Glycemic Status During Pregnancy in Gestational Diabetic & Non-Gestational Diabetic Women & its Effect on Maternal & Fetal Outcome

A. P. Sawant¹, S. S. Naik², V. D. Nagarkar²

Abstract

**Aims & Objectives:** 1. To study the time course of plasma glucose, in gestational diabetic and normal pregnant women. 2. To compare maternal outcome and fetal outcome in gestational diabetic and normal pregnant women. **Materials and Methods:** Five hundred pregnant individuals visiting the Antenatal Clinics of Rural Medical College, Loni in either half of the gestation were screened and gestational diabetes mellitus was diagnosed according to the WHO criteria. **Results:** The scope of diabetes and pregnancy encompasses not only diabetesics marching through pregnancy but also, any form of abnormal glucose tolerance developing during gestation, termed as gestational diabetes, abnormal glucose tolerance of any etiology recognized or unrecognized starting before pregnancy or revealed during pregnancy, is associated with a high risk of a poor maternal and fetal outcomes. In our study we found a significantly higher incidence of caesarean section in-patients with GDM when compared with the normal group (67% versus 25%, P < 0.001). In GDM cases, we observed fetal macrosomia, high birth weight etc. Naturally these are the factors, which add to the pre-existing unfavourable maternal factors affecting the process of labour adversely. We observed a significant difference in the incidence of preterm labour in between the GDM and non-GDM groups (22% Vs 13%, p<0.05). These individuals underwent a process of preterm labour at a gestational age of 32±3 weeks. Hyperglycemia and polyhydramnios are held responsible for preterm labour. The incidence rate of PIH was more in subjects with GDM as compared to the other group. However this difference failed to prove statistically significant at 5% level of significance. Though we did not get a significant difference in occurrence of PIH in between the GDM and non-GDM groups, we do agree with the comment that hyperglycemia earlier in the pregnancy is associated with greater incidence of PIH as three of the four cases who were diagnosed to have GDM in first half of pregnancy showed a presence of PIH. The present study revealed no association between Polyhydramnios and GDM. We found 16.65% incidence of polyhydramnios in GDM and 4.35% in non-GDM women. In our study maternal hyperglycemia was present in all cases of polyhydramnios so that osmotic imbalance could be involved in the pathogenesis of polyhydramnios. **Conclusion:** Diagnosis of gestational diabetes and subsequent treatment to attain normoglycemia will definitely lead to satisfactory maternal and/or fetal outcome.

Key words: Gestational Diabetes mellitus, PIH, Polyhydramnios, Fetal macrosomia

Introduction

The last half of the 20th century is rife with diabetes prevalence jeopardizing peoples’ death. The medical literature on Gestational Diabetes is voluminous but less illuminating though it has been recognized for decades. The potential significance of this condition, as well as criteria for screening and diagnosis remain controversial. The data on epidemiology, diagnostic criteria and maternal and fetal outcome of gestational diabetes mellitus is still either controversial or less illuminating. The present study was conducted to assess the impact of gestational diabetes mellitus on maternal as well as fetal outcome and also to know the prevalence of gestational diabetes mellitus in the drainage area of Rural Medical College Loni, Maharashtra.

The main bulk of the study population was formed by multiparous women (63.4%). Most of the women were below 25 years of age in both primiparous and multiparous, the youngest being 17 year old and the oldest being 37 years old. In our study 46 women were subjected for OGTT in first half and 71 in second half of pregnancy. A total of 18 cases were diagnosed to have GDM. Thus the incidence of GDM came out to be 3.6%.

<table>
<thead>
<tr>
<th>Category</th>
<th>Non GDM individuals [n=434 in 1st half and 482 in 2nd half]</th>
<th>GDM cases (n=18)</th>
<th>‘p’ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational Period</td>
<td>Plasma glucose level (mg%) + S.D.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting</td>
<td>71.92±8.39</td>
<td>97.55±13.20</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Post prandial</td>
<td>90.55±11.92</td>
<td>129.83±23.11</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Fasting</td>
<td>74.97±10.97</td>
<td>109.6±11.66</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Post prandial</td>
<td>92.81±18.66</td>
<td>149.66±14.05</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

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The rapidly accumulating data regarding the effect of gestational diabetes mellitus on the oral cavity suggest that oral tissues are adversely affected by uncontrolled diabetes mellitus similarly to other body systems. Prolonged high blood glucose levels can cause gum disease (periodontal disease) and other dental problems. Thus, study of dental problems related to GDM are equally important.

Material and Methods

Five hundred pregnant individuals visiting the Antenatal Clinic of Rural Medical College, Loni in either half of the gestation were screened and gestational diabetes mellitus was diagnosed according to the WHO criteria. A thorough record of carbohydrate profile, and all other investigations was conducted to assess the impact of gestational diabetes mellitus on the oral cavity suggest that oral tissues are adversely affected by uncontrolled diabetes mellitus similarly to other body systems. Prolonged high blood glucose levels can cause gum disease (periodontal disease) and other dental problems. Thus, study of dental problems related to GDM are equally important.

Observations

Table 1: Mean fasting and post prandial plasma glucose level in GDM and non-GDM individuals
outcome was also recorded. An appropriate statistical test was applied for the analysis and interpretation of the results.

**Impression**

1) Fasting as well as post prandial plasma glucose levels are significantly elevated in gestational diabetic group in both halves of pregnancy when compared to other group.

2) The difference in plasma glucose levels of GDM and Non-GDM individuals is further increased in 2nd half of gestation.

Table 2: Table showing fetal outcome in GDM and Non - GDM individuals

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Outcome</th>
<th>Non-GDM (n=482)</th>
<th>GDM (n=18)</th>
<th>'p' value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Normal</td>
<td>407 (84.43)</td>
<td>06 (33.33)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>2</td>
<td>IUD</td>
<td>17 (3.52)</td>
<td>2 (11.11)</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>3</td>
<td>Still Birth</td>
<td>15 (3.11)</td>
<td>01 (5.55)</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>4</td>
<td>IUGR</td>
<td>15 (3.11)</td>
<td>01 (5.55)</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>5</td>
<td>High Birth wt.</td>
<td>07 (1.45)</td>
<td>05 (27.77)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>6</td>
<td>Congenital ab(n)</td>
<td>07 (1.45)</td>
<td>02 (11.11)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>7</td>
<td>FDS</td>
<td>18 (3.73)</td>
<td>03 (16.67)</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

Chi- square (χ²) test with Yate's correction

**Impression**

1) Majority of the individuals without GDM (84%) are showing normal fetal outcome.

2) Babies with high birth weight, congenital anomaly and distress syndrome are present in high number in GDM group.

3) Presence or absence of GDM has not made any significant change in the incidence of IUGR, IUD and still birth.

Table 3: Table showing maternal outcome in GDM and Non- GDM subjects

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Outcome</th>
<th>Non-GDM (n=482)</th>
<th>GDM (n=18)</th>
<th>'p' value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>FTND</td>
<td>293 (60.78)</td>
<td>04 (22.22)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>2</td>
<td>C.S.</td>
<td>120 (24.89)</td>
<td>12 (66.66)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>3</td>
<td>Abortion</td>
<td>40 (8.29)</td>
<td>01 (5.55)</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>4</td>
<td>PIH</td>
<td>66 (13.69)</td>
<td>04 (22.22)</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>5</td>
<td>Preterm labour</td>
<td>25 (5.18)</td>
<td>04 (22.22)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>6</td>
<td>Polyhydramnios</td>
<td>21 (4.35)</td>
<td>03 (16.65)</td>
<td>&gt; 0.05</td>
</tr>
</tbody>
</table>

By Chi-square (χ²) test.

**Impression**

1. Incidence of preterm labour and caesarean section is more in individuals with GDM

2. Incidence of normal delivery is higher in individuals without GDM

3. Occurrence of post-datism, oligo/polyhydramnios, abortion and PIH does not differ significantly in both groups.

**Discussion**

The present study was undertaken with an aim to find out incidence of GDM in rural population and its impact on maternal and fetal outcome. The study has been done in the Dept. of Obstetrics and Gynaecology and Dept. of Biochemistry, Rural Medical College Loni, Maharashtra.

In our study 46 women were subjected for OGTT in first half and 71 in second half of pregnancy. A total of 18 cases were diagnosed to have GDM. Thus the incidence of GDM came out to be 3.6%. Many other studies related to the incidence of GDM have documented the wide range of incidence rate (2% to15%). Our result is falling in the previously reported range. Out of these, only 4 cases (22%) were detected in first half and 14 (78%) were detected in second half of gestation. This indicated the higher diabetogenic potential in second gestational half due to presence of anti-insulin hormones, increased insulin resistance and decrease in insulin response. We observed presence of post-prandial hyperglycemia (>200 mg%) in 17 out of 18 cases suggesting that post prandial hyperglycemia rather than fasting hyperglycemia is more commonly associated with GDM. Of the 18 gestational diabetic patients, the maximum of 7 patients (39%) belonged to the age group of 26-30 years and 6 patients (33%) were between 21 to 25 years i.e. 72% of all the gestational diabetic patients were between the ages of 21 to 30 years. We observed an incidence of GDM to be 3.8% and 3.4% in primigravida and multigravida respectively. Thus we did not find any influence of parity on the incidence of GDM.

In both gestational halves we noted a fasting plasma glucose level on lower side of a normal range in all normal pregnant women. Almost 70% of the individuals showed a fasting plasma glucose level of 60-80 mg% with a mean of 71.92 mg% and 74.97 mg% in second and third trimesters respectively. The rise in fasting plasma glucose level with advancing gestation is non-significant (p>1).

The fasting plasma glucose concentrations in gestational diabetic women are markedly raised in both gestational halves when compared to the non-diabetic pregnant women. In later half of gestation the magnitude of elevation in maternal fasting glucose level was further augmented. Also, the time course of fasting glucose concentration showed significant difference (97.55mg% to 109.61mg%, p<0.001) in gestational diabetic group. Though the fasting hyperglycemia was present in the first half of pregnancy, these are not cases of pregestational diabetes as only 4 out of 18 cases were diagnosed during first gestational half and remaining in second half of pregnancy. If they had preexisting diabetes, they would have proved to be gestational diabetic cases in first half of pregnancy.
In the present study, the 2-hour post-prandial plasma glucose levels were 90.55 mg% and 92.81 mg% in early and late gestations respectively in normal pregnancy suggesting that there was no significant difference in a time course of post-prandial plasma glucose in such individuals. However the corresponding values in GDM group were 129.83 mg% and 149.66 mg%. Thus, in both gestational halves these values differed significantly from the corresponding values in normal pregnant women. Furthermore, the rise by 20 mg% from second to third trimester was also remarkable. Because of the relatively small number of gestational diabetic subjects in our study population and the fact that they are not obese, we are cautiously stating that post-prandial hyperglycemia observed in GDM individuals can be explained on the basis of fall in first phase insulin response and/or insulin sensitivity.

Fetal Outcome in GDM and Non-GDM Individuals

Macrosomia

The infants of diabetic mothers are traditionally portrayed as being big. The birth weight pattern in our study differed remarkably between gestational diabetics and normal pregnant women. The average birth weights (mean + SD) were 2923 ± 878 gm and 2475 ± 523 gm in the gestational diabetic and non-gestational diabetic groups respectively. In GDM, maximum babies showed weights more than 3kg while for the other group the range was 2 to 3kg. The babies with birth weight > 4000 gm are called macrosomic. We have noticed 11% incidence of macrosomia in GDM versus 0.22% in the other group. The difference in weight pattern between the groups was obvious.

Smiti Nanda et al have reported the mean birth weight of the babies born to gestational diabetic mothers of 3075 ± 326 gm versus the babies born to mothers without GDM of 2790 ± 473 gm. The difference between mean birth weights in the two groups came out to be statistically significant. Witznitzer et al also were of similar opinion. In our study both, fasting and 2hr. post prandial plasma glucose concentrations were elevated significantly in gestational diabetic mothers who have given birth to babies weighing more than 3500 gm. However, few other studies have found correlation between increase in birth weight and either fasting or postprandial hyperglycemia. Smiti Nanda et al have found a presence of only fasting hyperglycemia and not post prandial hyperglycemia in these mothers. Similar results are also reported by Kim et al.and Veciena M et al. However Jovanovic et al suggested that the risk of fetal macrosomia was increased proportionally to the level of only post prandial hyperglycemia.

From our results, we conclude that both fasting as well as postprandial hyperglycemia influences the fetal birth weight in an inclining direction.

Fetal Distress Syndrome

In our study the overall incidence of fetal distress syndrome in gestational diabetic group was 16.67%. It was more common in multigravida than primigravida. All of these patients had hyperglycemia and hyperinsulinemia. Shelly Macfarlane and Tsakalakos et al have observed increased plasma lactate level and decreased pH in presence of hyperglycemia and hyperinsulinemia. According to them hyperinsulinemia was associated with an increased demand for oxygen leading to fetal hypoxia when the demand could not be fully met as for example in labour. Like Macfarlane and Tsakalakos, we attribute the increased rate of FDS in GDM to hyperglycemia and hyperinsulinemia leading to fetal hypoxia.

Congenital Anomalies

In the present study, nearly 12% cases of GDM delivered babies with obvious congenital abnormality. In normal pregnant women, this figure was only 1.45% One of the baby had meningomyelocele and other had cleft-palate. One patient was diagnosed to have GDM earlier in the pregnancy. Though diagnosed during second gestational half, another patient of GDM was having increased fasting and post-prandial glucose concentrations at 14-16 weeks of gestation also. Thus, we assume that these individuals had raised plasma glucose level profile at the time of organogenesis. Estimating plasma glucose values at the gestational age of 6-8 weeks would have confirmed this assumption.
Cousins have reported that 2-3% of newborns had a congenital abnormality at birth in normal pregnancy and the incidence ranged between 7.5% and 12.9% in diabetic pregnancies. In view of Ralf Tamura, it was estimated to occur with a frequency of 3% to 6% in diabetic women which was two to three fold greater than that of nondiabetic population. Our findings are nearer to those of Cousins. Many factors have been claimed in pathogenesis of congenital anomalies in pregnancy (like hyperglycemia, ketoacidosis, deficiency of arachidonic acid and myo-inositol, excess of sorbitol etc.) by many authors. According to Miller et al the anomalies occur by the 9th week of amenorrhea when organogenesis is maximum. Maternal hyperglycemia at this particular period is associated with major structural defects. Pinter et al studied the mechanism by which hyperglycemia produced dysmorphogenesis and proposed it to be hyperglycemia induced yolk sac failure and resulting compromise of nutrient transfer and oxygenation to the early embryo. Hod et al reported a hyperglycemia-associated increase in sorbitol and an inversely proportional reduction in myo-inositol levels. Goldman and associates suggested that hyperglycemia induced embryopathy was mediated by a functional deficiency of arachidonic acid.

Data from a study conducted by Mills did not totally corroborate these findings. The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus also did not find any association between a presence of GDM and congenital anomalies. However our results are matching with Miller et al and Goldman et al. Judging from just two cases and stating that congenital anomalies are more common in subjects with GDM will be a poorly justified conclusion. Looking back that organogenesis occurs rapidly in the first trimester and this is a vulnerable period for congenital anomalies and difficulty to differentiate between true GDM and overt diabetes in first few weeks of gestation, at the most we can conclude that hyperglycemia in first few weeks of gestation (may be of any origin) is probably associated with occurrence of congenital defects.

**Still Birth**

We noticed no difference between the normal pregnant and gestational diabetic women in the occurrence of stillbirth. We found it in 5.55% population of gestational diabetic versus 3.11% in the normal pregnancy. Previously many investigators found a strong association between stillbirth and GDM. But today in the modern era of Obstetrics and with improvement in the therapeutic approaches, this complication is no more strongly associated with GDM. However as reported by Hollingsworth, they still occur in women with no prenatal care or unrecognized and /or untreated gestational diabetes who present in at ≥41 weeks of gestation with no fetal movement. Mansha Dubey and Das reported still birth to be an important complication of GDM. Probable explanation for still birth is provided by Salvesen and colleagues who reported decreased fetal pH, and increased pCO2, lactate and erythropoetin suggestive of fetal acidosis in gestational diabetic women. They further added that hyperglycemia-mediated chronic aberrations in transport of oxygen and fetal metabolites might have produced still births. Kristina Adams did not show a single case of still birth in unrecognized GDM and non-diabetic control groups. The incidence of still birth was found to be only 2% in GDM patients and still low in non-diabetic pregnant women by Andres Aberg. Our results are also in accordance with those of Kristina Adams and Andres Aberg. Hyperglycemia per se alone is not a threatening factor for stillbirth unless and until other unfavourable factors operate simultaneously. Nowadays due to appropriate care and monitoring during antenatal period, occurrence of stillbirth is not increased in gestational diabetes mellitus.

**IUD and IUGR**

In our study we noticed that presence or absence of gestational diabetes mellitus does not make any change in the incidence rate of IUD or IUGR. In our study population, though we found IUD in 11.11% of women with GDM versus 3.52% in normal pregnant women, this difference is not important at 5% level of significance.

Many investigators have reported an increased incidence rate of IUD and IUGR in the past but nowadays it is very low. Mondenstein et al found that lower birth weight babies, smaller babies and growth-restricted babies had an increased risk of fetal death. They commented that women with poor glycemic control were usually at higher risk for fetal death compared to non-diabetic women. Their study indicated that increase in fetal death among women with poor glycemic control generally started at about 32 weeks, although it could have been earlier for individual cases. It would require a very large prospective study to examine the relationship between glycemic control and fetal death, which is beyond the scope of the present study.

**Maternal Outcome in GDM and Non-GDM Subjects**

**Caesarean Section**

We found a significantly higher incidence of caesarean section in-patients with GDM when compared with the normal group (67% versus 25%, P <0.001). The indications of caesarean section were mid pelvic contraction in two, unstable lie and high birth weight in one, precious pregnancy in one and fetal distress syndrome in one. In others it was attributed to higher birth weight, macrosomia or inability to induce labour.

Smiti Nanda et al have reported 60% incidence rate of caesarean section in GDM versus 36.3% in Non-GDM individuals. Wiznitzer et al, Ervin Pennison et al and Jens Svare et al also reported similar results. Not a single study has found a lack of association between gestational diabetes and caesarean section. Our results are similar to these observations.

In GDM cases, we observed fetal macrosomia, high birth weight, fetal distress syndrome etc. Naturally these are the
factors, which add to the pre-existing unfavourable maternal factors affecting the process of labour adversely. In most of the cases of caesarean section, a trial of labour was given initially. Only three underwent an elective caesarean section. Maternal hyperglycemia per se does not affect the pelvic diameters or the process of labour but fetal consequences make the obstetrician to plan a caesarean section. Thus, we conclude that maternal hyperglycemia and its fetal consequences are the culprits for increased rate of caesarean section in individuals with GDM.

Preterm Labour:
We observed a significant difference in the incidence of preterm labour in between the GDM and non-GDM groups (22% vs 13%, p<0.05). These individuals underwent a process of preterm labour at a gestational age of 32±3 weeks. Fetal complications like stillbirth in one, fetal distress syndrome in one, congenital anomaly in one and intrauterine death in one were associated with preterm labour.

Sibai and co-workers noticed that 9% of the women with hyperglycemia spontaneously delivered at 34 weeks or less compared with 4.5 % of non-diabetic normal women. Wiznitzer et al reported the prevalence of spontaneous preterm delivery as 10% in GDM and 7.1% in the non-diabetic women. Jens Svaré et al also reported a similar result. The authors found that patients of GDM had a significantly lower gestational age at delivery and this and women who were at high risk for GDM and who were diagnosed early in pregnancy had a significantly increased rate of preterm labour.

Mansha Dubey have blamed to polyhydramnios for a greater incidence of preterm labour. In our study polyhydramnios was absent in all women who underwent preterm labour. Thus, our results can be explained on the basis of hyperglycemia in individuals with GDM. However findings are not in agreement with the results obtained by Mansha Dubey.

PIH
In our study, the incidence rate of PIH was more in subjects with GDM as compared to the other group. However this difference failed to prove statistically significant at 5% level of significance. U.N. Das reported that both hypertension and pre-eclampsia were more frequent in women with GDM. In view of this, careful monitoring of blood pressure, weight gain and urinary protein excretion should be done regularly. A Wiznitzer et al also were of the same opinion. Their studies have shown that PIH was associated with poor glycemic control during the first trimester. In our study three of the four cases who were diagnosed to have GDM in first half of pregnancy showed a presence of PIH. Thus, thought we did not get a significant difference in occurrence of PIH in between the GDM and non-GDM groups, we do agree with the comment that hyperglycemia earlier in the pregnancy is associated with greater incidence of PIH.

Polyhydramnios
The present study revealed no association between Polyhydramnios and GDM. We found 16.65% incidence of polyhydramnios in GDM and 4.35% in non-GDM women. Though more incidence was present in GDM group, the difference between the groups came out to be statistically non-significant.

Dashe and co-authors in a study performed at Parkland Hospital found that amniotic fluid index (which denotes the quantity of amniotic fluid) paralleled the amniotic fluid glucose level among women with gestational diabetes. White and Dashe and co-authors documented that polyhydramnios resulted from poor maternal glycemic control, with an abnormal maternal or fetal osmotic balance leading to the excess fluid. In our study maternal hyperglycemia was present in all cases of polyhydramnios so that osmotic imbalance could be involved in the pathogenesis of polyhydramnios.

Conclusion
- Prevalence of gestational diabetes in our study was observed to be 3.6%
- Parity has no influence on incidence of GDM
- Hyperglycemia is a result of decreased insulin response and/or increased insulin resistance
- Hyperglycemia, Hyperinsulinemia contributes to macrosomia and increased fetal birth weight
- Congenital anomalies are due to hyperglycemia at the time of organogenesis
- Maternal hyperglycemia and its fetal consequences are culprits of increased rate of caesarean sections and Preterm labour in GDM
- IUD, IUGR and Polyhydramnios were not associated with Gestational Diabetes in the present study

References
8. Cousins L. Congenital anomalies among infants of diabetic mothers:


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