

VALIDITY OF TWO HOURS ORAL GLUCOSE TOLERANCE TEST AT 48-72 HOURS AFTER DELIVERY IN DETERMINING THE DEVELOPMENT OF TYPE 2 DIABETES AT SIX WEEKS POSTPARTUM IN PATIENTS WITH GESTATIONAL DIABETES MELLITUS

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ABSTRACT

Objective: To determine the validity of 2-hours oral glucose tolerance test (OGTT) conducted 48-72 hours after delivery in determining the development of type 2 diabetes at six weeks postpartum in patients with gestational diabetes mellitus (GDM).

Methodology: This was a prospective, cohort study conducted at Jinnah Allama Iqbal Institute of Diabetes & Endocrinology (JAIDE), Medical Unit-4, Jinnah Hospital, Lahore, from February, 2017 to July, 2017. Women diagnosed with GDM at 24-28 weeks of gestation using 75 grams OGTT were recruited in the study. The study outcomes were the calculation of sensitivity, specificity, and predictive values (positive and negative) of the 2 days postpartum OGTT results to predict diabetes mellitus and impaired glucose tolerance.

Results: The study was conducted on 138 female patients with mean age 28.6 ±9.2 years (range: 17–38 years). The mean fasting blood glucose level 48 hours and six weeks after delivery was 98.7 mg/dl and 86.6 mg/dl respectively (p <0.001). The frequency of diabetes was found out to be 4.3% and 9.4% at 48 hours and 6 weeks postpartum respectively. The sensitivity, specificity, positive predictive value and negative predictive value of OGTT conducted at 48-72 hours postpartum for diagnosis of diabetes mellitus was found out to be 76.2%, 96.1%, 67.4% and 94.1% respectively.

Conclusion: Oral glucose tolerance test performed 48-72 hours postpartum is a useful tool to predict diabetes mellitus in women with GDM. It is helpful in identifying those women who need further monitoring and testing for type 2 diabetes.

Key Words: Gestational diabetes mellitus, Oral glucose tolerance test, Postpartum

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INTRODUCTION

Gestational diabetes mellitus (GDM) is defined by the American Diabetes Association (ADA) as hyperglycemia occurring in the second and/or third trimester of pregnancy, in the absence of type 1 or type 2 diabetes mellitus (DM), and usually resolving after delivery¹. It complicates large number of pregnancies. Approximately 1 in every 7 women develops GDM². The International Association of Diabetes and Pregnancy Study Group (IADPSG) proposed 75gm OGTT as the diagnostic tool for GDM between 24 to 28 weeks of pregnancy³. Women

with GDM have seven fold increased risk of developing type 2 DM later in life than normal mothers⁴. Earlier studies have shown that almost 10% women with GDM developed type 2 DM and 12-36% had impaired fasting glucose or impaired glucose tolerance when screened 6–12 weeks after delivery⁵. Cumulatively, about 60% of GDM patients develop type 2 DM within 10 years⁶.

American Diabetes Association recommends oral glucose tolerance test (OGTT) at 6 weeks postpartum to screen for type 2 DM⁶. The OGTT is very cost effective and can detect type 2 DM very early specially in these

high risk women with GDM⁶. Despite presence of strong evidence of type 2 diabetes after GDM, less than 50% women receive 75 grams OGTT, 6 weeks postpartum as advised by ADA⁶. This indicates that early diagnosis and prompt treatment of type 2 DM after GDM is missed in a vast majority of patients in the 6 weeks postpartum period⁷.

This has been an area of interest for researchers to explore validity of earlier conduction of 75 grams OGTT. Recent studies have shown that OGTT conducted at 48–72 hours postpartum carries equal validity when compared to the conventional gold standard 75 grams OGTT conducted 6 weeks after delivery⁵. If patients at risk are identified on time, there is substantial evidence that appropriate life style modifications can effectively prevent and delay the development of type 2 DM in such patients⁸. We conducted literature search on PubMed, Google Scholar, EMBASE library and PakMediNet but could not find any published report from our country. The major limitation of earlier international studies was their limited sample size. So, this study was carried out to explore local data with a larger study population to determine the validity of 2-hours OGTT conducted 48–72 hours after delivery in determining the development of type 2 diabetes at 6 weeks postpartum in patients with GDM.

METHODOLOGY

This was a prospective, cohort study conducted in Jinnah Allama Iqbal Institute of Diabetes and Endocrinology (JAIDE), Jinnah Hospital, Lahore, after approval of its proposal from Ethical Review Board of Allama Iqbal Medical College, Jinnah Hospital, Lahore - Pakistan. The study was conducted from February, 2017 to July, 2017 following principles of good clinical practice as laid down in Declaration of Helsinki 2013. A written informed consent was obtained from all the study participants. The sample size was calculated using WHO Sample Size Calculator with 95% confidence interval, 5% margin of error and taking frequency of development of type 2 diabetes 6 weeks postpartum in patients with GDM to be 10%⁵. Patients were recruited using non-probability, purposive sampling. One hundred and thirty eight female patients, 25-50 years of age, diagnosed with GDM at 24–28 weeks of gestation using 75 grams OGTT, were recruited in the study after referral from Department of Gynaecology and Obstetrics, Jinnah Hospital and Akhtar Saeed Hospital, Lahore. Patients previously diagnosed with diabetes mellitus or taking any medications that were known to affect glucose metabolism e.g. glucocorticoids, anti-diabetic drugs etc. were excluded from the study. A specially designed proforma, pre-tested on ten patients, was used in the study after validation from a biostatistician. Age, height, weight, body mass index (BMI), family history of diabetes, educational status of the patient and hus-

band, history of previous GDM, mode of delivery in the previous pregnancies and the present pregnancy were recorded. Two hours 75 grams OGTT was carried 48 hours after delivery and blood sugar levels were recorded. Each patient was strictly followed up and 75 grams OGTT was repeated 6 weeks after delivery in the outpatient setting.

The collected information was entered and analysed in the statistical package for social sciences (SPSS) version 20.0 for Windows. Mean +SD was calculated for all quantitative variables like age, BMI etc. Frequency and percentage were calculated for patients who developed type 2 diabetes at 6 weeks postpartum. Similar analysis was done for those who had impaired fasting glucose or impaired glucose tolerance at 48 to 72 hours postpartum. The primary study outcome was the calculation of sensitivity, specificity, and predictive values (positive and negative) of the 2 days postpartum OGTT results to predict diabetes mellitus (defined as fasting blood sugar ≥ 126 mg/dl or 2-hours post-prandial blood sugar ≥ 200 mg/dl). The secondary outcomes included the calculation of sensitivity, specificity, and predictive values (positive and negative) of the 2 days postpartum 75 grams OGTT to predict abnormal fasting glucose (glucose 101-125 mg/dl) and abnormal glucose tolerance (2-hour glucose 140-199 mg/dl).

RESULTS

The study was conducted on 138 female patients with mean age 28.6 ± 9.2 years (range: 17-38 years). The mean values for parity and gestational age at the time of diagnosis of GDM were 3.8 ± 2.1 (range 1–7) and 25.5 ± 8.1 weeks respectively. As far as educational status is concerned, 71 (51.5%) reported to have successfully passed matriculation (10 years of formal education). Sixty (43.5%) patients gave a positive family history of diabetes mellitus. Analysis of the mode of delivery revealed that 80 (58.0%) gave birth through spontaneous vaginal delivery (Table 1). The mean glucose levels after 2-hours of 75 g OGTT were 135.2 mg/dl and 116.5 mg/dl after 48 hours and six weeks postpartum respectively ($p = 0.002$). Based on the results of 75 grams OGTT and the operational definitions of diabetes and impaired glucose tolerance stated earlier, the frequency of diabetes was found out to be 4.3% and impaired glucose tolerance was seen in 36.2% at 48–72 hours postpartum. Similarly, the frequency of diabetes and impaired glucose tolerance at 6 weeks postpartum was found out to be 9.4% and 23.2 % respectively (Table 2).

Table 3 gives the comparison of various characteristics of GDM patients who gave normal and abnormal values of OGTT 48–72 hours postpartum. The difference between the characteristics was statistically not significant ($p > 0.05$). The effect of mode of delivery (vaginal or caesarean section) on OGTT results at 48 to 72

Table 1: Baseline characteristics of the study population

Patient Characteristics	Mean ± S.D.
Age (years)	28.6 ± 9.2
Parity	3.8 ± 2.1
Pre-gestational BMI (Kg/m ²)	24.7 ± 7.2
Gestational Age at GDM Diagnosis (weeks)	25.5 ± 8.1
Positive Family History of Diabetes (%)	43.5
Positive Previous History of GDM (%)	7.9
Vaginal Delivery (%)	58.0
Delivery via C-Section (%)	42.0

Table 2: Comparison of 75 grams OGTT results carried out after 48-72 hours and 6 weeks postpartum

Parameter	OGTT at 48-72 Hrs Postpartum	OGTT at 6 Weeks Postpartum	P value
Fasting Blood Sugar (mg/dl)	98.7	86.6	0.658
Blood Sugar Level 2-h Post OGTT (mg/dl)	135.2	116.5	0.710
Frequency of Diabetes, n (%)	6 (4.3)	13 (9.4)	0.092
Frequency of Impaired Glucose Tolerance, n(%)	50 (36.2)	32 (23.2)	0.106

Table 3: Comparison of various characteristics of GDM patients who gave normal and abnormal OGTT results 48-72 hours after delivery

Variables	Normal OGTT (n = 82)	Abnormal OGTT (n = 56)	P Value
Age (years)	27.8 ± 8.1	28.9 ± 9.1	0.498
Pre-gestational BMI (kg/m ²)	23.4 ± 6.9	25.6 ± 7.2	0.258
BMI at Term (kg/m ²)	29.2 ± 7.6	31.3 ± 8.3	0.401
Positive Family History of diabetes, n (%)	30 (36.6)	26 (46.4)	0.019
Required Insulin during Pregnancy, n (%)	20 (24.4)	17 (30.4)	0.732
Gestational Age at Delivery (weeks)	39.8 ± 4.2	41.1 ± 3.9	0.826
Caesarean Section, n (%)	32 (39.0)	24 (42.9)	0.982

Table 4: Validity of 75 grams OGTT in diagnosing diabetes 48-72 hours after delivery

Validity Index	Diabetes	Impaired Glucose Tolerance
Sensitivity (%)	76.2	68.1
Specificity (%)	96.1	77.2
Positive Predictive Value (%)	67.4	36.8
Negative Predictive Value (%)	94.1	88.6

hours, and six weeks postpartum was also assessed. No statistically significant difference was found between the two groups ($p > 0.05$). Validity indices were calculated for diagnosis of diabetes mellitus and impaired glucose tolerance. We found that 75 grams OGTT conducted at 48-72 hours postpartum gave sensitivity of 26.2% and specificity of 96.1% for diagnosing DM; while it gave sensitivity of 68.1%, and specificity of 77.2% for diagnosing IGT, as shown in Table 4.

DISCUSSION

The primary objective of the study to assess the validity of 75 grams OGTT carried out after 48-72 hours postpartum for early diagnosis of diabetes mellitus in GDM patients was successfully met. To the best of our knowledge, this is the first study from Pakistan on the subject. Recently, two earlier studies were carried out to determine the utility of 48-72 hours postpartum OGTT in assessing development of diabetes mellitus in GDM patients^{1,5}. The idea of testing women with GDM soon after delivery was recently proposed and investigated by Werner et al⁹. The researchers reported that OGTT conducted at 48-72 hours postpartum was a feasible and very useful method for early identification of women with GDM at risk for later development of type 2 diabetes mellitus⁹. The idea was further explored by Nabuco et al⁵ who assessed the accuracy of the 75-grams OGTT conducted within 48-72 hours postpartum. The investigators reported that the test had a very high positive and negative predictive value of 16.7% and 97.9% respectively in identifying women with GDM who must be screened at 6 weeks postpartum for further risk evaluation⁵. Our results also match with the earlier reports as mentioned below.

The mean age of the patients was 28.6 ± 9.2 which differ slightly from the mean age reported earlier 32.2 ± 5.8 and 32.0 ± 5.2 years by Werner et al⁵ and Nabuco et al⁹ respectively. The lower mean age in our study population could be explained by a trend of early marriages in our country. The study population mainly consisted of an urban population. Had it been chosen from a rural population, even lesser mean age could have been recorded. The prevalence of diabetes mellitus on

OGTT 48-72 hours and 6 weeks postpartum was 4.3% and 9.4% respectively which is in accordance with earlier reports that have shown prevalence from 5-14%¹⁰⁻¹². We found that the pre-gestational BMI and gestational age at GDM diagnosis were 24.7 ± 7.2 Kg/m² and 25.5 ± 8.1 weeks respectively. These results are comparable to earlier study by Nabuco et al⁹ who reported pre-gestational BMI and gestational age at GDM diagnosis as 27.7 ± 5.3 Kg/m² and 23.1 ± 7.4 weeks respectively⁵.

Our study showed that all the plasma glucose levels were relatively higher in OGTT conducted 48-72 hours postpartum than those observed at 6 weeks (Table 2). This could be explained by differences in the hormonal levels in the body soon after delivery and after a period of 6 weeks postpartum. During pregnancy the levels of circulating oestrogen and progesterone are very high owing to placental production^{13,14}. These hormones are counter-regulatory to insulin and produce a state of insulin resistance and dysglycemia in the body¹⁴. However, soon after removal of placenta from the body, the levels of these hormones decline rapidly and reach pre-pregnancy levels in 5-7 days¹⁵. This is manifested by a better glycemic control and more regulated blood sugar levels at 6 weeks postpartum.

Our results showed that OGTT conducted soon after delivery carried a very high specificity and negative predictive values of 96.1% and 94.1% respectively meaning thereby that the GDM patients who tested negative 48-72 hours postpartum truly did not have diabetes mellitus. Werner et al⁵ and Nabuco et al⁹ reported a specificity of 94% and 60% respectively for utility of OGTT soon after delivery. Similar to earlier studies that showed a sensitivity of 100% and 71.4%, our findings also present a sensitivity of 76.2%^{5,9} (Table 4). The aforementioned validity indices imply that the OGTT conducted early in the postpartum period can be a very useful tool in identifying women who need further follow-up; and reduce the burden of excess testing by excluding those women who perform well on the test 48-72 hours postpartum. Besides, various studies have shown traumatizing life events to be the occasions when a significant lifestyle modification can be brought about in patients' lives¹⁶⁻¹⁸. The childbirth is considered a very emotional event in a women's life which provides an exceptional opportunity

to teach them about lifestyle modifications to overcome their different morbidities. So, OGTT conducted soon after birth helps us utilize this opportunity by educating the women with GDM about further follow-up and behavioural modifications that will not only improve their quality of life, but will also enable them to live a better life with their families. Further studies based on larger number of subjects will help establish definitive guidelines for utility of this test in following GDM patients.

CONCLUSION

Oral glucose tolerance test performed 48-72 hours postpartum is a useful tool in identifying those women who need further monitoring and testing for type 2 diabetes as well as lessens the burden on health care facilities by excluding those women who test normally in the early postpartum period.

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CONTRIBUTORS

AB conceived the idea, planned the study, and drafted the manuscript. AR, SM and ZAK helped acquisition of data. KS helped acquisition of data and did statistical analysis. KAK and SS critically revised the manuscript, did statistical analysis and designed the study. All authors contributed significantly to the submitted manuscript.