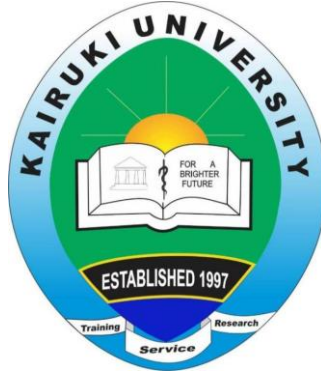


KAIRUKI UNIVERSITY



SCHOOL OF MEDICINE

DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY

RESEARCH REPORT

TITLE: ASSOCIATION OF MID-TRIMESTER SERUM β -hCG AND LIPID PROFILE WITH PRE-ECLAMPSIA IN HIGH-RISK PREGNANT WOMEN AT SELECTED HEALTH FACILITIES, UNGUJA.

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A Dissertation submitted in partial fulfillment of the requirements for Masters Degree in Obstetrics and Gynaecology at Kairuki University, 2025.

CERTIFICATION

It is hereby certified that the undersigned has read and hereby recommends acceptance by Kairuki University, a dissertation titled, "ASSOCIATION OF MID-TRIMESTER SERUM β -hCG AND LIPID PROFILE WITH PREECLAMPSIA IN HIGH-RISK PREGNANT WOMEN AT SELECTED HEALTH FACILITIES, UNGUJA" in partial fulfillment of the requirements for the degree of Master of Medicine in Obstetrics and Gynaecology of Kairuki University.


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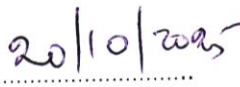
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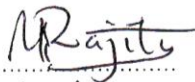
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DEDICATION

This work is dedicated to my supervisor Dr. Chiduo and my family who have helped me throughout my studying time.

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ABBREVIATIONS

KU	Kairuki University
HDP	Hypertensive disorders in pregnancy
BP	Blood Pressure
PB	Preterm Birth
DBP	Diastolic Blood Pressure
hCG	Human Chorionic Gonadotropin
TC	Total Cholesterol
HDL	High Density Lipoprotein
TG	Triglycerides
LDL	Low Density Lipoprotein
VLDL	Very Low Density Lipoprotein
LMP	Last Menstrual Period
PE	Pre-eclampsia
GA	Gestation Age
ANC	Antenatal Care
EMONC	Ethiopian National Emergency Obstetric and Newborn Care
ACOG	American College of Obstetrics and Gynaecology

OPERATIONAL DEFINITIONS

Pre-eclampsia:Pre-eclampsia is a multisystem progressive disorder characterized by the new onset of hypertension and proteinuria or the new onset of hypertension plus significant end-organ dysfunction with or without proteinuria, typically presenting after 20 weeks of gestation or postpartum (1).

Gestational Hypertension: New onset of systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg on at least 2 occasions at least 4 hours apart after 20 weeks of gestation in a previously normotensive individual(1).

Patients with systolic blood pressure ≥ 160 mmHg and/or diastolic blood pressure ≥ 110 mmHg should have blood pressure confirmed within a short interval (minutes) to facilitate timely administration of antihypertensive therapy(1,2).

Proteinuria: Proteinuria (≥ 300 mg per 24-hour urine collection, or protein:creatinine ratio ≥ 0.3 , or urinedipstick reading $\geq 2+$, if other quantitative methods are not available.

It is an important diagnostic criterion for pre-eclampsia and indicates kidney dysfunction. In a patient with new-onset hypertension without proteinuria, the diagnosis of preeclampsia can still be made if any features of severe disease are present(1,2).

Gestational Age: The duration of the pregnancy, measured from the first day of the last menstrual period (LMP) or estimated using ultrasound measurements. It is expressed in weeks and is essential for determining the timing of various prenatal assessments and interventions(3,4).

High-Risk Pregnancy: A pregnancy with increased risk for adverse maternal or fetal outcomes due to preexisting medical conditions (such as chronic hypertension or

diabetes), advanced maternal age, multiple gestation (e.g., twins), previous history of pre-eclampsia, or other factors that may predispose the woman to complications(4).

ABSTRACT

Background

Preeclampsia (PE) remains a leading cause of maternal and perinatal morbidity and mortality, with emerging evidence suggesting a role for biochemical markers such as serum β -human chorionic gonadotropin (β -hCG) and lipid abnormalities in its pathogenesis.

Objective: To investigate the association between mid-second trimester serum β -hCG levels, lipid profile alterations, and the subsequent development of preeclampsia.

Methods: A prospective cohort study was conducted among 325 pregnant women in their second trimester. Serum β -hCG and lipid profile were measured. Descriptive statistics were applied to evaluate variations in β -hCG and lipid levels. Subsequently, odds ratios (ORs) at 95% of confidence interval were computed using SPSS software version 25.0., to determine the strength of association between elevated β -hCG and lipid levels and the risk of developing preeclampsia.

Results: Elevated serum β -hCG levels during the mid-trimester were observed in 15.1% (n=49) of participants. Lipid abnormalities were prevalent, with elevated TC, LDL, and TG levels identified in 25.5 % (n=83), 30.5% (n=99), and 41.1 % (n=153) of participants, respectively, while 17.8% (n=58) had abnormally low HDL. Elevated β -hCG was associated with a 2.9 fold increased risk of developing preeclampsia by the end of the second trimester. Similarly, high LDL and TG levels were significantly ($p < 0.05$) associated with 7.1-fold and 6.4 fold increased risks of preeclampsia, respectively. Additionally, total cholesterol, low HDL, high LDL, high TG, and elevated TC were significantly ($p < 0.05$) associated with increased PE risk in the third trimester, with odds

ratios of 2.8, 16, 9.8 and 8.2 respectively. Elevated HDL levels, however, were not significantly associated with preeclampsia, suggesting a potential protective role.

Conclusion: Elevated mid-trimester serum β -hCG and dyslipidemia, particularly low HDL and high levels of LDL, TG, and TC, are strongly associated with increased risk of preeclampsia. These biomarkers may serve as useful predictors for early identification and risk stratification of PE, warranting further investigations in clinical screening protocols.

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background

Pre-eclampsia is hypertensive disorders in pregnancy that is characterized by persistent elevation of blood pressures above 140mmHg of systolic pressure or diastolic pressure above 90 mmHg and proteinuria or the new onset of hypertension plus significant end-organ dysfunction with or without proteinuria, typically presenting after 20 weeks of gestation or postpartum(1).

Pre-eclampsia constitute the most prevalent form of hypertensive disorder in pregnancy affecting 2-8% of pregnancies globally and constitute the leading causes of maternal and neonatal morbidity and mortality across the world, with developing countries bearing the brunt of this burden(2).

In developed countries a rate ranged between 1.8 to 16.7% is reported , while in low-income countries, the rate ranges from 2.2% to 6%(7,9). In Ethiopia, pre-eclampsia is the cause of 16% of direct maternal mortality and 10% of all maternal mortality , according to Ethiopian National Emergency Obstetric and Newborn Care (EMONC)(5).

In Tanzania, the prevalence of pre-eclampsia is 9% in Zanzibar and 4.2% in northern Tanzania(6).In addition, it is the second leading cause of maternal death in Tanzania and account for more than 19 % of maternal death(6).

Pre-eclampsia's cause still unknown. The majority of research, however, points to insufficient trophoblast penetration into maternal spiral arteries as the primary pathogenic mechanism(7). This would lead to reduced placental blood flow, trophoblast

death, and the release of pro-inflammatory cytokines(7).Recent studies utilizing placentas and maternal blood from preeclamptic pregnant mothers have suggested that the placenta may be the pathophysiological source of pre-eclampsia. Thus, it would be very beneficial to precisely predict pre-eclampsia by finding early biomarkers of placental malfunction so that interventions can be implemented timely in order to lower the occurrence of PE.

Thus , the predictive determinants of pre-eclampsia have been assessed using a number of biochemical indicators of placental malfunction prior to the onset of clinical signs(8). Human chorionic gonadotropin (β -hCG) has been linked to preterm birth (PB) according to several research , and screening for PE at 8–14 weeks gestational age has been suggested using β -hCG as a blood marker(8).

Although, inconsistency exist to the reliability on elevated serum beta HCG in second trimester to predict pre-eclampsia as several studies reported controversies result. In women with PE, some authors found that blood β -hCG levels had a substantial predictive value, whereas many other studies that examined the relationship between serum β -hCG levels and PE found no statistically significant correlation(10,11).

On the other hand, serum lipid was reported to be determinant of pre-eclampsia in high risk pregnant mother as observed in a study conducted by Salma and colleagues where dyslipidemia together with elevated BMI was observed to predict pre-eclampsia among 70 pregnant mother attending Sheba Hospital Kaligonj in Bangladesh(11). Similar findings were found in the study of Olalere and colleagues, among 240 pregnant mother attending Lagos teaching hospital in Nigeria where strong correlation between hyperlipidemia and preeclampsia was observed(12).

There is still scanty data on the association between β -hCG, serum lipid and PE in low income countries, Tanzania include.

1.2 Statement of the problem

Pre-eclampsia is a significant obstetric complication that contribute to increase morbidity and mortality in pregnant mothers and their neonates to the extent that it is directly responsible for 70,000 maternal fatalities globally each year, making it the second most common cause of direct maternal deaths(1,2).InTanzania, studies revealed that about 12 % of severe maternal outcomes were reported to be attributed to pre-eclampsia(6).

Pre-eclampsia remain a multifactorial disease .Nevertheless, serum biomarkers like serum β -hCG can contribute to detect pre-eclampsia early because of raised β -hCG that is associated with vasoconstriction and poor angiogenesis that lead to high blood pressure in PE patients(7,8).On the other hand, because hyperlipidemia causes endothelial dysfunction, serum lipids have also been shown to be a reliable serum biomarker that can initially predict PE(7,8).However, the reliability of these biomarkers remains controversial, with some authors claiming associations and others citing conflicting findings.

In addition, the reliability of serum β -hCG and lipid to predict pre-eclampsia remain understudy in low resource countries, Tanzania include.

This study aimed to assess the correlation between serum β -hCG and lipid levels with pre-eclampsia among mid-trimester pregnant mothers attending at selected health facilities in Zanzibar.

1.3 Rationale of the study

In resource-limited settings such as Zanzibar, there is a notable lack of research of potential of mid-trimester serum β -hCG and lipid profile as predictive markers for pre-eclampsia in high-risk pregnancies.

The results of this study will enhance timely management of patients who have a high risk of developing pre-eclampsia by offering a primary preventive measure and a more reliable screening and monitoring tool. The control burden associated with pre-eclampsia will also be aided by identifying the various factors that influence changes in serum β -hCG and lipid in high-risk pre-eclamptic pregnant women.

In addition, the results of this study will serve as a basis for further researchers in this area.

1.4 Research questions

1. What is the level of serum β -hCG among mid trimester high-risk pregnancies at Ijitimai district hospital, Fuoni and Mpendae health centers in Zanzibar?
2. What is the level of serum lipid among mid trimester high risk pregnant mothers?
3. What is the association between mid-trimester serum β -hCG and lipid levels with subsequent development of pre-eclampsia among high-risk pregnancies?

1.5 Objectives

1.5.1 Broad objective

To determine the relationship between mid-trimester serum β -hCG and lipid profile with pre-eclampsia among high-risk pregnancies at selected health facilities in Zanzibar.

1.5.2 Specific objectives

1. To determine the level of serum β -hCG among mid trimester high-risk pregnancies to preeclampsia.
2. To evaluate the level of serum lipid among mid trimester high risk pregnancies to preeclampsia.
3. To assess the association between mid-trimester serum β -hCG levels and serum lipid with subsequent development of pre-eclampsia among high-risk pregnancies.

1.6 Conceptual Framework

Pre-eclampsia is a hypertensive disorder characterized by high blood pressure, $\geq 140/90$ mmHg, proteinuria and/or multi-organ involvement which often develops after 20 weeks of gestation. High-risk pregnant women for developing pre-eclampsia include those with history of chronic or pre-pregnant hypertension, diabetes, previous pre-eclampsia, renal disease and advanced maternal age.

Elevated serum biomarkers specifically β -hCG and lipids correlate with higher risk of pre-eclampsia due to trophoblastic dysfunction. Serum β -hCG produced by placenta is essential for trophoblastic invasion and maintenance of pregnancy. Abnormal levels indicate trophoblastic dysfunction, which is a precursor to pre-eclampsia.

Changes in triglycerides, LDL, HDL and total cholesterol are common in early pregnancy. Elevated triglycerides, total cholesterol and LDL along with reduced HDL, contribute to endothelial dysfunction and oxidative stress leading to increased blood pressure and hence the development of pre-eclampsia.

INDEPENDENT VARIABLE

DEPENDENT VARIABLE

1. Medical/Obstetric factors.

- Chronic hypertension
- Previous history of PE.
- History of diabetes .
- History of renal diseases.
- Advanced maternal age.

2. Serum biomarkers

- Serum β -hCG
- Serum lipid



PRE ECLAMPSIA

CHAPTER TWO

2.0 LITTERATURE REVIEW

2.1 Level of serum beta hCG among mid trimester high-risk pregnancies.

Human chorionic gonadotropin (hCG) is produced by the placenta in a variety of forms, including hyperglycosylated hCG (hCG-h), which is the predominant form of hCG in the early stages of pregnancy and peak concentrations attained during the first six weeks of gestation(13). The human chorionic gonadotropin (hCG) is a glycoprotein composed of two non covalently linked subunits, α and β , and is produced by syncytiotrophoblast cells of the placenta(14). The production of hCG is made by placenta cells, it is generally accepted that cytotrophoblasts make very little hCG, whereas syncytiotrophoblasts produce large amount of hCG(13,14). Elevated hCG-h concentrations have been linked to enhance cytotrophoblast activity and have been found in prenatal trophoblastic disorders(13,14). Maternal serum hCG reaches its maximum at 8–10 weeks of pregnancy, after which it decreases to a plateau at 18–20 weeks(13,14). There are three possible origins of the free β -subunit: direct trophoblast cell production, the dissociation of hCG into free α - and free β -subunits, and nicking of the hCG molecule by neutrophil or macrophage enzymes(13,14). Only approximately 0.3–4% of total hCG is present in the form of free β -hCG circulating in maternal serum. There are several factors which have led to rise of serum β -hCG during pregnancy and the common reported include neoplastic trophoblastic conditions like molar pregnancies as well as twin(15).

A study carried out in India on expectant mothers who were at high risk of developing pre-eclampsia revealed that higher blood β -hCG at 14–18 weeks, with a cutoff of 67750 mIU/ml, can predict pregnancy-induced hypertension with a sensitivity and specificity of 51.85% and 88.54%, respectively(16). Predicting pregnancy-induced hypertension and preeclampsia was also found to be possible with blood β -hCG levels above 23180 mIU/ml at 24–28 weeks, exhibiting a 62.96% sensitivity and 72.61% specificity(16). Similar results were reported by Ritu Yadav and colleagues among pregnant mother attending antenatal consultation in their second trimester in India where high level of serum β -hCG was significantly elevated in women with high risk of PE(17).

The increase in serum β -hCG in pregnant mother with PE can be explained by the fact that vasoconstriction and impaired angiogenesis cause high blood pressure in women with PE. This, in turn, causes hypoxia and trophoblastic cell hyperplasia, which result in placental hormone hypersecretion and high levels of circulating β -hCG(14).

Furthermore, Sayran and colleagues' study of 125 pregnant women admitted to the labor ward of the Maternity Teaching Hospital in Erbil City, Kurdistan, Iraq, found that the rise in serum β -hCG was associated with the severity of preeclampsia. The mean β -hCG concentration for pregnant mothers with severe preeclampsia was 37,520.56 mIU/mL, while 16,487 mIU/mL for those with mild PE, and 11,699.82 mIU/mL for those with normotension(18). Similar findings were reported by Reham Elazab and colleagues among pregnant mother attending Mansura hospital in Egypt where they observed strong correlation between rise of serum beta HCG and occurrence of PE. In

addition they found that rise of serum β -hCG was strong predictor of severity of PE(19).

Serum β -hCG level remains understudy in pregnant mother in low income countries, Tanzania include and yet hypertensive disorders in pregnant mother still prevalent in those regions.

2.2 Levels of serum lipids among mid trimester high-risk pregnancies.

Serum lipid metabolism changes during different physiological change of pregnancy. It is said that the levels of TC, HDL-C, TG and LDL-C increase significantly after the first trimester. Up to 25–50% more TC, 60% more LDL, and 200% more TG are present(20). Triglyceride levels double and plasma cholesterol levels rise by 50% by the end of pregnancy compared to pre-pregnancy levels(26). Seldom do total cholesterol levels surpass 250 mg/dl, and the ratio of total cholesterol to HDL rises with each trimester of a typical pregnancy, contingent on body weight(21). Placental steroid synthesis requires cholesterol, and elevated levels of cholesterol during pregnancy encourage the formation of fetal membranes and the build-up of maternal fat reserves during the first two thirds of pregnancy(20). The first and second trimesters of a typical pregnancy are anabolic states for the women, marked by elevated progesterone levels(21). This causes dietary fat intake to rise, which in turn causes hepatic lipogenesis and chylomicron production, which in turn causes fat deposition and maternal hyperlipidemia(21).

A shift to a catabolic state with high-estrogen driven lipolysis during the third trimester causes an increase in the synthesis of VLDL. Like the other lipid fractions, lipoprotein a levels rise with gestational age throughout pregnancy and return to pre-pregnancy

levels six months after delivery(20). Lipoprotein is a known cardiovascular risk factor. While the elevated triglyceride levels rapidly normalize post-pregnancy, the smaller LDL particles remain in circulation and are associated with increased cardiovascular risk in women(20).

On the other hand, altered lipid profile has been shown as etiological factor of endothelial dysfunction which is considered as an important factor for the mechanism of increased blood pressure during pregnancy(22,23). This may be because increasing serum cholesterol can cause vascular oxidative stress and reduce nitric oxide bioavailability, both of which can lead to a rise in blood pressure by decreasing vasodilatation(22,23). Several authors have assessed the contribution of dyslipidemia in preeclamptic pregnant women. A case-control study was conducted at Sheba Hospital Kaligonj in Bangladesh among 35 normal pregnant and 35 pre-eclampsia women attending an antenatal clinic, where elevated serum lipid levels were significantly associated with pre-eclampsia(11). Similar findings were reported in Netherlands, in a cohort study conducted among 5,692 pregnant mother where elevated serum total-cholesterol, triglycerides, LDL were significantly associated with elevated BP and pre-eclampsia(24). Similar findings were reported in the study of Olalere and colleagues among 240 pregnant women attending Lagos teaching hospital in Nigeria where strong correlation between hyperlipidemia and preeclampsia was observed(12). However, Hillary Hosie and colleagues reported no correlation between dyslipidemia and occurrence of pre-eclampsia in a multi-center study among published review from Europe, African and Latin America(25). The findings of Hillary and colleagues were from retrospective review of medicals record.

2.3 Association between beta HCG levels and subsequent development of pre-eclampsia.

Elevated levels of circulating β -hCG in pregnant mothers have been linked to preterm pre-eclampsia. The rationale for this belief was that pre-eclampsia is likely a trophoblastic condition and high β -hCG is believed to indicate early placental dysfunction or injury. The blastocyst's implantation and maintenance depend on the placenta's early pregnancy synthesis of β -hCG.

In addition, it was observed that connection between abnormal placental invasion and the trophoblast response to hypoxia, may result in the establishment of a hypersecretory condition, and normal pregnancies(14). There may be an additional underlying mechanism contributing to the association of high β -hCG concentration with the increased risk of pre-eclampsia, such as hCG-modulating effects on immune cells which may respond differently depending on β -hCG level (26).

Though the exact origin of the high hormone levels in the bloodstream caused by the placenta is still up for debate, it is generally accepted that the placenta continues to be the primary source of β -hCG in individuals with pre-eclampsia.

There are several studies which have been conducted for searching contribution of high serum β -hCG with pre-eclampsia installation. In India, a study conducted among 50 pregnant women reported rise serum β -hCG among pregnant mother with pre-eclampsia compared to those without pre-eclampsia(16). However, the above studies recruited only pregnant mother on the third trimester between 28 and 37 week.

Pregnant mothers with elevated serum beta β -hCG levels in the second trimester have varying risks of developing hypertensive disorders, depending on whether they are in

the early or late pregnancy. In China, Wang and colleagues reported among women attending Liaocheng People's Hospital maternity ward that Higher circulating β -HCG level was correlated with severe pregnancy-induced hypertension at the end of pregnancy(27).The difference in biomarkers between early and late pregnancy was explained by the theory that early onset disease results from improper placental implantation, while late-onset disease is assumed to be the result of certain medical co-morbidities in the mother(28).

Several publications have documented disagreements regarding the relationship between an increase in serum β -hCG and the later development of pre-eclampsia. A study done on pregnant women attending prenatal clinics in China found no statistically significant difference in the higher levels of serum β -hCG in the second trimester between pregnant women who developed pre-eclampsia and those who did not(29). Similar findings were reported in a case control study conducted by Shin and colleagues in China, where there was no significant difference in rise of serum β -hCG and occurrence of PE(30).

More research is still required to distinguish between the role played by elevated serum β -hCG in the second trimester and other factors in the development of hypertension diseases, particularly in low-income nations where this subject is currently being studied.

On the other hand, serum β -hCG and lipids can be under influence of several factors such as socio-demographic, obstetrical and clinical factors. Among socio-demographic factors which can affect serum β -hCG include, maternal age, specifically extreme age such as younger women and advanced maternal age (>35 years)(31). In young

women, there is faster β -hCG rises in early pregnancy due to generally healthier reproductive systems. Also advanced maternal age (>35 years) may be linked to abnormal hCG trends, miscarriage, or chromosomal anomalies (31). In addition there is contribution of ethnicity and race. Some studies suggest variations in baseline β -hCG levels and rise patterns among different ethnic groups. For example, African American women may have slightly different β -hCG level during early pregnancy(32).

Furthermore, serum lipids have been also influenced by socio-demographic factors such age, social economic status among others. Advanced maternal age (>35 years) is associated with higher total cholesterol and LDL levels which may increase risk of metabolic syndrome, contributing to hyperlipidemia(32,21). Younger mothers typically exhibit more favorable lipid profiles. Low social economic status may contribute to poor diet quality (high in saturated fats, low in fiber)(32,21). Other factor is the limited access to prenatal care which may lead to unmonitored dyslipidemia which contribute to higher rates of obesity and insulin resistance. On the other side higher socioeconomic status is generally associated with a better nutrition and greater health awareness and lifestyle control.

For serum lipid similar factors can affect such gestational age which increase progressively serum lipid, especially in second and third trimesters. Multiple pregnancies can also lead higher maternal lipid levels due to greater metabolic demands. Gestational diabetes may induce elevated triglycerides, LDL, reduced HDL. High body mass index and obesity may strongly associate with hyperlipidemia in pregnancy(33).

CHAPTER THREE

3.0 METHODOLOGY

3.1 Study design

This was a hospital-based prospective cohort study in which pregnant women with high risk of pre-eclampsia in selected health facilities were followed to understand the relationship between the level of serum β -hCG and lipids with occurrence of pre-eclampsia. The quantitative approach was applied by using questionnaires, blood and urine tests in data collection. The patients follow up was done at ANC visit, starting at 20 weeks of gestation then monthly up to 38 weeks. For each visit urine for protein and BP were monitored.

3.2 Study area

This study was conducted at Ijitimai district hospital, Fuoni health centre and Mpendae health centre in Zanzibar. The purposive sampling was employed in selecting these health facilities based on specific criteria including high volume of antenatal care visits by pregnant women, and the laboratory capacity to analyze serum β -hCG and lipid levels.

Ijitimai district Hospital is situated in an urban area, however, serves as a representative health care facility for both urban and rural populations. This allows for the inclusion of pregnant women from various backgrounds, providing insights in pre-eclampsia incidence, risk factors, and management with in different settings. The obstetrics and gynaecology department is served by 5 registrars and 18 midwife nurses. The hospital serves about 1500 deliveries per year.

Fuoni is health centre located at western B District, in Zanzibar. This health care facility mostly serves the pregnant women residing in rural areas of western B District. The study was conducted in obstetrics department, which provides both outpatient and inpatient services. There are about 700 deliveries which are conducted per year. The labour ward has 4 delivery beds with sufficient privacy, 4 beds for observation after delivery, resuscitation unit and a nurse station.

Mpendae health centre is located at urban district, this will purely contribute to understanding PE in urban population. There are 2 medical officer, 3 clinical officers, 15 midwife nurses. The Labor ward has 4 delivery beds with sufficient privacy, 2 beds for observation after delivery, resuscitation unit and a nurse station. There are about 600 deliveries which are conducted per year.

3.3 Study population

All pregnant women with high-risk of pre-eclampsia.

3.4 Sample size

In this study, the sample size was calculated using Daniel formula (1999) :

$$n = \frac{Z^2 P(1-P)}{d^2}$$

where n = sample size, Z = Z statistic for a level of confidence,

P = 0.26 using the findings of the study conducted by Mwashamba and Angelina in Zanzibar where prevalence of pre-eclampsia was 26.4 %(34).

d = precision (in proportion of one; if 5%, d = 0.05).

Z statistic (Z): For the level of confidence of 95%, which is conventional, Z value is 1.96

$$n = \frac{1.96^2 \times 0.26(1-0.26)}{0.05^2} = 295$$

Adding 10% accounted for loss of follow up the estimated sample size was 325.

3.5 Sampling procedure

A simple random sampling technique of high-risk pregnant women in each selected health facility was conducted by using a random number table until the desired sample size of 325 was obtained.

3.5.1 Inclusion criteria

- ✓ Pregnant women attending Antenatal clinic at selected health care facilities.
- ✓ On second trimester, GA between 15 and 20 weeks.
- ✓ Presence of one or more high-risk factors, such as:
 - Advanced maternal age (typically defined as 35 years or older).
 - History of pre-eclampsia in the previous pregnancy.
 - Chronic hypertension.
 - Diabetes mellitus.
 - Renal disease.

3.5.2 Exclusion criteria

- ✓ Pregnant women with known pre-eclampsia at the time of enrollment.
- ✓ Patient having Trophoblastic disease.

3.6 Research participant recruitment

3.6.1 Procedure of recruitment

The study involved sequential enrollment and guidance through the consent process for women who visited the Antenatal Clinic at Ijitimai district hospital, Fuoni health centre and Mpendae health centre.

The pregnant women were firstly recruited at the second trimester of their gestational age between 15 to 20 weeks. Upon arrival, the principal investigator and research assistants who were one medical doctor and two midwives in each health facility promptly provided a structured questionnaire to participants who satisfied the inclusion requirements and consent to participate in the study. The questionnaire covered the following topics: socio-demographic variables like age, marital status, gestational age and obstetric variables like parity, gravity, gestational age, individual pregnancy-related hypertension, and documented prenatal blood pressure in the first trimester. Then venous blood sample was collected from the participants to investigate serum β -hCG and lipid levels.

3.6.2 Determination of serum β -hCG and lipid.

Blood samples for serum β -hCG and lipid were taken during the visit of antenatal period in second semester. A 3ml venous blood was collected into serum separating tubes (SST) and allowed to clot for a while and sent to laboratory for examination. The samples were centrifuged for 4000rpm in 10minutes to get a clear serum for measurement using MAGLUMI 800(China).

The chemiluminescent microparticle immunoassay (CMIA) method was used to estimate serum β -hCG.

Then 0.025ml sample and magnetic microbeads coated reagent with anti-hCG monoclonal antibody were mixed thoroughly and incubated to form immune complexes and then a wash cycle was performed. After addition of ABEI labeled with anti-hCG monoclonal antibody, the complexes bound to monoclonal antibody and incubated to form sandwich complexes. After a precipitation in a magnetic field, decanted the supernatant and then another wash cycle was performed.

Subsequently, the Starter 1+2 were added to initiate chemiluminescent reaction. The light signal was measured by a photomultiplier as a relative light unit (RLU), which is proportional to the concentration of β -hCG present in the sample.

The β -hCG levels were measured in mIU/ml. A serum β -hCG level range between 4,060-165,400 mIU/mL was considered as normal. And a serum β -hCG level above >165,400 mIU/mL was considered as elevated.

Then, the centrifuged sample was used to measure the lipids using SELECTRA PRO M (from ELITech, France).

The sample was mixed with reagents namely HDL, LDL, total cholesterol and triglycerides reagents for investigating the levels of HDL, LDL, total cholesterol and triglycerides respectively. A reaction took place. The concentration of the product of the reaction was determined via the absorbance measurements. As the behaviour of the reagents was well defined, this gave a clear indication for the concentration of a particular substance in the sample.

The lipid levels of triglycerides (mg/dL), high-density lipoprotein cholesterol (HDL-C, mg/dL), low-density lipoprotein cholesterol (LDL-C,mg/dL), and total cholesterol

(mg/dL) were measured using a standardized automated high enzymatic analysis using BS 240 spectrometer. Analysis of different serum lipids were measured using the low-density lipoprotein cholesterol (LDL-C) levels as per the Friedewald formula: $LDL-C = \text{total cholesterol} - (HDL + TG/5)$ (35). Serum triglyceride levels were measured using a cutoff of less than 150 mg/dL (1.7 mmol/L) as normal, 150 to 499 mg/dL (1.7 to 5.6 mmol/L) as mildly elevated, 500 to 886 mg/dL (5.6 to 10.0 mmol/L) as moderately increased, and more than 886 mg/dL as extremely high(12,35).

A level of less than 200 mg/dL (5.17mmol/L) of serum total cholesterol was regarded as normal. 200–239 mg/dL (5.17–6.18 mmol/L) of total cholesterol was considered to be on the borderline of high. A high total cholesterol level was defined as 240 mg/dL (6.21 mmol/L) or higher(12,35) . A cutoff of 130 mg/dL (3.4 mmol/L) for LDL cholesterol was regarded as normal (12,35) .

3.6.3 Blood pressure measurement.

Brachial artery blood pressure was taken in sitting position using manual Android BP machine (China). The first reading was manually obtained after five minutes of rest on an upper arm, and the second reading was obtained after ten to fifteen minutes of rest in order to confirm the blood pressure level. In this study, blood pressure readings between 120 and 139/80 and 89 mmHg was indicative prehypertension state, whereas readings below 120/80 mmHg was indicative of normal blood pressure. Furthermore, if persistently increased on at least two occasions, separated by four hours, blood pressure greater than or equal to 140/90 mmHg was indicative of hypertension. Patients BP was measured and recorded from 20 weeks, then monthly until 38 weeks of gestation.

3.6.4 Determination of protein in urine

Urine test was performed during ANC visits at GA of 20,24,28,32, 36 and 38 weeks. By using sterile gloves, 10mls of midstream urine was collected using sterile urine containers, and the specimen was labeled with the participant's complete name, age, or patient identification and then sent to the testing location.

A non-expired urine test strips (dipsticks) were immersed into the urine containers and rapidly withdrawn after being dipped into for about a second. Urine strip has pads that change colour based on concentration of different substances including protein. To allow the test pads to develop, place the test strip, test pads facing up, on a paper towel or pad and set a timer for 60 seconds. Test results were obtained and recorded for urine protein in milligrams and other patient management-relevant results like urobilinogen, bilirubin, ketone, blood, nitrite, leukocytes, glucose, specific gravity, and pH obtained in the same Dirui urine dipstick strip while holding the test strip vertically and the strip container upright. Each test pad was compared to the corresponding color blocks row on the bottle label. The initials of the person testing were written down, and the used materials discarded properly as medical waste.

Pre-eclampsia was defined as elevated blood pressure at $\geq 140/90$ mmHg after 20 weeks of gestation and proteinuria $\geq 1+$ dipstick.

3.6.5 Data collection tool.

A semi-structured questionnaire (Refer to Appendix II) was used to assess serum β -hCG and lipid imbalance and their correlation to occurrence to pre-eclampsia among high-risk pregnant mother to pre-eclampsia attending selected studies centers. The

tool was designed after reviewing different literature on the correlation between serum β -hCG and lipid and occurrence of pre-eclampsia and it will include five parts:

Part I: Health facility information such as name of the facility, district and region.

Part II: Socio-demographic characteristics like age, residence, occupation, and level of education.

Part III: Obstetrical factors such as gestational age number of pregnancies, gestational age, and parity.

Part IV: Risk factors of pre-eclampsia such as previous history pre-eclampsia, history of chronic hypertension, history of diabetes mellitus and age above 35 years.

Part V: Laboratory findings and blood pressure, which contained information concerning serum β -hCG, lipid, Urine test and blood pressure results.

3.7 Study variables.

3.7.1 Dependent variable.

- ✓ Pre-eclampsia.

3.7.2 Independent variables.

Medical-obstetric factors: Gravidity, parity, gestation age, family hypertension history, chronic hypertension, history of pre-eclampsia in previous pregnancy, diabetes history.

Serum biomarkers: serum β -hCG and lipids.

3.8 Data management

Data from questionnaires was entered and analyzed using SPSS software version 25.0., a statistical computer program. Continuous variables were summarized as means and

medians. For categorical data like sex, levels of education were summarized as proportions, percentages, and frequencies.

- **For Objective 1:** The level of serum β -hCG among pregnant women in high risk of pre-eclampsia attending antenatal clinics at Ijitimei district hospital, Fuoni and Mpendae Health centres were computed and descriptive statistic was used which consists to check the percentage of participant with highly elevated serum β -hCG of the total number of participants recruited.
- **For Objective 2:** The level of serum lipids among pregnant women in high risk of pre-eclampsia was computed and descriptive statistic was used which consists to check the percentage of participants with highly elevated serum lipids to the total number of participants recruited.
- **For Objective 3:** Association between high levels of serum β -hCG, serum lipids with occurrence of pre-eclampsia among pregnant women in high risk of pre-eclampsia were analyzed using logistic regression. The measure of association was reported as odds ratios (ORs) with corresponding 95% CI and p-values. Predictors with p-value <0.5 at univariate regression were computed at multivariate logistic regression model to estimate adjusted odds ratio. The variables that were statistically significant were considered associated with preeclampsia.

3.9 Ethical consideration

The KU Ethical Review Committee granted the study ethical approval before it was carried out at Ijitimei district hospital, Fuoni and Mpendae Health Centres.

On the other hand, the permit was granted from Second Vice President office and Ministry of health in Zanzibar, as well as Medical Officers in charge of the selected health facilities.

After receiving a patient's signed informed permission, enrolment began for all eligible participants who arrived at these Health care facilities. The participants were introduced about the aim and benefits of this study as well as the procedures done during data collection. The participant's identity was concealed by using numbers rather than names. The acquired information was coded and entered into a computer for records. By assigning each file a unique password that was known only to researchers, security was maintained. Only researchers had access to the written forms, which housed in a secure cabinet.

Withdraw criteria.

Participants were free to withdraw from the study at any time when they consented for any reason. Shifting from the original residence, for example from Unguja to Pemba for some women married in Unguja and need to continue with antenatal visits and deliver in their island (Pemba) as well as changing of health care facility for ongoing antenatal care visits were considered.

The researcher terminated a participant involvement whenever she failed to attend the visit and if a participant got any antenatal morbidity that led to referral to higher health facility.

Disclosure of potential conflicts. This research was conducted through self-funding which covered the expenses of each participant's study investigations, research assistant monthly payments. Also this fund was used to pay the fee that was needed

for study permit at the setting. Close relationship was built between the researcher and the health care providers and the study participants.

Vulnerable participants

We had limited the recruitment of vulnerable groups in this study, including pregnant women with mental illness and non-adult participants. However, the study's findings will also be advantageous to the vulnerable population.

Benefits of study to local community

There may not be a direct benefit for the participants of this study, however information obtained from this study will extensively benefit other patients that will come with related problems in the future, where early intervention will be given to avoid poor pregnancy outcomes.

Provision for compensation

This study was conducted through voluntary participation following informed consent, there was not any amount of money or incentives given to study participant.

Privacy and confidentiality

Anumerical code was used to identify the respondents to keep confidentiality of the patient. During the course of the study, the records were kept under lock and key for the case of paper documents and password protected documents for electronic data. Only study investigators had access to see and manipulate the participants' information.

CHAPTER FOUR

4.0 RESULTS

4.1 Study participants

In the present study, pregnant women identified as high-risk for developing pre-eclampsia were systematically screened and enrolled. High-risk status was determined based on established clinical risk factors including history of pre-eclampsia, chronic hypertension, diabetes, renal disease, or advanced maternal age (≥ 35 years). To ensure homogeneity of the study population and minimize confounding variables, the following exclusion criteria were applied, pre-existing pre-eclampsia at the time of enrollment, trophoblastic disease confirmed by ultrasound or history in the current pregnancies. Eligible participants were randomly enrolled from antenatal clinics until the target sample size of 325 was achieved.

4.2 Baseline sociodemographic factors of study participants.

Table 1. Baseline socio-demographic factors of study participants.

Characteristics	N=325(%)
Age(year)	
<25	28(8.6)
25 – 35	66(20.3)
>35	231(71.1)
Marital status	
Single	12(3.7)

Married	273(84)
Divorced	40(12.3)
Occupation	
Employed	132(40.6)
Entrepreneur	115(35.4)
House wife	78(24.0)
Level of education	
Informal	44(13.5)
Primary	48(14.8)
Secondary	166(51.1)
University	67(20.6)

71.1 % of study participants were over 35 years old and 84% were married. Of the participants, 51.1% had a secondary education and 40.6% were employed.

4.3 Baseline medicals and obstetrical factors of study participants.

Table 2. Baseline medical and obstetrical factors of study participants.

Characteristic	N=325(%)
	Mean (Minimum-maximum)
Gestational Age(weeks)	18.1(17.8-20)
Gravidity	
Primigravida	15(4.6)
Multigravida	206(63.4)
Grand multigravida	104(32.0)
Parity	
Nullipara	92(28.3)
Primipara	158(48.6)
Multipara	49(15.1)
Grand multipara	26(8.0)
Previous history of PE	
Present	79(24.3)
Absent	246(75.7)
History of HTN	
Present	43(13.2)
Absent	282(86.8)
History of DM	
Present	34(10.5)
Absent	291(89.5)
History of renal disease	
Absent	309(95.1)
Present	16(4.9)

63.4% of the study participants were multigravida, and 32.0 % were grand multigravida. Multipara made up 48.6% of the study participants. However, a history of PE, HTN, and DM was present in 24.3%, 13.2%, and 10.5% of the participants, respectively.

4.4 Magnitude of subsequent pre-eclampsia among study participants.

Table 3. Magnitude of subsequent pre-eclampsia among study participants.

Gestation age	Pre-eclampsia N=325		Cumulative frequency (presence)
	Presence n (%)	Absent n (%)	
20 weeks	9(2.8)	316(97.2)	9
24 weeks	11(3.4)	314(96.6)	20
28 weeks	8(2.5)	317(97.5)	28
32 weeks	16(4.9)	309(95.1)	44
36 weeks	26(8.0)	299(92.0)	70
38 weeks	28(8.6)	297(91.4)	98

In the current study, the prevalence of PE in the third trimester was 2.5%, 4.9%, 8.0%, and 8.6% at 28, 32, 36, and 38 weeks of pregnancy, respectively. The second trimester showed a low rate, with respective rates of 2.8%, and 3.4% at weeks 20 and 24.

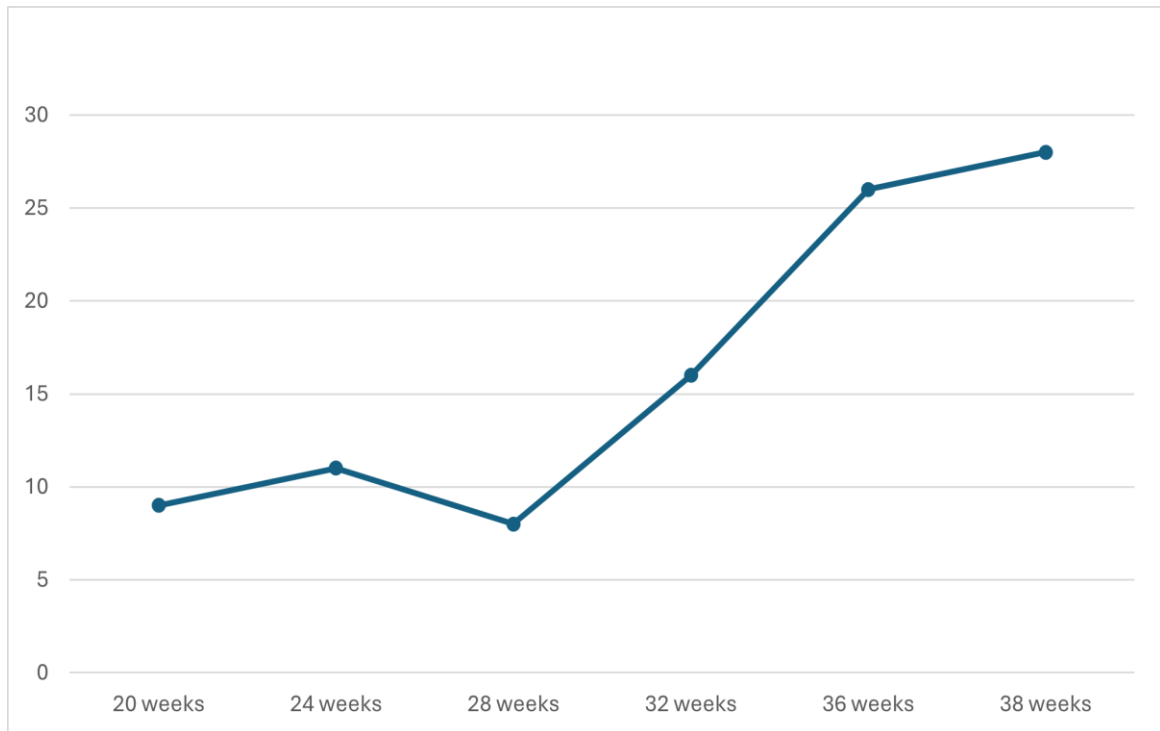


Figure 1. Graph showing magnitude of subsequent PE along the pregnancy.

4.4 Level of serum β -hCG among study participants.

Table 4. Level of serum β -hCG among study participants.

Serum β-hCG	N=325(%)
Normal(4,060-165,400 mIU/mL)	276(84.9)
Elevated (>165,400 mIU/mL)	49(15.1)

In this study, 15.1% of patients had elevated serum β -hCG.

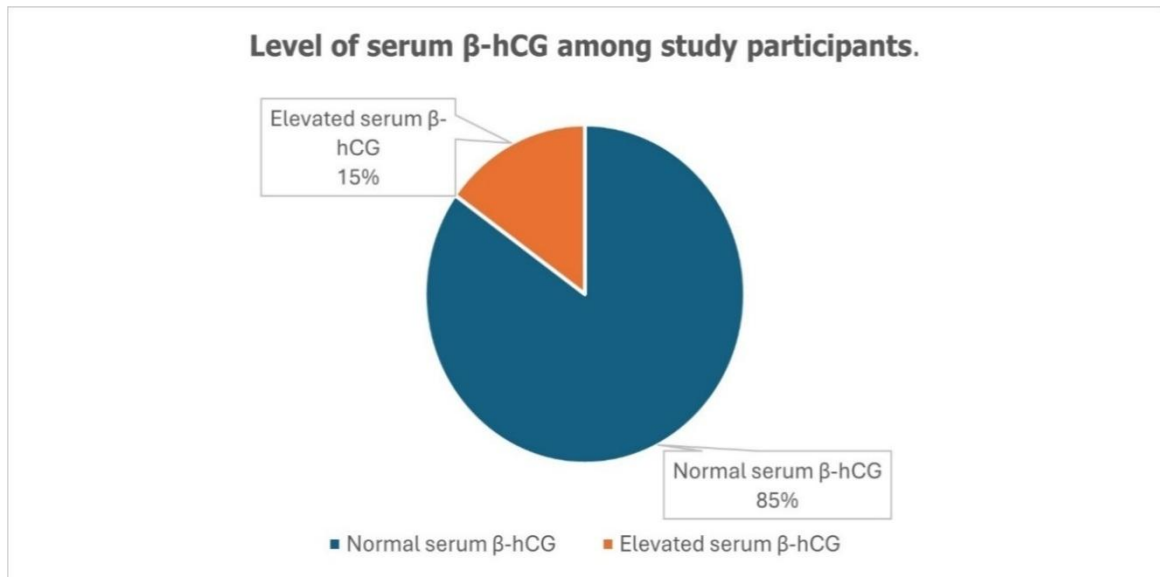


Figure 2. Pie chart showing level of serum β -hCG among study participants.

4.5 Level of serum lipid among study participants.

Table 5. Level of serum lipid among study participants

Serum lipid	N=325(%)
Total cholesterol (mmol/l)	
Normal (<6.2)	242(74.5)
Elevated (>6.2)	83(25.5)
HDL (mmol/l)	
Normal (1-2.2)	197(60.6)
Low (<1.0)	58(17.8)
Elevated (>2.2)	70(21.5)
LDL(mmol/l)	
Normal (<4.2 mmol/l)	226(69.5)

Elevated (>4.2 mmol/l)	99(30.5)
Triglyceride (mmol/l)	
Normal (<2.25)	172(52.9)
Elevated (>2.25)	153(47.1)

In the current study, there was an increase in TC, LDL, HDL, and triglycerides of 25.5%, 30.5%, and 41.1%, respectively. Additionally, among participants, 17.8% had low HDL.

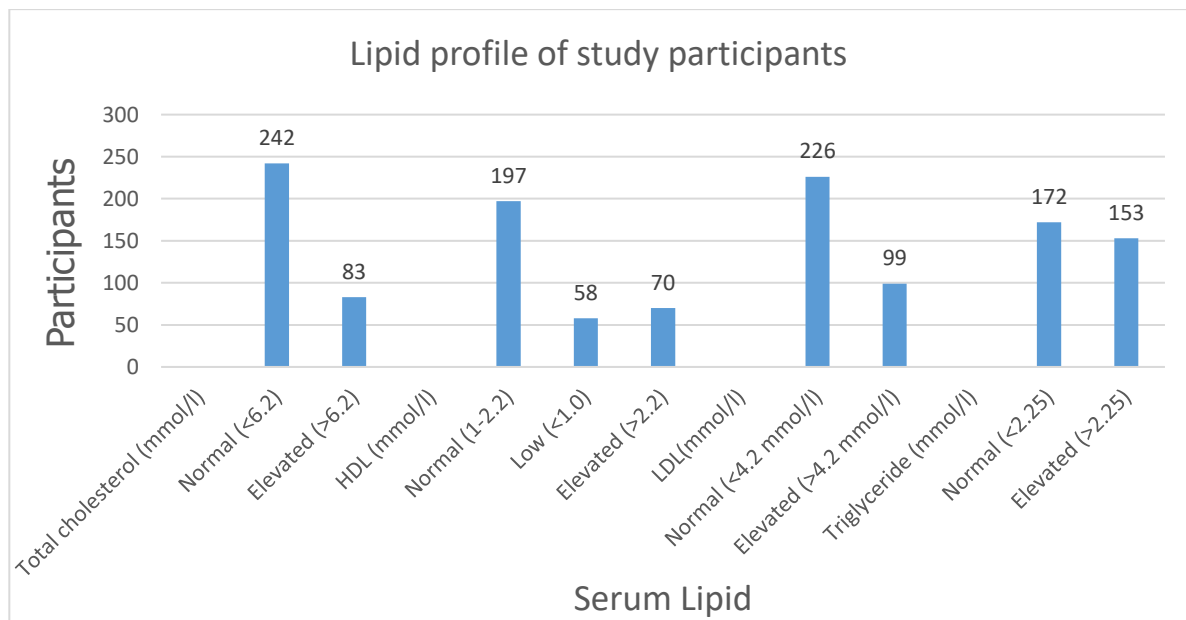


Figure 3: Histogram showing level of different serum lipid among study participants.

4.7. Association between mid-trimester serum β -hCG levels and serum lipid profile with subsequent development of pre-eclampsia among study participants.

Table 3. Association between mid-trimester serum β -hCG levels and serum lipids with subsequent development of pre-eclampsia in second trimester.

Characteristics	Pre-eclampsia					
	Present	Absent	Univariate		Multivariate	
	n=16(%)	n=309(%)	COR (95%CI)	P value	AOR (95%CI)	P value
Serum β-HCG levels						
Normal	2(0.8)	240(99.2)	Ref			
elevated	14(16.9)	69(83.1)	4(1.1-13.1)	0.001	2.9(2.1-11.1)	0.002
Total cholesterol(mmol/l)						
Normal (<6.2)	13(5.4)	229(94.6)	Ref			
Elevated (>6.2)	3(3.6)	80(96.4)	1.3(0.4-3.9)	0.5	6.2(0.8-17)	0.2
Low HDL (mmol/l)						
Low (<1.0)	8(3.0)	259(97.0)	Ref			
Normal (1-2.2)	8(13.8)	50(86.2)	0.6(0.14-2.9)	0.5	1.8(0.2-11)	0.5

High HDL (mmol/l)						
Normal	109(3.9)	245(96.1)	Ref			
Elevated	6(8.6)	64(91.4)	0.5(0.2-2.9)	0.1	7.3(1.3-40)	0.12
LDL (mmol/l)						
Normal (<4.2)	4(1.8)	222(98.2)	Ref			
Elevated (>4.2)	12(12.1)	87(87.9)	9.3(3.1-27)	0.005	7.1(2.7-26)	0.004
Triglyceride (mmol/l)						
Normal (<2.25)	2(1.2)	170(98.8)	Ref			
Elevated (>2.25)	14(9.2)	139(90.8)	8(3.1-23)	0.005	6.4(3.4-24)	0.003
Previous history of PE						
Absent	13(5.3)	283(94.7)	Ref			
Present	3(3.8)	76(96.2)	0.7(0.1-2.5)	0.7	0.3(0.05-1.9)	0.2
History of HTN						
Absent	15(5.3)	267(94.7)	Ref			
Present	1(2.3)	42(97.7)	3.1(0.3-27)	0.2	0.3(0.03-2.7)	0.2
History of DM						
Absent	14(4.8)	277(95.2)	Ref			

Present	2(5.9)	32(94.1)	1.9(0.2-14)	0.4	0.5(0.06-3.6)	0.5
History of renal disease						
Absent	15(4.9)	294(95.1)	Ref			
Present	1(6.2)	15(93.8)	0.7(0.08-7.3)	0.8	0.7(0.06-1.6)	0.8
Age						
<35 years	6(6.3)	89(93.7)	Ref			
>35 years	10(4.3)	220(95.7)	0.3(0.06-1.6)	0.18	0.3(0.06-1.6)	0.18

In the current study, participants who had increased serum β -HCG in the middle of the second trimester were 2.9 times more likely to present with PE at the end of the second trimester ($p=0.04$). Conversely, individuals with raised levels of LDL and serum triglycerides also had a significantly (p value <0.05) higher chance of presenting PE at the end of the second trimester, with respective risks of 7.1 and 6.4.

Table 4. Association between mid-trimester serum β -hCG levels and serum lipids with subsequent development of pre-eclampsia in third trimester.

Characteristics	Pre-eclampsia					
	Present	Absent	Univariate		Multivariate	
	n=33(%)	n=292(%)	COR(95%CI)	P value	AOR (95%CI)	P value
Serum β-hCG levels						
Normal	12(4.2)	264(95.7)	Ref			
Elevated	21(42.9)	28(57.1)	1.7(1.2-4.1)	0.002	2.4(1.1-13.1)	0.001
Total cholesterol(mmol/l)						
Normal (<6.2)	6(2.5)	236(97.5)	Ref			
Elevated (>6.2)	26(31.3)	57(68.7)	4.2(1.1-8.1)	0.01	2.8(1.9-8.1)	0.001
Low HDL (mmol/l)						
Low (<1.0)	21(36.2)	37(63.8)	15(2.7-12)	0.001	16(6.7-36.2)	0.002
Normal (1-2.2)	11(4.1)	256(95.9)				
High HDL (>2.2)						
Normal	19(7.5)	236(92.5)	Ref			
Elevated	13(18.5)	57(81.4)	0.6(0.1-0.9)	0.01	0.7(0.37-2.1)	0.07
LDL (mmol/l)						
Normal (<4.2)	2(0.9)	224(99.1)	Ref			
Elevated (>4.2)	30(30.3)	69(69.7)	10.0(2.1-17)	0.004	9.8(2.1-21.1)	0.04
Triglycerides						

(mmol/l)						
Normal (<2.25)	5(2.9)	167(97.1)	Ref			
Elevated (>2.25)	27(17.6)	126(82.4)	7.2(1.3-13.2)	0.001	8.2(2.6-15)	0.01
Previous history of PE						
Absent	26(10.6)	220(89.4)	Ref			
Present	6(7.6)	73(92.3)	0.6(0.2-1.7)	0.4	0.4(0.1-1.5)	0.2
History of HTN						
Absent	27(9.6)	255(90.4)	Ref			
Present	5(11.6)	38(88.4)	1.2(0.4-3.4)	0.6	1.1(0.3-3.2)	0.8
History of DM						
Absent	28(9.6)	263(90.3)	Ref			
Present	4(11.8)	30(88.2)	1.2(0.4-3.8)	0.5	0.6(0.18-2.6)	0.6
History of renal disease						
Absent	29(9.4)	280(90.3)	Ref			
Present	3(18.8)	13(81.2)	2.2(0.6-8.2)	0.2	1.7(0.4-6.8)	0.4
Age						
<35 years	12(12.6)	83(87.4)	Ref			
>35 years	20(8.7)	210(91.3)	0.6(0.3-1.40)	0.2	0.4(0.1-1.2)	0.1

Participants in this study had a significantly ($p < 0.05$) 2.4-time chance of developing PE if they had increased serum β -HCG in the mid trimester of their pregnancy. Participants with total cholesterol, low HDL, LDL, triglycerides, and increased serum TC had a 2.8, 16, 9.8 and 8,2 chance of developing a PE, respectively. However, there was no discernible risk of PE in the third trimester for those with high HDL.

CHAPTER FIVE

5.0 DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS OF THE STUDY.

5.1 Introduction.

This study aimed to determine mid trimester level of serum β -hCG, serum lipid and their association with subsequent development of pre-eclampsia among high-risk pregnant women.

5.2 Discussions.

In the current study, elevated levels of serum β -human chorionic gonadotropin (β -hCG) during the mid-second trimester were observed in 15.1% of the participants. Concurrently, an increase in lipid parameters was documented, with total cholesterol (TC), low-density lipoprotein (LDL), and triglycerides (TG) elevated in 25.5%, 30.5%, and 41.1% of the participants, respectively. Although high-density lipoprotein (HDL) was elevated in some cases, 17.8% of participants were found to have abnormally low HDL levels, a known cardiovascular risk factor.

Importantly, these biochemical alterations demonstrated a strong association with the development of pre-eclampsia (PE). Participants who exhibited elevated serum β -hCG levels in the mid-second trimester were found to be 2.9 times more likely to develop pre-eclampsia by the end of the second trimester compared to those with normal β -hCG levels. Similarly, elevated levels of LDL and triglycerides were associated with a 7.1-fold and 6.4 fold increased risk, respectively, of developing PE in the same timeframe. Furthermore, the risk escalated notably in the third trimester. Participants with persistently high serum β -hCG levels from mid-pregnancy exhibited a 2.4-fold increased likelihood of developing pre-eclampsia in the third trimester. Additionally,

those with dysregulated lipid profile specifically total cholesterol, low HDL, high LDL, high triglycerides, and elevated TC showed significantly increased risks of PE development, with odds ratios of 2.8, 16, 9.8 and 8.2 respectively. Conversely, elevated levels of HDL cholesterol were not significantly associated with an increased risk of pre-eclampsia in the third trimester, suggesting a potential protective role of high HDL against the development of hypertensive disorders in pregnancy.

A number of studies have evaluated the role that blood lipids and β -hCG levels play in predicting PE. In this study, we found that 15.1% of pregnant women exhibited elevated levels of serum β -human chorionic gonadotropin (β -hCG) during the mid-trimester. Importantly, women with elevated β -hCG levels at this stage were found to be 2.9 times more likely to develop pre-eclampsia by the end of the second trimester. Furthermore, persistently elevated β -hCG levels from mid-pregnancy into the third trimester were associated with a 2.4fold increased risk of developing pre-eclampsia later in pregnancy. These findings strongly underscore the potential of β -hCG as a predictive biomarker for hypertensive disorders of pregnancy, especially pre-eclampsia. The rise of serum β -human chorionic gonadotropin (β -hCG) during the mid-second trimester may be explained by explained by the fact that vasoconstriction and impaired angiogenesis cause high blood pressure in women with PE(29). This, in turn, causes hypoxia and trophoblastic cell hyperplasia, which result in placental hormone hyper secretion and high levels of circulating β -hCG(29). Different authors have also reported similar findings as in a study conducted by Ritu Yadav and colleagues among pregnant mother attending antenatal consultation in their second trimester in India where high level of serum β -hCG was significantly elevated in women with high risk of

PE(13). Furthermore, Sayran and colleagues found also that the rise of serum in serum β -hCG in mid second trimester was associated with the severity of preeclampsia(19). Similar findings were reported in China by Wang and colleagues reported among mother attending Liaocheng People's Hospital maternity ward that Higher circulating β -HCG level was correlated with severe pregnancy-induced hypertension at the end of pregnancy(27).However, other authors reported controversial results, such as a study of pregnant women attending Chinese prenatal clinics that found no statistically significant difference between pregnant women who developed pre-eclampsia and those who did not in terms of higher levels of serum β -hCG in the second trimester(33).However, the results above came from a retrospective analysis of the medical records of expectant women who visited a prenatal clinic. A case control study by Shin and colleagues in China revealed similar results, with no discernible difference between the incidence of PE and the rise in blood β -hCG(34).

On the hand, this study found that a high prevalence of dyslipidemia among pregnant women, with elevated total cholesterol, LDL and triglycerides. While high HDL was observed in 17.8% of participants, it was the low HDL levels, in combination with other lipid abnormalities, that were strongly associated with an increased risk of pre-eclampsia (PE).This could be because endothelial dysfunction, which is thought to be a key component of the process underlying elevated blood pressure during pregnancy, has been linked to the rise of altered lipid profiles(22,23). This can be due to the fact that elevated serum cholesterol can lower nitric oxide bioavailability and induce vascular oxidative stress, both of which can raise blood pressure by reducing vasodilatation(25) .These results were supported by a case-control study that was

carried out at Sheba Hospital Kaligonj in Bangladesh with 35 pregnant women who were normal and 35 women who were pre-eclamptic. The study found a substantial correlation between pre-eclampsia and high serum lipid levels (11). A cohort research of 5692 expectant mothers in the Netherlands revealed similar results, showing that elevated serum levels of total cholesterol, triglycerides, and LDL were strongly linked to elevated blood pressure and pre-eclampsia(26). In a meta-analysis and comprehensive review, Endalamaw and colleagues found similar results among pregnant African women at risk of pre-eclampsia(35). They also found a strong correlation between high VLDL, total blood cholesterol, and serum triglycerides. Endalamaw and colleagues' findings, however, showed no discernible link between HDL and pre-eclampsia(35). Some authors reported controversial results, such as a study conducted by Hillary Hosie and colleagues which found no correlation between dyslipidemia and occurrence of pre-eclampsia in a multi-center study among published review from Europe, African and Latin America(25). This disagreement with our findings may be explained by differences in the research population and design. Another meta-analysis conducted by Cassandra and colleague found that dyslipidemia was not a good indicator of pre-eclampsia at the end of the second and third trimesters (10). At the same time, they note that PE in late pregnancy is significantly correlated with increases in blood triglycerides and cholesterol.

5.3 Conclusion

This study provides compelling evidence that elevated serum β -hCG levels during the mid-trimester, in conjunction with abnormal maternal lipid profile, serve as significant biochemical predictors of preeclampsia. The observed association suggests that these

biomarkers, when measured early in pregnancy can help identify women at increased risk well before the onset of clinical symptoms. Notably, the risk was markedly higher among the women presenting with both persistently elevated β -hCG and concurrent lipid abnormalities, underscoring the synergistic impact of these parameters in the pathophysiology of preeclampsia. Furthermore, this study highlights the urgent need for integrating cost-effective, evidence-based risk stratification tools into maternal health care systems, especially in low-resource settings where the burden of preeclampsia remains disproportionately high.

5.4 Limitations

1. This was a single-time point biomarker assessment. β -hCG and lipid levels were measured only during the mid-trimester, without serial measurements. This prevents assessment of temporal trends and dynamic changes across pregnancy, which may provide more predictive accuracy.
2. Confounding variables may have not fully controlled. Potential confounders that could affect PE risk and biomarker levels included pre-pregnancy BMI, dietary habits, physical activities and insulin resistance.
3. Specificity and generalizability of populations. The results may not be as applicable to other groups with distinct ethnic, genetic, or environmental traits.

5.5 Recommendations.

The following are recommendations of the study.

1. Incorporate routine biochemical screening in Antenatal Care. Mid-second trimester screening for β -hCG and lipid profiles (including TC, LDL, HDL, and triglycerides) should be considered as part of standard antenatal assessments, particularly for women at higher risk of hypertensive disorders. Establish cut-off values for each biomarker to support early identification of women at risk for PE.
2. Enhanced antenatal monitoring. For women identified as high-risk, recommend a schedule of closer antenatal follow-ups. This should include more frequent blood pressure checks, urine protein analysis, ultrasounds for fetal growth, and Doppler flow studies to assess placental health.

3. Conduct further research. Promote longitudinal and multi-center studies to validate the predictive value of β -hCG and lipid biomarkers across diverse populations and settings. Explore intervention studies to assess the impact of early detection and management of dyslipidemia on preeclampsia outcomes.

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Appendices

APPENDIX 1: Informed Consent- in English

Greetings! My name is Dr. Hafidh Maulid Rajab, a postgraduate student at Kairuki University undertaking Masters Degree in Obstetrics and Gynaecology. The research is about investigating the correlation of mid-trimester serum β -hCG and lipid profile and the occurrence of pre-eclampsia in high-risk pregnancies.

If you agree to participate, you will be asked to answer a structured questionnaire about your medical history and demographics, provide blood samples during your antenatal care appointments for serum β -hCG and lipid level measurement, and allow the research team to access your medical records related to this study.

The procedures involved in this study are considered minimal risk. However, as this study will involve drawing blood, it is acknowledged that there may be slight pain or swelling when the needle is inserted for blood withdrawal, but researchers will take necessary precautions to ensure procedures are carried out with care and respect, providing assistance or clarification as needed. So, we ensure you that, in case of treatment needed for any acquired injury sustained during blood sample taking, as well as any medical or psychological issue of a participant during whole period of the study, the participant will be intended free of charge and followed up closely.

In terms of benefits, there may be no direct benefits to you, but the information obtained from this study may contribute to a better understanding of pre-eclampsia in high-risk pregnancies. Please be informed that all information collected will be kept confidential. Your name and any other identifying information will not be included in any reports or publications resulting from this study. Your participation in this study is

entirely voluntary. You may choose not to participate, and you may withdraw from the study at any time without penalty or loss of benefits to which you are otherwise entitled.

Confidentiality

The information that you provide will be tremendously respected and preserved in strictly confidential manner. Only the study staffs will have an access to your information and investigation results.

Contacts

In case of any problem or question about this study, you can communicate with:-

IREC chairperson,

Kairuki University,

P.O BOX 65300, Dar es Salaam,

Tanzania.

Email: irec@ku.ac.tz

Tel: +255 - 22-2700021/4

Principal investigator

Dr Hafidh M. Rajab

Tel: 0612 715 545

Supervisor

Dr Monica Chiduo

Department of Obstetrics and gynaecology

Tel: 0713 618 847

Participant Consent:

I have understood the information provided above, and I also understand the nature and purpose of the study. I have had the opportunity to ask questions, and any questions I have asked, have been answered to my satisfaction. I voluntarily agree to participate in this study.

Participant's Name: _____

Participant's Signature: _____ **Date:** _____

Investigator's Certification:

I confirm that the participant has been provided with the information needed to make an informed decision about participating in this study.

Investigator's Name:

Investigator's Signature: _____ Date: _____

APPENDIX 2: Informed Consent- in Kiswahili

Habari ya leo! Jina langu ni Dkt. Hafidh Maulid Rajab, mwanafunzi wa Chuo Kikuu cha Kairuki nachukua Shahada ya Uzamili katika fani ya magonjwa ya kina mama na afya ya uzazi. Utafiti huu ni kuhusu uchunguzi wa uhusiano kati ya viwango vya homoni ya ujauzito (β -hCG) na mafuta katika damu na kutokea kwa kifafa cha mimba kwa wanawake wajawazito walio katika hatari kubwa.

Ikiwa utakubali kushiriki katika utafiti huu, utaombwa kujibu maswali yanayohusu historia yako ya matibabu na takwimu zako za kibaiolojia, kutoa sampuli ya damu kwa ajili ya kupima kiwango cha homoni na mafuta na kuruhusu timu ya utafiti kupata rekodi zako za matibabu zinazohusiana na utafiti huu. Utafiti huu haukadiriwi kuwa na athari kwa washiriki. Hata hivyo, kwa kuwa utafiti huu unahusisha kuchukua damu, tunatambua kwamba inaweza kutokea maumivu kidogo au uvimbe katika sehemu iliyochomwa sindano, lakini watafiti watachukua tahadhari kubwa kuhakikisha utoaji damu unafanyika kwa uangalifu wa hali ya juu, na kutoa msaada au ufafanuzi kama unavyohitajika.

Ikiwa mshiriki atapata changamoto ya kiafya ndani ya muda wote wa utafiti huu, na kama kutahitajika tiba ya athari yoyote itakayopatikana kama vile maumivu wakati wa kutoa damu kwa ajili ya vipimo, mshiriki atatibiwa bure na atafuatiliwa kwa ukaribu zaidi.

Kuhusu faida, yawezekana hakutokuwa na faida moja kwa moja kwako, lakini taarifa za utafiti huu zitachangia kuelewa vizuri zaidi kifafa cha mimba kwa wanawake wajawazito walio katika hatari kubwa. Tafadhali elewa kuwa taarifa zote zitakazokusanywa zitabaki

kuwa za siri. Jina lako na taarifa nyingine yoyote ya kukutambua haitajumuishwa katika ripoti au machapisho yoyote yatakayotokana na utafiti huu. Ushiriki wako katika utafiti huu ni wa hiari. Unaweza kuchagua kutoshiriki, na unaweza kujitoa kwenye utafiti wakati wowote bila adhabu au kupoteza stahiki zako zozote.

Usiri

Taarifa zote utakazotoa pamoja na majibu ya vipimo vya damu utakavyofanyiwa katika utafiti huu vitakuwa siri. Wafanyakazi wa utafiti tu ndio watakaokuwa na haki ya kutumia taarifa zako kwa ajili ya utafiti.

Mawasiliano

Ikiwa una maswali yoyote kuhusu utafiti, tafadhali jisikie huru kuwasiliana na:-

Mwenyekiti, Kamati ya maadili ya utafiti,

Chuo kikuu cha Kairuki,

Sanduku la barua 65300, Dar es Salaam,

Tanzania .

Barua pepe : irec@ku.ac.tz

Nambari ya simu: +255 - 22-2700021/4

Mtafiti mkuu

Dkt Hafidh M. Rajab

Nambari ya simu: 0612 715 545.

Msimamizi mkuu,

Dkt Monica Chiduo

Idara ya magonjwa ya kina mama na afya ya uzazi

Nambari ya simu: 0713 618 847

Ridhaa ya Mshiriki:

Nimeelewa habari iliyotolewa hapo juu, na pia ninaelewa asili na lengo la utafiti. Nimepata fursa ya kuuliza maswali, na maswali yangu yote yamejibiwa kwa ufasaha. Kwa hiari yangu mwenyewe, nakubali kushiriki katika utafiti huu.

Jina la Mshiriki: _____

Saini ya Mshiriki: _____ **Tarehe:** _____

Uthibitisho wa Mtafiti:

Nathibitisha kwamba mshirikiamepewa habari zote anazohitaji kufanya uamuzi wa kushiriki katika utafiti huu.

Jina la Mtafiti:

Saini ya Mtafiti: _____ **Tarehe:** _____

APPENDIX 3: Data Collection Tool - in English

Research title: Correlation of mid-trimester Serum β -hCG levels and lipid profile with pre-eclampsia in high-risk pregnant women at Ijitimai district hospital, Fuoni and Mpendae health centres.

SECTION I: HEALTH FACILITY INFORMATION

Name of Health Facility: Region: District:

SECTION II: SOCIODEMOGRAPHIC DATA

1. Age: 2. Marital status: Single Married Divorced
2. Occupation: Employee Entrepreneur House wife
Other, specify;

3. Level of education: No formal education Primary education
Secondary education college/university

SECTION III: OBSTETRIC DATA

4. Gestational age:
5. How many times have you been pregnant (gravidity)? 1 2 -4 ≥ 5
6. Number of deliveries (parity) 0 1 2-4 ≥ 5

SECTION IV: RISK FACTORS OF PRE-ECLAMPSIA

7. Previous history of pre-eclampsia Yes No
8. History of chronic hypertension: Yes No
9. History of diabetes mellitus: Yes No
10. History of renal disease: Yes No
11. Age 35years or more: Yes No

SECTION V: laboratory findings and blood pressure

12. Second trimester β -hCG:

13. Serum cholesterol:

LDL:

HDL:

Total cholesterol:

Triglycerides:

14. Blood pressure and urine protein

Gestational age	Blood pressure (mmHg)	Urine for protein (dipstick)
20 weeks		
24 weeks		
28 weeks		
32 weeks		
36 weeks		
38 weeks		

APPENDIX 4: Data Collection Tool - in Kiswahili

SEHEMU YA I: TAARIFA ZA KITUO CHA AFYA

Jina la Kituo cha Afya:

Wilaya:

SEHEMU YAI: DATA YA SOCIODEMOGRAPHIC

1. Umri:

2. Hali ya mahusiano; Nimeolewa Sijaolewa Mtalaka

3. Kazi: Mwajiriwa Mjasiriamali Mama wa nyumbani

Nyingine, taja;

3. Kiwango cha elimu: Hakuna elimu rasmi Elimu ya msingi
Elimu ya sekondari chuo/chuokikuu

SEHEMU YA III : TAARIFA ZA UZAZI

4. Umri waujazito:

5. Umekuamjanzito (gravida) mara ngapi : 1 2 - 4 ≥ 5

6. Umejifungua mara ngapi : 0 1 2 - 4 ≥ 5

SEHEMU YA IV : MAMBO HATARI YA KUPATA PRE-ECLAMPSIA

6. Historia ya awali ya priklampsia: Ndio Hapana

7. Historia ya shinikizo la damu sugu: Ndio Hapana

8. Historia ya ugonjwa wa kisukari: Ndio Hapana

9. Historia ya ugonjwa wa figo: Ndio Hapana

10. Umri wamiaka 35 au zaidi: Ndio Hapana

SEHEMU YA V: Shinikizo la damu na matokeo ya maabara

11. Shinikizo la damu na protini ya mkojo

Umri wa ujauzito	Shinikizo la damu (mmHg)	Mkojo kwa protini (dip stick)
Wiki 20		
Wiki 24		
Wiki 28		
Wiki 32		
Wiki 36		
Wiki 38		

14. Trimester ya pili β -hCG:

15. Cholesterol ya Serum:

LDL:

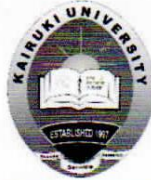
HDL:

Jumla ya cholesterol:

Triglycerides:

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Ref. No. KU/IREC/27.10/583

18 July, 2025

Dr. Hafidh Maulid Rajab,
Kairuki University,
70 Chwaku Street,
Mikocheni,
P. O. Box 65300.

Dar es Salaam, Tanzania.

RE: ETHICAL CLEARANCE CERTIFICATE FOR CONDUCTING HEALTH RESEARCH

I am pleased to inform you that the research titled: **Correlation of Mid-Trimester Serum β -hCG and Lipid Profile with Pre-Eclampsia in High-Risk Pregnant Women at Selected Health Facilities, Zanzibar (Rajab, H. M., 2025)** has been granted ethical approval.

This approval is in effect for one year from the above date.

- Any changes in the procedures should be reported to the Institutional Research Ethics Committee.
- Significant changes will require the submission of a revised request for ethical approval.
- You will be required to submit a **study progress report** every six months.

Permission to publish your findings should be sought from the National Institute for Medical Research (NIMR) before submission to a publisher and not concurrently.

CHAIRPERSON

Name: Prof. Frederick Kaijage

Signature:

SECRETARY

Name: Prof. Columba Mbekenga

Signature:



FUONI HEALTH CENTER,
WEST B,
URBAN WEST,
ZANZIBAR.

19TH JUNE 2025.

DR. HAFIDH M. RAJAB,
KAIRUKI UNIVERSITY,
S.L.P 65300,
DAR-ES-SALAAM,
TANZANIA.

**YAH: KURUHUSIWA KUFANYA UTAFITI WAKO KWA MAMA WAJAWAZITO JUU YA UWIANO
WA VINASABA BETA HCG NA MAFUTA KATIKA DAMU NA UTOKEAJI WA KIFafa CHA
MIMBA KWA WAJAWAZITO WALIO KATIKA HATARI KUBWA.**

Naomba husika na mada ilio juu.

Ruhusa imetoka ya kufanya utafiti wako katika RCH ya Hospital yetu kwa ajili ya kupata taarifa juu ya uhusiano ya viwango ya Beta HCG na mafuta katika damu na kujitokeza kifafa cha mimba (Edampsia) kwa wamama wajawazito walio katika viashiria vya hatari wanaohudhuria katika ANC.

Tunakutakia utafiti mwema, na kwa ushirikiano wowote unaouhitaji usisite kuona uongozi wa hospital yetu.





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IJITIMAI DISTRICT HOSPITAL
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KUMB: JDH/47/25

09/06/2025

Ndg. Haidh M. Rajab
Kairuki University
S.L.P 65300
DAR ES SALAAM


KUH: OMBI LA KUFANYA UTAFUTI" UHUSIANO KATI YA VIWANGO VYA BETA HCG NA MAFUTA KATIKA DAMU NA KUTOKEA NA KIFAPA CHA MIMBA KWA WANAWAKE WAJAWAZITO WALIO KATIKA HATARI KUBWA (HIGH RISK PREGNANCIES)" KATIKA HOSPITALI YA WILAYA JITIMAI.

Tafadhali husika na mada iliapo hapo juu.

Nimepokea barua yako kuhusu ombi la kufanya Utafiti katika taasisi yetu kuhusu" uhusiano kati ya viwango vya beta hcg na mafuta katika damu na kutokeakwa kifapa cha mimba kwa wanawake wajawazito walio katika hatari kubwa (high risk pregnancies)" katika hospital ya wilayaIjtimai.

Ombi lako limelibaliwa kufanya utafiti kulingana na maada husika

Ahsante kwa ushirikiano


DR. LWANYUMBA J. LWEGASILA
DAKTARI DHAMANA
HOSPITALI YA WILAYA JITIMAI


SEIF YAHYA ISSA
KATIBU HOSPITALI YA WILAYA IJITIMAI



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KUMB:JDH/47/25

13/06/2025

Ndg. Hafidh M. Rajab

Kairuki University

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DAR ES SALAAM

**REF: CORRELATION OF MID-TRIMESTER SERUM BETA HCG AND LIPID
PROFILE WITH PREECLAMPSIA IN HIGH-RISK PREGNANT WOMEN AT
SELECTED HEALTH FACILITIES ZANZIBAR.**

Tafadhali husika na mada iliapo hapo juu.

Nimepokea barua yako kuhusu ombi la kufanya Utafiti katika taasisi yetu kuhusu " uhusiano kati ya viwango vya beta hcg na mafuta katika damu na kutokea kwa kifafa cha mimba kwa wanawake wajawazito walio katika hatari kubwa (high risk pregnancies)" katika Kituo cha afya cha Mpendae.

Ombi lako limekubaliwa kufanya utafiti kulingana na maada husika

Ahsante kwa ushirikiano



DR. SALIM KHAMIS SALIM

DAKTARI DHAMANA

KITUO CHA AFYA MPENDAE

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DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY
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TITLE: ASSOCIATION OF MID-TRIMESTER SERUM β -HCG AND LIPID PROFILE WITH PRE-ECLAMPSIA IN HIGH-RISK PREGNANT WOMEN AT SELECTED HEALTH FACILITIES, UNGUJA.

Name: DR HAFIDH M. RAJAB
REG No: HK/PG/OG/22/0049

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