ORIGINAL ARTICLE

Evaluation of Fasting and Random Plasma Glucose for Diagnosis of Gestational Diabetes

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ABSTRACT

Objective: To compare different cut-off values of fasting and random plasma glucose as a screening test for diagnosis of gestational Diabetes in comparison to the 50 grams Glucose Challenge Test (GCT).

Study Design: Comparative, cross-sectional study.

Place and Duration of Study: This study was carried out between July 2006 to September 2007 at Departments of Pathology, Obstetrics/Gynaecology and Medicine, PNS Rahat Hospital, Karachi.

Methodology: A total of 53 pregnant subjects at 24-28 weeks of pregnancy were selected to undergo random and fasting blood sugar level estimation and 50-g GCT. All the subjects later underwent 100-g OGTT as well. The results were evaluated by both "Carpenter and Coustan criteria" and "NDDG criteria". The results of random plasma glucose random [cut-off: ≥ 11.1 mmol/L], fasting plasma glucose (cut-off: > 5.3 mmol/L and > 5.1 mmol/L) and plasma glucose results post 50-g GCT (cut-off: ≥ 7.8 mmol/L and ≥ 7.2 mmol/L) were evaluated against 100-g OGTT results through ROC curve analysis. Finally, various diagnostic parameters including sensitivity, specificity, predictive values, likelihood ratios (LR) and efficiency were evaluated.

Results: Nineteen subjects were diagnosed to have GDM as per the "Carpenter and Coustan criteria" and 13 met the "NDDG criteria" as per the results of 100-g OGTT. Fasting plasma glucose at was the most efficient investigation at cut-off of 5.1 mmol/L sensitivity=66.66%, specificity=81.25%, PPV=70%, NPV=78.78%, LR+=3.56, LR-=0.41, efficiency=75.47%. At the cut-off value of 5.3 mmol/L, the results had 64% sensitivity, 85.71% specificity, 80% PPV, 72.72% NPV, 4.48 LR+, 0.42 LR-, 75.97% efficiency]. It was followed by plasma glucose post 50-g GCT (53.57% sensitivity at cut-off of ≥ 7.2 mmol/L and 54.54% sensitivity at cut-off of ≥ 7.8 mmol/L).

Conclusion: Fasting plasma glucose is a better investigation for the screening of gestational Diabetes than plasma glucose post 50-g glucose challenge.

Key words: *Gestational Diabetes. Fasting plasma glucose. Glucose challenge test.*

INTRODUCTION

Gestational Diabetes mellitus is defined as hyperglycemia detected for the first-time during pregnancy.[1] Some of the known complications include caesarian section, pre-eclampsia, still birth, macrosmia, and neonatal hypoglycemia.[2] With recent urbanization trends and changes in lifestyles, there is a rapid rise in gestational Diabetes.[3]

The diagnosis of gestational Diabetes has multiple dimensions to it. Firstly, the hidden hyperglycemic tendency has to be screened through some simple biochemical method. Later, the confirmation of the presumptive diagnosis is confirmed through some definitive diagnosis.[4] Presently, there is a marked degree of heterogeneity related to the diagnostic criteria of gestational Diabetes mellitus.[5] These include the NDDG (National Diabetes Data Group) criteria of 1979, the consensus statement of the 4th international workshop on gestational Diabetes mellitus (recommending the Carpenter and Coustan criteria), WHO (World Health Organization) criteria and the position statement by the Australian Diabetes in Pregnancy Society.[6,7] These criteria and position statements have differences in terms of recommendations regarding diagnosis of GDM.[7] There are regional differences in methodologies and cut-off for diagnosing GDM according to their community-based requirements.[8] One local study showed WHO criteria to be better in the diagnosis of GDM.[9] Recently, there was another study by Chandna *et al.* suggesting a different cut-off for the glucose challenge test in pregnant subjects.[10] The screening modalities advocated by the ADA and NDDG require the incorporation of the original O' Sullivan method of measuring plasma glucose after one hour of subjecting the pregnant ladies with a 50-g glucose load. The very well appreciated and documented controversies and problems associated with this approach are the two cut-offs in vogue to define subjects with a "positive screening test" i.e., 7.2 mmol/L and 7.8 mmol/L after 50-g GCT.[11] The 50-g glucose challenge test requires a totally different strategy for routine use in clinical practice

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(vs. plasma glucose fasting in the diagnosis of Diabetes mellitus in non-pregnant subjects).[7] This problem is especially more prevalent in developing societies, where limitations like workload and the late introduction of evidence-based practices into clinical practices create a lot more confusion in terms of diagnostic algorithms for various diseases.[12]

Also the idea of the introduction of a newer approach to diagnose a hyperglycemia related disorder sometimes seems as an addition to the complexity of an already complex metabolic disorder. Simply trying the traditional approach or changing the traditional cut-off for plasma glucose fasting or random may match the reported advantage by 50-g GCT for detecting GDM. The 50-g GCT does not require any fasting requirements, and can be carried out at any time of the day; thus earlier food intake and specific activities like intake of juices and tea may create a varying picture of hyperglycemia in a 50-g glucose challenge test.[13] Moreover, there is some new evidence in literature, which has not shown 50-g GCT as a better investigative modality and has recommended alternative screening modalities including the use of plasma glucose fasting as a screening test for the diagnosis of gestational Diabetes mellitus.[14,15]

Hence, this study was conducted to the performance of fasting and random plasma glucose at various cut-off results against 50 grams glucose challenge test considering 100 grams OGTT as Gold standard.

METHODOLOGY

This comparative cross-sectional study was carried out at the Departments of Pathology, Obstetrics/ Gynaecology and Medicine, PNS Rahat Hospital, Karachi, from June 2006 to September 2007.

All subjects who presented at gynaecological/obstetrical OPD during the study period were targeted for further inclusion into the study. The population considered for this study comprised high risk subjects who were referred for screening of gestational Diabetes mellitus through 50-g GCT. Subjects who were not considered at risk for GDM were not further considered.

Subjects who had known Diabetes, hypertension, asthma or chronic ailments, or those who were on any treatment (except pregnancy related) were excluded from the study. Further, the sample size was narrowed down by excluding subjects who reported for testing before the 24th or after 28th week of pregnancy.

Finally selected subjects (n=53) were formally explained in detail the various procedural details and consequences of the study. The individuals were thoroughly evaluated through history and clinical examination. All individuals were advised to report twice.

The first appointment was given for 50 gram glucose challenge test (sometimes on the same day). The individuals were made to relax and after 20 minutes of rest were sampled for plasma glucose (random sample for plasma glucose). This was followed by 50 grams of glucose load intake. Later, sampling for plasma glucose was done after exact one hour ($\pm$5 minutes). All individuals were requested to report back on a second appointment in complete medical fasting state on any given working day before 08:00 hours ($\pm$30 minutes). Standard protocols were used while sampling to ensure limited pre-analytical errors.

On second appointment individuals were made comfortable by giving them a rest of 15 minutes. After rest they were subjected to 100-g OGTT. Sampling were done at '0' hour for fasting plasma glucose level and at 1, 2 and 3 hours after 100 grams glucose administration for first, second and third sample respectively.

All the samples were analyzed through glucose oxidase method on microlab-200 clinical chemistry analyzer. In order to reduce random errors, all samples were run in duplicate, and the average of the two readings was taken as the final result.

The results of fasting plasma glucose were evaluated at two cut-off i.e., 5.3 mmol/L, and 5.1 mmol/L. The results of plasma glucose random was considered positive if they were $\geq$ 11.1 mmol/L. For the 50 grams GCT, two cut-offs were evaluated i.e., $\geq$ 7.8 mmol/L, and $\geq$ 7.2 mmol/L. The results of the 100 grams oral glucose tolerance test were considered a positive diagnosis for GDM, if two out of four readings were $\geq$ to the values mentioned in Table I.

Table I: Cut-off values used in the 100-grams oral glucose tolerance test.

Time for fasting plasma glucose	Carpenter and Coustan criteria	NDDG criteria*
0 hour	$\leq$ 5.3 mmol/L	$\leq$ 5.8 mmol/L
1 hour	$\leq$ 10 mmol/L	$\leq$ 10.5 mmol/L
2 hour	$\leq$ 8.6 mmol/L	$\leq$ 9.2 mmol/L
3 hour	$\leq$ 7.8 mmol/L	$\leq$ 8.5 mmol/L

** National Diabetes data group criteria.*

All data was entered in SPSS version-15. Descriptive statistics, in terms of mean and standard deviation were calculated. Inferential statistics were used to compare the results of candidate fasting and random plasma glucose against the present in vogue 50-g GCT, keeping the results of 100-g OGTT as the Gold standard using Carpenter and Coustan criteria. Area under the curve (AUC) were calculated through ROC curve analysis for different cut-off of plasma glucose fasting, plasma glucose random and 50-g GCT against the Gold standard. This was followed by calculation of diagnostic performance parameters including sensitivity, specificity, predictive values, likelihood ratios and overall efficiency. A p-value of < 0.05 was considered significant.

RESULTS

The mean age in this data set was 29.90 $\pm$ 4.92 years. The differences for age between subjects with and without GDM were not significant. As per the results of

the Gold standard 100 grams OGTT, 19 subjects were shown to have gestational Giabetes mellitus according to "Carpenter and Coustan's criteria", and 13 subjects were declared to have GDM as per "NDDG criteria". The ROC curve analysis shows fasting plasma glucose to have the most AUC i.e., 0.824 (95%, CI:0.698-0.951), in comparison to random plasma glucose plasma glucose post 50-g GCT (Figure 1 and Table II).

Out of the three investigative modalities available for screening of GDM i.e., fasting plasma glucose, random plasma glucose and plasma glucose results post 50-g GCT, fasting plasma glucose remained the most efficient investigation at a cut-off of 5.3 mmol/L (Table III). Employing a lower cut-off for fasting plasma glucose i.e., 5.1 mmol/L only marginally improved sensitivity for the diagnosis of gestational Diabetes mellitus (Table III). On the other hand, the results of glucose challenge test showed sensitivity of 54% and 55% at cut-off of 7.2 mmol/L and 7.8 mmol/L respectively. Random plasma glucose was the least efficient of all modalities investigated as a marker for screening of gestational Diabetes mellitus. It showed an efficiency of only 55.8%.

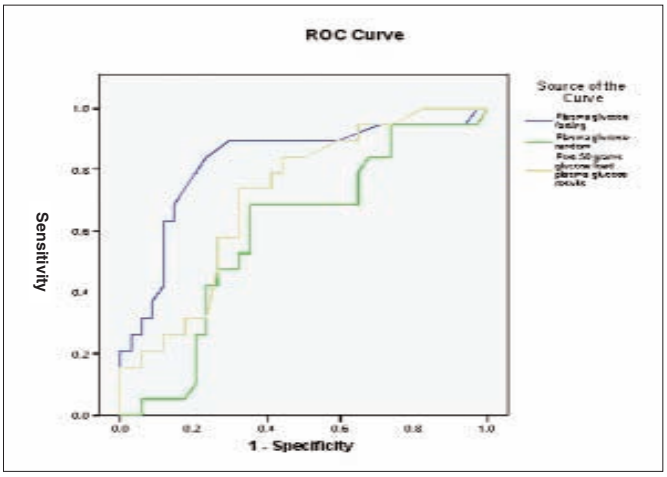

Figure 1: ROC analysis of fasting plasma glucose, random plasma glucose and plasma glucose post 50-g GCT keeping diagnosis through 100-g OGTT as gold standard.

Table II: Area under curve for fasting plasma glucose, random plasma glucose and plasma glucose post 50-g GCT for diagnosis of gestational diabetes mellitus.

Test variable(s)	Area under curve	Std. error*	Asymptotic sig.**	Asymptotic 95% confidence interval	
				Upper bound	Lower bound
Fasting plasma glucose	0.824	0.065	0.000	0.698	0.951
Random plasma glucose	0.598	0.081	0.239	0.440	0.756
Post 50 gram glucose load plasma glucose result	0.714	0.071	0.010	0.576	0.853

** Under the non-parametric assumption; ** Null hypothesis: true area=0.5.*

DISCUSSION

This study showed that screening for gestational Diabetes mellitus can be carried by investigating the fasting plasma glucose level. The overall efficiency (including sensitivity) of the fasting plasma glucose remained superior to other investigations like random plasma glucose and plasma glucose after 50-g GCT at selected cut-off levels of 5.1 mmol/L and 5.3 mmol/L. Some studies have shown similar conclusions [4,16,17] but on the whole this finding comes as a contrast to many other studies available in literature.[18,19]

What could be the possible reasons for these differences? Firstly, from a historic point of view, the requirement of demonstrating hyperglycemia in pregnant subjects arose when O'Sullivan demonstrated in his novel study that hidden hyperglycemic tendencies are to be highlighted through a 50-g GCT in 1964.[20] At that time, there were no consensus-based guidelines to diagnose Diabetes mellitus. The first ever consensus-based cut-off came to clinical practice in 1979 through NDDG.[21] Those guidelines had recommended 7.8 mmol/L as a cut-off for diagnosing Diabetes mellitus. This was later considered way too high to demonstrate hyperglycemia in adults in follow-up studies.[22] Later even the normality for plasma glucose fasting was lowered down to 5.6 mmol/L (ADA) and 6.1 mmol/L (WHO) in the general population.[22,23] The aim behind lowering these cut-offs was primarily to increase the sensitivity of diagnosis and to pick up hyperglycemia earlier.[22] Simply, adopting plasma glucose fasting at a lower cut-off will prove more beneficial not only on grounds of cost-effectiveness and clinical application, but will also give enhance sensitivity for GDM diagnosis

Table III: Diagnostic performance characteristics of fasting plasma glucose, random plasma glucose and 50-g GCT.

Parameter	Sensitivity	Specificity	Positive predictive value	Negative preddictive value	Positive likelihood ratio	Negative likelihood ratio	Efficiency
Fasting plasma glucose (Cut-off used=5.1 mmol/L)	66.66	81.25	70	78.78	3.56	0.41	75.47
Fasting plasma glucose (Cut-off used=5.3 mmol/L)	64	85.71	80	72.72	4.48	0.42	75.97
Random plasma glucose (Cut-off used=11.1 mmol/L)	52.94	57.69	45	65.21	1.25	0.82	55.8
50 grams GCT (Cut-off used=7.2 mmol/L)	53.57	80	75	60.60	2.68	0.58	66.037
50 grams GCT (Cut-off used=7.8 mmol/L)	54.54	74.19	60	69.69	2.113	0.61	66.03

as demonstrated in this study. There are studies which have shown that the mean plasma glucose fasting levels in subjects range from 5.0-5.7 mmol/L.[24] This particular fact can be utilized to improve the GDM diagnosis by incorporating a lower cut-off for plasma glucose fasting.

Secondly, different people take different kinds of diets. The effect of prior feeding, which may be a traditional fried-bread style breakfast or a simple cup of tea may not help standardize patient preparedness and thus differences due to prior feeding may appear and confound the diagnosis.[24] Lastly, there are many recent studies which have recommended the use of plasma glucose fasting as a screening modality for the diagnosis of GDM.[16,25,26] Even the ADA as part of its recommendations also includes a fasting plasma glucose of 7.0 mmol/L $\geq$ as simply confirmatory of GDM.[27] Moreover, the presentation of GDM in the local population could be different from the Western set-ups, as most of the studies recommending a screening approach other than performing a GCT have not been carried out in western set-ups.[16,26] So a point can be made about using plasma glucose fasting as a screening test in GDM in our set-up.

A few limitations of this study must be acknowledged: It was a hospital-based survey in which only high and moderate risk subjects were considered for inclusion into the study based upon clinical evaluation. Subjects considered “low risk” were not addressed further. The sample size may be considered small. It is recommended that a more comprehensive epidemiologically-based survey be carried out to further augment or disapprove our findings.

The clinical implications associated with this study are very important. Finding plasma glucose fasting as a superior screening investigative tool for the diagnosis of GDM may in future replace the existing protocol. This change may not only make the diagnostic protocols for GDM simple, but also easily interpretable and cost-effective.

CONCLUSION

Plasma glucose fasting is a better investigative choice for the screening of gestational Diabetes mellitus than plasma glucose post 50-g glucose challenge. Pregnant subjects with plasma glucose of $\geq$ 5.1 mmol/L are recommended to undergo 100-g OGTT for confirmation of GDM.

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