

# Effect of Various Degrees of Maternal Hyperglycemia on Fetal Outcome

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## ABSTRACT

- Objective** To find out the effect of various degrees of maternal hyperglycemia on fetal outcome.
- Study design** Comparative study.
- Place & Duration of study** Obstetrics and Gynecology Department, Liaquat National Hospital Karachi, from August 2007 to August 2009.
- Methodology** Healthy pregnant women with no co-morbids attending antenatal clinic were subjected to glucose challenge test (GCT) with 50 gm load of glucose in their 2<sup>nd</sup> trimester of pregnancy regardless of previous meal. Patients with established type II diabetes mellitus and pregnancies with medical disorders were excluded from study. Patient data was collected on predesigned performa and analyzed on SPSS 15 version.
- Results** A total of 228 antenatal women enrolled in the study. Higher rate of cesarean section were noted among women with gestational diabetes mellitus (GDM-68%) as compared to 45.2% and 46.8% ( $p < 0.009$ ) with mild gestational hyperglycemia (MGH) and control groups. Normal babies in GDM were 44% ( $p < 0.001$ ) while neonatal intensive care unit (NICU) admissions were significantly higher in GDM babies (54.7%  $p < 0.001$ ), as compared to other two groups. Rate of premature births in GDM mothers was higher than MGH and control. Gestational age of babies at birth for GDM was  $36.4 \pm 2.1$  weeks as compared to MGH ( $38.1 \pm 1.2$  weeks) and control groups ( $37.8 \pm 1.9$  weeks).
- Conclusions** The preponderance of maternal obesity, increasing maternal age and multiparity had strong association with the development of diabetes. In cases of unplanned pregnancies, the pre-pregnancy blood sugar levels are usually not known, therefore type II diabetes mellitus (DM) some times 1<sup>st</sup> diagnosed during pregnancy.
- Key words** GCT, Maternal hyperglycemia, Fetal outcome.

## INTRODUCTION:

Gestational diabetes mellitus is defined as glucose intolerance of varying degrees and severity with onset or first recognition, during pregnancy. This definition applies regardless of whether insulin or diet modification is used for treatment and whether or not the condition persists after pregnancy.<sup>1</sup> GDM may be associated with an increased risk of macrosomia, congenital malformations, birth trauma, neonatal metabolic abnormalities, NICU admission

and increased rate of cesarean or instrumental deliveries.<sup>1,2</sup>

Prevalence of GDM may range from 1-14% in all pregnancies, depending upon the population studied. According to American Diabetic Association, approximately 7% of all pregnancies are complicated by GDM, resulting in more than 200,000 cases annually.<sup>3</sup> The glucose challenge test has high specificity but low sensitivity. It is not cost effective test for screening, and it needs to be combined with random blood sugar levels.

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Gestational diabetes is a reversible condition and women who have adequate control of glucose level can effectively decrease the associated risks and with birth of healthy babies. Women with gestational diabetes are at high risk of developing type II diabetes

mellitus after pregnancy while their offsprings are prone to develop childhood obesity later in life. Most patients are treated only with diet modification and moderate exercise, while some need anti-diabetic drugs including insulin therapy.<sup>3,4</sup>

Recurrence rate of gestational diabetes is reported to be 30-70% and incidence of overt diabetes in women with gestational diabetes history is between 35.2-73 %.<sup>5,6</sup> Since GDM manifests itself after the period of organogenesis, malformations are rare except in cases who present for the first time in pregnancy with uncontrolled blood sugar levels. If gestational hyperglycemia is controlled by introduction of the insulin, the fetal outcome in gestational diabetic mothers can be improved.<sup>4</sup> The objective of this study was to assess the effect of various degrees of maternal hyperglycemia on fetal outcome.

#### **METHODOLOGY:**

The study was conducted at Obstetrics and Gynecology Department, Liaquat National Hospital Karachi, from August 2007 to August 2009. Healthy pregnant women with no co-morbid attending antenatal clinic were subjected to GCT with 50 gm glucose load in their 2<sup>nd</sup> trimester of pregnancy regardless of previous meal. One and half hour later their blood collected for glucose estimation. Patients with established type II diabetes and pregnancies with medical disorders were excluded from the study.

Blood glucose challenge test was done at 24 weeks, then repeated at 34 weeks of gestation in both MGH and woman with impaired oral glucose tolerance test (OGTT). The cutoff value for normal GCT was taken as <140 mg%. The women with impaired GCT were subjected to oral glucose tolerance test with 75 gm glucose load. Two samples were collected one hour apart. The cutoff values used to diagnose the GDM cases, and the normal readings of OGTT for reference were:

- Fasting blood glucose =95mg/dl
- After one hour =180 mg/dl
- After two hours =155 mg/dl

Mild gestational hyperglycemia was the term used for those patients whose OGTT results were normal but they were GCT screen test positive. Both groups were referred to endocrinologist in diabetic clinic for advice, either reassurance and follow up, diet modification or insulin therapy. Some women already on oral hypoglycemic agents like metformin, were continued on same. A 3<sup>rd</sup> group of women whose GCT results remained normal through out pregnancy was also enrolled. All three groups followed up in

antenatal period. These women delivered under tertiary care services and their babies observed in postnatal period. The pediatrician attended these babies at birth, in labor ward and operation room for presence of any developmental defects, need for resuscitation and assessment of Apgar score. Maternal parameters like age, parity, body mass index (BMI), gestational age and control of blood sugar with fetal outcome were noted. Fetal weight, gestational age at birth, and type of delivery were also recorded. Development of hypoglycemia and hyperbilirubinemia in neonate was assessed.

Informed consent was taken from all the patients. Numeric variables like age, parity, BMI, Apgar score, gestational age at birth were measured in mean + SD, and categorical variables like mode of delivery, perinatal outcome, weight of the baby, intrauterine death (IUD), neonatal death (NND), congenital anomalies were presented in frequencies and percentages. Chi square test was used to compare relative frequencies of categorical variables whereas ANOVA (Analysis of Variance) was used to compare mean + SD in all three groups (GDM, MGH and Normal). All data were entered and analyzed through SPSS version 15. P value < 0.05 was considered as statistically significant.

#### **RESULTS:**

Two hundred and twenty eight women recruited in three groups on the basis of GCT and OGTT results. One hundred and eleven women were normoglycemic (control group), forty two had mild gestational hyperglycemia while 75 women diagnosed with gestational diabetes mellitus. The mean age, parity and BMI of women in 3 groups is shown in table I. The correlation of variables significantly demarcated by the fact that gestational diabetes was more preponderant in women of growing age and multi-parity with the tendency of weight gain in these women.

A significantly higher rate of cesarean section noted in women with GDM (68%) whereas it was 45.2% in MGH and 46.8% in control groups (p 0.009) as shown in table II. The comparative analysis of three groups showed that the NICU admission was higher in babies of GDM mothers (54.7%; p<0.001). There were only 7/42 NICU (16.8%) admissions in MGH group while 14/111 (12.6%) in control group.

The number of healthy babies born to GDM mothers were significantly low (44%; p<0.001). Mostly the babies born to them were preterm as compared to other groups. Their mean gestational age was 36.4 ± 2 weeks, while mean gestational ages in MGH and normal pregnancies were 38.1 ± 1.2 and

Table I: Study Characteristics

Variables	GDM (n = 75)	MGH (n = 42)	Normal (n = 111)	p – value
Age (years)	32.2 + 5	28.5 ± 4.5	28.2 ± 4.1	< 0.001
Parity (number)	2.4 + 2.1	1.1 ± 1.3	1.3 ± 1.4	< 0.001
BMI (Kg/m <sup>2</sup> )	25.3 + 2.7	24.7 ± 3.9	23.4 ± 3.9	0.002
<b>OGTT</b> Impaired Normal	75 (100%) 0	0 42 (100%)	0 111 (100%)	< 0.001
<b>GCT</b> Impaired Normal	75 (100%) 0	42 (100%) 0	0 111 (100%)	< 0.001

37.8 ± 1.9 weeks respectively. No statistical difference found in Apgar scores, blood sugar at birth and metabolic disorders in three groups. Similarly the birth weight of neonates born to mothers of either of three groups was found to be average (p 0.044). It is evident from study results that optimum control of blood sugar through out pregnancy resulted in birth of average weight neonates. There were 2/42 (4.8%) babies in MGH and 3 babies in control who had birth weight > 4 kg.

The neonatal deaths (14.7%) were significantly high in GDM as compared to other two groups (table II). There were 54.7% of NICU admissions of GDM babies, who had diagnosis of neonatal jaundice in 33.3%, jaundice with sepsis 9.3%, and sepsis 4%. Other indications were prematurity, meconium aspiration syndrome and observation for hypoglycemia and hypocalcemia. Some of these babies required prolonged NICU services and antibiotic cover according to their blood and urine culture report. Early breast feeding was encouraged to prevent complication of hypoglycemia and hypocalcemia in babies.

No intrauterine demise occurred in MGH group. One fresh still birth found in control group at 28 week due to anencephaly; the labor was induced and the fetal weight was 0.9 kg. There was one fresh still birth in GDM group with anencephaly and meningo-myelocele at 34 weeks, who was delivered by cesarean section due to unstable lie.

There were five (6.7%) babies in GDM group born alive with congenital defects as compared to two (4.8%) babies in MGH and four babies (3.4 %) in control groups. Out of those 5/75 GDM mothers babies, multiple type of defects found including one

baby with polycystic kidneys, one with hyaline membrane disease, one with achondroplasia, two with hydrocephalus and one with cardiac defect. Out of 2/41 babies in MGH group one had renal cysts with bilateral hydronephrosis and other had holoprosencephaly. One baby died within 24 hours while other with renal defect was referred to pediatric surgeon. Out of 4/111 in control group, one baby had anencephaly, two babies born with renal tract anomalies and one had cardiac defect.

#### DISCUSSION:

The effect of maternal hyperglycemia at conception or in period of embryogenesis usually manifests itself as congenital anomalies where as glucose intolerance during pregnancy leads to large for gestational age fetuses, metabolic disturbances, fetal demise and need for admission in NICU. By literature search this is evident that the distinction between the non-insulin dependent diabetes and gestational diabetes mellitus is not usually clear. The trimester during which the insulin is used may identify the type of diabetes. The possibility always exists of an un-recognized non-insulin dependent diabetes mellitus in the 1<sup>st</sup> trimester, may become clinically overt in last trimester.<sup>9</sup>

The fetal outcome of mothers with mild gestational hyperglycemia in this study was nearly equal to mothers with normoglycemia. According to some studies it is evident that insulin dependent diabetes and uncontrolled blood sugars in early weeks of pregnancy have high rates of congenital defects in fetuses and our study results endorse these observations.<sup>7,9</sup> Whites P distinguished gestational diabetes into two subtypes, type A1 where the abnormal glucose tolerance test is followed by normal fasting and 2 hours postprandial blood sugar levels.<sup>10</sup>

In this condition only diet modification is sufficient. In type A2, abnormal OGTT is compounded by abnormal glucose levels during fasting and/or after meals. Here additional therapy with insulin is required. Based on different studies, the chances of development of GDM in subsequent pregnancies are between 30-84%, depending on ethnic background.<sup>4</sup>

Our observations in this study showed that fetal morbidity and mortality were more in women with GDM who had variations in blood sugar control

during pregnancy and those whose insulin requirement was high, especially in last trimester. The cesarean section rate was high in GDM mothers due to obstetrical and maternal reasons as compared to MGH and control group. These observations were similar to what were reported in a study where pregnant women aged 24 years were subjected to OGTT with 100 gm glucose. Compared to control group the borderline GDM women had higher rates of macrosomia (birth weight >4000g - 28.7% versus 13.7%,  $p < 0.001$ ), and increased rate of cesarean sections (29.6% versus 20.2%,  $p 0.02$ ).

**Table II: Delivery and Perinatal Outcome in Women with and without Gestational Diabetes (GDM) and Mild Gestational Hyperglycemia (MGH)**

Variables	GDM (n = 75)	MGH (n = 42)	Normal (n = 111)	p value
<b>Mode of Delivery</b>				
Vaginal Delivery	21 (28%)	21 (50%)	52 (46.8%)	0.016
Cesarean section	51 (68%)	19 (45.2%)	52 (46.8%)	0.009
Instrumental	03 (4%)	02 (4.8%)	07 (6.3%)	0.777
<b>Perinatal Outcome</b>				
Alive	33 (44%)	35 (83.3%)	95 (85.6%)	< 0.001
NICU Admission	41 (54.7%)	07 (16.7%)	14 (12.6%)	< 0.001
<b>Weight of Baby</b>				
< 2 kg	07 (9.3%)	01 (2.3%)	03 (2.7%)	0.084
2 – 3.9 kg	63 (84%)	39 (92.9%)	105 (94.6%)	0.044
4 or more kg	05 (6.7%)	02 (4.8%)	03 (2.7%)	0.429
<b>Apgar Score</b>				
At 1 min (mean + SD)	7.04 + 1.1	7.05 + 0.7	7.03 + 1.2	0.921
At 5 min (mean + SD)	8.5 + 1.2	8.6 + 0.7	8.5 + 1.3	0.606
<b>Baby's blood Sugar (mg%)</b>	62 + 50.8	64.9 + 33.8	60.3 + 12.8	0.748
<b>Gestational Age at Birth (weeks)</b>	36.4 + 2.1	38.1 ± 1.2	37.8 ± 1.9	< 0.001
<b>Intra Uterine Death</b>				
No	74 (98.7%)	42 (100%)	110 (99.1%)	0.625
Yes	01 (1.3%)	0	1 (0.9%)	
<b>Outcome</b>				
Neonatal Death	11 (14.7%)	01 (2.4%)	03 (2.7%)	0.014
Discharge Home healthy	64 (85.3%)	41 (97.6%)	108 (97.3%)	
<b>Jaundice</b>				
Neonatal Jaundice	25 (33.3%)	7 (16.7%)	15 (13.5%)	0.004
Sepsis	03 (4%)	0	02 (1.8%)	0.339
Jaundice + Sepsis	07 (9.3%)	1 (2.3%)	01 (0.9%)	0.013
<b>Normal</b>	40 (53.4%)	34 (81%)	93 (83.8%)	< 0.001
<b>Congenital Anomalies</b>				
Yes	5 (6.7%)	02 (4.8%)	04 (3.6%)	0.633
No	70 (93.3%)	40 (95.2%)	107 (96.4%)	

Cesarean delivery in this sub-group was associated with macrosomia (45.5% versus 23.5% p 0.03). Cesarean delivery rate was high, about 33%, due to various maternal risk factors.<sup>11</sup>

It is evident from some studies that fasting hyperglycemia >105mg% may be associated with an increased risk of intrauterine fetal death during last 4-8 weeks of gestation.<sup>12</sup> Neonatal hypoglycemia, polycythemia, jaundice and hypocalcaemia may complicate GDM babies.<sup>2,4</sup> The observations in this study suggested that optimum control of blood glucose level during pregnancy, vigilant obstetric care through out pregnancy and best neonatology services can give better fetal outcome.

Rizvi JH<sup>8</sup> in a study on screening of abnormal glucose in pregnancy on 2,230 women attending antenatal clinic found that women with abnormal glucose tolerance were older, usually had history of macrosomia, with family history of diabetes as compared to controls. There was higher incidence of preterm labor and cesarean section. In neonates higher rate of hypoglycemia and hyperbilirubinemia were noted. The fetal abnormality rate was 5.6% and mortality rate was 28/1.000 which was higher than controls.<sup>8</sup> According to present study the results of fetal structural defects were slightly more due to the selective inclusion of GDM cases.

In a study by Ramachandran, 211 GDM women were compared with 853 normal pregnancies. There was no case of early pregnancy loss while still births and number of premature births were higher in GDM pregnancies. Babies with weight = 3.5 kg were more among the GDM (p < 0.001) and there was no difference in occurrence of congenital anomalies in both the groups. The observations that adverse maternal and perinatal outcomes are seen with one elevated 50 gm glucose challenge test value > 200 mg%, warrants close glucose monitoring and treatment in this group even in the absence of a diagnostic abnormal OGTT.<sup>13</sup>

Limitations of this study were inclusion of referred cases with confirmation of diagnosis of gestational diabetes in their 2<sup>nd</sup> or 3<sup>rd</sup> trimesters. Since their blood sugars were uncontrolled, they required high doses of insulin. The pre-pregnancy blood sugar level was not known in some of the patients and the diagnosis of GDM was confirmed in postnatal period by carrying out postpartum OGTT.

#### CONCLUSIONS:

Maternal obesity, increasing maternal age and

multiparity had strong association with the development of diabetes. The pre-pregnancy blood sugar levels are usually not known, therefore sometimes disease is diagnosed first time during pregnancy. Postpartum OGTT after 6 weeks is thus recommended.

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