GESTATIONAL DIABETES MELLITUS RISK FACTORS AND PREGNANCY-RELATED OUTCOMES AMONG WOMEN IN KISUMU COUNTY, WESTERN KENYA

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A Thesis Submitted to the Graduate School in Partial Fulfilment of the Requirements for the Award of the Degree of Doctor of Philosophy in Public Health Of Jaramogi Oginga Odinga University Of Science And Technology

DECLARATION

This thesis is my original work and has not been presented for an award or conferment of a degree in any other university or institution.

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DEDICATION

I dedicate this thesis to my dear parents Jeremiah Ottaro and Josephine Ottaro and my lovely husband Rev. Fr. Willis Ondiek for their unconditional love, sacrifice, patience, encouragement and prayers.

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ABBREVIATIONS

BMI	Basal metabolic index
BP	Blood Pressure
DM	Diabetes Mellitus
GDM	Gestational Diabetes Mellitus
GWAS	Genome-wide association studies
GWG	Gestational weight gain
HIV	Human immunodeficiency syndrome
IADPSG	International association of diabetes and pregnancy study groups
IFAS	Iron- folic acid supplementation
JOOTRH	Jaramogi Oginga Odinga Teaching and Referral Hospital
JOOUST	Jaramogi Oginga Odinga University of Science and Technology
LMIC	Low- and Middle-Income Countries
NICU	Neonatal intensive care unit
OGCT	Oral glucose challenge test
OGTT	Oral glucose tolerance test
PCOS	Polycystic ovarian syndrome
PFOA	Perfluorooctanoic acid
PMTCT	Prevention of Mother-to- Child Transmission
SGA	Small to gestational age
SSA	Sub-Saharan Africa
TB	Tuberculosis

DEFINITION OF TERMS

BMI- Body Mass Index	This is weight in kgs divided by Height in m^2
Parity	Number of live child(ren) that the study participant has delivered
Employment status	Categorization of women based on the source of their income
Education qualification	Level of education attained in academic institutions
Physical activity	This refers to the time spent in carrying out either vigorous exercise or household chores **Active** (>3times weekly for at least 30mins) **Inactive** (<3times weekly for at least 30mins)
Diet	Food taken in daily in the right proportions Balanced (has carbohydrates, proteins, vitamins/minerals, water) Unbalanced (lacks one or more nutrients)
Maternal age	Age of the pregnant mother in years as they present at ANC clinic
Maternal height	This is the height measured in metres in erect position at the time of enrolment in the study
Nulliparous	A woman presenting to deliver for the first time at the time of enrolment in the study
Primiparous	Women who had given birth to one child at the time of enrolment in the study
Multiparous	Women who had given birth to two or more children at the time of enrolment in the study
GDM	Gestational Diabetes Mellitus

ABSTRACT

Evidence indicate that gestational diabetes mellitus (GDM) has a multifactorial aetiology and results in poor maternal and neonatal outcomes that vary based on geographic locations and ethnicity. However, in Kenya, despite GDM being a public health concern there are very few studies on the risk factors for GDM among pregnant women and its associated pregnancy –related outcomes. Therefore, the aim of this study was to determine the risk factors for GDM and the risk of pregnancy-related outcomes associated with GDM. To this end, a case-control study was carried out among 210 pregnant women attending antenatal clinic at Jaramogi Oginga Odinga Teaching and Referral Hospital (JOOTRH) in Kisumu County. Screening and diagnosis were performed using the 2013 WHO criteria. Descriptive and inferential statistical analysis were done in SPSS V.23 using Chi-square ($\chi 2$) test to test for associations and binary logistic regression analysis to determine predictors of GDM. Of the 105 GDM cases, majority 54(51%) were in 30-34 years age group, 59(56%) were overweight with a BMI of 25-29.9 kg/m2, 56(53%) had history of hypertension, 67(64%) had hypertensive relatives, 67(64%) had history of glycosuria, 72(69%)were multiparous, 64(61%) had history of caesarean delivery, 66(63%) had history of macrosomic delivery and 56(53%) had history of neonatal intensive care unit (NICU) admission. Multivariate analysis showed that having a diabetic relative (adjusted OR (aOR) 7.4, [95%CI: 1.2-76], p=0.049), history of CS delivery (aOR 7, [95%CI: 1.6-35.9], p<0.014), being on IFAS (aOR 16.6, [95%CI: 5-69.2], p<0.014) and having history of NICU admission (aOR 15, [95%CI: 3.5-86.9], p<0.001) were significantly associated with GDM. Further analysis revealed that gestational age at delivery ≥ 40 weeks (Adjusted Odds Ratio (aOR) 1.67, [95% CI 1.29-2.21, p<0.001), caesarean delivery (aOR7.28, [95%CI 3.17-18.0,p<0.001), induced labour (aOR 4.60, [95%CI 2.07-10.8, p<0.001),gestational hypertension (aOR15.2, 95%CI 3.92-103,p<0.001), foetal macrosomia (aOR 22.5, [95%CI 9.42-59.3, p<0.001) and neonatal admission to intensive care unit (aOR 16.2, [95%CI 3.73, 115, p<0.001) were significantly associated with GDM. This data suggests that having a diabetic relative, history of caesarean section, history of NICU admission and being on IFAS are predictors of GDM. GDM screening should be included in the standard routine ANC services for timely detection and treatment of GDM to achieve desirable pregnancy outcomes and limit adverse outcomes linked to GDM. Further, longitudinal multicentre studies should be carried out to explore long term effects of IFAS (in terms of duration and dosage) on GDM in order to provide an evidence-based nutritional interventions during pregnancy complicated by GDM. There is also need for implementation of lifestyle modification programs such as involvement in physical exercise and balanced diet to prevent the development of GDM and pregnancy-related complications being that a majority of cases were overweight. In addition, due to adverse pregnancy outcomes there is need for early screening and management of GDM among the high-risk populations.

CHAPTER ONE: INTRODUCTION

1.1 Background information

One of the most common non-communicable metabolic deregulation that present as glucose or carbohydrate intolerance of differing severity during pregnancy is Gestational Diabetes Mellitus (GDM) (Wang *et al*., 2022). It is a common pregnancy complication accounting for 90% of all pregnancy complicated by diabetes (Buse *et al*., 2020). It is results in poor neonatal and maternal outcomes and poses a significant health risk for both the mother and neonates (Muche *et al.,* 2019; Njogu *et al,* 2022). In 2013, the world Health Organization (WHO) adopted the international diagnostic and screening criteria for GDM that include performing oral glucose tolerance test (OGTT) in a fasting state (WHO, 2013). Despite the adoption of this criteria, the use of two-step screening and diagnostic methods involving measurement of glucose concentration following 50g glucose challenge test (GCT) and then again after 100g OGTT is still widely used in various settings (Coustan *et al.,* 2018; Natamba *et al.,* 2019). This lack of uniformity in diagnostic and screening protocols has partly contributed to variation in GDM prevalence across regions (Natamba *et al*., 2019).

The global prevalence of GDM varies from 1% to 28% depending on the study population genetics, environment and screening methods (Muche *et al*., 2019). Estimates indicate that sub-Saharan Africa (SSA) has a prevalence of 14%, North Africa (24.5%), North America (7%) and Europe (5.4%) (Njogu *et al*., 2022). In Africa, there is also geographic variation in GDM prevalence with North Africa (24.5%) and west Africa (14%) having a higher prevalence relative to East Africa (6%) (Muche *et al*., 2019). Moreover, even within East Africa region there is variation in prevalence with Rwanda having a prevalence of 8.3%), Tanzania having a prevalence of 5. 9%, Ethiopia a prevalence of 3.7% and western Kenya presenting with a prevalence of 2.6% (Muche *et al*., 2019; Njogu *et al*., 2022).

Recently, there is a significant shift in public health challenges facing sub-Saharan Africa (SSA) such as increases in incidences of obesity, diabetes and other non-communicable diseases due to changes in lifestyles such as physical inactivity or not eating healthier diets (Muche *et al*., 2019). Developing targeted interventions that will reduce the burden of the problem and result in improvement of both maternal and child health in SSA requires a thorough understanding of the risk factors of non-

communicable diseases such as GDM. Although there is still lack of data on the risk factors for GDM in SSA, previous studies revealed that maternal age, high parity, pregnancy overweight or obesity, family history of diabetes, being hypertensive, previous delivery of macrosomic infants and previous bad obstetric outcomes such as still birth and abortion are important risk factors for GDM (Natamba *et al*., 2019; Njogu *et al*., 2022). Other potential risk factors include low or high birth weight, smoking, physical inactivity, stature, socioeconomic factors, undernutrition during early life and exposure to Human Immunodeficiency virus and Tuberculosis (Nyirenda, 2016).

The Kenyan Ministry of Health policy on screening and treatment of GDM has not rolled it out as part of the routine antenatal care (ANC) services. Moreover, to our knowledge the only one study done in Eldoret in Uasin Gishu County, western Kenya, found a GDM prevalence of 2.6% (Pastakia *et al*., 2017). This study was focused on screening strategies and did not look at the predictors of GDM. Moreover, the lifestyle patterns (in terms of physical activity and dietary habits) in this region are different with that of Kisumu County. The true prevalence and risk factors for GDM in Kenya is not known. These data is needed to inform policy change and device evidence-based interventions for prevention, screening and treatment of GDM. Therefore, the purpose of this study was to determine predictors of GDM among pregnant women with GDM in western Kenya.

Adverse neonatal and obstetric outcomes associated with GDM pose a significant health risk for both the mother and neonates (Natamba *et al*., 2019; Njogu *et al*., 2022). The adverse obstetric outcomes include prolonged labour, hypertension, hyperglycaemia pre-eclampsia, caesarean section, infection and type 2 diabetes mellitus (T2DM), while the adverse neonatal outcomes include macrosomia, birth trauma, neonatal hypoglycaemia, preterm birth, congenital malformations, increased need for admission of neonates in the intensive care units (Muche *et al*., 2019; Natamba *et al*., 2019; Pastakia *et al*., 2017; Stogianni *et al*., 2019). To reduce these adverse neonatal and obstetric outcomes, there is need to maintain optimal levels of blood glucose for pregnant women (Stogianni *et al*., 2019). There is a paucity of data on adverse obstetric and neonatal outcomes in pregnancy complicated by GDM in Kenya. This study was conducted in western Kenya with a GDM prevalence of 2.6% (Pastakia *et al*., 2017). Early screening and detection of GDM before and/or during pregnancy

to ensure good maternal and neonatal outcomes requires of identification of factors that predisposes women with GDM to poor obstetric and neonatal outcomes.

Therefore, the aim of this study was to evaluate the proportion of neonatal and obstetric outcomes among pregnancy complicated with GDM relative to those with pregnancies not complicated by diabetes. All the outcomes were examined for potential predisposing factors such as maternal age, parity, marital status, obesity and weight gain.

1.2 Statement of the problem

Estimate indicate that Kenya has GDM prevalence of 2.6% with the prevalence rapidly increasing (Njogu *et al.,* 2022). In western Kenya, most health facilities do not have adequate technical capacity in terms of laboratories and personal to undertake the GDM test thus posing a huge challenge to pregnant women in terms of missed chances of early diagnosis (Pastakia *et al*., 2017). Moreover, some of the barriers to accessing this service include long distance from hospital and the fact most do not to routinely attend antenatal check-up in fasting state unless and otherwise informed. It is also challenging to convince women to undergo fasting so that they can test GDM test due stigma attached to diseases. Although GDM is fully treatable, early screening and diagnosis of GDM is critical as it informs clinical decision-making including life style changes, nutrition and insulin therapy, and antepartum foetal observation aimed at reducing poor pregnancy-related outcomes associated with GDM (Kouhkan *et al*., 2021; Seah *et al*., 2021). Despite this, the Kenyan Ministry of Health policy has not rolled out screening and treatment of GDM as part of the standard routine antenatal care (ANC) services. Moreover, GDM screening is done through dipstick glycosuria urinalysis, at the 16th week of gestation or at first antenatal care (ANC) visit. But then dipstick urine testing for glucose has challenges. In pregnancy, renal glomerular glucose reabsorption threshold is reduced, resulting to increased glycosuria at some point in about half of all pregnancies. However, hyperglycaemia without detectable glycosuria is not unlikely. Glycosuria being used as a routine screening test could possibly result in missed cases through false negatives resulting to many pregnant women with missed GDM diagnosis presenting adverse maternal and neonatal outcomes such as macrosomia, gestational hypertension, pre-eclampsia, antepartum haemorrhage, caesarean section, preterm birth, birth trauma and congenital anomalies (Pastakia *et al*., 2017). These outcomes are associated with the high morbidity and

mortality among mothers and infants (Njogu *et al*., 2022). Some risk factors including maternal age, maternal BMI, previous bad obstetric history among others have been pointed out to be predictors of GDM world-wide. In Kenya, there is a paucity of studies on the risk factors for GDM and associated pregnancy outcomes. This therefore, means little is understood about GDM and its associated risks factors plus the risk of pregnancy-related outcomes among GDM pregnant women that can inform policy on screening, diagnosis and identification of high-risk population. Consequently, the need to determine the risk factors for gestational diabetes in this setting and its relationship with pregnancy outcomes among women in western Kenya.

1.3 Justification

Several risk factors such as maternal age, maternal BMI, parity and adverse obstetric and neonatal outcomes have been associated with GDM (Muche *et al.,* 2019). However, there is variation on the prevalence of GDM based on population genetics, environment and diagnostic/screening methods (Bawah *et al*., 2019; Njogu *et al.*, 2022; Ye *et al*., 2022), suggesting that context-specific factors may not only influence the risk for GDM but also pregnancy related outcomes. However, in Kenya there is still a paucity of data on the risk factors for GDM and its pregnancy related outcomes. Hence the need for studies that look at the risk factors for GDM and associated pregnancy related outcomes to inform policy on GDM screening among the high-risk population.

1.5 General objective

To investigate on gestational diabetes mellitus risk factors and pregnancy-related outcomes among women attending antenatal clinic at JOOTRH in Kisumu County, western Kenya

1.5.1 Specific objectives

1. To determine gestational diabetes mellitus risk factors among pregnant women with GDM in Kisumu County, western Kenya
2. To evaluate pregnancy outcomes associated with GDM among pregnant women with GDM in Kisumu County, western Kenya
3. To determine the risk factors of pregnancy-related outcomes associated with GDM in Kisumu County, western Kenya

1.5.2 Hypothesis

1. Gestational Diabetes Mellitus is not associated with any risk factor among pregnant women with GDM
2. Gestational Diabetes Mellitus is not associated with pregnancy related outcomes among pregnant women with GDM
3. Gestational Diabetes Mellitus is not a risk factor for pregnancy related outcomes among pregnant women with GDM

1.6. Significance of the study

The results of this study showing that having a diabetic relative, history of caesarean delivery, history of NICU admission and being on IFAS are predictors of GDM. GDM screening should be incorporated in the standard routine ANC services for early detection and timely treatment in order to achieve optimal pregnancy outcomes and preventing complications linked to GDM. There is also need for implementation of lifestyle modification programs such as involvement in physical activity and healthier diet to prevent the development of GDM and obstetric complication being that a majority of cases were overweight. In addition, due to adverse pregnancy outcomes there is need for early screening and management of GDM among the high-risk populations.

1.8 Assumptions, limitations, and delimitations

1.8.1 Assumptions

- Participants understood, comprehended, and followed the instructions given by the researcher.
- Participants answered the questions honestly and to the best of their knowledge.
- Random sampling of women attending ANC clinic is representative of the general population.

1.8.2 Limitations

This study may have been negatively impacted by recall bias of the participants, since women were asked to recall events of their last pregnancy, which may have been months or years back. This was mitigated by abstracting and comparing some information about the study participant's medical records with the information obtained from the questionnaire.

1.8.3 Delimitations

The data for this study was obtained through administration of the data collection instruments by individuals at the facility. These study population consisted of women who had no mental illness attending the Antenatal care and maternity and child health clinics at the facility. Data collection tools were used to obtain data during hospital hours in the hospital.

CHAPTER TWO: LITERATURE REVIEW

2.1 Epidemiology of gestational diabetes mellitus (GDM)

Gestational Diabetes Mellitus (GDM) is a non-communicable disease characterized as glucose or carbohydrate intolerance of variable severity that start at or detected for the first-time during pregnancy (Wang *et al*., 2022). It is a common pregnancy complication accounting for 90% of all pregnancy complicated by diabetes (Buse *et al*., 2020). Increasingly, GDM is becoming a serious public health concern especially in low- and middle-income countries where it leads to maternal and neonatal morbidity and mortality (Njogu *et al.*, 2022). Pregnancy has been demonstrated to deregulate maternal glucose metabolism and insulin sensitivity resulting in maternal hyperglycaemia (Macaulay *et al.*, 2014). Although GDM is commonly diagnosed from 24 to 28 weeks of gestation, maternal hyperglycaemia during early pregnancy is a potential predisposing factor for developing GDM (Popova *et al*., 2016). Hence it is necessary to determine the circulating blood glucose levels early enough to prevent adverse pregnancy outcomes associated with GDM (Quaresima *et al*., 2020).This necessitated the adoption of the International diagnostic and screening criteria for GDM that include performing oral glucose tolerance test (OGTT) in a fasting state by WHO in 2013(WHO, 2013). However, despite the adoption of this criteria, the use of two-step screening and diagnostic methods involving measurement of glucose concentration following 50g glucose challenge test (GCT) and then again after 100g OGTT is still commonly used in various settings (Coustan *et al.,* 2018; Natamba *et al.,* 2019). This lack of uniformity in diagnostic and screening protocols, variations in population genetics and environmental factors have partly contributed to variation in GDM prevalence across regions (Natamba *et al*., 2019).

Global estimates indicate that the prevalence of GDM increased from 381 million in 2013 to 422 million in 2015 and is projected to reach 592million by 2035 (Jaffe *et al*., 2020). Globally, there is context-specific differences in GDM prevalence with prevalence varying from 1% to 28% (Muche *et al*., 2019). Sub-Saharan Africa (SSA) has a prevalence of 14%, North Africa 24.5%, North America 7% and Europe 5.4% (Njogu *et al*., 2022). In Africa, there is also geographic variation in GDM prevalence with North Africa 24.5% and West Africa 14% having a higher prevalence relative to East Africa 6% (Muche *et al*., 2019). Moreover, even within East Africa region there is variation in prevalence with Rwanda with prevalence of 8.3%, Tanzania with a

prevalence of 5. 9%, Ethiopia with a prevalence of 3.7% and western Kenya with a prevalence of 2.6 (Njogu *et al.,* 2022). Among the few studies carried out in Kenya on GDM, prevalence has been demonstrated to range from 1.1% to 16.7% (Pastakia *et al*., 2017; Njogu *et al*., 2022) with significant differences on the methodology used, and the population characteristics thus making it hard to define clearly the magnitude of GDM in Kenya. Recently, evidence indicate that there is an increase in the prevalence of incidences of obesity, diabetes and non-communicable diseases in SSA due to changes in lifestyles such as physical inactivity or not eating healthier diets (Muche *et al*., 2019). This calls for understanding of the aetiological factors of non-communicable diseases such as GDM in order to develop targeted interventions that will limit the burden of the problem and ultimately improve both maternal and neonatal outcomes in SSA.

2.2 Risk factors for GDM

Despite a few data on the predisposing factors for GDM in SSA, previous studies revealed that maternal age, multiparity, weight, history of close relatives having diabetes, being hypertensive, previous delivery of macrosomic infants and previous bad obstetric outcomes such as still birth and abortion are important predisposing factors for GDM (Erem *et al.,* 2015; Natamba *et al*., 2019; Njogu *et al*., 2022). Additionally, baby's birth weight ,smoking, physical inactivity, stature, socioeconomic factors, undernutrition during early life and exposure to Human immunodeficiency virus and tuberculosis prevalent in SSA are important predisposing factors of GDM (Nyirenda, 2016; Quinn *et al.,* 2016; Swisa *et al.,* 2017).

Several factors including a maternal age, history of close relatives having diabetes, previous history of GDM, foetal macrosomia, ethnic origin, pregnancy weight and smoking have been shown to predispose mothers to GDM (Plows *et al.,* 2018; Jaffe *et al*., 2020; Ye *et al*., 2022). It has been shown that history of parental smoking predisposing factors to the development of GDM among their daughters (Bao *et al*., 2016). Genetic studies have revealed that genetic polymorphism plays a critical role in the aetiology of GDM (Huang *et al.,* 2021; Li *et al.,* 2022). Environmental factors such as exposure to certain chemicals such as perfluorooctanoic acid (PFOA), an endocrine disruptor increases GDM risk (Heude *et al.,* 2012; Zhang *et al*., 2015). It has been shown maternal body weight before and during pregnancy, having close relatives with

GDM and polycystic ovarian syndrome (PCOS) are aetiological factors of GDM (Alejandro *et al.,* 2015; Juan *et al.,* 2020).

Evidence indicate that unhealthier or unbalanced diet and lack of physical exercise are crucial factors in the aetiology of GDM (Mijatovic-Vukas *et al*., 2018; Werner *et al.,* 2019; Rasmussen *et al*., 2020). Increased regular physical exercise among women limits the risk of GDM (Mijatovic-Vukas *et al*., 2018; Nelson *et al.,* 2020; Caniglia *et al.,* 2022). Unbalanced diet before and during pregnancy increases the odds of developing GDM (Yamamoto *et al.,* 2018; Rasmussen *et al*., 2020). It has been shown that levels of vitamin D and vitamin C and high fat consumption during pregnancy are critical aetiology factors of GDM (Loy *et al*., 2015;Oiye *et al.,* 2020; Egan *et al.,* 2021). High intake sugar-sweetened beverages, iron intake, processed food, animal fat and animal protein, a diet low in carbohydrate, meat and processed meat, refined grain products, sweets predisposes pregnant women to develop GDM (Chen *et al.,* 2009; Bao *et al.,* 2014; Bao *et al.,* 2016; Ye *et al.,* 2022). However, healthier dietary lifestyles such as consumption of fruits, fresh vegetables, poultry and fish products, nuts and fibre reduces the chances of developing GDM among pregnant women (Zhang *et al*., 2014; Hua *et al.,* 2020). Together, these findings indicate the important roles played by lifestyle factors in the aetiology of GDM among pregnant women.

2.3 Pregnancy-related outcomes

Estimates indicate that 1 in 25 pregnancies are complicated with GDM associated with poor pregnancy-related outcomes (Njogu *et al*., 2022; Akanmode *et al.,* 2022). There is a public health concern with increases in poor pregnancy-related outcomes and effects on the development of children born to mothers with a history of GDM (Stogianni *et al.,* 2019). GDM has also been shown to predispose mothers to have both maternal and neonatal complications, including caesarean delivery, macrosomia and birth trauma (Muche *et al*., 2019; Nguyen *et al.,* 2021). Other effects include shoulder dystocia, birth injuries, neonatal hyperbilirubinemia (Said *et al.,* 2016; Njogu *et al*., 2022). In the current study, these pregnancy outcomes were better categorized as maternal and neonatal outcomes.

2.3.1 Maternal outcomes

Pregnancy can result in a metabolic disorder leading to increased burden of GDM associated with poor pregnancy outcomes such as premature delivery, cesarean delivery and pregnancy induced hypertension (Moon *et al.*, 2022). The other outcomes include prolonged labour, hyperglycemia, risk of respiratory distress syndrome, pre-eclampsia, infection, type 2 diabetes mellitus (T2DM) and advanced gestational age at delivery (Lean *et al.*, 2017; Stogianni *et al*., 2019; Muche *et al.*, 2020; Kouhkan *et al*., 2021; Seah *et al*., 2021). Women with GDM have increased odds of developing T2DM (Beta *et al.*, 2019; Grunnet *et al.*, 2020; Vounzoulaki *et al*., 2020). GDM also increases the risk of postpartum metabolic disorder and cardiovascular disease (Xu *et al*., 2014; Tranidou *et al*., 2021). Normally, perturbed metabolic profiles including elevated cholesterol, triglycerides, high-density lipoprotein cholesterol and being overweight or obese before pregnancy increases the risk of developing GDM (Noussitou *et al.*, 2005; Billionnet *et al.*, 2017). Thus, the increased prevalence of metabolic disorders among overweight and obese women (Catov *et al*., 2020; Rajamoorthi *et al.*, 2022).

Findings from America, France and China revealed that women with GDM have more likelihood of undergoing caesarean delivery (Tian *et al.*, 2014; Kim *et al*., 2015; Billionnet *et al*., 2017; Song *et al.*, 2017). This can be partly attributed to maternal hyperglycemia that result in excessive fetal growth and macrosomia and/or the fact that women with GDM who are at increased risks of adverse neonatal and maternal outcomes are more likely to influence clinical-decision making of medical doctors leading to operative delivery (Gorgal *et al*., 2012; Logakodie *et al*., 2017; Wang *et al.*, 2021; Guo *et al.*, 2022). Additionally, women with GDM are have increased likelihood of presenting with pregnancy induced hypertension (Kong *et al.*, 2019; Basu *et al.*, 2021; Ye *et al*., 2022), associated with poor pregnancy outcomes such as preterm delivery, intrauterine growth restriction, placental abruption, small-for-gestational-age (SGA) infants and risk of perinatal mortality hence the need of caesarean delivery to limit poor pregnancy outcomes in women with pregnancy induced hypertension (Ye *et al.*, 2009; Hwu *et al.*, 2016; Bawah *et al.*, 2019). However, there is need for research to explore the potential underlying mechanisms.

Evidence indicate that inducing labour at 38 or 39 weeks among pregnant women with GDM reduces the risk of caesarean delivery in women who are giving birth for the first time and pregnancy-related hypertension those who have given birth several times (Melamed *et al*., 2016; Souter *et al.,* 2019). However, the odds of neonatal intensive care unit admission are increased if it performed at <39 weeks of gestation (Melamed *et al*., 2016). Hence inducing labour among pregnant women with GDM in clinical setting may be informed by clinical decision making to decrease the chances of caesarean delivery and other poor pregnancy outcomes (Feghali *et al.,* 2016). Increased odds of gestational age at delivery ≥ 40 weeks is common in pregnancy complicated by GDM (Feghali *et al*., 2016), this can result in increased likelihood having foetal macrosomia and consequently caesarean delivery due to increased birth weight with increasing gestational age at delivery (Feghali *et al*., 2016; Wang *et al*., 2021). Apart from poor maternal outcomes, GDM has also been associated with poor neonatal outcomes.

2.3.2 Neonatal outcomes

The poor neonatal outcomes among pregnant women with GDM include of foetal macrosomia, shoulder dystocia, neonatal injury, respiratory distress syndrome, preterm birth, caesarean birth, large for gestational age, neonatal intensive care unit admission, neonatal hypoglycaemia, jaundice, birth status, congenital malformations, neonatal hypoglycaemia and hyperbilirubinemia (Juan *et al.,* 2020; Sun *et al.,* 2020; Ye *et al*., 2022). The congenital malformations is common among mothers with GDM and high maternal BMI (Billionnet *et al*., 2017). It is important to diagnose GDM early so that appropriate management of pregnancy in terms of clinical advice on life style changes, nutritional advice and therapy, insulin therapy and antepartum foetal observation to reduce poor pregnancy outcomes (Cegolon *et al.,* 2020; Kouhkan *et al*., 2021; Seah *et al*., 2021). Although screening and diagnosis of GDM in asymptomatic pregnant women is still a challenge and controversial, healthcare providers need to identify and screen pregnant women predisposed to have GDM earlier using both traditional risk factors and novel biomarkers for efficient management of GDM and associated pregnancy outcomes (Logakodie *et al*., 2017).

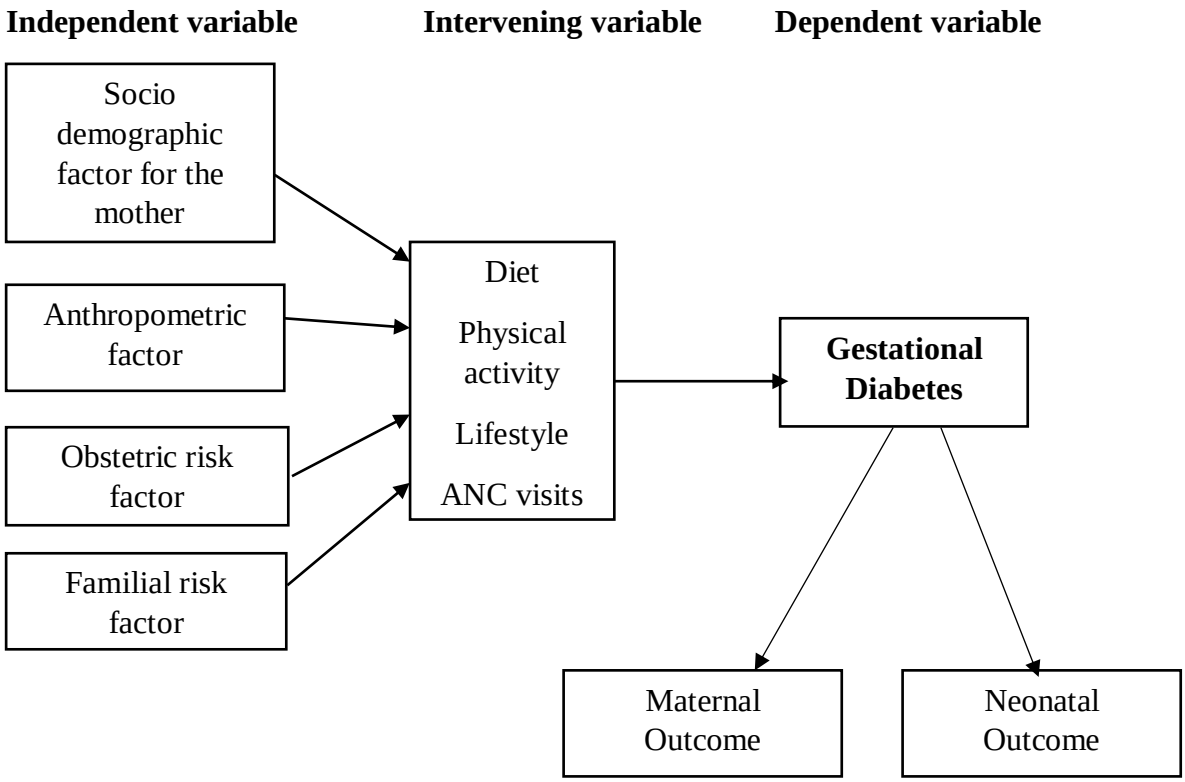
Macrosomia and neonatal admission to intensive care unit are common poor neonatal pregnancy related outcomes in pregnancy complicated with GDM (Srichumchit *et al.,*

2015; Seghieri *et al*., 2020; Wang *et al*., 2021). A study done in Thailand revealed that the rate foetal macrosomia is significantly high among pregnant women with GDM (Srichumchit *et al*., 2015; Quinn *et al.,* 2016; Sweeting *et al.,* 2019). Maternal hyperglycaemia in women with pregnancy complicated with GDM has been demonstrated to lead to excessive foetal growth that leads to macrosomia (Metzger *et al*., 2008; Seghieri *et al*., 2020; Atlaw *et al.,* 2022). Although the underlying pathomechanisms between maternal hyperglycaemia and macrosomia are still unclear, it is possible that maternal hyperglycaemia and insulin resistance lead foetal hyperinsulinemia and increased utilization of nutrients resulting foetal overgrowth and adiposity (Ye *et al*., 2009; Burris *et al.,* 2017; Li *et al*., 2020;). This increased foetal growth leads to macrosomia that can result in shoulder dystocia and increase the likelihood of caesarean delivery (Retnakaran *et al.,* 2017; Tandon *et al*., 2022; Deng *et al.,* 2022). Hence, there is need for public health interventions targeted at controlling maternal hyperglycaemia through engaging in physical exercise, eating healthier and nutritious foods and/or insulin therapy lower the risk of excessive foetal growth and caesarean delivery (Landon *et al*., 2009; Hull *et al.,* 2011; Yang *et al*., 2014).

The role of maternal GDM plays in the development of neonatal respiratory distress syndrome is not well elucidated, but is thought to be due to lack of maturity of lungs especially in preterm births (Mitanchez, 2010; Yee *et al.,* 2015; Billionnet *et al*., 2017). However, pregnant women with GDM who are undergoing insulin-therapy have increased likelihood of giving birth to neonates with neonatal respiratory distress syndrome especially in deliveries after that occur after 37 weeks (Billionnet *et al*., 2017). This may be partly explained by the fact that poor management of GDM delays expression phosphatidylglycerol which is pulmonary surfactant required for poor functioning of lungs in amniotic fluid after 34 weeks of pregnancy leading to dysfunctions of the lungs and respiratory distress in neonates(Piper, 2002;Qiu *et al.,* 2004; Kale *et al.,* 2005). Indeed, it has been shown that mothers with pregnancies complicated GDM and undergoing insulin therapy were more likely to give birth to neonates with respiratory distress syndrome especially if birth took place in after 33 weeks of gestation (Becquet *et al.,* 2015; Chivese *et al.,* 2019).

2.5 Conceptual framework

This conceptual framework shows the interactions between sociodemographic factors such age, BMI, employment status, residence, education level, marital status and clinical factors such as family history of GDM, prior diabetes test, history of caesarean delivery, history of hypertension, having a diabetic relative, induced labour, pre-eclampsia, miscarriage, birth injuries, abortion, macrosomia, neonatal death, still birth, respiratory distress syndrome with GDM.



CHAPTER THREE: MATERIALS AND METHODS

This chapter describes the methods and methodology applied in this study. It captures the study design, the study area, study population, the sampling procedures and the sample size .It also described the instruments that were used in data collection and the collection procedures.

3.1 Study site

The study was carried out at Jaramogi Oginga Odinga Teaching and Referral Hospital (JOOTRH) (Latitude: -0.08890391141913101 Longitude: 34.7702281343219) as shown in the map (*Appendix* I). The JOOTRH is one of the eight main national referral hospitals in Kenya located in Kisumu County. It serves a varied demography of patients from both rural, peri-urban and urban residents in the county and the larger western region of the country. The hospital handles an average of about 40 pregnant women daily who attend antenatal care and maternity and child health clinics during clinic days (Monday to Friday). Data was collected from participants visiting the hospital for antenatal check-ups. Several services are routinely provided at the clinics including PMTCT, screening for hypertension, malaria, anaemia, venereal diseases and urinary tract infections. The hospitals have staff of different carders including consultants, resident doctors, midwives, specialists and nurses. However, there are other services which were not routinely provided including screening and diagnosis for GDM. Approximately, 5 deliveries are conducted in a day. The hospitals have staff of different carders including consultants, resident doctors, midwives, specialists and nurses.

3.2 Study design

This was a hospital-based case-control study design study, employing quantitative data collection methods. The participants with GDM were categorized as (cases) group and those without GDM were in the (control) group. The relevant information was collected from the participants using structured questionnaire, gynaecological files and laboratory examinations.

3.3 Study population

3.3.1 Target population

The target population was all pregnant women attending ANC at JOOTRH.

3.3.2 Sample size determination

This study determined risk factors for GDM, therefore for sample size estimation maternal obesity as a risk factor was used. Sample size calculation was done using a formula for comparing two proportions (Riffenburgh, 2006) with the significance level (α) 0.05 and the power of study being (1-β) of 80%.

$$n = \frac{(z\alpha + z\beta)^2}{(P_0 - P_1)^2} * \mathrm{P}(1 - \mathrm{P})$$

Where:

P_0 =Proportion of women with obesity in Control group 26% (Orero *et al*., 1990)

P_1 = Proportion of women without obesity in Cases group 47%

$Z\alpha 0.05$ = 1.96

$Z\beta 0.80$= 0.84

=84 women

25% non-respondent was added as follows:

n =84+ 21=105

i. Women with GDM and associated risk factors (Cases)

= 105 Women

ii. Women without GDM and associated risk factors (Controls)

= 105 Women

Therefore, a minimum number of women to be sampled is (105×2) = 210 women

3.3.3 Inclusion criteria

All pregnant women who attended JOOTRH (antenatal care clinic, maternity and child health clinics) 18 years or older with singleton pregnancies, have been residents of Kisumu County for the past 12 months, mentally sound between 24 and 36 weeks gestation with a maximal range to 45 weeks, were eligible for inclusion and consented to participate in the study.

3.3.4 Exclusion criteria

The study excluded pregnant women with pre-existing diabetes, multiple gestations, chronic illnesses and/or taking drugs that would affect blood glucose control or pregnancy outcome, those with incomplete blood glucose values and those unwilling to participate. Those who had not resided in Kisumu County for the past 12 months and had not consented to participate in the study.

3.4 Sampling technique

The study used a simple random sampling procedure to select the study participants

3.5 Data collection procedure and research tools

Once pregnant women arrived at the clinic, objectives of the study were explained to all of them and those who fitted in the inclusion criteria were randomly sampled and screened for diabetes.

3.5.1 Screening for GDM

All participants who met the inclusion criteria were advised to eat regular diets and fast on the night prior to the appointment day for testing (not to eat anything after 10 o'clock night with exception to water). After which all the participants were given an appointment within 72hours. All appointments were scheduled for 8-10 o'clock in the morning. The participants underwent universal screening by 2 qualified laboratory technicians who performed a laboratory test (Glucose Oxidase method), which was conducted for Fasting blood glucose (FBG) using a capillary whole blood sample from a finger prick drawn aseptically from the participant and measured using a ONE TOUCH FLEX Plus glucometer machine (UK ProPharma Group, Richmond , UK). FBG: 5.1-6.9 mmol/l (92-125 mg/dl), was considered positive and subjected to oral glucose tolerance test (OGTT) two hours after ingestion of 75 gms of glucose dissolved in 250 ml of water. A blood glucose load of 7.8-11.0 mmol/l (153-199 mg/dl) was considered confirmatory for a GDM case. According to WHO recommendations: (FBG: 5.1-6.9 mmol/l (92-125 mg/dl) and 2-h post 75g oral glucose load 7.8-11.0 mmol/l (153-199 mg/dl). On the same day after diagnosis was completed, participants' both blood pressure and anthropometrical measurements were taken.

3.5.2 Anthropometrical measurements

The anthropometric measurements including height in meters (m) and weight in kilograms (kgs) were measured with the pregnant women wearing light clothes and without shoes. Height measurement were done with the women standing erect, touching the occiput and looking forward to measure with their back, hip, and heels on a straight measuring wall. Weighing machines placed on a flat surface were used to measure the weight of the pregnant women. The two measurements were used to calculate the Body mass index (BMI) dividing weight in (Kg) by height in (m^2). The

BMI was further stratified as <18.5 (underweight), 18.5-24.9 (normal), 25-29.9 (overweight) and > 30 (obese) kg/m^2.

2.5.3 Measurement of blood pressure

To reduce the variation of blood pressure (BP) value with resting blood pressure precaution was taken. If the pregnant mothers were excited they were first requested to rest for approximately 5 minutes in sitting position then BP was measured. The measurement was done by first wrapping an inflatable cuff around the right hand by a clinician. The clinician then inflated the cuff which gently tightened around the arm. The gauge on the cuff then gave the measurement of blood pressure which was then recorded in the mothers booklet.

3.5.4 Data collection

All the participants with abnormal OGTT were followed up to delivery for collection of data regarding delivery mode, maternal and neonatal outcomes, morbidity and mortality. These data on pregnancy outcomes was captured using a checklist (*Appendix* II). Face to face interviews of the study participants by trained research assistants were conducted using a validated structured questionnaire (*Appendix* III). Data was collected for both dependent and independent variables. Additional data such as maternal age and gestational age (in weeks) were collected from the mother-baby booklet. All the study participants had the clinic attendance booklets. The data collection considered a ratio of 1:1 (Cases : Control).Once a case was identified the immediate following participant who was a control was included. Data collection from all chosen participants continued until the sample size was reached for both cases and controls.

3.6 Study variables

3.6.1 Study variables for risk factors of GDM

The dependent variable was GDM. Upon enrolment in the study, the independent variables included anthropometric and sociodemographic data obtained using a structured questionnaire. The variables in this study consisted of both dependent variable GDM and independent variables: ***Socio demographic variables*** including mother-age, marital status, residence, educational level, occupational status of the women, monthly income of women and history of chronic infections; ***Anthropometrical factors*** including height, pregnancy weight gain, Body Mass Index (BMI); ***Obstetric factors*** such as parity and obstetric history (history of caesarean or

macrosomic delivery, abortion, stillbirth, history of miscarriage, history of infertility); ***Familial risk factors*** including previous history of GDM, previous history of diabetes and family history of hypertension; and ***Bio-chemical factors*** including history of glycosuria Fasting blood glucose (FBG) and oral glucose tolerance test (OGTT).

3.6.2 Study variables for pregnancy-related outcomes among pregnant women with GDM

Maternal characteristics assessed include age (years), type of diabetes (GDM) vs. no diabetes), employment was defined as employed or unemployed. Marital status was defined as married or unmarried, miscarriages, previous episodes of GDM, hypertension, BMI at first visit,), premature rapture of membrane. The maternal/neonatal outcomes investigated were induction of labour, gestational hypertension, frequency of abortion, gestational age at delivery, miscarriages, pre-eclampsia, neonatal death, congenital malformations, pre-term delivery (<37 weeks), vaginal/ caesarean delivery, macrosomia (birth weight >4500g), neonatal hypoglycaemia, hyperbilirunemia, respiratory distress syndrome, foetal injury, shoulder dystocia, neonatal intensive care admission.

3.7 Validity and Reliability

Face validity was done on the questionnaire. It was reviewed by three women, one health educator, and two lay persons both of whom were above 18 years and could read and write in English, were randomly chosen from the communities in Kisumu County. The questionnaire was revised accordingly. Content validity, was initially done by an epidemiologist who keenly reviewed the questionnaire and then revised accordingly. The draft questionnaire was then finalized for use. The checklist on other hand was reviewed by both a gynaecologist, midwife and paediatric nurses to make the items clear, and was checked to ensure content of the questions. After Ethical approval, pilot testing of the questionnaire was conducted in another health facility outside Kisumu County by the researcher and research assistants who verbally translated the questions in the questionnaire to Kiswahili for respondents that couldn't speak English thus ensuring the reliability of the tools. This was to identify gaps and the questions modified appropriately to ensure that respondents clearly understood what they were being asked. Data from both the questionnaire and checklist was double entered by the researcher and the assistants to reduce errors. The laboratory test results were double checked by two laboratory technicians by both overseeing each other's work for quality assurance.

3.7 Data management and analysis

3.7.1 Data management

Completed questionnaires were secured safely in locked cabinets and could only be accessed by the study staff. Data was then entered and saved in password restricted netbooks and accessed and used only by the study personnel without revealing the identities of individual participants. Data was downloaded daily from the netbooks into the hard disks and then transferred to the computer for cleaning. Cleaned data was stored electronically in the server with restricted access to only those concerned with handling the data.

3.7.2 Data analysis

The data from each participant was entered into an Excel spreadsheet. The data was cleaned to check for inconsistencies or double/wrong entries. Thereafter, transferred into SPSS version 23.0 for Windows. Both descriptive and inferential statistics were employed. Pearson Chi-square and Fisher's exact test were used for comparison of categorical variables between groups. Binary regression was performed with all variables with GDM as the dependent variable, yielding crude odds ratios (cOR) with 95% Confidence Interval (CI). All binary variables were tried in univariate regression analysis. Variables with p-value <0.25 for the specific outcome were included in multiple regression models with dependent variable for adjusted odds ratios (aOR). p-value≤0.05 was considered significant. The statistical analysis was carried out with SPPS (Statistical Package for the Social Sciences, Chicago, Illinois, version 23).

3.8 Ethical Considerations

Approval for this study was sought from Jaramogi Oginga Odinga University of Science and Technology Board of Postgraduate studies (*Appendix* IV). Ethical approval was sought from JOOTRH Ethics Review Committee (Approval Number: IERC/JOOTRH/220/2020) (Appendix V). Informed consent was sought from all the study participants using an approved consent form (Appendix V1). Privacy and confidentiality of the study participants and all raw data was strictly observed.

CHAPTER 4: RESULTS

This chapter presents the results based on each study objectives.

4.1 Risk factors for GDM

4.1.1 Sociodemographic and clinical characteristics of the study populations

The sociodemographic characteristics of study participants with GDM and those without GDM included in the study are given in Table 4.1. A total of 210 pregnant women (105 cases with GDM and 105 controls without GDM) were enrolled in this study. A majority of participants with GDM were in 30-34 years age group (54, 51%), married (79, 75%), had secondary education (54, 52%) and unemployed (37, 36%). In table 4.2, several participants were overweight with a BMI of 25-29.9 kg/m^2 (59, 56%), had no prior diabetes test (88, 84%), had history of hypertension (56, 53%), had hypertensive relatives (67, 64%), had no diabetic relative (65,62%) and had a history of glycosuria (67, 64%). Similarly in table 4.3, numerous women were multiparous (72, 69%), had history of caesarean delivery (CS) (64,61%), history of macrosomic delivery (66,63%) and history of intensive care unit (ICU) admission (56, 53%).

Pearson Chi-square and Fisher's exact test results revealed the prevalence of GDM increased with age ($p<0.001$), with highest prevalence in 30-34 (51%) and ≥35 (47%) year-old age groups. An association was observed between the prevalence of GDM with marital status ($p=0.038$), education level ($p=0.033$) and employment status ($p<0.001$). When BMI was considered, a positive association was observed between pregnancy BM1 and GDM ($p<0.001$). The prevalence of GDM increased with pregnancy BMI. The prevalence was highest in overweight (25-29.9 kg/m^2) group.

Diabetes mellitus was associated with women with history of hypertension ($p<0.001$), history of hypertensive relative ($p<0.001$), history of a diabetic relative ($p<0.001$) and history of glycosuria ($p<0.001$). GDM was more prevalent in multiparous women ($p<0.001$), those with history of miscarriage ($p=0.007$), history of CS ($p<0.001$), history of macrosomic delivery ($p<0.001$), history of neonatal intensive care unit admission (NICU) ($p<0.001$).

Table 4.1 Sociodemographic characteristics of the participants (n=210)

	Gestational Diabetes Status		
Variable	GDM = 105	no GDM=105	χ^2 p-value
Age in years			**<0.001**
<25	1(0.9)	41(39)	
25-29	1 (0.9)	48 (45.7)	
30-34	54 (51.4)	16 (15.2)	
≥35	49 (46.7)	0 (0%)	
Marital Status			**0.038**
Married	79 (75.2%)	82 (78%)	
Unmarried	26 (24.8%)	23 (21.9%)	
Residence			0.076
Rural	28 (26.7%)	35 (33.3%)	
Urban	39 (37.1%)	46 (43.8%)	
Peri-urban	38 (36.2%)	24 (22.9%)	
Education level			**0.033**
None	0 (0%)	1 (1.0%)	
Primary	28(26.7%)	16 (15.2%)	
Secondary	54 (51.4%)	70 (66.7%)	
Tertiary	23 (21.9%)	18 (17.1%)	
Employment status			**<0.001**
Employed	72 (68.6%)	41 (39%)	
Unemployed	33 (31.4%)	64 (61%)	

Table 4.2 Clinical characteristics of the participants (n=210)

	Gestational Diabetes status		
Variable	GDM = 105	no GDM=105	χ^2 p-value
BMI			**<0.001**
<18.5(Underweight)	0 (0%)	0 (0%)	
18.5-24.9(Normal)	18 (17.1%)	65 (61.9%)	
25-29.9 (Overweight)	59 (56.2%)	40 (38.1%)	
>30(Obese)	28 (26.7%)	0 (0%)	
Prior diabetes test			**0.003**
Yes	17 (16.2%)	7 (6.7%)	
No	88 (83.8%)	98 (93.3%)	
Chronic disease			>0.9
Yes	0 (0%)	0 (0%)	
No	105 (100%)	105 (100%)	
On IFAS			**<0.001**
Yes	99 (94.3%)	45 (42.9%)	
No	6 (5.7%)	60 (57.1%)	
History of hypertension			**<0.001**
Yes	56 (53.3%)	19 (18.1%)	
No	49 (46.7%)	86 (81.9%)	
Hypertensive relative			**<0.001**
Yes	67 (63.8%)	20 (19%)	
No	38 (36.2%)	85 (81%)	
History of glycosuria			**<0.001**
Yes	67 (63.8%)	0 (0%)	
No	38 (36.1%)	105 (100%)	
Diabetic relative			**<0.001**
Yes	40 (38%)	4 (3.8%)	
No	65 (62%)	101 (96.2%)	

BMI: Body Mass Index, IFAS: iron-folic acid supplementation

Table 4.3 Gynecological characteristics of the participants (n=210)

	Gestational Diabetes status		
Variable	GDM = 105	no GDM=105	χ^2 p-value
Parity			**<0.001**
Nulliparous (0)	12(11.4%)	25 (23.8%)	
Primiparous (1)	21(20%)	32(30.5%)	
Multiparous (2+)	72(68.6%)	48(45.7%)	
History of infertility			0.2
Yes	9 (8.6%)	7 (6.7%)	
No	96 (91.4%)	98 (9.3%)	
History of miscarriage			**0.007**
Yes	8 (7.6%)	0 (0%)	
No	97 (92.4%)	105 (100%)	
History of Cesarean delivery			**<0.001**
Yes	64 (61%)	13 (12.4%)	
No	41 (39%)	92 (87.6%)	
History of assisted delivery			>0.9
Yes	0 (0%)	0 (0%)	
No	105 (100%)	105 (100%)	
History of still birth			0.062
Yes	5 (4.8%)	0 (0%)	
No	100 (95.2%)	105 (100%)	
History of Neonatal death			0.12
Yes	4 (3.8%)	0 (0%)	
No	101 (96.2%)	105 (100%)	
History of Macrosomic delivery			**<0.001**
Yes	66 (62.9%)	16 (15.2%)	
No	39 (37.1%)	89 (84.8%)	
History of NICU admission			**<0.001**
Yes	56 (53.3%)	7 (6.7%)	
No	49 (46.7%)	98 (93.3%)	

NICU: neonatal intensive care unit admission

4. 1. 2 Risk factors for Gestational diabetes

To establish the independence of these variables binary logistic regression analysis was performed. As shown in Table 4.4, univariate analysis revealed women with a diabetic relative were more likely to have diabetes relative to those without (Crude Odds Ratio (cOR) 28, [95CI: 8.2-176], p<0.001), those with hypertensive relative were more like to have GDM relative to those without (cOR 7.9, [95%CI: 4.2-15.6], p<0.001), those who had prior diabetes test were likely to have GDM relative to those without prior diabetes test (cOR 5.8, [95%CI:1.9-25.4], p<0.001). When parity was considered, those who were primiparous (cOR 1.3, [95%CI: 0.5-3.2], p<0.001) and multiparous (cOR 3.5, [95%C: 1.6-8.1], p<0.001) were likely to have GDM relative to those who were nulliparous. Those with history of infertility were more like to have GDM relative to those without although not statistically significant (cOR 2.1, [95%CI: 0.7-7.9], p<0.22). The results reveal that those with history of hypertension were more likely to have GDM relative to those without (cOR 5.5, [95%CI: 2.9-10.9], p<0.001). Similarly, those with history of CS delivery (cOR 13, [95%CI: 6.3-29.2], p<0.001), on IFAS (cOR 21.9, [95%CI: 9.3-60.5], p<0.001), history of macrosomic delivery (cOR 10.4, [95%CI:5.3-21.9], p<0.001), history of NICU admission (cOR 20.1, [95%CI: 8.2-60.6], p<0.001) were more likely to have GDM relative to those without.

Multivariate analysis revealed that those with diabetic relative were more likely to have GDM relative to those without (Adjusted OR (aOR) 7.4, [95%Ci: 1.2-76], p=0.049), those with history of CS delivery were more likely to have GDM relative to those without (aOR 7, [95%CI: 1.6-35.9], p<0.014). Although statistically not significant the analysis revealed that those with hypertensive relative were more likely to have GDM than those without (aOR 1.1, [95%CI: 0.3-4], p=0.900). Those with prior diabetes test were more likely to have GDM relative to those without though not statistically significant (aOR 3.5, [95%CI: 0.6-25.3], p=0.200). Similarly, those with macrosomic delivery were more likely to have GDM than those without though not statistically significant (aOR 1.3, [95%CI: 0.3-6.6], p=0.700). Those on IFAS were more likely to have GDM relative to those not on IFAS (aOR 16.6, [95%CI: 5-69.2], p<0.014). Further analysis revealed that those with history of NICU admission (aOR 15, [95%CI: 3.5-86.9], p<0.001) were more likely to have GDM relative to those without.

Table 4.4. Risk factors for Gestational diabetes

	Univariate analysis			Multivariate analysis		
Variable	cOR[1]	95% CI[1]	p-value	aOR[1]	95% CI[1]	p-value
Diabetic Relative			<0.001			
No	*Ref.*	—		*Ref.*	—	
Yes	28.0	8.20, 176		8.09	1.44, 73.0	**0.031**
On IFAS			<0.001			
No	*Ref.*	—		*Ref.*	—	
Yes	21.9	9.33, 60.5		13.0	4.37, 47.8	**<0.001**
History of NICU admission			<0.001			
No	*Ref.*	—		*Ref.*	—	
Yes	20.1	8.23, 60.6		13.9	3.45, 70.5	**<0.001**
History of caesarean delivery			<0.001			
No	*Ref.*	—		*Ref.*	—	
Yes	13.0	6.26, 29.2		5.02	1.42, 19.5	**0.015**

cOR: crude odds ratio. aOR: adjusted odds ratio, CI: Confidence Interval, IFAS: iron-folic acid supplementation and NICU: neonatal intensive care unit admission

4.2 Maternal and neonatal outcomes associated with GDM

4.2.1 Maternal outcomes associated with GDM

As shown in Table 4.5, the proportion of women who delivered below 39 weeks of gestation n= 82(78.9%) and n=23(21.9%) that were delivered beyond the 40 weeks of gestation, n=35(33%) had pregnancy-induced hypertension, half of the women n=56(53%) had caesarean delivery, while n=40(38%) were induced with labour in the current pregnancy. Though, no significant statistically premature delivery was n= 5 (4.8%), premature rapture of the membrane n=3 (2.9%), intensive care admission n=3 (2.9%), pre-eclampsia n= 16(15%) and no cases of miscarriages were recorded among the study participants with GDM in the current pregnancy.

As shown in Table 4.5, Pearson Chi-square and Fisher's exact test revealed that GDM was associated with gestational age at delivery≥40 weeks, Caesarean Delivery, induced labour , pregnancy-induced hypertension (all p<0.001).

Table 4.5. Maternal outcomes associated with GDM

	Gestational Diabetes Status		
Variable	GDM = 105	No GDM = 105	χ^2 p-value
Gestation age at delivery (weeks)			**<0.001**
<39	82 (78%)	94 (89.5%)	
≥40	23 (21.9%)	11 (10%)	
Caesarean Delivery			**<0.001**
Yes	56 (53%)	15 (13%)	
No	49 (47%)	90 (87%)	
Induced Labour			**<0.001**
Yes	40 (38%)	17 (16%)	
No	65 (62%)	88 (84%)	
Pregnancy-induced hypertension			**<0.001**
Yes	35 (33%)	4 (2.2%)	
No	70 (67%)	101 (98%)	

4.2.2 Multivariate analysis of maternal outcomes associated with GDM

From table 4.6, univariate analysis revealed that gestational age at delivery ≥ 40 weeks (Crude Odds Ratio (cOR) 1.48, 95% CI 1.22- 1.83, p<0.001), caesarean delivery (cOR 7.71. 95% CI 3.87-16.4, p<0.001), induced labour (cOR 3.20, 95%CI 1.65-6.46, p<0.001), pregnancy induced hypertension (cOR 22.7, 95%CI 6.63-143, p<0.001) were the maternal outcomes associated with GDM. Multivariate logistic regression analysis indicate that gestational age at delivery ≥ 40 weeks (Adjusted Odds Ratio (aOR) 1.67, 95% CI 1.29-2.21, p<0.001), caesarean delivery (aOR7.28, 95%CI 3.17-18.0,p<0.001), induced labour (aOR 4.60, 95%CI 2.07-10.8, p<0.001) and pregnancy induced hypertension (aOR15.2, 95%CI 3.92-103,p<0.001) were significantly associated with GDM.

Table 4.6 Multivariate analysis of maternal factors associated with GDM

	Univariate analysis			Multivariate analysis		
Variable	cOR	95%CI	P-value	aOR	95%CI	P-value
Gestation age at delivery (weeks)			**<0.001**			
≤ 39	*Ref*	—		*Ref*	—	
≥ 40	1.48	1.22, 1.83		1.67	1.29, 2.21	**<0.001**
Caesarean Delivery			**<0.001**			
No	*Ref*	—		*Ref*	—	
Yes	7.71	3.87, 16.4		7.28	3.17, 18.0	**<0.001**
Induced Labour			**<0.001**			
No	*Ref*	—		*Ref*	—	
Yes	3.20	1.65, 6.46		4.60	2.07, 10.8	**<0.001**
Pregnancy-induced Hypertension			**<0.001**			
No	*Ref*	—		*Ref*	—	
Yes	22.7	6.63, 143		15.2	3.92, 103	**<0.001**

4.2.3 Neonatal outcomes associated with GDM

As shown in Table 4.7, majority of the neonates were unhealthy in terms of their birth status n=80 (76%), 70% were macrosomic (n=74) and n=1(0.5%) dead. A number of the neonates experienced neonatal hypoglycemia n=15(14%), n=37(35%), experienced respiratory distress syndrome, n= 11(10%) shoulder dystocia, n=9 (8.6%) had jaundice and n=31(30%) were admitted in the neonatal intensive care unit (NICU) with two thirds of the neonates being male n=69(66%) compared to females n=36(34%) in the current pregnancy. The number of neonates did experience fetal injury n=1(1.0%), n=1(1.0%) experienced hyperbilirunemia. Perinatal death n=1(1.0%) and Still birth n=3(2.9%) was observed. No congenital malformations, abortion and neonatal death were recorded among the outcomes in the current pregnancy. Pearson's Chi-square and Fischer's exact test analysis of neonatal outcomes associated with GDM revealed that macrosomia, respiratory distress syndrome **(**RDS), neonatal hypoglycaemia, fetal injury, shoulder dystocia, neonatal intensive care unit

admission, jaundice and birth status (all p<0.001) were significantly associated with GDM.

Table 4.7. Neonatal outcomes associated with GDM

	Gestational Diabetes Status		
Variable	GDM = 105	no GDM = 105	p-value
Sex of the baby			**0.03**
Male	69 (66%)	51 (49%)	
Female	36 (34%)	54 (51%)	
Macrosomia			**<0.001**
Yes	74 (70%)	12 (9.7%)	
No	31 (30%)	93 (90%)	
Neonatal Hypoglycemia			**<0.001**
Yes	15 (14%)	0 (0%)	
No	90 (86%)	105 (100%)	
RDS			**<0.001**
Yes	37 (35%)	3 (1.1%)	
No	68 (65%)	102 (99%)	
Shoulder dystocia			**0.001**
Yes	11 (10%)	0 (0%)	
No	94 (90%)	105 (100%)	
NICU admission			**<0.001**
Yes	31 (30%)	3 (2.2%)	
No	74 (70%)	102 (98%)	
Jaundice			**0.004**
Yes	9 (8.6%)	0 (0%)	
No	96 (91%)	105 (100%)	
Birth status			**<0.001**
Healthy	24 (23%)	100 (97%)	
Unhealthy	80 (76%)	5 (3.2%)	

NICU: Neonatal Intensive Care Unit, RDS: Respiratory distress syndrome

4.2.4 Multivariate analysis of neonatal outcomes associated with GDM

Univariate analysis of neonatal outcomes associated with GDM revealed that GDM was significantly associated with the neonate being male (cOR 1.96, 95%CI 1.11-3.49, p<0.02), having macrosomia (cOR 22.3, 95%CI 10.4- 52.8, p<0.001) and neonatal intensive care admission (cOR 19.1, 95%CI 5.52- 120, p<0.001).

As shown in Table 4.8, Multivariate analysis revealed that fetal macrosomia (aOR 22.5, 95%CI 9.42-59.3, p<0.001) and neonatal admission to intensive care unit (aOR 16.2, 95%CI 3.73, 115, p<0.001) were significantly associated with GDM.

Table 4.8 multivariate analysis of neonatal outcomes associated with GDM

Variable	cOR	95% CI1	p-value	aOR	95% CI1	p-value
Macrosomia			**<0.001**			
No	*Ref*	—		*Ref*	—	
Yes	22.3	10.4, 52.8		22.5	9.42, 59.3	**<0.001**
NICU admission			**<0.001**			
No	*Ref*	—		*Ref*	—	
Yes	19.1	5.52, 120		16.2	3.73, 115	**<0.001**

cOR: crude odds ration; aOR: adjusted odds ratio; CI: confidence interval and NICU: neonatal intensive care unit

4. 3 Risk factors for caesarean and macrosomic delivery among women with GDM

4.3. 1 Risk factors for Caesarean delivery among women with GDM

In this study a higher proportion of women had a history of caesarean delivery (64, 61%). As presented table 4.9 , the univariate analysis revealed women who were older age between 30-34 years (Crude Odds ratio (cOR)5.60, 95%CI 1.95- 20.4, p<0.001) and 35-39 years (cOR10.7, 95%C I3.57-40.0, p<0.001), employed (cOR 3.47, 95%CI, 1.86-6.66 , p<0.001), overweight (cOR 2.46, 95%CI 1.25- 4.99, p< 0.006), obese (cOR 3.69, 95%CI 1.47-9.44, p<0.006), had diabetic relatives (cOR 5.80, 95%CI 2.83-12.4, p<0.001), had relatives with blood pressure (cOR 11.3, 95%CI 5.73-23.4,p<0.001) and had high glucose levels (cOR 7.71, 95%CI 3.87, 16.4, p<0.001) were significantly more likely to have caesarean delivery.

Multivariate logistic regression analysis revealed that having a relative with a high blood pressure was significantly associated with cesarean delivery among women with GDM (aOR 5.89, 95%CI 2.69-13.3, p<0.001). Though not statistically significant, further analysis revealed that women with GDM aged between 30-34 years (aOR 1.72, 95%CI 0.45-7.67, p<0.8) and 35-39 years (aOR 1.07, 95%CI 0.10-9.16, p<0.9), who were employed (aOR 1.56,9 0.71- 3.55, p<0.3), who were overweight (aOR 1.22, 95% CI 0.47- 3.14, p<0.7), who were obese (aOR 1.98, 95% CI 0.29-3.34, p<0.9), had diabetic relatives (aOR 1.53, 95% CI 0.61-3.87, p<0.4) and had glycosuria (aOR 4.56, 95% CI 0.81-39.7, p<0.11) were more likely to undergo cesarean delivery.

Table 4.9 Multivariate logistic regression analysis of risk factors for caesarean delivery among women with GDM

	Univariate analysis			Multivariate analysis		
Variable	cOR	95% CI[1]	p-value	aOR	95% CI[1]	p-value
Hypertensive relative			**<0.001**			
No	*Ref*	—		*Ref*	—	
Yes	11.3	5.73, 23.4		5.89	2.69, 13.3	**<0.001**

cOR: crude odds ratio; aOR: adjusted odds ratio; CI: confidence interval; Ref: reference; GDM; gestational diabetes mellitus

4.3.2 Risk factors of macrosomic delivery among women with GDM

This study looked at the risk factors of macrosomic delivery among women with GDM. From univariate analysis in Table 4.10, women with GDM, who were aged between 30-34 years (cOR 3.91, 95%CI 1.57- 10.8, p<0.001) and 35-39 years (cOR 7.80, 95%CI 2.96-22.9, p<0.001), employed (cOR 7.99, 95%CI 4.15,-16.2, p<0.001), overweight (cOR 1.92, 95%CI 1.00-3.73, p<0.001), obese (cOR 6.87, 95%CI 2.70-19.0, p<0.001), had a diabetic relative (cOR 7.42, 95%CI 3.48-17.1, p<0.001) and glycosuria (cOR 10.4, 95%CI 5.27-21.9, p<0.001) were significantly more likely to have macrosomic delivery.

Multivariate logistic regression analysis revealed that women with GDM who were employed (aOR 8.05, 95%CI 3.31, 21.1, p<0.001), those with relatives with high blood pressure (aOR 10.9, 95%CI 4.47, 28.6, p<0.001) and had glycosuria (aOR 12.2, 95%CI 1.34-329, p<0.05) were significantly more likely to have macrosomic delivery. Though not statistically macrosomic delivery was associated with age between 30-34 years

(aOR 1.16, 95%CI 0.01-1.55, p<0.2), 35-39 years (aOR 1.27, 95%CI 0.01-3.36, p<0.4), were overweight (aOR 1.47, 95%CI 0.15-1.35, p<0.2), obese (aOR 1.80, 95%CI 0.42-8.18, p<0.4) and having a diabetic relative(aOR 1.81, 95%CI 0.27-2.37, p<0.7).

Table 4.10. Multivariate logistic regression analysis of risk factors for fetal macrosomia in women with GDM

	Univariate analysis			Multivariate analysis		
Variable	cOR	95% CI[1]	p-value	aOR	95% CI[1]	p-value
Employment Status			**<0.001**			
Unemployed	*Ref*	—		*Ref*	—	
Employed	7.99	4.15, 16.2		8.05	3.31, 21.1	**<0.001**
Hypertensive relative			**<0.001**			
No	*Ref*	—		*Ref*	—	
Yes	14.1	7.21, 29.1		10.9	4.47, 28.6	**<0.001**
Glycosuria			**<0.001**			
No	*Ref*	—		*Ref*	—	
Yes	10.4	5.27, 21.9		12.2	1.34, 329	**0.05**

cOR: crude odds ratio; aOR: adjusted odds ratio; CI: confidence interval; Ref: reference; GDM; gestational diabetes mellitus

CHAPTER 5: DISCUSSION

This chapter discusses the results per objectives of the study

5.1 Risk factors for GDM

This study examined the risk factors for GDM among pregnant women with GDM in western Kenya. The comparator were women without GDM . In the present study, 56% of the GDM women were overweight with a BMI of 25-29.9kg/m^2 and 26% were obese with BMI ≥30 kg/m^2, whereas 61% of women in the control group without GDM had normal BMI of while 40% were overweight. This study found that found an association between pregnancy BMI and GDM. This is consistent with previous observations linking GDM to maternal BMI (Muche *et al*., 2019; Stogianni *et al*., 2019; Egan *et al*., 2021). This may be due to suppressed insulin sensitivity among women who are overweight or obese resulting in maternal hyperglycaemia (Nelson *et al*., 2010) or due to lack of physical exercise by overweight and obese women (Muche *et al*., 2019). Significantly the increase in prevalence of overweight among women with pregnancies not complicated by diabetes is of great public health concern as it suggests that there will rise in GDM cases in the future in this region. Hence, there need for lifestyle interventions such as eating healthier and nutritious food, engaging in physical exercise and early detection of GDM that will ultimately lead to reduction of the risk of being overweight or obsess (Heude *et al*., 2012; Stogianni *et al*., 2019).

Pregnant women with pregnancies complicated with GDM tend to have advanced age and advanced maternal age increased the likelihood of having GDM. These findings are in agreement with studies from various countries globally that demonstrated an association between GDM and advanced maternal age (Karcaaltincaba *et al.,* 2009; Erem *et al.,* 2015; Stogianni *et al*., 2019; Njogu *et al*., 2022). This is probably due to the fact that mothers with advanced maternal age have given birth severally, pregnancy is known to initiate metabolic disorders such as increased insulin resistance and may result in obesity (Mdoe *et al.,* 2021). Poor obstetrical outcomes such as increased risk of CS and GDM is linked to advanced maternal age due to increase foetal growth in hyperglycaemic mothers (Mdoe *et al*., 2021). Hence maternal age should be considered when providing reproductive health care services especially screening for GDM during ANC visits.

The current study found that 61% of the women with GDM had a history of CS delivery in comparison to 11% of women without diabetes. This is in line with findings that CS is an adverse pregnancy outcome associated with GDM due to foetal macrosomia (Muche *et al*., 2019; Njogu *et al*., 2022). Similar findings of increased rate of operative deliveries among women with pregnancies complicated have been reported (Stogianni *et al*., 2019; Njogu *et al*., 2022). The rise in the CS is a serious public health challenge given that CS is associated with haemorrhage, intra-abdominal adhesion and mortality among pregnant women and development of allergic reaction or poor developmental outcomes in children (Huang *et al*., 2021;Ye *et al*., 2022). Hence there is a need to formulate and implement interventions geared towards reducing the rate of CS. Further analysis revealed that history of CS is a predictor of GDM suggesting that history of CS can be included in the algorithm for identification of pregnant women at high risk for GDM and interventions targeting this population for screening need to be put in place.

This study demonstrated that family history of diabetes increases the odds of having GDM. Similar observation has been reported in Tanzania, Turkey, Iran and USA (Muche *et al*., 2019; Mdoe *et al*., 2021). Increased risk for GDM has been associated with inheritance of genetic receptor B_3-adrenergic genes linked to weight gain and resistance from one generation to the next (Alejandro *et al*., 2015; Mdoe *et al*., 2021). Moreover, familial inheritance of genetic defects that cause β cell dysfunctions such as deregulated insulin production that lead to hyperglycaemia, insulin intolerance and development of diabetes (Alejandro *et al*., 2015; Swisa *et al*., 2017; Ye *et al*., 2022). Although this study did not look at the genetic factors, these findings suggest family history of diabetes is a predisposing factor to develop GDM and women with this history should be considered to be at high risk and prioritized for screening especially in poor countries where resources for universal screening are unavailable.

To prevent poor pregnancy-related outcomes due to iron and folic deficiencies, the WHO recommends that pregnant women should be given daily iron and folic supplementation (WHO, 2013). Based on this several countries including Kenya have included IFAS in ANC services (Oiye *et al.,* 2020). However, studies have shown associations between IFAS and the likelihood of developing GDM among pregnant women (Huang *et al*., 2019; Caniglia *et al*., 2022), with increased risk associated to taking IFAS for a longer period and/or taking higher doses (Huang *et al*., 2019). More

importantly, those using IFAS have higher GDM risk relative to non-users (Hua *et al*., 2020). Similar to this finding this study also demonstrate that being on IFAS is a predictor of GDM. Although the mechanisms underlying associations between IFAS and GDM is not known, it has been shown that elevated levels of unmetabolized folic acid can downmodulate natural killer cell immune responses and results into infiltration of β-cell in GDM (Swisa *et al.,* 2017). This finding indicate that there is need for large-scale epidemiological studies cohort studies to look at the of long-term effects of IFAS on GDM. This will lead to formulation optimal evidence-based nutrition interventions during pregnancy that will result in excellent pregnancy-related outcomes.

Another finding from the current study is that the proportion of women with history of neonatal intensive care unit admission was higher 53% among women with pregnancies complicated with GDM relative to 5.4% among women without diabetes. Further analysis revealed that having a history of NICU admission is a predictor of GDM. NICU admissions have been previously associated with maternal pregnancy BMI and CS (Quinn *et al*., 2016; Werner *et al*., 2019) that are also predictors of GDM. In addition, parity increases the likelihood of having both GDM and risk of NICU (Werner *et al*., 2019), suggesting that there is interaction between these factors.

5.2 Maternal and neonatal outcomes associated with GDM

Optimal management and clinical decision-making including life style changes, nutrition, hormonal therapy and antepartum foetal observation aimed at reducing adverse pregnancy outcomes associated with GDM are dependent on early diagnosis of GDM (Kouhkan *et al*., 2021; Seah *et al*., 2021). Currently there are a lot of challenges regarding screening and diagnosis of asymptomatic pregnant women for GDM, this despite the need of healthcare providers to identify and screen at risk pregnant women for GDM earlier for effective and efficient management of GDM and associated pregnancy-related outcomes (Logakodie *et al*., 2017). Therefore, this study evaluated the relationship between GDM and the associated risk factors of pregnancy-related outcomes among pregnant women attending ANC clinic at JOOTRH. The study found that gestational age at delivery ≥ 40 weeks, caesarean delivery, induced labour and pregnancy induced hypertension were significantly associated with GDM. This is similar to previous observations that GDM increases the odds of prolonged labour, caesarean delivery, pregnancy induced hypertension and gestational age at delivery (Lean *et al*., 2017; Stogianni *et al*., 2019; Muche *et al*., 2020; Kouhkan *et al*., 2021; Seah

et al., 2021). In addition, GDM increases the likelihood of macrosomia, respiratory distress syndrome **(**RDS), neonatal hypoglycaemia, foetal injury, shoulder dystocia, neonatal intensive care unit admission, jaundice and birth status. With GDM being an independent predictor of foetal macrosomia and neonatal admission to intensive care unit. This is consistent with previous studies showing increased odds of foetal macrosomia, shoulder dystocia, neonatal trauma, respiratory distress syndrome and increased admission to neonatal intensive care units among neonates born to mothers with pregnancy complicated by GDM (Chivese *et al.*, 2019; Muche *et al*., 2020; Kouhkan *et al*., 2021; Seah *et al*., 2021; Atlaw *et al*., 2022).

For poor maternal outcomes, women with GDM had increased chance of gestational age at delivery ≥ 40 weeks, caesarean delivery, induced labour and pregnancy induced hypertension in line with similar observations (Logakodie *et al*., 2017; Muche *et al*., 2020; Ye *et al*., 2022). In this study, observation that GDM increases the risk of CS delivery is in agreement with observations from the United States of America, France and China that demonstrated that increased rate of caesarean delivery among pregnant women with pregnancies complicated with GDM (Kim *et al*., 2015; Billionnet *et al*., 2017; Song *et al*., 2017). The elevated rate of caesarean delivery among pregnant women with GDM may be due to maternal hyperglycaemia that leads to excessive foetal growth and macrosomia that can lead to clinicians opting for operative deliveries in order to reduce the chances of poor pregnancy-related outcomes (Gorgal *et al*., 2012; Logakodie *et al*., 2017; Wang *et al*., 2021). This study also found increased odds of pregnancy induced hypertension among pregnant women with GDM similar to previous findings (Ye *et al*., 2022). Pregnancy induced hypertension leads to adverse pregnancy-related outcomes including preterm births, disruption of the placenta, retarded intrauterine growth and neonatal mortality, hence necessitating the need of caesarean delivery to limit adverse pregnancy-related outcomes in women with pregnancy induced hypertension (Ye *et al*., 2009). However, there is need for research to explore the potential underlying mechanisms.

In women with GDM, induction of labour at 38 or 39 weeks results in reduced odds of is caesarean delivery in women who are giving birth for the first time and reduces pregnancy-related hypertension in women who have given birth severally (Melamed *et al*., 2016; Souter *et al*., 2019). But this can lead to increased likelihood of neonatal intensive care unit admission if performed at <39 weeks of gestation (Melamed *et al*.,

2016). The increased odds of induced labour among pregnant with GDM found in this study may be informed by clinical decision making in clinical settings to limit the risk of caesarean delivery and other poor pregnancy-related outcomes (Feghali *et al*., 2016). This study also found that women with pregnancy complicated with GDM had increased odds of gestational age at delivery ≥ 40 weeks agreement with previous observations (Feghali *et al*., 2016). The increased gestational age may increase excessive foetal growth that ultimately increases the odds of foetal macrosomia and caesarean delivery among pregnant women with GDM (Feghali *et al*., 2016; Wang *et al*., 2021).

This study reveal that GDM is an independent predictor of foetal macrosomia and neonatal admission to intensive care unit. This finding is in agreement with data from various regions showing positive associations between GDM with macrosomia (Srichumchit *et al*., 2015; Seghieri *et al*., 2020; Wang *et al*., 2021). In Thailand, the rate of macrosomia is significantly high among pregnant women with GDM (Srichumchit *et al*., 2015). This may be due to excessive foetal growth that result from metabolic disorders such as maternal hyperglycaemia in women with pregnancies complicated with GDM (Metzger *et al*., 2008; Seghieri *et al*., 2020). This necessitates the of efficient and effective public health interventions such as eating healthier diets, engaging in physical exercise and adherence to insulin-therapy in order to control maternal hyperglycaemia and decrease the risk of macrosomia (Landon *et al*., 2009; Yang *et al*., 2014). Although the underlying patho-mechanisms between maternal hyperglycaemia and macrosomia are still unclear, it is postulated that maternal hyperglycaemia and insulin resistance result in foetal hyperinsulinemia and increased utilization of nutrients leading excessive foetal growth (Ye *et al*., 2009; Li *et al*., 2020). Of note, is that the increased foetal growth increases the risk of shoulder dystocia among macrosomic infants and caesarean delivery (Tandon *et al*., 2022). This can potentially lead increased rate of admission of neonates from mothers with pregnancies complicated with GDM in intensive care unit (Kouhkan *et al*., 2021; Tandon *et al*., 2022), similar to these previous observations this study reports that infants from pregnant mothers with pregnancy complicated with GDM more likelihood of intensive care unit admission.

5.3 Risk factors for caesarean delivery and macrosomia among pregnant women with GDM

This study examined maternal and fetal outcomes in pregnancies complicated with diabetes among pregnant women attending ANC clinic at Jaramogi Oginga Odinga Teaching and Referral Hospital in Kisumu city, in western Kenya. GDM increases the odds of poor pregnancy-related outcomes (Bawah *et al*., 2019; Grunnet *et al*., 2020). Similar to previous studies, this study also found that GDM increases the likelihood of poor maternal outcomes such as caesarean delivery, induced labor, gestational hypertension and gestational week at delivery (Grunnet *et al*., 2020). Additionally, this study reveal that women with pregnancy complicated with GDM present with poor neonatal outcomes such as neonatal hypoglycemia, respiratory distress syndrome, shoulder dystocia, history of NICU admission and jaundice. This is in agreement with studies that found neonates from mothers with GDM are increased likelihood of presenting with shoulder dystocia, asphyxia, hypoglycemia and prolonged intensive care admission (Quinn *et al*., 2016; Beta *et al*., 2019; Basu *et al*., 2021). Together these data indicate that GDM is increases the odds of presenting with poor pregnancy-related outcomes.

Evaluation of the risk factors for caesarean delivery revealed that that having a relative with high blood pressure, maternal age, being employed, being overweight, being obese having diabetic relatives and had glycosuria were independently associated with caesarean delivery. In fact, one of the poor maternal outcomes associated with fetal macrosomia among women with GDM is caesarean delivery (Muche *et al*., 2019;). Further analysis revealed that having a relative with high blood pressure is significantly associated with caesarean delivery among women with pregnancy complicated with GDM. The odds of caesarean delivery was 5.89 times greater in GDM women who's relative had high blood pressure compared to those whose relatives didn't have. Previous studies have demonstrated that CS rate among women with GDM is associated with medical maternal blood pressure and history of diabetes among close relatives (Kale *et al*., 2005; Tian *et al.*, 2014; Sweeting *et al*., 2019). History of hypertension among close family members increases the odds of also had increased blood pressure after delivery and delivery through caesarean section (Guo *et al*., 2022). Of note is that, most of the study participants with GDM were of advanced age and it has been reported that advanced maternal age increases the risk of elevated blood pressure after delivery

among women with history of pregnancy complicated with GDM in Taiwan (Hwu *et al*., 2016). Advanced maternal age can lead to metabolic dysregulation and perturbation vascular environments milieu potentiating the odds of having elevated blood pressure among women with pregnancy complicated with GDM (Retnakaran *et al.*, 2017).

The other factors that were significant at univariate levels but not at multivariate levels were advance age, being employed, being overweight, being obese, having diabetic relatives and having high glucose levels in urine were associated with CS delivery. GDM among pregnant women has been associated with advance age and having adverse maternal outcome such as CS delivery as a result of excessive fetal growth (Njogu *et al*., 2022). This imbalanced fetal growth is due to deregulated production of insulin, glucose, leptin, ghrelin, adiponectin, growth hormone and insulin-like growth factors that result in maternal hyperglycemia (Kong *et al.*, 2019). The maternal hyperglycemia indices excessive fetal growth by up-regulating the production of growth factors such as fetal insulin that acts with maternal to promote fetal growth (Kong *et al*., 2019; Rajamoorthi *et al.*, 2022). Of note data in this study, indicate that increased levels of glycosuria among of women with GDM increases the odds of CS delivery. Moreover, consistent with this, previous studies have shown that maternal weight determines the birth weight of the offspring birth weight (Kong *et al*., 2019; Guo *et al*., 2022), due to maternal and fetal deregulation of the production of glucose, insulin, lipid, and amino acid metabolism (Kong *et al*., 2019). Genetic studies have shown that gene polymorphisms associated with glucose metabolism and increase in maternal body weight in macrosomic neonates, indicating the potential role of genetic factors in the development of macrosomia (Deng *et al.*, 2022). These data suggest the physiological dysregulation and pathological changes in women with GDM may result into increased inter-uterine growth resulting in CS delivery. However, the increased rate of CS among women with pregnancy complicated with GDM can also be due to several factors including individual characteristics such as labor characteristics, fetal presentation or health system factors such gynecologist's decision-making, medico-legal issues and organization of the hospital (Cegolon *et al*., 2020).

This evaluated the risk factors for fetal macrosomia among women attending ANC clinic in Kisumu County. Fetal macrosomia refers to abnormal intrauterine fetal growth or a birth weight greater or equal to 4kg irrespective of gestational age (Said *et al.*,

2016; Sun *et al*., 2020). The excessive growth is partly due to maternal hyperglycemia and is associated with adverse maternal outcomes such as postpartum hemorrhage, caesarean delivery, prolonged labor, vaginal and perianal lacerations, and need for blood transfusion (Nguyen *et al.*, 2021; Akanmode *et al.*, 2022; Njogu *et al*., 2022). In addition, adverse fetal outcomes such as hypoglycemia, NICU admissions, shoulder dystocia, brachial plexus palsy, intracranial hemorrhage and death are associated with macrosomia (Beta *et al*., 2019; Nguyen *et al.*, 2021; Njogu *et al*., 2022). This study found that being employed, having relatives with high blood pressure and having glucose in urine were independent risk factors for macrosomic delivery.

Advanced maternal age, family history of diabetes and nutritional status are good predictors of adverse neonatal and obstetric outcomes for both the infant and the mother (Hwu *et al*., 2016; Sun *et al*., 2020). Studies have shown that being old, overweight or obese predispose pregnant women to GDM, hypertensive syndrome and disorders of fetal growth (Sun *et al*., 2020; Njogu *et al*., 2022). This study also show that though not statistically significant, macrosomic delivery was associated with advanced age maternal age, mothers being overweight or obese and having a diabetic relative. Dysregulated production of glucose, amino acids and free fatty acids among overweight and obese women with pregnancy complicated with GDM increases the likelihood of macrosomia (Hull *et al*., 2011; Hwu *et al*., 2016), indicating the maternal physiological perturbation play a central role in the etiology of fetal macrosomia . This reveal that women having close family members with GDM were 1.81 times more likely to have a macrosomic delivery relative to those without diabetic relatives. This is similar to previous data showing that having history of close relatives having diabetes increases both the likelihood of having GDM and ultimately fetal macrosomia (Plows *et al*., 2018). This possibly due to genetic polymorphisms associated with that influence glucose production and usage and those that regulate both maternal and fetal growth indicating the potential role of genetic variations in macrosomia

In high income countries, maternal employment status, education status, and income levels have been associated with poor pregnancy outcomes among women with pregnancy complicated with GDM (Yee *et al.*, 2015; Burris *et al.*, 2017). This study findings reveal that being employed increases the risk of macrosomic delivery significantly by 8.05 folds possibly due to the fact that employed women have transition

from traditional foods to western dietary lifestyles such as high intake of saturated fats, white bread, red meat, butter, sugar and lower intake of whole carbohydrates, fruits and vegetables (Yuste Gómez *et al.,* 2022). This increases the risk of GDM and macrosomic delivery by interfering with insulin signaling and inducing pathogenic factors (Plows *et al*., 2018; Yuste Gómez *et al*., 2022). In addition, this study found there was 12.2 times odds of having macrosomic neonates among pregnant GDM women with glycosuria. This is partly due to maternal hyperglycemia resulting from dysregulated production and/or elevated circulating levels of insulin, glucose, leptin, ghrelin, adiponectin and other growth hormones resulting in excessive fetal growth (Kong *et al*., 2019). This suggest that there is need for dietary interventions targeted at improving glycaemia and/or birth weight outcomes in women with GDM. However, findings in this study are not in agreement with previous observation that there is no significant association between maternal employment status with cesarean birth and macrosomia in women with GDM (Yuste Gómez *et al*., 2022).

History of gestational diabetes among close family members increases the odds of metabolic dysregulation such as maternal hyperglycemia and high blood pressure (Hedderson *et al.,* 2008). Insulin resistance contributes to both chronic and gestational hypertension and is thought a critical factor in the etiology of GDM (Carpenter, 2007). Evidence indicate that inflammatory markers such as C-reactive protein increases the likelihood of increasing the development of increased BP levels and GDM (Carpenter, 2007; Qiu *et al.,* 2004). More importantly, GDM is associated with both BMI and macrosomic delivery (Njogu *et al*., 2022). Therefore, data in this study shows having history of high blood pressure were 10.9 timely more likely to have macrosomic delivery. This data shows that there is need of public health interventions targeting at controlling high blood pressure among women with GDM to prevent macrosomic delivery. It has been observed that family history of hypertension increases the odds of having high blood pressure after delivery and caesarean section (Guo *et al.*, 2022). This study found that most women with pregnancy complicated with GDM advanced maternal age. Advanced maternal age is associated with development of blood pressure after delivery among women with pregnancy complicated with GDM (Hwu *et al*., 2016), due to perturbation of metabolic processes and deterioration of vascular environments milieu with advancing age leading to increased blood pressure among women with pregnancy complicated with GDM (Retnakaran *et al.,* 2017).

CHAPTER 6: CONCLUSION AND RECOMMENDATIONS

6.1 CONCLUSION

The predictors of GDM include having a diabetic relative, history of CS delivery and history of NICU admission in addition to being on IFAS. These indicate that GDM screening should be incorporated in the standard routine ANC services for early detection and timely treatment in order to achieve optimal pregnancy outcomes and preventing complications linked to GDM. There is need for prioritizing high risk women for screening based on their history of CS, history of macrosomic delivery and history of neonatal intensive care unit admission.

GDM was significantly associated with gestational age at delivery ≥ 40 weeks, caesarean delivery, induced labor and pregnancy induced hypertension. In addition, GDM is associated with macrosomia, respiratory distress syndrome (RDS), neonatal hypoglycemia, fetal injury, shoulder dystocia, neonatal intensive care unit admission and jaundice as the pregnancy outcomes.

Caesarean delivery is associated with family history of high blood pressure whereas having macrosomic delivery is associated with being employed, having glycosuria and family history of high blood pressure. Hence there is need for increased antenatal public health interventions that target management of pregnancy among women with GDM in order to reduce adverse maternal and neonatal outcomes.

6.2 RECOMMENDATIONS

6.2.1 Recommendation for action

I. Enlighten on the implications of GDM risk factors and effect on adverse pregnancy outcomes as it may lead to a vicious cycle of future development of gestational diabetes and other metabolic disorders to the offsprings and the mothers.

II. Health education should focus on these risk factors and pregnancy outcomes in our setting to avert potential development of GDM and loss of lives that may be a result to probable risk to both the mother and the fetus.

III. It is imperative for the clinicians to know the possible risk factors in this setting inorder to screen, educate and manage GDM early.

IV. IFAS association to GDM need to be taken with a lot of caution with regular monitoring during routine check ups.

6.3 Suggestions for future research

Further longitudinal multicenter studies should be carried out to explore long term effects of IFAS (in terms of duration and dosage) on GDM, establish the link between assosiated risk factors and pregnancy related outcomes with no statistical significance, with large data sets in order to provide an evidence-based antenatal care based interventions. There is also need for implementation of lifestyle modification programs such as involvement in physical activity and healthier diet to prevent the development of GDM and obstetric complications.

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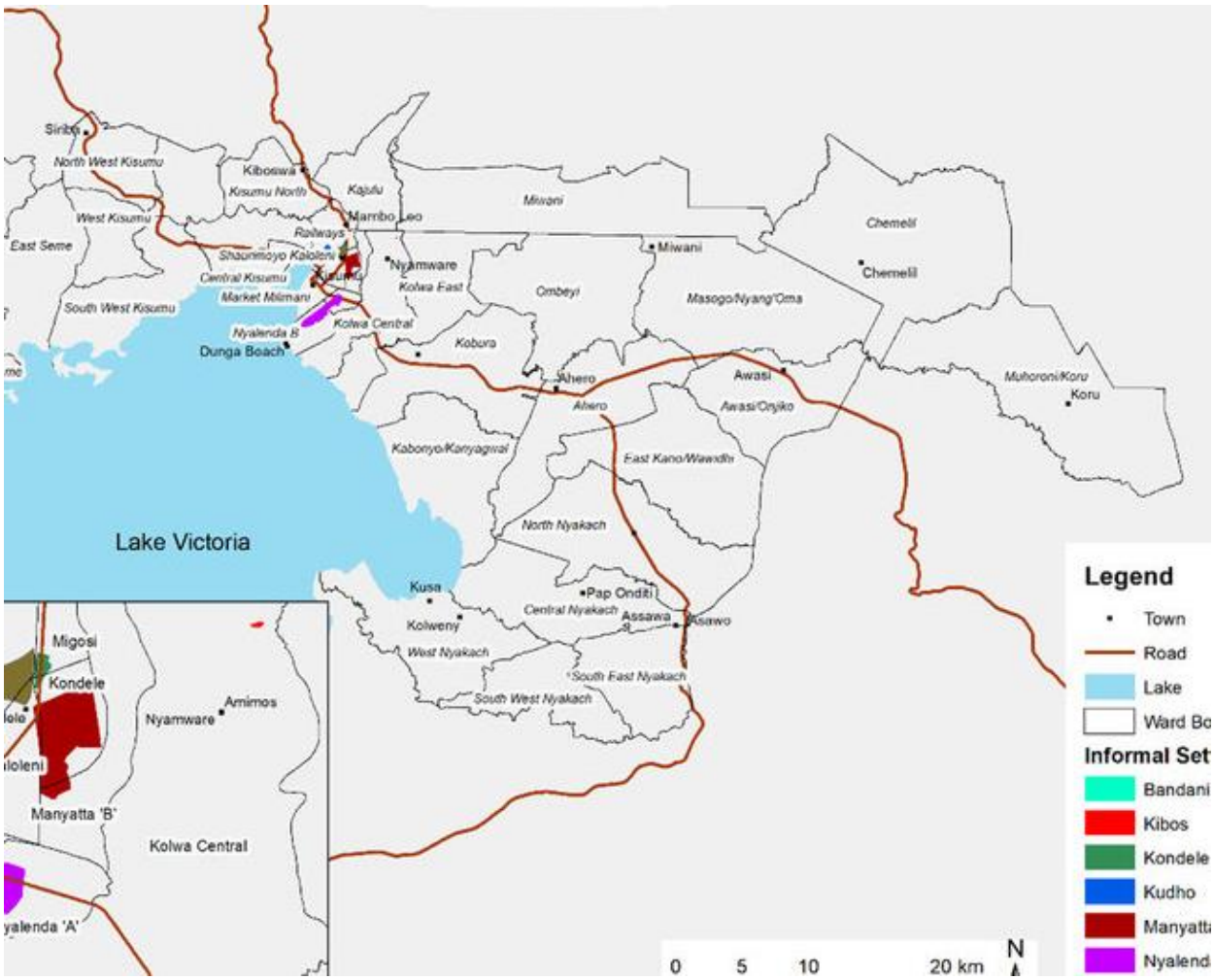
APPENDICES

APPENDIX 1: MAP OF THE STUDY AREA



APPENDIX II: PREGNANCY OUTCOME CHECKLIST (*Tick where appropriate*)

MATERNAL OUTCOMES	
	Gestational age at delivery *(in weeks)*
	Premature delivery *(delivery before 37weeks of pregnancy)*
	Premature rupture of the membrane *(rupture of membranes prior to beginning of labour and before 37weeks of pregnancy)*
	Caesarean delivery
	Induction of labour
	Intensive care admission
	Pre-eclampsia *(HBp after 20 weeks of pregnancy& protein in urine (>140mmHg systolic & 90mmHg diastolic)*
	Pregnancy induced hypertension *(HBp during pregnancy)*
	Miscarriage *(spontaneous expulsion of a foetus before viability)*
FOETAL/ NEONATAL OUTCOMES	
	Birth status (1-healthy 2-unhealthy 3- dead)
	Abortion *(deliver of dead baby before 22weeks)*
	Still birth *(delivery of a dead baby at/or after 22weeks of pregnancy)*
	Neonatal death *(death of infant within 28 days of life)*
	Birth weight *(Macrosomia- ≥4kgs)*
	Neonatal hypoglycaemia *(blood glucose level <2.2mmol/L (40 mg/dL))*
	Hyperbilirunemia *(lab report of bilirubin level ≥ 220mmol/L or neonatal treatment with phototherapy)*
	Congenital malformation *(malformation that required surgery and/ or resulted in permanent injury)*
	Respiratory distress syndrome(RDS) *(need for supplemental oxygen in the nursery at 4 hours after birth)*
	Foetal injury (Caput succedaneum**)**
	Shoulder dystocia
	Neonatal intensive care unit (NICU)admission
	Perinatal mortality *(death within 7 days of life)*
	Jaundice

APPENDIX III: QUESTIONNAIRE

Date: Study number:

Age (yrs.) Height (cm): BMI:

Blood pressure (mmHg): Systolic Diastolic

Mobile No:

A: Personal medical history

1. What was your weight in Kg before pregnancy?

□ Wt. [1] □Unknown [9]

If unknown, what was your weight at beginning of clinic?

2. What is your current weight today?

3. Have you experienced any of the following symptoms

□ Frequent urination [1]

□ Frequent thirst [2]

□ Increased appetite [3]

4. Have you ever had your blood glucose measured?

□ Yes [1] □ No [2]

When was this? ----------

What was the result?

□ Normal [1] □ Abnormal [2] □ Unknown [9]

5. Do you suffer from a chronic disease? Which one?

□ Liver disease [1]

□ Renal disease [2]

□ Cardiac disease [3]

□ None [4]

□ Don't know [9]

6. Are you currently on any medication?

□ Yes [1] □ No [2]

If yes, specify ----------

7. What is your HIV status

□ Positive [1] □ Negative [2]

I: Socio-demographic characteristics

8. What is your marital status?

□ Single [1] □ Married [2] □ Separated [3]

□ Other. Please state ---------- [4]

9. Where is your current residence? ----------

□ Rural [1]

□ Urban [2]

□ Peri-urban [3]

10. How long have you been staying in your current residence?----------

11. What is your level of education?

□ Primary [1]

□ Secondary [2]

□ Tertiary [3]

□ None [4]

12. What is your employment status?

□ Self-employed [1]

□ Employed [2]

□ Unemployed [3]

13. how often do you move in a week?

□ More than 3times weekly [1]

□ Less than 3 times weekly [2]

□ Hardly move [3]

14. What activities do you take part in?

□ House chores [1]

□ Digging [2]

□ Walking [3]

□ Exercise [4]

15. What food do you eat often

□ Starchy [1]

□ Meats [2]

□ Vegetables and fruits [3]

□ Stone and mud [4]

□ Water [5]

II: Obstetric and gynaecological history

Stage of pregnancy……..weeks

Parity: Gravida: Gestation by Dates:

16. Have you experienced any problem with conceiving?

□ Yes [1] □ No [2]

17. Have you suffered a miscarriage?

□ Yes [1] □ No [2]

18. If yes to 17 above at how many weeks gestation

□ 6-12 weeks [1]

□ 12 – 20 weeks [2]

□ 20-28 weeks [3]

□ Not known [9]

19. How many pregnancies have you delivered before 37 weeks?

□ None [1] □ All [2]

□ Some, specify how many---------- [3]

20. Have you had elevated blood pressures in this or prior pregnancies?

□ Yes [1] □ No [2]

21. Have you been told of you having glucose/sugar in your urine in this or prior pregnancies?

□ Yes [1] □ No [2]

22. Have you been diagnosed with diabetes?

□ Yes [1] □ No [2]

23. If yes to 22 above, when was diagnosis made?

□ Before becoming pregnant [1]

□ In the previous pregnancy [2]

24. Have you ever been told that your womb looks bigger than what is expected?

□ Yes [1] □ No [2]

25. If yes to question 24, was it related to increased amount of fluid in the uterus?

□ Yes [1] □ No [2] □ Don't know [9]

26. Have you delivered any of your babies by Caesarean section?

□ Yes [1] □ No [2]

27. If yes to 26 above what was the indication of C/S?

□ Big baby [1]

□ Failed induction [2]

□ Prolonged labour [3]

□ Foetal distress [4]

□ Other. Please state ---------- [5]

28. Have you been assisted to deliver before? If yes, by which method?

□ Vacuum [1]

□ Forceps [2]

□ Don't know [9]

29. Have you delivered any of your babies when they are already dead (still births)

□ Yes [1] □ No [2]

If yes, how many? ----------

30. Have you delivered a child who died after delivery?

□ Yes [1] □ No [2]

If yes, how many?----------

31. If yes to 30 above how long after delivery did the baby die?

□ Less than 24 hours [1]

□ 1 day – 7 day [2]

□ 7 days – 28 days [3]

□ Other [4]

32. Have you delivered a baby with an abnormality?

□ Yes [1] □ No [2]

33. If yes to Q 32 what kind of abnormality

□ Central Nervous System---------- [1]

□ Cardiovascular System---------- [2]

□ Genito-Urinary Tract [3]

□ Gastro-intestinal Tract [4]

□ Other. Please state---------- [5]

34. Have had a baby with a birth weight of 4 kg or more?

□ Yes [1] □ No [2]

35. Have had any of your babies admitted to nursery/new born unit?

□ Yes [1] □ No [2]

36. If yes to 35 above what was the indication?

□ RDS [1]

□ Prematurity [2]

□ Jaundice [3]

□ Other. Please state ---------- [4]

□ Don't know [9]

D: Family history

37. Do you have any relatives with diabetes?

□ Yes [1] □ No [2]

How many? ----------

What is their relationship to you? ----------

38. Have you had any relative with high blood pressure?

□ Yes [1] □ No [2]

What is their relationship to you? ----------

E: LABORATORY SCREENING FORM

Age *Study number*

Date *Time of last meal:*

Result:

Fasting Blood glucose

□Glucose intolerance (>5.9mmol/l) [1]

□No glucose intolerance (<5.9 mmol/l) [2]

75g Oral Glucose Tolerance Test

□ Gestational Diabetes (>7.8 mmol/l) [1]

□No Gestational Diabetes (<7.8 mmol/l) [2]

Results:

75g OGTT	mmol/l
Fasting blood glucose	
2 hr. blood glucose	

Thank you very much for taking the time to complete this questionnaire.

APPENDIX IV: ETHICAL APPROVAL FROM JOOTRH

MINISTRY OF HEALTH

Telegrams: "MEDICAL", Kisumu
Telephone: 057-2020801/2020803/2020321
Fax: 057-2024337
E-mail: medsuptnpgh@yahoo.com
When replying please quote

JARAMOGI OGINGA ODINGA TEACHING & REFERRAL HOSPITAL
P.O. BOX 849
KISUMU

Ref: IERC/JOOTRH/220/2020

Date June 2, 2020

To, Anita Amukhuma Ottaro
Dear Anita.

RE: STUDY TITLE:
RISK FACTORS FOR GESTATIONAL DIABETES AND PREGNANCY OUTCOMES AMONG WOMEN IN WESTERN KENYA

This is to inform you that ***JOOTRH IERC*** has reviewed and approved your above research proposal. Your application approval number is ***IERC/JOOTRH/220/2020.*** The approval period is ***June 2 , 2020 – June 2 , 2021.***

This approval is subject to compliance with the following requirements;

i. Only approved documents including (informed consents, study instruments, MTA) will be used
ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by ***JOOTRH - IERC***.
iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to ***JOOTRH - IERC*** within 72 hours of notification
iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to ***JOOTRH - IERC*** within 72 hours
v. Clearance for export of biological specimens must be obtained from relevant institutions.
vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. Attach a comprehensive progress report to support the renewal.
vii. Submission of an executive summary report within 90 days upon completion of the study to JOOTRH - ***IERC***.

Prior to commencing your study, you will be expected to obtain a research license from National Commission for Science, Technology and Innovation (NACOSTI) https://oris.nacosti.go.ke and also obtain other clearances needed.

In case the case of study site is JOOTRH, kindly report to Chief Executive Officer before commencement of data collection.

Yours sincerely,

SECRETARY,
IERC JOOTRH

APPENDIX V: APPOVAL TO COMMENCE DATA COLLECTION FROM BPS

JARAMOGI OGINGA ODINGA UNIVERSITY OF SCIENCE & TECHNOLOGY

BOARD OF POSTGRADUATE STUDIES

Office of the Director

Tel. 057-2501804
Email: bps@jooust.ac.ke

P.O. BOX 210 - 40601
BONDO

Our Ref: H162/4072/2015

Date: 3rd February 2020

TO WHOM IT MAY CONCERN

RE: ANITA AMUKHUMA OTTARO – H162/4072/2015

The above person is a bona fide postgraduate student of Jaramogi Oginga Odinga University of Science and Technology in the School of Health Sciences pursuing a PhD in Public Health. She has been authorized by the University to undertake research on the topic: ***"Risk Factors for Gestational Diabetes and Pregnancy Outcomes among Women in Poor Resource Setting".***

Any assistance accorded to him shall be appreciated.

Thank you.

Prof. Dennis Ochuodho
DIRECTOR, BOARD OF POSTGRADUATE STUDIES

APPENDIX VI: INFORMATION AND CONSENT FORM

Title of the study: GESTATIONAL DIABETES MELLITUS RISK FACTORS AND PREGNANCY-RELATED OUTCOMES AMONG WOMEN IN KISUMU COUNTY, WESTERN KENYA

Part A: INFORMATION SHEET

The information in this part is to assist you to understand this study with a view to enable you to give voluntary and informed consent to your participation. Kindly read it carefully before signing the consent form in Part B.

Name of Principal Investigator
Ms. Anita A. Ottaro
Jaramogi Oginga Odinga University of Science and Technology (JOOUST)
P.O.Box 210-40601
Bondo.
Tel; 0736-464522/0782-152561
And
Jaramogi Oginga Odinga Teaching and Referral Hospital (JOOTRH)
P.O.Box 849
Kisumu.
Tel; 057-2020801/2020803/2020321

Objective of the study

To determine gestational diabetes mellitus risk factors and pregnancy-related outcomes among women attending antenatal clinic at JOOTRH in Kisumu County, western Kenya. This is important, as the results of this study will contribute in improvement of strategies of GDM management and control.

The risks and discomforts of the study

You may not experience much discomfort during blood sample collection, a small prick will be made through the finger, this will cause a small pain onto the study subjects but this pain will disappear in a few minutes. You may also experience some cravings and hunger during the fasting period but this will only be for a short time after which you'll resume to your normal eating regime.

The benefits of the study

All participants diagnosed positive for GDM will be referred to the doctor in the hospital for proper management. All Screening and laboratory diagnosis will be free and no expenses will be incurred by the participants. Participation will also provide valuable information to the medical community for better treatment strategies.

Data security and confidentiality

All the information gathered by the research team will be used in confidence for the sole purpose of this research only. No names of individuals will be written down at any time. Information on diagnosis of the participants will be treated confidentially and will only be disclosed to authorize person's i.e. medical personnel in the health centres. Data will be kept in folders, which will be locked in cabinets for storage throughout the study period. Computer documents will have passwords only accessible to the researcher. The strict data management procedures are intended to ensure confidentiality of the study participants. The results of the study may be published for scientific purposes; however, your identity will not be revealed.

Withdrawal without prejudice

You are free to withdraw your consent and to discontinue participation in this study at any time without prejudice, without affecting the planned procedures and without any consequence for their treatment and any subsequent visits to the health facility later.

Cost of participation

There will be no cost to the participants for participation in the study. Therefore, participation is free.

Compensation

There will be no monetary compensation to the participants for participation as the study is based on voluntary participation.

Legal rights

You are not waiving any of your legal rights by signing this consent form.

Part B: CONSENT FORM

You are requested to carefully read the Information sheet in Part A before signing this consent form. By signing the space allocated below, you are indicating your voluntary willingness to participate in this study. Should you be having any issue, concern or questions about this study and your participation kindly feel free to contact the following principal investigator.

Ms. Anita A.Ottaro
Jaramogi Oginga Odinga University of Science and Technology (JOOUST)
P.O.Box 210-40601
Bondo
Tel; 0736-464522/0782-152561

Declaration

I have read the information sheet concerning this study and what is expected of my participation in this study and I have understood it.

_____

Signature of Participant Date

_____

Signature of Investigator Date