AVERAGE THIRD TRIMESTER FASTING BLOOD SUGAR LEVEL AND POOR PREGNANCY OUTCOMES AMONG WOMEN WITH PREGNANCY DIABETES AT KENYATTA NATIONAL HOSPITAL – RETROSPECTIVE DESCRIPTIVE COHORT

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H58/80768/2015

A DISSERTATION SUBMITTED IN PARTIAL FULFILMENT OF THE DEGREE OF MASTER OF MEDICINE IN OBSTETRICS AND GYNAECOLOGY AT THE UNIVERSITY OF NAIROBI

2020

DECLARATION

DECLARATION

This is to declare that this dissertation is my original work, carried out with guidance from my supervisors, and references made to work done by others have been indicated.

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This dissertation has been presented with our full approval as supervisors

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CERTIFICATE OF AUTHENTICITY AND DEPARTMENTAL APPROVAL

CERTIFICATE OF AUTHENTICITY AND DEPARTMENTAL APPROVAL

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ACKNOWLEDGEMENTS

This work would not have been possible without the help and hard work of my supervisors – Dr Joe Wanyoike and Dr Alfred Mokomba, my research assistants – Slavy Murungi and Peter Kuria, my statistician – Wycliffe Ayieko, my family and God.

DEDICATION

I dedicate this work to my family.

I also dedicate this work to all the women with diabetes in pregnancy.

FUNDING AGENCY

Funding was provided by Kenyatta National Hospital Research and Funding.

LIST OF ABBREVIATIONS AND ACRONYMS

OGTT – Oral Glucose Tolerance Test

GDM – Gestational Diabetes Mellitus

HAPO – Hyperglycaemia and Adverse Pregnancy Outcomes

SPSS 23 – Statistical Package for Social Sciences version 23

BMI – Body Mass Index

PPH – Postpartum Haemorrhage

FBS – Fasting blood sugar

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OPERATIONAL DEFINITIONS:

Gestational diabetes mellitus – hyperglycaemia recognized for the first time during pregnancy, with fasting blood glucose of 5.1-6.9mmol/L, 1-hour post 75g oral glucose load greater or equal to 10mmol/L or 2-hour post 75g oral glucose load 8.5-11mmol/L (1).

Overt/Pre-existing Diabetes in pregnancy – hyperglycaemia first detected by testing at any time during the course of pregnancy that meets the criteria for diagnosis of diabetes in the nonpregnant state, fasting plasma glucose greater or equal to 7.0mmol/L, and/or 2-hour 75g oral glucose tolerance test (OGTT) greater or equal to 11.1mmol/L, or random plasma glucose greater or equal to 11.1 mmol/L associated with signs and symptoms of diabetes (1).

Macrosomia – birth weight greater or equal to 4kg (2).

Stillbirth – a baby born with no signs of life at or after 28 weeks' gestation (3).

Neonatal hypoglycaemia – neonatal blood glucose ≤ 2.6mmol/L after birth (4).

Primary Postpartum haemorrhage – blood loss of 500 ml or more within 24 hours after birth due to uterine atony, genital tract trauma, uterine rupture or retained placental tissue (5).

Perineal Trauma – any damage to the genitalia during childbirth that occurs spontaneously or intentionally by surgical incision (episiotomy) (6).

Poor Glycaemic Control – average third trimester fasting blood sugar ≥ 5.3mmol/L

Good Glycaemic Control – average third trimester fasting blood sugar < 5.3mmol/L

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ABSTRACT

Background

The prevalence of Gestational Diabetes Mellitus, a form of hyperglycaemia recognised for the first time in pregnancy, is increasing globally. The prevalence at Kenyatta National Hospital was 11.6% in 2012.

Uncontrolled hyperglycaemia, a consequence of poor glycaemic control, can result in foetal macrosomia and stillbirths. Macrosomia can lead to a variety of pregnancy outcomes: shoulder dystocia, perineal trauma, postpartum haemorrhage, neonatal hypoglycaemia, neonatal hyperbilirubinemia, and later obesity along with type 2 diabetes in the neonate.

The level of glycaemic control and incidence of macrosomia and poor pregnancy outcomes among women with diabetes in pregnancy on treatment at Kenyatta National Hospital is unknown.

Objective

To determine the prevalence of poor glycaemic control and compare the incidence of poor pregnancy outcomes among women with diabetes in pregnancy who have poor glycaemic control (average third trimester fasting blood sugar ≥ 5.3mmol/L) with the incidence of poor pregnancy outcomes among women with diabetes in pregnancy who have good glycaemic control (average third trimester fasting blood sugar < 5.3mmol/L.

Methodology

Study Design: This was a retrospective descriptive cohort study.

Study Population: Women with diabetes in pregnancy (gestational diabetes and pre-existing diabetes) on treatment

Study Setting: Kenyatta National Hospital antenatal clinic, antenatal ward and labour ward.

Sample Size: A sample of 258 files of diabetic pregnant patients, with the exposed group of 230 with average third trimester fasting blood sugar level ≥ 5.3mmol/L, and

the unexposed group of 28 with average third trimester fasting blood sugar level < 5.3mmol/L

Data Collection: A structured questionnaire was used to retrieve data from patients' files.

Data Analysis: Data was entered and analysed with the use of SPSS 23. Demographic data was analysed and presented as means and standard deviations. The prevalence of poor glycaemic control (average third trimester fasting blood sugar ≥ 5.3mmol/L) was presented as proportion of women with levels at or above 5.3mmol/L. The incidences of the macrosomia and poor pregnancy outcomes were calculated.

Results

The prevalence of poor glycaemic control (average third trimester fasting blood sugar level ≥ 5.3mmol/L) was 89.1%. There was a higher incidence of macrosomia (25.7% vs 21.4%; p-value 0.627), stillbirths (17.9% vs 3.6%; p-value 0.058) and preterm birth (43.9% vs 21.4%; p-value 0.025) among diabetic pregnant women with poor glycaemic control compared to diabetic pregnant women with good glycaemic control. Furthermore, among those with poor glycaemic control, the pre-existing diabetics experienced significantly worse outcomes of stillbirths (20.9% vs 0%; p-value 0.004) and preterm births (47.2% vs 24.2%; p-value 0.014) than the gestational diabetics.

Conclusion

Poorly controlled diabetes in pregnancy heightens the risk of adverse pregnancy outcomes such as macrosomia, stillbirths and preterm births, with poorly controlled pre-existing diabetic women experiencing significantly worse outcomes of stillbirths and preterm births than poorly controlled gestational diabetics.

1.0: INTRODUCTION

Gestational diabetes mellitus is hyperglycaemia recognized for the first time in pregnancy, with fasting blood sugar of 5.1-6.9mmol/L, 1-hour post 75g glucose load ≥ 10mmol/L or 2-hour post 75g glucose load 8.5-11mmol/L (1).

Overt/Pre-existing Diabetes in pregnancy is hyperglycaemia diagnosed during pregnancy with fasting plasma glucose greater or equal to 7.0mmol/L, and/or 2-hour 75g OGTT greater or equal to 11.1mmol/L, or random plasma glucose at or above 11.1 mmol/L associated with diabetes symptomatology (1).

Worldwide, the prevalence of pregnancy diabetes is rising. According to the International Diabetes Federation, the global estimate of gestational diabetes prevalence for 2017 was 14%, that is, 18.4 million live births. The South East Asia region contributed 26.6%, while the Africa contributed 9.5% (7). At Kenyatta National Hospital, the prevalence was at 11.6% in a study by Bosire in 2012 (8). The screening for gestational diabetes is usually done at 24 – 28 weeks gestation; however, screening can be done at the first antenatal clinic visit.

Gestational diabetes mellitus occurs due to inadequate multiplication of the beta cells (inadequate insulin secretion) in response to the increased demand for insulin brought about by increased food intake in pregnancy along with elevated levels of somatolactogenic (insulin resistant) hormones (prolactin, growth hormone, placental lactogen, placental growth hormone). Hence, maternal hyperglycaemia occurs with increased transplacental glucose transport. This transplacental glucose transport is modulated by corticotropin releasing hormone (9) (10) (11).

According to the Pedersen Theory, maternal hyperglycaemia leads to foetal hyperglycaemia and hyperinsulinemia once the foetal pancreas becomes functional in the second trimester. Then foetal hyperinsulinemia increases central deposition of fat in the abdominal and interscapular areas. Finally, foetal macrosomia, a major indicator of hyperglycaemia, results (12) (13).

Foetal macrosomia heightens the risk of caesarean and instrumental delivery, shoulder dystocia, perineal and bladder trauma, and postpartum haemorrhage in the

mother. Furthermore, there is increased risk of fresh stillbirths, nerve injuries, bone fractures and hypoxia in the foetus (14).

Macrosomic babies of gestational diabetes mothers have a high likelihood delayed motor development (15), of gaining a lot of weight early in life and are at risk of getting type II diabetes when they are older. Furthermore, changes in the genes of a foetus of a gestational diabetes mother in utero could result in transmission of diabetes to future generations (12).

A 2017 case control study by Bunyoli on Factors related to foetal macrosomia at Kenyatta National Hospital revealed increased risk in advanced maternal age, higher BMI, gestational weight gain, history of previous macrosomic delivery, diabetes, higher parity and late term pregnancy (2).

Untreated or poorly controlled diabetes in pregnancy has great risk for poor pregnancy outcomes as well as long term adverse life incidences for mother and child. There is increased risk of macrosomia, neonatal hypoglycaemia, respiratory distress syndrome, hyperbilirubinemia, induced delivery, shoulder dystocia, birth trauma, and caesarean delivery. Furthermore, there is increased risk of preeclampsia. All the fore-mentioned adverse outcomes occur in the short term. In the long term, the child can develop obesity, diabetes and metabolic syndrome, while the mother is predisposed to metabolic syndrome and type 2 diabetes. This implies that continual follow-up of mother and child is of utmost importance (16).

Follow-up of pregnant women with diabetes is goal oriented with targeted blood sugar control. The pregnant woman is involved in her care, with daily self-monitoring of fasting and 1-hour postprandial blood sugar being ideal. This goes hand in hand with treatment, which includes regular exercise and a healthy diet. Indeed, exercise and a healthy diet improve insulin sensitivity. If despite these lifestyle changes blood glucose targets are not met, introduction of insulin and oral hypoglycaemic agents is prudent (16).

2.0: LITERATURE REVIEW

The HAPO Study revealed a strong relationship of maternal glucose level (starting from less than 4.2mmol/L upwards) with increased birth weight and increased foetal hyperinsulinemia above the 90th percentile. Fasting plasma glucose values 5.6mmol/L or more were related to a five-fold greater risk of macrosomia compared with a fasting blood sugar level less than 4.2mmol/L. There was also a linear relationship of maternal blood sugar levels and primary caesarean section, hypoglycaemia in the new-born, preterm delivery, shoulder dystocia and birth injury, neonatal critical care and hypertension in pregnancy (17).

Treating gestational diabetes reduces the likelihood of developing foetal macrosomia. The Australian Carbohydrate Intolerance Study, a randomized clinical trial investigating how treating gestational diabetes mellitus affects pregnancy revealed that treatment reduces preeclampsia, perinatal death, shoulder dystocia, birth weight, clavicular or humeral fracture, and nerve injury, while raising admission to the new-born unit and labour induction. Furthermore, the treated women were happier during pregnancy and three months postpartum. No significant differences in neonatal hypoglycaemia were elicited (18).

In addition, in the Australian Carbohydrate Intolerance Study Trial: risk factors for shoulder dystocia, the greater the maternal fasting blood sugar level, the higher was the risk of macrosomia with greater probability of shoulder dystocia (19).

A systematic review on effect of treating gestational diabetes mellitus revealed that treatment lowers weight at birth and risk of shoulder dystocia and gestational hypertension. In addition, the risk of foetal death around birth, new-born hypoglycaemia, birth injuries, preterm deliveries, pre-eclampsia, caesarean delivery and labour induction was low (15).

In a study by Badurudeen et al on glycated haemoglobin level and outcomes of pregnancy, comparing those with glycated haemoglobin above 6.5% with those < or = to 6.5%, the gestational diabetic patients with higher glycated haemoglobin had significantly higher rates of macrosomia, neonatal hypoglycaemia and new-born intensive care unit admissions (20).

In a cohort examining pregnancy outcomes of pre-existing diabetics, gestational diabetics discovered early in pregnancy and gestational diabetics discovered later in pregnancy, with achievement of fasting blood glucose target of less than 5.2mmol/L, poor pregnancy outcomes (hypertension, preterm birth, caesarean delivery and jaundice of the new-born) were more prevalent in pre-existing diabetics and in gestational diabetics diagnosed early in pregnancy than in gestational diabetics diagnosed later in pregnancy. Furthermore, rates of birth weight at or above 4kg, large for gestational age and neonatal critical care in gestational diabetics discovered before 12 weeks gestation were similar to rates seen in pre-existing diabetics (21).

The use of third trimester fasting blood sugar as a measure of glycaemic control is based on the findings of a cohort study of the population examining foetal growth trajectories in pregnancies with and without gestational diabetes. The study found that foetuses of gestational diabetic mothers tended to be smaller than foetuses of normal mothers in week 24 of pregnancy (this being before gestational diabetes was diagnosed), but thereafter grew faster until birth (22), a reflection of the effect of maternal hyperglycaemia. Furthermore, a HAPO Study examining how maternal glycated haemoglobin and blood glucose related with pregnancy outcomes, revealed that blood glucose was a stronger predictor of birth weight, percent body fat, and foetal hyperinsulinemia. It was also postulated that neonatal anthropometric outcomes such as weight and head circumference were more strongly associated with glycemia in later pregnancy (13). Other concerns of glycated haemoglobin use are the unclear reference intervals for healthy pregnant women, the controversy on its levels at different gestational ages, and the varying values depending on whether the diabetic patient has anaemia, uraemia, or increased haemoglobin level (23).

A 2013 systematic review on glucose targets in the third trimester in gestational diabetic women, including 34 studies - 9433 women, found that a third trimester fasting blood sugar level < 5.0mmol/L related strongly with reduced risk of birth weight above 4 kg, neonatal hypoglycaemia, hyperbilirubinemia and preeclampsia. There was inadequate data on pre-existing diabetics to determine an a link between different blood sugar levels and outcomes for any trimester (24).

A 2016 Cochrane review on different levels of blood sugar control for gestational diabetes patients concluded that evidence was lacking to guide clinical practice on

what blood glucose level to aim for to improve pregnancy outcomes without increasing risk (25).

There is an ongoing randomised trial (TARGET) comparing tight (fasting plasma glucose < or = 5.0mmol/L) and less tight (fasting plasma glucose <5.5mmol/L) blood glucose aims for gestational diabetics; the primary outcome being large for gestational age infants. (26).

According to the 2018 Kenya National Diabetes Guidelines, when treating gestational diabetes, aim to achieve a fasting blood sugar of < 5.0mmol/L, whereas the fasting blood sugar target for pre-existing diabetics is < 5.3mmol/L (39); Furthermore, in the first edition of the Kenya clinical guidelines, glycaemic targets for pregnancy were pre-prandial blood sugar of 3.5-5.5mmol/L and post-feeding blood sugar of 5-6.7mmol/L (27).

Concerning perineal tears, a cohort study examining the association between diabetes mellitus and perineal tears after vaginal delivery found that women with diabetes mellitus with all prior vaginal births, who delivered a term singleton vaginally, had the same risk of perineal tears as women without diabetes (28).

With regards to stillbirth, a retrospective cohort study examining the risk of stillbirth at different gestational ages in patients with gestational diabetes, found that waiting was better than delivering at 36 weeks, but at 39 weeks, giving birth then was better than waiting longer, meaning, it was safer to deliver at 39 weeks (29). In addition, a study examining the appearance of placental villi and vessels in hyperglycaemic women revealed that low maternal hyperglycaemia stimulates vascular proliferation in response to a lower hypoxia level, ensuring maternal and foetal exchange. However, further increase in glycaemic levels inhibits villous angiogenesis, interfering with maternal-foetal exchanges and increasing the risk of perinatal mortality (30).

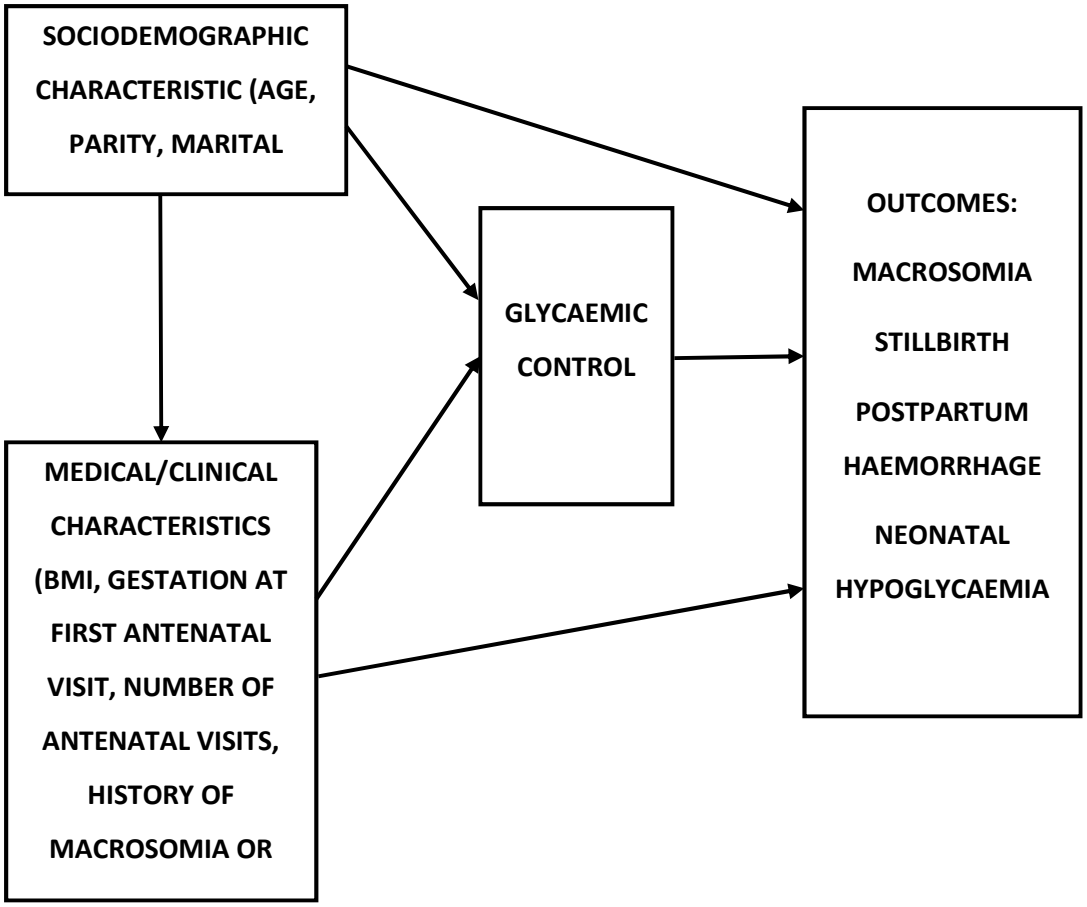
Sociodemographic factors influence glycaemic control. A prospective cohort study on social contributors to glycaemic control published in 2016 found that women with good blood sugar control were more likely to be married, educated and have higher household income, in addition to exercising regularly. Conversely, receipt of food stamps, a marker of poverty, adversely affected glycaemic control (31)

Other sociodemographic factors were investigated in a prospective study of Omani women, published in 2017. It revealed that increasing maternal age, body mass index

above 25kg/m2 before pregnancy and parity ≥ 4 were associated with higher incidence of GDM. Furthermore, a prior history of GDM and diabetes mellitus within the family were strong predictors for gestational diabetes (32)

The 2018 Kenya National Diabetes Guidelines recommend regular antenatal visits, assessing maternal and foetal wellbeing. Hence, regularity of antenatal visits as well as gestational age at first antenatal visit are important medical characteristics to consider (39).

3.0: CONCEPTUAL FRAMEWORK



3.1: Conceptual Framework Narrative

Concerning the conceptual framework, a variety of sociodemographic characteristics such as maternal age, parity, marital status, and employment status influence glycaemic control directly, as well as influencing medical/clinical characteristics such as gestation at first antenatal visit, number of antenatal visits and adverse pregnancy outcomes in previous pregnancy and current pregnancy. These medical/clinical characteristics in turn influence glycaemic control as well as pregnancy outcomes in current pregnancy. Also, level of blood sugar control influences the incidence of poor outcomes of pregnancy.

4.0: STUDY JUSTIFICATION

Diabetes in pregnancy, if poorly managed, has the potential for far reaching negative impact on the mother and new-born, besides the poor pregnancy outcomes conferred in the short term. Of note is the increased risk of type II diabetes, obesity and hypertension, all chronic disorders requiring continual use of hospital resources with increased hospital costs.

In the short-term, impaired blood sugar control in gestational diabetic pregnant women increases the risk of poor pregnancy outcomes: excessive foetal weight gain, stillbirths, preterm births, life-threatening low blood sugar in the new-born, postpartum haemorrhage and lower genital tract tears. These short-term implications markedly lower the quality of life of the woman in the postnatal period, besides increasing hospital costs.

On the other hand, gestational diabetes well managed, with good blood sugar control during the antenatal period can markedly improve pregnancy outcomes. Indeed, good glycaemic control is a marker of quality of care. Good glycaemic control reduces the likelihood of poor pregnancy outcomes, reducing hospital costs and length of hospital stay.

The third trimester fasting blood sugar level and risk of macrosomia and poor pregnancy outcomes in diabetic pregnant patients on treatment at Kenyatta National Hospital is unknown.

The knowledge gained from this study will reveal the quality of care being offered besides providing valuable information which can be used in the formulation of hospital protocols and standard operating procedures employed in the care of diabetic pregnant women.

Furthermore, this study will add to the pool of knowledge of diabetes in pregnancy in Kenya and Sub-Saharan Africa, an area where there is an insufficiency of studies in the area of gestational diabetes.

5.0: STUDY QUESTION

What is the incidence of poor pregnancy outcomes among pregnant women with pregnancy diabetes with average third trimester fasting blood sugars ≥ 5.3mmol/L and among those with average third trimester fasting blood sugars < 5.3mmol/L at Kenyatta National Hospital?

6.0: OBJECTIVES

6.1 Broad Objective

Among women with pregnancy diabetes at Kenyatta National Hospital, to determine the incidence of macrosomia and poor pregnancy outcomes in those with average third trimester fasting blood sugar greater or equal to 5.3mmol/L and in those with average third trimester fasting blood sugar less than 5.3mmol/L.

6.2 Specific Objectives

Primary Objectives

Among women with pregnancy diabetes at Kenyatta National Hospital:

1. To determine the prevalence of average third trimester fasting blood glucose level at or above 5.3mmol/L.
2. To determine the incidence of poor neonatal outcomes (macrosomia, stillbirths and neonatal hypoglycaemia) in those with average third trimester fasting blood glucose level at or above 5.3mmol/L and in those with average third trimester fasting blood glucose level below 5.3mmol/L.
3. To determine the incidence of poor maternal outcomes (perineal trauma, preterm birth and postpartum haemorrhage) in those with average third trimester fasting blood glucose level at or above 5.3mmol/L and in those with average third trimester fasting blood glucose level below 5.3mmol/L.

Secondary Objective

1. Among pregnant diabetic women with poor glycaemic control (average third trimester fasting blood glucose at or above 5.3mmol/L), to compare the incidence of poor pregnancy outcomes of those with pre-existing diabetes with the incidence of poor pregnancy outcomes of those with gestational diabetes.

7.0: METHODOLOGY

7.1 STUDY DESIGN: This was a retrospective descriptive cohort study examining the incidence of poor pregnancy outcomes of women with pregnancy diabetes with average third trimester fasting blood sugar ≥ 5.3mmol/L and with average third trimester fasting blood sugar < 5.3mmol/L.

7.2 STUDY AREA DESCRIPTION:

The study occurred at Kenyatta National Hospital; information being recovered from patients' files stored at Health Records Office.

Kenyatta National Hospital is the largest referral hospital in Kenya. It is a tertiary multidisciplinary hospital located in Nairobi. The antenatal clinic is an outpatient clinic, clinic 18, that is run by consultants, senior health officers and nurses. There is a labour ward and three antenatal wards (GFA, GFB and 1A) run by consultants, senior health officers and nurses, with daily ward rounds being done. Labour ward has a bed capacity of 24, but often hosts up to 100 patients due to overflow from surrounding facilities. Likewise, the antenatal wards each have a bed capacity of 35, but tend to host up to double that number of patients due to overflow from surrounding facilities.

At Kenyatta National Hospital, patients with gestational diabetes mellitus were identified through screening of pregnant women who attend antenatal clinic with fasting blood sugar level and OGTT. Gestational diabetes was diagnosed with fasting blood sugar of 5.1-6.9mmol/L, 1-hour post 75g oral glucose load ≥ 10mmol/L or 2-hour post 75g oral glucose load 8.5-11mmol/L. Once diagnosed, patients with gestational diabetes were put on treatment with lifestyle modification (diet modification), oral medication (metformin, glibenclamide) and insulin. A nutritionist and diabetologist were involved in the management of the patient. Regular clinic attendance continued with monitoring of fasting blood sugar level at subsequent visits and modification of treatment based on blood sugar level. In addition, monitoring for foetal wellbeing was done, including performance of an obstetric ultrasound. Post-delivery, the blood sugar of babies born to diabetic mothers were measured and recorded in the file of the mother.

In case a patient with diabetes in pregnancy had uncontrollably high blood sugars or other complications warranting hospital admission, they were admitted through labour

ward where acute management was conducted, after which, further management was done in the antenatal wards.

7.3 STUDY POPULATION:

All the files of pregnant patients with diabetes were retrieved from the health records. Then, based on an average of at least two third trimester fasting blood sugar levels from 26 gestational weeks to 37 gestational weeks, the files were divided into those with fasting blood glucose less than 5.3mmol/L (unexposed group), and those with fasting blood glucose ≥ 5.3mmol/L (exposed group), using consecutive sampling. A sample size of 258 was reached, 230 being the exposed group, and 28 being the unexposed group. Thereafter, using the structured questionnaire, data was retrieved from the files concerning baseline characteristics and poor pregnancy outcomes outlined in the specific objectives.

7.4.1 INCLUSION CRITERIA:

1. Pregnant women with gestational diabetes identified through fasting blood sugar of 5.1-6.9mmol/L and/or 1-hour post-75g OGTT ≥ 10mmol/L, or 2-hour post-75g OGTT of 8.5-11mmol/L.
2. Pregnant women with pre-existing/overt diabetes diagnosed through fasting blood sugar level ≥ 7mmol/L and 2-hour post 75g OGTT above 11mmol/L.

7.4.2 EXCLUSION CRITERIA:

1. Multiple gestation pregnancies may have complications such as preterm birth or twin-to-twin transfusion leading to foetal death. These complications may interfere with outcomes of interest such as macrosomia and stillbirths, which are dependent on maternal hyperglycaemia in this study.

2. Missing data on exposure, that is, missing data on at least two third trimester fasting blood sugar levels.

7.5 SAMPLE SIZE DETERMINATION

Sample size calculation for finite population (40)

$$n = \frac{Nz^2pq}{E^2(N-1) + z^2pq}$$

n = Desired sample size

N = population size (number of women with GDM approximately…… 258).

Z = value from standard normal distribution corresponding to desired confidence level (Z=1.96 for 95% CI)

p = expected true proportion (the proportion expected to be 31.9%, from a study conducted by Nakabuye B. et al (33)

$q = 1 - p$

E = desired precision (0.05)

$$n = \frac{258\ x\ 1.96^2\ x\ 0.319\ x\ 0.681}{0.05^2(258-1) + (1.96^2\ x\ 0.319\ x\ 0.681)} = 146$$

A Sample size of 146 participant files will be required for the study.

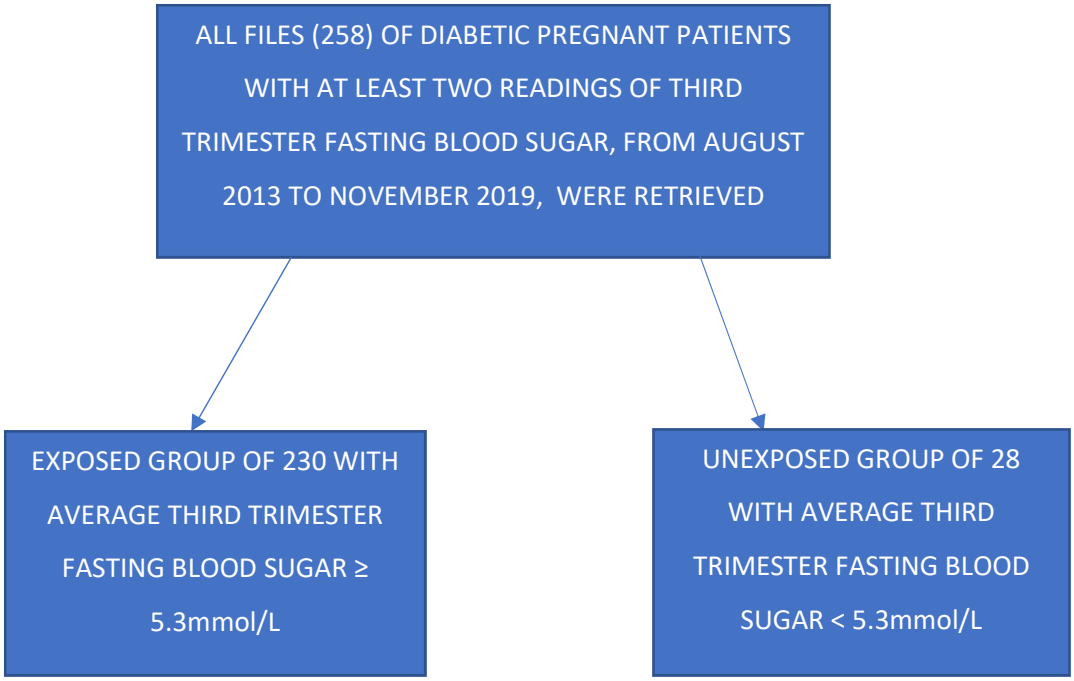
258 participant files (all available participant files) were used for the study.

7.6 SAMPLING PROCEDURE

At the Kenyatta National Hospital Health Records Office, patient files are coded according to diagnosis made at discharge from the hospital, and data regarding diagnosis and patient file number is recorded on a central processing unit. Through the use of these records and labor ward records, files of pregnant patients with diabetes managed in the antenatal clinic 18, labor ward and antenatal wards (GFA, GFB and ward 1A) were retrieved.

Consecutive sampling of patients' files was done from May 2011 to November 2019. Patient names and file numbers were accessible through labor ward records and statistics office at health records department. Labor ward records in the form of hard copies were available only up to May 2011, with records earlier than this period not being traceable. The statistics office at health records availed file numbers from August 2013 dating forwards. At the statistics office in the health records department, earlier records of file numbers before August 2013 were inaccessible due to a computer system crash in July 2013. Hence, 258 files of patients with pregnancy diabetes (gestational diabetes, pre-existing diabetes) with at least two readings of third trimester fasting blood sugar level were retrieved. The exposed group comprised of 230 files of patients with average third trimester fasting blood sugar ≥ 5.3mmol/L. The unexposed group comprised of 28 files of patients with average third trimester fasting blood sugar < 5.3mmol/L. The documentation of the patient sociodemographic data, medical/clinical characteristics, fasting blood sugar levels and outcomes of interest was in a structured questionnaire.

Figure 2: Participant Files



7.7 RECRUITMENT AND CONSENTING PROCEDURES

Since this study was retrospective and involved retrieving data from patients' files, there was no need for informed consent from patients.

7.8 DATA VARIABLES; Figure 3

INDEPENDENT VARIABLE	DEPENDENT VARIABLE	DATA SOURCE
THIRD TRIMESTER FASTING BLOOD SUGAR LEVEL	MACROSOMIA	PATIENTS' FILES
	STILLBIRTH	
	NEONATAL HYPOGLYCAEMIA	
	PRETERM DELIVERY	
	POSTPARTUM HAEMORRHAGE	
	PERINEAL TEARS	

7.9 DATA COLLECTION AND MANAGEMENT

After ethical approval, data was collected from patients' files using a structured questionnaire, by the principal investigator aided by trained research assistants. The principal investigator backed up data in an external hard drive. Data was accessible to the principal investigator, statistician and supervisors.

Data was analysed using SPSS 23. Demographic data was analysed and presented as means and standard deviations as well as medians with interquartile range where applicable. The incidence of macrosomia, stillbirth, neonatal hypoglycaemia, preterm delivery, primary postpartum haemorrhage and perineal tears will be calculated.

7.10 QUALITY CONTROL

The research assistants were trained by the principal investigator on proper filling of the questionnaires. Information entered into the questionnaires was double checked after filling to ensure completeness.

7.11 STUDY RESULTS DISSEMINATION PLAN

The final study results were presented to the Department of Obstetrics and Gynaecology and later published into a thesis for filing in the University of Nairobi Library Services. The findings will also be disseminated to Kenyatta National Hospital, and be summarized into papers and sent out to maternal health journals for publishing and wider dissemination.

7.12 ETHICAL CONSIDERATIONS

Approval to conduct the research was granted by Kenyatta National Hospital – University of Nairobi Ethics and Research Committee. License to conduct the study was sought from the Department of Obstetrics and Gynaecology and management of Kenyatta National Hospital. Information obtained from patients' files was kept confidential. Names or any data identifying particular patients was not recorded on the questionnaire. Data collected was only used for the purposes of this study.

7.13 STRENGTHS OF THIS STUDY

Quantifies the burden of poor glycaemic control and occurrence of poor pregnancy outcomes in women with diabetes in pregnancy.

7.14 STUDY LIMITATION

Some limitations were encountered during the conduct of this study.

1. Inaccessibility of data due to poor storage of patient diagnosis records and computer system failure. This could be improved by development of a proper filing system of patient diagnosis records, and adequate backup systems in place in the event of a computer system failure.
2. Body mass index was not routinely calculated and recorded at patient visits. In some cases, the height of women attending antenatal clinic was not recorded. High body mass index is an important confounder in this study. Where possible, the body mass index of patients was calculated using the recorded height and weight at first antenatal visit.
3. Missing data due to poor documentation. Files with missing data on exposure were excluded.
4. Non-differential misclassification bias where inaccuracy in the evaluated outcome affects both the exposed and non-exposed group

   Differential misclassification bias where inaccuracy in the evaluated outcome affects either the exposed or unexposed group.

   Problems of misclassification were countered by double-checking information collected in the questionnaire against patient's health records, besides having at least 2 recordings of third trimester fasting blood sugar from 2 separate occasions from which average third trimester fasting blood sugar was derived.

8.0: RESULTS

The following are the results of a retrospective descriptive cohort study conducted among 258 pregnant diabetics at Kenyatta National Hospital examining the prevalence of poor glycaemic control (average third trimester fasting blood sugar ≥ 5.3mmol/L), the incidence of adverse maternal and neonatal outcomes among those with poor glycaemic control (n=230) and those with good glycaemic control (n=28).

TABLE 1

Patient characteristics (Sociodemographic and Medical/Clinical Characteristics): poor glycemic control vs good glycemic control

	Poor (≥5.3mmol/L)	Good (<5.3mmol/L)	Total	p-value
Age				
Below 21	**2 (0.9)**	**0 (0.0)**	**2 (0.8)**	
21-30	**92 (40)**	**10 (35.7)**	**102 (39.5)**	
31-40	**124 (53.9)**	**17 (60.7)**	**141 (54.7)**	
>40	**12 (5.2)**	**1 (3.6)**	**13 (5.0)**	
Marital status				
Married	**204 (88.7)**	**26 (92.9)**	**230 (89.1)**	**0.504**
Single	**26 (11.3)**	**2 (7.1)**	**28 (10.9)**	
Employment				
Employed	**133 (57.8)**	**19 (67.9)**	**152 (58.9)**	**0.308**
Not employed	**97 (42.2)**	**9 (32.1)**	**106 (41.1)**	
Education				
Secondary and below	**147 (63.9)**	**13 (46.4)**	**160 (62.0)**	**0.072**
Above secondary	**83 (36.1)**	**15 (53.6)**	**98 (38.0)**	
Parity				
< 2	**93 (40.4)**	**14 (50.0)**	**107 (41.5)**	**0.332**

≥ 2	**137 (59.6)**	**14 (50.0)**	**151 (58.5)**	
History of macrosomia				
Yes	**56 (24.3)**	**9 (32.1)**	**65 (25.2)**	**0.370**
No	**174 (75.7)**	**19 (67.9)**	**193 (74.8)**	
History of pregnancy loss				
Yes	**91 (39.6)**	**8 (28.6)**	**99 (38.4)**	**0.259**
No	**139 (60.4)**	**20 (71.4)**	**159 (61.6)**	
History of Gestational DM				
Yes	**7 (3.0)**	**1 (3.6)**	**8 (3.1)**	**1.000**
No	**223 (97.0)**	**27 (96.4)**	**250 (96.9)**	
Family history of diabetes				
Yes	**50 (23.1)**	**8 (32.0)**	**58 (24.1)**	**0.327**
No	**166 (76.9)**	**17 (68.0)**	**183 (75.9)**	
Body Mass Index				
Below 30	**34 (44.2)**	**3 (30.0)**	**37 (42.5)**	**0.507**
30 and above	**43 (55.8)**	**7 (70.0)**	**50 (57.5)**	
Gestational age at first antenatal visit (weeks)				
< 24	**95 (48.5)**	**10 (43.5)**	**105 (47.9)**	**0.650**
≥ 24	**101 (51.5)**	**13 (56.5)**	**114 (52.1)**	
Number of ANC visits				
< 4	**85 (38.5)**	**7 (26.9)**	**92 (37.2)**	**0.250**
≥ 4	**136 (61.5)**	**19 (73.1)**	**155 (62.8)**	
Treatment Patient on				
Insulin				

Yes	**157 (68.3)**	**16 (57.1)**	**173 (67.1)**	**0.237**
No	**73 (31.7)**	**12 (42.9)**	**85 (32.9)**	
Oral hypoglycemics				
Yes	**82 (35.7)**	**6 (21.4)**	**88 (34.1)**	**0.134**
No	**148 (64.3)**	**22 (78.6)**	**170 (65.9)**	

The mean age of the entire population was 32.2y (SD=0.3), with 54.7% being in the 31-40 years category. Of the entire population, 89.1% of the women were married, 58.9% employed, 62% with secondary education and below, 58.5% with parity ≥ 2, 57.5% had body mass index ≥ 30, 52.1% had first antenatal visit at or above 24 gestational weeks, 62.8% had 4 or more antenatal visits, 58.5% delivered at or above 37 weeks gestation. The mean age for those with poor glycaemic control was 32.2 (SD=5.4) years, while the mean age for those with good glycaemic control was 32.4 (SD=4.2) years. The prevalence of being married was 88.7% and 92.9% for those with poor glycaemic control and good glycaemic control respectively; this was not statistically significant (p-value 0.504). The prevalence of being employed was 57.8% and 67.9% for those with poor glycaemic control and good glycaemic control respectively; this was not statistically significant (p-value 0.308). The prevalence of tertiary education was 36.1% and 53.6% for those with poor glycaemic control and good glycaemic control respectively; this was not statistically significant (p-value 0.0702). The prevalence of parity less than 2 was 40.4% and 50% for those with poor glycaemic control and good glycaemic control respectively; this was not statistically significant (p-value 0.332). The prevalence of history of macrosomia was 24.3% and 32.1% for those with poor glycaemic control and good glycaemic control respectively; this was not statistically significant (p-value 0.37).The prevalence of history of pregnancy loss was 39.6% and 28.6% for those with poor glycaemic control and good glycaemic control respectively; this was not statistically significant (p-value 0.259). The prevalence of family history of diabetes was 23.1% and 32% for those with poor glycaemic control and good glycaemic control respectively; this was not statistically significant (p-value 0.327). The prevalence of body mass index ≥ 30 was 55.8% and 70% for those with poor glycaemic control and good glycaemic control respectively;

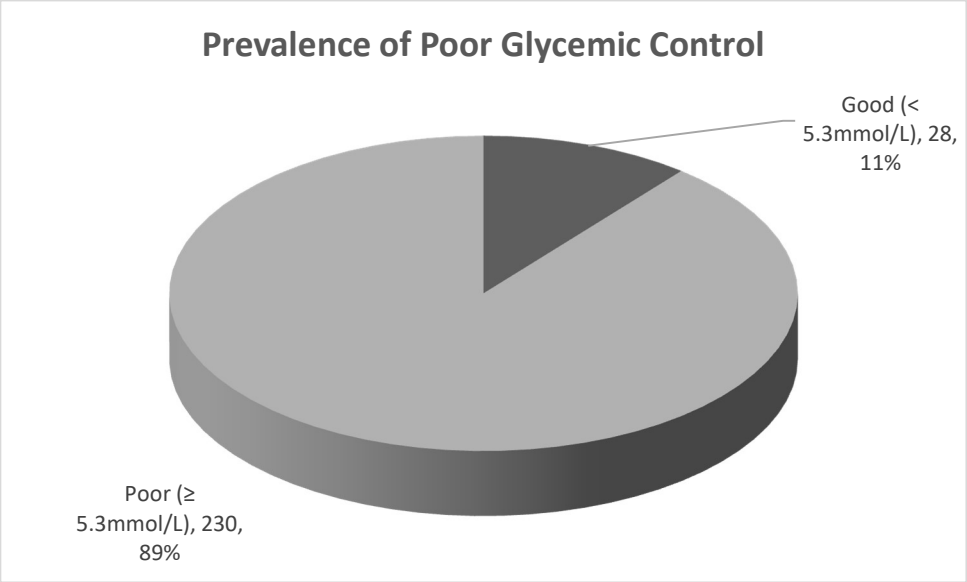
this was not statistically significant (p-value 0.507). The prevalence of being less than 24 weeks' gestation at first antenatal visit was 48.5% and 43.5% for those with poor glycaemic control and good glycaemic control respectively; this was not statistically significant (p-value 0.65). The prevalence of ≥ 4 antenatal visits was 61.5% and 73.1% for those with poor glycaemic control and good glycaemic control respectively; this was not statistically significant (p-value 0.25). The prevalence of insulin use was 68.3% and 57.1% for those with poor glycaemic control and good glycaemic control respectively; this was not statistically significant (p-value 0.237). The prevalence of oral hypoglycaemic use was 35.7% and 21.4% for those with poor glycaemic control and good glycaemic control respectively; this was not statistically significant (p-value 0.134).

TABLE 2

Prevalence of Poor Glycemic Control (Average third trimester Fasting Blood Sugar Level)

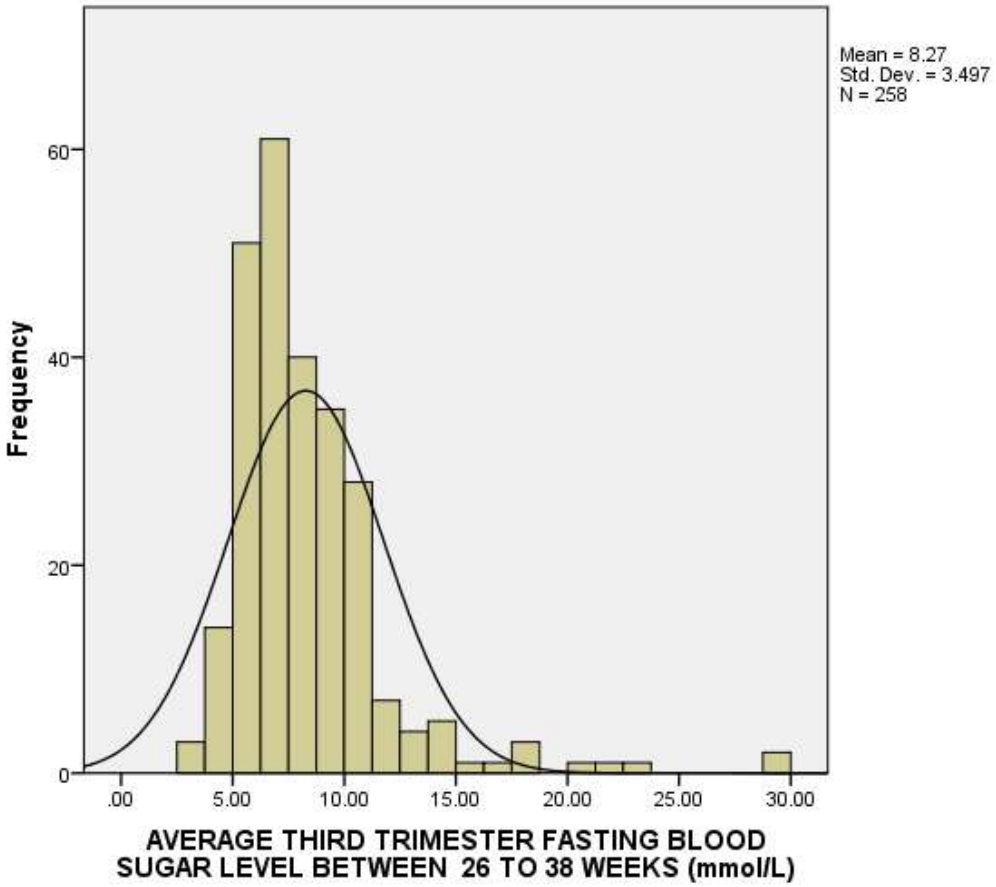
	Frequency n (%)
Good (< 5.3mmol/L)	**28 (10.9)**
Poor (≥ 5.3mmol/L)	**230 (89.1)**

Figure 4



The prevalence of poor glycaemic control was 89.1%.

Figure 5: Average Third Trimester Fasting Blood Sugar Level



The average third trimester fasting blood sugar level was 8.27mmol/L.

TABLE 3

Neonatal Outcomes: poor glycemic control vs good glycemic control

	Poor (≥5.3mmol/L)	Good (<5.3mmol/L)	Total	p-value
Birth weight				
Less than 4kg	**171 (74.3)**	**22 (78.6)**	**193 (74.8)**	**0.6**
≥ 4kg	**59 (25.7)**	**6 (21.4)**	**65 (25.2)**	
Baby alive				
Yes	**188 (82.1)**	**27 (96.4)**	**215(83.7)**	**0.058**
No	**41 (17.9)**	**1 (3.6)**	**42 (16.3)**	
Presence of neonatal hypoglycemia				
Yes	**38 (27)**	**6 (28.6)**	**44 (27.2)**	**0.9**
No	**103 (73)**	**15 (71.4)**	**118 (72.8)**	

The incidence of macrosomia was 25.7% and 21.4% for those with poor glycaemic control and good glycaemic control respectively; this was not statistically significant (p-value 0.627). The incidence of stillbirths was 17.9% and 3.6% for those with poor glycaemic control and good glycaemic control respectively; this was not statistically significant (p-value 0.058). The incidence of neonatal hypoglycaemia was 27% and 28.6% for those with poor glycaemic control and good glycaemic control respectively; this was not statistically significant (p-value 0.876).

TABLE 4

Maternal outcomes: poor glycemic control vs good glycemic control

	Poor (≥5.3mmol/L)	Good (<5.3mmol/L)	Total	p-value
Gestational age at delivery				
< 37	**101 (43.9)**	**6 (21.4)**	**107(41.5)**	**0.025**
≥ 37	**129 (56.1)**	**22 (78.6)**	**151 (58.5)**	
Presence of PPH				
Yes	**66 (28.9)**	**12 (44.4)**	**78 (30.6)**	**0.1**
No	**162 (71.1)**	**15 (55.6)**	**177 (69.4)**	
Perineal trauma				
Yes	**35 (15.3)**	**6 (22.2)**	**41 (16)**	**0.4**
No	**194 (84.7)**	**21 (77.8)**	**215 (84)**	

The incidence of preterm birth was 43.9% and 21.4% for those with poor glycaemic control and good glycaemic control respectively; this was statistically significant (p-value 0.025). The incidence of postpartum haemorrhage was 28.9% and 44.4% for those with poor glycaemic control and good glycaemic control respectively; this was not statistically significant (p-value 0.098). The incidence of perineal trauma was 15.3% and 22.2% for those who had poor glycaemic control and good glycaemic control respectively; this was not statistically significant (p-value 0.403).

POORLY CONTROLLED PRE-EXISTING VS POORLY CONTROLLED GESTATIONAL DIABETES

TABLE 5

Patient characteristics (Sociodemographic and Medical/Clinical Characteristics) of those with poor glycemic control (Average third trimester fasting blood sugar ≥ 5.3mmol/L)

	Poorly Controlled Pre-existing Diabetes	Poorly Controlled Gestational Diabetes	Total	p-value
Age	**N=197**	**N=33**		
Average age	**31.9 ± 5.3**	**33.5 ± 5.5**		**0.1**
Marital status				
Married	**174 (88.3)**	**30 (90.9)**	**204 (88.7)**	**1.0**
Single	**23 (11.7)**	**3 (9.1)**	**26 (11.3)**	
Employment				
Employed	**112 (56.9)**	**21 (63.6)**	**133 (57.8)**	**0.5**
Not employed	**85 (43.1)**	**12 (36.4)**	**97 (42.2)**	
Education				
Secondary and below	**127 (64.5)**	**20 (60.6)**	**147 (63.9)**	**0.7**
Above secondary	**70 (35.5)**	**13 (39.4)**	**83 (36.1)**	
Parity				
< 2	**81 (41.1)**	**12 (36.4)**	**93 (40.4)**	**0.7**
≥ 2	**116 (58.9)**	**21 (63.6)**	**137 (59.6)**	
History of macrosomia				
Yes	**44 (22.3)**	**12 (36.4)**	**56 (24.3)**	**0.1**
No	**153 (77.7)**	**21 (63.6)**	**174 (75.7)**	
History of pregnancy loss				
Yes	**75 (38.1)**	**16 (48.5)**	**91 (39.6)**	**0.3**

No	**122 (61.9)**	**17 (51.5)**	**139 (60.4)**	
History of Gestational DM in earlier pregnancy				
Yes	**2 (1.0)**	**5 (15.2)**	**7 (3.0)**	**0.001**
No	**195 (99.0)**	**28 (84.8)**	**223 (97.0)**	
Family history of diabetes				
Yes	**44 (23.0)**	**6 (24.0)**	**50 (23.1)**	**0.9**
No	**147 (77.0)**	**19 (76.0)**	**166 (76.9)**	
Body Mass Index				
Below 30	**31 (48.4)**	**3 (23.1)**	**34 (44.2)**	**0.1**
30 and above	**33 (51.6)**	**10 (76.9)**	**43 (55.8)**	
Gestational age at first antenatal visit (weeks)				
< 24	**81 (46.6)**	**14 (63.6)**	**95 (48.5)**	**0.1**
≥ 24	**93 (53.4)**	**8 (36.4)**	**101 (51.5)**	
Number of ANC visits				
< 4	**81 (42.6)**	**4 (12.9)**	**85 (38.5)**	**0.002**
≥ 4	**109 (57.4)**	**27 (87.1)**	**136 (61.5)**	
Treatment Patient on				
Insulin				
Yes	**137 (69.5)**	**20 (60.6)**	**157 (68.3)**	**0.3**
No	**60 (30.5)**	**13 (39.4)**	**73 (31.7)**	
Oral hypoglycemics				
Yes	**64 (32.5)**	**18 (54.5)**	**82 (35.7)**	**0.014**
No	**133 (67.5)**	**15 (45.5)**	**148 (64.3)**	

The mean age was 31.9 ± 5.3 years and 33.5 ± 5.5 years for the poorly controlled pre-existing diabetics and poorly controlled gestational diabetics respectively; this was not statistically significant (p-value 0.122). The prevalence of being married was 88.3% and 90.9% for the poorly controlled pre-existing diabetics and poorly controlled gestational diabetics respectively; this was not statistically significant (p-value 1). The prevalence of being employed was 56.9% and 63.6% for the poorly controlled pre-existing diabetics and poorly controlled gestational diabetics respectively; this was not statistically significant (p-value 0.465). The prevalence of tertiary education was 35.5% and 39.4% for the poorly controlled pre-existing diabetics and poorly controlled gestational diabetics respectively; this was not statistically significant (p-value 0.698). The prevalence of parity ≥ 2 was 58.9% and 63.6% for the poorly controlled pre-existing diabetics and poorly controlled gestational diabetics respectively; this was not statistically significant (p-value 0.703). The prevalence of history of macrosomia was 22.3% and 36.4% for the poorly controlled pre-existing diabetics and poorly controlled gestational diabetics respectively; this was not statistically significant (p-value 0.082). The prevalence of history of pregnancy loss was 38.1% and 48.5% for the poorly controlled pre-existing diabetics and poorly controlled gestational diabetics respectively; this was not statistically significant (p-value 0.258). The prevalence of history of gestational diabetes in earlier pregnancy was 1% and 15.2% for the poorly controlled pre-existing diabetics and poorly controlled gestational diabetics respectively; this was statistically significant (p-value 0.001). The prevalence of family history of diabetes mellitus was 23% and 24% for the poorly controlled pre-existing diabetics and poorly controlled gestational diabetics respectively; this was not statistically significant (p-value 0.914). The prevalence of body mass index ≥ 30 was 51.6% and 76.9% for the poorly controlled pre-existing diabetics and poorly controlled gestational diabetics respectively; this was not statistically significant (p-value 0.093). The prevalence of first antenatal visit at less than 24 weeks' gestation was 46.6% and 63.6% for the poorly controlled pre-existing diabetics and poorly controlled gestational diabetics respectively; this was not statistically significant (p-value 0.131). The prevalence of 4 or more antenatal visits was 57.4% and 87.1% for the poorly controlled pre-existing diabetics and poorly controlled gestational diabetics respectively; this was statistically significant (p-value 0.002).The prevalence of insulin use was 69.5% and 60.6% for the poorly controlled pre-existing diabetics and poorly controlled gestational diabetics respectively; this was not statistically significant (p-value 0.307). The

prevalence of oral hypoglycemic use was 32.5% and 54.5% for the poorly controlled pre-existing diabetics and poorly controlled gestational diabetics respectively; this was statistically significant (p-value 0.014).

TABLE 6

Neonatal Outcomes: Poorly controlled pre-existing diabetes vs poorly controlled gestational diabetes

	Poorly Controlled Pre-existing Diabetes	Poorly Controlled Gestational Diabetes	Total	p-value
Birth weight				
Less than 4kg	**148 (75.1)**	**23 (69.7)**	**171 (74.3)**	**0.5**
≥ 4kg	**49 (24.9)**	**10 (30.3)**	**59 (25.7)**	
Baby alive				
Yes	**155 (79.1)**	**33 (100)**	**188 (82.1)**	**0.004**
No	**41 (20.9)**	**0 (0.0)**	**41 (17.9)**	
Presence of neonatal hypoglycemia				
Yes	**31 (27.4)**	**7 (25.0)**	**38 (27.0)**	**0.8**
No	**82 (72.6)**	**21 (75.0)**	**103 (73.0)**	

The incidence of macrosomia was 24.9% and 30.3% for the poorly controlled pre-existing diabetics and poorly controlled gestational diabetics respectively; this was not statistically significant (p-value 0.509). The incidence of stillbirths was 20.9% and 0% for the poorly controlled pre-existing diabetics and poorly controlled gestational diabetics respectively; this was statistically significant (p-value 0.004). The incidence of neonatal hypoglycaemia was 27.4% and 25% for the poorly controlled pre-existing diabetics and poorly controlled gestational diabetics respectively; this was not statistically significant (p-value 0.795).

TABLE 7

Maternal outcomes: poorly controlled pre-existing diabetes vs poorly controlled gestational diabetes

	Poorly Controlled Pre-existing Diabetes	Poorly Controlled Gestational Diabetes	Total	p-value
Gestational age at delivery				
< 37	**93 (47.2)**	**8 (24.2)**	**101 (43.9)**	**0.014**
≥ 37	**104 (52.8)**	**25 (75.8)**	**129(56.1)**	
Presence of PPH				
Yes	**47 (24)**	**19 (59.4)**	**66 (28.9)**	**<0.001**
No	**149 (76)**	**13 (40.6)**	**162 (71.1)**	
Perineal trauma				
Yes	**30 (15.3)**	**5 (15.2)**	**35 (15.3)**	**1.0**
No	**166 (84.7)**	**28 (84.8)**	**194 (84.7)**	

The incidence of preterm birth was 47.2% and 24.2% for the poorly controlled pre-existing diabetics and poorly controlled gestational diabetics respectively; this was statistically significant (p-value 0.014). The incidence of postpartum haemorrhage was 24% and 59.4% for the poorly controlled pre-existing diabetics and poorly controlled gestational diabetics respectively; this was statistically significant (p-value < 0.001). The incidence of perineal trauma was 15.3% and 15.2% for the poorly controlled pre-existing diabetics and poorly controlled gestational diabetics respectively; this was not statistically significant (p-value 0.982).

9.0: DISCUSSION OF RESULTS:

The comparison of the sociodemographic (age, marital status, employment status, education level) and medical/clinical characteristics of diabetic pregnant patients with poor glycaemic control versus good glycaemic control revealed no statistically significant differences between the groups, with the mean age of those with poor glycaemic control being 32.2 years, and the average age of those with good glycaemic control being 32.4 years. However, those with poor glycaemic control had a higher incidence of pregnancy loss in earlier pregnancies (39.6% vs 28.6%; p-value 0.259). In addition, those with poor glycaemic control had fewer antenatal visits (p-value 0.25).

Prevalence of Poor Glycaemic Control (Average third trimester fasting blood sugar level at or above 5.3mmol/L):

The prevalence of poor glycaemic control was 89.1%. This reveals that majority of the women with pregnancy diabetes (pre-existing/overt and gestational) have poor glycaemic control, not in keeping with the 2018 Kenya National Diabetes Guidelines (39). This could be attributed to a lack of widespread knowledge of the glucose targets recommended by the Ministry of Health, leading to reduced practice in aiming for those targets.

Neonatal Outcomes:

The incidence of macrosomia was 25.7% in those with poor glycaemic control and 21.4% in those with good glycaemic control (p-value 0.627; not statistically significant). The incidence of macrosomia was lower in those with good glycaemic control than in those with poor glycaemic control. This is due to the direct relation of maternal glucose level on foetal weight gain as shown in the HAPO study which found that higher fasting plasma glucose values were related to a greater risk of macrosomia (17).

In an observational study of Saudi diabetic women on Glycaemic control and pregnancy outcomes, the incidence of macrosomia was 25% among those with poor glycaemic control (HbA1c > 6.5%) and 8.4% in those with good glycaemic control (20). The Saudi study had similar observations of macrosomia to this KNH study on glycaemic control and pregnancy outcomes.

A retrospective cohort examining pregnancy outcomes in Korean women with poorly controlled type 2 diabetes, found an incidence of macrosomia of 15% in those with

average third trimester fasting blood sugar of 5.86 – 8.41mmol/L (34). The incidence of 15% in the Korean study was lower than the incidence of macrosomia of 25.7% among poorly controlled diabetics in this KNH study on glycaemic control and pregnancy outcomes. In a Ugandan prospective study of hyperglycaemic women, the incidence of macrosomia was 8.1% (33); lower than the incidence of macrosomia in this KNH study (25.7%).

The incidence of stillbirths in those with poor glycaemic control was 17.9% and in those with good glycaemic control was 3.6%, with (p-value 0.058; not statistically significant).

In a retrospective study of Saudi diabetic women on Glycaemic control and pregnancy outcomes, the incidence of stillbirths was 6.7% among those with poor glycaemic control and 1.6% in those with good glycaemic control (20). In the Saudi study, the incidence of stillbirths was lower in those with good glycaemic control than in those with poor glycaemic control. The Saudi study had similar observations to this KNH study on glycaemic control and pregnancy outcomes, which found a lower incidence of stillbirths in those with good glycaemic control than in those with poor glycaemic control.

In a nationwide French 2012 cohort, the risk of perinatal death was 0.5% in women with gestational diabetes, 1.2% in women with type 1 diabetes and 2.4% in women with type 2 diabetes (35). There was no report on the glycaemic control in this survey. However, the incidence of stillbirths was much lower in the large French survey than in this KNH study.

In a Ugandan prospective cohort of hyperglycaemic pregnant diabetics the incidence of stillbirth was 4.1% (33); lower than the incidence of stillbirth of 17.9% in this KNH study.

In this KNH study on glycaemic control and pregnancy outcomes, the incidence of stillbirth in those with good glycaemic control was 3.6%.

In a cohort examining gestational diabetes mellitus in early pregnancy with good glycaemic control, the incidence of stillbirth was 1.8% in those with type 2 diabetes and 3.4% in those with gestational diabetes diagnosed at less than 12 weeks gestation (21). Our KNH study on glycaemic control found a similar incidence of stillbirth (3.6%) among those with good glycaemic control compared to the incidence of stillbirths

(3.4%) among the multi-ethnic cohort of gestational diabetics with good glycaemic control.

In our study, the incidence of stillbirths was higher in those with poor glycaemic control than in those with good glycaemic control (17.9% vs 3.6%; p-value 0.058). This could be explained by a study of placental villi and vessels in hyperglycaemic women, which revealed that increase in glycaemic levels inhibits villous angiogenesis, interfering with maternal-foetal exchanges and increasing the risk of perinatal mortality (30).

The incidence of neonatal hypoglycaemia was 27% in those with poor glycaemic control and 28.6% in those with good glycaemic control (p-value 0.876). These incidences of neonatal hypoglycaemia differed in trend from the findings of the HAPO study which demonstrated a direct relationship of maternal blood sugar levels and neonatal hypoglycaemia (17). Indeed, in a retrospective study of Saudi diabetic women in keeping with the HAPO study findings, the incidence of neonatal hypoglycaemia was 30% in those with poor glycaemic control and 6% in those with good glycaemic control (20). The contrast in research findings could be attributed to the smaller sample of files of women with good glycaemic control in this KNH study.

Maternal Outcomes:

The incidence of preterm birth was 43.9% in those with poor glycaemic control and 21.4% in those with good glycaemic control. This is a statistically significant finding with a p-value of 0.025. The incidence of preterm birth was higher in those with poor glycaemic control. This could be due to the higher probability of large for gestational age babies the higher the fasting blood glucose level, leading to more incidences of preterm labour and birth. Indeed, the HAPO study revealed a strong relationship of maternal glucose level with increased birth weight above the 90^{th} percentile and preterm birth (17).

The incidences of preterm birth in the KNH study on glycaemic control (43.9% vs 21.4%) were similar in trend to those of a Saudi retrospective study (Buhary) which had an incidence of preterm birth of 26.2% in those with poor glycaemic control and 13.5% in those with good glycaemic control (20). In a Korean study, the incidence of preterm birth among type 2 diabetics with poor glycaemic control was 9% (34). In contrast, in the KNH study on glycaemic control and pregnancy outcomes, the incidence of preterm birth in those with poor glycaemic control was 21.4%. There is

need for better glycaemic control among pregnant diabetics at Kenyatta National Hospital.

The incidence of postpartum haemorrhage among those with poor glycaemic control was 28.9% while the incidence of postpartum haemorrhage among those with good glycaemic control was 44.4%. This finding was not statistically significant (p-value 0.098).

In a Cameroon prospective cohort study examining maternal hyperglycaemia during labour and pregnancy outcomes (36), the incidence of postpartum haemorrhage was 3.2%; lower than the incidence of postpartum haemorrhage in those with poor glycaemic control (28.9%) in this KNH study. Similarly, in a retrospective cohort study in Delhi examining maternal and perinatal outcomes in gestational diabetes, the incidence of postpartum haemorrhage was 1.2%; with majority of birth weights being less than 3.5kg (37).

The incidence of perineal trauma was 15.3% in those who had poor glycaemic control and 22.2% in those who had good glycaemic control. This finding was not statistically significant (p-value 0.403).

In a Cameroon prospective cohort study of hyperglycaemic women (36), the incidence of perineal trauma was 13%; similar to the incidence of perineal trauma among those with poor glycaemic control (15.3%) in this KNH study. In a Ugandan prospective cohort study (33) of hyperglycaemic women, the incidence was 53.1%; higher than the incidence of perineal trauma among women with poor glycaemic control in this KNH study. In a Saudi retrospective study, the incidence of perineal trauma was 8.5% in those with poor glycaemic control and 2.5% in those with good glycaemic control (20); lower than the incidences of perineal trauma in this KNH study.

Poorly controlled diabetics were divided into pre-existing diabetics and gestational diabetics, and their pregnancy outcomes compared. The incidence of macrosomia was 24.9% in poorly controlled pre-existing diabetics, and 30.3% in the poorly controlled gestational diabetics, albeit, not statistically significant (p-value 0.509). The incidence of macrosomia was higher in poorly controlled (FBS 6.5mmol/L) gestational diabetics than in poorly controlled (FBS 9.1mmol/L) pre-existing diabetics (p-value 0.509). This could be due to the higher incidence of preterm births among the poorly

controlled pre-existing diabetics than among poorly controlled gestational diabetics (47.2% vs 24.2%), leaving fewer opportunities for birth of macrosomic babies among the poorly controlled pre-existing diabetics.

In a Saudi retrospective study (20), the incidence of macrosomia was 19.6% among type 2 diabetics, 19.3% among type 1 diabetics, and 35.2% among those with gestational diabetes; the poorly controlled pre-existing diabetics having a lower incidence of macrosomia than the poorly controlled gestational diabetics. The Saudi findings were similar to the incidences of macrosomia in this KNH study.

The incidence of stillbirths was 20.9% in the poorly controlled pre-existing diabetics, and 0% in the poorly controlled gestational diabetics. The incidence of stillbirths was significantly higher in the poorly controlled pre-existing diabetics than in the poorly controlled gestational diabetics (p-value 0.004). This could be attributed to placental insufficiency in the poorly controlled pre-existing diabetics who also had higher average third trimester fasting blood sugar level of 9.1mmol/L. This is in keeping with the findings in a study (30) examining the appearance of placental villi and vessels in hyperglycaemic women; it revealed that low maternal hyperglycaemia stimulates vascular proliferation in response to a lower hypoxia level, ensuring maternal and foetal exchange. However, further increase in glycaemic levels inhibits villous angiogenesis, interfering with maternal-foetal exchanges and increasing the risk of perinatal mortality (30).

In a Saudi retrospective study, the incidence of stillbirths was 7.69% in type 2 diabetics, 16.2% in type 1 diabetics, and 1.23% in gestational diabetics (20); similar in trend to this KNH study, with pre-existing diabetics with poor glycaemic control having a much higher incidence of stillbirths than gestational diabetics with poor glycaemic control.

The incidence of neonatal hypoglycaemia was 27.4% in the poorly controlled pre-existing diabetics and 25% in the poorly controlled gestational diabetics, with a p-value of 0.795 (not statistically significant). The incidence of neonatal hypoglycaemia was higher in the poorly controlled pre-existing diabetics than in the poorly controlled gestational diabetics. This could be due to the higher average fasting blood sugar level of the pre-existing diabetics leading to a higher incidence of foetal hyperinsulinemia, with resultant neonatal hypoglycaemia.

In a Saudi retrospective study, the incidence of neonatal hypoglycaemia was 33.3% in type 2 diabetics, 41% in type 1 diabetics, and 15.4% in those with gestational diabetes (20); similar in trend to those of this KNH study.

In a 1976 study examining maternal fasting blood sugar level and incidence of hypoglycaemia, the incidence of neonatal hypoglycaemia was 77% in the infants of diabetic mothers and 25% in the infants of mothers with gestational diabetes (38). The findings for pre-existing diabetics in the 1976 study were higher than those for this KNH study; however, the findings for those with gestational diabetes were similar to those of this KNH study.

The incidence of preterm birth was 47.2% in the poorly controlled pre-existing diabetics, and 24.2% in the poorly controlled gestational diabetics, with a statistically significant p-value of 0.014. The incidence of preterm birth was higher in the poorly controlled pre-existing diabetics than in the poorly controlled gestational diabetics. This could be due to the longer period of foetal exposure to hyperglycaemia in the pre-existing diabetics, leading to larger for gestational age babies, with distention of the uterus inducing preterm labour, resulting in preterm birth.

In a Saudi retrospective study (20), the incidence of preterm birth was 33.3% in type 2 diabetics, 25% in type 1 diabetics and 21.1% in gestational diabetics, similar in trend to this KNH study findings.

The incidence of postpartum haemorrhage was 24% in the poorly controlled pre-existing diabetics, and 59.4% in the poorly controlled gestational diabetics, with a statistically significant p-value of less than 0.001. The incidence of postpartum haemorrhage was lower in the pre-existing diabetics than in those with gestational diabetes. This could be due to the higher incidence of foetal macrosomia among the gestational diabetics, leading to overdistention of the uterus, with a predisposition for uterine atony and postpartum haemorrhage at third stage of labour.

No studies were found comparing the incidence of postpartum haemorrhage in pre-existing diabetics with that of gestational diabetics with poor glycaemic control.

The incidence of perineal trauma was 15.3% in the poorly controlled pre-existing diabetics, and 15.2% in the poorly controlled gestational diabetics, with a p-value of 0.982 (not statistically significant). There was no difference in incidence in the two groups. This could be attributed to the multifactorial nature of perineal trauma, with

possible causes including a large foetus, primiparity, malpresentation, position during childbirth or a decision to perform an episiotomy.

In a Saudi retrospective study, the incidence of perineal trauma was 7.84% in type 2 diabetics, 12.9% in type 1 diabetics and 8.45% in gestational diabetics (20).

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10.0: CONCLUSION

- The prevalence of poor glycaemic control was 89.1%.
- Poorly controlled pregnancy diabetes increases the risk of poor pregnancy outcomes such as macrosomia, stillbirths and preterm birth, with poorly controlled pre-existing diabetics sometimes experiencing worse outcomes than poorly controlled gestational diabetics.
- Indeed, this study found a higher incidence of macrosomia, stillbirths and preterm birth among those with poor glycaemic control compared to those who had good glycaemic control.
- Furthermore, among those with poor glycaemic control, the pre-existing diabetics experienced significantly worse outcomes of stillbirths and preterm births than the poorly controlled gestational diabetics.

10.1: RECOMMENDATIONS

- Information on risk factors for pregnancy diabetes, importance of early onset of and regular antenatal follow-up, timing and importance of screening for diabetes in pregnancy, symptoms of diabetes to watch out for, and glycaemic targets to aim for should be disseminated to patients and all cadres of health workers (nurses, medical officer interns, clinical officer interns, senior health officers) taking care of women of reproductive age.
- This study will contribute in the establishment of guidelines on the protocols for the management of diabetes in pregnancy by the Kenyatta National Hospital and the Ministry of Health.

11.1: STUDY TIMELINE

	Nov 2018- May 2019	June 2019	July - Oct 2019	Oct – Dec 2019	Dec – Feb 2020	Dec – Apr 2020
PROPOSAL DEVELOPMENT						
PROPOSAL PRESENTATION						
ETHICAL APPROVAL						
DATA COLLECTION						
DATA ANALYSIS						
REPORT WRITING AND PRESENTATION						
SUBMISSION TO DEPARTMENT						

11.2 BUDGET

	COMPONENTS	UNIT OF MEASURE	DURATION/NUMBER	COST (KSHS)	TOTAL (KSHS)
	Personnel				
1	Research Assistant	1	15	1,500.00	22,500.00
2	Statistician				30,000.00
	Printing				
1	Questionnaires	1	3	10.00	30.00
2	Interview Guide				-
3	Final Report	1	65	10.00	650.00
	Photocopying				
1	Questionnaires	160	3	3.00	1,440.00
2	Final Report	5	65	3.00	975.00
3	Final Report Binding	6	1	500.00	3,000.00
	Other Costs				
1	ERC Fees				2,000.00
2	Records Access Fees				1,500.00
3	Poster Printing				2,500.00
	Total				**64,595.00**

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APPENDICES

Appendix 1: Questionnaire

Date:

Serial Number:

1. AGE:

2. PARITY:

3. IF MULTIPARA, in previous pregnancy:

    a) History of macrosomia
    b) Pregnancy loss
    c) Gestational diabetes mellitus

4. MARITAL STATUS:

5. EMPLOYMENT:

6. EDUCATION:

7. FAMILY HISTORY OF DIABETES MELLITUS:

8. WEIGHT AT FIRST VISIT:

9. HEIGHT:

10. BODY MASS INDEX:

11. LAST NORMAL MENSTRUAL PERIOD:

12. FIRST TRIMESTER ULTRASOUND SCAN

YES	
NO	

13. EXPECTED DATE OF DELIVERY (EXTRAPOLATED FROM LAST NORMAL MENSTRUAL PERIOD OR FIRST TRIMESTER ULTRASOUND SCAN):

14. GESTATIONAL AGE AT FIRST ANTENATAL CLINIC VISIT:

15. NUMBER OF ANTENATAL CLINIC VISITS:

16. HOW WAS THE DIAGNOSIS OF GESTATIONAL DIABETES MELLITUS MADE?

Fasting blood sugar	
75g oral glucose tolerance test	

17. WHAT WERE THE BLOOD SUGAR LEVELS AT DIAGNOSIS OF GESTATIONAL DIABETES MELLITUS?

	BLOOD SUGAR LEVEL
Fasting blood sugar	
1-hr 75g oral glucose tolerance test	
2-hr 75g oral glucose tolerance test	

18. AT WHAT GESTATION WAS THE DIAGNOSIS OF GESTATIONAL DIABETES MELLITUS MADE?

19. WHAT TREATMENT WAS THE PATIENT PUT ON?

Lifestyle modification	
Insulin	

Oral medication (metformin, glibenclamide)	

20. FASTING BLOOD SUGAR LEVELS AT SUBSEQUENT ANTENATAL VISITS:

GESTATIONAL AGE	FASTING BLOOD SUGAR LEVEL
26 wk 0 days – 27 wk 6 days	
28 wk 0 days – 29 wk 6 days	
30 wk 0 days – 31 wk 6 days	
32 wk 0 days – 33 wk 6 days	
34 wk 0 days – 35 wk 6 days	
36 wk 0 days – 37 wk 6 days	

21. AVERAGE THIRD TRIMESTER FASTING BLOOD SUGAR LEVEL:

22. GESTATIONAL AGE AT DELIVERY:

23. BIRTH WEIGHT IN CURRENT PREGNANCY:

Less than 4kg	
Greater than or equal to 4kg	

24. Was the baby born alive?

25. What was the neonate’s blood sugar level?

26. What was the maternal blood loss in millilitres after giving birth?

27. Did the mother sustain any perineal trauma?

28. If perineal trauma was sustained, was it: (TICK AS APPROPRIATE)
    a) First-degree tear (involves the perineal skin only):

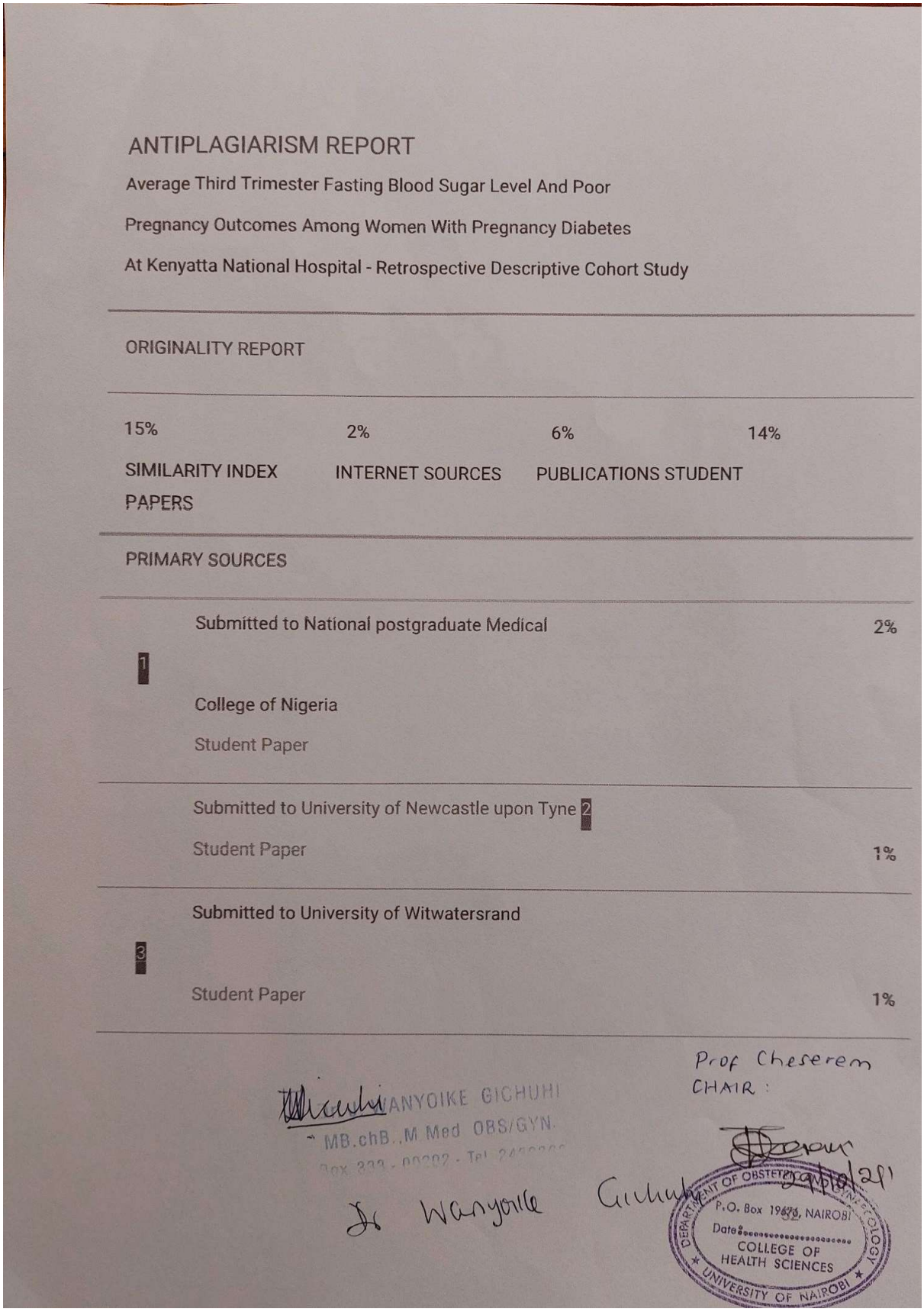
    b) Second-degree tear (involves the perineal muscles and skin):

    c) Third-degree tear (involves anal sphincter complex):

    d) Fourth-degree tear (involves anal sphincter complex and anal epithelium):

    e) Episiotomy:

Appendix 2: ANTIPLAGIARISM REPORT



ANTIPLAGIARISM REPORT

Average Third Trimester Fasting Blood Sugar Level And Poor Pregnancy Outcomes Among Women With Pregnancy Diabetes At Kenyatta National Hospital - Retrospective Descriptive Cohort Study

ORIGINALITY REPORT

15%	2%	6%	14%
SIMILARITY INDEX PAPERS	INTERNET SOURCES	PUBLICATIONS	STUDENT

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P.O. Box 19676, NAIROBI
Date
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Mohamed Esmat Abbass | Abdel Fattah et al.

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Publication

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Exclude bibliography	Off		

Appendix 3: Ethical Approval

Resub P532/06/2019

Salome Nolega Noreh
H58/80768/2015
Department of Obstetrics and Gynaecology
School of Medicine
College of Health Sciences
University of Nairobi

KENYATTA NATIONAL HOSPITAL RECEIVED 13 SEP 2019 KNH/UoN-ERC P.O. Box 20723-00202 NRB.

KENYATTA NATIONAL HOSPITAL APPROVED 02 OCT 2019 KNH/UoN-ERC P. O. BOX 20723 - 00202 NAIROBI

13th September 2019

To
KNH-UoN ERC

Dear KNH-UoN Ethics and Research Committee

RE REVISED RESEARCH PROPOSAL – THE ASSOCIATION BETWEEN AVERAGE THIRD TRIMESTER FASTING BLOOD SUGAR LEVEL AND POOR PREGNANCY OUTCOMES AMONG WOMEN WITH GESTATIONAL DIABETES MELLITUS ON TREATMENT AT KENYATTA NATIONAL HOSPITAL (P532/06/2019)

With reference to your letter referenced KNH-ERC/RR/799, several corrections have been made to my research proposal as follows:

1. **Length of Study Title:**
   The study title has been shortened: The Association between Average Third Trimester Fasting Blood Sugar Level and Poor Pregnancy Outcomes among women with Gestational Diabetes Mellitus on treatment at Kenyatta National Hospital. **Page 1**

2. **Background and Literature Review:**
   More literature has been cited. **Page 10, 11, 13**

3. **Conceptual Framework:**
   A clear figure has been printed. **Page 14**

4. **Study Design:**
   A brief description on the study design has been given on **Page 17**.

5. **Study Area:**
   Kenyatta National Hospital, the antenatal clinic, labour ward and the maternity wards, as well as how patients with gestational diabetes mellitus are identified and managed at KNH has been described in detail on **Page 17**.

6. **Study Population:**
   i. **The use of records from 2013 to 2018 vis a vis sample size of 146:**
   At Kenyatta National Hospital, approximately 90 patients with diabetes in pregnancy are managed in a year. However, of these 90, there is no breakdown into pre-existing diabetes and gestational diabetes. Therefore, 2013 to 2018 was an estimate of a period. However, I will consider the sample size of 146, because in the given period, I may not have achieved adequate number of patient files in the exposed or unexposed group, necessitating going beyond the period earlier stated. **Page 17**

   ii. **Identification of Patients and Retrieval of Records:**
   A detailed description has been given on **Page 17 -18**.

   iii. **Which Fasting Blood Sugar Level to Use:**
   An **average of AT LEAST TWO** third trimester fasting blood sugar levels from 27 – 37 weeks gestation will be used. **Page 18**

   iv. **Retrieval of Neonatal Records:**
   Blood sugar of the new-born is normally determined in the first hour after delivery and recorded in the mother's file in the nursing cardex. Therefore, I will not retrieve neonatal files. **Page 18**

7. **Inclusion and Exclusion Criteria:**
   These criteria have been clearly described on **Page 18**.

8. **Sampling Procedure:**
   The sampling process I will follow to identify records of patients has been described in detail plus illustration of a flow chart on **page 19 – 20**.
   I will document the level of fasting blood sugars and outcomes of interest in a structured questionnaire. **Page 29 – 31**

9. **Study Limitations:**
   The study limitations, including confounders, missing data and misclassification of data, including how to minimize them have been described on **Page 22**.

10. **Reference List:**
    Reference Number 2 has been properly cited, starting with the author. **Page 24**

11. **Dummy Table 1** has been modified to compare the exposed and unexposed groups. **Page 32**

12. **A letter granting permission** to use patient files from KNH Records Department has been **attached.**

Yours sincerely

Noreh

Salome Nolega Noreh

H58/80768/2015