Assessment of Diagnostic Accuracy of Early OGTT in Prediction of Gestational Diabetes Mellitus taking 2nd Trimester OGTT as Gold Standard

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Abstract

Background: Early diagnosis of gestational diabetes may have the potential to improve maternal and neonatal health outcomes.

Objective: To determine the diagnostic accuracy of early OGTT in the prediction of Gestational Diabetes Mellitus by taking 2nd-trimester OGTT as a gold standard.

Methodology: This was a cross-sectional study that enrolled 420 pregnant women with single pregnancy between 18 and 40 years of age, who had their first prenatal visit in PAF hospital at 1st or early 2nd trimester, from 1st August 2022 to 31st January 2023. All the women in their first trimester were subjected to 75g OGTT and the values of the plasma glucose concentration were recorded at fasting level, after 1-hr and after 2-hrs respectively. All these results were compared with 2nd trimester OGTT of the same patients taking 2nd trimester OGTT as a gold standard.

Results: The mean age of the women was 27±4 years. The mean BSF and 2-hr plasma glucose of women in 1st OGTT were 4.74±0.36 mmol/L and 6.58±0.63 mmol/L respectively. The mean BSF and 2-hr plasma glucose of women in 2nd OGTT were 4.89±0.32 mmol/L and 6.04±0.97 mmol/L respectively. The prevalence of GDM in 1st OGTT was 6.4% and in 2nd OGTT it was 20.5%. The sensitivity, specificity, PPV, and NPV of the 1st OGTT performed between 10 to 17 weeks of gestation were found as 26.7%, 98.8%, 85.18%, and 83.97% respectively.

Conclusion: The early OGTT performed during 10-17 weeks of gestation has good specificity, with good positive predictive and negative predictive values but poor sensitivity, taking the late 2nd trimester OGTT as a gold standard.

Keywords: GDM, OGTT, Diagnostic Accuracy, Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value

Introduction

Gestational diabetes mellitus (GDM) is a very complex disease, with a diverse presentation of medical complications that involves pregnant women who have a glucose intolerance and women having undiagnosed diabetes mellitus diagnosed in pregnancy.[1] GDM is termed as any level of dysglycaemia occurring for the first time or is diagnosed first time during pregnancy. It has been a serious public health problem for the world.[2] Most of the international guidelines suggest that GDM should be diagnosed during 24-28 weeks of pregnancy by an oral glucose tolerance test (OGTT).[3,4] However, there is not enough evidence as to why the test should be performed at this time. Although most of the cases of GDM are detected at 24 weeks of pregnancy, but it may develop before 24 weeks and potentially harm the fetus and mother by exposing the fetus to hyperglycemia.[5] However, the benefits of early detection of GDM especially before 24-28 weeks of the pregnancy are not well documented in the literature.[6,7] A case report presented by Najmi et al showed that the GDM testing in early pregnancy, which is best for early visits of antenatal care, as well as insulin therapy, plays a beneficial role in minimizing the pregnancy complications and improving fetal outcomes.[3] Early diagnosis of the GDM may increase the chances of the interventions which can lead to improved maternal plus fetal outcomes.[8] This study aimed to assess the diagnostic accuracy of early OGTT in the prediction of Gestational Diabetes Mellitus taking 2nd trimester OGTT as the gold standard.

Methodology

It was a cross-sectional study for test validation, carried out at PAF Hospital Islamabad from 1st August 2022 to 31st January 2023. The sample size was calculated with a sensitivity and specificity calculator taking a confidence level of 95%, Sensitivity of 91%, Specificity of 96.6%, Absolute precision of 9%, and Prevalence of

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GDM as 9.3%.[9] The sample size was 420 pregnant women. The data was collected by using a non-probability consecutive sampling technique. Women with singleton pregnancy, between 18 and 40 years of age, who had their first prenatal visit in PAF hospital during 1st and early 2nd trimester, were included in this study. The pregnant women who were in their mid-2nd and 3rd trimester at the start of data collection, women with pre-gestational diabetes, substance abuse, depressive disorder, heart disease, hypothyroidism, leukemia, epilepsy, anorexia, bulimia, asthma, autoimmune cirrhosis or multiple sclerosis and women on medication, corticosteroids, and antipsychotics were excluded from this study.

This study was started after obtaining approval from the **ethical and research board of PAF Hospital (Ref. No.........).** All women visiting the outpatient department of gynecology for booking in 1st and early 2nd trimester were included in the study. The objectives and significance of the current study were well explained to them and written informed consent was sought. The demographic data including age, parity, weight and height, clinical data including EDD, and family history of diabetes was taken from all women. All the women in their first trimester were subjected to a 75g oral glucose tolerance test and the values of plasma glucose concentration were recorded at fasting level, after one hour and after 2-hours respectively. All these results were compared with 2nd trimester OGTT of the same patients taking late 2nd trimester OGTT as a gold standard. All the information was recorded on a predesigned proforma by the trainee, which comprised the following variables: The age of women was recorded in years; gravidity, parity, and miscarriage were measured in numbers; the body mass index was calculated in scalar quantity. Later on, the categories of BMI were made according to the international classification of Body Mass Index during pregnancy.[10] The groups were made as: Under-weight: (BMI less than 18.5 kg/m^2), Normal weight: (BMI between 18.5 to 24.9 kg/m^2), Over-weight: (BMI between 25 to 29.9 kg/m^2), Obese: (BMI more than or equal to 30 kg/m^2); the family history was taken as nominal variable.

The 1st and 2nd OGTT done on patients recorded the following data. The gestational age during which the 1st OGTT was performed was recorded in

weeks; the fasting plasma glucose was measured in mmol/L and the cut-off≥5.1mmol/L was used to diagnose GDM; the one-hour plasma glucose was measured in mmol/L and the cut off ≥10mmol/L was used to diagnose GDM; the two-hour plasma glucose was measured in mmol/L and the cut off ≥8.5mmol/L was used to diagnose GDM according to IADPSG criteria. Patients having any one or more deranged values were categorized as having GDM.

All data was analyzed by using the SPSS 23 version. The descriptive statistics were presented as frequencies, percentages, and mean and standard deviation. In this study the variables such as sensitivity, specificity, positive predictive value, and negative predictive value were calculated and measured by using the following formulas: $TP/(TP+FN) \times 100$; $TN/(TN+FP) \times 100$; $TP/(TP+FP) \times 100$; $TN/(FN+TN) \times 100$ respectively.

Results

In this study, a total number of 420 pregnant women were enrolled. The mean age of the pregnant women was 27.77±4.87 years. The minimum age was noted as 18 years and the maximum age was 40 years. Most of the women 249 (59.3%) belonged to the age group 25-32 years, followed by 101 (24%) women in the age group 18-24 years, and 70 (16.7%) women in the age group 33-40 years.

Table I: Cross tabulation to determine the association of age, parity, BMI, and family history of women with GDM

Variable	Category	GDM Categories		% of GDM	X^2 (df)	P-value
		Positive	Negative			
Age groups (in years)	18 – 24 25 – 32 33 – 40	16 47 23	85 202 47	15.8 18.9 32.9	8.31 (2)	0.02
Parity	0 1-2 =3	10 57 19	81 224 29	11.0 20.3 39.6	15.79 (2)	<0.001
BMI	Under weight	2	21	8.7	26.10 (3)	<0.001
	Normal weight	44	244	15.3		
	Over weight	37	67	35.6		
	Obese	3	2	60.0		
Family History of Diabetes in 1st Degree Relatives	Negative	56	303	15.6	36.11 (1)	<0.001
	Positive	30	31	49.2		

The Chi-square Test of Independence showed a statistically significant association of women's age with GDM, χ^2 (2, n = 420) = 8.31, p = 0.02 (Table-I). The gravidity was 1 in 60 women, 2 in 157, 3 in 110, 4 in 59, 5 in 26 and 6 in 8 women. In this study, 304 women experienced no miscarriage, 91 women had 1, 20 women had 2, and 5 women had 3 miscarriages

in their lives. The Chi-square Test of Independence also showed a statistically significant association of women's parity with GDM, χ^2 (2, n = 420) = 15.79, p < 0.001. The Chi-square Test of Independence showed a statistically significant association of women's BMI with GDM, χ^2 (3, n = 420) = 26.10, p < 0.001. The Chi-square Test of Independence also showed a statistically significant association of family history of diabetes in the 1st degree relative of women with GDM, χ^2 (1, n = 420) = 36.11, p < 0.001 (Table-I).

Table II: Validity measurement of 1st OGTT

Test	GDM Positive	GDM Negative
1st OGTT Positive	23 (TP)	4 (FP)
1st OGTT Negative	63 (FN)	330 (TN)

In 1st OGTT, the mean BSF of women was 4.74±0.36 mmol/L. The minimum and maximum plasma glucose were 3.6 mmol/L and 5.9 mmol/L respectively. The mean 1-hr plasma glucose was 7.44±0.63 mmol/L. The minimum and maximum plasma glucose were 5.9 mmol/L and 10.5 mmol/L respectively. The mean 2-hr plasma glucose was 6.58±0.63 mmol/L. The minimum and maximum plasma glucose were 5 mmol/L and 9 mmol/L respectively. Among the pregnant women who were diagnosed with GDM in 1st OGTT, 23 women had only one deranged value of plasma glucose according to the cut-off criteria of IADPSG, three women had two deranged values and one woman had all three deranged values of plasma glucose, i-e, BSF, 1-hr and 2-hr plasma glucose.

In 2nd OGTT, the mean BSF of women was 4.89±0.32 mmol/L. The minimum and maximum plasma glucose were 3.9 mmol/L and 5.9 mmol/L respectively. The mean 1-hr plasma glucose was 7.15±0.92 mmol/L. The minimum and maximum plasma glucose were 5.4 mmol/L and 10.6 mmol/L respectively. The mean 2-hr plasma glucose was 6.04±0.97 mmol/L. The minimum and maximum plasma glucose were 4.2 mmol/L and 9.5 mmol/L respectively. Among the women who were diagnosed with GDM in the 2nd OGTT, 55 women had only one deranged value of plasma glucose according to cut-off criteria of IADPSG, 20 women had two deranged values and 10

women had all three deranged values of plasma glucose, i-e, BSF, 1-hr and 2-hr plasma glucose.

The prevalence of GDM in 1st OGTT was found as 6.4%. The prevalence of GDM in 2nd OGTT was found as 20.5%. Table-II is the 2x2 table to measure the validity of the 1st OGTT that was conducted during 10 to 17 weeks of the gestation. The table shows that the true positive value was 23, the false positive value was 4, the false negative value was 63, and true negative value was 330.

Table-III: Sensitivity, Specificity, Positive predictive value and Negative predictive value of 1st OGTT performed during 10 to 17 weeks of the gestation

Sensitivity	=	TP / (TP + FN) x 100
	=	23 / 86 x 100
Sensitivity	=	26.7%
Specificity	=	TN / (TN + FP) x 100
	=	330 / 334 x 100
Specificity	=	98.8%
Positive Predictive Value	=	TP / (TP + FP) x 100
	=	23 / 27 x 100
Positive Predictive Value	=	85.18%
Negative Predictive Value	=	TN / (FN + TN) x 100
	=	330 / 393 x 100
Negative Predictive Value	=	83.97%

Discussion

In the present study, the mean age of women was 27.77±4.87 years. Most of the women 249 (59.3%) belonged to the age group 25-32 years, followed by 101 (24%) women in the age group 18-24 years and 70 (16.7%) women in the age group 33-40 years. The findings revealed a significant association of women's age with gestational diabetes mellitus. The highest prevalence of GDM (32.9%) was found among women of the age group 33-40 years. Similar findings were revealed in the studies which demonstrated that the age of 30 years or above among pregnant women was a significant predictor of gestational diabetes mellitus.[8,11-13] This study also revealed a significant association of women's parity with the gestational diabetes mellitus. Fathy et al[13] and Li et al[11] also found multi-parity as a significant risk factor of the gestational diabetes mellitus.

The BMI of women was also significantly associated with the gestational diabetes mellitus in the current study. The findings clearly demonstrated that obese women had the highest prevalence (60%) of GDM, followed by overweight women who had a 35.6%

prevalence of GDM. Similar studies found that a BMI of more than 30 was significantly associated with gestational diabetes mellitus.[8,12,14] Larrabure-Torrealva et al identified that obese women had 1.64 times more chances of having GDM compared to non-obese women, after controlling for all possible confounders in the study.[15] The family history of the diabetes has been found to be statistically significantly associated with the occurrence of GDM as verified in previous literature.[11-13,15] The current study also found a significant association of positive family history of the diabetes in the 1st degree relatives of women with GDM. The women who had a positive family history of the diabetes in their 1st degree relative was found to have a 49.2% prevalence of GDM in this study, which was around three times more prevalent than women who had no family history of the diabetes (prevalence of GDM as 15.6%).

In the current study, the mean BSF, 1-hr and 2-hr plasma glucose of women in 1st OGTT were 4.74±0.36 mmol/L, 7.44±0.63 mmol/L, and 6.58±0.63 mmol/L respectively. The mean BSF, 1-hr, and 2-hr plasma glucose of women in 2nd OGTT were 4.89±0.32 mmol/L, 7.15±0.92 mmol/L, and 6.04±0.97 mmol/L respectively. The prevalence of GDM in 1st OGTT was found as 6.4% and in 2nd OGTT it was found as 20.5%. In a study by Larrabure-Torrealva et al, the prevalence of the GDM was found as nearly 16%.[15] A study that was conducted by Fathy et al found the prevalence of the GDM as 8%.[13]

The sensitivity and specificity of 1st OGTT performed during 10 to 17 weeks of the gestation were found as 26.7% and 98.8% respectively. The positive predictive value and negative predictive value of 1st OGTT performed during 10 to 17 weeks of the gestation were found as 85.18% and 83.97% respectively. In a similar study conducted by Lekva et al, the early OGTT performed between 14-16 weeks of gestation found sensitivity, specificity, and positive predictive value around 70-75%, 60%, and 20-40% respectively.[8] Another study conducted by Reyes-Munoz found that the OGTT performed between 11 to 35 weeks of gestation had sensitivity, specificity, positive predictive value, and negative predictive value of 91%, 97%, 64%, and 99% respectively.[9] The study carried out by Surapaneni et al performed the 75g OGTT in women during 24-28 weeks of gestation and found the sensitivity and specificity of fasting plasma glucose as 87.16% and 96.08% respectively. The sensitivity and specificity of the 1-hr test were found as 85.74 and 99.68% respectively.[16] In another study carried out by Phaloprakan et al on 193 pregnant women to diagnose gestational diabetes mellitus in 1st trimester by OGTT, the 1-hr plasma glucose values with cut-off 8.6mmol/L gave sensitivity, specificity, positive predictive value, and negative predictive value as 89.7%, 64.3%, 38.9%, 96.1%, and 0.77 respectively.[17] The findings of the current study will enhance the scientific insight for proposing the appropriate screening time for the gestational diabetes mellitus in pregnant women.

Conclusion
The early OGTT performed during 10-17 weeks of gestation has good specificity, positive predictive value, and negative predictive value but poor sensitivity, taking the late 2nd trimester OGTT as a gold standard.

Authors Contribution: SK: Conception of work, Acquisition and Analysis of data and Drafting. **AHK:** Acquisition and Analysis of data, Interpretation of data and revising. **MR:** Design of work, Acquisition and Analysis of data and revising. **MA:** Conception of work, Acquisition and Analysis of data and Drafting. **UH:** Acquisition and Analysis of data, Interpretation of data and revising. All authors critically revised and approve its final version.

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