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**Original Research Article**

# Comparative study of fetal outcomes in pregestational and gestational diabetes mellitus

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## ABSTRACT

**Background:** Diabetes mellitus is an emerging health problem worldwide and is now seen in increased frequency during pregnancy. Pregestational DM and GDM have an impact on the fetal outcome in terms of the baby weight, hypoglycemia, hyperbilirubinemia, respiratory distress syndrome and other complications in the fetus. This study was designed to study these effects in a comparative way between these two groups so as to equip ourselves better and provide better materno-fetal care.
**Method:** This was a prospective observational study conducted during a period of one year.All pregnant females attending the antenatal OPD were screened for diabetes mellitus. Those fulfilling the ADA criteria belonged to the pregestational diabetes mellitus group and those fulfilling the DIPSI criteria belonged to the GDM group. A proforma containing general information on demographic characteristics and neonatal outcome in terms of the baby status, baby weight, l, hypoglycaemia, hyperbilirubinemia, and respiratory distress syndrome was maintained. The whole data collected was then analyzed.
**Results:** The fetal outcome for Group DM was more adverse in comparison to the Group GDM. There was an increased incidence of macrosomia (27.9% vs. 8.25%), hyperbilirubinemia (87.1% vs. 53.1%), hypoglycemia and fetal wastage.
**Conclusions:** Pregnancy complicated with diabetes mellitus is a high risk pregnancy and the type of diabetes plays a crucial role in the fetal outcome of that pregnancy. An understanding of this can help provide better perinatal care and outcome.

**Keywords:** Foetal, Diabetes mellitus, High risk obstetrics

## INTRODUCTION

Diabetes is a chronic disease that occurs when the pancreas is no longer able to make insulin, or when the body cannot make good use of the insulin it produces.[1] Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance of variable severity with the onset or first recognition during pregnancy.[2] Pregestational diabetes mellitus is characterized by chronic hyperglycemia and other disturbances of carbohydrate and lipid metabolism along with increased incidence of microvascular as well as macrovascular complications.[3] All women have a 50-60% decrease in insulin sensitivity as the pregnancy progresses. [4] Normal pregnancy is considered to be a diabetogenic state characterized by exaggerated rate and amount of insulin release, associated with decreased sensitivity to insulin at cellular levels. Uncontrolled diabetes, pregestational as well as gestational is associated with fetal and neonatal effects including macrosomia, hypoglycemia and respiratory distress syndrome. Other complications include hypocalcemia, hyperbilirubinemia, shoulder dystocia, stillbirth and intrauterine death.

This study was designed to compare the fetal outcomes in babies born to mothers with pregestational and gestational diabetes in the immediate early neonatal period, as to whether the baby was born alive, still birth, was an intrauterine death or the pregnancy had resulted in an abortion. Other factors such as hypoglycemia, hyperbilirubinemia, respiratory distress syndrome, macrosomia and the APGAR score were also compared. It is important to know the impact these conditions (pregestational diabetes and GDM) can have on the fetal outcome, so as to equip ourselves better to provide better and improved health care.

## METHODS

The present study was a prospective observational cross-sectional study conducted in the Department of Obstetrics and Gynecology Kamla Nehru State Hospital for mother and child, IGMC Shimla for a period of one year. Two groups were formed and women with pre-existing diabetes mellitus, whether type1 or type 2, were included in the pregestational diabetes mellitus group (Group DM) based on their Fasting Blood Sugar, Post Prandial Blood Sugar and Random Blood Sugar. Criteria for labeling pregestational diabetes mellitus was based on the ADA classification.[5]

FPG ≥ 126 mg/dL (7.0 mmol/l). Fasting is defined as no caloric intake for at least 8 h.

OR

2-h PG ≥200 mg/dL (11.1 mmol/l) during OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75g anhydrous glucose dissolved in water.

OR

A1C ≥ 6.5% (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.

OR

In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dl (11.1 mmol/l)

The group GDM consisted of women with Gestational Diabetes Mellitus. All women attending the Antenatal OPD were subjected to a 75gm oral glucose tolerance test (75gmOGTT). In this test 75 gm anhydrous glucose was given after dissolving in approximately 300 ml of water, irrespective of their last meal timing which should have been completely ingested within 5-10 minutes.[6] Venous blood was drawn after 2 hours. The plasma glucose values was estimated in the hospital laboratory by the Glucose oxidase-peroxidase method. Patients were classified according to the DIPSI criteria.[7]

DIPSI criteria: Plasma glucose level <120 mg/dl-Normal, 121-139 mg/dl-Gestational Glucose Intolerance, 140-199 mg/dl-Gestational Diabetes Mellitus. Subjects with plasma glucose levels between 140-199 mg/dl were included in this study. A proforma containing general information on demographic characteristics and neonatal outcome in terms of the baby status, baby weight, APGAR at 1 minute and 5 minutes interval, hypoglycaemia, hyperbilirubinemia, and respiratory distress syndrome was maintained. The final maternal outcome was noted. The whole data collected was then analyzed.

### *Statistical analysis*

Association between categorical variables was analyzed by Chi-square test and continuous variable by independent sample t-test. For all statistical tests, $p<0.05$ was considered statistically significant.

## RESULTS

A total of 299 subjects were studied, out of which 56 of them had pregestational diabetes mellitus and 243 had gestational diabetes mellitus. It was observed that 13 (23.2%) of the pregnancies of subjects with pregestational diabetes mellitus resulted in an abortion. No such complication was seen in subjects with GDM and this was statistically significant ($p\leq0.001$).

The cause for the abortion was also noted which was as follows: In the Group DM, 23.2% of the fetuses were aborted (induced or missed), 21.4% had intrauterine fetal death and 1.8% had neonatal death. There were no such findings in the Group GDM. The neonatal death occurred due to severe tetralogy of fallot which was diagnosed on echocardiography at 34 weeks of gestation. There was a significant difference between the two groups in terms of distribution of Baby Status ($\chi2=123.566$, $p\leq0.001$).

**Table 1: Association between group and abortion (n=299).**

| Abortion | Group, N (%) | | | Fisher's Exact Test | |
|---|---|---|---|---|---|
| | DM | GDM | Total | χ2 | P Value |
| Yes | 13 (23.2) | 0 (0.0) | 13 (4.3) | | |
| No | 43 (76.8) | 243 (100.0) | 286 (95.7) | 58.975 | <0.001 |
| Total | 56 (100.0) | 243 (100.0) | 299 (100.0) | | |

In the Group DM 27.9% of the neonates were macrosomic whereas in the Group GDM 8.2% were macrosomic.

**Table 2: Cause of abortion.**

| Cause | N (%) |
|---|---|
| **Missed Abortion** | 4 (30.8) |
| **Anencephaly** | 3 (23.0) |
| **Multiple Anomalies** | 4 (30.8) |
| **Spontaneous** | 2 (15.4) |

There was a significant difference between the two groups in terms of distribution of Macrosomia ($\chi2$=14.235, p≤.001). In our study 25.8% of the neonates in the Group DM had APGAR <7 at 1 min whereas 2.9 % of the neonates in the Group GDM had APGAR <7 at 1 min. There was a significant difference between the two groups in terms of distribution of APGAR <7 at 1 min ($\chi2$=27.923, p≤0.001). In the Group DM 35.5% of the neonates developed RDS at some point after delivery whereas in the Group GDM 36.2% developed RDS.

**Table 3: Association between group and baby status (n=299).**

| Baby status | Group, N (%) | | | Fisher's Exact Test | |
|---|---|---|---|---|---|
| | DM | GDM | Total | $\chi2$ | P Value |
| **Alive And Healthy** | 30 (53.6) | 243 (100.0) | 273 (91.3) | | |
| **Abortion** | 13 (23.2) | 0 (0.0) | 13 (4.3) | | |
| **Intrauterine Death** | 12 (21.4) | 0 (0.0) | 12 (4.0) | 123.566 | <0.001 |
| **Neonatal Death** | 1 (1.8) | 0 (0.0) | 1 (0.3) | | |
| **Total** | 56 (100.0) | 243 (100.0) | 299 (100.0) | | |

**Table 4: Association between group and macrosomia (n=286).**

| Macrosomia | Group, N (%) | | | Fisher's Exact Test | |
|---|---|---|---|---|---|
| | DM | GDM | Total | $\chi2$ | P Value |
| **Yes** | 12 (27.9) | 20 (8.2) | 32 (11.2) | | |
| **No** | 31 (72.1) | 223 (91.8) | 254 (88.8) | 14.235 | <0.001 |
| **Total** | 43 (100.0) | 243 (100.0) | 286 (100.0) | | |

**Table 5: Association between group and APGAR at 1 min (n=274).**

| APGAR <7 at 1 min | Group, N (%) | | | Fisher's Exact Test | |
|---|---|---|---|---|---|
| | DM | GDM | Total | $\chi2$ | P Value |
| **Yes** | 8 (25.8) | 7 (2.9) | 15 (5.5) | | |
| **No** | 23 (74.2) | 236 (97.1) | 259 (94.5) | 27.923 | <0.001 |
| **Total** | 31 (100.0) | 243 (100.0) | 274 (100.0) | | |

**Table 6: Association between group and RDS (n=274).**

| RDS | Group, N (%) | | | Chi-Squared Test | |
|---|---|---|---|---|---|
| | DM | GDM | Total | $\chi2$ | P Value |
| **Yes** | 11 (35.5) | 88 (36.2) | 99 (36.1) | | |
| **No** | 20 (64.5) | 155 (63.8) | 175 (63.9) | 0.006 | 0.936 |
| **Total** | 31 (100.0) | 243 (100.0) | 274 (100.0) | | |

**Table 7: Association between group and hypoglycemia (n=274).**

| Hypoglycemia | Group, N (%) | | | Chi-Squared Test | |
|---|---|---|---|---|---|
| | DM | GDM | Total | $\chi2$ | P Value |
| **Yes** | 12 (38.7) | 71 (29.2) | 83 (30.3) | | |
| **No** | 19 (61.3) | 172 (70.8) | 191 (69.7) | 1.173 | 0.279 |
| **Total** | 31 (100.0) | 243 (100.0) | 274 (100.0) | | |

There was no significant difference between the two groups in terms of distribution of RDS ($\chi2$=0.006, p=0.936). In the Group DM 38.7% of the neonates developed hypoglycemia at some point after delivery whereas in the Group GDM 29.2% developed hypoglycemia. There was no significant difference between the two groups in terms of distribution of Hypoglycemia ($\chi2$=1.173, p=0.279). In the Group DM 87.1% of the neonates developed hyperbilirubinemia at

some point after delivery whereas in the Group GDM 53.1% developed hyperbilirubinemia.

There was a significant difference between the two groups in terms of distribution of Hyperbilirubinemia ($\chi 2=12.970$, $p \leq 0.001$).

**Table 8: Association between group and hyperbilirubinemia (n=274).**

| Hyperbilirubinemia | Group, N (%) | | | Chi-Squared Test | |
|---|---|---|---|---|---|
| | DM | GDM | Total | χ2 | P Value |
| Yes | 27 (87.1) | 129 (53.1) | 156 (56.9) | 12.970 | <0.001 |
| No | 4 (12.9) | 114 (46.9) | 118 (43.1) | | |
| Total | 31 (100.0) | 243 (100.0) | 274 (100.0) | | |

## DISCUSSION

Diabetes mellitus is a chronic condition characterized by increased glucose levels in the body. The long- term increased levels of glucose, called hyperglycemia, results in various health complications.[8,9] Pregnancy is a great stressful physiological condition in women during their reproductive period. Hyperglycemia at the time of conception and in early pregnancy, especially during organogenesis, results in a six-fold increase of midline defects in the developing embryo.[10] Even a mild increase in glucose levels during pregnancy can adversely affect both the mother and the fetus. The present study was conducted in the department of Obstetrics and Gynecology, KNSH for Mother and Child, IGMC Shimla to compare the maternal outcome in women with pregestational diabetes mellitus and gestational diabetes mellitus.

In our study there were a total of 299 subjects out of which 56 had pregestational diabetes mellitus and 243 had gestational diabetes mellitus. Out of the 56 subjects having pregestational diabetes, 13 of these pregnancies (23.2%) resulted in an abortion due to early intrauterine fetal demise or missed abortion (4, 30.8%), anencephaly (3,23%), multiple anomalies (4,30.8%) and spontaneous abortion (2,15.4%). High concentrations of glucose are a known teratogen. The risk of an anomaly increases linearly with the amount of maternal hyperglycemia during that crucial time.[4]

### *Neonatal status*

In our study, there were no neonatal mortalities in Group GDM. In the Group DM, however, there were 21.4% intrauterine deaths. There were 12 intrauterine deaths out of which 8 were macerated and 4 were fresh stillbirths. There was 1(1.8%) neonatal death. The neonatal death occurred due to severe tetralogy of fallot which was diagnosed on echocardiography at 34 weeks of gestation. In the study conducted by Wahabi et al there was increased incidence of stillbirth in the subjects with pregestational diabetes mellitus. (3.4% vs. 0.9%).[11] Also in the study conducted by Mustary et al there were increased perinatal mortalities in the subjects with pregestational diabetes as compared to gestational diabetes mellitus.[12]

### *Congenital anomalies*

There was an incidence of 26.8% of congenital anomalies for the Group DM in our study. Out of these 21.4% of the subjects had multiple anomalies which were detected on level two ultrasonography and were incompatible with life. Thus, they resulted in induced abortion. Ventricular Septal Defect was seen in 3.6% which was detected during the fetal echo, however there were no antenatal, intrapartum or postnatal complications in the fetus. One (1.8%) neonate had tetralogy of fallot which was detected at a later time in pregnancy, and resulted in neonatal death due to severity of the lesion. In the Group GDM the incidence of congenital anomalies was 0.8%, which was bilateral club feet. This is consistent with the study conducted my Mustary et al wherein there was increased incidence of congenital anomaly in the neonates of subjects with pregestational DM in comparison with GDM (8% vs. 2%).[12]

### *Macrosomia*

In our study, in the Group DM 27.9% of the neonates were macrosomic whereas in the Group GDM 8.2% were macrosomic. This is consistent with the study conducted by Wahabi et al where in the incidence of macrosomia was more in the neonates of the subjects with pregestational diabetes mellitus than GDM 11.2% vs. 5.3%.[11] In the study conducted by Pal et al 3% of the neonates of the subjects with GDM had macrosomia.[13] This difference occurs due to prolonged exposure of the fetus to maternal hyperglycemia with resultant prolonged fetal hyperinsulinemia and increased C peptide level and thus more severe effect on fetal weight gain and thus macrosomia.

### *APGAR <7 at 1 min*

In our study 25.8% of the neonates in the Group DM had APGAR <7 at 1 min whereas 2.9 % of the neonates in the Group GDM had APGAR <7 at 1 min. Decreased APGAR was seen in neonates of subjects with pregestational diabetes mellitus, which is consistent with the study conducted by Wahabi et al 4.3% vs. 1.1%.[11]

***Respiratory distress syndrome***

In our study 35.5% and 36.2% of the neonates belonging to Group DM and Group GDM respectively, developed respiratory distress syndrome. This was consistent with the study conducted by Naher et al (59.6% vs. 59.2%) and Mustay et al.[12,14]

The increased incidence of respiratory distress in our study, in both the groups, is consistent with the fact that increased amount of insulin resistance results in delayed lung maturity in the neonate.

***Hypoglycemia***

In our study, 38.7 % of the neonates in the Group DM had hypoglycemia whereas 29.2% of the neonates in the Group GDM developed hypoglycemia.

This was consistent with a study conducted by Naher et al as well as Mustary et al which had increased incidence of hypoglycemia in the neonates belonging to the subjects of the pregestational diabetes group.[12,14]

***Hyperbilirubinemia***

In this study there was a significant difference among the two groups in relation to hyperbilirubinemia in the neonate after delivery. In our study, 87.1% of the neonates had hyperbilirubinemia belonging to mothers of Group DM in comparison to 53.1% of neonates belonging to mothers of Group GDM. This is consistent with the study conducted by Naher et al wherein there was an incidence of 95.7% in the pregestational diabetes group and 73.5% in the GDM group.[14] Neonatal hyperbilirubinemia is caused by the breakdown of fetal hemoglobin which the neonatal liver is unable to manage efficiently. Increased in the number of premature deliveries in the Group DM resulted in increased incidence of hyperbilirubinemia.

## CONCLUSION

Diabetes in pregnancy is in itself a high-risk pregnancy resulting in adverse maternal outcomes, pregestational diabetes more so in comparison with GDM. The type of diabetes plays a crucial role in the maternal outcome of that pregnancy. With a better understanding of this and ensuring better facilities to equip ourselves in case of such complications, we can provide better maternal health care.

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