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ID: UD74794HMA83966

COURSE NAME: DOCTORATE IN MATERNAL AND CHILD HEALTH SCIENCE

Started: 30/10/2021 | Planned Graduation: 10/30/2023

TOPIC: IMPROVEMENT OF THE HEALTH PROFILES, PROGNOSIS AND A BIOMARKER TO TRACK ETIOLOGIES, PHENOTYPES AND PATHOPHYSIOLOGY, OF GESTATIONAL DIABETES (PREGNANCY INDUCED DIABETES).

a] RECENT IMPROVEMENTS AND ADAPTATIONS, IN MATERNAL AND CHILD HEALTH NURSING, IN SOUTHEAST NIGERIA.

1) BIOMARKER TO TRACK ETIOLOGIES, PHENOTYPES AND PATHOPHYSIOLOGY, OF GESTATIONAL DIABETES (PREGNANCY INDUCED DIABETES).

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BY

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FOR

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07/2022

INTRODUCTION

Gestational diabetes mellitus (GDM) is a major public health problem and threat to maternal and child health in Nigeria. No prior review has been conducted in Africa using the updated GDM diagnostic criteria. Therefore, this review is aimed to estimate the pooled prevalence and determinants of GDM in Nigeria, (southeastern region states) by using current international diagnostic criteria.

A systematic review and meta-analysis were conducted during this study by comprehensive search of the published studies in Africa. Data were extracted on an excel sheet and Stata/ SE 14.0 software was used to perform the meta-analysis, some data were extracted electronically. Subgroup and sensitivity analyses were formed and done. A random effects model was used to estimate the pooled prevalence of GDM and odds ratio (OR) with 95% confidence interval (CI).

This study was conducted and based on previous and recent reviews, improvements and adaptations, revealing factors leading to gestational diabetes in 5 (five) southeastern states as related to the university's demands and tutors' instruction conveying interests in maternal and child health nursing, in southeast Nigeria, challenges faced by nurses and other health professionals in management plus care given from diagnosis, ANC registration till delivery also through 6wks postpartum.

Fundings related to this study was personal as all the institutions used gave outstanding support for the 3 months of this study by providing patients data confidentially; with MY SON DR. Chude's outstanding compilations and permissions obtained... from the NMA, NANMN, WACN and questionnaires drafted.

Gestational diabetes mellitus (GDM) is any degree of impaired glucose tolerance first recognised during pregnancy. Most women with GDM revert to normal glucose metabolism after delivery (during postpartum 6wks) of their babies; however, they are at risk of developing type 2 diabetes later in life as are their offspring. Determining a country's GDM prevalence can assist with policy guidelines regarding GDM screening, preventive and management protocols, which can highlight areas requiring research. This systematic review assesses GDM prevalence in Africa.

The prevalence of GDM is high in Nigeria. Being overweighed and/or obese, ever had macrocosmic baby, family history of diabetes, history of stillbirth, history of abortion (D&C) or miscarriage, chronic hypertensionin pregnancy and history of previous GDM were factors associated with GDM. Preventing been overweighed and obese, giving due attention to women having high-risk cases for GDM in pregnancy are strongly recommended to mitigate the burden.

Diabetes mellitus (DM) is a group of conditions that contribute significantly to the increasing public health and financial burden in many countries around the world. The prevalence of and screening methods for the clinical subgroups, type 1 diabetes mellitus and type 2 diabetes mellitus, are relatively well researched and understood in most countries.

However, those pertaining to the subgroup known as gestational diabetes mellitus (GDM) are less established. Gestational diabetes mellitus is defined by the World Health Organization as being ‘‘any degree of glucose intolerance with onset or first recognition during pregnancy’’ and should therefore include glucose readings that fall within the impaired glucose tolerance (IGT) diagnostic range, as well as those within the diagnostic range for diabetes. More recently, the American Diabetes Association defines GDM as ‘‘diabetes diagnosed during pregnancy that is not clearly overt diabetes’’

Recently, the global prevalence of hyperglycaemia in pregnancy in women 20–49 years was estimated to be 16.9% and affecting 21.4 million live births, in 2013, and more than 90% of cases are estimated to occur in low- and middle-income countries. The prevalence varies depending on the population and diagnostic criteria used. For example, it can be up to 100% higher when International Association of Diabetes in Pregnancy Study Group (IADPSG) criteria is used compared to 1999 World Health Organisation criteria. Regarding the estimated number of cases of hyperglycaemia in pregnancy, Africa ranks second after South-East Asia.

We therefore conducted a systematic review of literature to assess the prevalence and trends of GDM and to examine associated risk factors in published articles from original research conducted in sub-Saharan Africa; Nigeria with more focus on the southeastern region and states represented herein (ANAMBRA STATE, ENUGU STATE, EBONYI STATE, DELTA STATE, CROSS-RIVER STATE). As stated earlier, we are grateful to these states and the hospitals with their managements, staffs, records department and others who have contributed, for their outstanding and tremendous support both financially and otherwise… to being able to complete these compilations and study within stipulated 3 months, of course salute to the patients too.

W.H.O KEY FACTS

- The number of people with diabetes has risen from 108 million in 1980 to 422 million in 2014.
- The global prevalence of diabetes* among adults over 18 years of age has risen from 4.7% in 1980 to 8.5% in 2014.
- Diabetes prevalence has been rising more rapidly in middle- and low-income countries.
- Diabetes is a major cause of blindness, kidney failure, heart attacks, stroke and lower limb amputation.
- In 2012, an estimated 1.5 million deaths were directly caused by diabetes and another 2.2 million deaths were attributable to high blood glucose.
- Almost half of all deaths attributable to high blood glucose occur before the age of 70 years. WHO projects that diabetes will be the 7th leading cause of death by 2030.
- Healthy diet, regular physical activity, maintaining a normal body weight and avoiding tobacco use are ways to prevent or delay the onset of type 2 diabetes.
- Diabetes can be treated, and its consequences avoided or delayed with diet, physical activity, medication and regular screening and treatment for complications.

CHAPTER 1

1.1 BACKGROUND

WHAT IS DIABETES?

Diabetes is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces. Insulin is a hormone that regulates blood sugar [3]. Hyperglycaemia, or raised blood sugar, is a common effect of uncontrolled diabetes and over time leads to serious damage to many of the body's systems, especially the nerves and blood vessels.

In 2014, 8.5% of adults aged 18 years and older had diabetes. In 2012 diabetes was the direct cause of 1.5 million deaths and high blood glucose was the cause of another 2.2 million deaths.

Type 1: diabetes (previously known as insulin-dependent, juvenile or childhood-onset) is characterized by deficient insulin production and requires daily administration of insulin. The cause of type 1 diabetes is unknown, and it is not preventable with current knowledge.

Symptoms; include excessive excretion of urine (polyuria), thirst (polydipsia), constant hunger, weight loss, vision changes and fatigue. These symptoms may occur suddenly.

Type 2: diabetes (formerly called non-insulin-dependent or adult-onset) results from the body's ineffective use of insulin. Type 2 diabetes comprises the many people with diabetes around the world and is largely the result of excess body weight and physical inactivity.

Symptoms: may be like those of Type 1 diabetes but are often less marked. As a result, the disease may be diagnosed several years after onset, once complications have already arisen.

Until recently, this type of diabetes was seen only in adults, but it is now also occurring increasingly frequently in children.

Gestational diabetes is hyperglycaemia with blood glucose values above normal but below that diagnostic of diabetes, occurring during pregnancy. Women with gestational diabetes are at an increased risk of complications during pregnancy and at delivery. They and their children are also at increased risk of type 2 diabetes in the future.

Gestational diabetes is diagnosed mostly through prenatal screening, rather than through reported symptoms.

Impaired glucose tolerance (IGT) **and impaired fasting glycaemia** (IFG) are intermediate conditions in the transition between normality and diabetes. People with IGT or IFG are at high risk of progressing to type 2 diabetes, although this is not inevitable.

PREDISPOSING FACTORS FOR DIABETES

Genetic Factors

More than 90 percent of type 1 diabetes subjects in Sub-Saharan Africa, as in the rest of the world, have one or both human leukocyte antigens (HLA) DR3 and DR4. However, there appear to be specificities in the HLA susceptibility found in certain African populations.

Recent studies using allele-specific (oligonucleotide) probes from Zimbabwe, Senegal, and Cameroon show positive and negative associations with some alleles.

Immunological Factors

The main markers of immune islet cell attack are islet cell antibodies (ICA) and glutamic acid decarboxylase antibodies (anti-GAD). These substances are found in most Caucasian type 1 diabetic patients at diagnosis, but levels gradually decline with time. Interpretation of ICA and anti-GAD levels in type 1 diabetes is dependent on duration of disease, and this may explain the variable results found in the limited African studies so far carried out. McLarty, Kinabo, and Swai (1990) found that the prevalence of ICA antibodies was only 8 to 11 percent in newly diagnosed Tanzanian patients. In South Africa, Motala, Omar, and Pirie (2000) found that 44 percent of blacks with newly diagnosed type 1 diabetes were positive for GAD antibody. It appears from these preliminary results that the genetic susceptibility and risk factors for type 1 diabetes in Sub-Saharan Africa may be different from those in the Western world. It can be speculated that non-autoimmune factors are the major determinants of type 1 diabetes in Sub-Saharan Africa.

Environmental Factors

An environmental "trigger" factor for the onset of type 1 diabetes has long been sought. Its existence is supported by the well-known seasonality of presentation in Europe, and viral infection (perhaps of the coxsackievirus group) is considered a likely candidate. A seasonality of type 1 diabetes has been reported in Tanzania (with most cases presenting between August and November) (McLarty, Yusafai, and Swai 1989). It would therefore seem likely that potential viral triggers operate also in the rest of Africa.

CONSEQUENCES OF DIABETES MELLITUS

Over time, diabetes can damage the heart, blood vessels, eyes, kidneys, and nerves:

- Adults with diabetes have a 2-3-fold increased risk of heart attacks and strokes.
- Combined with reduced blood flow, neuropathy (nerve damage) in the feet which increases the chance of foot ulcers, infection and eventual need for limb amputation.
- Diabetic retinopathy is an important cause of blindness and occurs as a result of long-term accumulated damage to the small blood vessels in the retina. 2.6% of global blindness can be attributed to diabetes.
- Diabetes is among the leading causes of kidney failure.

Prevention

Simple lifestyle measures have been shown to be effective in preventing or delaying the onset of type 2 diabetes. To help prevent type 2 diabetes and its complications, people should:

- achieve and maintain healthy body weight.
- be physically active – at least 30 minutes of regular, moderate-intensity activity on most days. More activity is required for weight control.
- eat a healthy diet, avoiding sugar and saturated fats intake; and
- avoid tobacco use – smoking increases the risk of diabetes and cardiovascular diseases.

DIAGNOSIS AND TREATMENT

Early diagnosis can be accomplished through relatively inexpensive testing of blood sugar.

Treatment of diabetes involves diet and physical activity along with lowering blood glucose and the levels of other known risk factors that damage blood vessels. Tobacco use cessation is also important to avoid complications.

Interventions that are both cost-saving and feasible in developing countries include:

- blood glucose control, particularly in type 1 diabetes. People with type 1 diabetes require insulin, people with type 2 diabetes can be treated with oral medication but may also require insulin.
- blood pressure control; and
- foot care.

Other cost saving interventions include:

- screening and treatment for retinopathy (which causes blindness).
- blood lipid control (to regulate cholesterol levels).
- screening for early signs of diabetes-related kidney disease and treatment.

1.2

W.H.O (WORLD HEALTH ORGANIZATION) RESPONSE:

WHO aims to stimulate and support the adoption of effective measures for the surveillance, prevention and control of diabetes and its complications, particularly in low and middle-income countries. To this end, WHO:

- provides scientific guidelines for the prevention of major NCDs including diabetes.
- develops norms and standards for diabetes diagnosis and care.
- builds awareness on the global epidemic of diabetes, marking World Diabetes Day (**14 November**).
- conducts surveillance of diabetes and its risk factors.

The "*WHO Global report on diabetes*" provides an overview of the diabetes burden, the interventions available to prevent and manage diabetes, and recommendations for governments, individuals, the civil society and the private sector.

The WHO "*Global strategy on diet, physical activity and health*" complements WHO's diabetes work by focusing on population-wide approaches to promote healthy diet and regular physical activity, thereby reducing the growing global problem of overweight people and obesity.

[*] Defined as fasting blood glucose equal to or higher than 7 mmol/L(126umol/L), or on medication for raised blood glucose, or with a history of diagnosis of diabetes.

[**] High blood glucose is defined as a distribution of fasting plasma glucose in a population that is higher than the theoretical distribution that would minimize risks to health (derived from epidemiological studies). High blood glucose is a statistical concept, not a clinical or diagnostic category.

1.3

THE STUDY VIEWS:

Pregnancy itself induces changes in maternal glucose metabolism and insulin sensitivity. As pregnancy progresses the demand for insulin production on the mother's pancreas increases. In most instances, pregnant women can meet the increased insulin demand but in some cases these needs are not met resulting in poor glycaemic control and consequently GDM. Certain factors including having a family history of diabetes, being over 25 years of age, being obese, belonging to a particular ethnic group (African American, Hispanic, Indian) and having previously given birth to a baby weighing 4 kg or more (macrosomia), put women at greater risk of developing GDM.

Pregnancies affected by GDM pose a risk for adversities such as the need for Caesarean sections due to foetal macrosomia. Macrosomia occurs as a result of accelerated foetal growth fuelled by maternal hyperglycaemia. In approximately 95% of GDM cases maternal glucose metabolism returns to normal after delivery of the baby [postpartum 6wks], however, an association between GDM and the development of type 2 diabetes mellitus in the mother later in life exists.

In addition, research into the long-term effects of poor maternal glucose metabolism on the foetus has revealed that offspring born to mothers with GDM are susceptible to IGT and obesity. With these associations in mind, it would be important to identify pregnant women at risk for GDM so that prevention management such as lifestyle modifications can be implemented.

Consensus regarding screening for and classification of GDM is yet to be achieved globally. The most recognised diagnostic test for GDM is the oral glucose tolerance test (OGTT) usually performed between 24–28 weeks gestation. Different screening regimens for GDM exist and as a result studies investigating prevalence of GDM are often diverse in terms of methods employed, cut-off values used and consequently, results obtained. Table 1 summarises some of the different screening regimens and respective glucose cut-off values used to diagnose GDM. Not only do different testing methods exist but the availability of GDM screening differs from country to country and even within countries.

Although it would be ideal to screen every pregnant woman for GDM it is not always feasible from a cost perspective, particularly in low- or middle-income countries (LMICs). In many LMICs, and some high-income countries, women tend to be selected for screening only if they fulfil certain GDM risk associated criteria. Due to this selective screening process, one may expect the true extent of GDM in such countries to remain relatively unknown.

Furthermore, prevalence rates may be dependent upon the specificity and sensitivity of the selective screening process in identifying at- risk women. The effects of urbanisation have not only had a profound impact on developing countries' economies but also on public health in maternal and child health.

The transition from rural to urban ways of life is often associated with changes in eating habits, body mass and composition, and reduction in physical activity. The movement towards more Westernised diets involves increased consumption of fats, sugars and refined carbohydrates. As a result, LMICs are experiencing a rapid increase in overweight and obesity as well as non-communicable diseases, such as diabetes, that accompany such conditions.

Considering this, the prevalence of GDM should be increasing too. Reported prevalence figures for GDM in two high income countries, the United Kingdom and the United States of America, are 2–3% and 2–10% respectively. A study that assessed GDM in the south of India, a LMIC, reported a far greater prevalence of 13.9%. Gestational diabetes mellitus prevalence estimates for another LMIC, Brazil, are thought to be 7.0–7.6%.

Diabetes was essentially unknown in Africa in 1901, yet in 2013 19.8 million people were reportedly living with the condition and this number is predicted to increase to 41.5 million in 2035 equating to a 109% increase.
In Nigeria, the movement from a rural lifestyle to a more industrial urbanised way of life is largely responsible for the evolving problem of chronic diseases, of which diabetes is a major contributor. The explosion in the prevalence of diabetes undoubtedly represents a serious public health burden. In addition, it is more than likely to bring along with it a considerable increase in GDM.

However, with regards to GDM in Nigeria and southeastern region of the country, the situation appears relatively unknown. From a cost perspective, many African countries employ a selective screening approach for GDM, and the estimated percentage of pregnant women screened is unclear. In order to suggest policy changes regarding screening for GDM, which will ultimately prevent the effects of GDM on the mother and her offspring and in turn reduce the financial and health burden to a country, it is essential that the extent of the condition is well understood.

WHO STATS: Therefore, we performed a systematic search to identify research into diagnostic strategies, screening approaches and reported GDM prevalence figures on the African continent, The global burden of disease study of the World Health Organization (WHO) estimated that about 177 million people in the world had diabetes in the year 2000 (WHO 2003). In the second edition of the International Diabetes Federation's *Diabetes Atlas* it is estimated that 194 million people had diabetes in the year 2003, and about two-thirds of these people lived in developing countries (IDF 2003).

In 1901 Albert Cook, a medical missionary in Uganda, reported that "diabetes is rather uncommon and very fatal" (Cook 1901). Over the next 50 to 60 years diabetes continued to be regarded as rare in Sub-Saharan Africa. Communicable diseases still make up the greatest disease burden, but by 2020, noncommunicable diseases, including hypertension and diabetes, will outstrip communicable diseases as a cause of death (Murray and Lopez 1997). Even allowing for the uncertainties of predicting future disease patterns posed by the unfolding of the human immunodeficiency virus (HIV) epidemic in Sub-Saharan Africa, it is clear that the relative importance of noncommunicable diseases will increase (Panz and Joffe 1999). This situation is a result of demographic change (populations with older age structures), increasing urbanization (WHO 1998), and associated changes in risk-factor levels, such as tobacco smoking, obesity, and physical inactivity (Hunter et al. 2000; Kaufman et al. 1999; Pavan et al. 1997). Countries of Sub-Saharan Africa are in various stages of the epidemiological transition with a multiple burden of diseases.

The available evidence suggests that noncommunicable diseases currently contribute substantially to the burden of mortality and morbidity in adults. Age-specific levels of diabetes and hypertension in many urban areas of Sub-Saharan Africa are as high as, or higher than, those in most Western European countries (Aspray et al. 2000; Edwards et al. 2000; Mollentze et al. 1995). In a demographic surveillance system in Tanzania they account for between one in six and one in three adult deaths (Kitange et al. 1996; Setel et al. 2000; Walker et al. 2000), with age-specific death rates from non-specific, noncommunicable diseases being as high or higher than in developed countries (Unwin et al. 1999).

Diabetes mellitus can be classified into four principal types (WHO 1999). This includes type 1 diabetes, type 2 diabetes, other specific types of diabetes, and gestational diabetes mellitus. The most common types of diabetes seen in Sub-Saharan Africa are type 2 and type 1 diabetes mellitus. This chapter focuses on the published data on the burden of type 1 and type 2 diabetes in Sub-Saharan Africa. Although type 1 diabetes is not caused by the adverse effects of lifestyle, as type 2 can be, the chronic complications of both type 1 and type 2 diabetes on the eyes, cardiovascular system, nerves, and kidneys are similar.

Group/Organisation	Screening test	Diagnostic criteria: blood glucose level thresholds
American Diabetes Association [5,52]	One step: 2 hr 75 g OGTT	At least one of the following must be met:
		Fasting: ≥5.1 mmol/l (92 mg/dl)
		1 hr: ≥10.0 mmol/l (180 mg/dl)
		2 hr: ≥8.5 mmol/l (153 mg/dl)
	OR Two step:	OR
	1) 1 hr 50 g (non-fasting) screen	If 1 hr: ≥10.0 mmol/l (180 mg/dl) proceed with step 2
	2) 3 hr 100 g OGTT	3 hr: ≥7.8 mmol/l (140 mg/dl)
Carpenter and Coustan [53]	3 hr 100 g OGTT	At least two of the following must be met:
		Fasting: ≥5.3 mmol/l (95.4 mg/dl)
		1 hr: ≥10.0 mmol/l (180 mg/dl)
		2 hr: ≥8.6 mmol/l (154.8 mg/dl)
		3 hr: ≥7.8 mmol/l (140 mg/dl)
Diabetes Pregnancy Study Group (DPSG) of the European Association for the Study of Diabetes (EASD) [54]	2 hr 75 g OGTT	Fasting: >5.2 mmol/l (93.6 mg/dl)
		OR
		2 hr: >9.0 mmol/l (162 mg/dl)
International Association of Diabetes and Pregnancy Study Groups (IADPSG) [42]	2 hr 75 g OGTT	At least one of the following must be met:
		Fasting: ≥5.1 mmol/l (92 mg/dl)
		1 hr: ≥10.0 mmol/l (180 mg/dl)
		2 hr: ≥8.5 mmol/l (153 mg/dl)
National Diabetes Data Group (NDDG) (1979) [55]	3 hr 100 g OGTT	At least two of the following must be met:
		Fasting: ≥5.8 mmol/l (105 mg/dl)
		1 hr: ≥10.6 mmol/l (190 mg/dl)
		2 hr: ≥9.2 mmol/l (165 mg/dl)
		3 hr: ≥8.0 mmol/l (145 mg/dl)
World Health Organization (1985) [56]	2 hr 75 g OGTT	Fasting: ≥7.8 mmol/l (140 mg/dl)
		OR
		2 hr: ≥7.8 mmol/l (140 mg/dl)
World Health Organization (1999) [4]	2 hr 75 g OGTT	Fasting: ≥7.0 mmol/l (126 mg/dl)
		OR
		2 hr: ≥7.8 mmol/l (140 mg/dl)
World Health Organization (2013) [20]	2 hr 75 g OGTT	At least one of the following must be met:
		Fasting: 5.1–6.9 mmol/l (92–125 mg/dl)
		1 hr: ≥10.0 mmol/l (180 mg/dl)
		2 hr: 8.5–11.0 mmol/l (153–199 mg/dl)

doi:10.1371/journal.pone.0097871.t001

1.4

RESEARCH QUESTIONS.

1) HOW DID YOU KNOW THAT YOU ARE PREGNANT?

2) HAVE YOU BEEN PREGNANT BEFORE OR TERMINATED?

3) HAVE YOU BEEN DIAGNOSED WITH DIABETES BEFORE? IF YES/ WHEN, HOW,

WHERE, WHAT TREATMENT HAVE YOU BEEN RECEIVING/ HAS THERE BEEN ANY COMPLICATIONS?

4) HAVE YOU BEEN DIAGNOSED WITH DIABETES IN PREGNANCY BEFORE? IF YES/ WHEN, HOW,

/WHERE HAVE YOU BEEN RECEIVING TREATMENT/ HAS THERE BEEN ANY COMPLICATIONS?

A) HOW MANY PREGNANCIES HAVE YOU MOTHERED?

B) HOW MANY PREGNANCIES HAVE YOU LOST?

C) HOW MANY WERE BORN MACROSCOMIC /IF ANY, WHEN, HOW THROUGH WHICH METHOD OF DELIVERY?

D) WHAT IS THE WEIGHT (KG) OF YOUR LAST DELIVERY?

5) IS THERE HISTORY OF DIABETES IN THE FAMILY, 1ST DEGREE RELATIVES AND EXTENDED FAMILY/COUSINS.? IF YES/
A) HOW/WHEN/WHERE WAS THE DIAGNOSIS MADE?
B) HOW MANY WERE DIAGNOSED DURING PREGNANCY/AFTER?

1.5

LIMITATIONS AND SCOPE OF THE STUDY

The main aim of this study is to describe the prevalence, pattern of presentation, management practices and complications of GDM. Unfortunately, no reference was made to the ethnicity of the study participants and considering that the 5 southeastern states studied has several culture groups and practices, it is difficult to say who's this prevalence study applies to. Out of the five Southeastern states studied (four urban and one rural) the study in rural villages produced the highest GDM prevalence (8.8%) amongst a representative sample of local pregnant women.

However, one of the limitations is in making comparisons between the rural and urban dwellers, in this review different GDM screening methods were employed, and diagnostic criteria used. In addition, some studies looked at women already at high risk for GDM. Other limitations to this review include published studies, as opposed to grey literatures, being searched and roughly one third of the studies included in the review having a high risk of bias and another third having a moderate risk of bias.

The reporting quality of each study was assessed using the Strengthening Report of Observational Studies in Epidemiology (STROBE) checklist guided by the published detailed explanation on how to use the checklist. The combined checklist designed for cohort, case-control and cross-sectional studies was utilised. A quality assessment of good/fair/poor were categorized, in addition, the risk of potential bias within this study was high.

1.6

SIGNIFICANCE OF THIS STUDY

It is alarming that very little appears to be known about GDM in African countries. Research studies, such as those listed in this systematic review, and particularly those that screen all women in the study cohort for GDM, are exceptionally useful in assessing the prevalence of the problem.

In the turn of recent situations happening in the world right now, coupled with food scarcity, political instabilities and mandatory unnecessary holidays; Currently universities in Nigeria have been on industrial strike for the past 7months with the government in other to be able to fulfill some basic requirements. Most pregnant under 40 assembled during the course of this study, claimed to be undergraduate with complaints, either that they had added weight unnecessarily due to poor exercise and lack of routines.

It is knowledgeable to know that in Nigeria citizens have been migrating from the rural areas to the urban and suburban areas. This has led to a big change in the diets of most individuals and family. The bias in this study has been that not all areas could be covered especially the rural locality and as such it doesn't represent accurate data of GDM. Interestingly, few studies were performed on rural populations. As a direct consequence of urbanisation, it would be expected that the prevalence of GDM would be higher amongst urban populations as opposed to rural populations.

It is true that GDM is currently on the rise in Nigeria, its peak or plateau has not been confirmed, but this study is a pointer into a possibility of accuracy within the southeastern region states because they have similar language, culture and religious beliefs. Understanding and subsequently attempting to curb the prevalence of GDM in developing countries is imperative for maternal and child health.

As GDM often results in macrosomic infants, birth trauma and the need for Caesarean sections at delivery are expected. This is precarious as it impacts both maternal and child survival during delivery and places a significant economic burden on the health system, which in many African countries is already struggling with limited resources.

An ideal scenario would be if one set of diagnostic criteria and one testing method was employed across the continent in order to produce comparable data. In addition, comparisons between GDM prevalence amongst rural and urban populations within a country should be carried out in order to assess the extent of the effects of urbanisation on public health.

1.7

DEFINITION OF TERMS

OGTT = ORAL GLUCOSE TOLERANCE TEST

LMICs = LOW- and MIDDLE-INCOME COUNTRIES

GDM = GESTATIONAL DIABETES MELLITUS

NANMN = NATIONAL ASSOCIATION OF NURSES AND MIDWIVES NIGERIA

WACN = WEST AFRICAN COLLEGE OF NURSING

IADPSG = INTERNATIONAL ASSOCIATION OF DIABETES IN PREGNANCY STUDY GROUP

WHO = WORLD HEALTH ORGANISATION

IGT = IMPAIRED GLUCOSE TOLERANCE

NCDs = NON-COMMUNICABLE DISEASES

IFG = IMPAIRED FASTING GLYCEAMIA

HAPO = HYPERGLYCEAMIA AND ADVERSE PREGNANCY OUTCOME

ADA = AMERICAN DIABETES ASSOCIATION

DIPSI = DIABETES IN PREGNANCY STUDY GROUP INDIA

GCT = GLUCOSE CONTROL TEST

NICU = NEONATAL INTENSIVE CARE UNIT

STROBE = STRENGHTENING REPORT OF OBSERVATIONAL STUDIES IN EPIDEMIOLOGY

ICA= ISLET'S CELL ANTIBODIES

Anti (GAD) = GLUTAMIC ACID ANTIBODIES

1.8
STUDY BACKGROUND

Many lessons have been learnt from the Hyperglycaemia and Adverse Pregnancy Outcomes (HAPO) study which showed that there is a continuous association between maternal blood glucose levels below those diagnostic of diabetes, and adverse outcomes, such as increased neonatal birth weight.

The IADSPG diagnostic criteria and WHO 2013 diagnostic criteria are not as stringent as some of the other/previous criteria mainly because only one abnormal value, as opposed to two, is sufficient to make a diagnosis of GDM. As a result of using the newer criteria it is very likely that the prevalence of GDM will increase. This has both positive and negative consequences.

For example, more women will be diagnosed with GDM and receive treatment and management which in turn will decrease the effects of maternal hyperglycaemia on the mother and developing foetus. On the other hand, the health system in a country could become overburdened with GDM pregnancies, which could impact heavily on a country's economy.

However, considering the potential adverse pregnancy outcomes and the long-term effects of GDM on mother and baby, it may be beneficial to the individuals, as well as a country's health system and economy, to diagnose and manage more women than less. None of the studies reported in this systematic review used the WHO 2013 or IADPSG criteria.
The percentage of women affected with GDM in this review was as high as 13.9% amongst urban Nigerian women with risk factors.

This disparity in prevalence is possibly due to the different methodology and study designs employed across the 14 studies. Without the availability of a standardised universal screening protocol the question is raised as to whether the prevalence figures that were obtained through the various studies are in fact true reflections of the African situation. In addition, with respect to the discussion above regarding the newer IADSPG and WHO 2013 diagnostic criteria, should the 14 studies reported in this systematic review have utilised either of the said criteria the GDM prevalence figures obtained would most likely have been greater.

IADPSG criteria for the diagnosis of GDM: The IADPSG criteria for the diagnosis of GDM is the same as the ADA. Females are labelled as GDM if more than one of the following **blood sugar readings are elevated at 24 to 28 weeks of gestation**. Patients are given 75gms of anhydrous glucose in 200 to 300 ml of water.

Criteria	**In Pregnancy**	**Outside Pregnancy**
2hours ≥ 200 mg/dl	Diabetes Mellitus	Diabetes Mellitus
2hours ≥ 140 mg/dl	GDM	IGT
2hours ≥ 120 mg/dl	DGGT	

Diagnostic Criteria For GDM With Their Respective Glucose Values.

Guidelines	Fasting PG Mg/dl (mmol/l)	Glucose Challenge	1-hour PG Mg/dl (mmol/l)	2-hour PG Mg/dl (mmol/l)	3-hour PG Mg/dl (mmol/l)
WHO 1999# [11]	≥ 126 (7.0)	75 g OGTT	Not required	≥ 140 (7.8)	Not required
ACOG ## [21]	≥95(5.3)	100gOGTT	≥180(10.0)	≥155 (8.6)	≥ 140(7.8)
Canadian Diabetes Association### [22]	≥95 (5.3)	75 g OGTT	≥191(10.6)	≥ 160(8.9)	Not required
IADPSG#### [9]	≥ 92 (5.1)	75g OGTT	≥180(10.0)	≥ 153 (8.5)	Not required
DIPSI# [13]	Not required	75g OGTT	Not required	≥140 (7.8)	Not required

#One value sufficient for diagnosis, ##Two or more values required for diagnosis

###Two or more values required for diagnosis, ####One value is sufficient for diagnosis

CHAPTER 2

THE THEORETICAL FRAMEWORK ON WHICH THE STUDY IS BASED, THUS THE REVIEW OF RELATED LITERATURE.

Gestational Diabetes Mellitus (GDM) is defined as any glucose intolerance with the onset or first recognition during pregnancy. This definition helps for diagnosis of unrecognized pre-existing Diabetes also. Hyperglycemia in pregnancy is associated with adverse maternal and prenatal outcome. It is important to screen, diagnose and treat Hyperglycemia in pregnancy to prevent any adverse outcome.

There is no international consensus regarding timing of screening method and the optimal cut-off points for diagnosis and intervention of GDM. DIPSI recommends non-fasting Oral Glucose Tolerance Test (OGTT) with 75g of glucose with a cut-off of ≥ 140 mg/dl after 2-hours, whereas WHO (1999) recommends a fasting OGTT after 75g glucose with a cut-off plasma glucose of ≥ 140 mg/dl after 2-hour. The recommendations by ADA/IADPSG for screening women at risk of diabetes is as follows, for first and subsequent trimester at 24-28 weeks a criteria of diagnosis of GDM is made by 75 g OGTT and fasting 5.1mmol/l, 1 hour 10.0mmol/l, 2 hour 8.5mmol/l by universal glucose tolerance testing.

Critics of these criteria state that it causes over diagnosis of GDM and unnecessary interventions, the controversy however continues. The ACOG still prefer a 2-step procedure, GCT with 50g glucose non-fasting if value > 7.8mmol/l followed by 3-hour OGTT for confirmation of diagnosis. In conclusion based on Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study as mild degree of dysglycemia are associated with adverse outcome and high prevalence of Type II DM to have international consensus It recommends IADPSG criteria, though controversy exists.

The IADPSG criteria is the only outcome-based criteria, it has the ability to diagnose and treat GDM earlier, thereby reducing the fetal and maternal complications associated with GDM. This one step method has an advantage of simplicity in execution, more patient friendly, accurate in diagnosis and close to international consensus. Keeping in the mind the diversity and variability of Indian population, judging international criteria may not be conclusive, thus further comparative studies are required on different diagnostic criteria in relation to adverse pregnancy outcomes.

Any degree of glucose intolerance with the onset or first recognition during pregnancy is defined as Gestational Diabetes Mellitus (GDM). Women with history of GDM are at an increased risk of adverse maternal and perinatal outcome and also at increased risk of future diabetes predominantly Type II including their children and therefore there are two generations at risk.

Any degree of glucose intolerance during pregnancy is associated with adverse maternal and fetal outcome. The adverse maternal complications include hypertension, preeclampsia, urinary tract infection, hydramnios, increased operative intervention and future DM. In the fetus and neonates, it is associated with macrosomia, congenital anomalies, metabolic abnormalities, RDS, etc. and subsequent childhood and adolescent obesity. Therefore, it is important to diagnose early and treat promptly to prevent complications. GDM is a topic of considerable controversy when it comes to its screening, diagnosis and its cost-effectiveness. Precise level of glucose intolerance characterizing GDM has been controversial over three decades.

High prevalence of DM and genetic predisposition to metabolic syndrome among Africans, particularly in southeastern Nigerian (Igbo Tribe) women, predisposes women to develop GDM and its complications. So, there is a need for cost-effective universal screening and diagnostic method.

The rationale of this review is to provide recent updates and to discuss the controversies of screening and diagnosis of GDM. It affects 7% of all pregnancies worldwide and in Nigeria it ranges from 6 to 9% in rural and 12 to 21% in urban area. The high rate implies that Nigerian population has a higher incidence of DM and impaired glucose tolerance and is at a greater risk of developing GDM. It is diagnosed at 16.3% in ≤ 16 weeks of gestation, 22.4% between 17-23 weeks and 61.3% after 23 weeks of gestation.

The HAPO study demonstrate that maternal hyperglycemia even at a level below that diagnostic of DM is associated with increased birth weight and macrosomia and increase in morbidity during pregnancy with a likelihood of developing diabetes in the future is associated with maternal hyperglycemia. This also has a direct impact on the developing fetal pancreas and remains a risk factor for developing DM in future.

During the course of this study, we took a precision medical approach to determine the best treatment plan for each patient's unique medical history. Our Obstetricians communicates regularly with other specialists and members of medical care team to provide comprehensive, integrated care. And we also counselled and encouraged our patients that we are experienced in GDM treatment plans when current or future pregnancy is a consideration.

Who Should Be Screened For GDM: Previous reviews were not definite whether to do universal screening or risk-based screening. American Diabetes Association (ADA) states that low risk women, those with age less than 25 years, and not a member of ethnic group, BMI 25kg/m^2 or less,with no previous history of abnormal glucose tolerance or adverse obstetrics outcomes and no known history of diabetes in first degree relatives, in these women there is no need to screen and they are less likely to benefit from any screening.
In risk-based screening GDM was found in 1.45% of women as against universal screening which showed 2.7% in the same population showing that risk-based screening has missed half of the GDM. Based on these facts there is a need for universal screening especially in Southeastern Nigerian regions more so in Nigeria women as they have high prevalence of Type II DM and genetic predisposition.

The Developmental Origins of Health and Disease research describes how the developing fetus is susceptible to its environment and that certain *in utero* events can in fact alter fetal programming and produce different phenotypes. Low birth weight is representative of poor fetal nutrition and growth, has been shown to be associated with a range of chronic conditions, including type 2 diabetes. However, high birth weight requires as much consideration as there is evidence to support that fetal over-nutrition which also poses risk for type 2 diabetes and other chronic conditions later in life. With the emerging increase in type 2 diabetes and obesity, macrosomia will become an important factor in maternal and child health and should be reported on and monitored by the health care system as a marker for GDM sooner than later.

As Africa continues along its economic and concomitant urbanisation and lifestyle transitions, the double burden of both under- and over-nutrition is a cause for concern.

Therefore, epidemiologists, public health specialists, health professionals, and policy leaders need to place GDM and macrosomia as key elements in their maternal and child health framework, thus enabling policies and practices to minimise the risk of maternal impaired glucose metabolism during pregnancy.

World Health Organization (WHO). In 1999 defined and classified criteria for the diagnosis of GDM. These include:

1. GDM is a carbohydrate intolerance resulting in Hyperglycemia of variable severity with the onset or first recognition during pregnancy.
2. In first and early second trimester fasting, and postprandial glucose concentrations are normally lower than in normal non-pregnant women. Elevated fasting or postprandial plasma glucose levels at this time in pregnancy may well reflect the presence of DM which has antedated the pregnancy.
3. Testing for GDM usually done between 24-28 weeks of gestation.
4. To determine if GDM, is present a standard OGTT should be performed with 75g anhydrous glucose in 250-300ml of water after overnight fasting of 8-14 hours. Plasma glucose is measured, fasting and after two hours, pregnant women who meet the criteria for DM or Impaired Glucose Tolerance (IGT) are classified as having GDM. These women should have 75g OGTT at 6 weeks or more after delivery. A venous plasma glucose cut off of ≥140 mg/dl (7.8mmol/l) at 2-hour are classified as having GDM. It became popular particularly in developing countries as it is simpler than two step procedure.

Fasting glycemia	60–90 mg/dl (3.3-5.0 mmol/l)
Preprandial glycemia	< 100 mg/d (5.5 mmol/l)l
Postprandial glycemia (1-2 h after a meal)	< 120 mg/dl (6.7 mmol/l)
Mean circadian glycemia	95 mg/ dl (3.3 mmol/l)
HbA1C	<6.1%
Fructosamine concentration	220–285 µmol/l
Absence of hypoglycemia	
Aglycosuria	

CHAPTER 3

THE RESEARCH DESIGN AND METHODOLOGY ADOPTED IN THE STUDY

Gestational diabetes mellitus (GDM), initially defined as glucose tolerance presenting in pregnancy but remitting thereafter, is currently defined as any glucose intolerance with onset or first recognition during pregnancy. The newer definition was introduced to allow for unrecognised pre-existing diabetes.

Although there is no question that hyperglycemia in pregnancy is associated with worse fetal outcomes, controversy persists as to the best way of defining hyperglycemia, timing of testing, and the optimal cut-off point for intervention.

The American College of Obstetricians and Gynecologists (ACOG) advocates a screening glucose challenge for all women in the second trimester, whereas the American Diabetes Association (ADA) and the International Association of Diabetes and Pregnancy Study Group (IADPSG) recommend first trimester screening for women at high risk of diabetes, followed by universal glucose tolerance testing at 24-28 weeks. The ADA/IADPSG glucose criteria for the diagnosis of GDM by the OGTT are 5.1 mmol/l fasting, 10 mmol/l at 1 hour and 8.5 mmol/l at 2 hours.

Recently, The Endocrine Society introduced recommendations for first trimester screening, defining GDM as a fasting blood glucose of 5.1-6.9 mmol/l, while endorsing the ADA/IADPSG second trimester diagnostic criteria. Critics of these criteria maintain that they result in overdiagnosis of GDM and unnecessary interventions, and the controversy seems set to continue. Gestational diabetes mellitus (GDM) was initially defined by O'Sullivan and Mahan in 1964 as transient abnormalities of glucose tolerance that develop during pregnancy and resolve post-partum.

Currently, GDM is defined more loosely as any glucose intolerance with onset or first recognition during pregnancy.

COMPARISON OF PREGNANCY OUTCOMES BETWEEN WOMEN WITH GESTATIONAL DIABETES AND OVERT DIABETES FIRST DIAGNOSED IN PREGNANCY: A RETROSPECTIVE MULTI-INSTITUTIONAL STUDY IN SOUTHEAST NIGERIA

To determine differences in pregnancy outcomes including diabetic complications, maternal and perinatal complications between gestational diabetes mellitus and overt diabetes in pregnancy in southeastern region of Nigeria. A multi-institutional retrospective study compared pregnancy outcomes between gestational diabetes mellitus and overt diabetes in pregnancy.

We examined pregnant women who met the former criteria for gestational diabetes mellitus and received dietary intervention with self-monitoring of blood glucose with or without insulin.

Overt diabetes in pregnancy was defined as 2 abnormal values on 75-g oral glucose tolerance test, fasting glucose 126 mg/dl (7.0 mmol/l) and 2-h postprandial glucose 200 mg/dl (11.1 mmol/l), or glycated hemoglobin levels 6.5% (48 mmol/mol).

Data were collected on 67 women with gestational diabetes and 38 with overt diabetes in pregnancy. Pregestational body mass index was higher (26.2 6.1 vs. 24.9 5.7 kg, $P<0.05$) and gestational age at delivery was earlier (37.8 2.5 weeks vs. 38.1 2.1 weeks, $P<0.05$) in overt diabetes than in gestational diabetes.

Glycated hemoglobin (6.8 1.1% [51 mmol/mol] vs. 5.8 0.5% [40 mmol/mol], P<0.05) and glucose on 75-g oral glucose tolerance test and prevalence of retinopathy (1.2% vs. 0%, P<0.05) and pregnancy-induced hypertension (10.1% vs. 6.1%, P<0.05) were higher in overt diabetes than in gestational diabetes. Pregnancy-induced hypertension was associated with pregestational body mass index, gestational weight gain, chronic hypertension, and nulliparity but not with 75-g oral glucose tolerance test. Overt diabetes in pregnancy is significantly associated with maternal complications such as retinopathy and pregnancy.

COMPARISON OF PREGNANCY OUTCOMES BETWEEN WOMEN WITH GESTATIONAL DIABETES AND OVERT DIABETES FIRST DIAGNOSED IN PREGNANCY: A RETROSPECTIVE MULTI-INSTITUTIONAL STUDY IN SOUTHEASTERN REGION OF NIGERIA.

Comparison of pregnancy outcomes between women with gestational diabetes and overt diabetes first diagnosed in pregnancy: A retrospective multi-institutional study in southeastern states provided the Author links open to overlay panel and records in NAUTH, Nnewi and other institutions, in other to determine differences in pregnancy outcomes including diabetic complications, maternal and perinatal complications between gestational diabetes mellitus and overt diabetes in pregnancy within the region.

A multi-institutional retrospective study compared pregnancy outcomes between gestational diabetes mellitus and overt diabetes in pregnancy. We examined pregnant women who met the former criteria for gestational diabetes mellitus and received dietary intervention with self-monitoring of blood glucose with or without insulin.

Overt diabetes in pregnancy was defined as 2 abnormal values on 75-g oral glucose tolerance test, fasting glucose 126mg/dl (7.0mmol/l) and 2-h postprandial glucose 200mg/dl (11.1mmol/l), or glycated hemoglobin levels 6.5% (48mmol/mol). Data were collected on 67 women with gestational diabetes and 38 with overt diabetes in pregnancy.

Pregestational body mass index was higher (26.26.1 vs. 24.95.7kg, P<0.05) and gestational age at delivery was earlier (37.82.5 weeks vs. 38.12.1 weeks, P<0.05) in overt diabetes than in gestational diabetes. Glycated hemoglobin (6.81.1% [51mmol/mol] vs. 5.80.5% [40mmol/mol], P<0.05) and glucose on 75-g oral glucose tolerance test and prevalence of retinopathy (1.2% vs. 0%, P<0.05) and pregnancy-induced hypertension (10.1% vs. 6.1%, P<0.05) were higher in overt diabetes than in gestational diabetes. Pregnancy-induced hypertension was associated with pregestational body mass index, gestational weight gain, chronic hypertension, and nulliparity but not with 75-g OGTT.

BLOOD PRESSURE IN GDM: Hypertension and preeclampsia have been over the period known to be associated with gestational diabetes mellitus as one of the most common complications with a difficult task for clinicians in co-managing both morbidities and also not overlooking or monitoring biophysical profile and fetal wellbeing.

During the course of this study a couple of vital signs were obtained with consent from the subjects/patients and it was further worked on statistically by standard deviation using mean in order to provide insight with the relationship of the hemodynamic status to GDM and its outcome. We adopted the proposed white's criteria and also classified hypertension related in pregnancy within indicating the number of subjects affected.

Variable	White B	White C	White D	White R	White F	*p* for trend
n (%)	208 (19)	282 (26)	375 (34)	121 (11)	108 (10)	
SBP (mmHg)						
1st trimester	118.5±11.6 [194]	118.6±12.0 [252]	121.7±14.7 [343]	125.3±14.9 [113]	134.0±14.9 [101]	<0.001
2nd trimester	119.4±11.9 [204]	121.0±12.9 [269]	122.9±13.7 [361]	127.5±15.0 [118]	139.3±17.0 [105]	<0.001
3rd trimester	130.6±19.2 [202]	134.2±19.6 [274]	137.6±20.5 [374]	147.5±23.2	159.9±19.9 [106]	<0.001
DBP (mmHg)						
1st trimester	72.6±9.1 [194]	72.4±9.2 [252]	74.9±9.4 [343]	77.0±8.6 [113]	81.7±8.9 [101]	<0.001
2nd trimester	73.6±9.0 [204]	74.4±8.4 [269]	75.1±8.6 [361]	77.4±9.1 [118]	84.3±10.0 [105]	<0.001
3rd trimester	80.8±12.2 [202]	83.9±11.5 [274]	84.0±11.2 [374]	87.6±11.4	94.3±8.9 [106]	<0.001
SBP ≥140 mmHg and/or DBP ≥90 mmHg						
1st trimester	11 (5.7) [194]	21 (8.3) [252]	42 (12.2) [343]	20 (17.7) [113]	42 (41.6) [101]	<0.001
2nd trimester	17 (8.3) [204]	26 (9.7) [269]	49 (13.6) [361]	25 (21.2) [118]	54 (51.4) [105]	<0.001
3rd trimester	53 (26.2) [202]	97 (35.4) [274]	160 (42.8) [374]	80 (66.1)	90 (84.9) [106]	<0.001
Chronic hypertension	11 (5.3)	12 (4.3) [280]	27 (7.2) [374]	12 (9.9)	21 (19.4)	<0.001
Gestational hypertension	30 (14.4)	33 (11.8) [280]	44 (11.8) [374]	28 (23.1)	22 (20.4)	0.03
Pre-eclampsia	17 (8.2)	54 (19.3) [280]	93 (24.9) [374]	44 (36.4)	52 (48.1)	<0.001

Data are means±SD or frequencies (%)
The number of subjects is presented in square brackets if different
For definitions of White's classes, please refer to the footnotes of Table 1
DBP, diastolic BP; SBP, systolic BP

DIABETES MELLITUS AND PREGNANCY

Practice Essentials Gestational diabetes mellitus (GDM) is defined as glucose intolerance of variable degree with onset or first recognition during pregnancy. A study by Stuebe et al found this condition to be associated with persistent metabolic dysfunction in women at 3 years after delivery, separate from other clinical risk factors.

Infants of mothers with preexisting diabetes mellitus experience double the risk of serious injury at birth, triple the likelihood of cesarean delivery, and quadruple the incidence of newborn intensive care unit (NICU) admission. Gestational diabetes mellitus accounts for 90% of cases of diabetes mellitus in pregnancy, while preexisting type 2 diabetes accounts for 8% of such cases. Screening for diabetes mellitus during pregnancy for the benefit of Gestational diabetes the following 2-step screening system regarding gestational diabetes is currently recommended in the ministry of health Nigeria.

Alternatively, for high-risk women or in areas in which the prevalence of insulin resistance is 5% or higher (eg, the southwestern and southeastern of Nigeria), a 1-step approach can be used by proceeding directly to the 100-g, 3-hour OGTT. The US Preventive Services Task Force (USPSTF) recommends screening for gestational diabetes mellitus after 24 weeks of pregnancy. The recommendation applies to asymptomatic women with no previous diagnosis of type 1 or type 2 diabetes mellitus.

The recommendation does not specify whether the 1-step or 2-step screening approach would be preferable. In Type 1 diabetes the disease is typically diagnosed during an episode of hyperglycemia, ketosis, and dehydration which is the most commonly diagnosed in childhood or adolescence; the disease is rarely diagnosed during pregnancy Patients diagnosed during pregnancy most often present with unexpected fluctuating glucose levels.

What Are The Existing Diagnostic Criteria?

O' Sullivan and Mahan in 1964 proposed the first diagnostic criteria for GDM, assaying whole blood glucose with the Somogyi-Nelson method, during a three-hour oral glucose tolerance test (OGTT). Glucose levels of 90, 165, 145 and 125 mg/dl (for fasting, one-hour, two-hour and three-hour post glucose load respectively) were proposed as diagnostic thresholds for GDM.

More than a decade later, in 1979, the National Diabetes Data Group (NDDG) suggested measuring plasma instead of whole blood glucose and set new threshold values (105, 190, 165 and 145 mg/dl). In 1982, Carpenter and Coustan proposed changing the values to 95, 180, 155 and 140 mg/dl9. According to the NDDG and Carpenter and Coustan criteria, the diagnosis of GDM is established if two or more glucose values are higher than the defined cut-offs during a three-hour OGTT.

In 1989, Sacks et al proposed the more inclusive criteria of 96, 172, 152 and 131 mg/dl, after calculating glucose concentrations in paired whole blood and plasma specimens of 995 consecutive pregnant women. All the aforementioned diagnostic thresholds were based on data from women who were diagnosed with diabetes after gestation and not on any short-term adverse pregnancy outcomes.

In 2010, the International Association of Diabetes and Pregnancy Groups (IADPSG) proposed a new set of criteria, based on the incidence of adverse perinatal outcomes, as assessed in the Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study.

According to these criteria, the diagnosis of GDM is made if at least one value of plasma glucose concentration is equal to or exceeds the thresholds of 92, 180 and 153 mg/dl (for fasting, one-hour and 2-hour post glucose load glucose values respectively), after performing serial analysis.

CHAPTER 4

THE DATA COLLECTION AND ANALYSIS AND PRESENTATION OF FINDING

In this study, the prevalence rates used is dependent upon the specificity and sensitivity of the selective screening process in identifying at- risk women. As we already know from the previous chapters that there are more than 2 investigative screening processes proposed and adopted by different countries and the WHO.

Nigeria is amongst the low middle income countries but has been taking advance steps to upgrade her health system and improve health education. The Nigerian ministry of health strongly frowns at and for all undocumented and unrecorded maternal morbidity and mortality hence have tried to enjoin some partners to help reduce the burden of public health especially maternal morbidity and mortality.

Southeastern region of Nigerian is amongst the part of the nation with the most educated population burdened with continuous migration to urbanization and modern lifestyle, increasing the risk of GDM. This region is also amongst the region encouraging health research, continuous medical education and training of staffs as such improving healthcare.

However, a more widely studied, considered and taught diabetic screening procedure and classification adopted worldwide has been the WHITE'S classification of diabetes complicating pregnancy and its proposed treatment protocol with associated therapy.

BRIEF HISTORY

+Priscilla White was a pioneer in the treatment of Diabetes complicating pregnancy

1. She proposed the famous White classification
2. It emphasizes the importance of 3 factors
    a. Age of patient
    b. Duration of diabetes
    c. Presence of vasculopathy
3. It was modified by the American College of Obstetricians and Gynaecologists in 1986
4. The original version consists of 7 classes
5. The modified version splits class A – consisting of patients who developed diabetes during pregnancy – into 2 subcategories – A1 and A2
6. A1 corresponds to those who have carbohydrate intolerance detected during 100g 3-hour glucose tolerance test, but fasting and post prandial glucose levels are less than 105mg/dl and 120mg/dl respectively
7. In the A2 subcategory, the fasting and post prandial glucose levels are more than 105mg/dl and 120mg/dl respectively.

CLASSIFICATION OF DIABETES COMPLICATING PREGNANCY
PART 1 – GESTATIONAL DIABETES

Class	Onset	Fasting Plasma Glucose	2-hour postprandial glucose	Therapy
A1	Gestational	<105mg/dl	<120mg/dl	Diet
A2	Gestational	>105mg/dl	>120mg/dl	Insulin

Class	Onset (age in years)	Duration (years)	Type of vascular disease
A1	Gestational – diet-controlled	–	None
A2	Gestational – treated with medication/ insulin	–	None
B	20	<10	None
C	10–19 *or*	10–19	None
D	<10 *or*	20	Benign retinopathy
F	Any	Any	Nephropathy
R	Any	Any	Proliferative retinopathy
T	Any	Any	Prior renal transplant
H	Any	Any	Coronary artery disease

PART 2 – OVERT DIABETES

Class	Age of Onset	Duration (years)	Vascular disease	Therapy
B	Over 20	<10	None	Insulin
C	10-19	10-19	None	Insulin
D	>20	>20	Benign retinopathy	Insulin
E	Any	Any	Nephropathy	Insulin
R	Any	Any	Proliferative retinopathy	Insulin
G	Any	Any	Cardiac involvement	Insulin

Class	Onset	Plasma Glucose Level: Fasting	Plasma Glucose Level: 2-Hour Postprandial	Therapy
A_1	Gestational	< 105 mg/dL	< 120 mg/dL	Diet
A_2	Gestational	> 105 mg/dL	> 120 mg/dL	Insulin
Class	**Age of Onset (yr)**	**Duration (yr)**	**Vascular Disease**	**Therapy**
B	Over 20	< 10	None	Insulin
C	10 to 19	10 to 19	None	Insulin
D	Before 10	> 20	Benign retinopathy	Insulin
F	Any	Any	Nephropathy[a]	Insulin
R	Any	Any	Proliferative retinopathy	Insulin
H	Any	Any	Heart	Insulin

[a]When diagnosed during pregnancy: proteinuria ≥ 500 mg/24 hr before 20 weeks' gestation.

There is need to review every and all articles accessible during the course of this study as all have possible vital information that will benefit subjects/ patient during counselling and management of which without prompt intervention and specialized care poor outcome is inevitable. Some screening procedures are cheap and readily available and as such are the preferred e.g., NICE recommendations.

NICE Guidelines 2015 for Screening and Diagnosis of GDM

1. Assess risk of GDM using risk factors in a healthy population. If women had GDM in previous pregnancy do 75g OGTT as soon as possible, if negative repeat again at 24-28 weeks. Other women with any other risk factors screen at 24-28 weeks by 2-hour OGTT with 75 g glucose load.
2. **Do not use fasting plasma glucose, random blood glucose, HbA_1C, glucose challenge test or urine analysis for glucose to assess risk of developing GDM.**
3. Glycosuria of 2+ or more on one occasion or of 1+ or above on 2 or more occasions by regent strip on ANC needs further testing to exclude GDM.
4. Diagnosis of GDM made if the women has either fasting plasma glucose level of 5.6mmol/l or above or a 2-hour plasma glucose level of 7.8mmol/l or above.

RHETORIC QUESTIONS?

1) By seeing all these criterias and guidelines where do we stand? What would be ideal in developing and developed countries is still a question.

2) What is needed is a correct diagnosis, prompt treatment to prevent adverse maternal and perinatal outcome and development of future diabetes both in mother and child.

3) Will a single glucose test value be diagnostic to serve as a standard of care? If a single glucose test determination such as fasting plasma glucose or any other value would have been sufficient for the diagnosis, a full OGTT can be avoided.

The relative independent contribution of the fasting, 1-hour and 2-hour glucose test values were considered by IADPSG in concordance with HAPO trial. Each of these values contributed at least partially as an independent predictor of adverse outcome and therefore IADPSG, recommended the full 2-hour 75g OGTT.

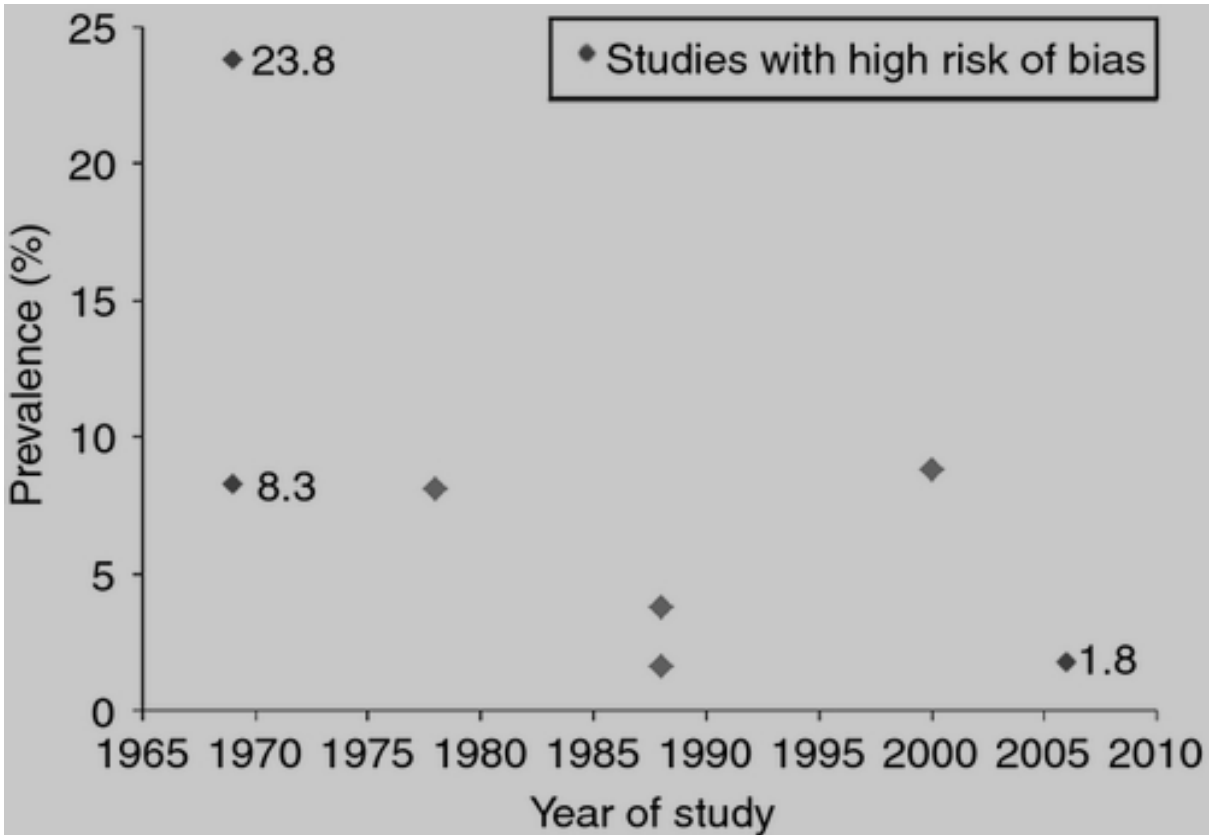
Among HAPO cohort, 11.1% had only one elevated result, 3.9% had 2 elevated results and 1.1% had elevation of all these results. Diagnosis of GDM by a single glucose value may be acceptable in low resource community with a cost of decreased sensitivity which will exclude many women with GDM from being diagnosed and deny them the benefit of treatment.

However, Diagnosis of GDM by a single glucose test value should be accepted in low resource centers and community with proper counselling on the test result outcome and dieting encouraging further antenatal care visit with a cost-effective package for each patient, this will improve patients' confidence and trust in the center and the ability of her healthcare giver and skilled provider assuring them of a beneficial expectation even in the conditions of lack of money.

Statistical Methods And Analysis

The data were entered into Microsoft Excel, exported into STATA/SE version 14 software for analysis. The heterogeneity test of the included studies was assessed by using the I^2 statistics and Q test with its respective *p*-value. The presence of heterogeneity was considered to I^2 test statistics results > 50% and Q test and its respective *P*-value < 0.05.
Furthermore, the heterogeneity was presumed in the protocol based on an estimate of a potential variation across studies and depicted in the analyses, we used a random effects model as a method of analysis.
The publication bias was assessed using the Egger's regression test objectively and funnel plot subjectively. Any asymmetry of a funnel plot and statistical significance of Egger's regression test (P-value < 0.05) was suggestive of publication bias.

Therefore, the Duval and Tweedie nonparametric trim and fill analysis using the random effect analysis was performed. Forest plots used to present the combined prevalence and 95% confidence interval (CI). Subgroup analyses for prevalence were performed by sub regions of states, publication year of studies, quality of the study and study design.
In addition, a sensitivity analysis was done to point out the study (s) that caused variation. The different factors associated with GDM were presented using odds ratios (ORs) with 95% confidence interval (CI).

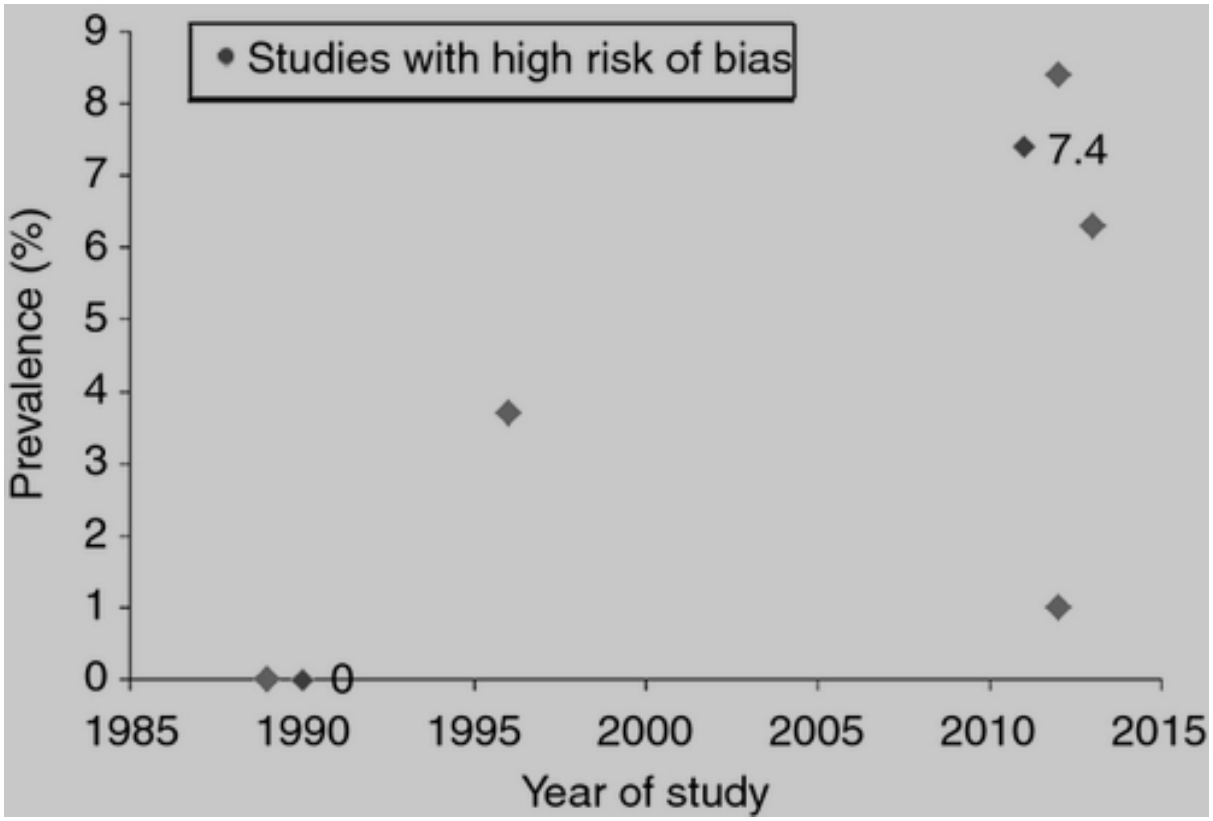


The random effect pooled prevalence of GDM in the southeast state region was 13.61% (95% CI: 10.99, 16.23; $I^2 = 96.1\%$, $p < 0.001$). However, there was a publication bias (Egger's test, $\beta o = 7.98$, p-value < 0.001).

The trim and fill analysis added ten studies and the pooled prevalence of GDM in Africa varied to 6.81% (95% CI: 3.96, 9.7).

There was significant heterogeneity ($I^2 = 96.1\%$) and Q test (Tau-squared = 35.6783, p-value $p < 0.001$) in the prevalence of GDM in the southeast states, which is likely due to differences prevalence in sub regions of Nigeria, publication year of studies, risk of bias and study design.

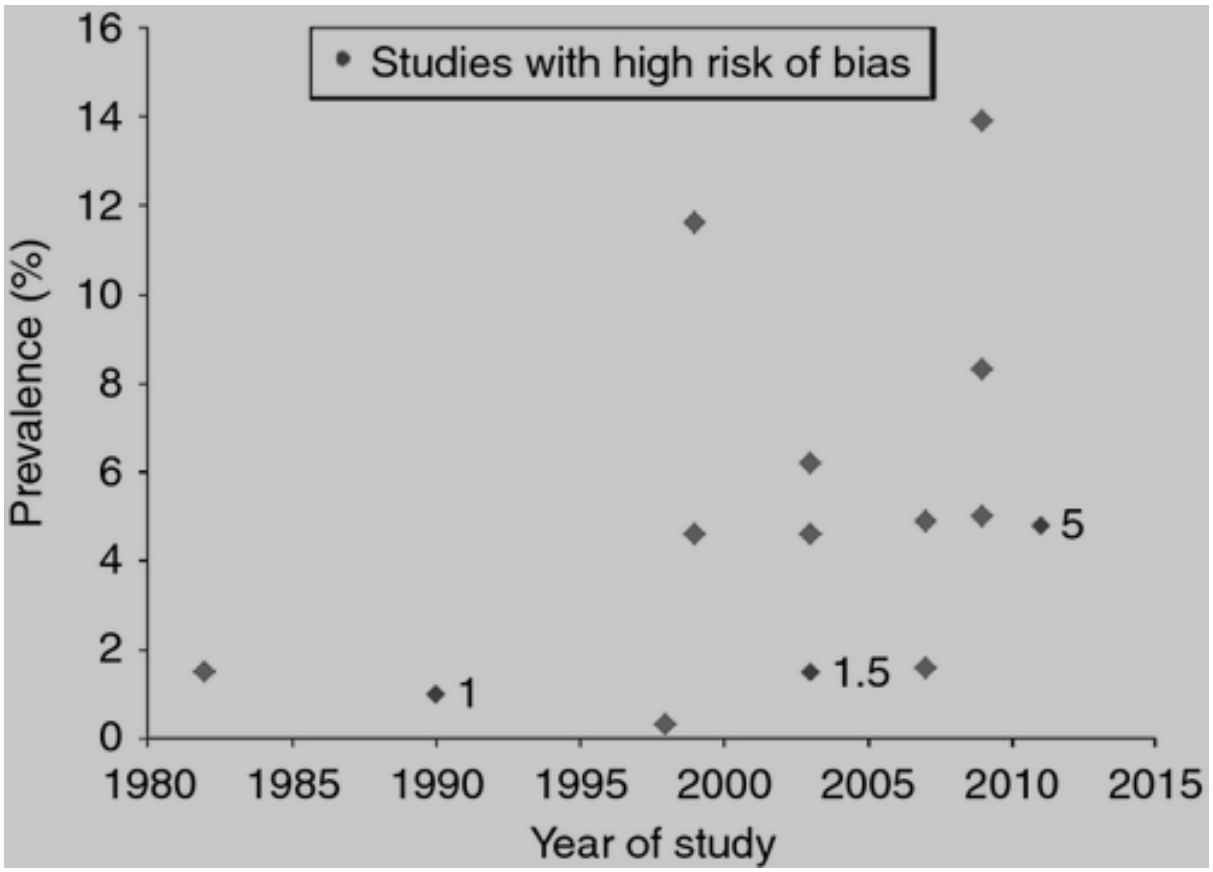
Therefore, this sub-group analysis showed that the pooled prevalence of GDM in southeastern region was 14.28% (95% CI: 11.39, 17.16; $I^2 = 96.4\%$, $p < 0.001$).



Data were extracted from each study regarding name of author (s), state and sub-region, Study design, setting, year of publication, year of study conducted (year of survey), sample size, response rate, gestational age when GDM screen, participant selection, age of pregnant women, test approach (one step vs two step), screening criteria (Universal vs selective), Blood glucose levels measured by (Glucometer vs Laboratory method), prevalence of GDM (including percentage and 95% CI), odds ratio, relative risk of certain risk factors.
The outcome measures extracted were prevalence of GDM and risk factors in terms of differences of proportion/percent of GDM in the total pregnant women were participated.

Data Extraction And Quality Assessment

The selected papers were fully reviewed and the required information for the systematic review was extracted and summarized using an extraction table in Microsoft Office Excel software. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline were followed throughout the review and analysis processes.



The study quality or risk of bias was assessed using the adopted a risk of bias tool developed by Hoy et al. and modified it to suit to our study. The tool consists of ten items that assess sampling, attrition, measurement and reporting bias. The validity of methodology, appropriateness and reporting of results were also assessed.

When the information provided was not adequate to assist in making judgment for a certain item, we agreed to grade that item with a 'NO' meaning high risk of bias. Each study was graded depending on the number of items judged 'YES' as low (≥ 8), moderate (6 to 7) or high risk of bias (≤ 5).

CHAPTER 5

SUMMARY, CONCLUSION, AND RECOMMENDATIONS MADE OF THE STUDY

5.1

SUMMARY

Screening and diagnosis of GDM and treating it effectively not only prevent adverse maternal and perinatal outcome but also future diabetes in both mother and child. Whatever method used it is important to do universal screening in Southeast Nigerian states.

More effective and simpler strategies should be developed in future clinical practice by which the need for performing an OGTT can be avoided. In HAPO study risk of adverse outcomes were very low when fasting plasma glucose was ≤ 4.4mmol/l (80mg/dl).

Further evaluation is required before recommending FPG as a screening method which may potentially identify pregnancies with very low risk of GDM because it is almost always accessible and of low cost. After reviewing all the related articles on GDM, one important aspect which comes to mind is that the Nigerian population is diverse and variable, hence judging international criteria on Nigerian population may not be conclusive. So, we need further comparative study on different diagnostic criteria in relation to pregnancy outcomes.
Although still low, this regional representation is better than the one found in the former review. This highlights the fact that little seems to be known about the prevalence and potential burden of GDM in African countries with specific focus to Nigerian southeast region known for different culture, religious beliefs and tribes.

Before health care policies and guidelines can successfully be drawn up and implemented, it is important for one to establish the extent of a particular problem. It is evident that the extent of GDM in Nigeria is not well investigated. Nigeria has been plagued with under-nutrition, unceasing inflation and GDM may be considered a public health concern.

However, as Nigeria shifts economically with government negligence to her subjects coupled with reduction in circulating funds, non-payment and poor payment of workers, no support for the underprivileged and capped with scarcity of farm products a double burden of under- and over-nutrition emerges combining its health burden. There is increase in poor feeding or over-nutrition, particularly in females and babies, GDM cannot be naively overlooked.

5.2

CONCLUSION

The countries with the most studies pertaining to GDM in literatures were South Africa and Nigeria. In addition, Nigeria and South Africa have reported relatively recent figures on macrosomia rates. In Nigeria it is thought that macrosomia accounts for 7.5% [45] to 8.1% [46,47] of births which ties in with the high GDM prevalence figures of 8.3% [35] and 13.9% [27] as reported by the two Nigerian studies in this review. **This Suggests Macrosomia May Be A Marker For GDM Prevalence.**

Interestingly, few studies were performed on rural populations. As a direct consequence of urbanisation, it would be expected that the prevalence of GDM would be higher amongst urban populations as opposed to rural populations.

It is alarming that very little appears to be known about GDM in African countries. Research studies, such as those listed in this systematic review, and particularly those that screen all women in the study cohort for GDM, are exceptionally useful in assessing the prevalence of the problem.

However, one of the limitations in making comparisons between the rural and urban studies in this review is the different GDM screening methods employed and diagnostic criteria used. In addition, some studies looked at women already at high risk for GDM. Other limitations to this review include only published studies, as opposed to grey literature, being searched and roughly one third of the studies included in the review having a high risk of bias and another third having a moderate risk of bias.

This comprehensive systematic review has illustrated a gap in the knowledge of GDM in Africa with only 11% of the African continent being represented. More epidemiological based studies on GDM in African countries and the 4 geographical regions of Nigeria need to be performed in order to provide reliable information and thus clarity on the extent of GDM.

5.3

RECOMMENDATIONS

Understanding and subsequently attempting to curb the prevalence of GDM in developing countries is imperative for maternal and child health. As GDM often results in macrosomic infants, birth trauma and the need for Caesarean sections at delivery are expected.

This is precarious as it impacts both maternal and child survival during delivery and places a significant economic burden on the health system, which in Nigeria is already struggling with limited resources and health system negligence. It is necessary for continuous update training of medical workers.
Furthermore, for most countries' macrosomia appears to have been overlooked with the justified focus on low birth weight and small for gestational age statistics.
The Developmental Origins of Health and Disease research describes how the developing fetus is susceptible to its environment and that certain in utero events can infact alter fetal programming and produce different phenotypes.

Low birth weight is representative of poor fetal nutrition and growth and has been shown to be associated with a range of chronic conditions, including type 2 diabetes and hypertensives diseases in pregnancy.

However, high birth weight requires as much consideration as there is evidence to support that fetal over-nutrition which also poses risk for type 2 diabetes and other chronic conditions later in life.

With the emerging increase in type 2 diabetes and obesity, macrosomia will become an important factor in maternal and child health and should be reported on and monitored by the health care system as a marker for GDM sooner than later.

5.4

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