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Oral glucose tolerance outcomes among pregnant women receiving antenatal care in Calabar and environs – A pilot study

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ABSTRACT

Objectives: Dysglycemia is a common metabolic alteration during pregnancy with adverse effects on both mother and fetus. This is related to the fact that pregnancy is associated with insulin resistance which is a harbinger for hyperglycemia. This study was carried out to find out the prevalence of gestational diabetes mellitus (GDM) among pregnant women in Calabar area using International Association of Diabetes and Pregnancy Study Group (IADPSG) diagnostic values.

Material and Methods: This was a prospective, observational, cross-sectional study among pregnant women attending antenatal care in four health facilities in Calabar and adjoining areas conducted from September 2018 to August 2019. All consenting pregnant women were given 75 g glucose in 250–300 mL of water after 8–10 h overnight fast, without regard to the presence or absence of GDM risk factors. GDM diagnosis was made if any of the following glucose values were met or exceeded: (1) Fasting >92 mg/dl, (2) 1 h post-glucose load >180 mg/dl, and (3) 2 h post-glucose load >153 mg/dl. Data were analyzed using IBM Statistical Package for the Social Sciences version 20.0 and results were presented using tables and a Venn diagram.

Results: There were 345 pregnant women aged 18–50 (28.7 ± 6.3) years at 24–41 (29.6 ± 4.1) completed weeks of gestation. GDM was diagnosed in 48 (13.9%) women. Fasting plasma glucose cutoff diagnosed 81% while 37.5% and 50.0% met the diagnostic cutoff for 1 h and 2 h, respectively, and 15 (31.3%) women were positive for all three diagnostic cutoffs. Diabetes mellitus in a first-degree relative was the most common risk factor identified while hypertension in a first-degree relative and history of GDM was the least. Some 36.5% of women had no identifiable risk factors. Those who had positive fasting plasma glucose only (6.1%) were more than twice those diagnosed by 1 and 2 h only (2.6%) combined. The number of women with glucose values in the diabetic range was 6 (1.72%) but was classified as GDM since they were not previously known diabetics.

Conclusion: This study has shown that the prevalence of GDM is 13.9% among women in Calabar and environs using the IADPSG criteria. Fasting plasma glucose can identify more than twice GDM patients than 1 and 2 h values combined. GDM still remains a major health issue among pregnant women hence there should be a national policy on routine screening for GDM with more studies being encouraged to determine the preferred glucose cutoff among Nigerians.

Keywords: Gestational diabetes mellitus, Dysglycemia, International Association of Diabetes and Pregnancy Study Group criteria, OGTT, Calabar

INTRODUCTION

Dysglycemia is currently regarded as a very common metabolic alteration during pregnancy.[1] This is related to the fact that pregnancy is associated with insulin resistance[2] which is a harbinger for hyperglycemia. It has been shown that during pregnancy, there is a uniform 50–60% decrease in insulin sensitivity with advancing gestation in both normal glucose tolerance and gestational diabetes.[2] However, the significant decrease in insulin sensitivity in late gestation observed in women with gestational diabetes in comparison with a matched control group is reflections of a decreased insulin sensitivity that may exist before pregnancy.[1,3] The prevalence rate of GDM, therefore, is said to reflect the prevalence of IGT in young reproductive women as well as the background prevalence of type 2 diabetes in the given population.[4]

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance diagnosed in the second or third trimester of pregnancy that is not clearly overt diabetes.[1,5] The prevalence of GDM ranges from less than 2% in low-risk populations such as in Sweden to 17.8% in urban Indian women.[4] In Nigeria, prevalence ranging from 1.13%[6] to 13.9%[7] depending on the population studied and the diagnostic criteria used have been reported. GDM increases the risks of various complications of pregnancy and delivery.[8] There is a greater frequency of miscarriages, macrosomia, and perinatal mortality among women that developed diabetes during pregnancy.[9] Their offspring is not spared either as the intrauterine exposure to maternal glucose intolerance places them at increased risks for long-term adverse outcome.[9] Furthermore, women with a history of GDM are also at increased risk of future cardiovascular disease.[10]

Various methods of screening and diagnostic criteria for GDM have been used by different professional bodies with calls for consensus.[11] Most screening strategies adopt the presence or absence of risk factors such as age, body mass index, previous fetal macrosomia, family history of diabetes among others, and these indices have been significantly correlated with a diagnosis of GDM.[12,13] Universal screening has been recommended by many researchers to be a more objective method of assessing the prevalence of GDM[11,14,15] to forestall under diagnosis. However, in many low- and medium-income countries and even in some high-income countries, screening is selective involving only those presenting with at least one risk factor for GDM.[16] This selective screening may underestimate the prevalence of the disorder in these countries[16] with grave consequences as shown by a landmark hypoglycemic and adverse pregnancy outcome (HAPO) study involving over 25,500 women.[17] To avoid the untoward effects of a possible missed diagnosis both to the fetus and mother, we undertook to screen all consenting pregnant women with a view to determining the prevalence of the disorder in the population using the diagnostic criteria proposed by the International Association of Diabetes and Pregnancy Study Group (IADPSG).[18] The IADPSG diagnostic criteria were determined based on recommendations from the HAPO study.

MATERIAL AND METHODS

Study area

The protocol of this study was approved by the Health Research Ethics Committee of the University of Calabar Teaching Hospital (UCTH/HREC/33/681). It was carried out in the metabolic disease research unit of the Department of Chemical Pathology, UCTH. It included data from the UCTH, General Hospital, Calabar, which is a secondary health-care facility with about 50 beds and two Primary Health Centres (PHC) in Akpabuyo Local Government Area located about 15–20 km North of Calabar metropolis. The UCTH is a tertiary health facility with over 500 beds, located in Calabar South Local Government. Calabar is a metropolitan town and comprises Calabar Municipality and Calabar South Local Governments. It also serves as administrative capital of Cross River State in the South-South geopolitical zone of Nigeria.

UCTH serves as a referral center to other primary and secondary health facilities in Cross River State and neighboring Akwa Ibom State. Women who are pregnant receive antenatal care services every week day at the department of obstetrics and gynecology. Low-risk pregnancies are seen every 4 weeks till 28 weeks of gestation, every 2 weeks till 36 weeks, and weekly till delivery. High-risk pregnancies are seen every 2 weeks till 28 weeks of gestation and every week thereafter till delivery. At booking, the investigations carried out include packed cell volume, hemoglobin solubility, blood grouping, Venereal Disease Research Laboratory test, urinalysis, hepatitis B surface antigen, hepatitis C virus, as well as human immunodeficiency virus by voluntary counseling and testing. Any additional investigations are tailored to clinical indications. Screening for GDM is selective depending on the presence or absence of risk factors. Little or no elaborate screening is undertaken in the other centers included in this study where at best urinalysis is done to rule out the presence of proteinuria or glycosuria which are associated with preeclampsia or GDM, respectively.

Study design

This was a prospective, observational, cross-sectional study conducted from September 2018 to June 2019. Pregnant women, 18–50 years, who gave consent were recruited during antenatal clinic visits if they were 24 weeks of gestation and

over. Women who were beyond 28 weeks of gestation were also screened because a considerable number of women usually commence ANC late in their second trimester. Selection was carried out without regard to the presence of risk factors. However, those with identifiable risk factors were documented.

Inclusion criteria

Pregnant women aged from 18 years and above attending ANC; with gestation age from 24 completed weeks to term; without a previous history of diabetes mellitus; with or without presence of risk factors for GDM; and gave consent to participate in the study.

Exclusion criteria

Pregnant women who are known type 2 diabetics on treatment; with GA below 24 completed weeks. Those who did not give consent were excluded from the study.

Sample size determination

This was done using Fisher's formula below:

$$n = \frac{Z^2 p(1-p)}{I^2} \quad (1)$$

Where:
n = Sample size (where population is >10,000)

Z = Normal deviation at the desired confidence interval. In this case, it will be taken at 95%, Z value at 95% is 1.96

P = Proportion of the population with the desired characteristics (reported to be 13.9%[7] in Nigeria)

Q = Proportion of people without the desired characteristics (1-p)

I^2 = Degree of precision; will be taken to be 5%

$$\text{Sample size } (n) = \frac{Z^2 p(1-p)}{I^2} \quad (2)$$

$$n = \frac{3.84 \times 13.9/100 \left(1-13.9/100\right)}{0.05 \times 0.05} = 183.8 \quad (3)$$

An attrition rate of 10% = 18 was added to account for dropouts.

Therefore, a minimum of 184 + 18 = 201 participants was considered for recruitment into the study.

Sampling technique

Participants were recruited randomly to avoid bias. The researchers explained the details of the study to the women during routine ANC visits and those that met the inclusion criteria and were willing to participate in the study were asked to volunteer. No inducement was given for participation. At least 50 participants were recruited from each center to ensure adequate representation.

Baseline evaluation

On the morning of the test, a written consent was obtained from each participant. Data including age, gestational age of index pregnancy, medical, obstetrical, and family history were collected by interviewer-administered questionnaire. A physical examination was carried out including blood pressure (BP) using an Accoson mercury column sphygmomanometer (A. C. Cossor and Sons Ltd, London), weight and height were recorded with the aid of HANA bathroom weighing scale (Kion Classics, China) and a wooden measuring rule graduated in centimeters, respectively. The rule was placed vertically against a straight wall and height was read with participants standing in front of the rule without shoes and head scarf. BP was taken twice 30 min apart with patient in sitting position. Hypertension was defined by systolic or diastolic BP above 139/89 mmHg on more than 1 occasion or taking BP-lowering medications. Inquiry was made about the presence of risk factors for GDM including DM in a first-degree relative, hypertension in index pregnancy, history of GDM, hypertension in first-degree relative, and history of macrosomic baby (birth weight >4.0 kg).

Sample collection and analysis

Participants were allowed to rest for about 30 min after arrival. Two milliliters of venous blood were drawn by standard venepuncture techniques into sample bottle containing fluoride oxalate as anticoagulant. Munro Glucose-D (Brian Munro Limited, Lagos, Nigeria) was weighed into 75 g with the aid of KERN Balances and Weights (KERN & Sohn GmbH, Ziegelei 1, Germany). It was dissolved in 250–300 mL of water and given to each participant to take orally within 5 min. This was time 0 h. After the glucose loading, 2 ml of blood was drawn at 1 and 2 h using standard venepuncture techniques, into fluoride oxalate bottle for glucose assay. Samples were separated after centrifugation at 3500 rpm for 5 min. Plasma was collected and analyzed on the same day using enzymatic glucose oxidase method with the aid of a spectrophotometer.

Diagnosis of GDM

GDM diagnosis was made using the criteria by IADPSG[18] if any of the following criteria were met or exceeded: (1) Fasting plasma glucose ≥92 mg/dl (5.1 mmol/l), (2) 1 h post-glucose load of glucose ≥180 mg/dl (10 mmol/L), or (3) 2 h post-glucose load ≥153 mg/dl (8.5 mmol/l).

Statistics

Data were entered into Microsoft Excel and exported into IBM Statistical Package for the Social Sciences version 20.0 software for analysis. Sociodemographic characteristics of the participants were analyzed for differences and express as mean ± standard deviation. A correlation was made between risk factors and GDM. $P < 0.05$ was considered to be statistically significant for all tests.

RESULTS

The study participants included 345 pregnant women 18–50 years of age with a mean age of 28.7 ± 6.3 years. Mean gestational age of all participants was 29.6 ± 4.1 ranging from 24 to 41 completed weeks. The women who were found to have GDM were 48/345 (13.9%) while 297/345 (86.1%) had normal response. Table 1 shows the characteristics of the study participants.

Table 2 represents the different number of women that were diagnosed as positive for GDM by the different time points using OGTT. More women were diagnosed by the fasting plasma glucose than the 1 h or 2 h. Those who had positive FPG only (6.1%) were more than twice those diagnosed by 1 and 2 h only (2.6%) combined.

Table 1: General characteristics of the study participants.

Variable	Mean±SD	Frequency (%)
Age (years) *n*=345	28.7±6.3	
<35	-	225 (65.2)
≥35	-	120 (34.8)
EGA at testing (weeks)	29.6±4.1	
24–28	-	195 (56.5)
>28	-	150 (43.5)
Risk factors		
One or more	-	60 (17.4)
None	-	285 (82.6)
0 h glucose (mmol/L)	3.9±1.1	-
1 h glucose (mmol/L)	5.7±2.2	-
2 h glucose (mmol/L)	5.1±2.2	-
Weight (kg)	68.8±14.0	-
Height (m)	1.6±0.1	-

Table 2: OGTT time points meeting GDM diagnosis by IAGPSG criteria.

Time (hours)	Number (%) (*n*=345)
0	39 (11.3)*
1	18 (5.2)
2	24 (7.0)
0 and 1 only	57 (16.5)
0 and 2 only	63 (18.3)
1 and 2 only	42 (12.2)
0, 1, and 2	15 (4.3)
0 only	21 (6.1)
1 only	3 (0.9)
2 only	6 (1.7)
GDM	48 (13.9)

*Percentages of all subjects (*n*=345)

Figure 1 is a Venn diagram showing the interactions of OGTT time points among the GDM subjects. About 81% (39/48) met the diagnostic criterion using fasting plasma glucose while 37.5% (18/48) and 50.0% (24/48) met the diagnostic cutoff for 1 h and 2 h, respectively. GDM was most frequently diagnosed by fasting plasma glucose, followed by 2 h glucose. The number of women with glucose values in the diabetic range was 1.72% (6/348) but was classified as GDM since they were not previously known diabetics.

Table 3 shows the comparison between the GDM group and the non-GDM group. The women with GDM were older than those without GDM and this difference was statistically significant ($P = 0.001$). The weight and height were all higher among the GDM group but the difference did not reach statistical significance. The systolic and diastolic BPs were higher among the GDM group than the non-GDM group with the difference in systolic BP alone reaching statistical significance ($P = 0.001$).

Table 4 shows the distribution of risk factors among the study population. There were very few risk factors identified among the study population. A very large number of the women are not aware of the presence of any of such risk factors and were unable to volunteer any.

DISCUSSION

Our study has shown that the prevalence of GDM is high among women in our environment. At 13.9% prevalence rate, we have the same prevalence that was reported among women with risk factors in Ibadan, Southwest Nigeria, using the 1999 WHO guidelines.[7] That was the highest prevalence reported in Nigeria at the time. However, our

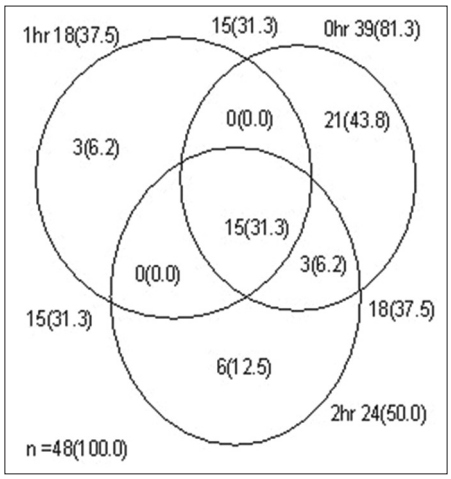

Figure 1: Venn diagram showing the interactions of the OGTT time points for GDM diagnosis.

Table 3: Comparison between GDM and normal pregnancy demographic information using unpaired Student's *t*-test.

Variable/group	GDM *n*=48 (mean±SD)	Non-GDM *n*=297 (mean±SD)	*t*-value	*P*-value
Age (years)	33.13±6.34	27.70±5.85	3.312	0.001*
Gestational age (weeks)	29.13±3.68	29.68±4.16	0.347	0.730
Weight (Kg)	75.63±10.77	67.60±14.21	1.520	0.134
Height (m)	1.61±0.06	1.58±0.09	0.987	0.328
BMI (Kg/m^2)	29.24±4.86	26.81±5.00	1.126	0.266
Systolic pressure (mmHg)	118.75±22.75	104.51±9.91	2.906	0.006*
Diastolic pressure (mmHg)	68.88±6.67	66.90±7.75	0.657	0.515

Values are expressed as mean±standard deviation, GDM: Gestational diabetes mellitus, significant at $P<0.05$

Table 4: The distribution of GDM risk factors among pregnant women.

Risk factor	Frequency	Percentage
DM in a first-degree relative	18	5.2
Previous macrosomic baby (birth weight ≥4.0 kg)	12	3.5
Hypertension in index pregnancy	12	3.5
Past history of GDM	9	2.6
Hypertension in a first-degree relative	9	2.6
No risk factors detected	126	36.5
No response/ignorance of risk factors	159	46.1
Total	345 (100)	100.0

reported prevalence is lower than what was reported among Cameroonians (20.5%) using the IADPSG diagnostic criteria.[19] A review article on GDM in Africa carried out about 6 years ago reported a prevalence as low as 0% in rural Tanzania and as high as 13.9% among urban Nigerian women with risk factors.[16] All studies in the review had used the risk factor approach to select their participants and the study with the highest prevalence was carried out among urban dwellers with risk factors among whom the prevalence of GDM is expectedly high.[7,8,20] Another review article on GDM in low- and middle-income countries reported a prevalence ranging from 8.9 to 20.4% in studies that used the IADPSG criteria and these were among the highest prevalence reported.[21] The number of studies that used the universal screening criteria was 87% (39/45) showing a shift toward adoption of the universal screening for all pregnant women without regard to the presence or absence of GDM risk factors.

The use of the IADPSG criteria has been reported to return an increased prevalence of GDM in the population. Imoh *et al*. compared different GDM diagnostic criteria on the same population of pregnant women and reported widely varying prevalence rate for GDM. They reported a prevalence of 2.2% versus 15.9% in the same population using the 1999 WHO versus the IADPSG criteria, respectively.[22] The reason for the significant difference is the recommended diagnostic cutoff values. The 1999 WHO and the IADPSG criteria use fasting blood glucose ≥7.0 mmol/L versus ≥5.1 mmol/L and 2 h post 75 g glucose load of ≥7.8 mmol/L versus ≥8.5 mmol/L, respectively. The IADPSG has an additional 1 h post-glucose load cutoff ≥10.0 mmol/L. It is, therefore, obvious that the reported prevalence by Kuti *et al*.[7] would have been higher if the IADPSG criteria were used.

Screening all pregnant women for GDM has been advocated as the gold standard to avoid missing any case.[11,18] Although some have argued that it will increase financial burden in resource poor countries like Nigeria,[23] there are indications that the universal screening method is gradually becoming popular even among low- and middle-income countries.[21] This is a welcomed development. It has been adopted by some obstetricians in some centers in Nigeria.[22] The implications of a missed diagnosis including poor pregnancy outcome, high risk of future maternal diabetes, and cardiometabolic conditions make it appear to be more cost effective in the long run to screen all pregnant women.[18] It has been reported that as much as a quarter of Nigerian women with GDM may not have any identifiable risk factors.[22] This further emphasizes the need to screen all pregnant women at the recommended time and intervene when necessary.

One factor that may work against selective risk factor approach is literacy level. We did not inquire about the educational level of the women who participated in this study but it was evident that almost half of participants, especially from the PHCs located in rural areas, were not aware of the presence or absence of risk factors for GDM. History of previous home deliveries under traditional birth attendants (TBAs) is usually high among rural dwellers and this will further limit identification of some risk factors such as fetal macrosomia, hypertension, and previous history of GDM, among others. These factors are rarely excluded during routine ANC under TBAs. In this study, about 50% of participants were unaware of the presence of any risk factors. The most reliable way of excluding the presence of these risk factors for GDM remain by routine OGGT in all facilities carrying out ANC.

Body mass index has been shown to correlate positively

with GDM among different ethnic groups.[7,20,22] In a large cohort of 123,040 women without evidence of pregravid diabetes, it was observed that as much as 65% and 23% of pregnant African-American and Asian women, respectively, could be prevented from developing GDM if their pregestational BMI was ≤25 mg/kg^2.[24] In this present study, we did not classify the women into different BMI classes because they were all in their second or third trimester where BMI is an unreliable guide. However, BMI was higher among the GDM group relative to the non-GDM but the difference did not reach statistical significance. Another setback to assessing pre-pregnancy BMI is that most pregnant women start attending ANC late in pregnancy, making it difficult to measure their pregravid or first trimester body weight. Community-based studies will aid to provide such data.

This is probably the first report on the prevalence of GDM from our center. It is also the 1st time the universal screening criteria will be applied on pregnant women in our hospital and beyond. GDM screening in our environment is presently done only on the basis of the presence of risk factors. We are unaware of a national policy in Nigeria for routine GDM screening during ANC. This is not the case with some countries like India.[25] By the said Government of India Order, issued in 2007, all pregnant women are screened for GDM between 24 and 28 weeks of gestation using a 75 g OGTT without regard to time of last meal. The justification for this directive is that more than 90% of women with GDM can be managed by meal plan alone without using pharmacotherapy.[14] Others may require only lifestyle modification during follow-up postpartum and prevented from progressing to full-blown DM since pharmacotherapy did not show any advantage over lifestyle modification as reported by some researchers.[26] This means that screening all pregnant women for GDM may be cheaper in the long run considering the enormous economic cost of treating diabetes mellitus. It may be pertinent to considered routine GDM screening with the aim of reducing DM burden among our women.

Fasting glucose was more sensitive in the diagnosis of dysglycemia among participants in this study as has been observed in other studies using the IADPSG criteria.[20,22] Women who were diagnosed by fasting plasma glucose were twice as much as those who were diagnosed by 1 h and 2 h values combined. This was observed by some researchers who raised concern that FPG value of 5.1 mmol/l as recommended by the IADPSG will increase both GDM prevalence and the rate of false-positive diagnosis.[22,26] While this may sound plausible, it is to note that the value was not assigned arbitrarily. It was based on the recommendations from data from the HAPO study which revealed that the risk of adverse maternal, fetal, and neonatal events increased continuously as a function of maternal glycemia, even within intervals that were previously considered normal for pregnancy.[17] Apparently, diagnosing GDM will allow for prevention of future onset of DM in the woman with a potential for saving medical cost of treatment and improvement of quality of life.[27] Since the benefit of diagnosing GDM far outweighs a missed diagnosis, it will seem wise to advocate for the adoption and use of the IADPSG criteria and universal screening option.

The most common risk factor among our study participants was DM in a first-degree relative. This was the same observation reported by Kuti *et al*. among women at high risk of developing GDM.[7] GDM and type 2 diabetes are believed to share common pathogenic pathways that manifest as impaired beta cell function and increased insulin resistance.[28] However, the expression of GDM is multifactorial requiring the interaction of genetic with environmental factors as well as family history and obesity.[29] Such environmental factors will include cigarette smoking, alcohol consumption, and dietary habit some of which may be ignored when evaluating risk factors for GDM.[30] Studies have examined the roles of single-nucleotide polymorphisms, DNA methylation, and microRNAs as possible biomarkers for GDM and their interaction with environment may account for the variation of GDM prevalence among different populations.[31] Some researchers did not find any relationship between family histories of DM in a first-degree relative with GDM.[32] One possible reason for this finding may be due to the high rate of undiagnosed DM in sub-Saharan Africa making it hard for relations to note such disorder among family members.[20]

Another factor that has been observed to be associated with GDM is history of fetal macrosomia.[9] In this study, this was the second most common risk factor along with hypertension in index pregnancy. Researchers in Jos, North-Central Nigeria, observed that women with a history of fetal macrosomia have a higher risk of developing GDM.[33] It was not easy to get all the risk factors that our participants were presenting with due to educational levels of some of our participants, especially those in the rural PHCs. We, therefore, cannot claim that the number of women who reported history of fetal macrosomia was representative. A good number of our participants were unable volunteer any risk factors since they were either not aware of the presence of any due to lack of previous screening. However, risk factor like hypertension in index pregnancy was identified by taking the BP of the participants during OGTT screening.

Subjects with GDM were older than the non-GDM group and the difference in age was statistically significant. Some researchers in Nigeria had reported that age above 30 years was an independent risk factor for GDM.[7] Eweninghi *et al*. also observed that the prevalence of GDM increased with advancing age and the difference was statistically

significant (P = 0.035). They reported prevalence of 3.3%, 4.2%, and 17.6% across different age groups of 15–24 years, 25–34 years, and 35–44 years, respectively, with the overall prevalence being 4.8% across all age groups.[20] Although the mean age of our participants was about 29 years, majority (>65%) were above 35 years. The age factor may also have contributed to the relatively high prevalence of GDM in this study. The age of our study participants is an indication that women are becoming pregnant at a more advanced age as has been reported in some studies.[34]

One limitation of this study was that the number of participants from whom no risk factors were gotten was very high. This was due to the literacy level of some of our study volunteers and the PHC where they were attending ANC did not routinely screen for GDM. Therefore, any association between GDM and some of these risk factors may not be representative.

CONCLUSION

This study has shown that the prevalence of GDM is 13.9% among women in Calabar and environs using the IADPSG criteria. We have seen that fasting plasma glucose can identify more than twice GDM patients than 1 and 2 h values combined. We are advocating for a national policy on the screening of GDM with more studies being encouraged to determine the preferred glucose cutoff among Nigerians.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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