A COMPARATIVE STUDY OF SERUM LIPID PROFILE IN PREGNANT WOMEN WITH TYPE 2 DIABETES MELLITUS AND GESTATIONAL DIABETES MELLITUS

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ABSTRACT

BACKGROUND

Diabetes mellitus is one of the most common medical complications that occurs in pregnancy. Changes in serum lipid levels in diabetic pregnancy is associated with preeclampsia, future diagnosis of GDM, induced preterm delivery, LGA infants etc. So, it is important to measure the serum lipid levels to reduce future complications. This present study was carried out in pregnant women with type 2 DM and GDM, to explore if there is any significant variation in serum lipid levels between the two.

MATERIALS AND METHODS

The study (Prospective comparative) was conducted in Assam Medical College and Hospital, Dibrugarh, for a period of one and a half year from January 2013 to May 2014. The study included all pregnant women who were diagnosed as GDM or Type 2 DM during antenatal check-ups or diagnosed beforehand in the department or outside. A total of 29 pregnant women diagnosed with GDM and 13 women with type 2 DM were enrolled who fulfilled the inclusion criteria. Pregnant women with diagnosed lipid metabolism disorders, extremely obese (BMI > 35), malnourished (BMI < 18), endocrine disorders, eclampsia or preeclampsia were excluded from the study. Data were collected on a standard proforma after getting proper permission from the Institutional Ethics Committee (No. AMC/EC/PG/13343) and patient consent.

RESULTS

There was no statistical difference between the groups in terms of maternal age, gestational age, BMI, Gravida and Socio-economic status of the pregnant women. Mean HbA1C levels in the GDM and Type 2 DM groups (in %) were 6.41 ± 0.42 and 6.34 ± 0.47 were homogenous (p = 0.633). Mean total cholesterol, triglyceride, LDL and HDL levels (in mg/dL) in the GDM were 268.49 ± 42.124, 325.52 ± 45.456, 137.15 ± 22.32 and 50.35 ± 11.12, respectively. The levels (in mg/dL) in Type 2 DM were 261 ± 21.27, 327 ± 56.28, 143.95 ± 27.14 and 44.24 ± 13.31, respectively. The results were homogenous (p= 0.549, p= 0.929, p= 0.399 and p= 0.129 respectively).

CONCLUSION

Among the pregnancies complicated by diabetes, incidence of GDM is more than Type 2 DM. No significant lipid level changes were noted between the two groups.

KEYWORDS

Diabetes, Pregnancy, Lipid Profile, GDM, Type 2 DM.

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BACKGROUND

Diabetes mellitus comprises a group of metabolic disorders that result in hyperglycaemia due to defects in insulin secretion, insulin action or both, influenced by the complex interaction of genetics, environmental and lifestyle factors.[1]

Diabetes is the most common medical complication in pregnancy. It affects about 1 to 5% of all pregnancies.[2] It may antedate pregnancy (pre-gestational diabetes) or may be detected for the first time during pregnancy.[3]

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Gestational Diabetes Mellitus (GDM) is defined as carbohydrate intolerance of variable severity with onset or first recognition during pregnancy; irrespective of treatment with insulin or not.[4] Few women with gestational diabetes mellitus may have undiagnosed type II diabetes mellitus (type 2 DM).[5]

The prevalence of gestational diabetes mellitus is variable depending on the population under study. Indian women are considered to be high-risk population for developing gestational diabetes mellitus and have 11 fold increased risk compared to Caucasians.[3] The prevalence of gestational diabetes mellitus in India is 10.6 - 35.8% in urban, 7.8 - 48.4% in semi urban and 8.2 - 29.6% in rural area.[3] The increase is due to obesity and sedentary lifestyle.[3] In general, gestational diabetes mellitus is said to complicate 1 - 16% of all pregnancies,[6] while out of all pregnant women with diabetes 90% have GDM and the incidence of Type 2 DM with pregnancy is increasing.[6] Physiological changes during pregnancy result in a naturally transient hyperlipidaemic and

hyperglycaemic state, and can often serve as an antecedent to the development of Type II diabetes and cardiovascular disease.[7]

Maternal metabolism is designed to provide adequate nutrition for foetal growth in the form of glucose, ketones, lipids and other fuels. In early pregnancy, maternal metabolism is anabolic, which combined with pregnancy-related hyperphagia, results in increased maternal fat stores. In the third trimester, maternal metabolism becomes more catabolic to support the acceleration of foetal growth.[8] Increased maternal insulin resistance combined with peripheral adipose tissue lipolysis results in increased maternal lipoprotein concentrations and elevated lipoprotein content including VLDL (very low density lipoprotein), HDL (High Density Lipoprotein), LDL (Low Density Lipoprotein) and Triglyceride (TG).

In women with pre-existing diabetes or GDM (Gestational Diabetes Mellitus), there is deviation from the usual pattern of pregnancy associated changes in maternal lipids. Changes in maternal lipoproteins or differences in the triglyceride, cholesterol or apolipoprotein content of the maternal lipoproteins have been reported in pregnancies complicated by diabetes.[9]

Data on lipids in women with type 2 diabetes in pregnancy are very few. Studies have shown higher free fatty acid levels compared with normal pregnancy[10] and higher triglyceride and lower HDL-C levels in the first trimester when compared with women with type 1 diabetes in pregnancy[11] or no difference in any lipoprotein compared with either type 1 diabetes or GDM.[12]

In women with GDM, maternal triglycerides have been reported to be increased in all trimesters of pregnancy,[13] although this is not a universal finding. Similarly, maternal cholesterol has been reported as increased[14] or unchanged[10,14,15] across gestation. Studies in women with GDM have shown no difference[12] or a decline in LDL-C concentration,[15] but with increased levels of small, dense LDL[14,16] and increased LDL oxidation.[13]

There are various studies in both national and international literatures that show the changes of lipid profile in pregnancies complicated by type 2 DM and GDM. However, majority of the studies focused on lipid profile changes and pregnancy outcome in GDM. This present study was therefore carried out in pregnant women with type 2 DM and GDM, in our hospital to explore if there is any significant variation in serum lipid levels between the two.

MATERIALS AND METHODS

This study was conducted in the Department of Obstetrics and Gynaecology, Assam Medical College Hospital, Dibrugarh, after approval of the Institutional Ethics Committee (No. AMC/EC/PG/13343) and permission from the Srimanta Sankaradeva University of Health Sciences, Assam for a period of one and a half year from January 2013 to May 2014 as a hospital-based prospective comparative study.

The study included all the pregnant women in the age group of 18 to 35 years who were diagnosed as diabetes both, GDM or type 2 DM in AMCH or outside in the last trimester (29 - 40 weeks) of gestation. We have included all the cases attending the Institution, fulfilling our criteria as the number of diabetic pregnancies was less. Two study groups were**:**

GDM Group

All the pregnant women with GDM attending antenatal outpatient department as well as indoor admitted cases and patient admitted in emergency ward. Screening of the group for Diabetes was done in between 24 - 26 weeks.

Type 2 DM Group

All the pregnant women with type 2 diabetes, diagnosed beforehand, attending antenatal outpatient department as well as indoor admitted cases and patient admitted in emergency ward.

Exclusion Criteria

- Pregnant women having diagnosed of lipid metabolism disorders and receiving hypolipidaemic drugs.
- Extremely obese (BMI > 35) and malnourished (BMI < 18) pregnant women.
- Pregnant women with pre-pregnant hypertensive and other endocrine disorders.
- Patients having eclampsia or preeclampsia were also excluded from our studies.

Methodology of Case Selection

Whenever a pregnant woman visited the outpatient department or emergency, risk stratification was done for diabetes. Already a diagnosed GDM or type 2 diabetic pregnancy was included in our study. As Indian (Asian) women considered to belong to the high risk group for GDM[16], were included for one step diagnostic strategy to diagnose GDM.[17] After 8 hours of overnight fasting, fasting blood sample was collected. Then the patient was asked to drink 75 grams of glucose with 200 mL of water (at 24 - 28 weeks of gestation, not previously diagnosed with overt diabetes). The blood sample was then collected at 1, 2 hours for sugar estimation.[16,17] The diagnosis of GDM was made if any of the below mentioned values were met.[16,17]

- Fasting: 92 mg/dL
- 1 hour: 180 mg/dL
- 2 hours: 153 mg/dL

Type 2 DM was diagnosed according to the standards laid down by IADPSG and ADA.[16] Women with random plasma glucose > 200 mg/dL with classical signs and symptoms such as polydipsia, polyuria and unexplained weight loss are diagnosed as overt diabetes in pregnancy. Overt diabetes was diagnosed if the following values are met.[16]

- Fasting plasma glucose: 126 mg/dL
- HbA1C: 6.5%
- Random plasma glucose: 200 mg/dL with classical signs and symptoms.

Once the diagnosis was established, patients were divided into 2 groups. Serum lipid profile (including TC, TG, LDL and HDL) was estimated in the third trimester. All samples were taken in the morning within 2 hours of breakfast to minimise confounding in the results. The glycaemic status was checked periodically by FBS and PPBS and also by HbA1C levels. The patient's treatment profile, BMI, socioeconomic status and complete obstetrical history was recorded. Complete physical and obstetrical examination results were obtained and recorded.

Parameters	Normal Reference Values (mg/dL)
Serum Triglyceride	30 - 200
Serum Total Cholesterol	< 200 (desirable)
Serum HDL cholesterol	40 - 60
Serum LDL Cholesterol	< 100 (optimal)

Table 1. The Normal Reference Values of Serum Lipid Profile[18]

The results obtained were subjected to statistical analysis using Microsoft Excel 2013 to calculate mean, standard deviation and student t-test in GraphPad prism.

RESULTS

Data was collected from a total of 42 subjects, 29 pregnant women with gestational diabetes mellitus and 13 pregnant women with type 2 diabetes that fulfilled the criteria as mentioned above.

Parameters	GDM	Type 2 DM	Significance (p value)
Age	28.43 ± 3.13	29.80 ± 4.12	0.242
BMI	26.7 ± 3.2	24.47 ± 3.7	0.053
HbA1C	6.41 ± 0.42	6.34 ± 0.47	0.633

Table 2. General Characteristics

Socioeconomic Class	GDM (n = 29)	Type 2 DM (n = 13)	Total (n = 29)
Upper	0 (0.00%)	0 (0.00%)	0 (0.00%)
Upper Middle	1 (3.44%)	0 (0.00%)	1 (2.38%)
Lower Middle	2 (6.89%)	1 (7.69%)	3 (7.14%)
Upper Lower	10 (34.48%)	5 (38.46%)	15 (35.71%)
Lower	16 (55.17%)	7 (53.85%)	23 (54.76%)
Inference	P=0.377		

Table 3. Socioeconomic Status of the Groups (according to Modified B. G. Prasad Classification Updated on 2014)[19]

Gravida	GDM (n = 29)	Type 2 DM (n =13)
G1	11 (37.93%)	4 (30.76%)
G2	7 (24.13%)	5 (38.46%)
G3	8 (27.58%)	4 (30.76%)
G4 and Above	3 (10.34%)	0 (0.00%)
Inference	P = 0.0911	

Table 4. Gravida Distribution

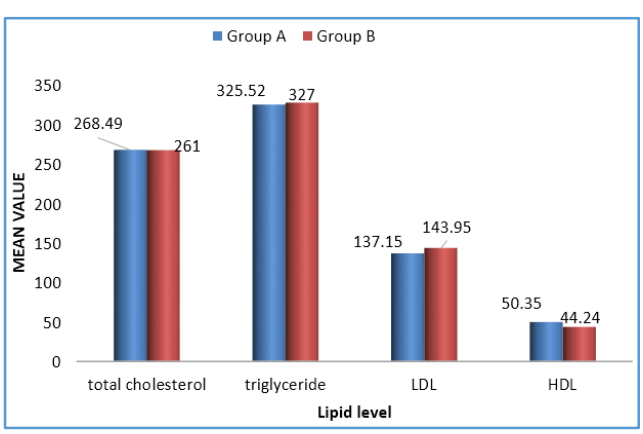

Figure 1. Mean Lipid Profile of the Groups

DISCUSSION

Diabetic pregnancies are associated with changes in maternal lipids. Pregnancies with gestational diabetes and type 2 diabetes have conflicting results regarding changes of lipid profile. Women with pre-existing type 2 DM may have higher TG and lower HDL-C levels in the first trimester without significant change in LDL-C and Lp (a) in comparison to normal. Women with gestational diabetes may have increased to unchanged TG and TC levels and stable LDL fractions throughout gestation, although these results have been equivocal.[20,21,22,23] Maternal obesity on the other hand with or without overt gestational diabetes is linked with atherogenic lipid profile and adverse pregnancy outcome, in part due to inflammation and endothelial dysfunction.[20,21,22,23] Gestation in obese women is more frequently associated with elevated TG and small, dense LDL fractions with low HDL-C levels.[20,21,22,23] While some studies show increased levels of triglyceride and others show lower levels of HDL.

In our study, the mean ages of the groups were 28.43 ± 3.13 (GDM) and 29.80 ± 4.12 (Type 2 DM) years, respectively (p = 0.242). In a longitudinal study by Montelongo et al,[9] the mean age was 30.8 ± 2.1 and 29.0 ± 1.3 years for the patients with GDM and pre-gestational diabetes (p > 0.005). Another study by Toescu et al,[10] the mean age for GDM and Type 2 diabetic pregnant women with diabetes were 32.8 ± 1.5 and 32.50 ± 1.6 years, respectively (p > 0.05). The mean age of the type 2 diabetic pregnancy in the study by Clause et al[24] was 33.4 years and it was 34.0 ± 5.0 years in the study by Valk et al.[25]

Based on revised modified BG Prasad socioeconomic classification scale, January 2014[19] most of the participants in GDM had come from a lower (L) socioeconomic status (55.17%) and in Type 2 DM from upper lower status (53.85%). Total 54.76% of patients belonged to the lower class in our study; 34.48% in both the groups came from Upper Lower (UL) socioeconomic status. Other studies eliminated the selection bias by including the patients belonging to the same socio-economic class.

Pregnancy mean BMI in the present study in GDM and Type 2 DM were 26.7 ± 3.2 and 24.47 ± 3.7, respectively (p = 0.053). In a longitudinal study by Montelongo et al,[9] the mean BMI was 23.27 ± 0.64 and 22.20 ± 0.28 for the patients with GDM and pre-gestational diabetes (p > 0.05). Another study by Toescu et al,[10] the mean BMI for GDM and Type 2 diabetic pregnant women with diabetes were 30.9 ± 1.7 and 30.7 ± 2.2, respectively.

Present study shows that most of the patients in GDM were primigravida 39.1%, while in type 2 DM it was in gravida 2 (50.00%). The association between gravida, parity and diabetes seems consistent in different studies. Women with higher parity are frequently heavier and older. Therefore, no study that evaluates parity could ignore age adjustments.

In the present study, mean HbA1C levels in GDM and Type 2 DM were 6.41 ± 0.42 and 6.34 ± 0.47%, respectively (p = 0.633). The median value of HbA1C in the two groups were 6.2 and 6.35, respectively. In the study by Montelongo et al,[9] the mean HbA1C was 4.90 ± 018 and 5.52 ± 0.17% for the patients with GDM and pre-gestational diabetes (p > 0.05). Clause et al[24] (5.9%) and Gibson et al[26] (5.8 ± 0.76%) found the mean HbA1C level comparable to our study population in the third trimester of type 2 diabetic mother. These values

were comparable with our study in terms of glycaemic control.

The mean total cholesterol levels in the GDM and Type 2 DM were 268.49 ± 42.124 and 261 ± 21.270 mg/dL respectively (p = 0.549). Triglyceride levels in the groups were 325.52 ± 45.456 and 327 ± 56.28 mg/dL respectively (p = 0.929). The mean LDL cholesterol levels in the GDM and Type 2 DM were 137.15 ± 22.32 and 143.95 ± 27.14 mg/dL, respectively (p = 0.399). The mean HDL cholesterol levels in the groups were 50.35 ± 11.12 and 44.24 ± 13.31 mg/dL respectively (p = 0.129).

These results were similar in comparison to the other studies by He B et al[27], Montelongo et al[9] found similar TG/HDL ratio in the two groups. They found statistical significance of TG/HDL level between pregnant women with type 1 diabetic and GDM; type 1 diabetic and type 2 diabetic pregnant women. Toescu et al[10] did not find any statistical significant differences between the groups in third trimester for lipid levels TG, TC, LDL and HDL.

But our findings were not consistent with the study of Chen DQ et al[28]. They found lowest mean value of TC, LDL and TG in GDM group, while lowest mean value of HDL in pre-gestational diabetes.

CONCLUSION

From our study it was established that of all the pregnant women suffering from diabetes, GDM has a major contribution. There is no significant change of lipid profile in the pregnancies complicated by GDM and type 2 diabetes, although it should be more widely studied.

Limitation

The study population was very small, so it was difficult to draw a conclusion. Systemic studies in a larger population of people in different parts of the world in different ethnic groups will help in this regard.

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