International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Jaja MA et al. Int J Reprod Contracept Obstet Gynecol. 2024 Mar;13(3):505-514
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20240447

Original Research Article

Assessment of risk factors and glycosylated haemoglobin in early pregnancy as predictors of diabetes in pregnancy

Mary A. Jaja[1], Mkpe Abbey[2]*, Olufemi A. Oloyede[3], Paul L. Kua[2], Simeon C. Amadi[2], Tehemen Kasso[1], F. Allison[1], Eghuan K. Okagua[2], Rose S. Iwo-Amah[2], Joseph N. Kwosah[2], Nestor M. Innimgba[4], Uduak S. Ocheche[4]

[1]Department of Obstetrics and Gynaecology, University of Port Harcourt Teaching Hospital, Rivers State, Nigeria
[2]Department of Obstetrics and Gynaecology, Rivers State University Teaching Hospital, Port Harcourt, Rivers State, Nigeria
[3]Fetal-Maternal Medicine Unit, Department of Obstetrics and Gynaecology, Olabisi Onabanjo University Teaching Hospital, Sagamu, Ogun State, Nigeria
[4]PAMO University of Medical Sciences, Port Harcourt, Rivers State, Nigeria

Received: 17 December 2023
Revised: 15 February 2024
Accepted: 16 February 2024

***Correspondence:**
Mkpe Abbey,
E-mail: mkpeabbey@aol.com

ABSTRACT

Background: The aim of the study was to determine the performance of history of risk factors and universal HBA1c testing as screening tools for diabetes mellitus in the first trimester of pregnancy using OGTT as a gold standard.
Methods: A prospective cross-sectional study conducted between 8 and 13±6 weeks in 305 consecutive pregnancies in the antenatal clinics of the University of Port Harcourt Teaching (UPTH) and Rivers State University Teaching Hospital (RSUTH) between January and August 2020. Each woman had oral glucose tolerance test (OGTT), and glycosylated haemoglobin (HBA1c) levels estimation. Multivariate logistic regression analysis was carried out with history of risk factors and HBA1c level as independent variables and OGTT as the dependent variable for the assessment of their predictive performances.
Results: The prevalence of DM was 28.85%, 2.62% and 31.48% for GDM, pre-gestational and for both respectively. Family history of DM was associated with high specificity (91.4%) and negative predictive value (NPV) of 68.7% but low sensitivity (9.4%) and positive predictive value (PPV) (33.3%). The receiver operator characteristic curve for HBA1c revealed a significant area under the curve value: 0.653 (CI: 058-0.72), p<0.01. The optimal cut-off for HBA1c from Youden index was 5.25%. HBA1c levels had high specificity (88.5%) and NPV (75.2%) with low sensitivity (36.5%) and PPV (59.3%). Multivariate logistic regression analysis showed HbA1c as the only independent predictor of GDM (p=0.0001).
Conclusions: The high prevalence of diabetes (31.48%), underscores the need for universal screening in early pregnancy. The high NPV and specificity of the risk factors for GDM and HBA1c levels better predict pregnancies that are not likely to develop GDM, but they are not suitable for diagnosis because of the low sensitivity and PPV.

Keywords: Risk factors, Glycosylated haemoglobin, Early pregnancy, Predictors, Diabetes, Pregnancy

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized by hyperglycaemia due to defects in insulin secretion, action or both.[1] It can be classified into pre-gestational namely (type I or insulin-dependent and type II or non-insulin-dependent diabetes) and gestational diabetes mellitus (GDM).[2]

The global prevalence of the disorder remains in the upward trends in both pregnant and non-pregnant population.[2-4] Among antenatal patients generally in Nigeria, the prevalence rose from 0.3% in the 1980s to 15.3% in 2014.[3,4] In the first trimester, using fasting blood glucose as a predictor, the prevalence of GDM and pre-gestational diabetes were 21.2% and 2.4% respectively, totalling 23.6%.[5] Screening for DM as early as possible is recommended in order to commence targeted interventions and limit the occurrence and severity of complications. In this respect, the first trimester screening should be desirable.

The commonly used risk factors for screening such as maternal characteristics [maternal age≥35 years, body mass index (BMI)≥30, excessive weight gain in pregnancy, family history of diabetes, previous large-for gestational-age baby, still birth and glycosuria] may lead to as much as 38% to 50% unidentified gestational diabetes.[6,7]

One of the newer screening methods is the application of glycosylated haemoglobin HBA1c. HbA1c threshold of 6.5% (48 mmol/mol) is associated with missed diagnosis in 47% of the pregnancies. However, HbA1c values between 5.8 and 6.0% (40-42 mmol/mol) were shown to have a high specificity and positive predictive value for detecting women who met OGTT criteria for GDM at some stage in pregnancy.[8,9]

In the Niger Delta where the study was conducted, there was paucity of information on the performance of screening using risk factors or HBA1c for diabetes in the first trimester of pregnancy. The aim of the study was to determine the usefulness of history of risk factors and universal HBA1c testing as screening tests for diabetes mellitus in the first trimester of pregnancy using OGTT as a gold standard.

METHODS

Study design and protocol

The study was of a cross-sectional design carried out between January and August 2020, among consecutive antenatal clinic attendees of 2 university teaching hospitals in the Niger Delta (RSUTH and UPTH). Women who had dating scans, confirmed to be 8-14 weeks pregnant and consented to the study were recruited. Those with known pre-existing diabetes mellitus, previous babies with birth defects, including genetic and chromosomal abnormalities were excluded.

Data about socio-demography, namely age, tribe, educational status, maternal and husband's occupation, social history, gravidity, parity, anthropometric measurements (weight, height and body mass index) and clinical findings were recorded on a proforma. Obstetric, gynaecological, general medical and family history were also obtained. Blood for oral glucose tolerant test (OGTT) and HBA1c was obtained from all the participants and routine antenatal follow-up were continued till delivery.

Diagnostic criteria for diabetes in pregnancy

The WHO 2014 diagnostic criteria for interpretation of OGTT results were applied.[2] GDM was diagnosed with the following results: Fasting blood glucose (FPG)≥5.1-6.9, 1 hr plasma glucose levels≥10.0 mmol/l or 2 hr plasma glucose levels≥8.5-11 mmol/l. Pre-gestational diabetes was diagnosed if fasting blood glucose ≥7.0 mmol/l or random (2 hr postprandial) blood glucose level≥11.1. Plasma glucose levels of ≤2.5 mmol/l were also abnormal and required further clarification. Women who were diagnosed with gestational diabetes were treated according to a standard protocol.

Sample size calculation

The sample size of 305 was calculated using sample size formula for descriptive cross-sectional study with a prevalence of 23.6%, precision of 5%, and standard normal deviation of 1.96 at 95% confidence interval. The 23.6% was taken from a prevalence study that was conducted at the University of Port Harcourt Teaching hospital, using fasting blood glucose.[9] Prevalence of diabetes in pregnancy was used because the performance of HBA1c was to be compared with that of the OGTT and fasting blood glucose which is a component of OGTT was used in that study which gave a prevalence of 23.6% in the Niger Delta.

$$n = \frac{(Z)^2 PQ}{d^2}$$

Where, n=sample size, Z=proportion of normal distribution corresponding to the required significance level (5%) which is 1.96, P=prevalence of GDM in the first trimester of pregnancy, Q=(1.00-P), d=precision of 0.05

$$n = \frac{(1.96)^2 \times 0.236 \times (1 - 0.236)}{(0.05)^2}$$
$$= \frac{3.8416 \times 0.236 \times 0.764}{0.0025} = 277.06$$
$$= 277$$

Attrition rate was considered to be 10% (28), to give total sample size of 305.

Data analysis and presentation

The socio-demographic, clinical and the blood tests results of the patients were entered into an Excel file cleaned and then uploaded onto the Statistical Package for Social Sciences (SPSS) version IBM SPSS Statistics 28.0.1, 2021 for analysis.

Data were presented in prose format, frequency distribution tables, and charts as appropriate. Quantitative

variables were summarized using means and standard deviation while qualitative variables were expressed as frequencies and proportions.

The usefulness of history of risk factors for GDM and HBA1c as screening tools for diabetes mellitus in the first trimester of pregnancy, using OGTT as the gold standard was assessed using validity tests of sensitivity, specificity, positive and negative predictive values.

$$\text{Sensitivity} = \frac{\text{True Positive}}{\text{True Positive} + \text{False Negative}} \times 100$$

$$\text{Specificity} = \frac{\text{True Negative}}{\text{True Negative} + \text{False Positive}} \times 100$$

$$\text{Positive Predictive Value (PPV)} = \frac{\text{True Positive}}{\text{True Positive} + \text{False Positive}} \times 100$$

$$\text{Negative Predictive Value (NPV)} = \frac{\text{True Negative}}{\text{True Negative} + \text{False Negative}} \times 100$$

Receiver operating characteristic curve for the determination of the accuracy of HBA1c as a screening tool for GDM, using OGTT as the gold standard for diagnosis

The test results of HBA1c and that of OGTT were obtained as continuous values and require a process of conversion and interpretation into a dichotomous form to determine the presence of diabetes. The receiver operating characteristic curve (ROC) curve was used to assess the diagnostic accuracy of HBA1c by comparing its results with those of the gold standard OGTT in the diagnosis of diabetes (Figure 4).

The ROC curve was created by plotting the sensitivity on the Y-axis and 1 minus specificity on the X-axis for various cut points of HBA1c as a diagnostic criterion for diabetes with the OGTT as the goal standard. The cut point was used to determine the diagnostic results, e.g., positive or negative, diseased or healthy.[10]

Determination of the optimal cut off point of HBA1c in the diagnosis of diabetes in the first trimester using the Youden index

The Youden index is a summary measurement of the receiver operating characteristic (ROC) curve for the accuracy of a diagnostic test with ordinal or continuous endpoints (Figure 5). The range of the cut point on the ROC is generally from -1 to +1. It is of interest to find the optimal cut point to increase the accuracy of a diagnostic test.[11]

The Youden Index (J) is a well-known tool for the ROC curve to measure the clinical diagnostic ability of a test.[12]

$$J = Max[Sen(c) + Spe(c) + 1]$$

Where, c is the cut point.

Diagnostic tests with higher J values would be preferable. The Youden index is an optimal trade-off between sensitivity and specificity with an equal weight being assigned to sensitivity and specificity. For a given total sample sizes in the diseased group and the non-diseased group, the optimal cut point would determine the maximum number of subjects being correctly diagnosed. Although the theoretical range of the Youden Index is from -1 to 1, the practical range in use is often from 0 to 1 since negative values of the Youden Index do not have meaningful interpretation in practice. J=1 represents a prefect diagnostic test and J=0 indicates that the diagnostic test is not effective to determine the disease status.

Validation of the usefulness of HBA1c and multiple logistic regression involving the screening tools (risk factors and HBA1c) and OGTT

HBA1c was validated in the diagnosis of diabetes against the gold standard OGTT. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPP) of HBA1c were calculated as were done when risk factors were validated as seen above. Multivariate logistic regression analysis was carried out using OGTT as the dependent variable and the screening tools (history of risk factors for GDM and HBA1C) as the independent variable. Confidence intervals in statistical analyses were set at 95% level and a $p<0.05$ was considered statistically significant.

Ethical consideration

Ethical approval for the study was obtained from the Research Ethics Committee of the University of Port Harcourt Teaching Hospital. The ethical clearance certificate number was UPTH/ADM/90/S.II/VOL.XI/902. All participating pregnant women were adequately counselled and a written consent from each patient was obtained before enrolment. The study was carried out under strict confidentiality.

RESULTS

Socio-demographic characteristics

Three hundred and fifteen (315) patients were recruited for the study. Ten patients were left out because they could not continue with oral glucose tolerant test. Details of the socio-demographic characteristics of the participants are shown in Table 1 and Figure 1.

Summary of the results of the oral glucose tolerance test among the study population

The result was as shown in Table 2 and Figure 2 and 3. Using only the fasting blood glucose (FBG) as a diagnostic criterion, 83 (27.2%) and 7 (2.35) out of the 305 participating patients were diagnosed with gestational and pre-gestational DM respectively. With 1 hr and 2 hr plasma glucose, only 6 new cases of abnormal glycaemia were added to the already diagnosed abnormal cases that were picked up, using fasting plasma glucose (FPG) as a diagnostic criterion- 5 cases of GDM and I case of pregestational diabetes. Therefore out of the total 305 study population the prevalence of diabetes was 83+5=88 (28.85%), 7+1=8 (2.62%) and 88+8=96 (31.48%) patients for GDM, pre-gestational and for both respectively.

Distribution of risk factors for GDM among the pregnant women in the study

Table 3 shows the risk factors for GDM; 8.9% had family history of DM, 1.3% had previous history of unexplained still birth, 43.3% were obese and 7.2% had previous macrosomic babies (fetal weight≥4 kg). Among the study participants, 168 (55.1%) women had at least one risk factor for GDM.

Validity tests for history of any of the risk factors for GDM as a predictor for GDM among the participants

Tables 4 show the results of the validity tests for the risk factors as screening tools for GDM, using OGTT as a gold standard for diagnosis. The sensitivity, specificity, PPV and NPV were calculated using OGTT as the gold standard. History of any of the positive risk factor for GDM in Table 4 had highest sensitivity of 87.5%, the specificity of 13.9%, PPV- 31.8% and NPV was 70.7%.

$$Sensitivity = \frac{True\ Positive}{True\ Positive + False\ Negative} \times 100$$

$$Sensitivity = \frac{84}{84 + 12} = 87.5\%$$

$$Specificity = \frac{True\ Negative}{True\ Negative\ +\ FalsePositive} \times 100$$

$$Specificity = \frac{29}{29 + 180} = 13.9\%$$

$$Positive\ Predictive\ Value\ (PPV) = \frac{True\ Positive}{True\ Positive + False\ Positive} \times 100$$

$$PPV = \frac{84}{84 + 180} = 31.8\%$$

$$Negative\ Predictive\ Value\ (NPV) = \frac{True\ Negative}{True\ Negative\ +\ False\ Negative} \times 100$$

$$NPV = \frac{209}{209 + 12} = 70.7\%$$

In Table 5, which shows the validity tests for all the risk factors for GDM as predictors of GDM using OGTT as a gold standard, obesity was associated with the highest sensitivity of 46.9%, and NPV of 75.1% but the specificity and PPV were 58.0% and 28.8% respectively.

ROC for the determination of the accuracy of HBA1c as a screening tool for GDM, using OGTT as the gold standard for diagnosis of GDM

The ROC curve used to assess the diagnostic accuracy of HBA1c by comparing results with those of the gold standard OGTT in the diagnosis of DM (Figure 4) showed the AUC of 0.655 (95% CI: 0.59-0.72, p=0.001), which was considered to be meaningful since it was greater than 0.5.

Determination of the optimal cut off point of HBA1c in the diagnosis of diabetes in the first trimester using the Youden index

The Youden index=0.250; the optimal cut off for HBA1c was therefore determined as 5.25% (Figure 5).

Validation of HBA1c in the diagnosis of diabetes against the gold standard OGTT

The sensitivity, specificity, PPV and NPP of HBA1c when validated against the gold standard OGTT in the diagnosis of diabetes were 36.5%, 88.5%, 59.3% and 75.2% respectively (Table 6). The optimal cut-off value for predicting GDM was 5.25%; that was gotten from the Youden index (Figure 5). Using the new cut-off this means that HbA1c could be used to screen out the true negative cases thereby reducing the number of people that will progress to do OGTT.

$$\text{Sensitivity} = \frac{\text{True Positive}}{\text{True Positive} + \text{False Negative}} \times 100$$

Sensitivity=35=36.5%

35+61

$$\text{Specificity} = \frac{\text{True Negative}}{\text{True Negative} + \text{False Positive}} \times 100$$

$$\frac{185}{185 + 25} = 88.5\%$$

$$\text{PPV} = \frac{\text{True Positive}}{\text{True Positive} + \text{False Positive}} \times 100$$

$$PPV = \frac{35}{35+24} = 59.3\%$$

$$\text{Negative Predictive Value (NPV)} = \frac{\text{True Negative}}{\text{True Negative} + \text{False Negative}} \times 100$$

$$NPV = \frac{185}{185+6} = 75.2\%$$

A mmultivariate logistic regression was done using OGTT as the dependent variable and the screening tools (history of risk factors for GDM and HBA1C) as the independent variables. It showed that HBA1c levels was the only independent predictor of abnormal OGTT ($p<0.05$).

Those with abnormal HBAIc were five times more likely to have abnormal OGTT than those with normal HBA1c (OR: 5.076, 95% CI: 2.71-9.51) as shown in Table 7.

Table 1: Socio-demographic and anthropometric characteristics of the participants in the first trimester.

Variables (N=305)	N	%
Age category (years)		
≤24	19	6.2
25-29	95	31.1
30-34	124	40.7
35-39	57	18.7
≥40	10	3.3
Marital status		
Single	6	2.0
Married	294	96.4
Separated/divorced	5	1.6
Educational level		
Secondary	45	14.8
Tertiary	260	85.2
Employment status		
Unemployed	52	17.0
Employed	253	83.0
Smoking		
Yes	0	0.0
No	305	100.0
Alcohol intake		
Yes	23	7.5
No	282	92.5
BMI		
Underweight	1	0.3
Normal	51	16.7
Overweight	131	39.7
Class I	94	30.8
Class II	24	79
Class III	14	48

Table 2: Summary of the results of oral glucose tolerance test among the pregnant women in their first trimester.

Time interval	Blood glucose (mmol/l)	
	Mean±SD	Median (range)
Zero hour (fasting blood glucose)	4.83±0.98	4.70 (3.20-13.80)
One-hour	7.80±1.88	7.70 (3.80-19.80)
Two-hour	6.46±1.58	6.20 (2.40-19.80)

Table 3: Distribution of risk factors for GDM among the pregnant women in the study.

Variables (N=305)	N	%
Family history of DM		
Yes	27	8.9
No	278	91.1

Continued.

Variables (N=305)	N	%
Previous history of unexplained stillbirth		
Yes	4	1.3
No	301	98.7
Previous history of delivery of baby ≥4 kg		
Yes	22	7.2
No	283	92.8
History of glycosuria		
Yes	9	3.0
No	296	97.0
Maternal age above 40 years		
Yes	3	1.0
No	302	99.0
BMI ≥30.0 kg/m^2		
Yes	132	43.3
No	173	56.7
Recurrent UTI/candidiasis		
Yes	26	8.5
No	279	91.5
History of GDM in previous pregnancy		
Yes	1	0.3
No	304	99.7
History of any of the risk factors for DM		
Yes	264	86.56
No	41	13.44

Table 4: Validity tests for history of any of the risk factors for GDM as a predictor for GDM (OGTT) among women in their first trimester of pregnancy.

History of any of the risk factors for GDM (screening test)	OGTT (gold standard)		
	GDM	**No GDM**	**Total**
Positive	84 True positive	180 False positive	264
Negative	12 False negative	29 True negative	41
Total	96	209	305

Table 5: Validity tests for all the risk factors for GDM as a predictor for GDM (OGTT) among the participants.

Risk factors	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Family history of diabetes mellitus	9.4	91.4	33.3	68.7
Previous history of unexplained still birth	2.1	99.0	50.0	68.8
Previous history of delivery of big baby (≥4 kg)	8.3%	93.3	36.4	68.9
Previous history of glycosuria	4.2	97.6	44.4	68.9
Maternal age above 40 years	2.1	99.5	66.7	68.9
BMI≥30 kg/m^2	46.9	58.0	28.8	75.1
History of recurrent UTI	7.3	90.9	26.9	68.1
GDM in previous pregnancy	0.0	99.5	0.0	68.4

Table 6: Validity tests for HbA1c category as a predictor for GDM (OGTT) among women in their first trimester of pregnancy.

HbA1c category from test results	OGTT (gold standard)		
	GDM	**No GDM**	**Total**
GDM (>5.25%)	35 True positive	24 False positive	59
No GDM (≤5.25%)	61 False negative	185 True negative	246
Total	96	209	305

Table 7: Multiple logistic regression showing predictors of GDM (OGTT) among women in their first trimester of pregnancy.

Factors	Coefficient(B)	Odds ratio (OR)	95% CI	p-value
Family history of DM				
Yes	0.352	1.422	0.47-4.28	0.532
No [R]		1		
Previous history of unexplained stillbirth				
Yes	0.735	2.085	0.25-	17.70
No [R]		1		
Previous history of delivery of baby≥4 kg				
No	0.054	1.056	0.35-3.19	0.923
Yes [R]		1		
Previous history of glycosuria				
No	0.200	1.221	0.25-5.89	0.804
Yes [R]		1		
BMI ≥30.0 kg/m^2				
Yes	0.512	1.669	0.51-5.45	0.396
No [R]		1		
History of recurrent UTI				
No	0.813	2.254	0.61-8.35	0.224
Yes[R]		1		
History of any of the risk factors for GDM				
No	0.484	1.623	0.44-5.94	0.464
Yes [R]		1		
HbA1c level				
Abnormal	1.624	5.076	2.71-9.51	0.0001*
Normal[R]		1		

Note: *-Statistically significant, R=ratio.

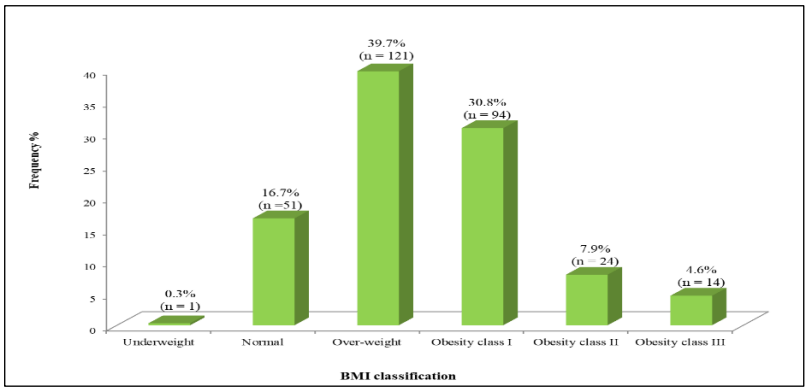

Figure 1: BMI classification of the pregnant women.

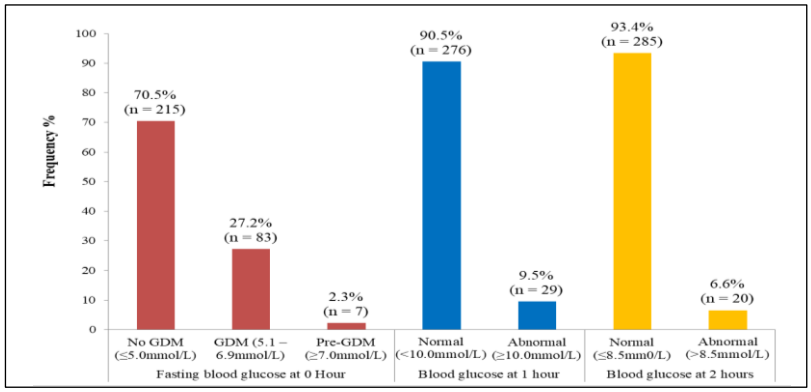

Figure 2: Distribution of blood glucose levels at different time intervals among the participants.

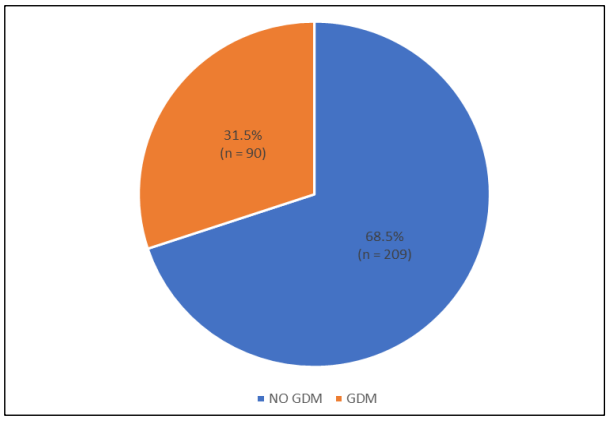

Figure 3: The prevalence of GDM among pregnant women in their first trimester.

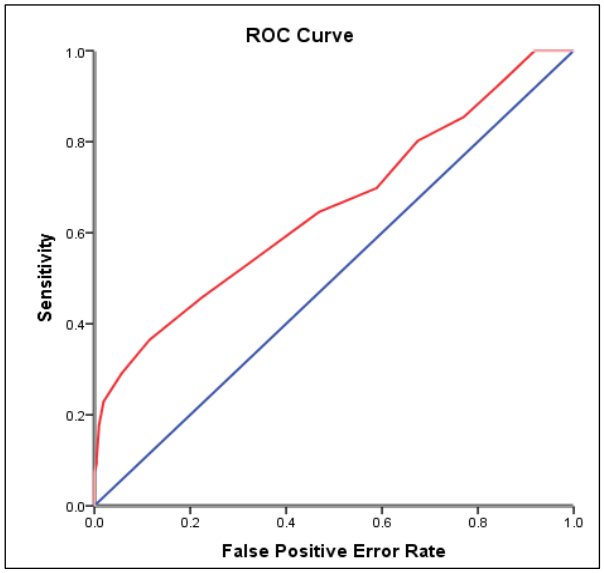

Figure 4: Receiver operating characteristics (ROC) curve for HbA1c in predicting GDM among women in their first trimester of pregnancy.

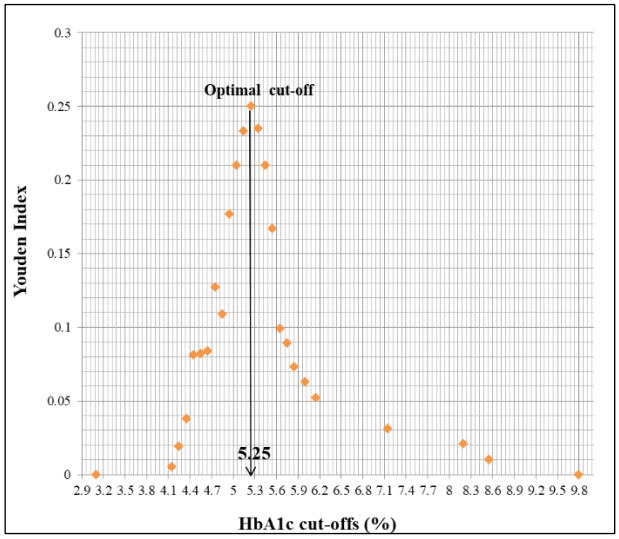

Figure 5: Determination of optimal cut off point for HbA1c from Youden index.

DISCUSSION

The study was prompted by the high prevalence of diabetes in the Niger Delta as demonstrated in the previous studies that were carried out in the same tertiary health facility where the present study was executed.[3,5,13,14]

The prevalence of 31.5% for diabetes mellitus in pregnancy found in the present study using the gold standard OGTT was closer to the prevalence of 23.6% noted in the previous one where fasting blood glucose only was used but higher than the findings from other studies in the same centre.[5,13,14] It was also higher than the prevalence of 4.8% recorded in Jos Nigeria, United States (14 %), China (6.8% and 10.4%) but similar to 27.5% recorded in India.[15-17] The findings were also in contrast to those of the IADPSG 2010 review of HAPO study.[18,19]

Therefore, early screening, diagnosis of the disorder and offering a suitable and adequate care to women who had DM early in pregnancy could largely impact on maternal and perinatal morbidity and mortality. It would also help in arresting the increase in the prevalence of the disorder in children delivered by mothers with diabetes mellitus and also in their future generations.[20]

Out of the total 305 study population, 264 patients had risk factors for gestational diabetes while 41 did not. Family history of diabetes was identified in 27 (8.9%) patients and that was lower than 29.3% found in another study.[21] Obesity was found in the highest number of patients 132(43.3%) while history of any of the risk factors for GDM was found in 264 patients (86.56%); this could be one of the reasons responsible for the high prevalence of GDM in the study population. Previous history of delivery of macrosomic babies (≥4 kg) was found in 7.2%, patients; that was similar to 10% that was recorded in one previous study.[22] Recurrent UTI/candidiasis were registered in 26 (8.5%) and history of glycosuria in 9 (3%) patients.

Regarding the presence of any of the risk factors, although the sensitivity for predicting GDM was high at 87.3%, the specificity was only 13.9% and the PPV and the NPP were 31.8% and 70.7% respectively. It can therefore not be used for screening women that are likely to develop diabetes in pregnancy. However, considering the risk factors on their individual merits, the moderately high NPV and high specificity exhibited associated with them showed that they could be used to predict those who did not have GDM and are therefore useful as a tool for screening for GDM. They could not be used for diagnostic purposes since they had low sensitivity and PPV.

A non-pregnancy threshold for HBA1c of 6.5% (48 mmol/mol) could not be recommended in pregnancy. Applying an HbA1c threshold of 48mmol/mol (6.5%) led to missed diagnosis in 47% of the women. Its levels might be affected by a variety of genetic, haematological and illness-related factors.[23] The ROC curve for HbA1c showed a significant area under the Curve (AUC) value of

0.655 (95% CI: 0.59-0.72, p=0.001) which was considered to be meaningful since it was greater than 0.5 but it was generally interpreted as 'poor'.[24] Therefore, HBA1c was not as good as the OGTT for diagnosing diabetes in pregnancy. The result was similar to the AUC obtained for ROC curve in other studies were they were 0.649 and 0.679 respectively.[25,26] It was however lower than 0.852 and 0.98 that were obtained from other studies, the last been for IADPSG study.[19,27] In a large observational study in early pregnancy, the optimal HbA1c for diagnosis of diabetes in pregnancy , using the IADPSG OGTT criteria before 20 weeks was 41 mmol/mol (5.9%).[5] The same HbA1c threshold detected all cases of diabetes and was highly specific 98.4% (95% CI 97-99%) for early GDM.

In the present study, the Youden index was 0.250; the optimal cut off point for HBA1c in the diagnosis of diabetes in pregnancy was therefore determined to be 5.25%. Using the optimal cut-off point of 5.25% that was determined by Youden index in the present study, the sensitivity, specificity, the PPV and the NPV of HbA1c levels against the Gold standard OGTT in the diagnosis of GDM were 36.5%, 88.5%, 59.3%, 75.2% respectively. HbA1c did not have adequate sensitivity and PPV for diagnosis of GDM but it had high specificity and moderately high NPV. It could not replace the gold standard OGTT in the diagnosis of GDM. A negative result will however screen out women that were unlikely to develop GDM in pregnancy, thereby reduce the number of women that would proceed to do OGTT. That means that any pregnant woman with an HbA1c level less that 5.25% in early pregnancy was unlikely to have GDM in the index pregnancy. On the other hand, any pregnant woman with HbA1c of 5.25% and above in the first trimester would have to do the confirmatory test OGTT for GDM diagnosis.

The optimal cut-off value and the NPV recorded in this study were similar to the values that were obtained in previous studies.[28] The sensitivity of 36.5% was in contrast with 63.9% that was recorded by Soumya et al.[28] The differences in sensitivity and specificity might be due to the difference in the prevalence of the disease, differences in diagnostic criteria, screening approach and study design. In addition, the HbA1c assay had not been well standardized in many countries; variety of factors namely genetic, haematological and illness-related factors affect its assay.[23] More studies need to be conducted with correction for those factors that affects the levels of HBA1c.

A multiple logistic regression was carried out to predict the contribution of each of the risk factors for GDM to its diagnosis and to build a logistic regression model to predict the disease. HBA1c estimation was the only independent predictor of abnormal OGTT (p<0.05). Those with abnormal HBAIc were five times more likely to have abnormal OGTT than those with normal HBA1c. This was in contrast with the findings in one previous study where the maternal risk factors had high predictive value in the diagnosis of GDM.[29] The findings in the previous study may have differed from the findings in the present study due to the different diagnostic criteria, difference in study design and screening approach adopted. The present study was done in first trimester using current WHO 2013 criteria and involved the universal screening of women and was carried out in two tertiary centres while the previous study was a multicentre study.

Limitations

This study was carried out between January and June 2020 at the peak of COVID-19 pandemic and therefore some patients could not attend antenatal clinic during the lockdown as movement was restricted. That delayed the work so much that it was stretched beyond June. The study was carried out in tertiary institutions and therefore those in the rural areas were not captured. Many of the pregnant women registered for antenatal care late, mostly in the second and third trimester; that also affected the recruitment of patients into the study.

CONCLUSION

The high prevalence of diabetes in the first trimester of 31.5% underscored the urgent need for universal screening of pregnant women early in pregnancy so that timely diagnosis could be made and treatment initiated. The moderately high NPV and high specificity exhibited by the risk factors for GDM and HBA1c levels in the first trimester of pregnancy showed that they could be used to predict those who did not have GDM but they could not be used for diagnostic purposes. The area under the ROC curve (AUC) for HBA1c was 0.653%, 95% CI=0.59-0.72, p=0.001. The Youden index was 2.50 and the optimal cut off for HBA1c for diagnosis of diabetes was 5.25%. On multiple logistic regression analysis, HBA1c (not risk factors for GDM) was the only independent predictor of abnormal OGTT (p<0.05).

ACKNOWLEDGEMENTS

Authors are thankful to all patients, staff members and Lecturers of department of Obstetrics and Gynaecology, Rivers State University Teaching Hospital and University of Port Harcourt Teaching Hospital who participated in the study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2011;34(1):S62-9.

2. Diagnostic criteria and classification of hyperglycaemia first detected in pregnancy: a World Health Organization Guideline. Diabetes Res Clin Pract. 2014;103(3):341-63.
3. Chinenye S, Ogu R, Korubo I. Diabetes advocacy and care in Nigeria: A review. Nigerian Health J. 2015;15(4):145-50.
4. Chodick G, Elchalal U, Sella T, Heymann AD, Porath A, Kokia E, etal. The risk of overt diabetes mellitus among women with gestational diabetes: a population-based study. Diabet Med. 2010;27(7):779-85.
5. Abbey M, Kasso T. First trimester fasting blood glucose as a screening tool for diabetes mellitus in a teaching hospital setting in Nigeria. Asian J Med Health. 2018;10(4):1-9.
6. Berger H, Crane J, Farine D, Armson A, De La Ronde S, Keenan-Lindsay L, et al. RETIRED: Screening for gestational diabetes mellitus. J Obstet Gynaecol Can. 2002;24(11):894-912.
7. Keely E, Berger H, Feig DS, Diabetes Canada Clinical Practice Guidelines Diabetes in Pregnancy Expert Committee. New Diabetes Canada Clinical Practice Guidelines for Diabetes and Pregnancy - What's Changed? J Obstet Gynaecol Can. 2018;40(11):1484-9.
8. Bell R, Glinianaia SV, Tennant PW, Bilous RW, Rankin J. Peri-conception hyperglycaemia and nephropathy are associated with risk of congenital anomaly in women with pre-existing diabetes: a population-based cohort study. Diabetologia. 2012.
9. Anaka O, Houlihan C, Beim R, Ranzini AC. Does first-trimester hemoglobin A1C predict gestational diabetes and fetal outcome?. Obstet Gynaecol. 2014;123(1):S38-9.
10. Kumar R, Indrayan A. Receiver operating characteristic (ROC) curve for medical researchers. Indian Pediatr. 2011;48(4):277-87.
11. Schisterman EF, Perkins N. Confidence Intervals for the Youden Index and Corresponding Optimal Cut-Point. Commun Stat Simul Comp. 2007;36:549-63.
12. Youden WJ. Index for rating diagnostic tests. Cancer. 1950;3(1):32-5.
13. Chinenye S. Living with diabetes in Nigeria: the cure and prevention. An inaugural lecture series in University of Port Harcourt. 2015;126.
14. Chinenye S, Ogu R, Korubo I. Diabetes advocacy and care in Nigeria: A review. Nigerian Health J. 2015;15(4):145-50.
15. Anzaku AS, Musa J. Prevalence and associated risk factors for gestational diabetes in Jos, North-central, Nigeria. Arch Gynecol Obstet. 2013;287(5):859-63.
16. Bhattacharyya OK, Shah BR, Booth GL. Management of cardiovascular disease in patients with diabetes: the 2008 Canadian Diabetes Association guidelines. CMAJ. 2008;179(9):920-6.
17. Guariguata L, Linnenkamp U, Beagley J, Whiting DR, Cho NH. Global estimates of the prevalence of hyperglycaemia in pregnancy. Diabetes Res Clin Pract. 2014;103(2):176-85.
18. HAPO Study Cooperative Research Group; Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, et al. Hyperglycemia and adverse pregnancy outcomes. N Engl J Med. 2008;358(19):1991-2002.
19. International Association of Diabetes and Pregnancy Study Groups Consensus Panel; Metzger BE, Gabbe SG, Persson B, Buchanan TA, Catalano PA, et al. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care. 2010;33(3):676-82.
20. Roura LC, Arulkumaran SS. Facing the noncommunicable disease (NCD) global epidemic--the battle of prevention starts in utero--the FIGO challenge. Best Pract Res Clin Obstet Gynaecol. 2015;29(1):5-14.
21. Syngelaki A, Pastides A, Kotecha R, Wright A, Akolekar R, Nicolaides KH. First-Trimester Screening for Gestational Diabetes Mellitus Based on Maternal Characteristics and History. Fetal Diagn Ther. 2015;38(1):14-21.
22. Berger H, Crane J, Farine D, Armson A, De La Ronde S, Keenan-Lindsay L, et al. RETIRED: Screening for gestational diabetes mellitus. J Obstet Gynaecol Can. 2002;24(11):894-912.
23. Gallagher EJ, Le Roith D, Bloomgarden Z. Review of hemoglobin A(1c) in the management of diabetes. J Diabetes. 2009;1(1):9-17.
24. Nahm FS. Receiver operating characteristic curve: overview and practical use for clinicians. Korean J Anesthesiol. 2022;75(1):25-36.
25. Amadi SC, Ogu RN, Odum E, Ojule J, Enyindah CE, Ugboma HAA. Effectiveness of Glycated Haemoglobin in the Diagnosis of Gestational Diabetes Mellitus among Pregnant Women in Port Harcourt, Nigeria. Nigerian Med J. 2022;62(4):171-7.
26. Benaiges D, Flores-Le Roux JA, Marcelo I, Mañé L, Rodríguez M, Navarro X, et al. Is first-trimester HbA1c useful in the diagnosis of gestational diabetes? Diabetes Res Clin Pract. 2017;133:85-91.
27. Ryu AJ, Moon HJ, Na JO, Kim YJ, Kim SJ, Mo SI, et al. The Usefulness of the Glycosylated Hemoglobin Level for the Diagnosis of Gestational Diabetes Mellitus in the Korean Population. Diabetes Metab J. 2015;39(6):507-11.
28. Soumya S, Rohilla M, Chopra S, Dutta S, Bhansali A, Parthan G, Dutta P. HbA1c: A Useful Screening Test for Gestational Diabetes Mellitus. Diabetes Technol Ther. 2015;17(12):899-904.
29. Syngelaki A, Pastides A, Kotecha R, Wright A, Akolekar R, Nicolaides KH. First-Trimester Screening for Gestational Diabetes Mellitus Based on Maternal Characteristics and History. Fetal Diagn Ther. 2015;38(1):14-21.

Cite this article as: Jaja MA, Abbey M, Oloyede OA, Kua PA, Amadi SC, Kasso T, et al. Assessment of risk factors and glycosylated haemoglobin in early pregnancy as predictors of diabetes in pregnancy. Int J Reprod Contracept Obstet Gynecol 2024;13:505-14.