



Original Article

Assessment of Fructosamine and Corrected Fructosamine as A Screening Test for Gestational Diabetes Mellitus

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ABSTRACT

Background: The prevalence of Gestational Diabetes Mellitus (GDM) is on the increase, and screening with Oral Glucose Tolerance Test (OGTT) is time consuming. Fructosamine offers an alternative in its simplicity and can be assayed anytime of the day compared to OGTT. This study aimed to evaluate serum fructosamine and corrected fructosamine usefulness in detecting GDM. **Method:** This was a cross-sectional study which included 160 pregnant women. recruited from the antenatal clinic of Federal Medical Centre, Makurdi. Plasma glucose, serum fructosamine and serum total protein assays were assessed. Diagnosis of GDM was made using World Health Organization (WHO) 2013 diagnostic criteria. **Results:** Majority of the participants 130 (81.3%) had normal blood glucose levels while those with GDM were 25 (15.6%) and Diabetes in Pregnancy (DIP) were 5 (3.1%). The mean (SD) fructosamine was higher in women with GDM [223.6 (17.6) $\mu\text{mol/L}$] compared to women without GDM [217.9 (15.0) $\mu\text{mol/L}$], however, this difference was not statistically significant, $p = 0.091$. Also, the mean (SD) corrected fructosamine was slightly higher in women with GDM [254.9 (19.1) $\mu\text{mol/L}$] compared to women without GDM [251.2 (22.3) $\mu\text{mol/L}$]. This difference was also not statistically significant, $p = 0.435$. Receiver Operator Characteristics of Fructosamine and Corrected Fructosamine to detect GDM, the Area under the curve (AUC) for fructosamine and corrected fructosamine were 0.584 and 0.594 respectively. Suggesting that they may not be good markers for detecting GDM.

Conclusion: Serum fructosamine and corrected fructosamine have limited use as a screening tool for GDM.

Keywords: Gestational Diabetes Mellitus, Hyperglycaemia in pregnancy, Diabetes in pregnancy, Fructosamine,

INTRODUCTION

Hyperglycaemia is a common medical condition seen in pregnancy.¹ It could be due to diabetes in pregnancy

2) antedating pregnancy, or diabetes first diagnosed during pregnancy but satisfies the World Health Organization (WHO) criteria for a non-pregnant state.¹ GDM has been defined as any degree of glucose intolerance with first onset or recognition in pregnancy. It could occur at any time in pregnancy but most likely after 24 weeks of gestation.¹⁻⁴

The occurrence of GDM in a given population parallels the prevalence of Impaired Glucose Tolerance (IGT), obesity and type 2 diabetes mellitus (T₂DM).¹ Worldwide, these conditions are on the rise.¹ Child bearing age is on the increase while the age of onset of diabetes mellitus and pre-diabetes mellitus is decreasing.¹

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(DIP) or gestational diabetes mellitus (GDM).^{1, 2} DIP may either have been pre-existing diabetes (type 1 or type

Hence, more women becoming pregnant will have risk factors for hyperglycaemia in pregnancy.¹

The International Diabetes Federation (IDF) estimates that out of 100 pregnancies with hyperglycaemia, 16% are due to DIP while the majority, 84%, are due to GDM.^{1, 5} There is a wide variation in global GDM prevalence rates which may be related to ethnic heterogeneity among different population as well as different screening and diagnostic criteria used. This gives a wide range of GDM prevalence ranging from 1-28% globally.^{1, 6} A study in Nigeria has put the prevalence of GDM to be up to 11.6% depending on the diagnostic criteria used and suggested a rise in the incidence with the global trend.⁷

GDM is associated with increased incidence of maternal and foetal morbidity, including spontaneous abortion, pre-eclampsia, caesarean delivery and future overt diabetes mellitus. Foetal complications include macrosomia, congenital abnormalities, still birth, neonatal death, and higher risk of obesity, IGT and future overt diabetes mellitus.^{1, 3, 4, 8}

There is great emphasis on screening for GDM during antenatal care to facilitate early diagnosis and management of GDM to prevent the associated complications.^{1, 5, 6, 7, 9, 11-13} Oral Glucose Tolerance Test (OGTT) has been widely used for this screening. Its reliability has however been questioned and the lengthy procedure, non-compliance from patients have further hampered its routine use.^{14, 15}

Some studies indicate that the 50g 1-hour Glucose Challenge Test is sensitive for GDM screening while others have reported a poor performance. Thus, GCT has not been universally accepted.¹⁵ Fasting blood glucose (FBG) and Random Blood Glucose (RBG) are commonly used for pre-screening of GDM.^{16, 17}

Glycated proteins [glycated haemoglobin (HbA_{1c}) and glycated albumin (Fructosamine)] have been used to monitor glucose control. HbA_{1c} assesses glucose control over the preceding 8-12 weeks and is affected by recent blood loss, haemolytic anaemia or haemoglobinopathies such as sickle cell anaemia.¹⁵ Fructosamine assesses glucose control over a shorter term of 2-3 weeks and is more sensitive in conditions like pregnancy where hormonal changes cause greater short-term fluctuations in blood glucose levels.¹⁵

The commonly used screening method is OGTT using 100g or 75g glucose, which involves obtaining 3-4 blood samples at specified time points. This is further complicated by variable diagnostic criteria in use, and time spent by the women staying at the clinic or laboratory for several hours.¹⁸ There is a need for a simple one sample test with good specificity and sensitivity that would encourage patients' compliance. The fact that fructosamine assesses glucose control over a shorter period and can be sampled at any time of the day makes it a good preposition as an alternative marker

of hyperglycaemia in pregnancy. However, the use of fructosamine as a screening tool for GDM has not been well studied and local studies to determine the correlations with glucose levels in pregnancy are rare. This study is aimed at providing data concerning the clinical utility of fructosamine in pregnancy in Nigerian pregnant women.

MATERIALS AND METHODS

Background Of the Study Area

This study was conducted at the Federal Medical Centre, located in Makurdi, the capital city of Benue State. The city is cosmopolitan with nearly all ethnic groups and social classes replicating the Nigerian society.

Study Population

The study population included pregnant women visiting the antenatal clinic of Federal Medical Centre, Makurdi which holds on Mondays, Wednesdays and Fridays.

Study Design

This study was a cross-sectional study and recruited pregnant women consecutively after obtaining consent, who booked before 28 weeks of pregnancy at the antenatal clinic of the Federal Medical Centre, Makurdi.

Inclusion Criteria

This included consenting pregnant women who booked before 28 weeks of gestation dated by either the last menstrual period (LMP) or ultrasonography.

Exclusion Criteria

- i. Pregnant women whose first antenatal visit is after 28 weeks of gestation.
- ii. Pregnant women with pre-gestational diabetes (known to have DM before pregnancy).
- iii. Age younger than 18 years.
- iv. Multiple gestation.
- v. Pregnant women on drugs that affect glucose metabolism such as steroids, β -Adrenergic blockers and thiazide diuretics.
- vi. Patients with suspected plasma cell dyscrasias
- vii. Chronic liver or kidney disease patients.
- viii. Pregnant women with hyperthyroidism.

Sample Size Determination

The sample size has been arrived at using Fisher's formula.

$$\text{Sample size (n)} = \frac{Z_{1-\alpha/2}^2 P(1-p)}{d^2}$$

Where $Z_{1-\alpha/2}$ = standard error = 1.96 at 5% type 1 error ($P < 0.05$)

P = Prevalence of GDM in North-Central Nigeria¹⁹ = 8.3% (0.083)

d = Absolute precision set by the researcher = 0.07 μmol/L

$$\text{Therefore, } n = \frac{(1.96)^2 \times 0.083 \times (1-0.083)}{0.05^2} \approx 120$$

A minimum of 120 was calculated. To enrich the study a total number of 160 participants were recruited for the study.

Study Procedure

Each study participant was administered a pre-tested questionnaire. The questionnaire was completed by the researcher or his trained assistant. It addressed sociodemographic factors such as age, weight, height, last menstrual period (LMP), and estimated gestational age (EGA) calculated from the LMP or by ultrasonography. The questionnaire also documented drug history and history of present or past illness that may interfere with the study as well as risk factors for GDM.

A 2-hour OGTT with 75g glucose load was carried out on all the subjects at 24-28 weeks of gestation and blood specimen obtained from the cubital vein for plasma glucose estimation at 0, 1 and 2 hours. The serum from the fasting specimen was used for analysis of fructosamine and serum total protein for calculating corrected fructosamine^{10,21}. The participants were grouped into two namely GDM, and Normoglycaemia based on the results obtained from the OGTT using 2013 WHO diagnostic criteria.

Five millilitres of venous blood was aseptically collected into fluoride oxalate vacutainer tubes from the cubital vein of each participant at 0hr, 1hr and 2hrs during the standard OGTT. Samples for fructosamine and total protein were collected at point 0hr into plain vacutainer tubes. The specimens were separated after centrifugation at 3000 rpm for 5 minutes, Plasma glucose and serum total protein estimation were assayed on the same day of sample collection. Serum for fructosamine was stored at -80°C²² until analysis within 3 months of collection,

Analysis of Blood Samples

Plasma samples were analysed for glucose using the hexokinase method, while serum samples were analysed for total protein using the biuret method and fructosamine

using the Nitroblue Tetrazolium Reaction estimation. All assays were analysed using the Roche/Hitachi (c) Cobas c311 automated, discrete, clinical chemistry analyser. Analytical accuracy and precision were assured by simultaneous analyses of pooled plasma and commercial quality control specimen, at low and high control ranges with each batch of samples from Cobas Roche Diagnostic GmbH, Sandhofer Strasse 116, D-68305 Mannheim, Germany.

Statistical Analysis

The data collected was analysed using Statistical Package for Social Sciences (SPSS® Incorporated Chicago Version 25.0) software for Descriptive statistics were presented as mean ± SD or medians with interquartile ranges (IQRs) for nonnormal continuous variables, and proportions (as percentages) for categorical variables. Mann-Whitney U test was used to test the difference in medians of continuous variables between groups and Chi-square and fisher's exact was used to test relationships among variables. A Receiver Operator Characteristics curve (ROC) was used to determine the sensitivity and specificity of fructosamine and corrected fructosamine for the prediction of GDM. The significance level was set at $p \leq 0.05$.

Ethical Consideration

This study was carried out after approval from the Ethical Committee of Federal Medical Centre, Makurdi was obtained. Permission was also sought from the Head of Department, Obstetrics and Gynaecology to allow the study on their patients. Informed consent was also obtained from all participants.

RESULTS

Characteristics Of Study Population

One hundred and sixty (160) pregnant women were recruited for the study, with mean ± SD age of 29.9(4.9) years. The mean (SD) gestational age at Oral glucose tolerance testing was 27.1(0.6) weeks. The mean (SD) Fasting glucose, 1-hour glucose and 2-hour glucose levels were 4.8(0.8) mmol/L, 7.2(1.9) mmol/L, 6.7(1.5) mmol/L respectively. The mean (SD) fructosamine and corrected fructosamine levels were 221.0(21.3) μmol/L and 253.7(25.4) μmol/L respectively. One hundred and thirty participants (81.3%) were found to have normal glucose tolerance following a 75g glucose load OGTT and using the 2013 WHO diagnostic criteria. Among pregnant women with abnormal glucose tolerance, 25

(15.6%) had GDM while 5 (3.1%) had DIP (see figure 1). Other clinical and biochemical indices of the study population are summarised in Tables 1 and 2.

Table 1: Clinical and Biochemical Indices of Study Population

Characteristics	Mean $\pm$ SD
Age (years)	29.9 $\pm$ 4.9
Gestational Age (weeks)	27.1 $\pm$ 0.6
Gravidity	3.1 $\pm$ 1.8
0-hour glucose (mmol/l)	4.8 $\pm$ 0.8
1-hour glucose (mmol/l)	7.2 $\pm$ 1.9
2-hours glucose (mmol/l)	6.7 $\pm$ 1.5
Fructosamine (μ mol/l)	221.0 $\pm$ 21.3
Corrected Fructosamine (μ mol/l)	253.7 $\pm$ 25.4
Total Protein (g/l)	63.1 $\pm$ 6.0

Table 2: Percentile of Fructosamine and corrected Fructosamine

	Fructosamine (μ mol/l)	Corrected Fructosamine (μ mol/l)
25 th Percentile	208.0	225.5
50 th Percentile	216.0	247.8
75 th Percentile	229.0	266.2
95 th Percentile	247.2	293.7

The mean (SD) gravidity, parity and weight were significantly higher in women with GDM compared to women without GDM. Fasting glucose ($p=0.003$), 1-hour glucose ($p=0.001$) and 2-hour glucose ($p=0.001$) were significantly higher in women with GDM compared to normoglycemic women. The mean (SD) fructosamine was higher in women with GDM [223.6 (17.6) μ mol/L] compared to normoglycemic women [217.9 (15.0) μ mol/L], however, this difference was not statistically significant, $p=0.091$. Also, the mean (SD) corrected fructosamine was slightly higher in women with GDM [254.9 (19.1) μ mol/L] compared to women without GDM [251.2 (22.3) μ mol/L]. This difference was also not statistically significant, $p=0.435$. This is shown in table 3.

The mean (SD) fructosamine levels were even much higher in women with DIP [289.9 (52.2) μ mol/L] compared to their normoglycemic counterpart [217.9 (15.0) μ mol/L] and this difference was statistically significant ($p=0.037$). The mean (SD) corrected fructosamine levels in women with DIP [313.9 (52.6) μ mol/L] was higher than among normoglycemic women [251.2 (22.3) μ mol/L], this difference though was not statistically significant ($p=0.055$).

Figure 1 shows Receiver Operator Characteristics of Fructosamine and Corrected Fructosamine to detect

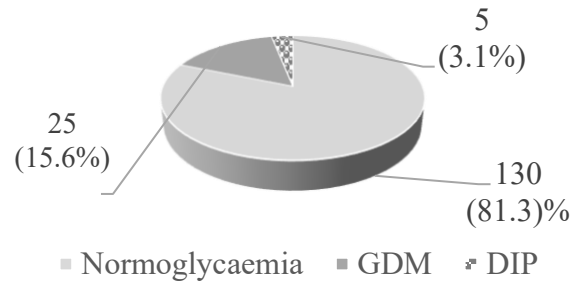


Figure 1: Pie Chart showing the Classification of Glycaemic status

GDM, the Area under the curve (AUC) for fructosamine and corrected fructosamine were 0.584 and 0.594 respectively

Table 3 shows the Sensitivity and specificity to detect GDM at selected cut-of values (representing selected percentiles). At 216.0 μ mol/L, the sensitivity, specificity of fructosamine to detect GDM for all participants was 84.0%, 28.5% respectively. At 247.2 μ mol/L, it was 12.0% and 96.9% respectively.

The sensitivity and specificity to detect GDM at selected cut-of values (representing selected percentiles). At 247.8 μ mol/L, the sensitivity and specificity of corrected fructosamine to detect GDM for all participants was 64.0%, and 54.6%, respectively. At 293.7 μ mol/L, it was 4.0% and 95.4% respectively. Table 11 summarises this.

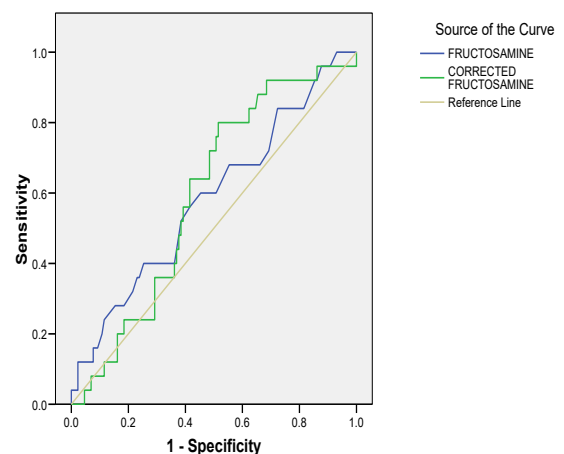


Figure 1: Receiver Operator Characteristics of Fructosamine and Corrected Fructosamine to predict GDM.

Table 3: Clinical and Biochemical Characteristics of GDM and Normoglycaemic participants

Variable	GDM n= 25	Normoglycaemia n=130	p- value
Age [years, mean (SD)]	31.5(4.8)	29.6(4.9)	0.065
Gestational Age [weeks, mean (SD)]	27.1(0.7)	27.1(0.5)	0.978
Gravidity mean (SD)	4.2(2.3)	2.8(1.6)	<0.001
Parity mean (SD)	2.1(1.8)	1.1(1.2)	0.001
Weight [Kg, mean (SD)]	84.9(14.4)	76.0(16.0)	0.011
Height [M, mean (SD)]	1.6(0.1)	1.6(0.1)	0.300
Fasting Glucose [mmol/L, mean (SD)]	5.4(0.5)	4.5(0.3)	<0.001
1 Hour Glucose [mmol/L, mean (SD)]	8.7(1.6)	6.7(1.0)	<0.001
2 Hour Glucose [mmol/L, mean (SD)]	7.7(1.2)	6.3(0.9)	<0.001
Total Protein [g/L, mean (SD)]	63.4(5.6)	62.9(6.2)	0.691
Fructosamine [μ mol/L, mean (SD)]	223.6(17.6)	217.9(15.0)	0.091
Corrected Fructosamine [μ mol/L, mean (SD)]	254.9(19.1)	251.2(22.3)	0.435

Table 3: Sensitivity and Specificity of Fructosamine and Corrected Fructosamine for Predicting GDM at selected cut-off values

Selected cut-offs (μ mol/L) {percentile}	Sensitivity (%)	Specificity (%)
Fructosamine		
208.0 {25 th }	84.0	28.5
216.0 {50 th }	60.0	52.3
229.0 {75 th }	32.0	78.5
247.2 {95 th }	12.0	96.9
Corrected Fructosamine		
225.5 {25 th }	96.0	8.5
247.8 {50 th }	64.0	54.6
266.2 {75 th }	24.0	75.4
293.7 {95 th }	4.0	95.4

DISCUSSION

The prevalence of GDM in this study was found to be 15.6% which falls within the global prevalence of 1-28%.^{1,6} This is higher than the prevalence in other parts of Nigeria of 11.6%⁷ in Ilorin, Nigeria by Prince et al and approximately twice the prevalence of 8.3% obtained in Jos in a study by Anzaku et al.¹⁹ Another study carried out in Jos by Imoh et al in 2015, reported a prevalence of 13.8%.¹³ The finding in this work is in keeping with the global trend of the increasing prevalence of GDM and

DM and can also be due to the lower cut-off values used in the 2013 WHO criteria for screening of GDM. It was 61%²³ in Nigeria and 84% globally^{1,5} according to International Diabetes Federation.

The mean $\pm$ SD of serum fructosamine values found in this study was 217.9 $\pm$ 15.0 μ mol/L and 223.6 $\pm$ 17.6 μ mol/L for those without GDM and those with GDM respectively. Huter et al²⁴ had a mean fructosamine of 172.0 $\pm$ 25 μ mol/L in those with GDM and 160.0 $\pm$ 15 μ mol/L in those without GDM. The mean serum fructosamine values in this study were higher but statistically insignificant when compared between those

with GDM and those without GDM. Haladu et al²⁵ in their study obtained a mean (SD) of corrected fructosamine to be 300.39 (123) $\mu\text{mol/L}$ and 337.39 (146) $\mu\text{mol/L}$ in pregnant women without GDM and pregnant women with GDM respectively. Their mean values were higher than the mean (SD) value of 251.2 (22.3) $\mu\text{mol/L}$ for normoglycaemic women and 254.9 (19.1) $\mu\text{mol/L}$ for GDM group in this study respectively. The distribution of fructosamine levels in this study was in keeping with findings in pregnancy in previous studies.

Fructosamine levels in non-pregnant healthy individuals was found to be within the reference limits of 195 $\mu\text{mol/L}$ to 285 $\mu\text{mol/L}$ depending on the method of assay and the studied population.^{26,27} In this study, the fructosamine values at the 2.5 and 97.5 percentiles of pregnant women in mid pregnancy with no risk factor for GDM were 175.6 and 261.7 $\mu\text{mol/L}$ respectively and this may represent the reference intervals for fructosamine in mid-pregnancy in a Nigerian population. This is similar to the range found in Caucasians (176-252 $\mu\text{mol/L}$) and in Asians (176-240 $\mu\text{mol/L}$).²⁶ These values are lower than the reference limits in the non-pregnant population.^{26,27}

In this study fructosamine is poorly correlated generally with glucose values in OGTT. This finding is corroborated by studies conducted by Huter et al²⁴ and Gingras et al²⁸ who reported poor correlation between fructosamine and glucose levels at OGTT. They, however, did not compensate for the falling fructosamine values with increasing gestational age which was as a result of falling total protein. Hughes et al considered this fall in fructosamine levels with increasing gestational age,²¹ where they obtained a sensitivity and specificity of 79.4% and 77.3% respectively.

Earlier research about fructosamine and GDM by Roberts et al²⁹ had shown good correlation between fructosamine and glucose values. Hughes et al²¹ corroborated this finding in his work using a second generation fructosamine corrected for total proteins. However, Robert et al³⁰ in a follow-up work published four years later found poor agreement of fructosamine with glycaemic status and concluded that fructosamine may not be a good screening tool for GDM as defined. These discrepancies in results obtained may be explained by methodological differences in the study design. The diagnostic criteria used by Roberts and Baker in the previous study detected severe forms of hyperglycaemia as gestational diabetes. The severe forms of glucose intolerance correlated better with fructosamine levels. Furthermore, more than 40 percent of the study participants with elevated glucose, had their fructosamine measured 8 weeks after the OGTT.³¹ This is unlike later studies including this one where GDM was diagnosed with lower glucose cut points and the fructosamine levels assessed at OGTT.

Although Nasrat et al³² found a poor correlation between fructosamine and glucose values generally, a

better correlation ($r=0.40$) between fructosamine and fasting glucose was found only in early pregnancy (< 20 weeks of gestation). Given that fructosamine levels falls as pregnancy progresses, it is plausible that higher fructosamine levels in early pregnancy may correlate better with hyperglycaemia in early pregnancy. Indeed, one reason for poor correlation of fructosamine and hyperglycaemia in pregnancy may be that proteins and therefore fructosamine predictably falls as pregnancy progresses, but this fall may be disproportional among pregnant women. This may weaken any expected correlation between fructosamine and hyperglycaemia.

This discordance between fructosamine and glucose values appears to be more pronounced at lower hyperglycaemic ranges which is likely in GDM as opposed to very high glycaemic ranges such as found in diabetes in pregnancy. This may explain why higher fructosamine and corrected fructosamine levels were found in women with DIP and why women with DIP had significantly higher fructosamine and corrected fructosamine compared to women with GDM and normoglycaemic women. Huter et al²⁴ found fructosamine to correlate only with post load glucose values more than 10 mmol/L at 2-Hour.

Although the fructosamine and corrected fructosamine were higher in women with GDM compared to normoglycaemic women, this difference was not statistically significant. Thus, at lower glycaemic levels, glycation of proteins as reflected by fructosamine levels does not show very good discriminatory ability between hyper and normoglycaemia. The implication of this is that the fructosamine may not provide sufficient discriminatory ability when used to screen for GDM. However, it may be better in detecting or differentiating DIP from GDM or normoglycaemia. This finding has been corroborated by the results in previous studies. Vermes et al³³ and Haladu and Yahaya²⁵ in a recent study in northern Nigeria did not find a significant difference in fructosamine levels in women with GDM and normoglycaemic women. However, earlier studies conducted by Khan et al¹⁴ had shown that corrected fructosamine was higher in pregnant women with very elevated hyperglycaemia compared to normoglycaemic women. A similar result was obtained in Thailand by Ayyappan et al.³⁴ In these two studies, random blood glucose was employed in their assessment and their mean RBG in the hyperglycaemic groups were 9.9 mmol/L and 12.7 mmol/L respectively.^{14, 34}

Correction of fructosamine levels to control for fluctuations in albumin and total protein levels have been suggested to improve diagnostic performance of fructosamine as a marker for hyperglycaemia.^{35,36, 37} In this study, fructosamine, following correction with serum total protein remained poorly correlated with glucose values in OGTT for women with GDM and women without GDM. Correction with serum proteins also did

not improve the discriminatory ability of fructosamine between women with and without GDM. A similar result was obtained by Vermes et al, although serum albumin and not serum total protein was used for fructosamine correction.³³

The plausible reasons for this could be the difference in profile of albumin and total protein in the study population compared to other populations where correction of fructosamine has been studied. The mean $\pm$ SD total protein (63.1 ± 6.0 g/L) in this study was close to the lower reference interval of 60 g/L.³⁸ This is compared to a mean $\pm$ SD total protein of 69 ± 6 g/L by Rodrigues in Spain.³⁹ The formula for corrected fructosamine as employed in this study was from studies among Caucasians, in which the average protein or albumin levels for the population is used. Local formulae for correction of fructosamine that considers the apparently lower proteins may improve the correction among our population. Furthermore, as suggested earlier, the protein levels may not fall in a predictable linear fashion in pregnancy, and this may distort the relationship between hyperglycaemia and protein glycation.

In their study to assess Mid-Pregnancy Fructosamine Measurement—Predictive Value for Gestational Diabetes and Association with Postpartum Glycaemic Indices, Gingras et al²⁸ used cut-offs' of $\geq 222 \mu\text{mol/L}$ (50th percentile), $\geq 256 \mu\text{mol/L}$ (75th percentile), $\geq 312 \mu\text{mol/L}$ (95th percentile). The sensitivity and specificity of fructosamine for predicting GDM were 54.8% and 48.6%, 26.0% and 74.9% and 6.9% and 95.1% respectively. This was similar to our findings in this study were at $\geq 216.0 \mu\text{mol/L}$ (50th percentile), $\geq 229.0 \mu\text{mol/L}$ (75th percentile), and $\geq 247.2 \mu\text{mol/L}$ (95th percentile), the sensitivity and specificity of fructosamine for predicting GDM were 60.0% and 52.3%, 32.0% and 78.5% and 12.0% and 96.9% respectively. The AUC was 0.584 (95% CI 0.459-0.708). This represents a poor performance for fructosamine as a screening test for GDM. This implies that fructosamine could not be used as a screening test for the detection. Correction of fructosamine did not improve the predictive performance of fructosamine as a predictor of GDM. We observed that at $\geq 247.8 \mu\text{mol/L}$, $\geq 266.2 \mu\text{mol/L}$, and $\geq 293.7 \mu\text{mol/L}$, the sensitivity and specificity of corrected fructosamine for predicting GDM were 64.0% and 54.6%, 24.0% and 75.4% and 4.0% and 95.4% respectively.

The AUC for corrected fructosamine was 0.594 (95% CI 0.487-0.702). Our finding however is in contrast with the report of Hughes et al,⁴⁰ who observed an optimal performance of corrected fructosamine at a cut off of 215 that achieved a 79.4% sensitivity and a 77.3% specificity for a diagnosis of GDM confirmed by a glucose tolerance test using Carpenter's modified criteria. This is plausible because the higher glucose load and cut-offs values in this diagnostic criterion allows for

a more distinct discrimination between hyperglycaemic and normoglycaemic pregnancies.

Limitation

We did not assess fructosamine in relation to other diagnostic criteria in this study which may limit making inferences regarding comparison with other criteria. Another limitation of this study is the absence of widely acceptable reference limits of cut-off values for fructosamine. Also, correction with protein levels is not standardized given that levels vary among populations. Therefore, applying cut-offs value and formulae derived from other population may affect the findings from this study. Nevertheless, this study has shown that fructosamine and corrected fructosamine levels are not significantly different in the GDM and normoglycaemic pregnant women classified based on the WHO 2013 criteria for GDM diagnosis. Suggesting that they may not be good markers for detecting mild forms of hyperglycaemia.

CONCLUSION

We therefore conclude that serum fructosamine and corrected fructosamine have limited use as a screening tool for GDM based on the WHO 2013 diagnostic criteria for GDM.

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