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Assessment of Diagnostic Accuracy of Early OGTT in Prediction of GDM taking 2nd Trimester OGTT as Gold Standard

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Abstract: Objectives: To determine the diagnostic accuracy of early OGTT in prediction of GDM taking 2nd trimester OGTT as gold standard.

Methods: This study cross-sectional study 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. All the women in their first trimester were subjected to 75g OGTT and the values of 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 same patients taking 2nd trimester OGTT as gold standard.

Results: The mean age±SD of women was 27.77±4.87 years. The mean±SD 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±SD 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%. The sensitivity and specificity of 1st OGTT performed between 10 to 17 weeks of gestation was found as 26.7% and 98.8% respectively. The positive predictive value and negative predictive value of 1st OGTT performed between 10 to 17 weeks of gestation was found as 85.18% and 83.97% respectively.

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.

Key Words: GDM, OGTT, Diagnostic Accuracy, Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value.

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INTRODUCTION:

Gestational diabetes mellitus (GDM) is a diverse medical complication that involves pregnant women who have glucose intolerance and women having undiagnosed diabetes mellitus diagnosed in pregnancy.(McIntyre et al., 2019) 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.(Lee et al., 2018) Most of the international guidelines suggest that GDM should be diagnosed during 24-28 weeks of pregnancy by oral glucose tolerance test (OGTT).(Cosson et al., 2020; Najmi, Atal, Sadasivam, Singh, & Ray, 2019) 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 fetus to hyperglycemia.(Cho, Jung, & Kim, 2016) However, the benefits of early detection of GDM before 24-28 weeks of pregnancy are not well documented in literature.(Benhalima et al., 2019; Farrar et al., 2017) A case report presented by Najmi et al showed that 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.(Najmi et al., 2019) Early diagnosis of GDM may increase the likelihood of interventions to improve maternal and fetal outcomes.(Lekva et al., 2018) This study aimed to determine the diagnostic accuracy of early OGTT in prediction of GDM taking 2nd trimester OGTT as gold standard.

MATERIAL AND METHODS

It was a cross-sectional validation study, carried out at PAF hospital Islamabad from 1st August 2022 – 31st Jan 2023. The sample size was calculated with sensitivity specificity calculator taking: Confidence level of 95%, Sensitivity of 91%, Specificity of 96.6%, Absolute precision of 9% and Prevalence of GDM as

9.3%.(Reyes-Muñoz et al., 2018) The sample size was 420 pregnant women. The data was collected by using 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 at 1st and early 2nd trimester were included in the study. 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, leukaemia, epilepsy, anorexia, bulimia, asthma, autoimmune cirrhosis or multiple sclerosis and women on medication, corticosteroids and antipsychotics were excluded from this study.

The study was conducted after obtaining approval from the ethical and research board of PAF hospital. All women visiting the out-patient department of gynecology for booking in 1st and early 2nd trimester were included in the study. The objectives and significance of the study were explained to them and a written informed consent was taken. 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 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 same patients taking late 2nd trimester OGTT as gold standard. All the information was recorded on a predesigned performa by the trainee, which comprised of 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.(Simko et al., 2019) The groups were made as: Under-weight: (BMI <18.5 kg/m2), Normal weight: (BMI = 18.5–24.9 kg/m2), Over-weight: (BMI = 25.0–29.9 kg/m2), Obese: (BMI ≥30 kg/m2); 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 performed was recorded in weeks; the fasting plasma glucose was recorded in mmol/L and the cut off ≥5.1mmol/L was used to diagnose GDM; the one-hour plasma glucose was recorded in mmol/L and the cut off ≥10mmol/L was used to diagnose GDM; the two-hour plasma glucose was recorded 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 SPSS 23 version. The descriptive statistics were presented as frequencies, percentages and mean±SD. The sensitivity, specificity, positive predictive value and negative predictive value were measured by using the following formulas: TP/(TP+FN) x 100; TN/(TN+FP) x 100; TP/(TP+FP) x 100; TN/(FN+TN) x 100.

RESULTS:

A total number of 420 pregnant women were enrolled in the study. The mean age ± SD of women was 27.77 ± 4.87 years. The minimum age was 18 years and maximum age was 40 years. Most of the women 249 (59.3%) belonged to age group 25 – 32 years, followed by 101 (24.0%) women in age group 18 – 24 years and 70 (16.7%) women were in age group 33 – 40 years. The Chi-square Test of Independence revealed a significant association of women's age with GDM, $\chi 2$ (2, n = 420) = 8.31, p = 0.02 (Table 1).

The gravidity was 1 in 60 women, 2 in 157, 3 in 110, 4 in 59, 5 in 26 and 6 in 8 women. 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 found a significant association of women's parity with GDM, $\chi 2$ (2, n = 420) = 15.79, p < 0.001. The Chi-square Test of Independence revealed a significant association of women's BMI with GDM, $\chi 2$ (3, n = 420) = 26.10, p < 0.001. The Chi-square Test of Independence also revealed a significant association of family history of diabetes in 1st degree relative of women with GDM, $\chi 2$ (1, n = 420) = 36.11, p < 0.001 (Table 1).

Table 1: Chi-square Test of Independence to determine the association of age, parity, BMI and family history of women with GDM

		Positive	Negative	% of GDM	X^2 (df)	p-value
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 wt. Normal wt. Over weight Obese	2 44 37 3	21 244 67 2	8.7 15.3 35.6 60.0	26.10 (3)	<0.001
Family History of Diabetes in 1st degree relatives	Negative Positive	56 30	303 31	15.6 49.2	36.11 (1)	<0.001

In 1st OGTT, the mean BSF ± SD 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 ± SD 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 ± SD was 6.58 ± 0.63 mmol/L. The minimum and maximum plasma glucose were 5.0mmol/L and 9.0mmol/L respectively. Among the women who had been diagnosed with GDM in 1st OGTT, 23 women had only one deranged value of plasma glucose according to 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 ± SD 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 ± SD was 7.15 ± 0.92 mmol/L. The minimum and maximum plasma glucose were 5.4 mmol/L and 10.6mmol/L respectively. The mean 2-hr plasma glucose ± SD 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 had been diagnosed with GDM in 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 2 is the 2x2 table to measure the validity of 1st OGTT performed between 10 to 17 weeks of gestation. The table is showing that the true positive value was 23, false positive value was 4, false negative value was 63 and true negative value was 330.

Table 2: Validity measurement of 1st OGTT

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

The sensitivity, specificity, positive predictive value and negative predictive value of 1st OGTT performed between 10 to 17 weeks of gestation is measured by using the following formulas (Table 3):

Table 3: Sensitivity, specificity, positive predictive value and negative predictive value of 1st OGTT performed between 10 to 17 weeks of gestation

Sensitivity	=	**TP / (TP + FN) x 100**
		23 / 86 x 100
Sensitivity		**26.7%**
Sensitivity	=	**TP / (TP + FN) x 100**
		23 / 86 x 100
Sensitivity		**26.7%**
Sensitivity	=	**TP / (TP + FN) x 100**
		23 / 86 x 100
Sensitivity		**26.7%**
Sensitivity	=	**TP / (TP + FN) x 100**
		23 / 86 x 100
Sensitivity		**26.7%**

DISCUSSION

In the present study, the mean age ± SD of women was 27.77 ± 4.87 years. Most of the women 249 (59.3%) belonged to age group 25 – 32 years, followed by 101 (24.0%) of women were in age group 18 – 24 years and 70 (16.7%) of women were in 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 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.(Benhalima et al., 2020; Fathy, Khalil, & Mahmoud, 2018; Lekva et al., 2018; F. Li et al., 2020) This study also revealed a significant association of women's parity with gestational diabetes mellitus. Fathy et al(Fathy et al., 2018) and Li et al(F. Li et al., 2020) also found multi-parity as a significant risk factors of gestational diabetes mellitus.

The BMI of women was also significantly associated with gestational diabetes mellitus in the current study. The findings clearly demonstrated that obese women had highest prevalence (60%) of GDM, followed by overweight women who had 35.6% prevalence of GDM. The similar studies found that BMI more than 30 was significantly associated with gestational diabetes mellitus.(Benhalima et al., 2020; Lekva et al., 2018; G. Li et al., 2020) 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.(Larrabure-Torrealva et al., 2018) The family history of diabetes has been found significantly associated with GDM as verified in previous literature.(Benhalima et al., 2020; Fathy et al., 2018; Larrabure-Torrealva et al., 2018; F. Li et al., 2020)The current study also found a significant association of positive family history of diabetes in 1st degree relatives of women with GDM. The women who had positive family history of diabetes in their 1st degree relative had 49.2% prevalence of GDM found in this study, which was around three times more prevalence than women who had no family history of diabetes (prevalence of GDM as 15.6%).

In the current study, the mean ± SD 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 ± SD 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 the study of Larrabure-Torrealva et al, the prevalence of GDM was found as nearly 16%.(Larrabure-Torrealva et al., 2018) A study conducted by Fathy et al found the prevalence of GDM as 8%.(Fathy et al., 2018)

The sensitivity and specificity of 1st OGTT performed between 10 to 17 weeks of gestation was found as 26.7%

and 98.8% respectively. The positive predictive value and negative predictive value of 1st OGTT performed between 10 to 17 weeks of gestation was 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 a sensitivity, specificity and positive predictive value around 70-75%, 60% and 20-40% respectively.(Lekva et al., 2018) 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 as 91%, 97%, 64% and 99% respectively.(Reyes-Muñoz et al., 2018) The study carried out by Surapaneni et al performed the 75g OGTT in women between 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 1-hr test was found as 85.74 and 99.68% respectively.(Surapaneni, Nikhat, & Nirmalan, 2013) 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.(Phaloprakarn & Tangjitgamol, 2008) The findings of the current study will enhance the scientific insight for proposing the appropriate screening time for gestational diabetes mellitus among 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.

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