PERFORMANCE CHARACTERISTICS OF THE 50 GRAM GLUCOSE CHALLENGE TEST COMPARED TO THE 75 GRAM ORAL GLUCOSE TOLERANCE TEST FOR GESTATIONAL DIABETES SCREENING AT THE KENYATTA NATIONAL HOSPITAL.

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DECLARATION:

This dissertation is my original work and has not been presented elsewhere. This research project is my original work and has not been presented for academic award in any other university. References to work done by others have been clearly indicated.

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This research is dedicated to you.

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LIST OF ABBREVIATIONS

ACOG	-	American College of Obstetrics and Gynaecology
ADA	-	American Diabetic Association
ADIPS	-	Australian Diabetes In Pregnancy Society
AIDS	-	Acquired Immuno Deficiency Syndrome
ANC	-	Ante-Natal Clinic
ATP	-	Adenosine Tri-Phosphate
BMI	-	Body Mass Index
BOH	-	Bad Obstetric History
C/S	-	Caesarean section
DIPSI	-	Diabetes In Pregnancy Study group in India
DM	-	Diabetes Mellitus
EASD	-	European Association for the Study of Diabetes
FBS	-	Fasting Blood Glucose
FFA	-	Free Fatty Acid
FOGSI	-	Federation of Obstetrics and Gynaecological Society of India
GCT	-	Glucose Challenge Test
HBA1c	-	Glycated haemoglobin
HAPO	-	Hyperglycemia and Adverse pregnancy outcome study
HIV	-	Human Immunodeficiency Virus
HPL	-	Human Placental Lactogen
IADPSG	-	International Association of Diabetes in Pregnancy Study Groups
IDF	-	International diabetic federation

KNH	-	Kenyatta National Hospital
KDHS	-	Kenya Demographic and Health Survey
LGA	-	Large for Gestational Age
MODY	-	Maturity Onset Diabetes Of The Young
NBU	-	New born unit
NDDG	-	National Diabetic Data Group
OGTT	-	Oral Glucose Tolerance Test
RBS	-	Random Blood Sugar
SEMDSA	-	Society for Endocrinology, Metabolism and Diabetes of SouthAfrica
SSA	-	Sub-Saharan Africa
T2DM	-	Type 2 Diabetes Mellitus
WHO	-	World Health Organization

OPERATIONAL DEFINITION OF TERMS

Hyperglycemia is an abnormally high glucose level circulating in the blood plasma

Macrosomia refers to fetal growth beyond a specific threshold, regardless of gestational age. The most commonly used threshold is weight beyond 4000 or 4500g.

"One Step" Procedure" entails performing OGTT in the morning after an overnight fast of ≥ 8 hours, followed by plasma glucose measurement fasting, 1-hour and 2-hour (cut-off criteria varies depending on guidelines used)

Operative Vaginal Delivery refers to a delivery in which the clinician uses forceps, a vacuum, or other devices to extract the fetus from the vagina, with or without the assistance of maternal pushing.

Pre-eclampsia is a disorder of pregnancy characterized by the onset of high blood pressure.

Sensitivity is the proportion of truly diseased persons in the screened population who are identified as diseased by the screening test. Sensitivity indicates the probability that the test will correctly diagnose a condition, or the probability that any given case will be identified by the test.

Specificity is the probability that the test will correctly identify a non-diseased person. A specific test is one that picks up only the disease in question.

Shoulder Dystocia is a specific case of obstructed labour whereby after the delivery of the head, the anterior shoulder of the infant cannot pass below, or requires significant manipulation to pass below, the pubic symphysis. It is diagnosed when the shoulders fail to deliver shortly after the fetal head is delivered.

"Two Step" Procedure" entails performing 50-gram glucose challenge test irrespective of last meal in women not having preexisting diabetes; if Plasma Glucose at 1-hour after load is ≥ 140mg/dl (7.8 mmol/l) 100g glucose OGTT is performed.

Positive predictive value: PPV of a test is the proportion of people with a positive test result who actually have the disease.

Negative predictive value: NPV of a test is the proportion of people with a negative test result who do not have the disease.

Likelihood ratios: are used for assessing the value of performing a diagnostic test. Two versions of the likelihood ratio exist; positive and negative likelihood ratios.

Positive likelihood ratio: the probability of a person who has the disease testing positive divided by the probability of a person who does not have the disease testing positive.

Negative likelihood ratio: the probability of a person who has the disease testing negative divided by the probability of a person who does not have the disease testing negative.

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ABSTRACT:

TITLE: PERFORMANCE CHARACTERISTICS OF THE 50 GRAM GLUCOSE CHALLENGE TEST COMPARED TO THE 75 GRAM ORAL GLUCOSE TOLERANCE TEST FOR GESTATIONAL DIABETES SCREENING AT THE KENYATTA NATIONAL HOSPITAL.

Introduction: The International Diabetes Federation (IDF) in 2015 estimated that, 16.2% of livebirths were complicated with hyperglycaemia in pregnancy(1), 81.5% due to GDM(1). The prevalence of GDM at Kenyatta National Hospital (KNH) is estimated at 11.6-16.7%(2)(3).The International Association of Diabetes and Pregnancy Study Groups recommend a universal one-step 75-g oral glucose tolerance test (OGTT) as a screening strategy for GDM(4). The American College of Obstetricians and Gynaecology (ACOG) prefer a universal two-step screening strategy using a 50-g glucose challenge test (GCT) to determine candidates for an OGTT(5).There are insufficient studies on the various screening and diagnostic criteria and cut off for a GCT compared to OGTT especially in this setting.

Objectives: to evaluate the performance characteristics (sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and likelihood ratios) and receiver-operator characteristic curve (ROC)) of the 50g GCT compared with 75g OGTT; assess the correlation between abnormal GCT and OGTT to Glycated hemoglobin (HbA1c) levels and determine the risk factors for GDM.

Study setting: the study was conducted at Kenyatta National Hospital antenatal clinic and antenatal wards.

Methodology: This was a hospital based cross-sectional study where 438 eligible antenatal clients, at 24-28 weeks of gestation without pre-gestational diabetes underwent a 50g GCT followed by a 75g OGTT within two weeks. Plasma glucose level of >7.8mmol/l on GCT was considered as positive test and used to estimate the performance characteristics of the GCT. The ROC curve was generated, area under the curve (AUC) calculated. The best threshold value of the GCT for detecting GDM was obtained from the ROC curve. The performance characteristics of the test was determined at different cut-offs. Positive samples on both the 50g GCT and 75g OGTT were also correlated to HbA1c levels. Risk factors for development of GDM were determined. P-value was significant at $p<0.05$.

Results: Of the 438 patients enrolled, 100 (23%) had GDM based on a 75g OGTT. A total of 107 had a positive GCT at a cut off plasma glucose levels of >7.8mmol/l, out of whom 54 (50%) had abnormal OGTT. The sensitivity, specificity, PPV, NPV, PLR, NLR of the 50g GCT at a cut off of ≥7.8 mmol/l was 56%, 85%, 52%, 87%, 3.71 and 0.52 respectively. The ROC curve gave a GCT cut off of 7.5mmol/l and area under the curve of 0.7 hence sensitivity and specificity of 92% and 73% respectively. The HbA1c was positive (≥6.5%) in only 13 (13%) of the diabetic patients and 12 (11%) of GCT positive patients making it a poor screening tool for GDM. Glycosuria was associated with GDM in both univariate and multivariate analysis.

Conclusion: The 50 gram GCT at a threshold of 7.8mmol/l is a good screening test in this setting due to its high specificity and high negative predictive value making it a useful test in excluding GDM. The sensitivity of the test at the 7.8mmol/l cut off was lower, however lowering the threshold to 7.5mmol/l raises the sensitivity but lowers the specificity of the test. Lowering the current recommended threshold of 7.8mmol/l will lead to unnecessarily performing an OGTT. HbA1C levels do not correlate with abnormal GCT and OGTT. Glycosuria was associated with increased risk of GDM.

Recommendations: Universal screening for GDM with 50gram GCT is justified. 1-hour plasma glucose of >7.8mmol/l should be evaluated by 75g OGTT.

SECTION 1.0:

INTRODUCTION:

Background

Gestational Diabetes (GDM) is the commonest metabolic disorder in pregnancy and is associated with adverse maternal and fetal outcomes (6). In 2015, the International Diabetes Federation (IDF) estimated that 20.9 million (16.2%) live births were affected with hyperglycaemia in pregnancy, with GDM accounting for 85.1% of those cases (1)

GDM constitutes a major health problem worldwide, the prevalence of which is escalating tremendously due to the high prevalence of obesity and other associated risk factors for type 2 diabetes mellitus (DM)(7)(8). The rise in global prevalence of GDM has also been attributed to the advent of newer screening and diagnostic criteria that were derived from the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study(9). The shift from selective screening for GDM to universal screening has further contributed to rising prevalence of GDM(10).

GDM is associated with adverse maternal and fetal outcomes (6)(11). The potential adverse outcomes associated with GDM are maternal complications such as obstructed labour, increased operative interventions, pregnancy-induced hypertension, preeclampsia, infection and post-partum haemorrhage(12). Associated neonatal complications include macrosomia, birth trauma, preterm birth, and congenital anomalies (13). In the long term, mothers with GDM and their children are at an increased risk for obesity, type 2 diabetes mellitus (T 2DM) and other cardiovascular diseases (14)(15) (16)(17).

GDM is a condition that can be effectively controlled, thereby decreasing the associated complications and eventually leading to the delivery of healthy infants. Therefore Prompt

screening and diagnosis of GDM is the first step towards effective management and prevention of adverse outcomes.

Despite this, consensus regarding a universal screening and diagnostic criteria is yet to be achieved globally (18). The International Association of Diabetes and Pregnancy Study Groups (IADPSG) recommend a universal one-step 75-g oral glucose tolerance test (OGTT) as a screening strategy for GDM while the American College of Obstetricians and Gynaecologists (ACOG) prefer a universal two-step screening strategy using a 50-gram glucose challenge test (GCT) to triage candidates for an OGTT(19)(5). Apart from the lack of a universal screening method, the best threshold of GCT to identify women at risk for GDM remains controversial. American Diabetes Association (ADA) and ACOG recommend the 7.8mmol/l threshold(5). In Kenyatta National Hospital (KNH), screening for GDM is largely risk–factor based.

There is great diversity in the methods and criteria used for identifying women with hyperglycaemia in pregnancy, which makes it difficult to make comparisons between studies (20)(21). Therefore, to further evaluate and compare the usefulness of the relatively cheaper and easier to perform 50-gram GCT as a screening tool for the detection of GDM in this setting, we examined the performance characteristics of this screening test in comparison to the universally recommended WHO 75-gram OGTT.

SECTION 2:

LITERATURE REVIEW:

Section 2.1: Prevalence of GDM

2.1.1 Global prevalence

International Diabetes Federation (IDF) in 2017 estimated that 21.3 million (16.2%) of live births were affected by hyperglycemia in pregnancy. An estimated 86.4% of those cases were due to GDM, 6.2% due to pre-gestational diabetes (1). The global prevalence of GDM varies widely, depending on sociodemographic characteristics of a population, screening and diagnostic criteria used(22).

2.1.2 Regional prevalence

GDM is becoming a public health concern in Sub-Saharan Africa (SSA), although there is limited data available about the prevalence in the general population. A meta-analysis by Mwanri et al. estimated the prevalence of GDM in SSA to be 14% in high-risk pregnant women, depending on the diagnostic criteria used (23)**.** A systematic review by Eskinder et al in 2017 reported that the most commonly employed method for GDM screening in SSA was the 75-gram OGTT with glucose reference ranges as set by the WHO 1985 or 1999 diagnostic criteria.(24) (Table 2). The prevalence of GDM in this review was as low as 4.8% in Nigeria and as high as 11.6% in Kenya (2) (24).

2.1.3 Local prevalence

In Kenya, the overall prevalence rates are not available; however, a prospective study done in western Kenya gives a 2.9% prevalence of GDM(25). A study done by Bosire et al at the KNH in 2011, reported prevalence of GDM at 11.6% (2); this was lower than the, 16.7% prevalence reported by Adelaide in 2009 (26), in the same institution.

Section 2.2:

Pathophysiology of Gestational Diabetes Mellitus:

Women with GDM represent a diverse group; a larger proportion have unrecognized pre-existing non-insulin-dependent diabetes (type 2) and, a smaller proportion have insulin-dependent type 1 diabetes, with onset during pregnancy. The underlying pathophysiology of GDM is decreased maternal insulin sensitivity, or increased insulin resistance, which begins mid-pregnancy and progresses in the third trimester to levels similar to those seen with type 2 diabetes (27) (28).

Insulin resistance results from a combination of increased maternal adiposity and the insulin-desensitizing effects of hormonal products of the placenta such as progesterone, cortisol, placental lactogen, prolactin, and growth hormone (28). Majority of women with GDM appear to have β cell dysfunction that occurs on a background of chronic insulin resistance, with the main biological difference between women with and without GDM is failure of insulin to rise in response to insulin resistance resulting from pregnancy(29)**.**

In less than 10% of GDM patients, defects of β-cell function can be due to autoimmune destruction of pancreatic β-cells, i.e. type 1 diabetes**,** (30)(31) or caused by monogenic mutations, i.e. autosomal dominant inheritance pattern, commonly referred to as maturity-onset diabetes of the young (MODY)(30). These include mutations in genes coding for glucokinase, hepatocyte nuclear factor 1α and insulin promoter factor 1(32).

Section 2.3:

Risk factors for the development of Gestational Diabetes Mellitus:

It is estimated that 50% of GDM patients lack risk factors(18). Fifth International Workshop–Conference on Gestational Diabetes recommended risk assessment for detecting GDM as l*ow risk* , *average risk* and *high risk* as summarized in table 1 (33).

Table 1: Risk Assessment for Detecting Gestational Diabetes

Adapted from: The Fifth International Workshop–Conference on Gestational Diabetes:

GDM risk assessment: Should be ascertained at the first prenatal visit **Low Risk** – if all of these are present no need for routine screening • Member of an ethnic group with a low prevalence of gestational diabetes • No known diabetes in first-degree relatives • Age less than 25 years • Weight normal before pregnancy • No history of abnormal glucose metabolism • No history of poor obstetrical outcome • Weight Normal at birth
Average Risk – screen at 24 – 28 weeks. Screen with either • Two-step procedure: 50 g glucose challenge test (GCT) followed by a diagnostic oral glucose tolerance test in those meeting the threshold value in the GCT. • One-step procedure: Diagnostic oral glucose tolerance test performed on all subjects. • Include Women of Hispanic, African, Native American, South or East Asian origins
High risk – screen as soon as feasible if one or more are present • Women with marked obesity, strong family history of type 2 diabetes, prior gestational diabetes, or glycosuria, delivery of large-for-gestational-age infant.
N/B: If GDM is not diagnosed blood glucose should be repeated at 24 -28 weeks and anytime a patient exhibits signs and symptoms of hyperglycemia

The escalating prevalence of obesity worldwide has led to a resultant rise in GDM prevalence. In a meta-analysis by Chu et al. which looked at twenty studies published between 1980 and

2006, the risk of developing GDM was approximately 2, 3, and 6 times higher among overweight, obese, and severely obese women respectively, as compared with normal-weight pregnant women (34). Kim et al calculated the percentage of GDM attributable to overweight (15.4%), obesity (9.7%), and extreme obesity (21.1%) where the overall population attributable fraction was 46.2% (35).

A systematic review by Onubi et al. conducted to investigate the current evidence on maternal obesity in Africa revealed that the prevalence of maternal obesity across Africa ranged from 6.5 to 50.7%, with older and multiparous mothers more likely to be obese. Obese mothers had an increased risks of adverse maternal and neonatal outcomes (36)**.** The Kenya Demographic and Health Survey (KDHS) of 2009 showed that the national prevalence of overweight and obesity for women between 15 and 49 years in Kenya was 23%(37). The proportion of overweight and obese women was higher in urban areas than in rural areas, with Nairobi having the highest prevalence of 41% (37)**.**

GDM varies according to ethnicity/racial differences, with some ethnic or racial groups being at relatively higher risk than others, irrespective of their BMI, all non-European ethnic groups are at greater risk than European women (38)(39). A large cohort study in Northern California examined ethnic disparities in the prevalence of GDM by BMI. The authors reported that prevalence increased with increasing BMI (40). Asian and Filipino women had a GDM prevalence of 9.9% and 8.5%, respectively at a BMI of 22.0–24.9 kg/m2, whereas in Hispanic, non- Hispanic white, and African American women, had a slightly lower prevalence at 8.0% at a higher BMI of ≥28 kg/m2 (40).

Maternal age is an established risk factor for GDM. Terence et al reviewed the prevalence of GDM, in singleton pregnancies managed in Queen Mary Hospital from 1998 to 2001. The authors reported that the risk of GDM increases significantly with increasing age (41). Makgoba et al found that older age and higher BMI interact with racial group in relation to the prevalence of GDM particularly in women of South Asian and Black African racial origin(42).

Other most commonly known risk factors include; history of macrosomia, ethnicity, essential or gestational hypertension, polycystic ovarian syndrome, history of spontaneous abortion and unexplained still births, strong family history of T2DM diabetes specifically with first degree relatives, history of GDM in a previous pregnancy and persistent glucosuria (43)(44)(45)(46).

Infertility (47) and history of depression(48) have also been reported as risk factors for GDM. There is rising evidence from systematic reviews that maternal birth weight, low or high, is also a risk factor for GDM(49)(50). Increased parity(38)(51) multiple versus singleton pregnancy(52) and weight gain between pre-pregnancy and post-partum examination are additional risk factors for GDM (38). In relation to parity, it is possible that the period of hyperglycaemia during GDM leads to deterioration in maternal pancreatic β-cell function. Subsequent pregnancies appear to have an additive deleterious effect on the β-cell function, culminating in a potentially earlier onset of type 2 DM(53).

Section 2.4: Screening for Gestational Diabetes Mellitus:

2.4.1: Approaches to screening for Gestational Diabetes Mellitus:

Different approaches have been used to screen GDM **(table 2)**, these are:

- Universal approach versus risk-factor/selective approach
- "One-step" versus "two- step" approach

2.4.2: Universal screening for Gestational Diabetes Mellitus:

WHO, in the 2013 guidelines endorsed the IADPSG 2010 criteria. The WHO 2013 criteria recommended the use of universal screening using the one-step 75g OGTT approach (54). Using this approach, all pregnant women irrespective of having risk factors for GDM undergo GDM screening. The IADPSG recommends that all women not known to have prior diabetes undergo a 75-gram OGTT (55).

The American College of Obstetricians and Gynecologists (ACOG) practice bulletin states that universal screening for gestational diabetes should be done at 24 to 28 weeks' gestation, but early screening is recommended in women with risk factor (5)**.** The United States Preventive Services Task Force on Preventive Health Care concluded that there is not enough evidence to support or deny universal screening for GDM (56).

The updated guidelines by the Society for Endocrinology, Metabolism and Diabetes of South Africa (SEMDSA) recommends universal screening at 24 - 28 weeks' gestation using the World Health Organization (WHO) 2013 criteria (57)(58).

2.4.3: Selective/risk factor based screening for Gestational Diabetes Mellitus:

Selective screening approaches entail risk-factor based screening followed by OGTT for women who exhibit risk factors for GDM. The American Diabetes Association (ADA) states that low risk women, those with age less than 25 years, not members of ethnic group (African-American, Hispanic, Asian) BMI 25kg/m2 or less, no previous history of abnormal glucose tolerance or adverse obstetrics outcomes and no known history of diabetes in first degree relatives are less likely to benefit from any screening (59).

2.4.4: Universal versus Selective screening for Gestational Diabetes Mellitus:

There is no international consensus regarding the timing of screening method and the optimal cut-off points for diagnosis and intervention of GDM (18). A prospective randomized study in Dublin compared a risk-factor based screening programme with a universally based one. In risk factor-based screening, GDM was found in 1.45% of women versus 2.7% in universal screening in the same population, which showed that risk factor-based screening had missed half of the GDM (60).

A retrospective cohort study which was conducted in a tertiary academic perinatal center in Paris aimed at estimating the proportion of women with GDM who would be missed by selective versus universal screening from 2011 to 2012 (61). Using the IADPDG criteria, 2187 women were universally screened for GDM, 14% had GDM, of whom 83% had one or more risk factors (61). The proportion of women who had GDM despite the absence of any risk factor was 2.4% therefore, selective screening would have missed one-sixth of GDM cases (61). From these studies, it can be concluded that universal screening has improved the sensitivity for detecting GDM as well as improved pregnancy outcomes(62)(60). Selective screening in contrast, identifies the cases of GDM who are at highest risk of complications (61)(60).

2.4.5: 50g GCT as a screening tool for gestational diabetes:

The 50-g glucose challenge test (GCT) was first described by O'Sullivan et al. as part of their screening program for GDM in which a single blood glucose assessment was made an hour after a 50-gram oral glucose load (63). This technique showed to have a high degree of sensitivity and specificity of 79% and 87% respectively (63). U.S Preventive Services Task Force conducted a systematic review of various screening tests for GDM which showed that the joint estimates of sensitivity and specificity of the 50g GCT were 85% and 83%, respectively, using a cut-off point of 7.8 mmol/L (64). Ben Halima et al performed a multicentric prospective cohort study in Belgium between 2014 and 2017 and they found that the GCT has a moderate diagnostic accuracy in a universal two-step screening strategy for GDM using the 2013 WHO criteria(65) At GCT threshold of 7.8 mmol/l the sensitivity and specificity was 59.6% and 81% respectively and sensitivity rates of ≥70% were achieved at lower thresholds of 7.2 mmol/l(65).

A systematic review by M. Van Leeuwen et al in 2015 aimed to calculate estimates of the sensitivity and specificity of the 50 gram GCT found that the pooled estimate of sensitivity and specificity for a threshold value of 7.8mmol/l ranged between 74%-83% and 72%-85% depending on the OGTT threshold used for diagnosis of GDM (66). The authors concluded that the 50-g glucose challenge test is acceptable to screen for GDM, but cannot replace the OGTT (66). Juntarat et al in Thailand evaluated the cut-off value of GCT for detecting GDM by using ROC curve, they found that at 7.8mmol/l cut-off, sensitivity and specificity was 95.3% and 48.6% respectively(67)(68) They observed using lower thresholds of 7.5mmol/l and 7.2mmol/l raised the sensitivity but lowered the specificity leading to performing unnecessary OGTTs (68). The authors recommend threshold of 7.8mmol/l for the 50-gram GCT in screening high-risk pregnancy.

Akram et al in Pakistan compared the efficiency of the GCT with a 75 g OGTT for detection of GDM (69). They subjected 1000 Pakistani women to both GCT and OGTT regardless of their risk-factors. They found at the 7.8mmo/l cut-off, GCT had a sensitivity, specificity, PPV and NPV of 90.90%, 91.07%, 88.88%, 92.72% respectively. The authors emphasized on the use of universal screening with the GCT especially in poor resource settings (69).

In Nigeria, a study by Adegbola et al. determined the predictive value of the oral 50-gram GCT in the detection of GDM. They found the sensitivity and negative predictive values were 100% at thresholds of 7.2mmol/l and 7.8mmol/l, while the specificity was 82.4% and 91% at thresholds of 7.2mmol/l and 7.8mmol/l respectively (70). Locally, a cross-sectional study done at the KNH by Bosire et al, aimed at determining the specificity and sensitivity of screening using risk factor classification with the use of 50g GCT as a gold standard. The authors reported that, compared to the 50-gram GCT, the risk factor classification had a low sensitivity and specificity of 43.48% and 75.27% respectively, compared to 100% and 85.1% respectively of the GCT (using 7.2mmol/l threshold) (2). The diagnostic yield was 46.7% at 7.2 mmol/l while the diagnostic yield was higher at 71.7% with 7.8mmol/l threshold.

2.4.6: 'One-step' versus 'Two-step' screening for gestational diabetes:

Two approaches have been proposed for screening GDM that is the "One step" and "Two step" approaches. In 2013, WHO endorsed the IADPSG 2010 criteria that recommends universal screening of all pregnant women with the "One-step approach" with 75-g OGTT (71). The "One-Step" Procedure" entails performing OGTT in the morning after overnight fast of ≥ 8 hours, with plasma glucose (PG) measurement fasting, 1-hour and 2-hour (as per IADPSG threshold) at 24-28weeks (72).

The “Two Step” Procedure” on the other hand entails performing 50 gram glucose challenge test irrespective of last meal at 24-28 weeks in women not having preexisting diabetes; if PG at 1-hour after load is ≥ 140mg/dl (7.8 mmol/l) 100g glucose OGTT is conducted(5). In the latest guideline, the Canadian Diabetic Association (CDA) 2013 recommends screening all women with the GCT between 24-28 weeks, and if between 7.8-11.0 mmol/L, they should undergo the 75-g OGTT using thresholds recommended by them (73). Unlike ACOG the CDA “two-step approach” is slightly different in that they recommend the 75g OGTT and not 100g OGTT (73). The cut-offs of CDA 2013 are similar to the IADPSG 2010 thresholds (74).

The ADA proposes 2 methods for screening and diagnosis of GDM (75): “One Step” and “Two Step” approach which involves performing 50-gram glucose challenge test irrespective of last meal at 24-28 weeks gestation in women not having preexisting diabetes; those with plasma glucose (PG) at 1-hour after load of ≥ 7.8mmol/l proceed to 100g glucose OGTT (75)(59).

The HAPO study demonstrated that hyperglycemia at levels below those diagnostic for GDM using the old criteria were associated with adverse maternal and neonatal outcomes (76). For this reason, IADPSG convened a workshop conference in 2008 where they recommend using new cut-offs published in 2010 for the 75g OGTT (76). There is significant discordance in the adoption of the IADPSG recommendation between the ADA which has embraced these recommendations, and the ACOG which has not (5). ACOG has always endorsed the two-step approach to GDM. In its August 2013 bulletin, ACOG has retained the two-step procedure using the thresholds for the 100-g OGTT of the National Diabetes Data Group (NDDG) or Carpenter and Coustan criteria (5).

A prospective cohort study in the U.S.A done from 2011 to 2012 looked at the screening of GDM using one-step versus two-step approaches (58). The study showed that the "one-step" screening for GDM is associated with an increased rate of GDM, without improving maternal or neonatal outcomes (58). The "one-step" screening was shown to be less convenient because patients must be fasting, and it took longer to complete than the non-fasting, one-hour test for the first part of the "two-step" testing protocol (58). Contrary to this, Sevket et al in turkey in a randomised trial comparing the clinical outcomes of patients diagnosed with GDM using the one-step versus two-step approach found that women diagnosed with GDM using one-step approach had better perinatal outcomes compared to the latter(77).

In Africa, a published systematic review by Macaulay et al. showed that most studies utilised the two hour 75-gram oral glucose tolerance test and applied the WHO's diagnostic criteria (78). Nigeria published a national guideline modified in 2013which recommends risk assessment at booking; 75-g OGTT or two-step method (50-gram GCT with 100-gram OGTT) using carpenter and coustan criteria for diagnosis (79)**.**

The Society for Endocrinology, Metabolism and Diabetes of SouthAfrica (SEMDSA) recommends that pregnant women considered at high-risk for diabetes should be offered a 75g OGTT at their first visit and a further test at 24-28 weeks if the first test is normal(80).

Despite the availability of a guideline on GDM in Nigeria, practice still varies across obstetric units. There is no recommendation on the screening or diagnostic approach for women outside tertiary care facilities as 50-gram GCT or OGTT are not readily available in primary health care settings (81). Nigeria reflects some of the problems seen with GDM screening in Africa and stresses the importance of addressing the specific needs of the sub-Saharan Africa region. Due to the unavailability of resources, it is increasingly becoming difficult for international guidelines to be applied to the low and middle income countries (LMIC) (82)(83).

In Kenya there is no consensus on which guideline to use for GDM screening. The ministry of health 2018 guidelines on diabetes recommend the selective screening approach whereby screening for GDM should be done on antenatal mothers who are "high risk" with the 75g OGTT (84)(85).

2.4.7: Role of Glycated Hemoglobin (HBA1C) in GDM screening:

Glycated haemoglobin (HbA1C) reflects average glycaemia over approximately three months. It is a reliable method of detecting undiagnosed diabetes in the first 20 weeks of pregnancy (86). An HbA1C of ≥ 6.7% suggests probable undiagnosed diabetes. According to the screening, diagnosis and management of GDM in New Zealand 2014 guidelines, universal screening using HBA1C of all women on their first antenatal visit (early pregnancy) is recommended(87)(88). Women with HbA1C ≥ 50 mmol/mol (6.7%) are considered to have undiagnosed diabetes. All women with HbA1c 41–49 mmol/mol (5.9%-6.6%) in early pregnancy should receive an OGTT at 24–28 weeks (88), the guidelines however clearly state that HbA1c is not a diagnostic test for gestational diabetes as it is not sensitive enough to detect gestational diabetes (88).

Measurement of HbA1C is currently recommended by many international diabetes societies as a screening test for diabetes in early pregnancy i.e. (88) <20 weeks gestation (59). A Japanese study assessed four different approaches to detecting GDM: 50g GCT, RPG, HbA1C and FPG and compared screening in the first and second trimesters of pregnancy (89) GDM was confirmed with a 75 g OGTT within four weeks of being screened. The 50g GCT was found to be the optimal test for gestational diabetes screening based on assessments of different thresholds of the tests used (89). The authors concluded that first trimester screening for glucose intolerance was important as it suggests that the problem was probably present before pregnancy (89).

In the New Zealand STEP study (Screening for Type 2 diabetes in Early Pregnancy) 16,122 pregnant women were screened with an HbA1C and RPG on the first antenatal visit (88). Women with HbA1C ≥ 5.6% or RPG ≥ 5.5 mmol/L and control group of a consecutive series of 1000 women with results below these thresholds were invited to take a 75 g OGTT before 20 weeks' gestation. Diabetes in pregnancy and GDM were diagnosed by WHO criteria (88). In this study, the uptake of OGTT was very low: 16.4% of the control group and 21.3% of cases participated. Only 0.6% of the study population had probable undiagnosed diabetes. The authors concluded that the HbA1C test was superior to RPG in detecting probable undiagnosed diabetes in pregnancy. They also stated that HbA1C is likely to be a cost-effective addition to the first antenatal screen, especially in a population with a high prevalence of diabetes (90).

Limited data support the use of HbA1C as a screening test at 24–28 weeks. A study conducted in the United Arab Emirates aimed to evaluate HBA1C as a screening tool for GDM on 442 pregnant women between 24-28 weeks gestation. A confirmatory 75g OGTT was also done using the WHO criteria. Using an HbA1C value of <5.5% to rule out GDM lacked specificity (21%) despite good sensitivity (82%). Using a threshold of HBA1c 7.5% to rule-in GDM, the specificity was 95.8% with 15 of 21 patients over the threshold being false-positives (91).

A study in India by Rajput et al. evaluated the utility of HbA1C in combination with OGTT for diagnosis of GDM on 607 pregnant women between 24 and 28 weeks gestation. The mean HbA1c value in women with GDM was significantly higher than in women without GDM. An HbA1c cutoff value of 5.95% had a sensitivity and specificity of 28.6% and 97.2% respectively, while a lower HbA1c cutoff value of 5.45% had a higher sensitivity of 85.7% and lower specificity of 61.1% in diagnosing GDM. The authors concluded that HbA1c in combination with OGTT can obviate the need for OGTT in almost two-thirds of women with GDM (92).

2.4.8: When to screen for GDM

Globally, screening for GDM is usually done between 24 and 28 weeks of gestation because insulin resistance increases during the second trimester and glucose levels rise in women who do not have the ability to produce enough insulin to adopt this resistance (55).

Placental hormones mediate insulin resistance which increases the risk for development of GDM as the pregnancy advances so testing too early may not be helpful in some patients. Likewise, performing tests too late in the third trimester limits the time in which metabolic interventions can take place. Because of these reasons, it is advised to perform the tests at 24-28 weeks of gestation. The IADPSG, in a recommendation endorsed by the ADA, and based on the HAPO study, advocates testing using fasting plasma glucose, HbA1C or random plasma glucose in all women, at the first encounter. If results are not diagnostic of overt DM and fasting plasma glucose $\geq$ 5.1mmol/l, a diagnosis of GDM is made. If fasting glucose is $\geq$ 5.1mmol/l at the first antenatal visit, a 2-hour 75g OGTT should be repeated at 24-28 weeks (19).

Table 2: Comparison of screening and diagnostic criteria for gestational diabetes globally(93)

Area	Advising body	Year	Advise for screening	Method of screening (positive cut-off ≥)	Glucose load in grams	Glucose thresholds (mmol/L)				OGTT values for diagnosis ≥
						FBS	**1-h**	**2-h**	**3-h**	
North America	NDDG	1979	None	50-g GCT (7.8)	100	5.8	10.5	9.2	8.0	2
	ADA	2003	All but for those at low risk	50-g GCT (7.8)	100	5.3	10.0	8.6	7.8	2
					75	5.3	10.0	8.6	-	2
	C and C	1982	None	-	100	5.3	10.0	8.6	7.8	2
	IADPSG	2010	All	75-g OGTT	75	5.1	10.0	8.5		1
	CDA	2003	All	50-g GCT (7.8)	75	5.3	10.6	8.9	-	2
	CDA	2013		50-g GCT (7.8)	75	5.3	10.6	9.0	-	1
	SOGC	2002		50-g GCT (7.8)	100	5.3	10.0	8.6	7.8	2

			All except low risk		75	5.3	10.0	8.6	-	2
South America	BSD	2007	All	FPG (4.7)	75	-	7.0		7.8	1
	BSD	2014	All	FPG (4.7)	75	5.1	10.0	8.5		1
Europe	NICE	2015	Clinical risk	75-g OGTT	75	5.6	-	7.8	-	1
	EASD	1991	NS	NS	75	5.5 or 6.0			9.0	1
Asia	JDS	2013	All	50-g GCT (7.8)	75	5.1	10.0	8.5	-	2
	DIPSI	2009	-	-	75	-	-	7.8		
Australia	ADIPS	2014	All, unless resources limited	75-g OGTT	75	5.1	10.0	8.5	-	1
	NZSSD	1998	All	50-g GCT (7.8)	75	5.5	-	9.0	-	1
				75-g (8.0)						

Global criteria	WHO	2013	All	75-g OGTT	75	5.1	10.0	8.5	-	1

Key:

ADA: American Diabetes Organization;

ADIPS: Australian Diabetes in Pregnancy Society;

BSD: Brazilian Society of Diabetes; CDA: Canadian Diabetes Association;

C and C: Carpenter and Coustan;

EASD: European Association for the Study of Diabetes;

DIPSI: Diabetes in Pregnancy Study group in India;

IDF: International Diabetes Federation;

FPG: Fasting plasma glucose; JDS: Japan Diabetes Society; NDDG: National Diabetes Data Group; NZSSSD: New Zealand Society for the Study of Diabetes;

NICE: National Institute for Health and Care Excellence;

SOGC: Society of Obstetricians and Gynecologists of Canada;

WHO: World Health Organization.

FBS: fasting blood sugar

RPG: Random plasma glucose;

NS: Not specified;

SECTION 3.0: CONCEPTUAL FRAMEWORK

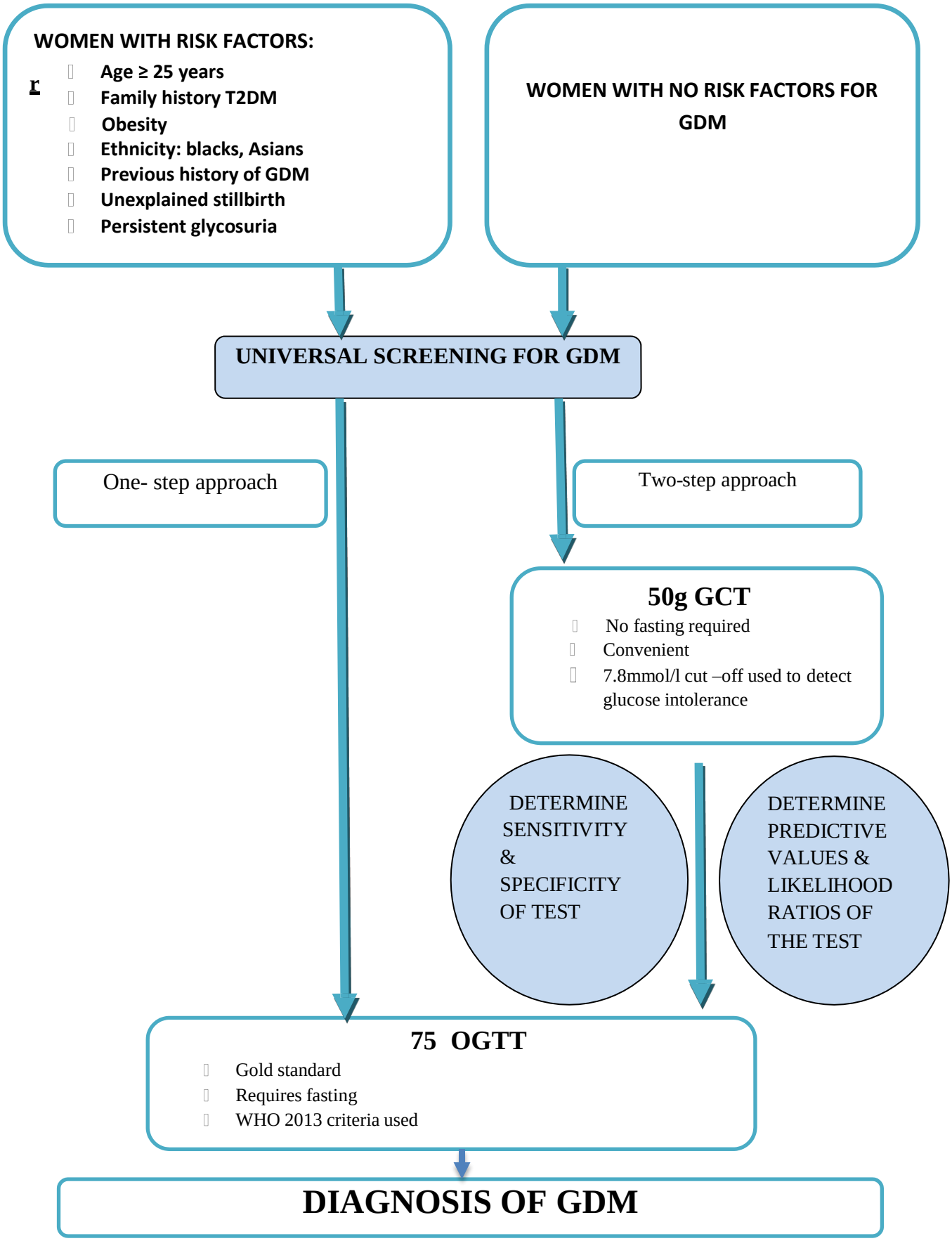


Figure 1: Conceptual framework

CONCEPTUAL FRAMEWORK NARRATIVE:

Several risk factors are associated with the development of GDM. The most common risk factors include obesity, previous history of GDM, history of delivery of LGA infant, family history of type 2 diabetes, glycosuria/impaired glucose metabolism, history of poor obstetric outcome. However, in up to 50% of mothers with GDM have no risk factors.

Early screening and diagnosis of GDM is associated with good perinatal outcomes. The WHO 2013 criteria recommends the use of universal screening using the one-step 75-gram OGTT approach (54). Using this approach, all pregnant women irrespective of having risk factors for GDM undergo screening. There are two approaches for screening GDM that is the "One-step" and "Two-step" approaches. The "One-Step" Procedure" entails performing OGTT in the morning after an overnight fast of ≥ 8 hours, with PG measurement fasting, 1-hour and 2-hour (WHO reference range in table 4) at 24-28weeks.

The "Two Step" Procedure" on the other hand entails performing 50g GCT irrespective of last meal at 24-28 weeks if PG at 1-hour after load is ≥ 140mg/dl (7.8 mmol/l) it is suggestive of glucose intolerance.

The study sought to determine the sensitivity and specificity, positive predictive value, negative predictive value and likelihood ratios of the 50g GCT and compare its performance with 75g OGTT which is diagnostic of GDM.

SECTION 4.0:

STUDY JUSTIFICATION

In approximately 95% of GDM cases maternal glucose metabolism returns to normal after delivery of the baby (94); however, an association between GDM and the development of type 2 DM in the mother later in life has been proven (28) (95). Research done to show the long term effects of poor maternal glucose metabolism on the fetus has revealed that children born to mothers with GDM are susceptible to glucose intolerance and obesity (11) (96). With these associations in mind it is important to identify pregnant women at risk for GDM so that prevention management such as lifestyle modifications can be instituted early (97).

GDM is a condition that can be effectively controlled, thereby decreasing the associated complications and eventually leading to the delivery of healthy infants. Effective prevention strategies for gestational diabetes are not costly. However, in health and economic terms, neglecting chronic diseases such as diabetes is very expensive. The costs of treatment of life-threatening complications of GDM (e.g. neonatal ICU care, maternal end-organ damage) and loss of productivity (GDM affects the most productive age group in the society) undermine and stunt economic growth. If Kenya can successfully strengthen its health systems to improve the coverage of interventions that reduce infectious disease and maternal and childhood conditions, it can equally build further capacity to address the rising burden of diabetes. Therefore Prompt screening and diagnosis of GDM is the first step towards effective management and prevention of adverse outcomes.

Hence, it is essential to use a reliable, simple screening test to be applied for the antenatal population. Globally, there is no consensus on the criteria for screening and diagnosis of GDM hence posing a unique challenge (73). This challenge percolates through the health system in Kenya as well, where there are no clear guidelines and policies on screening for GDM. Due to limited GDM related data, policy enactment has been hindered especially in routine screening at Maternal and Child Health clinics (MCH) and integration of GDM in essential package for health (EPH).

WHO recommends universal screening of all mothers with 75g OGTT (71). However due to resource constraints in developing countries that recommendation poses a challenge. Furthermore the 75-gram OGTT requires a mother to come in a fasting state which further poses a challenge. Therefore it was important to look into other alternatives which are cost effective and convenient like the non-fasting 50-gram GCT.

SECTION 5.0:

RESEARCH QUESTION

What is the performance characteristic (sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and likelihood ratios) of the one step 50g GCT compared with 75g OGTT in pregnant mothers between 24 and 28 weeks gestation attending the antenatal clinic at KNH in 2018?

SECTION 6.0:

BROAD OBJECTIVE

To evaluate the performance characteristic (sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and likelihood ratios) of the one step 50-gram GCT compared with 75-gram OGTT within one week in pregnant mothers who are between 24 and 28 weeks gestation attending KNH in 2018.

SECTION 7.0:

SPECIFIC OBJECTIVES

Primary objectives:

Among antenatal mothers at 24 and 28 gestation age attending the KNH in 2018, administered with the one step 50-gram GCT and 75g OGTT, to

1. Determine the sensitivity and specificity of 50-gram GCT in identifying women with GDM
2. Determine the PPV, NPV and likelihood ratios of 50-gram GCT in identifying women with GDM
3. Assess the risk factors for the development of GDM in pregnant mothers attending the antenatal clinic at the KNH.

Secondary objective:

Among antenatal mothers at 24 and 28 gestation age attending the KNH in 2018, administered with the one step 50-gram GCT and 75-gram OGTT, to:

Determine the association between abnormal 50-gram GCT and abnormal 75-gram OGTT with HBA1C levels

SECTION 8.0: STUDY METHODOLOGY:

Section 8.1

Study Design:

This was a cross-sectional study design, where all mothers fulfilling the eligibility criteria were subjected to 50-gram Glucose Challenge Test (GCT) and 75-gram Oral Glucose Tolerance Test (OGTT) within two weeks, and an assessment of the glucose levels determined for comparison. Positive tests in either of the 50-gram GCT and 75-gram OGTT were correlated to the HbA1c (glycated hemoglobin) levels.

The risk factors associated with the development of GDM at the Kenyatta National Hospital (KNH) were determined.

Section 8.2

Study Site:

The study was conducted in at the Kenyatta National Hospital (KNH) antenatal wards and clinics from December 2018 to April 2019. The KNH is the largest public referral and teaching hospital to the University of Nairobi and Kenya Medical Training College. The hospital mostly serves women in the middle to low income socio-economic groups. The obstetrics unit consists of three antenatal/postnatal wards, labour ward, a maternity operating theatre, antenatal and post-natal clinics. The KNH labour ward has >1000 admissions per month. The antenatal clinic runs from Monday to Thursday. On average, a total of 400 women attend ANC clinic per week; out of these, the proportion with gestation age of between 24 and 28 is approximately 50%.

The clients in the clinic are first registered then triaged where their vitals are taken, urinalysis is also done. For first time clients an antenatal profile involving VDRL, HIV status, blood group, haemoglobin and random blood sugar. The clients are then seen by the resident doctors and consultant obstetricians. Patients suspected of having GDM in the clinic i.e. by virtue of a previous macrosomic baby, or recurrent abortions, glycosuria, history of GDM or unexplained stillbirths , the client is sent for an OGTT. In this set up, there is usually no routine screening

done for GDM. The hospital has a well-equipped ISO certified biochemistry laboratory which is regularly subjected to internal and external quality control measures. The lab performs the 100 gram OGTT when requested, the cut-off used are as per the Carpenter –Coustan criteria.

Section 8.3:

Study population:

The study population were the antenatal women between 24 and 28 weeks gestation, managed at the KNH antenatal wards and clinics from December 2018 to April 2019.

Section 8.4:

Inclusion criteria:

- Pregnant women between 24-28 weeks gestation attending antenatal clinic and admitted in the antenatal wards at the KNH from December 2018 to April 2019.
- Women who gave an informed consent.

Section 8.5:

Exclusion criteria:

- Women with pre-gestational Diabetes
- Women on long-term use of steroids and other diabetogenic drugs
- Pregnant women unable to complete study protocol

Section 8.6:

Sample size determination:

The sample size of women to be included in the study was calculated using Buderer's formula (98) for sample size calculation in diagnostic accuracy studies at the required absolute precision level for sensitivity and specificity as follows:

Sample size (n) based on sensitivity = $\frac{Z^2_{1-\alpha/2} \times S_N \times (1-S_N)}{L^2 \times Prevalence}$

And

Sample size (n) based on specificity = $\frac{Z^2_{1-\alpha/2} \times S_P \times (1-S_P)}{L^2 \times (1-Prevalence)}$

Where n = required sample size

S_N = anticipated sensitivity

S_P = anticipated specificity

α= size of the critical region (1 – α is the confidence level = 0.05)

$Z_{1-\alpha/2}$ = standard normal deviate corresponding to the specified size of the critical region (α), and

L = absolute precision desired on either side (half – width of the confidence interval) of sensitivity or specificity

Using a prevalence of 16.7% (26) sensitivity of 95% for 50gGCT (99).

95% level of confidence, the sample size calculation for this study was **438.**

Section: 8.7

Sampling procedure:

This study used a consecutive sampling method to recruit 438 participants from the women attending antenatal clinic and antenatal wards at the KNH between December 2018 and April 2019. The gestation age of women attending ANC was established from the patients' records, history of last normal menses, and where in doubt, clinically or ultra-sonographic confirmation was sought. Five hundred and ten women were screened, 72 participants were excluded due to not fulfilling the study criteria (figure 1), and 438 participants were recruited.

The clients were first counselled about the study, those who satisfied the inclusion criteria were recruited and informed consent (annex 2) was obtained by the principal investigator or the trained research assistants. The enrolled participants were subjected to the interview questions and sample collection procedures (figure 1).

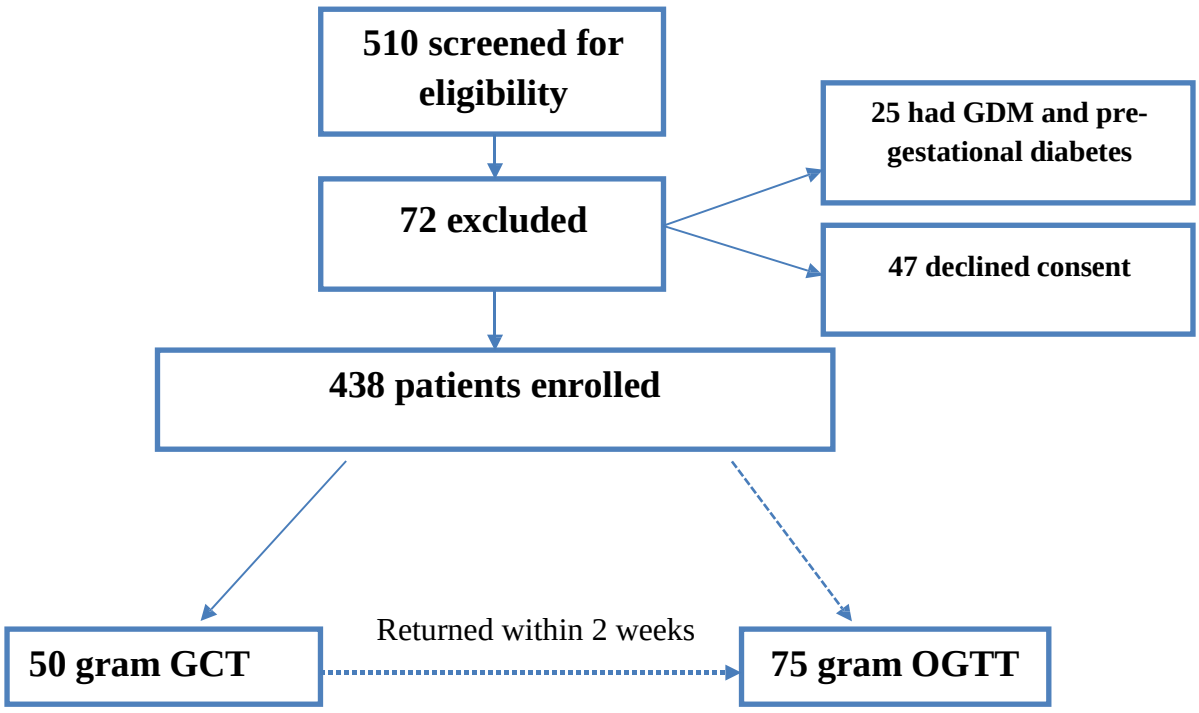


Figure 2: Flowchart of sampling procedure

Section: 8.8: **Study procedure:**

The study was a clinical based cross-sectional study as it sought to establish the performance characteristics (sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and likelihood ratios) of 50-gram GCT as a screening tool in comparison to 75g OGTT as the gold standard in the antenatal population attending KNH. Eligible patients were enrolled into the study after giving consent and a pre-tested structured questionnaire was administered. Data collected through interviewer-administered questionnaires included sociodemographic, reproductive and medical characteristics of the study participants according to the study's standard operating procedures. Eligible participants underwent a 50g GCT. Blood glucose measurement was determined an hour after ingestion of the glucose load. These participants came back within two weeks in a fasting state (≥8 hours) and were subjected to a 75-gram OGTT after a fasting blood sugar measurement. Blood sugar levels were then determined at 1 hour and 2 hours after the OGTT.

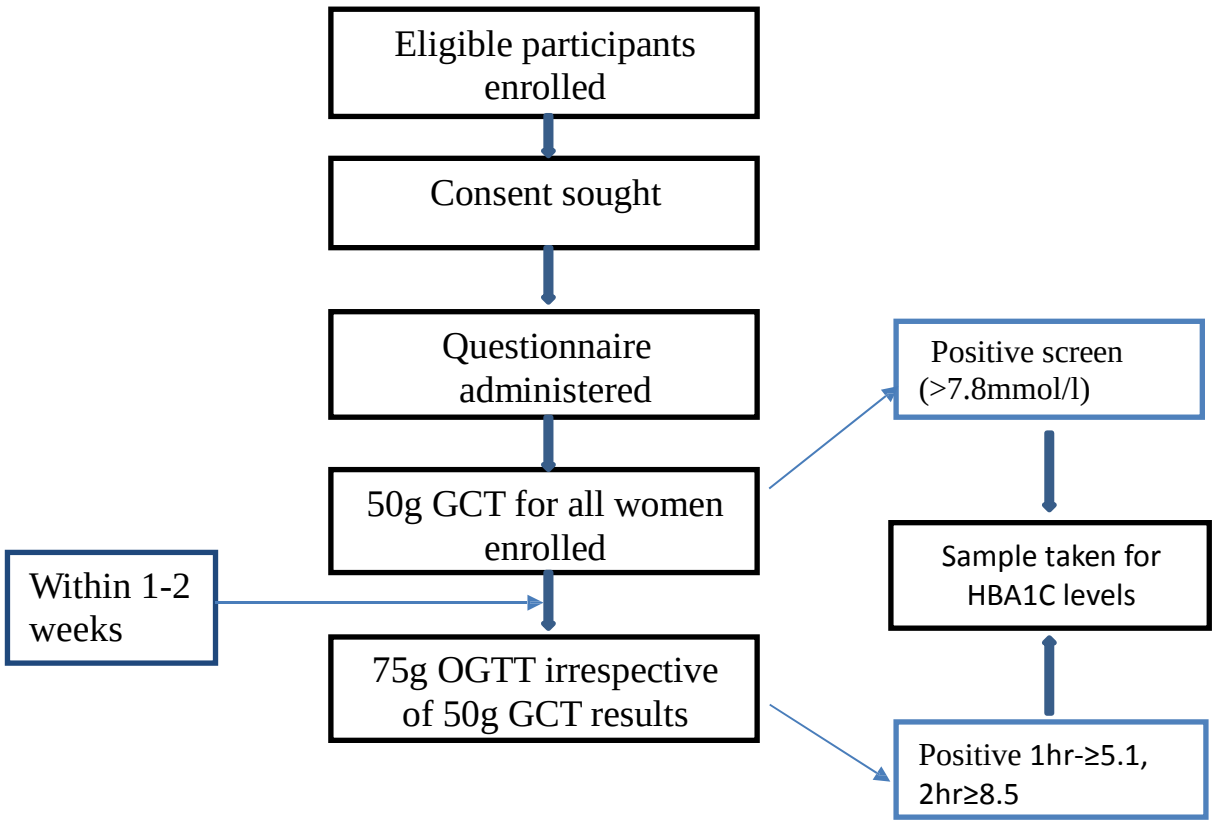


Figure 3: Flowchart of study procedure

Section: 8.9

Data variables:

Objective	Exposure variable	Outcome variable	Source of data
Determine sensitivity and specificity of 50g GCT in identifying women with GDM	50g GCT	Sensitivity and specificity of 50g GCT	ROC curve
Determine the PPV, NPV and likelihood ratios of GCT in identifying women with GDM	50g GCT	PPV, NPV and likelihood ratios of GCT	Sensitivity and specificity of 50g GCT
Assessment of risk factors for of GDM in antenatal mothers at KNH	risk factors for GDM: • Obesity • Previous GDM • Hx of delivery of LGA infant • Family hx of type 2DM • Glycosuria/impaired glucose metabolism • History of poor obstetric outcome	GDM	Patient Questionnaire
Correlation between abnormal 50g GCT and abnormal 75g OGTT with HBA1C levels	Positive 50 g GCT and 75 g OGTT	Elevated HbA1C	Elevated PG levels post the 50 g GCT and 75 g OGTT

Section 8.10

Data collection

The data for this study were collected using a standard data collection tool as attached in annex 3. The questionnaires were administered in a consultation room for privacy. The respondents selected gave informed consent for the research before administration of the questionnaires by the researcher and research assistants. A check list was used to note the number of respondents per day to keep tract of progress and any challenges. This ensured that the sample size for the research was achieved. Data on the glucose levels was collected from the KNH laboratory and entered into the data collection tool.

Tools:

A pre-tested structured questionnaire was used to assess for the presence of risk factors and symptom, e.g. past obstetrics history, past history of gestational diabetes or family history of diabetes and hypertension were elicited. The socio-demographic data of these clients were also collected by use of the questionnaire. At the end of the questionnaires the results of the client GCT using the 7.8mmol/l cut off and results of the 75g OGTT using the WHO protocol as well as HbA1C levels (if applicable) were documented.

Equipment:

The lab used blood glucose testing kits to measure the blood glucose levels at the time of testing. This included a glucometer with cuvettes. A glucometer is a quality machine that was well calibrated to read both venous and capillary glucose levels, and underwent regular quality control. Glucose load, both 50-gram and 75-gram glucose load were prepared by the laboratory. Sterile swabs and lancets, syringes and hypodermic needles were used to collect blood.

Procedure:

Approval to carry out the study was sought from the Ethics Review Board of Kenyatta National Hospital, the nursing officer sensitized the participants about the study at the antenatal clinic. The participants, who gave consent were recruited into the study, and questionnaire administered. Their weight was obtained from measurement using a calibrated weighing scale. The weighing scale used is the weighted health-o meter, which has been shown to have consistency in results over time. The participants were given 50-gram glucose load in 150ml of water which they ingested. Their blood glucose measurement were obtained an hour after ingestion of the glucose load. These participants then came back within two weeks in a fasting state (>8 hours) where their fasting blood glucose was determined before being given a 75-gram load in 250ml of water. Subsequently blood glucose measurement after 1 hour and 2 hours were obtained. Participants were advised to restrict physical activity over the duration of the test. The participants with positive 50-gram GCT (glucose level ≥7.8mmol/l) and positive 75g OGTT undertook the HbA1c test. The sample for HbA1c was obtained through 2ml of venous blood sample.

The lab procedures in this study were done as per the quality assurance protocols attached in annex 7.

Laboratory method:

Venous blood was withdrawn for the clients undergoing the GCT and OGTT and the blood sugars were measured using the glucometer/reflectance meters. The HbA1c sample drawn was also venous. The results were collected from the lab by the principle investigator and research assistants and disclosed to the patient. The results were entered into a data base by double entry method. Those who were diagnosed as having gestational diabetes were referred to the maternal-fetal clinic for management and follow up as per KNH protocol. Patients who

experienced vomiting due to gastric irritation caused by the glucose load were advised to be seen subsequently and, a glucose load mixed with chilled water was given.

Test interpretation:

The 50 g glucose challenge test results was interpreted according to the following criteria:

Blood glucose 1 hour after 50 g oral glucose ≥7.8 mmol/L

The 75 g OGTT was interpreted according to the WHO criteria. The HAPO/IADPSG Diagnostic criterion requires one abnormal glucose level from the range given in table 2.

- Fasting blood sugars: ≥5.1mmol/l
- 1 hour post 75 glucose load >10.0mmol/l
- 2hr post 75 gram glucose load >8.5mmol/l

HbA1c levels of more than 6.5% is suggestive of poor glycemic control.

Section: 8.11

Data management and analysis

Quality control measures included developing standard operating procedures (SOPs) and data collection manual to guide data collection. Quality assurance was enhanced continuously throughout the study period to maximize on the validity and reliability of the findings. The questionnaires were checked for completeness at the end of each day by the principal investigator during data collection period to ensure completeness and accuracy of data collected. The questionnaires were availed in English and Kiswahili and pre-testing of study instrument was carried out to correct it for bias, misinterpretation of the questions and ambiguity. The validity of the study was ascertained by ensuring that the data collection instruments reflect the objectives of the study. The research instrument was validated by the University of Nairobi supervisors.

Data were received in paper form as the questionnaires were assigned unique identifiers. Data verification was done by the principal investigator on a daily basis. The verified data were then entered into a password protected excel spreadsheet by two data clerks through the double data entry technique. This was done to check on duplicity, missing data and inaccuracies.

Data were exported from the Excel spreadsheet into R studio software version 3.5.1 for analysis. Quality assurance measures was implemented through designing a customized database using the study questionnaire structure with data stored in numeric coded format, and text for open ended questions. The design was intended to minimize data entry errors. In addition, range and consistency checks were built into the database to identify implausible values due to possible data collection errors. Data cleaning and analysis was then conducted. In cases where data entry errors were noted cleaning involved validating entries by referring back to the study questionnaire using the unique study identifier contained in each questionnaire. Any inconsistency between the questionnaire and data contained in the database was resolved by checking patient records and re-entering the data contained in the records. All data including questionnaires and electronic databases were archived in a secure lockable cabinet. The final master copy of received data was archived and backed up for future reference.

Descriptive data for the patients' bio-data such as age, parity, marital status, family history of diabetes or any chronic illness was analyzed and presented inform of tables. Measures of dispersion such as the mean were used to describe continuous data variables such as age. Categorical variables were compared using the chi-square test. The risk factors associated with the development of GDM such as BMI, family history of DM, previous history of GDM were assessed .Multivariable logistic regression models were used to determine the risk factors that are significantly associated with GDM. In these regressions all factors that showed significant

association with GDM in the univariate analysis were included as explanatory factors in a logistic regression. Associations of variance were determined using multivariate analysis models and chi-square tables. Tables were used to present the data. Odds ratio was used to quantify any association and a p-value of <0.05 taken as significant.

Sensitivity, specificity, negative and positive predictive values for the 50g screening were computed and the validity of the test conducted. Further analysis was done and presented using Receiver Operating Curves to further characterize 50-gram screening test outcomes. A p-value of 0.05 was taken as significant.

Section 8.12: Ethics considerations:

8.12.1 Ethical approval

Permission was sought from the KNH and UON Ethics Research Committee to carry out this study as part of the University of Nairobi (UON) thesis dissertation. Copies of this protocol, the informed consent form were presented to the committee for written approval before commencing the study. Informed, written consent was obtained from the participants before study commenced. Ethical approval number: (P524/07/2018)

8.12.2 Risk to participants

There was no risk to participants because the participants ingested a glucose load that was not contaminated. The common side effects which were experienced include gastric irritation, delayed emptying, and gastrointestinal osmotic imbalance, leading to nausea although these side effects were not common. This was minimized by giving chilled water with glucose as well as a lemon slice after ingestion.

The participants had a total of 5 ml of blood drawn from their veins for carrying out the tests. These tests are recommended by WHO and routinely done in KNH for patients suspected to have GDM. Infection prevention and safety was observed while collecting blood samples. Clean, sterile methods of collecting the blood samples, injection safety and body tissue rules when it comes to disposing of the sharps and blood collected from the participants were applied. Research assistants were trained on the above.

8.12.3 Confidentiality

All information was handled with uttermost confidentiality throughout the tenure of the study, held in trust by the investigator, research assistants and the study institution. A password protected computer with access by the primary investigator and research assistant was used. The participants were given study identification numbers and no information concerning the study participants was released to an unauthorized third party without prior written approval of the study institution or the Ethics Research Committee.

8.12.4 Informed consent

We obtained a written informed consent from participants. Adequate explanation and counseling was done before attaining consent. Participant's partners were informed about the study. Participant requests for the partner's presence or advice before consenting was granted if the partner was within the hospital at the time of the request. The partner then appended their signature as a witness as provided for in the consent form. However, the participant's approval was considered as tacit approval from the partner, unless otherwise specified. The informed consent form described the purpose of the study, the procedures to be carried out and the risks and benefits in accordance with applicable regulations. The consent form was translated into Swahili for ease of understanding.

Literate participants appended their signatures at the provided space in the consent form. Non-literate participants documented their approval by marking the form using their thumbprint, in the presence of a literate third-party witness. Local ERC requirements for obtaining informed consent from non-literate persons were followed. Participants or their parents/ guardians were provided a copy of their informed consent forms.

8.12.5 Benefits of the study

GDM is associated with adverse maternal and neonatal outcomes which can be prevented with early screening and diagnosis. This study will help increase the knowledge of GDM screening to health care givers therefore improving service provision. The study recommendations are expected to inform policy on diagnosis and management of GDM. In addition the outcome of the study will demonstrate the risk factors that lead to the development of GDM and how they could be adjusted for the promotion of a healthy lifestyle among pregnant women. The data from the study will also aid in the development of guidelines and implementation of policies on GDM screening.

Section 8.13

Study limitations:

Problematic fasting: Patients need to fast for ≥8 hours for the 75g OGTT, this was not easy to achieve as some patients forgot and come having eaten something. In addition, some patients may have taken some food and fail to disclose this information on the day of the OGTT.

To counter this, patient phone numbers were taken for follow up before the day of testing to remind them to fast before the test. Subsequently, the principal investigator called the participants to remind them on their return visit. Text messages sent the day before were included to encourage the patient to return.

We couldn’t differentiate the participants with undiagnosed pre-gestational diabetes from those with gestational diabetes

HbA1c levels were performed on selected cases, i.e. those with positive OGTT and 50 gram GCT therefore we couldn't ascertain the performance characteristics of HbA1c in comparison to the other screening tests used. We were not able analyze the relationship between 50 gram GCT with maternal and fetal outcomes.

Section 8.14

Dissemination of research findings:

All participants in the research were given a report of the findings, and encouraged to comment on them.

- Dissemination of the results will take place by three methods:
- Production of a report that was sent to the Department Of Obstetrics And Gynaecology. A report was also sent to the KNH/UON ethics and research committee (KNH-UON-ERC).
- Publishing papers in specialist and general, national and international journals.
- Presentation of papers at both national and international conferences.

SECTION 9: RESULTS

The study period was from December 2018 to April 2019. A total of 438 antenatal women were recruited. 24% (107) of antenatal women had positive 50 gram GCT (1 hour plasma glucose ≥7.8mmol/l), with 52 % (56) among the 107 participants later diagnosed with GDM. A total of 100 antenatal women were diagnosed with gestational diabetes based on a positive OGTT resulting in 23% (95% CI 19%-27%) prevalence of gestational diabetes. The participants with positive 50 gram GCT and 75 gram OGTT had their HbA1c levels done for correlation as in figure 4 below.

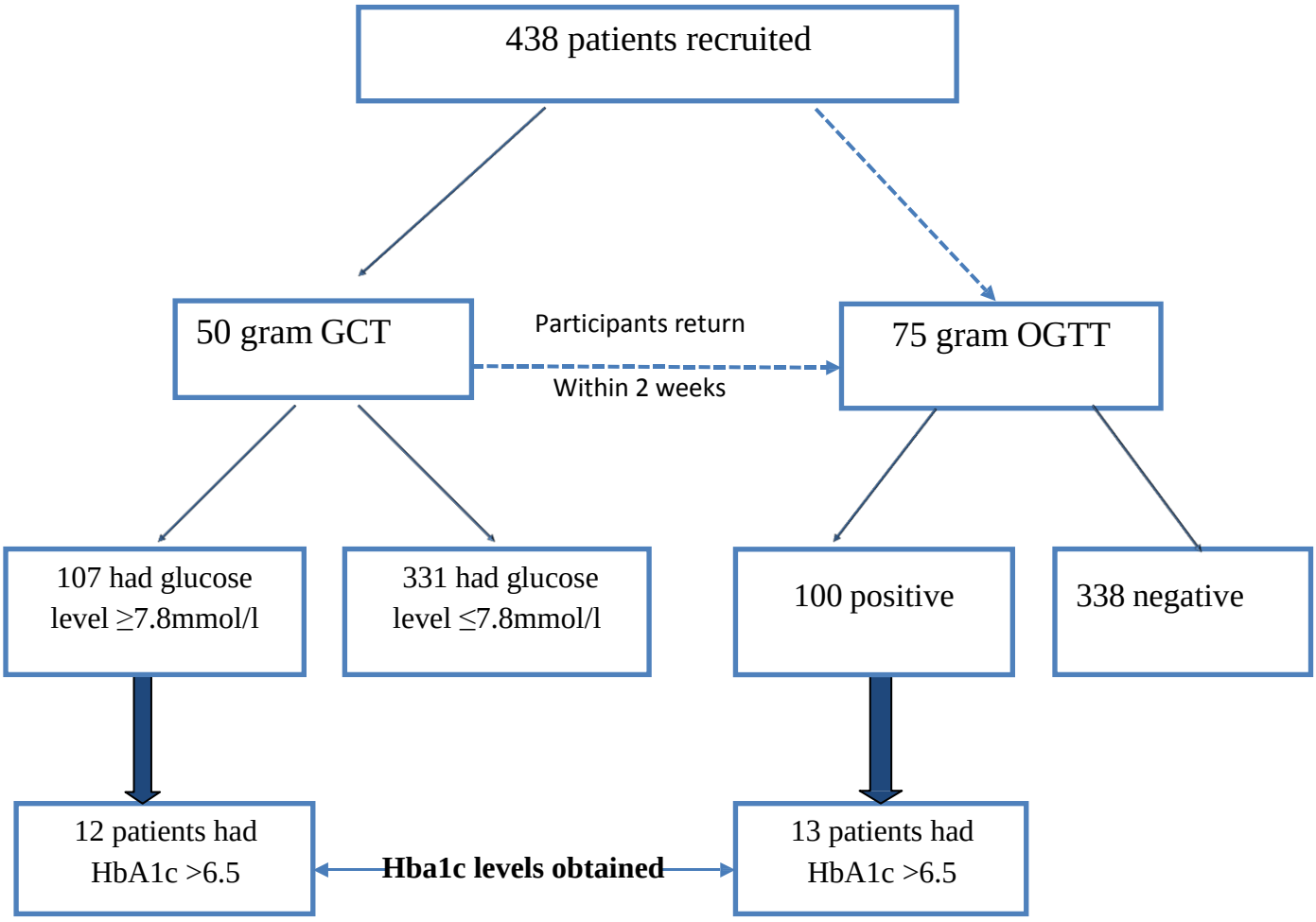


Figure 4: Characteristics of glucose levels and frequency of GDM amongst the study participants

Section 9.1:

Baseline characteristics of the study participants

Table 3: Baseline sociodemographic characteristics of the study participants who underwent screening for GDM at KNH between December 2018 and April 2019:

Variables	Frequency (n=438)	Percentage (%)
Age		
> 25 years	381	87
< 25 years	57	13
Marital Status		
Married	393	87
Single	45	13
Residence		
Urban	334	76
Rural	103	24
Level of Education		
Tertiary	191	44
Secondary	204	47
Primary	43	9
Employment status		
Self employed	220	50
Employed	127	29
Unemployed	91	21
Income per month		
> 30, 000	55	13
15, 000 - 30, 000	154	36
6, 000 - 15, 000	130	30
< 6, 000	90	21

Most participants were above the age of 25 (87%) and married (87%). Most participants (76%) resided in urban areas. Half of the participants were self-employed (50%) and majority had received at least secondary education and above (Table 3)

Table 4: Baseline clinical characteristics of the study participants who underwent screening for GDM at KNH between December 2018 and April 2019:

Variables:	Frequency n=438	Percentage (%)
Gravidity		
Primigravidae	141	32
Multigravidae	297	68
History of Miscarriage		
Yes	109	25
No	329	75
Macrosomia		
Yes	17	4
No	421	96
History of C/S		
Yes	112	26
No	336	74
History of NBU Admission		
Yes	43	10
No	395	90
Hypertension		
Yes	28	6
No	410	94
Family History of DM		
Yes	92	21
No	346	79
Family History of hypertension		
Yes	115	26
No	323	74
Glycosuria		
Yes	57	13
No	380	87
Pre-Pregnancy BMI		
Normal Weight	197	45
Overweight	168	38
Obese	73	17

Majority of the participants were multigravidae (87%). History of miscarriage was reported in 25% of the participants. Only 4% had a previous delivery of a macrosomic baby. A quarter of the participants (26%) had previously delivered via a c/section and 6% of the participants had been treated for hypertensive disorders. About 21% of participants gave a positive family history of diabetes while 26% had a family history of hypertension. Glycosuria was seen in 13% of participants. More than half of the participants were either obese or overweight; 17% and 38 % respectively (Table 4)

Section 9.2: Sociodemographic factors associated with GDM:

Table 5: Association between socio-demographic characteristics and gestational diabetes amongst the participants screened for GDM at KNH between December 2018 and April 2019:

Variables	Oral Glucose Tolerance Test			
	Negative	**Positive**	**OR (95 % CI)**	**P-Value**
Age				
> 25 years	291	90	1.45 (0.73-3.15)	0.3100
< 25 years	47	10		
Mean Age **(SD)**	29.8 (5.1)	31.7 (5.1)	1.96 (0.83-3.09)	0.0007
Marital Status				
Married	301	92	1.41 (0.67-3.37)	0.3960
Single	37	8		
Residence				
Urban	259	75	0.90 (0.54-1.54)	0.7010
Rural	78	25		
Level of Education				
Tertiary	151	40	0.92 (0.44-2.03)	0.8282
Secondary	155	49	0.77 (0.37-1.72)	0.5064
Primary	32	11		
Employment status				
Self employed	162	58	1.56 (0.86-2.93)	0.1520
Employed	102	25	1.07 (0.54-2.14)	0.8530
Unemployed	74	17		
Income per month				
> 30, 000	43	12	1.04 (0.45-2.34)	0.9200
15, 000 - 30, 000	121	33	1.02 (0.54-1.95)	0.9530
6, 000 - 15, 000	96	34	1.32 (0.70-2.54)	0.3910
< 6, 000	71	19		

In relation to the socio-demographic characteristics, there was a significant difference between the mean age of participants with GDM (31.7 years) compared to the mean age of non- GDM participants (29.8 years). The participants with GDM were therefore generally older than those with no GDM (p =0.0007). Marital status, area of residence, level of education, employment status and monthly income were not significantly associated with GDM (table 5).

Section 9.3: Clinical characteristics associated with GDM:

Table 6: Association between clinical characteristics and gestational diabetes amongst the participants screened for GDM at KNH between December 2018 and April 2019:

Variables	Oral Glucose Tolerance Test			
	Negative	**Positive**	**OR (95 % CI)**	**P-Value**
History of Miscarriage				
Yes	71	38	1.31 (1.42-3.72)	0.0007
No	267	62		
Macrosomia				
Yes	9	8	3.18 (1.16-8.54)	0.0207
No	329	92		
History of C/S				
Yes	67	45	3.31 (2.05-5.33)	<0.0001
No	271	55		
History of NBU Admission				
Yes	25	18	2.75 (1.41-5.26)	0.0024
No	313	82		
Hypertension				
Yes	17	11	2.33 (1.03-5.11)	0.0364
No	321	89		
Family History of DM				
Yes	67	25	1.35 (0.79-2.26)	0.2650
No	271	75		
Family History of Hypertension				
Yes	83	32	1.45 (0.88-2.34)	0.1380
No	255	68		
Glycosuria				
Yes	4	53	96.2 (37.3-324)	<0.0001
No	336	44		
Gravidity				
Multigravidae	216	81	2.41 (1.42-4.26)	0.0016
Primigravidae	122	19		
Pre-Pregnancy BMI				
Obese	45	28	3.60(1.95-6.69)	<0.0001
Overweight	125	43	1.99 (1.18-3.39)	0.0100
Under/ Normal	168	29		

Table 6: There was significant association between GDM status and history of miscarriage (p=0.0007), fetal macrosomia (p=0.0207), and history of C/section (p<0.0001), hypertension (p=0.0364), glycosuria (p<0.0001), multigravidae (p=0.0016), obesity (p<0.0001) and overweight (p=0.0100). There was no significant association found between first degree relatives with diabetes / hypertension and gestational diabetes.

Section 9.4: Multivariate Analysis of Clinical Characteristics associated with Gestational diabetes:

Table 7: Adjusted odds ratios of clinical characteristics associated with GDM:

Variables	Oral Glucose Tolerance Test			
	Negative	**Positive**	**Adjusted OR (95 % CI)**	**P-Value**
History of Miscarriage **Yes** **No**	 71 267	 38 62	1.38 (0.68-2.69)	0.3610
History of Macrosomia **Yes** **No**	 9 329	 8 92	3.49(0.67-15.9)	0.1130
History of C/S **Yes** **No**	 67 271	 45 55	1.76 (0.82-3.76)	0.1410
History of NBU Admission **Yes** **No**	 25 313	 18 82	1.02 (0.34-2.80)	0.9730
Hypertension **Yes** **No**	 17 321	 11 89	1.34 (0.40-4.01)	0.6170
Glycosuria **Yes** **No**	 4 336	 53 44	83.2 (31.2-261)	<0.0001
Gravidity **Multigravidae** **Nulligravidae**	 216 122	 81 19	0.84 (0.40-1.81)	0.6540
Pre-Pregnancy BMI **Obese** **Overweight** **Under/ Normal**	 45 125 168	 28 43 29	 1.69 (0.85-4.99) 2.07 (0.84-3.45)	 0.1050 0.1440

Table 7: the significant factors associated with GDM were fitted into a multivariate logistic regression model, all the odds ratios became non-significant apart from glycosuria ($p < 0.0001$).The participants with glycosuria were 83 times more likely to have gestational diabetes compared to the participants without glycosuria.

Section 9.5:

Prevalence of glucose intolerance:

The prevalence of glucose intolerance using the 50gram GCT cut-off ≥7.8mmol/l is estimated at 24% (95% CI; (0.20, 0.29) n=107

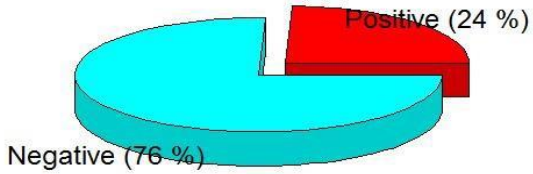


Figure 5: Prevalence of glucose intolerance with use of 50g GCT at 7.8mmol/l (n=107)

Section 9.6:

Prevalence of gestational diabetes:

Prevalence of GDM as determined by the standard diagnostic OGTT (WHO 2013 criteria) is estimated at 23%. (95% CI; (0.19, 0.27) n=100

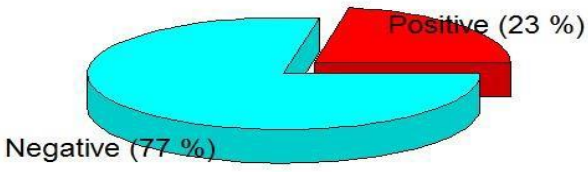


Figure 6: Prevalence of GDM with use of 75g OGTT (n=100)

Section 9.7:
Diagnostic utility of GCT against OGTT:

Table 8: Measures of Diagnostic Accuracy and Effectiveness of 50g GCT:

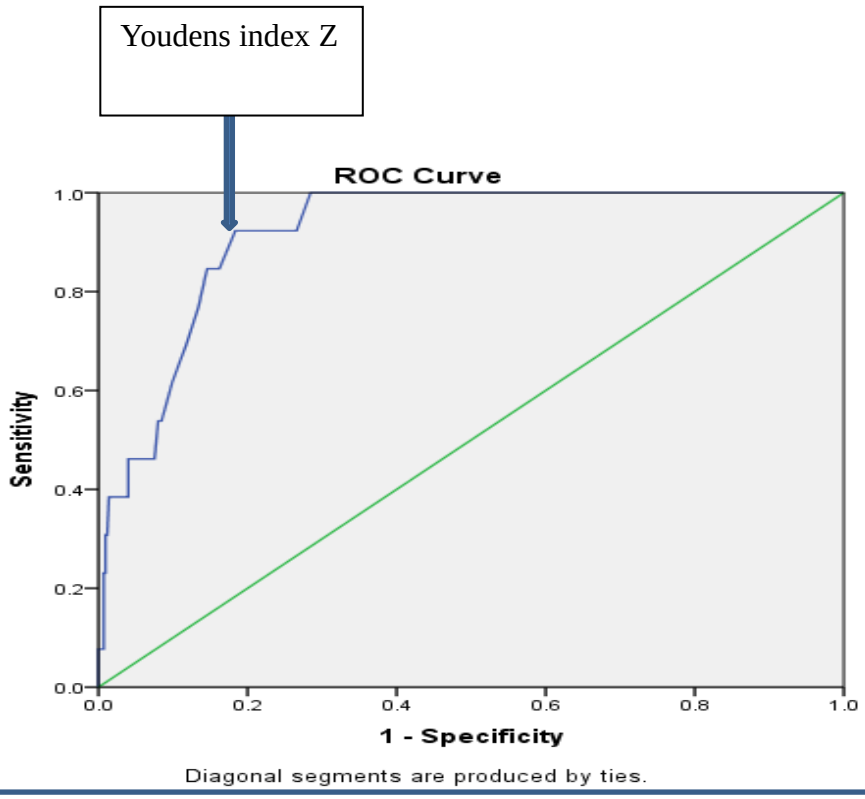
50g GCT	OGTT		
	Positive	Negative	Total
Positive (≥7.8 mmol/l)	56	51	107
Negative (<7.8 mmol/l)	44	287	331
Total	100	338	438
Prevalence of Glucose intolerance with use of 50g GCT (7.8 mmol/l cutoff)	24%(20%-29%)		
Prevalence of GDM with use of 75g OGTT	23%(19%-27%)		
Sensitivity	56%(46%-66%)		
Specificity	85%(81%-89%)		
Positive Predictive Value	52%(42%-62%)		
Negative Predictive Value	87%(83%-90%)		
Positive Likelihood Ratio	3.71(2.73-5.04)		
Negative Likelihood Ratio	0.52(0.41-0.65)		
Area Under ROC Curve (AUC)	0.7(0.64-0.75)		

All accuracy measures are displayed with 95% CI
OGTT: Oral Glucose Tolerance Test

Table 8: The diagnostic utility of the 50 GCT at 7.8mmol/l cut-off in screening for gestational diabetes is shown in table 2. There were 51 false positive cases and 44 false negative cases. At this threshold, the sensitivity was low at 56% (95% C.I 46%-66%) with a high specificity of 85% (95% C.I 81%-89%). The positive predictive value (PPV) was low at 52% (95% C.I 42%-62%) however the negative predictive value was high at 87% (95% C.I, 83%-90%). GCT had a positive likelihood ratio of 3.71 (95% C.I (2.73- 5.04)), which is greater than 1 indicating that a positive GCT was associated with presence of GDM.

Section 9.7.1:

The best-cut-off value of the GCT for detecting GDM as per the receiver-operator characteristic (ROC) curve



Using ROC curve the best Cut off of is 7.5mmol/l sensitivity of 92%, specificity of 73%

Youden's index = use to determine optimal cut-off which gives the least number of

Figure 7: Receiver Operator characteristic (ROC) curve of the 50-gram Glucose Challenge Test for screening of gestational diabetes mellitus using 75 gram OGTT (WHO criteria)

Receiver -operator characteristic (ROC) curve was generated. The ability of the GCT results to predict the diagnosis of GDM is depicted graphically (Figure 1). The area under the curve (AUC) curve is 0.7. The best cut-off value of the 50 gram GCT for detecting GDM was determined using the ROC curve (figure 7).

Section 9.7.2:

Table 9: Comparison of sensitivity and specificity of the GCT across different thresholds for the 50 gram GCT

Cutoff	Sensitivity	Specificity
7.5mmol/l	92%	73%
7.8mmol/l	56%	85%

Reducing the threshold of the GCT from 7.8mmol/l to 7.5mmol/l increased the sensitivity from 56% to 92% while reducing specificity from 85% to 73% (table 9).

Section 9.8:

Correlation between abnormal 50g GCT and OGTT with HbA1C:

9.8.1: Correlation of HbA1c with positive 50g GCT

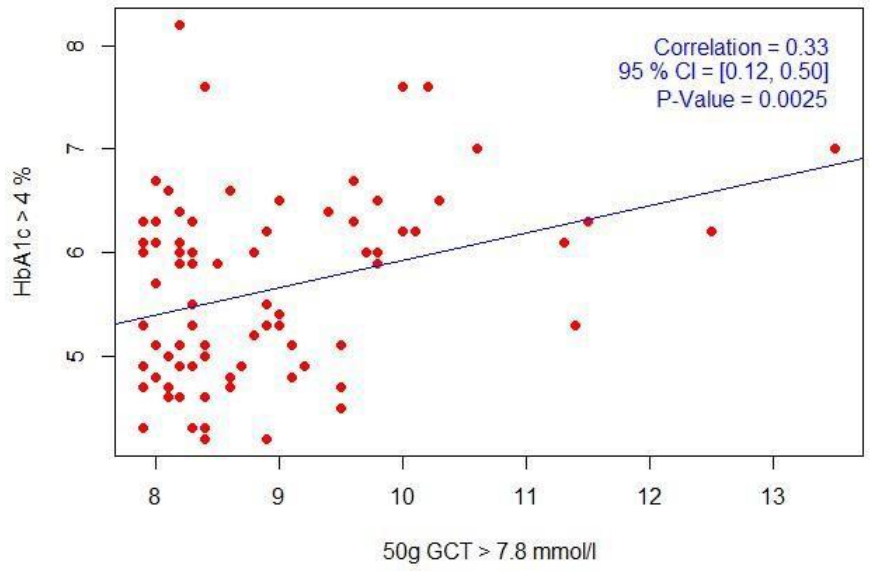


Figure 8: Correlation between abnormal 50g GCT and HbA1c levels

A total of 107 participants had a positive 50 gram GCT undertook the HbA1c test. 12 (11%) out of the 107 participants had an HbA1c cut-off of >6.5%. There was a significant (p=0.0025) but relatively weak positive linear correlation (correlation = 0.33) between the HbA1c measurements above 4% and that of 50g GCT above 7.8 mmol/l, (figure 8).

9.8.2: Correlation of HbA1c with abnormal OGTT:

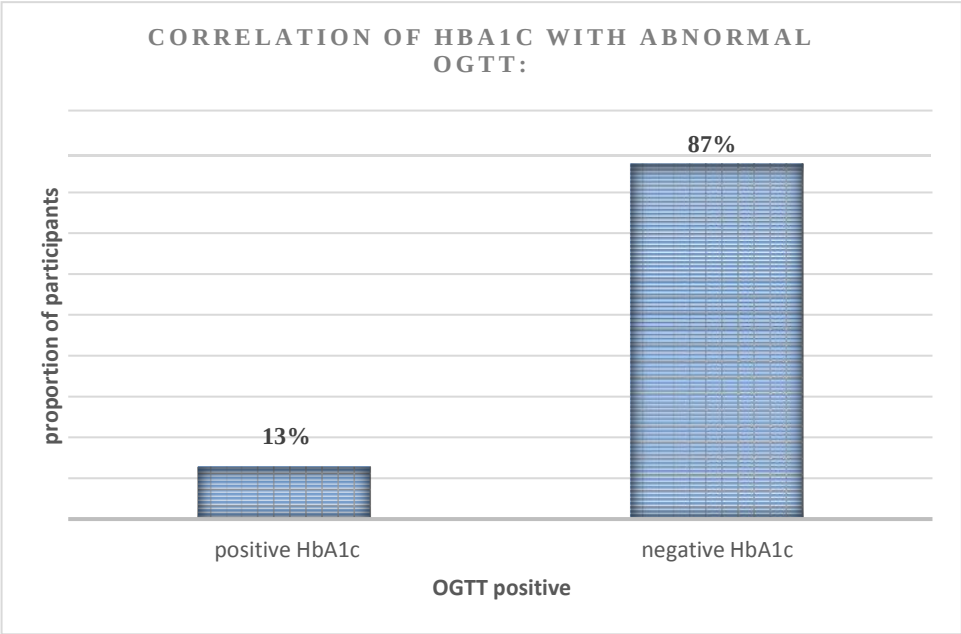


Figure 9: Correlation between abnormal OGTT and HbA1c levels

The bar plot above shows 13 out of the 100 participants had HbA1c levels >6.5% while remaining 87 had HbA1clevels of <6.5%. Therefore HbA1c test at a cut-off of 6.5 gave a high number of false negatives (87 out of 100 participants).

SECTION 10:

DISCUSSION:

The aim of this study was to determine the performance characteristic of the 50 gram GCT (at 7.8 mmol/l cut-off) as a universal screening tool in comparison to the 75gram Oral Glucose Tolerance Test (OGTT-2013 WHO criteria), and correlation of abnormal results with HbA1c. Risk factors associated with GDM were also determined.

The 50 gram GCT effectively ruled out gestational diabetes (GDM) due to the high specificity and negative predictive value (NPV) of the test. At the 7.8mmol/l threshold, the GCT had a low sensitivity and positive predictive value (PPV). The ROC curve generated showed an area under the curve (AUC) of 0.7 and best 50 gram GCT cut-off of 7.5mmol/l. We observed that reducing the threshold of the GCT, increased the sensitivity of the test but led to a resultant decrease in specificity. The prevalence of glucose intolerance and GDM was 23% and 24% respectively. Glycosuria was significantly associated GDM in both univariate and multivariate analysis. An eighth of the participants with GDM had an HbA1c level of ≥6.5%.

In our study we found a low sensitivity and high specificity of the 50g GCT at a cut off of ≥7.8 at 56%, 85% respectively. Our findings were similar to those reported by Ben halima et al who reported a sensitivity and specificity of 59.6% and 81% respectively (100) and Perucchini et al who reported sensitivity and specificity of 59% and 91% respectively (101). However Akram et al in Pakistan reported higher sensitivity and specificity at the 7.8mmol/l threshold of 90.90% and 91.07% respectively (102). Variations may be due differences in prevalence of GDM in different ethnicities and populations. Discrepancies in values could also be explained by variations in social, cultural and economic characteristics in different populations.

An important finding in this study is the high specificity and NPV of the GCT at 85% and 87% respectively thereby suggesting the usefulness of the test in excluding GDM. This was comparable to other studies (69). We found a PPV of 52%. This implies that 52% of the

participants with screening values at or beyond 7.8mmol/l would be correctly diagnosed with GDM. The converse is that over-diagnosis would occur in 48%. Ben-halima et al found lower positive predictive values of 31.7% leaving a large percentage of participants with an unnecessary diagnosis of GDM. On the contrary, Akram et al in Pakistan found a higher PPV of 88.8%(69). The predictive values of a test are dependent on the prevalence of the disease in a particular population, therefore the difference in prevalence of GDM could explain the discrepancies in the values at different settings. GCT had a positive likelihood ratio (PLR) and negative likelihood ratio of (NLR) of 3.71 and 0.52 respectively. The PLR is greater than 1 indicating that a positive GCT was associated with presence of GDM. Benhalima et al found similar values at 3.1 and 0.50 respectively (103).

ROC curve was generated to graphically depict the relationship between GCT and GDM. To define an effective screening test with an ROC curve, the area under the curve (AUC) should approach the upper left corner of the graph (i.e. near to value of 1). The AUC for the 50 gram GCT in our study was 0.7. The best cut-off value of the GCT as generated by the ROC curve was 7.5mmol/l. The sensitivity increased at this threshold value, however there was a resultant decrease in specificity. Perucchini et al and Benhalima et al made similar observations (101)(65). At the 7.8mmol/l threshold, the number of participants with true negatives was 287 compared to 246 at a lower threshold. Lowering the threshold would improve the sensitivity of the test but would lead to unnecessarily performing an OGTT. If threshold of 7.5mmol/l is used, 21% of women will undergo unnecessary OGTT therefore leading to unnecessary costs and inconvenience to the patient.

Prevalence of glucose intolerance and GDM was 24% and 23% respectively. Adelaide et al and Bosire et al in 2009 and 2011 documented lower GDM prevalence of 16% and 8.9% respectively, in the same setting (26)(2). We found a similar prevalence to Adam S et al in South Africa who found a prevalence of 25.8% using the 2013 WHO criteria (57). Akram et al

in a similar study in Pakistan found a higher prevalence at 44%. In our setting, most of or study participants were observed to be obese and above 25 years of age. These factors have been associated with an increased likelihood for GDM. Due to the lower diagnostic threshold of the 2013 WHO criteria and the use of universal screening we were able to detect more cases of GDM which further contributed to the the high prevalance.

When determining risk factors associated with GDM we found, using a multivariate logistic regression model, the participants with glycosuria were 83 times more likely to have gestational diabetes compared to the participants without glycosuria. Bosire et al found a similar association between glycosuria and GDM (2). There was no statistical difference between the parity, pre-pregnancy BMI, history of miscarriage, history of previous caesarean section, fetal macrosomia, history of hypertension or family history of hypertension and diabetes. This is contrary to a meta-analysis by akwilina et al in 2015 who reported being overweight/ obese, family history for type 2 diabetes, previous stillbirth, previous macrosomic child and age >30 years to be significant risk factors for GDM(104). This could attribute to low numbers of study participants for these particular variables in our study.

Our secondary objective was to correlate abnormal 50 gram GCT and OGTT results to HbA1C levels. We found a relatively weak positive linear correlation between the HbA1c measurements and that the GCT. An eighth of the GDM patients in this study had HbA1c levels ≥6.5%, giving a high number of false negatives. Paula renz et al in 2015 found at 6.5% cut-off the sensitivity and specificity of the HbA1C was 7% and 100% respectively(105) however lowering the threshold to 5.0% raised the sensitivity to 89.7% but lowered specificity to 32.6% (105).

Our study was limited in that we were not able analyze the relationship between 50 gram GCT and maternal and fetal outcomes. In addition, the HbA1c was only performed on a fraction of the study population therefore our study was not powered to make any inference in terms of the performance characteristics of the HbA1c as a screening tool for GDM.

The strength of our study is that it was the first study in this setting to universally screen antenatal women with both GCT against the 75 g OGTT, thus we did not discriminate based on risk-factors or a negative GCT.

CONCLUSION:

The 50 gram GCT at a threshold of 7.8mmol/l is a good screening test in this setting due to its high specificity and high negative predictive value making it a useful test in excluding GDM. The sensitivity of the test at the 7.8mmol/l cut off was lower, however lowering the threshold to 7.5mmol/l raises the sensitivity but lowers the specificity of the test. Lowering the current recommended threshold of 7.8mmol/l will lead to unnecessarily performing an OGTT. HbA1C levels do not correlate with abnormal GCT and OGTT. Glycosuria was associated with increased risk of GDM.

RECOMMENDATIONS:

Due to the high prevalence of GDM in our population, universal screening for GDM is justified. Although we recommend the GCT as a screening test, the association between GCT level and the pregnancy outcome has not been studied in this setting. Therefore follow-up studies to evaluate the maternal and neonatal outcomes on the antenatal women diagnosed with glucose intolerance and GDM are recommended.

SECTION 11:

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SECTION 12:

ANNEXES:

ANNEX 1: LETTER TO ERC

Dr. Souha Athman Al-kindy

H58/80771/2015

The Chairperson,

Ethics, Research and Standards Committee,

Kenyatta National Hospital and University of Nairobi,

P.O. Box 20723,

NAIROBI

Dear Sir,

RE: SUBMISSION OF MASTERS DEGREE RESEARCH PROPOSAL FOR APPROVAL

I wish to submit my research proposal for approval by your committee. I am currently a 3rd-year student pursuing a Master's Degree in Obstetrics and Gynaecology at the University of Nairobi, College of Health Sciences.

Yours Sincerely,

Dr. Souha Athman Al-kindy

Senior House Officer,

Department of Obstetrics and Gynecology,

College of Health Sciences

University of Nairobi

ANNEX 2: DATA ABSTRACTION TOOLS

Consent Form - English

Date (date/month/year): _____

Study Title: SENSITIVITY AND SPECIFICITY OF 50G GLUCOSE CHALLENGE TEST (GCT) IN COMPARISON TO 75G OGTT AS THE GOLD STANDARD IN GESTATIONAL DIABETES SCREENING.

Principal Investigator:

Dr. Souha Athman Al-kindy (MBChB)

Department of Obstetrics and Gynaecology, University of Nairobi.

Telephone Number: 0724-219219

Investigator's Statement:

We are requesting you to kindly participate in this research study. The purpose of this consent form is to provide you with the information you will need to help you decide whether to participate in the study. This process is called 'Informed Consent'. Please read this consent information carefully and ask any questions or seek clarification on any matter concerning the study with which you are uncertain. You are free to ask any questions about the study. The investigator will be available to answer any questions that arise during the study and afterward.

Purpose of the study

The purpose of this study is to determine the best screening method for gestational diabetes and to determine the the risk factors for development of gestational diabetes in pregnant mothers attending antenatal clinic at the Kenyatta National Hospital. This study will benefit you in that it would be possible to determine whether you suffer from gestational diabetes and thus be able to prevent and/or treat any complication that arises from this disease, in either you or your unborn child. You will receive your blood glucose results and be able to be reviewed by the attending obstetrician in the clinic. Your participation in the study may benefit others in future from the information we find in this study

Procedure

I and my research assistant will obtain information about you using a questionnaire. You would subsequently give you a glucose drink that you will drink in 5 – 10 minutes. An hour after ingestion of the drink then you will have some blood withdrawn from you for

measurement of the blood glucose level. It is requested that over this hour there be no activity. Within one week you will be requested to come back for the second part of the study at 8am in the morning and not having eaten since midnight of that day. On arrival to hospital then you shall have your blood glucose taken, then given another glucose load. This time your blood again will be drawn at 1 hour and 2 hours after ingestion of the drink. You might be requested to undertake a blood test further test known as the HbA1c should you test positive for the above tests. Your results will then be availed to you and be advised as to review by the attending obstetricians at the ANC clinic. You will still receive standard antenatal care as you participate in the study.

Risk or discomfort

Completing your questionnaire would take approximately 5 minutes of your time. Blood testing would take less than 5 minutes. If you are found to have glucose intolerance, then you would require follow up in the antenatal clinic. Slight pain will be felt on obtaining the blood for testing. It is estimated that you will undergo a maximum of 5 pricks to get your blood. You may have slight discomfort to the glucose load, if taken too quickly it may give you nausea. There is no danger caused by the testing to you or your unborn child.

Voluntariness:

The study will be fully voluntary. There will be no financial rewards to you for participating in the study. One is free to participate or withdraw from the study at any point. Refusal to participate will not compromise you or your child's care in any way.

Confidentiality:

All the information obtained from you will be held in strict confidentiality. Any information that may identify you or your child will not be published or discussed with any unauthorized persons. No specific information regarding you, your child or your family will be released to any person without your written permission. Your research number will be used in place of your names.

Access of health records:

You may apply for access to your own records, or may authorize third parties such as lawyers, employers, or insurance companies to do so on your behalf. The Principal

Investigator can be contacted if access to health records is required.

Sharing of results:

Study staff will protect your personal information closely so no one will be able to connect your responses and any other information that identifies you. Federal or state laws may require us to show information to university or government officials (or sponsors), who are responsible for monitoring the safety of this study. Directly identifying information (e.g. names, addresses) will be safeguarded and maintained under controlled conditions. You will not be identified in any publication from this study.

Problems or Questions:

If you ever have any questions about the study or about the use of the results you can contact the principal investigator, Dr. Souha Athman Al-kindy by calling 0724-219219. If you have any questions on your rights as a research participant you can contact the Kenyatta National Hospital Ethics and Research Committee (KNH- ESRC) by calling 020-2726300 Ext. 44355

Participant's Statement:

I _____having received adequate information regarding the study research, risks, benefits hereby AGREE / DISAGREE (Cross out as appropriate) to participate in the study. I understand that my participation is fully voluntary and that I am free to withdraw at any time. I have been given adequate opportunity to ask questions and seek clarification on the study and these have been addressed satisfactorily.

Participant's name: _____

Signature/thumb print: _____

Date _____

Witness name: _____

Signature/thumb print: _____

Date: _____

I _____ declare that I have adequately explained to the above participant, the study procedure, risks and benefits and given her time to ask questions and seek clarification regarding the study. I have answered all the questions raised to the best of my ability.

Interviewer's name and Signature: _____

Date: _____

Problems or Questions:

If you ever have any questions about the study or about the use of the results you can contact.

Principal investigator:

Dr. Souha Athman Al-kindy

P.O. BOX: 98705-80100, Mombasa

Tel: 07242189219

Email: souhaalkindy@gmail.com

Dr. Alfred Osoti.

P.O Box 30197-00100,

Nairobi.

Tel: 0733886664

Email: alfosoti@gmail.com

Dr. Rose JepchumbaKosgei.

P.O Box 30197-00100,Nairobi.

Tel:0722273443

Email: salikabon@gmail.com

Secretary, KNH-UoN ERC

P.O Box 19679-00202

Tel: (254-020) 2726300-9

Email: uonknherc@uonbi.ac.ke 40

Consent Form – Swahili version

FOMU YA RIDHAA

Tarehe (siku/mwezi/mwaka): _____

Study Title: SENSITIVITY AND SPECIFICITY OF 50G GLUCOSE CHALLENGE TEST (GCT) IN COMPARISON TO 75G OGTT AS THE GOLD STANDARD IN GESTATIONAL DIABETES SCREENING.

Mtafiti Mkuu:

Dkt. Souha Athman Al-kindy(MBChB)

Idara ya Uzazi na Afya ya kina mama, Chuo kikuu cha Nairobi.

Nambari ya simu: 0724-219219

Taarifa ya mtafiti:

Tunakuomba wewe kushiriki kwenye utafiti huu. Lengo la fomu hii ya idhini ni kukupa habari utakayohitaji iliikusaidie kuamua ikiwa utashiriki kwenye utafiti. Utaratibu huu unaitwa 'Idhini ya kujulishwa'. Tafadhali soma ujumbe wa idhini hii kwa uangalifu na uulize ma swali yoyote au ufafanuzikwa mambo yoyote yanayohusisha utafiti ambayo hauna uhakika nayo. Uko huru kuuliza ma swali yoyote kuhusu utafiti. Mtafiti atakuwe kokujibu maswali ya takayotokea wakati wa utafiti na baadaye.

Lengo na faida la utafiti:

Lengo la utafiti huu ni kuamua ni uchunguzi gani bora kabisa ambao unafaa kutumika kwa upimaji wa ugonjwa wa kisukari kipindi cha uja uzito na pia kuamua ni hali gani zinazochangia hatari ya kupata ugonjwa wa kisukari kipindi cha uja uzito, miongoni wa akina mama waja wazito wanao hudhuria kliniki ya wajawazito katika hospitali ya kitaifa ya Kenyatta. Kama mshiriki utafaidika na utafiti huu kwa sababu utapata kujua hali yako kama unauguwa kutokana na ugonjwa wa kisukari kipindi cha uja uzito, na kwa hivyo kuweza kuzuia au kutibu matatizo yeyote ambao yanaweza kuibuka kutokana na maradhi haya, aidha kwako ama kwa mtoto wako. Utakabidhiwa majibu yako ya vipimo vya sukari na yataweza kuonekana na daktari wa uzazi katika kliniki. Kushiriki kwako kwenye utafiti kwaweza wafaidi wengine wakati wa usoni kutokana na habari tutakoyopata kwenye utafiti huu.

Utaratibu:

Fomu ya maswali yaliyo na mpangilio ita tumika kuchukua habari yako ya uzazi, matibabu yaliyopita na maswala mengineo kukuhusu. Baada ya hapo utapatiwa kinwaji cha glukosi ambacho utatakiwa kunywa baina ya muda wa dakika tano na kumi. Baada ya muda wa saa moja, utatolewa damu na kiwango chako cha sukari kupimwa. Wakati unapongoja saa moja ipite unashauriwa kutulia na kutofanya shughuli yoyote. Baada ya muda wa wiki moja, utaombwa urudi kwa sehemu ya pili ya utafiti, saa mbili kamili asubuhi, hali ya kuwa umefunga kutoka saa sita usiku. Utakapowasili hospitali, utapimwa kiwango cha sukari kwenye damu, baada ya hapo utapewa kinwaji chenye glukosi na utapimwa tena kiwango cha sukari kwenye damu baada ya saa moja na mbili mtawalia. Kulingana na majibu yatakavyotokea, majibu yanayoonyesha ishara ya ugonjwa wa kisukari kipindi cha ujauzito, utahitajika kufanya kipimo kimoja zaidi cha damu inayoitwa HbA1c. Utakabidhiwa majibu yako ya vipimo vya sukari na yataweza kuonekana na daktari wa uzazi katika kliniki.

Hatari ama Usumbufu:

Itachukuwa takriban dakika tano za muda wako kukamilisha kujaza fomu ya maswali. Kuchukua vipimo vya damu itachukua takriban dakika tano zingine za muda wako. Ukitambulika kuwa na ugonjwa wa kisukari kipindi cha uja uzito utapaswa kufuatiliwa katika kliniki ya wajawazito. Inkadiriwa utadungwa takriban mara tano ili kupata vipimo vya sukari vya mwili wako.

Baada ya kunywa kinwaji cha glukosi, pindi utakapokinwa kwa haraka, unaeza hisi kichefuchefu. Inatakiwa ufahamu hakuna hatari yeyote itakayosababishwa na uchunguzi huu kwako wala kwa mtoto wako.

Kujitolea:

Utafiti utakua wa kujitolea. Hakuta kuwa na malipo ya kifedha kwa kushiriki kwenye utafiti huu. Mtu ako huru kushiriki au kujiondoa kwenye uta fiti kwa wakati wowote. Kukataa kushiriki hakutaathiri malezi yako au ya mwanao hata.

Usiri:

Habari yoyote itakayotolewa kwako itawekwa kwa usiri wa hali ya juu. Habari yoyote ya kukutambulisha wewe au mwanao haitachapishwa au kujadiliwa na watu wasiona kibali.

Hakuna habari maalum kukuhusu, kuhusu mwanao au mtu wa familia yako itapeanwa kwa mtu mwingine bila ruhusa yako iliyoandikwa. Nambari yako ya utafiti itatumika badala ya jina lako.

Kupata rekodi za kimatibabu:

Unaweza kuomba ku weza kufikia rekodi zako au kuruhusu watu wengine kama vile mawakili, waajiri au kampuni za fidia kufunya hivyo kwa niaba yako. Mtafiti mkuu anaweza fikiwa ikiwa rekodi zako zahitaji kufikiwa.

Kujulisha wengine matokeo:

Wafanyakazi wa utafiti watalinda habari sana habari yako ya kibinafsi ilimtu yeyote asije akajua akaunganisha majibu yako na habari inayoweza kukutambulisha. Sheria za serikali zatuhitaji kuonyesha habari kwa wawakilikilishi wa serikali (wafadhili) au chuo kikuu ambao wana jukumu la kufuatilia usalama wa utafiti huu. Habari inayotambulisha moja kwa moja (majina, anwani) zitalindwa na kuwekwa katika hali salama. Hautatambulishwa na chapisho lolote kutoka na utafiti huu.

Shida au Maswali:

Ikiwa una maswali kuhusu utafiti au matumizi ya majibu waweza asiliana na mtafiti mkuu, Dkt. Souha Athman Al-kindy kwa kupiga number ya simuya rununu 0724-219219. Ikiwa una maswali kuhusu haki yako kama mshiriki waweza wasiliana na kamati ya madili na tafiti ya hospitali kuu ya (KNH- ESRC) kwa kupiga number ya simu 020-2726300 Ext. 44355.

Fomu ya Idhini: Taarifaya Mshiriki:

Mimi_____ Nimepewa habari ya kutosha kuhusiana na utafiti , hatari, faida, NIMEKUBALI/NIMEKATAA (weka alama inavyostahili). kushiriki kwenye utafiti. Ninaelewa kwamba kushiriki kwangu ni kwa kujitolea na niko huru kujiondoa wakati wowote. Nimepewa nafasi ya kutosha ya kuuliza maswali na kuuliza ufafanuzi wa utafiti na nimeelezewa haya nikatosheka.

Jina la muhusika: _____

Sahihi/alama ya kidole: _____

Tarehe _____

Jina la mshahidi: _____

Sahihi/alamayakidole: _____

Tarehe: _____

Mimi_____Natangaza yakwamba nimemwelezea mshiriki aliye hapo juu yakutosha, taratibu za utafiti, hatari na faida na nimempa wakati wakuuliza naswali nakuuliza ufafanuzi kuhusu utafiti. Nimejibu maswali yake yote kwa uwezo wangu wote.

Jina la anayeuliza ma swali na sahihi: _____

Tarehe: _____

Ikiwa una maswali kuhusu utafiti au matumizi ya majibu waweza asiliana na:
Mtafiti mkuu:

- Dkt Souha Athman Al-kindy

SLP: 98705-80100, Mombasa
Number ya rununu : 07242189219
baruapepe: souhaalkindy@gmail.com

- Dkt Alfred Osoti. S.L.P:

30197-00100,Nairobi. Number
ya rununu: 0733886664
Barua pepe: alfosoti@gmail.com

- Dkt. Rose JepchumbaKosgei.

S.L.P: 30197-00100,Nairobi.
Number ya rununu :0722273443
Barua pepe: salikabon@gmail.com

- Mwenyekiti;

Hospitali Kuu ya Kitaifa ya Kentyatta,
Kitengo cha Ukaguzi wa Kimaadili
S.L.P:19679-00202
Simu: (254-020) 2726300-9
Barua pepe: uonknherc@uonbi.ac.ke 40

ANNEX 3: STUDY QUESTIONNAIRE.

Indicate all times using the 24 hour clock, and dates in this format date/month/year.

Date: _ _/_ _/ _ _ _ _

Enrollment number: _____

Age: _____

The numbers in brackets are pre-coded numerically.

a) Socio-demographic characteristics

Maternal demographics :

Date of birth	_ _/ _ _/ _ _ _ _ (dd/mm/yyyy)
Weight (kg)	_ _ kg
Height (cm)	_ _ _ cm
BMI (kg/m2) *To be calculated*	_ _ _. _ kg/m2
BP	

What is your marital status?

Single [1]

Married [2]

Separated [3]

Other. Please state ---------- [4]

Where is your current residence

Rural formal [1]

Rural informal [2]

Urban – High income [3]

Urban Middle income [4]

Urban Low income [5]

Urban Informal [6]

How long have you been staying in your current residence?	----------
What is your level of education?	Lower Primary [1] Upper Primary [2] Secondary [3] Tertiary [4] None [5]
What is your employment status?	Self employed [1] Employed [2] Unemployed [3] Other. Please state ---------- [4]
What is the total level of income per month in your family?	<6000 ksh/month [1] 6,000- 15,000 Ksh/month [2] 15,000- 30,000 Ksh/month [3] >30,000 Ksh/month [4]

b) <u>Personal medical history:</u>

What was your weight in Kg before pregnancy?	Weight _____Kg Unknown If unknown, what was your weight at beginning of clinic?-------- Kg

Have you experienced any of the following symptoms

Frequent urination [1]

Frequent thirst [2]

Increased appetite [3]

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]

Do you suffer from a chronic disease? Which one?

Liver disease [1]

Renal disease [2]

Cardiac disease [3]

None [4]

Don't know [9]

Are you currently on any medication?

Yes [1]

No [2]

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

What is your HIV status

Positive [1]

Negative [2]

If unknown what are the results obtained from antenatal clinic screen?

---

c)<u>Obstetric and gynaecological history:</u>

LNMP:

(if not sure of LNMP extrapolated on an early scan, first ANC visit and quickening) --/--/----

Parity

Gravida

GBD:

Obstetric history:						
	Date (Year)	Place Home or HF*	GA** at delivery	Mode of Delivery	Maternal Complications	Neonatal Outcome
1						
2						
3						
4						
5						

*HF- Health Facility

GA** Gestational age

Have you experienced any problem with conceiving?

Yes [1]

No [2]

Do you have a history of polycystic ovarian syndrome?	Yes [1] No [2]
Have you suffered a miscarriage?	Yes [1] No [2]
If yes to 15 above at how many weeks gestation	6-12 weeks [1] 12 – 20 weeks [2] 20-28 weeks [3] Not known [9]
How many pregnancies have you delivered before 37 weeks?	None [1] All [2] Some, specify how many---------- [3]
Have you had elevated blood pressures in this or prior pregnancies?	Yes [1] No [2]
Have you been told of you having glucose/sugar in your urine in this or prior pregnancies?	Yes [1] No [2]
Have you been diagnosed with diabetes?	Yes [1] No [2]
If yes to 20 above, when was diagnosis made?	Before becoming pregnant [1] In the previous pregnancy [2]

Have you ever been told that your womb looks bigger than what is expected?	Yes [1] No [2]
If yes to question above was it related to increased amount of fluid in the uterus?	Yes [1] No [2] Do not know [9]
Have you delivered any of your babies by Caesarean section?	Yes [1] No [2]
If yes to above what was the indication for the C/S?	Big baby [1] Failed induction [2] Prolonged labour [3] fetal distress [4] Other. Please state ---------- [5]
Have you been assisted to deliver before? If yes, by which method?	Vacuum [1] Forceps [2] Don't know [9]
Have you delivered any of your babies when they are already dead (still births)	Yes [1] No [2] If yes, How many?
Have you delivered a child who died after delivery?	Yes [1] No [2] If yes, How many?

If yes to 28 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]
Have you delivered a baby with an abnormality?	Yes [1] No [2]
If yes to above what kind of abnormality	CentralNervousSystem[1] CardioVascularSystem [2] Genito-Urinary Tract [3] Gastro-intestinal Tract [4] Other. Please state---------- ---------- [5]
Have had a baby with a birth weight of 4 kg or more?	Yes [1] No [2]
Have had any of your babies admitted to nursery/new born unit?	Yes [1] No [2]
If yes to 33 above what was the indication?	RDS [1] Prematurity [2] Jaundice [3] Other. Please state --------- ---------- [4] Do not know [9]

D: <u>Family history:</u>

Do you have any relatives with diabetes?	Yes [1] No [2]

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

Have you had any relative with high blood pressure?

Yes [1]
No [2]

What is their relationship to you?

E) Laboratory Screening Results:

50g Glucose Challenge Test:

Date: ___/___/_____

Glucose intolerance (<7.8mmol/l) [1]

Glucose intolerance (>7.8mmol/l) [2]

75g Oral Glucose Tolerance Test: date:____/____/_____v

75g OGTT	mmol/l
Fasting blood glucose	
1 hr Blood glucose	
2hr blood glucose	

Gestational Diabetes [1]

No Gestational Diabetes [2]

HbA1c level : _____ date:___/___/____

ANNEX 4: STUDY TIMELINE/TIME FRAME:

	2017				**2018**			
	Jan to Mar	**Apr to Jun**	**Jul to Sep**	**Oct to Dec**	**Jan to Mar**	**Apr to Jun**	**Jul to Sep**	**Oct to Dec**
Concept note								
Proposal Development								
Proposal Presentation								
Ethics Review Committee								
Data Collection								
Data Analysis and presentataion								
Results Presentation								
Publication								

ANNEX 5: BUDGET AND BUDGET JUSTIFICATION

Components	**Duration/Number**	**Cost (kshs)**	**Total (kshs)**
Personnel			
Research assistant	4	20,000	80,000
Statistician	1	40,000	40, 000
Laboratory costs			600,000
Printing			
Consent form	450	20	9000
Questionnaires	450	40	18000
Stationary	10	1000	10000
Miscellaneous			
Airtime	1	5000	5000
Transport cost for clients	450	100	45000
Total		**KSH 807,000**	

ANNEX 6: LABORATORY STANDARD OPERATING PROCEDURES (SOP):

a) SOP HbA1C

b) SOP 50g Glucose Challenge Test

c) SOP 75g Oral Glucose Tolerance Test

TECHNICAL OPERATING PROCEDURE

PROCEDURE	GLYCATED HAEMOGLOBIN ENZYMATIC ASSAY METHOD
SOP	KNH/LAB MED – BIOCHEM /SYP/017F7
COPY NO.	

(ANALYZER: DIRUI CS 4000 AUTOMATED CHEMISTRY ANALYZER)

1.1 Equipments for the Analysis

1.1.1 DIRUI CS 4000 Clinical Chemistry analyzer

The machine, above was used for sample analyses. DIRUI CS 4000 is a discrete, random access clinical analyzer capable of performing a wide range of chemical tests in a single run.

1.0 Purpose/Applicability

This document establishes the procedure for testing, reporting, transmission and dispatch of test results for HbA1c.

2.0 Scope

This SOP applies to all the specimens which have been appropriately received and logged in by the Biochemistry Laboratory, Kenyatta National Hospital for the purpose of determining glycated or glycosylated haemoglobin in the reportable units of percentage (HbA1 C %).

Equipment and Reagent

3.1 Equipment

3.1.1 EDTA vacutainers or Heparinised Vacutainers for specimen collection or Eppendorf tubes.

3.1.2 Adjustable pipette capable of measuring 100 - 1000 µl (1.0 ml) for haemolysin aliquoting.

3.1.3 Adjustable pipette capable of measuring 10 - 100 µl (1.0 ml)

For erythrocyte aliquoting

3.1.4 The Automated analyser in use for the test **(Dirui CS 4000).**

3.1.5 3.1.5 Centrifuge for specimen preparation.

3.1 Reagents

R1	Tris buffer	2.7 mol/l
R2	Peroxidase	1500U/L
	Fructosyl peptide Oxidase	1500 U/L
Pre-treatment Solution	Haemolysin	5 g / L
Calibrator	Concentration is specific to the lot number and is on the container label.	
Quality Control	Concentration is specific to the lot number and is on the container label.	

4.0 METHODOLOGY

4.1.1 Background

Haemoglobin (Hb) consists of four protein chainswith four haem portions , and is the red pigment located in the red blood cells (Erythrocytes).Its main function is to transport oxygen and Carbon dioxide in blood .Each Hb molecule is able to bind four oxygen molecules.Hb consists of a variety of subfractions and derivatives.Among this heterogeneous group of haemoglobins , HbA1C is one of the glycated haemoglobins , a subfraction formed by the attachment of various sugars to the Hb molecule.HbA1C is formed in two steps by the non-enzymatic reaction of glucose with the N- terminal amino groups of the Beta –chain of normal adult haemoglobin(HbA) .The first step is reversible and yields labileHbA1c.This slowly rearranges in the second reaction step to yield stable HbA1c.In the erythrocytes , the relative amount of stable HbA converted to stable HbA1c increases with the average concentration of glucose in the blood.The conversion of stable HbA1c is limited by the erythrocytes's lifespan of approximately 100 to 120 days.As a result , HbA1c reflects the average blood glucose level during the preceding 2 to 3 months.HbA1c is thus

suitable for monitoring long term blood glucose control in individuals with diabetes mellitus.More recent glucose levels have a greater influence on the HbA1c level.The approximate relationship between HbA1c and mean blood glucose value during the preceding 2 to 3 months has been analysed by several studies.

4.1.2 TEST OR ASSAY PRINCIPLE

In the first reaction , the concentration of haemoglobin is measured at an absorbance of fixed wavelength , and simultaneously the fructosyl dipeptides are generated from the N – terminal amino groups of the beta-chain of HbA1c by the reaction of protease.In the second reaction , the reaction of Fructosyl peptide oxidase (FPOX) with fructosyl dipeptides , the generated hydrogen peroxide allows 10-carboxymethylaminocarbonyl)-3,7-bis(dimethylamino) phenothiazine sodium salt to develop a colour in the presence of peroxidase.The change

inabsorbance is measured for HbA1c determination.The combined assay results for haemoglobin and HbA1c are used to calculate and express HbA1c (%).

4.2 Test procedure

Refer to appendix 1

6.3 Results dispatch and archiving.

6.3.1 For results outcome and interpretation **(Refer to appendix 1)**

6.3.2 The Health information personnel dispatches the validated results directly to the patient who shall sign for the collection.

6.4 Quality Control

6.4.1 Commercial controls are available for scheduled IQC.

6.5 Possible interferences

6.5.1 Use of expired reagents

6.5.2 Use of specimen haemolysed during phlebotomy

6.6 Calculation of the results

Refer to appendix 1

6.7 Biological reference intervals

Refer to appendix 1

6.8 Reportable intervals

Refer to appendix 1

6.9 Critical values

It is used as a monitoring test so critical values are not significant.

6.10 Potential source of variation

Failure to observe the expiry dates of reagents or sample integrity.

7.0 References

7.1 ISO 15189: 2012(E) Standard.

7.2 Junge w , Wilke B , et al.Determination of reference intervals

in adults for Haemoglobin A1C (HbA1c).Poster presentation 18th International Diabetes Federation Congress , Paris , 2003.

7.3 CLSI.Evaluation Of Precision Performance Of Quantitative

Measurement Methods;Approved Guideline – Second Edition.CLSI document EPs – A2[ISBN 1-56238 -542-9.CLSI,940 West ValleyRoad,SSuite1400,Wayne,Pa19087 USA ,2008.

8.0 Appendices

8.1 Appendix 1: Test procedure

8.2 Appendix 2: Staff training record

Kenyatta National Hospital
Department Of Laboratory Medicin
Biochemistry Laboratory

Hospital Road off Ngong Road
P.O. Box 20723
Nairobi, TEL: 020 272 6300

Appendix 1

1.1 Specimen Receiving and Registration

Responsible staff Health Information personnel at the reception.Verify the integrity of each specimen in terms of packaging, right container, volumes and whether the test is done in Biochemistry Laboratory .Refer to the specimen rejection and acceptance criteria (Refer to: KNH / LAB MED – BIOCHEM /SYP /017F4 Separate urgent or emergency specimens from routine ones and mark them with a colour as'P' to denote priority. Priority samples shall be run within one hour from the time of registration in the Laboratory. Unmarked or routine samples shall be run within two hours from the time of registration at the Biochemistry Laboratory reception immediately hand over the priority specimens to the testing personnel for processing, testing and reporting.

1.1 Specimen Preparation and assaying

Centrifuge or spin the whole blood at 2000 revolutions per minute **(2,000 RPM**) for **5 minutes.**

3.2.2 Aliquot **25µ**l of the deposited red blood cells into a sample cup or Eppendorf microfuge tube, using the calibrated pipette in use.

3.2.3 Add **500µ** l of the haemolysin / denaturant or pretreatment solution to the **25 µl** of the aliquoted erythrocytes.

3.2.4 Shake the mixture vigorously in a closed ependorf microfuge tube or vacutainer till lysis is achieved.

3.2.5 Homogeneously mix the resultant haemolysate gently and then run the assay after 5 minutes using the appropriate automated analyzer.

3.2.6 Whole blood is stable for 3 days at 15 - 25 ^{0}c or 7 days at 2-70°c.(Haemolysate is stable for 8 hours and 24 hours respectively) at the same temperatures quoted.

3.3 Result Validation, Interpretation and Indication for Repeat Testing

Responsible Staff: Laboratory In - charge, Testing Personnel

3.3.1 Refer to reporting of results SOP (KNH / LAB MED - BIOCHEM /SYP/ 017F5)

3.4 Transcription and release of ready results

Responsible Staff: Laboratory In – charge, Testing Personnel

3.4.1 Validate / verify test results and in appropriate reporting units.

3.4.2 Sign or initial the relevant column of the request/printed report form.

3.4.3 Result entry or matching with request forms can be done by trainees or competent staff whilst authorization is only done by competent technical staff

3.4.4 Immediately take the completed request/ result form to reception for dispatch either to specific patients or into pigeon holes.

3.4.5 Misplaced Results

3.4.5.1 Ask the client at the reception, for the attendance card and date when test was performed or the receipt.

3.4.5.2 Search in the Laboratory register for the log in number previously.

. 3.4.5.3 Search results in the History mode using the Laboratory number and

Reprint once confirmed as correct.

3.4.5.4 A competent technical staff verifies the results and signs or initials the reprint copy.

3.4.5.5 Write a remark to the effect that results were initially lost on the

Comment column of the request form and dispatch.

3.5Reference Ranges

SAMPLE TYPE		SI UNITS (%)
Whole Blood	According to IFCC	2.9 ----- 4.2
	According to NGSP / DCCT	4.8 ---- 5.9
	According to JCCLS	4.3 ------ 5.8

50 GRAM GLUCOSE CHALLENGE TEST SOP:

1.0 This procedure defines how to use the glucometer in conducting blood glucose testing.

2.0 SCOPE

The procedure covers all the steps required to be followed when carrying out blood glucose testing using this glucometer.

3.0 TERMS AND DESCRIPTIONS

Coding- setting the calibration of the meter using a provided Chip with a number that identifies the strips to use.

Lancet- the sharp-pointed tool used for pricking a person in order to get blood from a given site.

4.0 RESPONSIBILITY

4.1 Responsibility

All technical personnel performing the test at any given time are to follow the steps of the procedure.

4.2 Safety

Any personnel doing the test must observe safety precautions as laid out in the safety SOPs in order to ensure that there are is no exposure to disease or injuries**.**

5.0 EQUIPMENT AND REAGENTS

5.1 Equipment

- Cera-chek glucometer
- Cera-chek sensor strips

5.2 Reagents

None apart from the ones above

6.0 METHOD

6.1 Principle

The test is based on the measurement of an electrical current generated by the reaction of glucose with the reagent of the test strip. The glucometer measures the current and displays the corresponding blood glucose level. The strength of the current produced by the reaction depends on the amount of glucose in the blood sample.

6.2 Procedure

Refer to appendix 1

6.3 Results

The results are reported in mmol/l and recorded in the request form or monitoring book of the client.

6.4 Quality Control

This is done every morning using a commercial normal and an abnormal control material.

6.5 Interferences

- Leaving the glucometer in very hot or very cold conditions.
- Heavy fall of the glucometer(dropping and heavy impact)
- Poor maintenance
- Dust, dirt and blood presence inside the testing compartment of the glucometer.

6.6 Calculation of results

This displays automatically on the screen in mmol/L.

6.7 Biological reference intervals

The linearity range is 0.6 --- 50.0 mmol/L (The lowest and highest values the glucometer can read)

6.8 Reportable intervals

This is the section of the reference ranges (Refer to appendix 1).

6.9 Critical values

These are the figures that can cause immediate patient death if too low or too high.

6.10 Potential source of variation

6.1.1 Testing persons who are severely hypotensive or in shock.

6.1.2 Severe dehydration

6.1.3 Critical illness

7.0 REFERENCES

7.1 Cera-chek glucometer insert

7.2 American Diabetes Association; Diabetes Care, January 2013,Vol.36,Supplement 1.

8.0 APPENDICES

8.1: The stepwise testing procedure

Appendix 1: The stepwise testing procedure

i. Welcome the client and let him/her sit comfortably.

ii. Dissolve 50g of glucose into 150 to 200 milliliters of water (a Glass of water)

iii. Give the client the glucose solution to drink

iv. Determine the client's blood sugar after 1 hour

v. Remove the test strip from the vial and immediately close the cap.

vi. Insert the strip (sensor) into the insert port of the glucometer and await the blood symbol to blink on the glucometer screen.

vii. Choose the site to be punctured and disinfect using the available disinfectant.

viii. Obtain a blood sample.

ix. A generous homogenous sample is put on the glucometer sensor (strip) till the confirmation window is full of blood.

x. After 5 seconds an accurate result display appears on the glucometer screen.

xi. Record it and sign in the request form or book and inform the client of the result before she goes back to the clinician.

xii. The result is automatically stored in the test meter memory.

RESULTS AND INTERPRETATION:

Glucose Intolerance
GCT negative : Glucose : ≤ 7.8mMol/L at 1 Hour
GCT positive : Glucose : ≥ 7.8 mMol/L at 1 Hour
Overt Diabetes : Glucose ≥ 11.1mMol/L at 1Hour

ORAL GLUCOSE TOLERANCE TEST

4.0 Equipment and Reagents

4.1 A quality controlled glucometer

4.2 Venupuncture material

4.3 A graph paper for drawing the trend.

4.4 A ballpoint pen

4.5 **75 gram** of commercial glucose powder in a packet

4.6 A packet of commercial citric acid powder if the client is pregnant.

5.0 Method

5.1 Principle

This is an instruction procedure .There is no need for a principle.

6.2 Testing procedure

6.1.1 To perform the OGTT (**Refer to appendix 1**)

6.1.2 Report the test results using name and time of test completion.

6.1.3 Plot a curve of the test results behavior in **duplicate** as one copy is filed for reference**.** Hand over the results to the pathologist or a second technical personnel for validation

6.3 Results dispatch and archiving.

6.3.1 For results outcome and interpretation **(Refer to appendix 1)**

6.3.2 The Health information personnel dispatches the validated results directly to the patient who shall sign for the collection.

6.3.3 The technical personnel to file the duplicate copy in the OGTT file.

6.4 Quality Control

6.4.1 Before using the glucometer the technical personnel performs daily internal quality control using the glucometer accompanied controls or commercial controls available and use is made of both normal and abnormal controls.

6.5 Possible interferences

6.5.1 None compliant client in terms of adherence to the instructions

6.5.2 Failure to run quality control on the glucometer

6.5.3 Drugs the client is on.

6.6 Calculation of the results

Refer to appendix 1

6.7 Biological reference intervals

Refer to appendix 1

6.8 Reportable intervals: Refer to appendix 1

6.9 Critical values

Refer to appendix 1

6.10 Potential sources of variation

6.10.1 Undivulged information on the drugs a client is on.

6.10.2 Failure to comply with issued instruction

7.0 References

7.1 Documents of external origin File in the Biochemistry Laboratory.

7.2 All the kit inserts used for the various blood glucose testing methods and glucometers.

7.3 SOP/KNH/CORP/001

7.4 KNH/QM/01/2010.

7.5 A Global Health care Public Foundation (AGHPF) accreditation mentorship.

7.6 ISO 15189:2012 International Standard.

8.0 Appendices.

8.1 Appendix 1: Test procedure and results interpretation.

8.2 Appendix 2: Patient OGTT booking sheet

8.3 Staff training record

Appendix 1: OGTT Patient booking instructions:

Patient booking and instruction before the test

1. The client will be advised to remain on his or her usual diet till supper preceding the day of the test.

2. The Client will be advised by the technical personnel not to eat anything after supper and also to avoid breakfast on the day of the test.

TEST PROCEDURE:

The technical personnel shall;

Let the client sit on a comfortable seat where the noise levels and other forms of disturbance are minimal

a. Perform a fasting blood sugar of the client before loading the client with glucose.

b. Dissolve 75 g of glucose into 150 to 200 milliliters of water (a Glass of water)

c. Determine the client's blood sugar at 1 minute intervals for the next tw using a glucometer or any other analyzer for sugar.

d. Plot the measured values on the OGTT graph, verify and report the results.

e. The Pathologist or a second technical personnel shall validate the results.

RESULTS INTERPRETATION:

Gestational Diabetes(Any Two of the outcomes)	***Overt diabetes***
Fasting : ≥ 5.1 mMol/L	**Fasting: 7.0 mmol/L**
GTT: Glucose : ≥ 10 mMol/L at 1 Hour	**GTT: Glucose : ≥11.1 mMol/L at 2 Hour**
GTT: Glucose : ≥ 8.5mMol/L at 2 Hours	