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# RECLASSIFICATION OF GESTATIONAL DIABETES MELLITUS POSTPARTUM –A PROSPECTIVE STUDY

Obstetrics & Gynaecology

**Dr Binu K** MS OBG, DNB Senior Resident Department Of Obstetrics And Gynecology, Government Medical College Kozhikode Kerala

**Dr Menon Nalini Sekharan** Additional Professor, Department Of Obstetrics And Gynecology, Government Medical College Kozhikode Kerala

**Dr Bindu Vijaykumar*** Additional Professor, Department Of Obstetrics And Gynecology, Government Medical College Kozhikode Kerala *Corresponding Author

## ABSTRACT

**Introduction** Gestational diabetes mellitus (GDM) is historically defined as "any degree of glucose intolerance with onset or first recognition during pregnancy", and may or may not persist after labor. Women who had pregnancies complicated by GDM are at an increased risk of developing T2DM in the postpartumperiod when compared with those with normal plasma glucose levels during pregnancy.

**Aims &Objectives**

- To re-evaluate the glycemic status in women with history of GDM and to identify the progression to different glycemic outcomes at six weeks post partum

**Materials And Methods** Aa one group prospective cohort study, conducted in Institute of Maternal & Child Health, Kozhikode, on Pregnant women diagnosed with Gestational Diabetes Mellitus diagnosed at any gestational age, from April 2017 to March 2018. A total of 256 study subjects who were diagnosed with GDM who fulfilled the above criteria were followed upto 6 weeks postpartum. The clinical and demographic characteristics were studied .These pregnancies were followed up during their antepartum ,intrapartum and postpartum periods.The maternal and fetal outcomes were studied and they were followed up at 6 weeks postpartum andand the 75gm OGTT was used to test their glycemic control and progression to glucose intolerance. **Results** 35% of patients above 30 years had persistent glucose intolerance after delivery.Around 30% of patients who developed postpartum glucose tolerance were multigravidas. An excessive weight gain during pregnancy imparts 2.86 times increased risk of developing abnormal glucose tolerance at six weeks postpartum when compared with those who had a normal weight gain in the antenatal period,Similarly there was significant association beween obesity ,family history and previous history of GDM and the persistence of glucose intolerance p[ostpartum.

## KEYWORDS

### INTRODUCTION:

Gestational diabetes mellitus (GDM) is defined as "any degree of glucose intolerance with onset or first recognition during pregnancy", and may or may not persist after delivery[1]. This concept had limitations, considering the inclusion of pregnant women with type 2 diabetes mellitus (T2DM) not previously diagnosed[2]. Thus, it was modified after Hyperglycemia and Adverse Pregnancy Outcome (HAPO)study, which evaluated more than 25,000 pregnant women and planned to find the cutoff point of the maternal plasma glucose associated with the increase of adverse perinatal events.The diagnostic patterns for GDM were revised, and the recommendation according to the International Association of Diabetes and Pregnancy Study Groups (IADPSG) since 2010 is that pregnant women who fit the diagnosis of T2DM at the first prenatal appointment be diagnosed as having overt diabetes.

Women who had pregnancies complicated by GDM are at an increased risk of developing T2DM in the postnatal period and beyond when compared with those with normal plasma glucose levels during pregnancy[9]. A meta-analysis evaluated 28 studies including women with previous GDM, with follow-up ranging between 6 weeks and 28 years after the end of pregnancy, and showed rates of T2DM between 2.6 and 70%, depending on ethnicity, diagnostic criteria, and the follow-up period[5,10,11]. Literature proves that one in 10 pregnancies is associated with diabetes, 90% of which are GDM.

In India, rates of GDM are estimated to be 10-14.3% which is much higher than the west[12]. As of 2010, there was an estimated 22 million women with diabetes between the ages of 20 and 39 & an additional 54 million women in this age group with impaired glucose tolerance(IGT) or pre-diabetes with the potential to develop GDM if they become pregnant. The incidence of GDM is expected to increase to 20%, i.e. one in every 5 pregnant women is likely to have GDM.

With the prevalence of type 2 diabetes (T2DM) and prediabetes growing in epidemic proportions, it is important to promote strategies to delay or prevent the onset of T2DM among high risk populations. The incidence of gestational diabetes mellitus (GDM) is also increasing owing to advancing maternal age and increasing obesity rates[13-17]. This demands for improved screening and treatment for GDM with the aim of improving maternal and fetal outcomes.

### AIMS &OBJECTIVES

1.To re-evaluate the glycemic status in women with history of GDM and to identify the progression to different glycemic outcomes at six weeks post partum:

- Normal glycemic control,
- Impaired fasting glucose,
- Impaired glucose tolerance
- Type 2 Diabetes Mellitus.

2. To determine risk factors for developing glucose intolerance postpartum which may lead to diabetes mellitus in future

### METHODOLOGY

This is a one group prospective cohort study, conducted in Institute of Maternal & Child Health, Kozhikode, on Pregnant women diagnosed with Gestational Diabetes Mellitus diagnosed at any gestational age, from April 2017 to March 2018. Screening was done using one step diagnostic 75g 2hour OGTT with cut off of Fasting plasma glucose : >92mg/dl and Post 1 hour : >180mg/dl and Post 2 hour : >153mg/dl, a single abnormal value is enough to diagnose GDM[3].Pregnant women newly diagnosed with Gestational Diabetes Mellitus having normal levels of HbA1c at the time of diagnosis were included in the study. Patients with diagnosed T1DM or T2DM and patients with comorbidities like gestational hypertension, dyslipidemia,other metabolic disorders and those who were lost to follow up were excluded from the study.

A total of 256 study subjects who were diagnosed with GDM who fulfilled the above criteria were followed upto 6 weeks postpartum. The clinical and demographic characteristics were studied .These pregnancies were followed up during their antepartum ,intrapartum and postpartum periods.The maternal and fetal outcomes were studied and they were followed up at 6 weeks postpartum andand the 75gm OGTT was used to test their glycemic control and progression to glucose intolerance. The degree of glucose intolerance was assessed and the study subjects were re-classified accordingly .ADA guidelines

were used in interpreting the results. Data is entered in MS Excel. Data analysis was done using SPSS2 Software by applying appropriate statistical tests.

**RESULTS&OBSERVATIONS**

As seen in Table 1, of the 256 cases, majority of study subjects belonged to the age group of 20-30years, i.e137 cases (53.5%). The average age was 27.

Among these, 43.7% cases reverted back to normal glucose tolerance postpartum. 35% of patients above 30 years had persistent glucose intolerance after delivery.Age more than 30 years has a statistically significant increased risk of approximately 2 times of developing postpartum glucose intolerance (RR 1.92, 95% CI 1.21-3.05, P=0.006). And younger patients were protected from developing glucose intolerance, though the results are not significant statistically (RR 0.7, 95% CI 0.29-1.71. P=0.426).

Most of the study subjects were multigravidae (62.9%). Among these women, 69.6% patients were having normal glucose tolerance at six weeks postpartum. When compared to primigravidae, multigravidae was seen to have increased risk of developing glucose intolerance at six weeks postpartum, which was statistically significant (RR 3.21, 95% CI 1.65-6.24, P=0.0001) as depicted by Figure 1.

As seen in Table 2 ,Out of the 256 cases, 132 cases were having a positive family history of diabetes in first degree relatives (51.6%). Majority of them were having a history of diabetes in one of their parents or siblings. Patients with family history of Diabetes has shown to have a statistically significant increased risk of developing postpartum glucose intolerance at six weeks postpartum (RR 2.19, 95% CI 1.34-3.57, P=0.001).

74 patients in the study cohort had a history of GDM in their previous pregnancy (28.9%). 88.8% of patients who were diagnosed as Type2 Diabetes in the six weeks postpartum OGTT had a previous history of GDM. As seen in Figure 2 ,Previous history of GDM imparts a very much increased risk of developing glucoseintolerance postpartum (95% CI 2.72-10.04, P=<0.00001).

133 cases among the 256 study subjects who were diagnosed with GDM in the third trimester had normal glucose tolerance postpartum (83.6%). All those patients diagnosed with GDM before 20 weeks in the study cohort had some form of persistent glucose intolerance in the postpartum OGTT. Hence ,as seen in figure 3, lesser the gestational age at diagnosis of GDM, more increased is the risk of abnormal glucose tolerance in the postpartum period (RR 6.12, 95% CI 4.3-8.69, P=<0.00001).

Excessive weight gain was defined according to the most recent Institute of Medicine (IOM) guidelines. 52.3% of the study population had excessive weight gain during pregnancy. An excessive weight gain during pregnancy imparts 2.86 times increased risk of developing abnormal glucose tolerance at six weeks postpartum when compared with those who had a normal weight gain in the antenatal period, which is statistically significant (95% CI 1.65-4.96, P=0.00005)as seen in table 3.

93 cases were managed with Medical Nutritional Therapy (36.3%). Only 11 cases out of the 256 subjects were put on metformin (4.3%). Majority of the patients, i.e. 152 cases were managed with insulin (59.4%).

Overall, 187 patients had good glycemic control antenatally (73%). Out of these 187 well controlled diabetics, 156 had reverted back to normal glucose tolerance levels postpartum. All those 9 patients who showed results consistent with Type2 Diabetes according to the postpartum OGTT were having uncontrolled sugars during pregnancy despite being tried to be managed appropriately. There is a significant association between the mode of management of Gestational diabetes mellitus and postpartum glucose tolerance . Hence those managed with insulin, presumed to be so due to the uncontrolled sugars despite being managed with MNT or metformin are found to have abnormal glucose tolerance at six weeks postpartum. Those patients who had poor glycemic control at the time of delivery are more prone to have persistent glucose intolerance postpartum, which is proven statistically (RR 2,36, 95% CI 1.53-3.65, P=0.0001).

84.4% babies born to these diabetic mothers were under 4kg weight. 8 patients of the 9 cases who developed diabetes postpartum had macrosomic babies (88.8%). When compared with the patients who had babies of normal birth weight, those who had macrosomic babies are at increased risk to continue to be have glucose intolerance postpartum as shown by statistics (RR 2.24, 95% CI 1.42-3.52, P=0.001).

Those patients who developed other co-morbidities like gestational hypertension during the course of pregnancy were excluded from the study cohort.

Those complications attributable to diabetes were seen among those patients who developed Type2 Diabetes in the postpartum OGTT. 1 patient had a macrosomic baby with shoulder dystocia, birth asphyxia associated with third degree perineal tear and atonic PPH for the mother. 3 babies were delivered by vacuum extraction. 9% babies had hypoglycemic episodes and one among them had seizures. 4% babies had respiratory distress syndrome. Caesarean sections were also high among these patients. A higher incidence of wound infection was seen among diabetic mothers. There is a statistically significant increased risk for the patients who had perinatal complications to develop postpartum glucose intolerance when compared to those had did not have the same (RR 2.12, 95% CI 1.29-3.5, P=0.007)

Out of the 256 cases, 198 patients had normal glucose tolerance at the six weeks postpartum OGTT (77.3%).

8.5% cases, i.e. 22 patients showed impaired fasting glucose and 15 patients showed impaired glucose tolerance (5.9%).

Impaired fasting glucose along with impaired glucose tolerance was seen among 12 cases in the study cohort (4.8%).

There were 9 cases who showed results within the Type2 Diabetes range (3.5%). A total of 22.7% cases in the study population showed abnormal glucose tolerance at six weeks postpartum.

81 patients who were managed with Medical Nutritional Therapy were having normal glucose tolerance at six weeks postpartum (87.2%). 8 cases showed impaired fasting glucose (8.6%). There were 3 cases with impaired glucose tolerance (3.2%) andone case showing impaired fasting glucose with impaired glucose tolerance (1%). None of those patients on MNT developed Type 2 Diabetes at six weeks.

There were only 11 cases among the study cohort who were put on metformin (4.3%). Among them, 90.9% cases, i.e. 10 cases reverted back to normal glucose tolerance at six weeks postpartum. Only one case showed impaired fasting glucose , i.e. 9.1%.

Out of the 152 cases managed with insulin, 70.5% cases had normal glucose tolerance at the six weeks postpartum OGTT, i.e. 107 cases. All the patients who developed Type2 Diabetes in the postpartum OGTT were managed with insulin in the antenatal period, 9 cases. 8.5% patients on insulin showed impaired fasting glucose and 7.9% cases had impaired glucose tolerance. 11 cases, i.e. 7.2% had both impaired fasting glucose along with impaired glucose tolerance.

Basically those having uncontrolled sugars with MNT and OHA and had to be put on insulin were at higher risk of glucose intolerance in future life.

**DISCUSSION**

22.7% of women were detected to have glucose intolerance by 6 weeks postpartum, underlining the importance of early screening for diabetes. It also shows the importance of screening within 1 year window period in women who missed screening or screened negative at 6 weeks postpartum because there is a significantly increased risk of developing glucose intolerance in our population as seen in this study.

Studies have proven that development of abnormal glucose tolerance postpartum is attributed to the presence of risk factors like advanced maternal age, highBMI, family history of T2DM , previous history of GDM, HbA1c, weight gain during pregnancy and birth weight of the baby [1,7,8].

Several studies have revealed that maternal BMI at baseline

(independent of weight gain) is an independent risk factor for subsequent development of glucose intolerance[6]. As seen in previous studies, the current study also revealed that BMI ⩾25 kg/m$^2$ is an independent risk factor for postpartum glucose intolerance in South Indian women. In our study,Overweight women with GDM are seen to have an increased risk of developing postpartum glucose intolerance with a relative risk of 2.61 (95% CI 1.67-4.08, P=0.0001) compared to the patients with normal BMI. Underweight has shown to be protective, but not statistically significant (RR 0.7, 95% CI 0.19-2.61, P=0.742) .

The incidence of Impaired fasting glucose, Impaired glucose tolerance and diabetes, in this study, were 8.5%, 5.9% and 3.5%, respectively. The results showed that women who developed glucose abnormalities (IFG, IGT and diabetes) were significantly more obese.A significantly higher proportion from this group had a family history of T2DM and they needed insulin more frequently and higher doses, for control of glycemic status than the other group.

The incidence of IGT reported in this study is slightly lower than that reported in a national survey conducted in India which showed that 25% of the adult population have prediabetes. These differences may be due to the difference in the distribution of the risk factors between the general population and the participants of this study.

This study showed that the risk factors for developing hyperglycemia were significantly more frequent in women who developed diabetes and IGT compared to those who remained normoglycemic in the postpartum period. These include factors existing before pregnancy such as pre-pregnancy weight and a family history of T2DM, factors which occurred during the index pregnancy such as the need to use insulin and furthermore higher doses to control GDM.

Those patients with GDM who needed insulin to achieve euglycemia when compared to those controlled with nutrition therapy and metformin and women who developed perinatal problems like delivering a macrosomic baby ,shoulder dystocia are also likely to progress to impaired glucose tolerance later on.This points to the fact that severity of hyperglycemia and its related adverse outcomes in pregnancy is associated with the progression to Diabetes later. Although the odds for developing hyperglycemia after GDM were not statistically significant in this study, this, however, may be due to the small number of participants.

## CONCLUSION-

Glucose intolerance is very frequent in early postpartum in Indian women with GDM. Early screening in the postpartum period particularly in overweight women can identify women who are likely to progress to glucose intolerance and thus help plan preventive strategies for delaying the onset of T2DM in them.Postpartum glucose screening is not warranted for women at low risk who do not require insulin during pregnancy. The incidence of postpartum glucose intolerance in this group is very low(3.2%). Women with risk factors should compulsorily receive postpartum screening. Elevated BMI at booking, previous history of GDM, family history of Type2 Diabetes Mellitus, need for insulin therapy, birth weight of neonate more than 4000gms and earlier gestational age at time of diagnosis of gestational diabetes were found to be most predictive of an abnormal postpartum glucose tolerance test result. Well-defined lifestyle interventions specific to women with a history of glucose intolerance during pregnancy can reduce the chance of progression to overt Diabetes later in life.

### Implication to Practice

I. Establishing a national program for screening women with a history of GDM for diabetes and prediabetes should be a priority in a strategy for controlling the epidemic of diabetes in the country.

II. Implementation of evidence-based national guidelines for the treatment of GDM that includes lifestyle modification is an important step in the control of later progression to T2DM.

The Study Was Approved By The Instituitional Research And Ethics Committee.

### Conflict Of Interest:

All authors have participated in (a) conception and design, or analysis and interpretation of the data; (b) drafting the article or revising it critically for important intellectual content; and (c) approval of the final version.

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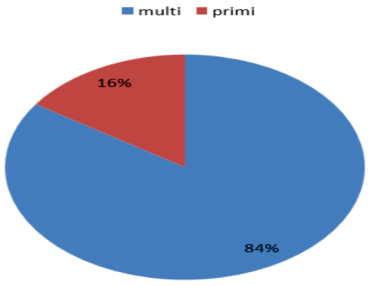


**Figure 1 Parity and postpartum glucose tolerance**

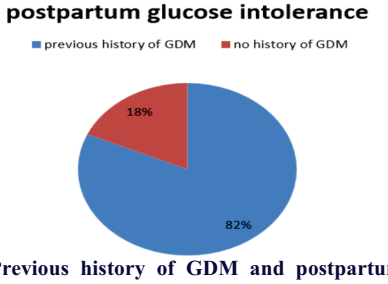


**Figure 2 Previous history of GDM and postpartum glucose tolerance.**

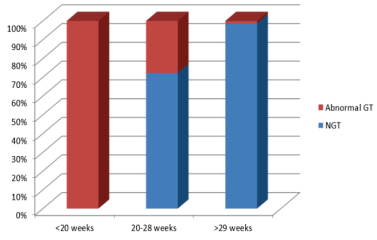


**Figure 3 Gestational age at diagnosis (weeks) and postpartum glucose tolerance**

**Table 1 Age group of patients (years) and postpartum glucose tolerance**

| Age (years) | Normal GT | Abnormal GT | RR | Pvalue |
|---|---|---|---|---|
| <20 | 34 | 5 | 0.7 (0.29-1.71) | 0.426 |
| 20-29 | 112 | 25 | 1 | |
| >30 | 52 | 28 | 1.92 (1.21-3.05) | 0.006 |

**Table 2 Family history of diabetes and postpartum glucose tolerance**

| Family history | NGT | Abnormal GT | RR | Pvalue |
|---|---|---|---|---|
| Present | 85 | 39 | 2.19 (1.34-3.57) | 0.001 |
| Absent | 113 | 19 | 1 | |

**Table 3 Gestational weight gain (kg) and postpartum glucose tolerance**

| Wt gain | NGT | Abnormal GT | RR | Pvalue |
|---|---|---|---|---|
| >12 | 90 | 44 | 1 | |
| <12 | 108 | 14 | 2.86 (1.65-4.96) | 0.00005 |

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