Research article DOI: https://doi.org/10.4038/jccp.v54i2.8010

Diagnostic significance of individual glucose values in oral glucose tolerance test and the associated risk factors for gestational diabetes mellitus in pregnant mothers: A cross-sectional study

De Silva UH[1], Dissanayake M[2], Amarasiri SS[1]

Journal of the Ceylon College of Physicians, 2023, **54**, 100-106

Abstract

Background: The diagnosis of gestational diabetes mellitus (GDM) is mainly based on oral glucose tolerance test (OGTT) in Sri Lankan clinical setting. The present study was to assess the diagnostic significance of individual glucose values in 75g OGTT in a group of pregnant mothers, to modify the test procedure to make it more convenient and cost-effective and to identify the associated risk factors for GDM.

Methods: A total of 150 pregnant women within the second trimester and attending the antenatal clinics at Teaching Hospital Mahamodara were recruited for the study. Data collection was carried out via an interviewer-administered questionnaire followed by retrieval of laboratory data on OGTT.

Results: Seventeen pregnant women (11.33%) were diagnosed with GDM by OGTT based on the WHO criteria. Diagnosis was based on either fasting or 2-hour glucose values alone or by increased levels in more than one of those parameters. None of them were diagnosed based on the 1-hour glucose value alone. The AUC values were 0.951 (0.884, 1.000), 0.829 (0.715, 0.942) and 0.859 (0.776, 0.943) respectively for fasting, 1-hour and 2-hour glucose concentrations (CI 95%). GDM was associated with uncontrolled sweet consumption ($\chi^2=5.86$, $p=0.015$) and no association was observed with reference to maternal age, parity, BMI, positive family history of diabetes, and prior history of GDM or diabetes mellitus.

Conclusion: Fasting and 2-hour plasma glucose values have higher diagnostic accuracy over 1-hour glucose values and the findings suggest the performance of fasting and 2-hour samples alone in the standard 75g OGTT procedure for the diagnosis of GDM.

Key words: diagnostic accuracy, gestational diabetes mellitus, oral glucose tolerance test, pregnant women

Introduction

Gestational diabetes mellitus (GDM) is a common health complication in pregnancy.[1] It is diagnosed as a state of hyperglycemia which occurs during pregnancy affecting maternal and neonatal wellbeing.[1] Even though the exact mechanisms underlying the disease are not yet completely understood, beta cell dysfunction and chronic insulin resistance have been recognized to play a crucial role in the pathogenesis of GDM.[2]

The WHO diagnostic criterion for GDM is based on the oral glucose tolerance test (OGTT), which is used as a screening tool during 24-28 weeks of gestation.[3] OGTT supports accurate diagnosis of GDM with sufficient sensitivity and specificity. The reported sensitivity of the test is twice as the random glucose measurement whereas the degree of disease severity measured by OGTT was the same as that of the random glucose estimation.[4]

[1]*Department of Medical Laboratory Science, Faculty of Allied Health Sciences, University of Ruhuna, Galle, Sri Lanka,* [2]*Chemical Pathology Laboratory, Teaching Hospital, Karapitiya, Sri Lanka.*

Correspondence: SA, e-mail: amssamarasiri@ahs.ruh.ac.lk

https://orcid.org/0000-0003-1136-1197

Received 3 September 2023, accepted 20 November 2023.

The GDM diagnosis by OGTT is based on the findings on fasting (8-14 hour), 1-hour and 2-hour plasma glucose values following a load of 75g of anhydrous glucose in 250-300mL of water.[5] An abnormality of one or more of the following values; fasting plasma glucose 5.1-6.9 mmol/L (92-125mg/dL), 1-hour plasma glucose ≥10.0mmol/L (180mg/dL), 2-hour plasma glucose 8.5-11 mmol/L (153-199 mg/dL) after the oral glucose dose would be considered during the diagnosis.[3] This procedure has been practiced over the past few decades in Sri Lankan clinical settings for the diagnosis of GDM among pregnant mothers.[6]

However, the OGTT procedure is often invasive and distressing due to the collection of three venous blood samples with one-hour intervals. Usually, the pregnant mothers have to wait for several hours at the phlebotomy or visit the laboratory several times for sample collection for OGTT, making the procedure time consuming. Moreover, analysis of glucose concentration in three consecutive samples causes additional costs as well.[7] Therefore, the search for a novel, cost effective, and efficient method for diagnosing GDM is quite essential, more importantly for the current Sri Lankan healthcare setting with the financial crisis.

Modification of the traditional OGTT procedure, and reducing the number of samples collected would be a possible answer to the issue mentioned above. However, numerous studies carried out to modify the procedure of OGTT at different study settings revealed controversial findings on the reliability of test results. Most of the studies have focused on estimating 2-hour glucose value alone in 75g OGTT procedure for the diagnosis of GDM. Several studies among them reported the appropriateness of 2-hour glucose value in the diagnosis of the disease, whereas some other studies state the importance of having all three measurements in the diagnosis.[8-11] Therefore, the reliability of using a single value alone in the standard OGTT procedure is a matter of concern. Hence, the present study was undertaken with the intent of assessing the validity of individual glucose values in 75g OGTT, in order to modify the test procedure to make it more convenient, efficient, and cost effective for the accurate diagnosis of GDM. Further, an assessment of potential risk factors was carried out in the selected study population in order to identify the independent predictors of GDM and to identify the safest group to rule out additional glucose testing.

Methods

A descriptive cross-sectional study was carried out including 150 pregnant mothers attending the antenatal clinics at Teaching Hospital Mahamodara, Galle, Sri Lanka. The pregnant mothers above the age of 18 years and within the second trimester (24-28 weeks) of their pregnancy were recruited for the study. Non-probability purposive sampling technique was used to collect data considering the time and resource limitations. The study was approved by the Ethics Review Committee of the Faculty of Allied Health Sciences, University of Ruhuna, Sri Lanka (Reference no: 131.07.2022). Informed written consent was obtained from the participants prior to data collection.

The sample size was determined with the consideration of existing prevalence of GDM (10.3%), expected sensitivity of 80%, and the possible marginal error (5%) using an online sample size calculator.[6,12] The study subjects below the age limit and having a prior history of diabetes mellitus were excluded from the study after examining previous medical records.

The details on maternal age, parity, family history of diabetes, past obstetric history, early screening, and lifestyle modification approaches were collected using an interviewer-administered questionnaire. The body mass index (BMI) was calculated using pregnancy weight and the height of the pregnant mothers. The laboratory data on OGTT of the relevant pregnant mothers were collected from the Chemical Pathology Laboratory at the Teaching Hospital, Mahamodara.

The GDM prevalence was assessed based on the WHO diagnostic criteria which indicate diagnosis of the disease at any time in pregnancy based on high values in one or more of the samples collected during the 75g OGTT procedure. Accordingly, fasting plasma glucose values within the range 5.1-6.9 mmol/L (92-125 mg/dL), 1-hour plasma glucose values ≥10.0 mmol/L (180 mg/dL) and 2-hour plasma glucose values within 8.5-11.0 mmol/L (153-199 mg/dL) were considered in the GDM diagnosis.[3] Further, mothers were categorized under impaired glucose tolerance based on fasting plasma glucose values within 6.1-6.9 mmol/L (110-125 mg/dL) and 2-hour plasma glucose <7.8 mmol/L (<140 mg/dL), and as diabetes in pregnancy based on fasting plasma glucose ≥7.0 mmol/L (126 mg/dL) and/or 2-hour plasma glucose ≥11.1 mmol/L (200 mg/dL).[3]

Statistical analysis

SPSS version 25 was used for statistical analysis. Descriptive analysis was done to explain the variation in the variables studied. Receiver operating characteristic (ROC) curve analysis was done and area under the curve (AUC) values were calculated for the

assessment of diagnostic accuracy of fasting, 1-hour and 2-hour plasma glucose values post 75g oral glucose load. The chi-square test of independence, logistic regression analysis, and Spearman correlation were performed to evaluate the relationship between variables. The values were considered significant at $p<0.05$.

Results

Socio-demographic and clinical characteristics of study population

Among the total of 150 pregnant mothers participated in this study, 145 were Sinhalese, three mothers were Tamils, and two mothers were Muslims. Majority of them were from the Galle district (90.7%) and a few mothers were from Matara (8.7%) and Hambanthota (0.7%) districts as well. Among them, 40 (26.7%) pregnant mothers were within the age group 19-25 years. Majority of the study subjects (91; 60.7%) were within the age group 26-35 years and 19 pregnant mothers were at the age of 36-44 years. Six mothers had a previous history of diabetes mellitus and eight mothers had been diagnosed with GDM during previous pregnancies. None of the study subjects had any kind of genetic disorders. Further, none of them had infants with hyperglycemia or macrosomia in previous pregnancies.

Prevalence of GDM, impaired glucose tolerance and diabetes in pregnancy among the participants

According to the WHO diagnostic criteria mentioned above, 17 mothers were diagnosed with GDM by OGTT from the total of 150 pregnant mothers showing a 11.33% prevalence of GDM among pregnant mothers attending the antenatal clinics at Teaching Hospital Mahamodara. The diagnosis was based on individual values of fasting (n=12) or 2-hour (n=2) glucose concentrations or by increased levels in more than one of those parameters (n=3). However, none of the mothers were diagnosed solely based on the 1-hour glucose values. Further, two mothers were categorized under diabetes in pregnancy. However, none of the pregnant mothers were diagnosed as impaired glucose tolerance based on the criteria which consider fasting plasma glucose values within 6.1-6.9 mmol/L (110-125 mg/dL) and 2-hour plasma glucose <7.8 mmol/L (<140 mg/dL). The variations of plasma glucose concentrations and the findings on possible diagnoses of pregnant mothers are shown in Table 1.

Table 1. Variation of plasma glucose concentrations in the study population (n=150)

	Normal glucose tolerance	*Gestational diabetes mellitus*	*Impaired glucose tolerant*	*Diabetes mellitus*
Fasting plasma glucose				
<5.1 mmol/L	135	-	-	-
5.1-6.9 mmol/L	-	14	-	-
≥7.0 mmol/L	-	-	-	1
1-h post 75g oral glucose load				
<10.0 mmol/L	146	-	-	-
≥10.0 mmol/L	-	4	-	-
2-h post 75g oral glucose load				
<8.5 mmol/L	145	-	-	-
8.5-11.0 mmol/L	-	4	-	-
≥11.1 mmol/L	-	-	-	1

Diagnostic accuracy of individual glucose values in 75g OGTT

Among the 17 GDM pregnant mothers diagnosed based on the WHO criteria, 64.71% (11/17) and 11.76% (2/17) mothers were diagnosed solely based on fasting and 2-hour plasma glucose values respectively. However, none of the pregnant mothers were diagnosed for GDM based on 1-hour plasma glucose value alone. Diagnosis of GDM was made based on both fasting and 1-hour plasma glucose values in one pregnant mother (17.65%) and based on all three plasma glucose concentrations in three pregnant mothers (5.88%) in the study population.

The diagnostic accuracy of fasting, 1-hour and 2-hour glucose values were assessed in terms of the ROC curve. The findings are shown in Figure 1. The AUC values generated with the ROC curve provides a measure of discrimination between pregnant mothers with GDM and those without GDM. In the present study, the AUC values reported for fasting, 1-hour and 2-hour glucose values were 0.951 (0.884, 1.000), 0.829 (0.715, 0.942) and 0.859 (0.776, 0.943) respectively with a 95% confidence interval, indicating a moderate (AUC; 0.7-0.9) to high (AUC; >0.9) level of diagnostic accuracy in all three tests. However, the findings show a better performance in fasting glucose values compared to the other two tests.

Assessing the risk factors for GDM among pregnant mothers

Among the selected study population, the mean maternal age of GDM was 29.41 years, and it was 29.38 years among the mothers with normal glucose tolerance. There were seven (4.7%) and 55 (36.7%) primigravida mothers among GDM and normal glucose tolerance subjects respectively. A summary of the findings on the associated risk factors for GDM among the pregnant mothers attending the antenatal clinics at Teaching Hospital Mahamodara are shown in Table 2. Among the study population, the majority of the GDM mothers (52.9%; 9/17) were categorized as overweight. However, GDM was observed in all the categories of BMI. Prior history of GDM, diabetes mellitus, or a family history of diabetes mellitus was observed with a few numbers of pregnant mothers with GDM. Genetic disorders and glycosuria conditions were not observed among the study population.

Early screening and lifestyle modification approaches were assessed in terms of regular checking of blood glucose levels, controlled/reduced consumption of sweets/high carbohydrate diet, use of a diet plan during pregnancy, and engagement in maternal exercises. The findings are shown in Figure 2. Among the GDM diagnosed pregnant mothers, 58.82% (10/17) haven't controlled sweets during pregnancy. From the selected study population, only two mothers were on reduced consumption of high carbohydrate diets and they were among the normal glucose tolerance mothers. None of the mothers used a diet plan during pregnancy or engaged in maternal exercises. Only one mother was doing regular checks of blood glucose level and she was among the normal glucose tolerance mothers. However, from the risk factors considered, a significant association with GDM was observed only with respect to the uncontrolled sweet consumption ($p<0.05$).

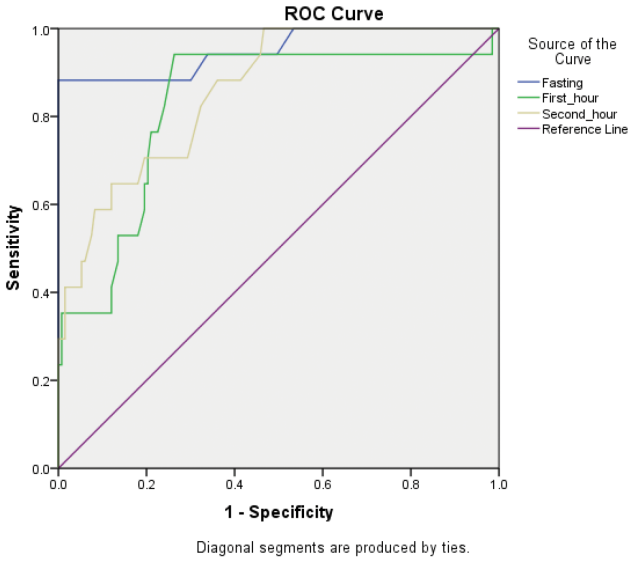

Figure 1. The receiver operating characteristic curves comparing fasting, 1-hour and 2-hour glucose values for diagnosis of Gestational Diabetes Mellitus.

Table 2. Associated risk factors for gestational diabetes mellitus among the pregnant mothers attending the antenatal clinics at Teaching Hospital, Mahamodara

	Normal glucose tolerance	*GDM*	*P value*
Age			0.771
<30 years	66	9	
>30 years	67	8	
BMI			0.920
Under weight (BMI<18.5)	11	1	
Normal (BMI 18.5-25)	62	7	
Overweight (BMI 25.1-30)	46	9	
Obese (BMI >30.1)	14	0	
Parity			0.992
One	41	4	
Two to five	37	6	
More than five	0	0	
Family history of diabetes			0.242
Positive	37	6	
Negative	96	11	
Prior DM history			0.215
Positive	6	0	
Negative	127	17	
Prior GDM history			0.136
Positive	7	1	
Negative	126	16	
Sweet consumption			0.027
Controlled	29	7	
Uncontrolled	104	10	

BMI; Body Mass Index, DM; Diabetes Mellitus, GDM; Gestational Diabetes Mellitus

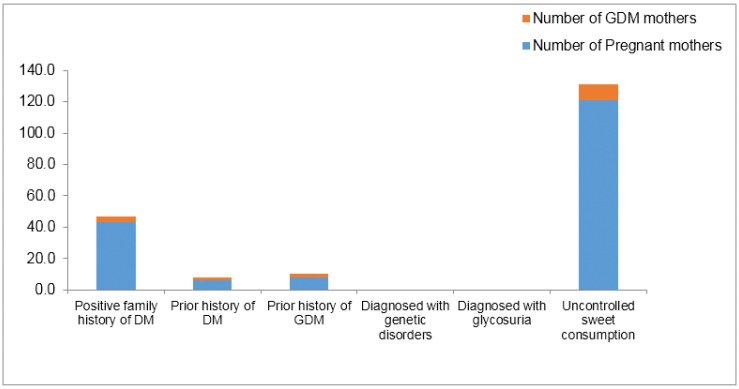

Figure 2. Associated risk factors for gestaional diabetes mellitus among the pregnant mothers attending the antenatal clinics at Teaching Hospital, Mahamodara.

DM; Diabetes Mellitus, GDM; Gestational Diabetes Mellitus.

Chi-square test of independence was performed to evaluate the relationship between GDM and the risk factors. A significant association was observed only with reference to the uncontrolled sweet consumption in the present study (χ^2=5.86, p=0.015), indicating that uncontrolled sweet consumption is more likely to cause GDM. However, no significant association was observed in variables such as maternal age (>30 years) (χ^2=0.066, p=0.797), parity (χ^2=1.777, p=0.777), BMI (χ^2=1.146, p=0.564), positive family history of diabetes (χ^2=0.247, p=0.619), prior history of GDM (χ^2=1.571, p=0.210) and diabetes mellitus (χ^2=3.010, p=0.083). Further, simple logistic regression, followed by multiple logistic regression analysis was carried out to identify the independent predictors of GDM in the present study. However, none of the risk factors showed a significant association with GDM (p>0.05). Moreover, assessment of the Spearman correlation between fasting, 1-hour and 2-hour glucose values with potential risk factors revealed no significant correlations in either factor with the glucose tests (p>0.05).

Discussion

Over the past few years, GDM has become a common health complication in pregnancy.[1] Even though the reported prevalence of GDM in Sri Lanka was 10.3%, a higher GDM prevalence (11.33%) was observed in the present study among the pregnant mothers attending the antenatal clinics at Teaching Hospital Mahamodara.[6]

In line with the previous literature, prior history of diabetes mellitus, prior history of GDM, and maternal overweight showed a positive relationship with the diagnosis of GDM in the present study.[13] We identified uncontrolled sweet consumption as a major risk factor for GDM among the pregnant mothers in our study population.

The main objective of the present study was to assess the diagnostic accuracy of individual plasma glucose values in the standard 75g OGTT procedure, to present it as a simple, more patient-friendly, reliable, and economical test for the diagnosis of GDM. Even though previous literature emphasized the diagnostic accuracy and intimacy of 2-hour glucose value alone in GDM diagnosis, present findings did not show complete agreement with those published reports. However, fasting glucose values showed a significant impact on GDM diagnosis in the study population. There was no significant difference between the diagnosis of GDM based on 1-hour and 2-hour glucose values alone (p=0.565) in the present study and none of the pregnant mothers were diagnosed based on 1-hour glucose value alone. Moreover, the fasting and 2-hour glucose values showed higher AUC values indicating better diagnostic accuracy compared to the 1-hour glucose value. These findings indicate that 1-hour glucose values were having less impact on the diagnosis of GDM compared to fasting and 2-hour values. These findings further corroborate the findings of Meltzer et al., which revealed the accurate diagnosis of GDM by two - step OGTT procedure which involved fasting and 2-hour glucose values.[14] Therefore present findings suggest the omission of the step of measuring 1-hour glucose value following the 75g glucose load in the standard OGTT procedure currently employed for the diagnosis of GDM. These modifications would make the current test procedure cost effective, less invasive, and more efficient as well.

In order to identify the independent predictors of GDM, simple logistic regression analysis followed by multiple logistic regression analysis was carried out in the present study, and none of the risk factors showed significant associations with GDM (P>0.05). This might be due to the small sample size of pregnant mothers with GDM, which is a limitation of this study. However, as shown in Table 2, no considerable variations were observed with respect to age, BMI, and parity among the pregnant mothers categorized as GDM in the present study. Further, the findings were contradictory with reference to family history and previous histories of diabetes mellitus and GDM. Majority of the GDM mothers did not have a family history of diabetes and almost all the GDM mothers did not have a previous history of diabetes mellitus or GDM. Further assessment of Spearman correlation between fasting, 1-hour and 2-hour glucose values with potential risk factors revealed no significant correlations in either factor with the glucose tests. These findings make it more complex to identify the safest group to rule out the 1-hour glucose test and warrant further studies with a large cohort of GDM mothers.

Conclusions

The present findings revealed that fasting and 2-hour plasma glucose values have higher diagnostic accuracy over 1-hour glucose values. These findings suggest the performance of fasting and 2-hour samples alone in the standard 75g OGTT procedure for the diagnosis of GDM. However, further studies are warranted with a large cohort of GDM mothers in order to identify the safest group to rule out the 1-hour glucose test for the proper diagnosis of GDM.

Author declaration

Ethical approval

Ethical approval for the study was obtained from

the Ethics Review Committee of the Faculty of Allied Health Sciences, University of Ruhuna, Sri Lanka (Reference no: 131.07.2022).

Competing interests

There are no competing interests to declare.

Funding

No funding was received to this study.

Author contribution

UHDS, MD and SSA drafted the study protocol. UHDS, and SSA were involved in the execution, data entry, data analysis and manuscript writing. All authors approved the final version of the manuscript.

Acknowledgements

The authors wish to thank the pregnant mothers who participated in this study and the laboratory staff at Teaching Hospital, Mahamodara for their support in conducting the study.

References

1. McIntyre HD, Catalano P, Zhang C, Desoye G, Mathiesen ER, Damm P. Gestational diabetes mellitus. *Nat. Rev. Dis. Primers* 2019; **5**: 1-19. DOI: 10.1038/s41572-019-0098-8
2. Plows J, Stanley J, Baker P, Reynolds C, Vickers M. The Pathophysiology of gestational diabetes mellitus. *Int. J. Mol. Sci.* 2018; **19**: 1-21. DOI: 10.3390/ijms19113342
3. Diagnostic criteria and classification of hyperglycaemia first detected in pregnancy (No. WHO/NMH/MND/13.2). World Health Organization 2013. Available at: https://www.who.int/publications/i/item/WHO-NMH-MND-13.2
4. Anderberg E, Källén K, Berntorp K, Frid A, Åberg A. A simplified oral glucose tolerance test in pregnancy: compliance and results. *Acta Obstetricia et Gynecologica* 2007; **86**; 1432-6. DOI: 10.1080/00016340701532444
5. Saisho Y, Miyakoshi K, Tanaka M, et al. Beta cell dysfunction and its clinical significance in gestational diabetes. *Endocr. J*. 2010; **57**: 973-80. DOI: 10.1507/endocrj.K10E-231
6. Wijeyaratne C, Ginige S, Arasalingam A, Egodage C, Wijewardhena L. Screening for gestational diabetes mellitus: the Sri Lankan experience. *Ceylon Med J*. 2006; **51**: 53-8.
7. Jamieson EL, Spry EP, Kirke AB, Atkinson DN, Marley JV. Real-World Gestational Diabetes Screening: Problems with the Oral Glucose Tolerance Test in Rural and Remote Australia. *Int. J. Environ. Res. Public Health*. 2019; **16**: 1-18. DOI: 10.3390/ijerph16224488
8. Bogdanet D, O'Shea P, Lyons C, Shafat A, Dunne F. The Oral Glucose Tolerance Test-Is It Time for a Change? – A Literature Review with an Emphasis on Pregnancy. *J. Clin. Med*. 2020; **9**: 1-22. DOI: 10.3390/jcm9113451
9. Hanna FWF, Peters JR. Screening for gestational diabetes; past, present and future. *Diabetic Medicine* 2002; **19**: 351-8. DOI: 10.1046/j.1464-5491.2002.00684.x
10. Rodriguez-Hervada AD, Pascual ALC. Diagnostic criteria for gestational diabetes: The debate goes on. *Endocrinologiay Nutricion* 2015; **62**: 207-9. DOI: 10.1016/j.endoen.2015.05.003
11. Schmidt MI, Duncan BB, Reichelt AJ, et al. Gestational diabetes mellitus diagnosed with a 2-h 75-g oral glucose tolerance test and adverse pregnancy outcomes. *Diabetes Care* 2001; **24**: 1151-5. DOI: 10.2337/diacare.24.7.1151
12. Arifin WN. Sample size calculator [online]. 2023 Available at: http://wnarifin.github.io
13. Kjos SL, Buchanan TA. Gestational diabetes mellitus. *NEJM*. 1999; **341**: 1749-56. DOI; 10.1056/NEJM199912023412307
14. Meltzer S, Snyder J, Penrod J, Nudi M, Morin L. Gestational diabetes mellitus screening and diagnosis: a prospective randomised controlled trial comparing costs of one-step and two-step methods. *International Journal of Obstetrics and Gynaecology* 2010; **117**: 407-15. DOI: 10.1111/j.1471-0528.2009.02475.x