ORIGINAL ARTICLE

Maternal Lipids in Pregnancies with Gestational Diabetes Mellitus

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ABSTRACT

Objective: To study the effect of gestational diabetes mellitus (GDM) on indices of lipid profiles in maternal blood samples and compare them with normal pregnancies.
Methodology: Blood samples were collected from 50 normal pregnant women and 46 women with GDM. Fasting blood sugar and hemoglobin A1c were estimated by colorimetry. Serum lipids and lipoproteins (Total cholesterol, triglycerides, LDL-Cholesterol, VLDL-cholesterol and HDL- cholesterol) using automated clinical analyzer.
Results: The results of the lipid profile showed no significant difference between GDM and controls. However HDL-cholesterol was significantly reduced in GDM group B ($P<0.001$).
Conclusion: In gestational diabetes mellitus the lipid profile alters in such manner that could be atherogenic and possibly harmful to the fetus.
Keywords: Gestational diabetes mellitus, Hyperlipidemia, Hemoglobin A1c

INTRODUCTION

A series of metabolic abnormalities results from insulin insufficiency and these causes complications that remain a major cause of morbidity and mortality. Abnormalities of plasma lipids and lipoproteins concentration are commonly observed in diabetic individuals[12]. Lipid abnormalities include so called diabetic dyslipidemia, characterized by an elevation in triglycerides (TG), a decrease in HDL-cholesterol and a moderate elevation or normal levels of LDL-cholesterol concentration in blood[10]. Normal pregnancy induces major alterations in carbohydrates, lipids and amino acids metabolisms[11]. Plasma concentration of TG, cholesterol, phospholipids and free fatty acids all increase during pregnancy. The most dramatic change is the rise in fasting TG concentration [27], which increases approximately four folds during pregnancy probably due to increased hepatic synthesis and reduced removals, induced by placental hormones[16]. Plasma cholesterol levels also change significantly during pregnancy. LDL-cholesterol levels peak at approx 36th week. Until week 32 and remains constant for the remainder of pregnancy. It is believed to be caused by estrogens[5].

Prior to the introduction of insulin treatment, diabetes was a rare complication of pregnancy due to high incidence of amenorrhoea, infertility and miscarriage in women with diabetes[11], maternal and perinatal mortality being over 50%. In 1921, Frederick Banting and colleagues isolated insulin, since then the maternal and perinaltal outcome has continued to improve[3]. Diabetes or impaired glucose tolerance develops in 2-3 percent pregnant women, previously non-diabetic, most often in the last trimester of pregnancy, when the burden is most [1]. This condition is referred to as gestational diabetes mellitus (GDM). It is defined as any degree of glucose intolerance with onset or first recognition during pregnancy. The definition applies regardless of whether insulin or only diet modification is used for treatment or whether the condition persist after pregnancy. GDM represents nearly 90percent of all pregnancies complicated by diabetes. (Expert Committee on the Diagnosis and Classification of diabetes mellitus, 1997). The insulin resistance of normal pregnancy may also contribute to GDM in women in whom the capacity for insulin secretion is not sufficient to meet the increased insulin demands of pregnancy[8]. Clinical recognition of GDM and control of diabetes mellitus is important and because therapy including diet and insulin and antipartum fetal surveillance can reduce the well described perinatal morbidity and mortility and maternal complications associated with these conditions. Also there is evidential support for the hypothesis which connects adulthood hypertension, insulin resistance and dyslipidemia to adverse intrauterine conditions during gestation[25], especially in diabetic pregnancy[24]. Our study aimed to determine the changes in serum lipids and lipoproteins during last trimester of gestational diabetes and compare these with serum lipids and lipoproteins levels in normal pregnancies. The increased specific activity of hepatic lipase induced

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by progesterone in turn likely results in increased concentration of HDL-cholesterol. Maternal lipoprotein lipase activity favours hypertriglyceridemia

MATERIAL & METHODS

This study was conducted in the Department of Biochemistry, Basic Medical Sciences, Jinnah Postgraduate Medical Center, Karachi. A total of 96, age matched, pregnant women, with single active fetus in their last trimester of pregnancy were screened for this study. The subjects were chosen from Gynae and Obstetrics wards 8 and 9 JPMC and Ward 7 Diabetic Clinic JPMC. The total number of subjects was divided into two groups. Group A consisted of 50 non-diabetic female in last trimester of pregnancy and 46 pregnant females, who were diagnosed with diabetes for the first time during pregnancy i.e., suffering from GDM were listed in Group B.

All women in Group B had GDM diagnosed based on a 75gm oral glucose tolerance test with determination of three glucose values in capillary blood using hexokinase method. At least two values had to exceed the criteria endorsed by the American Diabetes Association (95/180/155mg/dl) for measurement in venous plasma[23]. Women suffering from Type-I or II DM, thyroid diseases, liver diseases, those taking medicine which alter lipids metabolism e.g., cholesterol lowering drugs were not included in the study.

The subjects were informed and consent was taken, than asked to come in the morning after an overnight fast of at least 12-14 hours. About 10ml of blood was drawn from anticubital vein after all aseptic measures. 1 cc blood was used to estimate HbA1C, by fast ion exchange resin separation method, using Kit supplied by Human Germany, Cat No. 10658. Serum was separated from rest of the blood sample. Serum was used to estimate glucose by enzymatic calorimeter (GOD-PAP) method, using kit, Cat No Cod.1001191 supplied by spinreact, SA, Spain. Serum total cholesterol, triglycerides and HDL-cholesterol were determined by enzymatic calorimeter methods using automated clinical analyzer with the kits supplied by clinical Carvico (BG) Italy. LDL-cholesterol was calculated according to Friedwald's formula[9] and VLDL-cholesterol was calculated by Wilson cited by Delong et al[4]. Results were compared with SPSS version 10.

RESULTS

A total of 96 subjects were studied and table-I shows the distribution of subjects from both the Group-A and B with normal pregnancy and pregnancy with GDM respectively.

Table 2 shows mean values with standard error (±) of mean (SEM) and intergroup comparison of age, gestational age, height, weight and body mass index (BMI) of both groups. No statistically significant difference was seen in age, gestational age and height of these groups. But the mean weight of group B was significantly less ($p<0.01$) than group A and as a results of this mean BMI of group-B was significantly low ($p<0.001$).

Table-3 depicts the mean values and inter group comparison of serum blood glucose, HbA1C, total cholesterol, T.G, LDL-cholesterol, VLDL cholesterol, HDL-cholesterol and total cholesterol: HDL-cholesterol ratios. Where we noticed highly significant increase ($p<0.001$) in fasting serum glucose and HbA1C levels of group-B subjects when compared to group A. No significant difference was found in inter group comparison for total cholesterol, T.G, LDL-cholesterol and VlDL-cholesterol though the values were on higher side in group-B. HDL-cholesterol levels were significantly low ($p<0.001$) in group B when compared to group-A. Total cholesterol: HDL-cholesterol ratio was significant high in GDM group ($p<0.001$) when compared to non-diabetic group.

Table 1: Distribution of subjects according to diabetic status

Group	Distribution of Subjects	Diabetic Status
A	50	Non-Diabetic
B	46	Diabetic (GDM)

Table 2: Comparison of age, gestational age, height, weight and BMI of Group A and B.

Variables	Group A	Group B
Age (years)	26.85±1.27	27.50±1.06
Gestational age (weeks)	31.30±0.90	32.20±0.82
Height (m)	1.57±0.006	1.58±0.009
Weight (kg)	61.87±1.43	57.90±0.99
BMI (kg/m^2)	25.02±0.53	23.30±0.48

Table 3: Comparison of FBS, HbA1c, Total Cholesterol, T.G, HDL, LDL, VLDL and Total Cholesterol: HDL-cholesterol ratio of Group A and Group B.

Variables	Group A	Group B
FBS (mg/dl)	70.60±3.64	97.20***±4.97
HbA1c (%)	6.04±0.16	7.50***±0.43
Total cholesterol (mg/dl)	187.55±8.57	197.0±10.99
T.G (mg/dl)	186.55±11.83	216.20±15.18
HDL-cholesterol (mg/dl)	38.60±1.02	28.40***±2.10
LDL-cholesterol (mg/dl)	111.73±7.67	125.00±10.19
VLDL-cholesterol (mg/dl)	37.25±2.35	43.20±3.05
Total cholesterol: HDL-Cholesterol ratio	4.75±0.22	7.10***±0.50

*p<0.05, **p<0.01, ***p<0.001

DISCUSSION

Women with GDM are at high risk of maternal and fetal complications during pregnancy. Recent studies on experimental animals points towards an important role of intrauterine metabolic environment in the development of fetal malformation associated with GDM[6,29]. Disturbances of maternal metabolism are well known factors affecting growth of fetus. Because diabetes produces changes in maternal metabolic fuels and because diabetic pregnancy is often associated with complications, the effects of maternal diabetes on lipid metabolism are unclear[17].

The plasma lipids and lipoproteins changes in diabetic pregnancy have been studied by many researchers[24,25,7]. The recent study was designed to observe the changes in lipid profile and glucose tolerance in normal pregnancy (Group-A) and GDM subject (Group-B). It was confirmed decades ago that during pregnancy plasma glucose value is lowered during pregnancy[2] due to the utilization of glucose by conceptus. In our study the glucose levels in GDM patients were significantly high ($p<0.001$) actual levels being (97.2±4.97mg/dl) when compared to group-A (70.60±3.64mg/dl). Similarly HbA1C measurement provides a retrospective index of glycemic control over 4 to 8 weeks prior to determination and poor glycemic control in diabetic patients have generally been found to have elevated serum lipid levels[28]. In a study conducted by MD Kilby et al[15] in UK[19]. It was found that HbA1C was significantly greater in type-I diabetic mellitus than non-diabetic pregnancies being 9.6 percent and 6.8 percent respectively. Another study done by Ersanali et al[7] on GDM associated with fetal macrosomia showed significant higher values of HbA1C in GDM subjects. When compared to non-diabetic control. Results of our study showed mean levels of HbA1C as 7.5±0.43 Group-B which are significantly higher ($p<0.01$) than group-A. These results are in accordance to other studies done on same subjects by[7,15].

Hyperlipidemia is a common feature in normal pregnancy and consist primarily of tryglycerides with smaller rises in cholesterol[20]. Total cholesterol was studied in normal and GDM pregnancies by de Arcos [26] and results reported to show a trend towards being higher in diabetic patients, but no significant difference were encountered. In our study results, there was also an elevation of total serum cholesterol in group-B when compared to group-A but increase is not significant. Regarding the triglycerides (T.G) non-diabetic pregnancy and GDM did not show any significant difference though diabetic subjects were with higher mean values (216.20±15.18 mg/dl) than group-A (186.55±11.83). These results are in confirmation of all the studies consulted for lipidemia of pregnancy[2,13,28].

LDL-cholesterol and VLDL-cholesterol also elevates in pregnancy along with other lipids. A study done in 1982 by Hollingworth[18] depicts changes in LDL-cholesterol where GDM patients failed to demonstrate a rise with pregnancy. Study results of deArcos[26] showed non-significant rise in LDL and VLDL-cholesterol in GDM patients when compared to normal pregnancy. Montelonge[20] reported significant increase in LDL-cholesterol in GDM groups in comparison of normal pregnancies. Our results are in agreement with the results of Hollingsworth and deArcos where no significant difference was seen in LDL and VLDL-cholesterol values among the groups A and B. There is some evidence that not only TG and cholesterol are elevated but also the concentration of HDL-cholesterol is increased in pregnant women. Hollingsworth studied HDL-cholesterol in GDM and values were found lower than normal pregnancy status. Our results showed significantly lower ($P<0.001$) values than normal pregnancy actual values being (38.60±1.02) and (28.40±2.1) in group-A and group-B respectively. From above results it seems that diabetic subjects have lower HDL-cholesterol values which do not increase even under the influence of pregnancy hyperlipidemia.

In the end we also calculated total cholesterol: HDL cholesterol ratio which was found in pathological range in group-B, mean value (7.10±0.50) where as normal pregnancy group-A (4.75±0.22) did not show any change from normal values being 4-5. These results are in confirmation of other studies as of Mazurkiewicz[18,13,22].

To summarize this discussion our study shows that hyperlipidemia of normal pregnancy is due to increase in TG, HDL-cholesterol, VLDL-cholesterol. In GDM subjects these results were accumulated along with a decrease in HDL-cholesterol.

CONCLUSION

The present findings demonstrate that circulating maternal lipids in GDM subjects were not significantly different from the normal pregnancy levels except for HDL-cholesterol results. TG, VLDL-cholesterol and LDL-cholesterol did not show any significant difference in both the groups. HDL-cholesterol dropped significantly low ($p<0.00$)) in diabetic pregnancy Group B. The lowering of HDL-cholesterol in GDM increased the ratio of total cholesterol: HDL-cholesterol towards the high risk figure i.e., 7.10 + 0.50 which is significantly high ($p<0.001$) than normal pregnancies. It can be concluded from the above facts hyperlipidemia of normal pregnancy is counter

balanced by increase in HDL-cholesterol which protects from unfavourable effects of hyperlipidemia. In GDM the lipid profile alters in such a manner that could be harmful. Extended studies are required to see the effect of these alterations on fetus. Our results are not complete accordance with western repents. This could be due to ethnic and environmental factors.

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