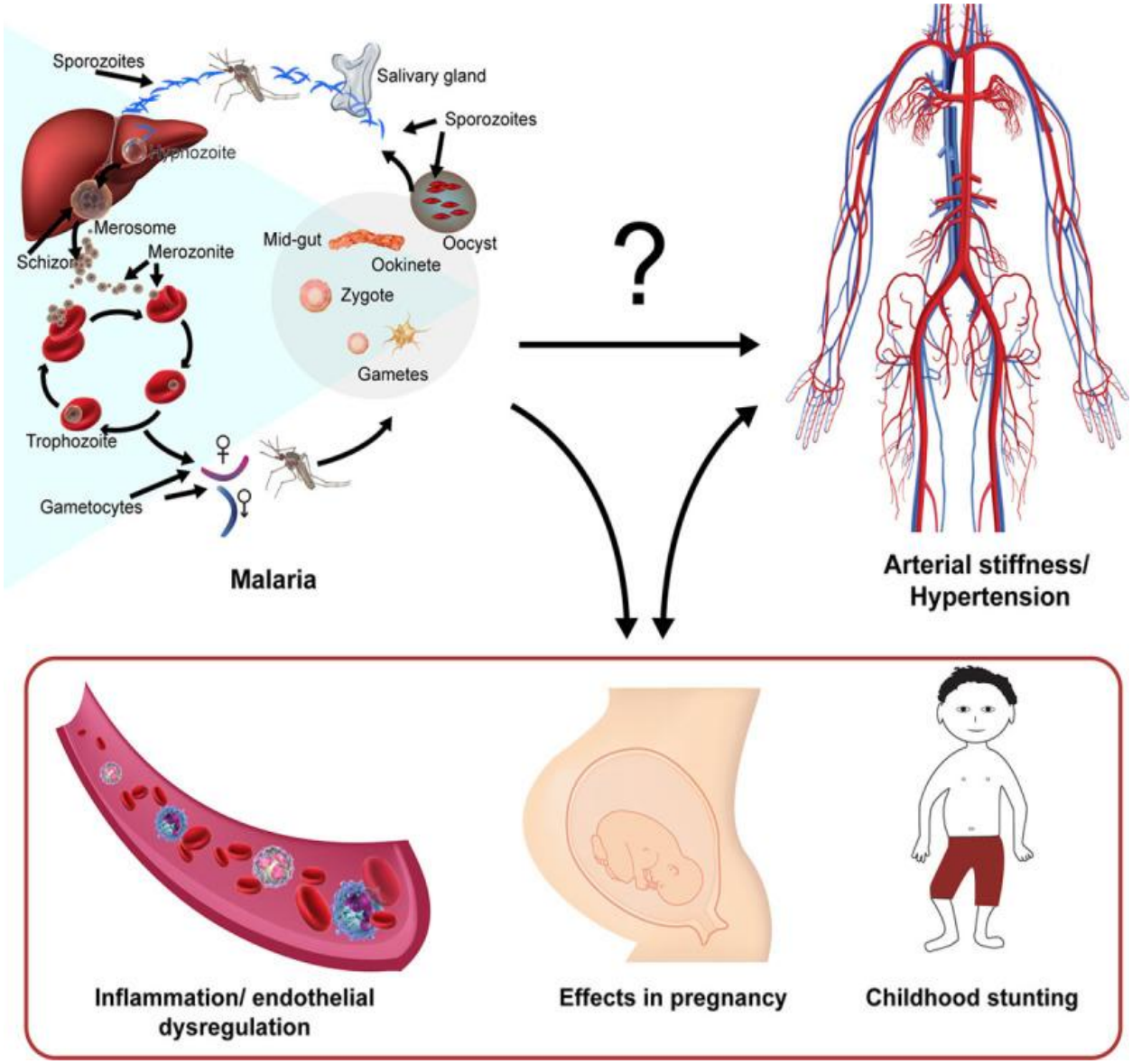


Figure 2.1: The Malaria – High Blood Pressure Hypothesis.

2.3 Empirical Framework

A population – based survey in Cote d' Ivoire carried out by Eze, Bassa, Fidele & Probost – Hensch (2019) showed positive associations with hypertension in participants with elevated body temperature [>36.5^{o}C; OR: 2.93 (95% CI 0.94 – 14)]. According to Eze *et al.* (2019) malaria parasitemia and hypertension are

prevalent and seemly linked co- morbidities in Africa settings. They explained that the link between malaria parasitemia and hypertension may depend on malaria parasitemia symptomaticity/latency where individuals with more latent/asymptomatic malaria parasitemia have lower risks of hypertension and those with more acute/systematic malaria parasitemia have a tendency toward higher blood pressure.

A longitudinal cohort study conducted by Duffy (2019) in Ouelessebougou, Mali on malaria immunology and pathogenesis in pregnant women and young children reported that pregnancy malaria is associated with gestational hypertension.

Onuigbo, *et al.*(2015) in a study Okigwe, Abia State, Nigeria, on malaria and pre - eclampsia among pregnant women attending ante – natal clinic in Okigwe Local Government Area reported that the prevalence of malaria infection, proteinuria and high blood pressure among pregnant women attending antenatal clinic in Okigwe Local Government Area concluded that malaria infection was high (26.1%) pregnant women and suggested that malaria during pregnancy may be an

Independent factor for pre – eclampsia, and that proteinuria and high blood pressure are the major cause of pre –eclampsia.

In a related study performed by Abdulazeez, Yau and Kufi (2017) in Kano State, Nigeria on association of hypertension and activity of angiotensin converting enzyme in malaria patients attending Sheik Muhammad Jida General Hospital,

Kano State found out that out of a total of 300(66.6%) patients tested positive for malaria, of which 60 (20%) were hypertensive. They concluded that prevalence differed significantly by gender, age group and occupational status. Bodkin, Gordon, Sawchuk and Dadelszen (2012) in a study in Vancouver, Canada on Placental malaria Infection as a risk factor for hypertensive disorders of pregnancy in malaria endemic regions reported that they did not find a significant association between PMI and the risk of HDP.

Mruma, McQuillan and Norrie (2018) a comparative cohort studies in London, United Kingdom on the association of malaria infection and gestational hypertension in Africa: Systematic review and meta-analysis reported that by using critical appraisal skills program (CASP) checklist tool they identified four good quality case-control studies. The total sample size was 1281 women out of which 518 were cases. These studies together show malaria is associated with Gestational Hypertension (GH) with an overall odds ratio of 2.67, 95% confidence interval

(CI) = 1.58-4.53. Heterogeneity of the individual studies supported fixed effect modeling assumptions ($I^2 = 0\%$). From their study they concluded that malaria infection may have a constant effect on GH across different African populations.

In 2009, Ndao *et al,* found a relation between placental malaria infection (PMI) and gestational hypertension in pregnant women living in a malaria-hypoendemic setting in Senegal. In a multivariate analysis, they found that the prevalence of PMI

was 4.6% for eclampsia, 4.0% for preeclampsia, and 11.6% for gestational hypertension. This suggests that malaria during pregnancy maybe an independent risk factor for hypertensive disorder. In another study, Muehlenbachs et al, 2006 discovered that young first-time mothers with placental malaria had significantly increased risk of hypertension in Tanzania.

CHAPTER THREE

METHODOLOGY

This chapter describes the methods that were applied by the researcher in carrying out this research work. It involves the study design, study setting, study population, sample size and sampling technique, instrument for data collection, validation of instrument, reliability of instrument, method of data collection, data analysis and ethical consideration.

3.1 Study Design

This is a hospital-based cross sectional study. The pregnant women were recruited based on their exposure to malaria. The cross sectional study design involves looking at data from a population at one specific point in time. In the study, antenatal procedure and data relevant to the study was collected once, as the design involves a cross sectional investigation of the obstetric conditions of the women.

3.2 Study Setting

This study was carried out at Abia State University Teaching Hospital, Aba in Abia State. Abia State is one of the five South Eastern states in Nigeria. Abia state occupies about 6,320 square kilometers. Abia is mainly peopled by the Igbo ethnic group. The Igbo people, who are the indigenous peoples of Southeastern part of

Nigeria, make up 95% of the population. Their traditional language, Igbo is in widespread use. English is also widely spoken, and serves as the official language in governance and business. The hospital is one of the largest hospitals in Abia State with many medical departments and wards. The present Abia State University Teaching Hospital (ABSUTH) is located at Umueze Road, Abayi, in the town of Aba, Abia State. The bearing of the hospital site is 70°, 24.06" North and 90°, 50.29" East. The old site of ABSUTH cuts across three roads, it lies between Eziukwu Road, Jubilee Road, and Queen's Road. The new ABSUTH site houses the following: College of Medicine and Health Sciences, Medical Laboratories, School of Nursing and Midwifery, Ophthalmology, Obstetrics &Gynecology, Pharmacy, Administrative Office Blocks, Staff Quarters and Hostels, Laundry etc.

ABSUTH is centrally located and easily accessible to all Aba neighborhoods and neighboring cities. This characteristic puts it in a pole position of proffering immediate solution to the needs of her customers, to understand the pressures confronting them and to develop innovations well suited to their needs. Aba is in Aba South L.G.A. of Abia State, South-East Nigeria. The city is one of the commercial nerve centers of the country and is more cosmopolitan in nature. Aba has a tropical climate with mean daily maximum air temperature range from 28°C-35°C and means daily minimum air temperature range from 19°C-24°C (Nwoke and Uwazie, 1991). Aba is located between latitude 5° 7'N and longitude 7° 22'E (Amaechi and Ukpai, 2013). The highest temperature occurs between March and

April and the lowest occurs in January. Wet and dry seasons are distinct in the area. Wet season spans from March to October giving an annual rainfall of between 1,700mm-2,000mm. The inhabitants are mainly traders and artisan with a few civil servants. Aba is a city with infrastructural facilities, tertiary institutions, one of which is Abia State University Teaching Hospital (ABSUTH), a general hospital, a few private clinics and Primary Health Care Centers.

Aba's vegetation is typically rainforest. It is an urban town spotting a lot of bushes, open drains, puddles and inefficient waste disposal with huge refuse litters found in strategic areas of the town. Flooding is widespread in the rainy season creating breading sites for mosquito vectors and ideal transmission conditions for malaria.

3.3 Study Population

The study population was 71 pregnant women attending antenatal clinic at Abia State University Teaching Hospital Aba in the month of March, 2018. The hospital was visited on the antenatal days which were Thursdays. On each visit, the number of pregnant women who came for antenatal was determined and identification numbers given to them to avoid counting one person twice. This process was carried out between 8am and 2pm, women who came after 2pm were not included in the study population. This was done for three weeks.

3.4 Sample Size and Sampling Method

3.4.1 Sample Size

A total of 60 women were drawn from seventy-one (71) pregnant women. The sample size was determined at 95% confidence level using the Taro Yammane sample size formula. (Yammane, 1967) (Appendix A).

3.4.2 Sampling Method

The hospital was on antenatal days which were Thursdays. On each visit, all the women who came for antenatal clinic were first sensitized and the objectives of the study were fully explained to them. Those who consented were tested with rapid diagnostic test kit (RDT) to confirm malaria. Only those who were positive made the daily study population and identification numbers given to them to avoid counting one person twice. Taro Yammane sample size formula was used to determine the sample size each day from the study population confirmed to be malaria positive and simple random sampling technique (balloting) was used in selecting participants for the study after determining the study population for each day. This was done for a period of eight weeks and sixty (60) pregnant women were recruited.

Inclusion Criteria: Pregnant women with malaria and no previous history of hypertension.

3.5. Instruments for Data Collection

i. A structured questionnaire was used to obtain data on the socio-obstetrics characteristics of the pregnant women. Gestational age was recorded in trimesters. Number of Children was recorded in parity and Maternal Age was recorded in years as independent variables and data regarding the pregnant women's history of hypertension were obtained.

ii. Laboratory Procedure

a. Malaria parasite identification and parasite density estimation was done using microscopy.

b. Paramed Professional Aneroid Sphygmomanometer Blood Pressure curve was used in measuring the blood pressure. BP was recorded in mmHg.

c. Urinalysis was done using Macherey-Nagel Medi-Test Combi 9 test strips.

3.6 Validity of Instrument

The questionnaire was validated using face validity. The questionnaire was carefully prepared by the researcher and was vetted by the supervisor and two experts in public health in relevance to the topic, contents, objectives and appropriateness of language. The corrections were used to modify the instrument and the final draft was approved (Appendix B).

3.7 Reliability of Instrument

Parallel reliability test was used to test the reliability of the instrument. Two sets of the copies of the questionnaire of equivalent contents were administered to 10 women that were not part of the study at the same time (five from Federal Medical Centre, Umuahia and five from General Hospital, Aba).The two sets of results were ranked and Spearman's rank co-relation was used to calculate the co-relation co-efficient. The Spearman's rank co-relation co-efficient takes values between -1 and +1 (i.e. 0.1 to 1.0). Co-efficient of 0.70 – 1.0 is most acceptable and the co-efficient co-relation reliability of the instrument was 0.88 (Appendix C).

3.8. Method of Data Collection

3.8.1 Questionnaire Administration

The questionnaire was administered orally. Questions on Socio-obstetric characteristics were asked to the women and the answered while the research assistants write down the answers on the questionnaire. Each questionnaire was administered in less than 3minutes.

3.8.2. Laboratory Examination

a. Malaria Microscopy

This test was done to determine malaria parasite density in the blood of the pregnant women. After cleaning the volar surface of the arm with cotton

wool moistened with methylated spirit, venous blood samples was collected with 5ml syringe which was stored in an ethylenediamine tetraacetic acid (EDTA) containers and was taken to ABSUTH laboratories for examination. Thick blood smears as described by Chesbrough [31] were made from each of these blood samples and labeled accordingly. These slides were stained for 10 seconds with Geimsa A solution (pH 7.2) after which it was rinsed off with water and subsequently, stained with Geimsa B solution which was allowed to dry and fix on the slide. Slides prepared can be stored for several months for future usage. This is the gold standard used for malaria microscopy. Malaria parasite was confirmed using, x45 objective lens and subsequently x100 objective lens for parasite identification and counting in each case. Identification of species was done using the thin blood smear. The parasite density was estimated on the thick smear under oil immersion and was viewed using x100 objective lens. The parasite density determination was done by counting the number of asexual forms of *Plasmodium falciparum* parasites against at least 100 leucocytes and 200 leucocytes for definitive count.The number of asexual parasites was calculated using this formula:

$$\text{Parasites}/\mu\text{L} = \frac{no of asexual parasite \times 8{,}000\ leucocyte}{200\ leucocytes}$$

Positive findings were graded on the thick smear using the 'plus' system scale:

+ (1 to 9 trophozoites in 100 fields); ++ (1 to 10 trophozoites in 10 fields); +++ (1 to 10 trophozoites per field); ++++ (>10 trophozoites per field). These scores were used to estimate parasite densities:

10 to 90 parasites/μL = + or mild

100 to 1,000 parasites/μL = ++ or mild

1,000 to 10,000 parasites/μL = +++ or moderate

> 10,000 = ++++ or severe

Quality control was ensured by using freshly reconstituted and filtered Geimsa stains.

b. Blood Pressure

Blood pressure reading of the pregnant women was determined as described by Brusie and Nall (2018). The mercury sphygmanometer is widely recognized as the "gold standard" for BP measurement (Ogedegbe and Pickering, 2010). The concern of mercury toxicity (Nnabuike and Jagidesa, 2019), continues to phase out their role as regards BP measurement. Automated BP reading devices have been gradually used in replacing the use of mercury sphygmanometer. Prior to the measurement, the subjects sat and rested for about 10 minutes. A digital Omron sphygmomanometer was used to measure the subjects BP. A cuff of suitable size was applied evenly on the exposed arm. The cuff was rapidly inflated until it is

fully filled with air. This was done by pressing the electronic button which automatically sends signal for cuff inflation. At full inflation, the digital analyzer read the results and the results Systolic Blood Pressure, (SBP), Diastolic Blood Pressure (DBP) appear on the screen. According to the American Heart Association (Cherney, 2018), gestational high blood pressure or hypertension is considered as a blood pressure reading <140/90mmHg.

c. Urinalysis

This test is done in order to detect protein (albumin) in urine (proteinuria) samples of pregnant women as this is one of the signs of preeclampsia. Sterile and clean containers were given to the pregnant women to collect their mid-stream urine.

Macherey-Nagel Medi-Test Combi 9 test strips were used to detect the presence and amount of protein present in the urine samples. A testing stick with a specially treated chemical strip is placed in the urine, the strip changes color depending on the presence of protein and also shows how much protein is present; this ranges from low (traces) to high (excess). A result of 3^+ is a further indication that the pregnant woman might be at risk for certain conditions such as preeclampsia.

The socio-obstetrics characteristics such as trimester, parity, maternal age of the pregnant women were ascertained using questionnaires. The structured pre-tested questionnaires were administered to the women after an informed consent was obtained. Literate pregnant women were allowed to fill the questionnaires

themselves but non-literate ones were assisted to answer the questions as they were asked in local language and their responses were filled by the researcher.

3.9. Classification of Cases

Cases were classified into three groups according to the National High Blood Pressure Education Programme Guidelines (Onuigbo, Elendu and Ekekeme, 2015):

I. Gestational hypertension (BP = $\frac{140}{90}$with albumin dosage of 2 (200mg).

II. Pre-eclampsia (BP = $\frac{140}{90}$ with albumin dosage of 3^{+} (300mg) without seizures).

III. Eclampsia (BP= >$\frac{140}{90}$ with albumin dosage of 3^{+} (300mg) with seizures and coma).

3.10 Data Analysis

Descriptive method of data analysis was used to summarize the data characteristics. Frequency distribution tables were constructed for all class variables which were expressed as the percentage of the distribution. Risks ratio was calculated for objectives which sought to determine the association between malaria and hypertension among the pregnant women. Chi-square test was used to analyze the results and significance was interpreted as calculated value < statistical table value at $P<0.05$.

3.11. Ethical Clearance/Informed Consent

The research proposal was submitted to the Ethical Review Board Committee (ERB) of School of Health Technology, Department of Public Health, Federal University of Technology Owerri for review and approval (Appendix D). Also, prior to the commencement of the study, ethical clearance was sought for by writing to the Chief medical Director (CMD) of ABSUTH explaining the purpose of the study and to seek for permission to use the health facility as well as the co-operation of their staff. On receiving approval, officers in charge of the Laboratory section were also consulted having received approval from the CMD. (Appendix E). Verbal informed consent was also obtained from respondents that participated in the study after the purpose, content and significance of the study had been adequately explained to them. They were informed that participation was voluntary and they will not suffer any consequences if they chose not to participate.

CHAPTER FOUR

RESULTS AND DISCUSSION

4.1 Results

4.1.1 Socio-Obstetrics Characteristics of Pregnant Women Attending Antenatal Clinic in ABSUTH Aba

The result on socio- obstetrics history of the pregnant women (Table 4.1.1) focused on three parameters; material age, parity and trimester.

The result on maternal age of the pregnant women showed that 10(16.7%) women were less than 18 years, 18(30%) women were between 18-25 years, 28 (46.7%) women were between 26-44 years and 4(6.6%) women were 45 years and above.

The results on parity of the pregnant women showed that 16(26.0%) women were primiparous, 12(20.0%) were secundiparous and 32(53.4%) women were multiparous.

Result on trimesters of the pregnant women showed that, 14(23.3%) women were in their first trimester. 34(56.7%) women were in their second trimester and 12(20.0%) women were in their third trimesters.

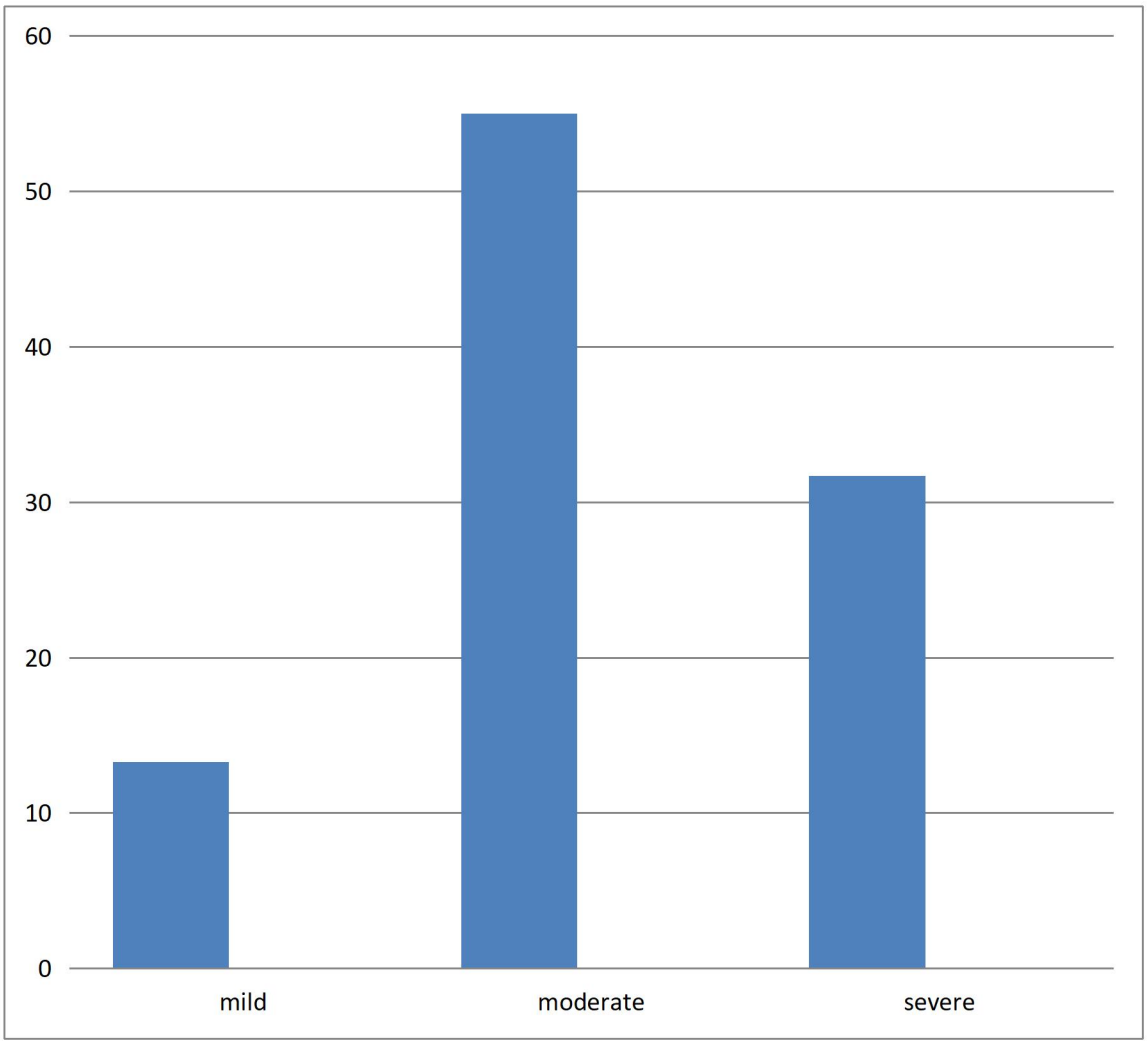
Result on the distribution of hypertensive disorders shows that 19(31.7) pregnant women had hypertensive disorders while 41(68.3) pregnant women had no hypertensive disorders.

Table 1: Socio-Obstetric Characteristics of Pregnant Women Attending Antenatal Clinic in ABSUTH.

VARIABLES	FREQUENCY N-60	PERCENTAGE
MATERNAL AGE		
>18	10	16.7
18-25	18	30.0
25-44	28	46.7
<45	4	6.6
Total	60	100.0
PARITY		
Primiparous	16	26.0
Seundiparous	12	20.0
Multiparous	32	53.4
Total	60	100.0
TRIMESTER		
1st trimester	14	23.3
2nd trimester	34	56.7
3rd trimester	12	20.0
Hypertensive Disorders		
Positive	19	31.7
Negative	41	68.3
Total	60	100

4.1.2 Distribution of Malaria Parasite among Pregnant Women Attending Antenatal Clinic at ABSUTH

Figure 2 shows that the sixty women who participated in this study all had malaria at varying parasite densities. Eight (8) pregnant women had mild parasite density (1,00 -10,000 parasites/ul) while nineteen (19) pregnant women had severe parasite density(> 10,000 parasite/ul).



Mild:10 – 1000parasites/µl; Moderate: 1000 – 10,000parasites/µl, Severe: >10000 parasites/µl

Fig 4.2: Distribution of Malaria Parasite Density among Pregnant Women Attending Ante-Natal Clinic at ABSUTH

4.1.3. Relationship between Hypertensive Disorder and Malaria Parasite Density among Pregnant Women Attending Antenatal Clinic at ABSUTH.

The result on the relationship between hypertensive disorder and malaria density among the pregnant women showed that, among 8 (13.3%) women with mild malaria, 3(37.5%) had hypertensive disorder and 5(62.5%) had non hypertensive disorder.

Also among 33 (55.0%) pregnant women with moderate malaria, 6(15.2%) had hypertensive disorder and 27(18.8%) had non hypertensive disorder.

Furthermore, among 19(31.7%) pregnant women, 10(52.6%) had hypertensive disorder and 9(47.4%) had non hypertensive disorder.

Statistical Analysis showed a significant relationship between hypertensive disorders and malaria density among the pregnant women ($X^2 = 6.85$, P-value = 0.032, d.f = 2)

Table 2: Relationship between Hypertensive Disorder and Malaria Parasite Density among Pregnant Women Attending Antenatal Clinic at ABSUTH.

Malaria Parasite Density	N=60	Hypertensive Disorders	Non-Hypertensive Disorders
Mild	8 (13.3)	3(37.5)	5 (62.5)
Moderate	33 (55.0)	6(18.2)	27 (81.8)
Severe	19(31.7)	10(52.6)	9 (47.4)
Total	60(100.0)	19(31.7)	41 (68.3)
$X^2 = 6.85$,	P= 0.034,	df= 2.	

4.1.4. The Influence of Maternal Age on Hypertensive Disorders of Pregnant Women with Malaria.

The result of the influence of maternal age on hypertensive disorders of pregnant women with malaria showed that 2(20.0%) out of 10 women within the age of 18 years and below had hypertensive disorders while 8(80.0%) women had non-Hypertensive disorder. Chi-square analysis showed a significant influence of material age on hypertensive disorder of pregnant women with malaria (X^2 – 4.788, P =0.091, d.f= 2) within the age group 18 years and below.

Also among pregnant women within the age group 19-25 years, 2(11.1%) had hypertensive disorder, each with moderate and severe malaria respectively. While 16(88.9%) presented with non-hypertensive disorders with mild malaria 1(100.0%), moderate malaria 11(91.7%) and severe malaria 4(80.0%). A Chi-square analysis showed no significant influence of maternal age on hypertensive disorder of pregnant women within the age group 19-25 years (X^2 = 15.11, P <0.001, d.f = 2).

Among pregnant women within the age group 26-44 years, 12(42.9%) had hypertensive disorder, out of which 3(75.0%) had mild malaria, 4(26.7%) had moderate malaria and 5(55.5%) had severe malaria. While among 16(57.1%) women with no hypertensive disorders, 1(25.0%) had mild malaria, 11(73.3%) had moderate malaria and 4(44.5%) had severe malaria. A Chi-square analysis showed a significant influence of maternal age on hypertensive disorders of pregnant

women with malaria within the age group of 26-44years (X= 3.84, P=0.146, d.f= 2).

Furthermore, among pregnant women within the age group 45 years and above, 3(75.0%) had gestational hypertension with severe malaria while 1(25.0%) had non hypertensive disorders with severe malaria.

Table 3: The Influence of Maternal Age on Hypertensive Disorder of Pregnant Women with Malaria

Maternal Age/Parasite Density	Hypertensive Disorder	Non-Hypertensive Disorder	Total	X^2	P- value
> 18					
Mild	0.(0.0)	3(100.0)	3 (30.0)		
Moderate	1 (16.7)	5 (83.3)	6 (60.0)		
Severe	1(100.0)	0.(0.0)	1 (10.0)		
Total	2(20.0)	8 (80.0)	10(100.0)	4.788	0.091
19 – 25					
Mild	0.(0.0)	1 (100.0)	1 (5.5)		
Moderate	1(8.3)	11 (91.7)	12 (66.7)		
Severe	1 (20.0)	4 (80.0)	5 (27.8)		
Total	2(11.1)	16 (88.9)	18(100.0)	15.11	<0.001
26 -44					
Mild	3(75.0)	1 (25.0)	4 (14.3)		
Moderate	4(26.7)	11(73.3)	15 (53.6)		
Severe	5(55.5)	4(44.5)	9(32.1)		
Total	12(42.9)	16(57.1)	28(100.0)	3.84	0.146
< 45					
Mild	0(0.0)	0.(0.0)	0.(0.0)		
Moderate	0(0.0)	0.(0.0)	0.(0.0)		
Severe	3(75.0)	1(25.0)	4(100.0)		
Total	3(75.0)	1(25.0)	4 (100)	0.000	

4.1.5 The Influence of Trimester On Hypertensive Disorders Of Pregnant Women With Malaria Attending Antenatal Clinic at ABSUTH.

The result on the influence of trimester on hypertensive disorders of pregnant women (table 5) with malaria showed that among 2(14.2%) pregnant women with hypertensive disorder in the first trimester, 1(33.3%) had moderate and severe malaria respectively while 12 (85.0%) had non-hypertensive disorder. Among the 12(85.8%) women that had non-hypertensive disorders 2(100.0%) had mild malaria, 7(87.5%) had moderate malaria and 3(66.6%) had severe malaria. A Chi-square analysis showed a significant influence of trimester on hypertensive disorders among of pregnant women with malaria in their first trimester (X^2 = 0.737, P =0.691, d.f=2).

Among pregnant women in the second trimester, 8(23.5%) hypertensive disorders, out of which 1(25.0%) had mild malaria, 2(9.5%) had moderate malaria and 5(55.5%) had severe malaria. Also among 26(76.5%) women with non hypertensive disorder, 3(75.0%) had mild malaria, 19(90.5%) had moderate malaria and 4(44.5%) had severe malaria. A Chi-square analysis showed a significant (X^2 = 8.313, P = 0.015, d.f =2) influence of trimester on hypertensive disorders among pregnant women with malaria in the second trimester.

Among pregnant women in the third trimester, 9(75.0%) had hypertensive disorders, out of which 2(100.0%) had mild malaria, 3(75.0%) had moderate malaria and 4(66.7%) had severe malaria. However 3(25.0%) had non-hypertensive disorder but with moderate 1(25.0%) malaria and severe 2(33.3%) malaria respectively. A chi-square analysis showed a significant influence of trimester on hypertensive disorder among pregnant women with malaria in the third trimester ($X^2 = 0.890$, P =0.640, d.f= 2).

Table 4: The Influence of Trimester on Hypertensive Disorders of Pregnant Women with Malaria Attending Antenatal Clinic at ABSUTH.

Trimester/ Malaria parasite Density	Hypertensive disorders	Non- Hypertensive Disorders	Total	X^2	P- value
First Trimester					
Mild	0(0.0)	2(100.0)	2(14.2)		
Moderate	1(12.5)	7(87.5)	8(57.2)		
Severe	1(33.3)	3(66.7)	4(25.6)		
Total	2(14.2)	12 (85.0)	14(100.0)	0.737	8.691
Second Trimester					
Mild	1 (25.0)	3(75.0)	4(11.7)		
Moderate	2(9.5)	19(90.5)	21(61.7)		
Severe	5(55.5)	4(44.5)	9(26.6)		
Total	8(23.5)	26(76.5)	34(100.0)	8.313	0.015
Third Trimester					
Mild	2(100.0)	0(0.0)	2(16.7)		
Moderate	3(75.0)	1(25.0)	4(33.3)		
Severe	4(66.7)	2(33.3)	6(50.0)		
Total	9(75.0)	3(25.0)	12(100.0)	0.890	0.690

4.1.6. The Influence of Parity on Hypertensive Disorder of Pregnant Women with Malaria attending antenatal clinic at ABSUTH.

The result on the influence of parity on hypertensive disorder of pregnant women showed that among 9(56.3) women with hypertensive disorder, 1(25.0%) had mild malaria, 4(50%) had moderate and 4(100%) had severe malaria. Also among 7(43.7%) pregnant women with non-hypertensive disorder, 3(75.0%) had mild malaria and 4(50%) had moderate malaria. A chi square analysis showed a significant influence of parity on hypertensive disorder of pregnant with malaria (X^2=4.82, P = 0.089, d.f = 2) among primiparous women.

Among secundiparous women, 6(50.0%) had hypertensive disorders out of which 1(50.0%) had mild malaria, 1(16.7%) had moderate malaria and 4(100.0%) had severe malaria. Also among 6(50.0%) pregnant women with non-hypertensive disorder, 1(50%) had mild malaria and 5(83.3%) moderate malaria. A Chi-square analysis showed a significant influence of parity on hypertensive disorder of pregnant women with malaria (X^2 =1.32, P-value = 0.517, d.f =2).

Also among 4(12.5%) multiparous women with hypertensive disorders were 1(50.0%) mild malaria, 1(5.3%) moderate malaria and 2(18.2%) severe malaria. Also 28(87.5%) had non-hypertensive disorder among them were 1(50.0%) mild malaria, 18(94.7%) had moderate malaria and 9(18.2%) had severe malaria. A Chi-

square analysis showed a significant influence of parity on hypertensive disorders of pregnant women with malaria ($X^2 = 4.78$, $P = 0.093$, $d.f = 2$).

Table 5: The Influence of Parity on Hypertensive Disorders of Pregnant Women with Malaria Attending Antenatal Clinic at ABSUTH.

Parity/ Malaria parasite Density	Hypertensive disorders	Non- Hypertensive Disorders	Total	X^2	P- value
Primiparous					
Mild	1(25.0)	3(75.0)	4(25.0)		
Moderate	4(50.0)	4(50.0)	8(50.0)		
Severe	4(100.0)	0(0.0)	4(25.0)		
Total	9(56.8)	7(43.7)	16(100.0)	4.82	0.089
Secundiparous					
Mild	1 (50.0)	1(50.0)	2(16.7)		
Moderate	1(16.7)	5(83.3)	6(50.0)		
Severe	4(100.0)	0(0.0)	4(33.3)		
Total	6(50.0)	6(50.0)	12(100.0)	1.32	0.517
Multiparous					
Mild	1(50.0)	1(50.0)	2(6.2)		
Moderate	1(53.0)	18(94.7)	17(59.4)		
Severe	2(18.2)	9(81.8)	11(34.4)		
Total	4(12.5)	28(87.5)	32(100.0)	4.75	0.093

4.2 Discussion

4.2.1. Prevalence of Hypertensive Disorders among Pregnant Women Attending Antenatal Clinic at ABSUTH

Table 2 shows the prevalence of hypertensive disorders among the study population. Gestational hypertension was found to be the predominant hypertensive disorder. In this study, 6.7% of the pregnant women had preeclampsia. This is in line with 6% prevalence of preeclampsia, chronic hypertension with superimposed preeclampsia as was recorded in Sokoto (Singh, Ahmed, Egondu and Ikechukwu, 2014). The prevalence of preeclampsia in this study also agrees with the 5-10% of other studies carried out in Lagos, Ibadan, Calabar, Kano and other parts of the world. (Emuveyan 1995; Itam and Ekabule, 2002; Myers and Baxer, 2002; Audu and Ekele, 2002; Omole-Ohonsi and Shehu, 2001; Hayman, 2003).

It is worthy of note to state that no case of eclampsia was recorded. This occurrence maybe attributed to the extremity that is associated with the disease which usually results to death of the pregnant woman. Furthermore, it could indicate the provision of improved antenatal care coverage which involves close monitoring and early intervention. This affirms that measures which promote awareness and enlightenment of the importance of early booking for antenatal care

services will contribute to prevention of progression of hypertensive disorders. This will thereby reduce the incidence of maternal morbidity, mortality and fetal outcomes associated with hypertensive disorders of pregnancies.

4.2.2 Relationship between Hypertensive Disorders of Pregnancy and Malaria Density among Pregnant Women Attending ABSUTH

Findings from the study indicated that the pregnant women with moderate parasite density had the highest prevalence of malaria with 33in which 5 had gestational hypertension, one (1) had pre-eclampsia and 27 had non hypertensive disorder.

Furthermore, 19 had severe parasite density with 7 having gestational hypertension, 3 had pre-eclampsia and 9 had non hypertensive disorder.

The Chi-square (X^2cal) statistical analysis shows X^2value of 10.40 with P-value = 0.034, which is significant since P value < 0.05. Therefore, the null (H_O) hypothesis which states that there is no significant relationship between malaria and hypertensive disorders among pregnant women obtaining antenatal care at ABSUTH is rejected while the alternate (HΛ) hypothesis which states that there is a significant relationship between malaria and hypertensive disorders among pregnant women obtaining antenatal care at ABSUTH is accepted. Thus, this finding from this study infers that there is significant relationship between malaria parasite density and hypertensive disorders among pregnant women attending antenatal clinic in ABSUTH, Aba.

Finding from this study confirms the study carried out by Mruma *et al.* (2018) which reported that malaria parasitemia is associated with gestational hypertension and that malaria may have a constant effect on gestational hypertension across different African population. Also, the finding from this study is in consonance with the study of Ndao *et al* (2009) which found a relationship between placental malaria and gestational hypertension in pregnant women living in a malaria hypo-endemic setting in Senegal

4.2.3. Influence of Maternal Age on the Hypertensive Disorders of Pregnant Women with Malaria attending Antenatal Clinic at ABSUTH, Aba.

In this study, there was a significant relationship between maternal age and the occurrence of hypertensive disorders in pregnant women with malaria. Ordinarily, age has been implicated to be a risk factor for developing malaria and hypertensive disorders especially among primigravids and young pregnant women. (Marielle et al, 2003 : Adam, Khamis and Elhassan, 2003 : Agomo and Oyibo, 2013 : Kumari, Dash and Singh, 2006 : Zibaeenazhad et al, 2010 : Sheraz et al, 2006 : Sajith et al, 2014 : Duckitt et al, 2005)

Agehas an important influence on the incidence of HDP among pregnant women (Kumari, Dash and Singh, 2006). A report by Zibaeenazhad *et al* 2010, showed that young pregnant women and pregnant women over 30 years especially primigravid ones have an increased chance of hypertension. Sheraz *et al*, 2006,

reported the same finding and stated that preeclampsia is more frequent in patients younger than 21 years and patients older than 35 years. In the present study, preeclampsia was found among pregnant women between 26 – 44 yrs. The finding from this study is not in consonance with the study carried out by Adam *et al.* (2011) which reported that there is no significant association between maternal age and malaria parasitemia.

Gestational hypertension was the predominant hypertensive disorder seen among the pregnant women in all maternal age groups in the present study. Furthermore, it was recorded more among pregnant women with within 26 – 44 years and was seen in all cases of malaria unlike preeclampsia, which was seen among women with moderate and severe cases of malaria only. Lou et al, (2020) reported that the risk of gestational hypertension and preeclampsia were associated with advanced maternal age. The association of malaria with maternal age in the study is not clear and the distribution of malaria cases among different maternal age groups may have occurred by chance

4.2.4 Influence of Trimester on the Hypertensive Disorders of Pregnant Women with Malaria attending Antenatal Clinic at ABSUTH, Aba.

Gestational hypertension was the predominant hypertensive disorder observed among the three trimester groups in this study. Gestational hypertension was recorded more among pregnant women in their third trimester and also among

pregnant women with severe malaria across the three trimesters as well as among women with severe malaria across the trimesters. This is an indication that severe malaria maybe associated to gestational hypertension especially during the last trimester of pregnancy. This finding is in line with the study of Mruma, McQuillan and Norrie (2020) which reported a significant association of malaria with gestational hypertension at different trimesters in different parts of Africa. Furthermore, Ndao et al, (2009) found a relation between placental malaria and gestational hypertension in pregnant women living in a malaria- hyperendemic setting in Senegal and have suggested that malaria during pregnancy maybe an independent risk factor for hypertensive disorders. The present study recorded one case of preeclampsia in the first trimester which may have occurred by chance. Also, three cases of preeclampsia were recorded in the study, all with severe cases of malaria. This is consistent with the previous study in Central Sudan, where women who had placental malaria infections in their second trimester were twice at high risk of preeclampsia when compared with women without placental malaria infection.

4.2.5. Influence of Parity on Hypertensive Disorders of Pregnant Women with Malaria attending Antenatal clinic at ABSUTH, Aba

The present study showed a significant association between parity and hypertensive disorders of pregnancy. Among primiparous women, there are more

cases of gestational hypertension and preeclampsia than secundiparous and multiparous groups. Studies have shown that prevalence of HDPs decline with increase parity (Singh, Ahmed, Egondu and Ikechukwu,2014). Primiparous women have been reported in previous studies to be at risk of HDPs, especially gestational hypertension and preeclampsia. (Luo et al, 2007; Meazaw, Chojenta, Muluneh, and Loxton, 2020; Watkins and Saldanha, 2019). This is in line with the results of the present study. The distribution of malaria parasitemia among parity showed that malaria affected all the women in the three parity groups in this study. Malaria can have adverse effects on both mother and fetus including; maternal anemia, fetal loss, premature delivery, intrauterine growth retardation and delivery of low birth weight infants (CDC, 2018). Severe malaria was recorded among primiparous and secundiparous women in the study. Some studies have reported that primigravid women experience the most severe consequences of pregnancy associated malaria (Meuris et al, 1993; Shulman et al, 1996).

CHAPTER FIVE

CONCLUSION AND RECOMMENDATIONS

5.1 Conclusion

The present study showed that malaria affects the blood pressure of pregnant women. This results to gestational hypertension, pre-eclampsia or eclampsia in worse case scenarios. Also these hypertensive disorders of pregnancies can be influenced by maternal age, trimester and parity. It is therefore necessary that pregnant women visit antenatal clinics at the early stage of their pregnancy to ensure that malaria is immediately treated if they are found to have malaria, also to ensure that their blood pressure is normal at all stages of their pregnancy.

5.2. Recommendations

Considering the outcome of this study, the following recommendations were made:

i. There should be an increased awareness for pregnant women to be enlightened on the importance of early antenatal visits, as this step will greatly help in detecting risks factors for high blood pressure and proteinuria in pregnant women less than eight weeks.

ii. Pregnant women should endeavor to practice more effective ways of preventing and controlling malaria infection either by prescribed treatments or vector control.

iii. Quality of antenatal care services should be further improved and extended to rural areas and provision of subsidized antenatal care services by health care providers is imperative.

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APPENDIX A

SAMPLE SIZE DETERMINATION

The study population was 60 pregnant women drawn from an initial population of 71 pregnant women, attending antenatal clinic at Abia State University Teaching Hospital Aba in the month of March, 2018.

Thus: $n = \frac{N}{1+Ne^2}$

Where N= Total Population

e= margin error (0.05).

n= sample size.

$$= \frac{71}{1+71(0.0025)} = 60.2 \cong 60$$

APPENDIX B

INSTRUMENT FOR DATA COLLECTION

A QUESTIONNAIRE ON "HYPERTENSIVE DISORDERS AMONG PREGNANT WOMEN WITH MALARIA ATTENDING ABSUTH, ABA, ABIA STATE."

Socio – Obstetrics Characteristics

Name: ……..

Occupation: …….

Maternal Age: ……

Gestational Age (Trimester): 1st ……. 2nd …… 3rd ……

Parity (No of Children): ……

Previous History of Hypertension: Yes/No.

TO BE FILLED BY RESEARCHER

Malaria Parasite Density: Mild: ……...

Moderate: ……

Severe: …….

Blood pressure reading: ……

Proteinuria: ……

APPENDIX C

CO-EFFICIENT CO – RELATION RELIABILITY OF INSTRUMENT

Marks of responses From ABSUTH Aba (x)	Marks of Responses General Hospital Aba (d)	Rank ($x = d_x$)	Rank ($y = d_y$)	$d = d_x - d_y$	d^2
75	78	2	1	1	1
50	65	3.5	3	+0.5	0.25
50	60	3.5	4	-0.5	0.25
45	50	5	5	0	0
80	70	1	2	-1	1
					2.50

Therefore using the Spearman's Rank Co-relation

We have = $r_s = 1 - \frac{6 \sum_d 2}{n(n^2-1)}$

n = 5, $n^2 = 25$, $\sum_d 2 = 2.5$

Putting these values in the formula above

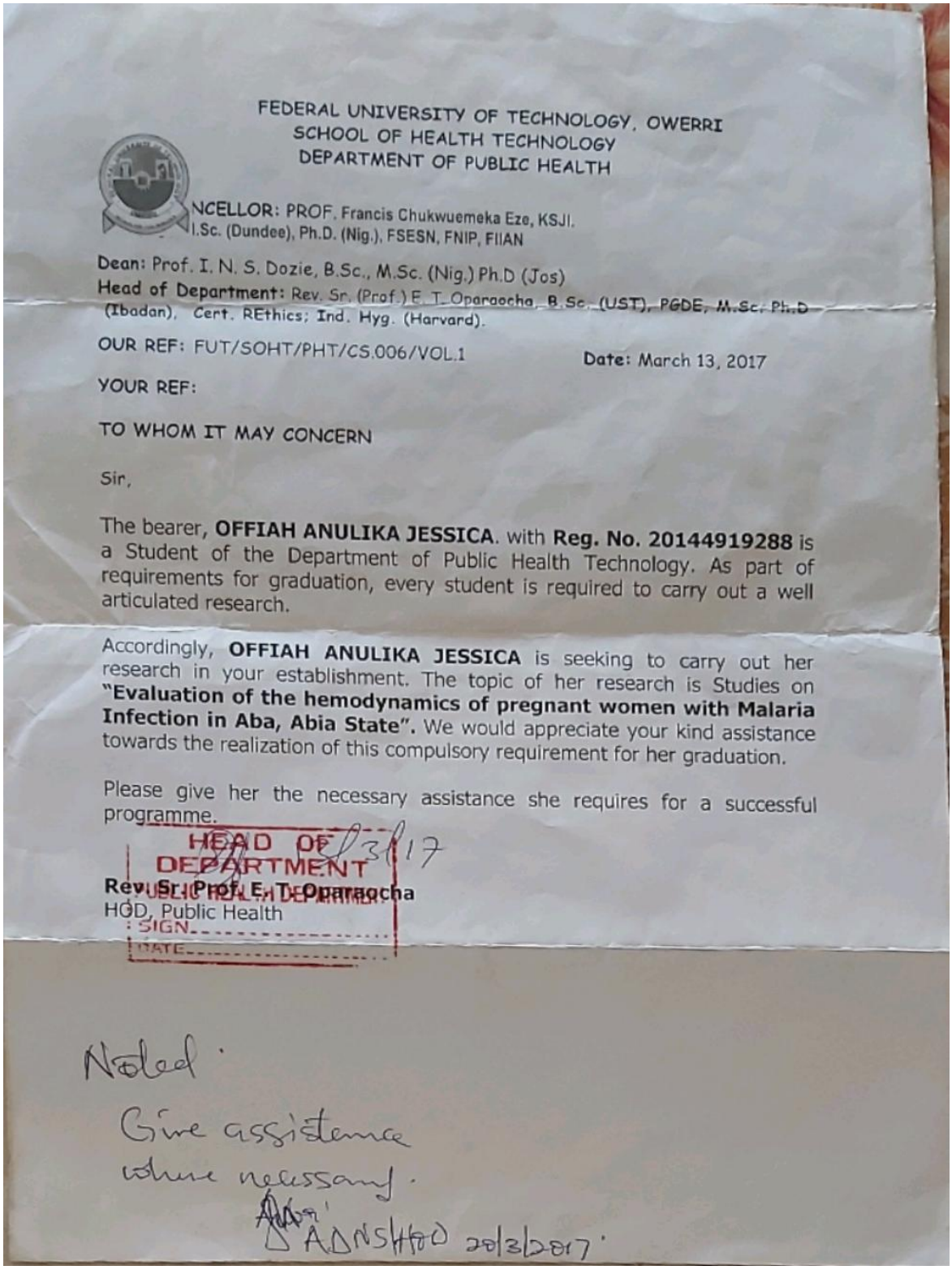
$r_s = 1 - \frac{6\ (2.5)}{5(25-1)} = 0.875 \approx 0.88$

A co-relation of 0.88 was obtained.

APPENDIX D

INFORMED

CONSENT



FEDERAL UNIVERSITY OF TECHNOLOGY, OWERRI
SCHOOL OF HEALTH TECHNOLOGY
DEPARTMENT OF PUBLIC HEALTH

NCELLOR: PROF. Francis Chukwuemeka Eze, KSJI.
I.Sc. (Dundee), Ph.D. (Nig.), FSESN, FNIP, FIIAN

Dean: Prof. I. N. S. Dozie, B.Sc., M.Sc. (Nig.) Ph.D (Jos)
Head of Department: Rev. Sr. (Prof.) E. T. Oparaocha, B.Sc. (UST), PGDE, M.Sc. Ph.D (Ibadan), Cert. REthics; Ind. Hyg. (Harvard).

OUR REF: FUT/SOHT/PHT/CS.006/VOL.1 Date: March 13, 2017

YOUR REF:

TO WHOM IT MAY CONCERN

Sir,

The bearer, **OFFIAH ANULIKA JESSICA**. with **Reg. No. 20144919288** is a Student of the Department of Public Health Technology. As part of requirements for graduation, every student is required to carry out a well articulated research.

Accordingly, **OFFIAH ANULIKA JESSICA** is seeking to carry out her research in your establishment. The topic of her research is Studies on **"Evaluation of the hemodynamics of pregnant women with Malaria Infection in Aba, Abia State".** We would appreciate your kind assistance towards the realization of this compulsory requirement for her graduation.

Please give her the necessary assistance she requires for a successful programme.

HEAD OF DEPARTMENT
PUBLIC HEALTH DEPARTMENT
SIGN
DATE

Rev. Sr. Prof. E. T. Oparaocha
HOD, Public Health

Noted.

Give assistance where necessary.

ADNSH&D 20/3/2017.

APPENDIX E

ETHICAL APPROVAL

ABIA STATE UNIVERSITY TEACHING HOSPITAL

P.M.B. 7004 ABA

Chairman Board of Management
DR. KINGSLEY N. ENWEREMADU
M.B.B.S. FCBE&T, FAGP, FICA, DMPN

Director of Administration/Secretary to the Board
MR. MODESTUS NWAOBASI
Bsc (Sociology)

Chief Medical Director
PROF. CHUKS KAMANU
MBBCh (Cal), FWACS, F.I.C.S.
Dipl Reproductive Medicine and Embryology (Germany)
+2347030857540

Chairman Medical Advisory Committee
ASSOC. PROF. ASSUMPTA CHAPP JUMBO
MBBS (NIG), FWACPaed

Our Ref: ABSUTH/MAC/117/VOL.I/23

Your Ref:

Website: www.absuthng.org
E-mail: info@absuthng.org, ict@absuthng.org
cmd@absuthng.org

Date: 11/04/2018

Jessica Offiah
Department of Public Health
Federal University of Technology
Owerri, Imo State.

Dear Madam,

RE: ETHICAL APPROVAL OF RESEARCH PROJECT

Please your research project titled **"ASSESSMENT OF HIGH BLOOD-PRESSURE RELATED HEALTH RISK ASSOCIATED WITH MALARIA AMONG PREGNANT WOMEN IN ABA, ABIA STATE"** has been granted ethical approval.

However, you are not permitted to draw patients' blood samples for analysis at a laboratory facility outside Abia State University teaching Hospital. You are required to comply with the Helsmki declaration on biomedical research involving human subjects.

Thank you.

Sincerely,

ABIA STATE UNIVERSITY TEACHING HOSPITAL

DR. CHIGBU B. 12/04/18
FICS, FWACS
Chairman Ethics Committee
ABA