

## Feto-maternal Outcome in Patients with Gestational Diabetes Mellitus in Western India: A Two Years Follow up Study

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### Abstract

**Objective:** Untreated gestational diabetes mellitus (GDM) may lead to increased risk of macrosomia, congenital anomalies, unexplained stillbirth, hypoglycemia and jaundice in newborns. This prospective study was conducted to evaluate feto-maternal outcome in women with GDM.

**Materials and Methods:** Two hundred pregnant women underwent 75grams glucose challenge test according to Diabetes in Pregnancy Study of India (DIPSI) criteria. All 26 GDM patients were managed by medical nutrition therapy (MNT), metformin and insulin. Monitoring was done through six-point and seven-point plasma glucose profile, anomaly scan between 18-20 weeks, every three weeks fetal sonography after 28 weeks, fetal echocardiography at 25 weeks, weekly non-stress test and amniotic fluid index after 32 weeks. Descriptive statistics and chi square were used to analyze data.

**Results:** Mean ( $\pm$ SD) age of studied patients was 24.26 ( $\pm$  3.75) years. Two (7.6%) patients with GDM developed vaginal candidiasis. Six (23.7%) patients underwent caesarean and two (7.6%) underwent vacuum-assisted delivery. One (3.8%) underwent spontaneous abortion. Neonatal outcome was affected by hyperbilirubinemia (12%) in three and shoulder dystocia in one (3.8%) neonate.

**Conclusion:** Timely screening of all pregnant women for glucose intolerance, achieving euglycemia in them and ensuring adequate nutrition can reduce adverse feto-maternal outcomes and promote healthy families. The successful maternal, perinatal and neonatal outcome rests on both the obstetrician's intrepidity and patients' awareness of her condition, its implications, management and long term prospects.

**Keywords:** Gestational diabetes mellitus, Pregnancy complication, Glucose tolerance tests

### Introduction

Pregnancy induces progressive changes in maternal carbohydrate metabolism. Gestational Diabetes Mellitus (GDM) is defined as carbohydrate intolerance of with onset or first recognition during pregnancy. Women with a history GDM are at increased risk of Type-2 diabetes mellitus (T2DM) in future; also their children are at the risk of

T2DM (1,2). Underlying insulin resistance, diabetogenic stress due to human placental lactogen and compensatory increase in insulin secretion are associated with adverse fetomaternal outcome. Untreated GDM may lead to increased risk of macrosomia, congenital anomalies, unexplained stillbirth, hypoglycemia and jaundice in the offspring. Infants of mothers with pre-existing diabetes experience the risk of serious birth injuries, caesarean delivery and the incidence of NICU admissions more than other. The adverse effects of abnormal maternal glucose metabolism on the offspring have been documented. The childhood metabolic syndrome includes childhood obesity, hypertension, dyslipidemia, and glucose intolerance. Congenital malformations, respiratory distress syndrome and extreme prematurity and perinatal deaths are in correlation with gestational diabetes (3-5). Despite GDM, maintaining euglycemia state can prevent from adverse fetomaternal outcome. This prospective study was conducted to evaluate fetomaternal outcome in women diagnosed with GDM over a two years period from May 2012 to Apr 2014.

### Materials and Methods

The prospective comparative study was conducted on 200 pregnant women presenting to the antenatal clinic of a 1600-bedded tertiary-care hospital and medical teaching institute in Western India from May 2012 to Apr 2014 after approval from Institutional ethics committee (AFMC/2011-14/OBG/01) and written informed consents. Blood plasma glucose levels >140 mg/dl by glucose-peroxidase method from venepuncture drawn sample two hours after administration of anhydrous 75 gm oral glucose tolerance test (OGTT) at <20 weeks and at 24-28 weeks period of gestation (POG) irrespective of glycemic state was considered for diagnosis of GDM under Diabetes in Pregnancy Study group of India (DIPSI) criteria (1). All patients with GDM were included whereas patients with past history of GDM, impaired glucose

tolerance (IGT), T2DM, unexplained stillbirth, macrosomia, congenital anomalies or birth injuries were excluded.

All 26 patients diagnosed with GDM were managed throughout the prenatal and perinatal period by medical nutrition therapy (MNT), oral antihyperglycemic medicines and insulin. MNT was appropriated according to patients' ethnicity, cultural and food preferences, as outpatients or inpatients, and recorded in a diet-diary. Daily calorie requirement was calculated according to pre-pregnancy body mass index (BMI) and present body weight; with 30 kcal/kg/day for BMI <20 Kg/m<sup>2</sup>, 25 kcal/kg/day for BMI between 21-29 Kg/m<sup>2</sup>, and 20 kcal/kg/day for BMI >30 Kg/m<sup>2</sup>; with a 100 calorie increment with each trimester. Food items with high glycemic index were avoided. Seven days after MNT, six-point plasma glucose at fasting, after breakfast, before lunch, after lunch, before dinner and after dinner was checked. Patients with pre-meal and 2-hour post-meal plasma glucose levels more than or equal to 95 mg/dl and 120 mg/dl were treated with metformin. Patients having further impaired glycemic profile were treated with human mixtard insulin 0.7, 0.8 and 0.9 units/kg body weight in first, second and third trimesters respectively with titrated dosages as required. Insulin therapy was monitored by seven-point plasma glucose including additional plasma glucose tested at 3 AM every night. MNT was continued in parallel to metformin and insulin (6).

All patients were followed for MNT, metformin or insulin therapy, anomaly scan between 18-20 weeks, every three weeks fetal sonography after 28 weeks, fetal echocardiography at 25 weeks, weekly non-stress test, amniotic fluid index after 32 weeks and termination of pregnancy at 39 completed weeks. Glycated hemoglobin (HbA1c) was as treatment index.

All patients with GDM were monitored as per guidelines for labor monitoring in high risk pregnancy. Plain insulin as per sliding-scale with a 2 hours capillary glucose monitoring was administered along with continued

surveillance and management in the perinatal period. Termination of pregnancy was planned at 39 weeks for uncomplicated controlled gestational diabetes mellitus patients.

Demographic, clinical, management and outcome profile were collected for descriptive statistics including frequency, percentages and 95% confidence intervals (95% CI). Chi square test with Yates correction for categorical variables was applied keeping  $P < 0.05$  as significant through Microsoft Excel and SPSS version 10.

### Results

All 200 patients were monitored during the study without any dropouts. Mean ( $\pm$ SD) age of patients was 24.26 ( $\pm$  3.75) years. A total of 26 patients were diagnosed with GDM. All patients tolerated oral medicines and insulin without major adverse effects. Seven-point glucose monitoring post-insulin was found

within normal limits for all patients. No patient was found to have abnormal HbA1c. Two patients with GDM developed vaginal candidiasis in the antenatal period. Six patients underwent caesarean and two underwent vacuum-assisted delivery. One underwent spontaneous abortion (Tables 1-2). Neonatal outcome was affected by hyperbilirubinemia in three and shoulder dystocia in one neonate (Table 3). Chi square revealed no significance between observed values and no macrosomia was seen.

### Discussion

GDM represents the tip of an iceberg as the risks of inadequate glycemic control has multipronged effects to the mother and offspring both during and beyond the perinatal period extending future risks of metabolic inadequacy (7,8). The ACOG committee report has found five-fold higher association

**Table 1. Obstetric outcome in gestational diabetes mellitus**

Antenatal complication	GDM		Total
	Present	Absent	
Preeclampsia/Gestational hypertension	0	11 (6.3%)	11
Urinary Tract Infection	0	2 (1.1%)	2
Vaginal Candidiasis	2 (7.6%)	4 (2.2%)	6
Polyhydramnios	0	0	0

**Table 2. Delivery-related obstetric outcomes in gestational diabetes mellitus**

Mode of delivery	GDM		Total
	Present	Absent	
Assisted breech delivery	0	1 (0.5%)	1
Caesarean	6 (23.07%)	21 (12.06%)	27
Full term normal delivery	15 (57.6%)	122 (70.11%)	137
Preterm vaginal delivery	0	10 (5.7%)	10
Spontaneous abortion	1 (3.8%)	1 (0.57%)	2
Twin vaginal delivery	1 (3.8%)	5 (1.15%)	6
Vacuum delivery	2 (7.6%)	9 (5.17%)	11
Vaginal birth after caesarean	1 (3.8%)	5 (2.9%)	6
<b>Total</b>	<b>26</b>	<b>174</b>	<b>200</b>

**Table 3. Neonatal outcomes in gestational diabetes mellitus**

Variable		GDM		Total	P-value
		Present	Absent		
Hypoglycemia	Present	1 (4%)	3 (1.6%)	4	0.33
	Absent	20	176	196	
Hyperbilirubinemia	Present	3 (12%)	5 (2.7%)	8	0.11
	Absent	18	174	192	
Shoulder dystocia	Present	1 (4%)	2 (1.1%)	3	0.19
	Absent	20	177	197	
Macrosomia	Present	0	0	0	-
	Absent	25	175	200	

Results analyzed through chi square test with  $P$ -value  $> 0.05$  for significance

between maternal hyperglycemia, large for gestational age infants, macrosomia, cord blood C-peptide (evidence of fetal hyperinsulinemia), neonatal hypoglycemia, neonatal jaundice and caesarean delivery (9,10).

In all women with inadequate glycemic control, there is 9-14% rate of miscarriage corresponding to the degree of hyperglycemia, which may revert with excellent glycemic control. Approximately 30% of fetuses of women with GDM are large for gestational age and 15-45% of neonates suffer from macrosomia (11,12). However, a well-managed GDM can have favorable outcome according this study (13-15).

During a healthy pregnancy, mean fasting blood sugar levels decline progressively to a remarkably low value of  $74 \pm 2.7$  mg/dl. On the other hand, peak postprandial blood sugar values rarely exceed 120 mg/dl. Meticulous replication of the normal glycemic profile during pregnancy has been demonstrated to reduce the macrosomia rate. Specifically, when two postprandial glucose levels are maintained less than 120 mg/dl, approximately 20% of fetuses demonstrate macrosomia. Conversely, if postprandial levels range up to 160 mg/dL, macrosomia rates rise to 35% (16).

Persistent maternal hyperglycemia can induce increase in beta cell mass and insulin secretion in the fetus by 16th week period of gestation. Surging maternal and fetal glucose levels are accompanied by episodic fetal hyperinsulinemia. Fetal hyperinsulinemia promotes excess nutrient storage, resulting in macrosomia. The energy expenditure associated with the conversion of excess glucose into fat causes depletion in fetal oxygen levels. These episodes of fetal hypoxia are accompanied by surges in adrenal catecholamine, which, in turn, cause hypertension, cardiac remodeling and hypertrophy, stimulation of erythropoietin, red cell hyperplasia, and increased hematocrit. Polycythemia (hematocrit >65%) occurs in 5-10% of newborns of diabetic mothers (17,18).

In women with overt diabetes and suboptimal glycemic control prior to conception, the likelihood of a structural anomaly is increased 4-8 fold compared to 1-2% otherwise. When the frequency of congenital anomalies in patients with normal or high first-trimester maternal HbA1c was compared with healthy patients, the rate of anomalies was only 3.4% with HbA1C < 8.5%, whereas patients with poor glycemic control in the periconceptional period (HbA1C >8.5%) had a 22.4% rate of malformations (19-21).

Most of the birth injuries occurring to infants of diabetic mothers are associated with difficult vaginal delivery, shoulder dystocia, brachial plexus trauma, facial nerve injury and cephalohematoma. While shoulder dystocia occurs in 0.3-0.5% of vaginal deliveries among healthy pregnant women, the incidence is 2-4 folds higher in women with diabetes. Warning signs during labor (labor protraction, suspected fetal macrosomia, and need for operative vaginal delivery) successfully predict only 30% of these events (22,23).

Preeclampsia is more frequent among women with diabetes, occurring in approximately 12% as compared to 8% of the non-diabetic population. The risk of preeclampsia is also related to maternal age and the duration of preexisting diabetes. Fasting blood glucose <105 mg/dl has been associated with 7.8% rate of preeclampsia, which reaches 13.8% beyond 105 mg/dl.

Limitations of the study include limitations of sample size, control arm, developing country cohort and resources, which can prove to be a limitation towards conclusive interpretation. In pregnancy, the decision to perform a placebo controlled trial requires clinical equipoise and hence no untreated pregnant controls were used (24).

A multifaceted approach involving obstetrician, diabetologist, neonatologist, laboratorian, diabetes educator, dietitian and midwife is required to optimize diagnosis and management of GDM and consequent feto-maternal outcome. A short-term intensive care gives a long term pay off in the primary

prevention of obesity, impaired glucose tolerance and diabetes in the offspring, as preventive medicine starts before birth. Patients need to be educated on the implications of GDM for her baby and herself, dietary and exercise recommendations, self-monitoring of blood glucose, self-administration of insulin and dose adjustment, identification and treatment of hypoglycemia, safe physical activity, stress reduction and coping with denial (25,26).

## Conclusions

Timely screening of all pregnant women for glucose intolerance, achieving euglycemia in them and ensuring adequate nutrition can reduce adverse fetomaternal outcomes and promote healthy families. The successful maternal, perinatal and neonatal outcome rests on both the obstetrician's intrepidity and patients' awareness of her condition, its implications, management and long term prospects.

## Conflict of Interest

The Authors declare that there are no conflicts of interest.

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