INTRODUCTION:

Gestational Diabetes Mellitus (GDM) is one of the most common metabolic disorders of pregnancy which is characterized by glucose intolerance detected for the first time during pregnancy due to decreased insulin sensitivity combined with insufficient insulin secretion (1). The incidence of GDM has been increasing due to the increased age of pregnant women and the rising rates of obesity in population. India being capital of Diabetes, there is increased prevalence of GDM in south Indian population. It is reported to be about 16% (2).

During pregnancy, the metabolism of carbohydrates and lipid undergoes adaptations to ensure a continuous input of energy and nutrients to the fetus which are mediated by placental hormones mainly estrogen and placental lactogen and by altered insulin levels and changes in insulin sensitivity (3). The maternal serum lipid levels are elevated during mid to late gestation in normal pregnancy which is a part of maternal adaptation to maintain stable fuel distribution to fetus. The triglyceride levels increase continuously from early pregnancy and by term there is two- to threefold elevation (4).

The impact of altered maternal lipid profile levels on maternal and perinatal outcome in women with Gestational Diabetes Mellitus

Vijaya.S(1), Sudha.S(2)

Abstract

Context: Gestational Diabetes Mellitus is associated with an increased risk of various short- and long- term adverse maternal outcomes and perinatal outcome.

Aims: To identify the impact of altered lipid levels on maternal outcome and neonatal outcomes in women with gestational diabetes mellitus.

Settings and Design: Institutional based study and a prospective case control study.

Methods and Material: The fasting lipid profile was taken for about 200 women with Gestational diabetes diagnosed by DIPSI criteria. The patients were divided into two groups based on their lipid profile values. The patient were then followed throughout the antenatal period and the occurrence of maternal complications and neonatal complications were studied.

Statistical analysis used: Statistical analysis was performed by the student t-test.

Results: Among the altered lipid profile group 78.2% of the patients were in age group above 25 years, 66.7% of patients were in BMI of range 25 to 29 kg/m². About 41.7% of the patients with altered lipid profile developed Preeclampsia, 15.4% had Gestational hypertension, 43.6% had polyhydramnios, 55.4% had caesarean section. There was about 11.5% macrosomic babies, 30.8% babies had respiratory distress syndrome, 12.2% babies had hypoglycemia, 14.1% of babies had hyperbilirubinemia, 2.6% babies had anomalies, 23.7% babies had NICU admissions more than 3 days among the babies born to GDM patients with altered lipid profile.

Conclusions: In our study, lipid profile alterations detected were increased total cholesterol, serum triglycerides in GDM patients and lower HDL levels. There was increased incidence of adverse maternal outcome and perinatal outcomes among GDM cases with altered lipid profile.

Key-words: Gestational Diabetes, Total cholesterol, Serum triglycerides, maternal outcome, perinatal outcome.
These metabolic changes that occur in normal pregnant women are progressive and are accentuated in GDM patients(2). There are alterations in fasting, postprandial, and integrated 24-hour plasma concentrations of amino acids, glucose, and lipids. There is three-fold elevation of plasma triacylglycerol concentrations towards term, elevation of plasma fatty acids, delayed postprandial clearance of fatty acids and elevation of branched-chain amino acids(7). In GDM there is a state of dyslipidemia consistent with insulin resistance. The lipid abnormalities in GDM are elevated triglycerides, elevated LDL cholesterol and low HDL cholesterol(8).

GDM is associated with adverse maternal and perinatal outcome, which includes increased likelihood of birth defects, preterm birth, caesarean delivery, macrosomia, pre-eclampsia and gestational hypertension(10). It is found that even with strict glycemic control there is higher incidence of complications. The abnormalities in carbohydrate metabolism occurring in GDM may lead to abnormalities in insulin resistance and metabolism of lipid(9). The insulin resistance causes inflammation, endothelial dysfunction and formation of reactive oxygen species. During pregnancy there is imbalance of HDL and LDL cholesterol due to oxidative stress, which is more enhanced in GDM where excess glucose acts as principle oxidative substrate used for fetal growth(16).

SUBJECTS AND METHODS:

Study place:
The study was conducted at the Institute of Social Obstetrics, Government Kasturiba Gandhi Hospital, Madras Medical College, Chennai.

Study Design:
This was an prospective case control study.

Study Period:
The study was conducted for a period of two years.

Participants:
The study group consisted of 200 patients after considering the exclusion and inclusion criteria.

Inclusion criteria:
- All patients above 18 years and below 35 years with Pregnancy Diagnosed with GDM either newly detected or on follow up by DIPSI (Diabetes In Pregnancy Study Group India) criteria as follows. 75g glucose given to pregnant woman at her first antenatal check-up visit irrespective of the gestational age and fasting state. GDM is diagnosed if 2-h venous glucose sample is ≥140mg/dl.
  - Singleton pregnancy
  - Antenatal mothers with records of pre-pregnant BMI, previous pregnancy details and outcome
  - Primi and multigravida
  - Cephalic presentation
  - Women booked and immunized at KGH
  - Women with regular antenatal visits

Exclusion Criteria
- Overt Diabetes
- Associated medical complications like hypothyroidism, hypertension complicating pregnancy, known lipid disorders
- Multiple pregnancy.
- Previous history of IUD
- Previous history of abortions
- First visit to KGH with no previous records
- Abnormal presentation
- Normal antenatal mothers

Method of study:
All selected women were subjected to a detailed history taking comprising of age, parity, prepregnant body weight, medication history, family history, medical history, detailed obstetric history. Then they were subjected to clinical examination and routine laboratory investigations. Oral glucose challenge test (OGCT) was performed in antenatal women attending the outpatient clinic at the first visit. The pregnant women diagnosed GDM are subjected to fasting lipid

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Std Error</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Altered Lipid</td>
<td>28.4615</td>
<td>4.5314</td>
<td>0.3628</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Normal Lipid</td>
<td>24.6136</td>
<td>4.2274</td>
<td>0.6373</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Altered Lipid</td>
<td>26.0369</td>
<td>2.54944</td>
<td>0.20543</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Normal Lipid</td>
<td>22.5899</td>
<td>2.80753</td>
<td>0.4433</td>
<td></td>
</tr>
</tbody>
</table>
profile on the next day.
The patients are divided as,

- Group A: GDM Women with altered lipid profile taken as cases
- Group B: GDM Women with normal lipid profile taken as controls

Fasting blood samples (4ml) were collected from these patients on the next day and subjected to lipid profile analysis. Total Cholesterol calculated by CHOD POD method, HDL by Enzymatic selective protection method, Triglycerides levels by Enzymatic Calorimetric method and LDL levels were estimated by Homogenous Enzymatic Calorimetric assay and the levels of VLDL was calculated indirectly from serum triglyceride values. OGCT is repeated at 24 – 28 weeks when the first test is negative and repeated again at 32-34 weeks and fasting lipid profile was done in patients diagnosed as GDM on the next day. GDM mothers attending antenatal clinics during study period were tested with fasting and postprandial blood sugar [2 hours] to know their glycemic control and manage with medical nutrition therapy and Insulin depending on their blood glucose levels. The maternal and perinatal outcome were studied.

Statistical analysis

Statistical analysis between two groups was performed by the student t-test.

RESULTS:

Among the altered lipid profile group multiparous women constitute 59%, 78.2% of the patients were in age group above 25 years, 66.7% of patients were in BMI of range 25 to 29 kg/m² and family history of diabetes was present in 46% of the patients. About 86% of GDM were detected in 2nd trimester and 14% in third trimester in the altered lipid profile group. About 41.7% of the patients with altered lipid profile developed Preeclampsia, 15.4% had Gestational hypertension, 43.6% had polyhydramnios, 46.2% of patients required Inj. Insulin therapy, 11% had preterm delivery, 55.4% had caesarean section out of which CPD was the most common indication for caesarean section. There was about 11.5% macrosomic babies, 30.8% babies had respiratory distress syndrome, 12.2% babies had hypoglycemia, 14.1% of babies had hyperbilirubinemia, 2.6% babies had anomalies, 23.7% babies had NICU admissions more

<table>
<thead>
<tr>
<th>Lipid profile</th>
<th>Groups</th>
<th>Mean</th>
<th>Standard Deviation(SD)</th>
<th>Significant (P Value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Cholesterol(TC)</td>
<td>Altered lipid</td>
<td>220.6</td>
<td>26.71</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>Normal lipid</td>
<td>165.25</td>
<td>19.04</td>
<td></td>
</tr>
<tr>
<td>Triglycerides(TGL)</td>
<td>Altered lipid</td>
<td>265.37</td>
<td>66.96</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>Normal lipid</td>
<td>138.99</td>
<td>38.94</td>
<td></td>
</tr>
<tr>
<td>Very Low Density Lipoprotein(VLDL)</td>
<td>Altered lipid</td>
<td>42.28</td>
<td>21.65</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>Normal lipid</td>
<td>27.84</td>
<td>7.73</td>
<td></td>
</tr>
<tr>
<td>Low Density Lipoprotein(LDL)</td>
<td>Altered lipid</td>
<td>112.58</td>
<td>41.25</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>Normal lipid</td>
<td>88.61</td>
<td>18.95</td>
<td></td>
</tr>
<tr>
<td>High density lipoprotein (HDL )Cholesterol</td>
<td>Altered lipid</td>
<td>49.34</td>
<td>9.58</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>Normal lipid</td>
<td>52.34</td>
<td>9.15</td>
<td></td>
</tr>
</tbody>
</table>
than 3 days, 2.6% IUD, 1.9% perinatal mortality among the babies born to GDM patients with altered lipid profile.

DISCUSSION:

Our study included 200 pregnant women diagnosed with Gestational Diabetes Mellitus. Among them about 156 patients had altered lipid profile and were grouped as altered lipid profile group and the remaining 44 women with normal lipid profile were taken as normal lipid profile group.

In our study about 78.2% of the GDM mothers with altered lipid profile are above 25 years. It was concluded that there was significant association between age with GDM with altered lipid profile since P value < 0.0001. In our study about 59% of GDM cases with altered lipid profile were multiparous women. Since P value <0.001 there was significant association between parity and GDM cases with altered lipid profile. In our study about 66.7% of GDM cases with altered lipid profile group had pre-pregnant BMI between 25-29 kg/m2 which is statistically significant as p value is <0.0001.

In our study family history was present in 46% of GDM cases. Since P value 0.547, there was no significant association between family history of diabetes and the occurrence of GDM in cases with altered lipid profile.

In our study the mean fasting total cholesterol and triglyceride levels were 220.6±26.71 and 265.37±66.94 mg/dl respectively. In another study from Iran, mid pregnancy Fasting serum triglyceride (mg/dl) was 213.9 ± 77.7 mg/dl (17). In our study 86% GDM cases were detected in 2nd trimester, 14% of GDM cases were detected in 3rd trimester. In the present study, Total cholesterol, serum triglycerides were higher in GDM patients and there was lower HDL levels.

MATERNAL OUTCOME:

Among the altered lipid profile group the incidence of preeclampsia in GDM cases was 41.7%. Wiznitzer et al reported that elevated serum level of triglycerides are associated with Gestational hypertension and pre-eclampsia, compared to women with low TG levels (14). Llurba et al showed that 16 of 34 women with pre-eclampsia, had TG levels>250 mg/dl (p<0.001) (16). Donovan McGrowder et al (19) showed Gestational diabetes mellitus is associated with increased risk of Gestational hypertension, preeclampsia and other maternal and fetal complications of pregnancy. The GDM patients had significantly increased total cholesterol and triglyceride concentrations and the study concluded that the GDM cases with dyslipidemia were at risk of developing preeclampsia. Arnon Wiznitzer et al (22) in their study compared and the lipid profile of pregnant women with and without GDM and or Preeclampsia. The abnormal lipid levels are associated with increased pregnancy complications.

In our study, polyhydramnios occurred in about 43.6% of

<table>
<thead>
<tr>
<th>TABLE 3-Comparison of maternal outcome between altered lipid profile and normal lipid profile group:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alter</strong></td>
</tr>
<tr>
<td>----------</td>
</tr>
<tr>
<td>Gestational hypertension</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>Preeclampsia</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>Polyhydramnios</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>Mode of delivery</td>
</tr>
<tr>
<td>Labour Natural</td>
</tr>
<tr>
<td>Instrumental delivery</td>
</tr>
<tr>
<td>LSCS</td>
</tr>
<tr>
<td>Repeat LSCS</td>
</tr>
</tbody>
</table>
GDM patients with altered lipid profile. About 46.2% of GDM patients in altered lipid profile group required Inj. Insulin for optimal control of blood sugar. Preterm deliveries occurred in about 11% of GDM patients with altered lipid profile. Evers et al (20) reported about 44% of caesarean section. Yoge et al (21) reported about 30%. The percentage of patients who had caesarean section was 55.4% (Both LSCS and repeat LSCS), the most common indication being CPD which is about 44% and previous about 27%. (TABLE-3). Ga Hyun Son et al (24), showed that maternal hypertriglyceridemia is a predictor of large for date babies born to GDM mothers. Ute M. Schaefer-Graf et al (23), explained that the association of maternal lipids as determinants of fetal growth and fetal environment in GDM patients.

In the present study, the incidence of macrosomia was 11.5%, RDS 30.8%, hypoglycemia 12.2%, hyperbilirubinemia 14.1%, Anomaly 2.6%, IUD 2.6%, perinatal mortality 1.9%, NICU admission requiring more than 3 days of admission was 23.7%.

There was a significant association between altered lipid profile in GDM cases and the occurrence of macrosomia, Respiratory distress syndrome hypoglycemia, hyperbilirubinemia and NICU admission > 3 days in neonates. (TABLE-4). There was no significant association between altered lipid profile in GDM cases and the occurrence of anomaly, IUD, perinatal mortality.

**CONCLUSION:**

In the present study, lipid profile alterations detected were increased total cholesterol, serum triglycerides in GDM patients and lower HDL levels. There was increased incidence of adverse maternal outcome such as preeclampsia, gestational hypertension, polyhydramnios, preterm labour and increased caesarean section rate and adverse perinatal outcome such as macrosomia, RDS, hypoglycemia, hyperbilirubinemia, NICU admissions and increased perinatal morbidity among GDM cases with altered lipid profile.

**REFERENCES:**

4. Coustan DR, Carpenter MW, O’Sullivan PS, SR. Gestational diabetes: predictors of subsequent disordered

**TABLE 4:** Comparison of perinatal outcome between altered lipid profile and normal lipid profile group:

<table>
<thead>
<tr>
<th></th>
<th>Altered Lipid Profile %within group(count)</th>
<th>Normal Lipid Profile %within group(count)</th>
<th>Pearson Chi-Square</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2.5 kg</td>
<td>5.8%(9)</td>
<td>0.0%(0)</td>
<td>14.617</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2.5-3.5 kg</td>
<td>66.7%(104)</td>
<td>95.5%(42)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;3.5 kg</td>
<td>27.6%(43)</td>
<td>4.5%(2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 min Apgar</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 7</td>
<td>28.2%(44)</td>
<td>4.5%(2)</td>
<td>10.848</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥ 7</td>
<td>71.8%(112)</td>
<td>95.5%(42)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory distress</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>30.8%(48)</td>
<td>11.4%(5)</td>
<td>6.635</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No</td>
<td>69.2%(108)</td>
<td>88.6%(39)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>12.2%(19)</td>
<td>2.3%(1)</td>
<td>3.743</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>No</td>
<td>87.8%(137)</td>
<td>97.7%(43)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperbilirubinemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>14.1%(22)</td>
<td>2.3%(1)</td>
<td>4.179</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>No</td>
<td>85.9%(134)</td>
<td>97.7%(43)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NICU Admission</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>23.7%(37)</td>
<td>0%(0)</td>
<td>12.805</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No</td>
<td>76.3%(119)</td>
<td>100%(44)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ACKNOWLEDGEMENT:

All the GDM patients who participated in the study