

# Alterations in lipid profile in gestational diabetes mellitus (GDM) and type 2 DM women during pregnancy

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## Abstract

**Objective:** To study the effect of gestational diabetes mellitus (GDM) and type 2 diabetes mellitus (DM) on indices of lipid profile in maternal blood samples and compare them with normal pregnancies. **Methodology:** Blood samples were collected from 45 normal pregnant women and 30 women with GDM and 15 women with type 2 DM during pregnancy. Serum lipids which include Total Cholesterol, Triglycerides, Very Low Density Lipoprotein, Low Density Lipoprotein and High Density Lipoprotein were estimated using semi-automated clinical chemistry analyzer. **Results:** The results of the lipid profile showed elevated levels of Total Cholesterol, Triglycerides, Very Low Density Lipoprotein and Low Density Lipoprotein in women with GDM and pregnant type 2 DM women compared to controls. On the other hand, the High Density Lipoprotein levels were significantly elevated in controls. **Conclusion:** In Gestational Diabetes Mellitus and type 2 DM during pregnancy, the lipid profile alters in such manner that could be atherogenic and possibly harmful to the fetus.

**Keywords:** Gestational Diabetes Mellitus, Total Cholesterol (TC), Triglycerides (TGL), VLDL (Very Low Density Lipoprotein), LDL (Low Density Lipoprotein), HDL (High Density Lipoprotein)

## Introduction

Diabetes or impaired glucose tolerance develops in 2-3 percent pregnant women, previously non-diabetic, most often in the last trimester of pregnancy. 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. GDM represents nearly 90 percent of all pregnancies complicated by diabetes. 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 [1].

Diabetes during pregnancy is associated with increase in maternal and perinatal morbidity. The hallmark of this condition is increased insulin resistance. Maternal hormones are thought to interfere with the action of insulin as it binds to the insulin receptor. Since insulin

promotes the entry of glucose into most cells, insulin resistance prevents glucose from entering the cells. As a result, glucose remains in the bloodstream, where glucose levels rise. More insulin is needed to overcome this resistance; more insulin is produced than in a normal pregnancy.

Macrosomia [2], congenital cardiac and central nervous system anomalies, skeletal malformations and respiratory distress syndrome are some of the well-known complications occurring in infants of diabetic mothers. Moreover, human epidemiological and animal studies suggest that the intrauterine diabetic environment increases the risk of hypertension, obesity, and type II diabetes in adulthood in the offspring of diabetic mothers. Fetal hyperinsulinemia at birth acts as a marker of this risk and it may also have potential prognostic implications. Thus, higher insulin levels in utero might be a cause of later metabolic complications [3] [4] [5].

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Normal pregnancy induces major alterations in carbohydrate; lipid and amino acid metabolisms [6]. Our study aimed to determine the changes in serum lipids during last trimester of gestational diabetes and type 2 DM during pregnancy and compare these with serum lipid levels in normal pregnancies. Lipid abnormalities include so called diabetic dyslipidemia, characterized by an elevation in triglycerides (TGL) and a moderate elevation or normal levels of LDL-cholesterol and total cholesterol concentrations in blood [7]. Plasma

concentration of TGL, cholesterol, phospholipids and free fatty acids increase during pregnancy. The most dramatic change is the rise in fasting TGL concentration [8], which increases approximately four folds during pregnancy probably due to increased hepatic synthesis and reduced removals, induced by placental hormones [9]. Maternal lipoprotein lipase activity also favours hypertriglyceridemia. The increased specific activity of hepatic lipase induced by progesterone in turn likely affects the concentration of HDL-cholesterol.

## Materials and methods

### Study Population:

#### a. Cases :

The study sample comprised 30 women with GDM and 15 women with type 2 DM during pregnancy during the third trimester. GDM women were diagnosed with oral glucose tolerance test (ADA Criteria)[10]. Both GDM and Type 2 DM women were on treatment with diet modifications, exercise and insulin.

#### b. Controls :

Comprised 45 normal pregnant women attending the antenatal clinic

### Inclusion Criteria

Women aged between 25-35 years and without any other medical complications of pregnancy

### Exclusion Criteria

Mothers with complications like preeclampsia, preterm deliveries, twin pregnancies and those on medications which alter lipid metabolism e.g., cholesterol lowering drugs were not included in the study.

### Sample Collection and Processing

#### Sample collection

Patients' overnight fasting blood samples were drawn into vacutainer tube. The samples were made to stand for 1 hour for sera to separate. The samples were then centrifuged at 3000 rpm for 5 minutes. Sera were aliquoted and stored at -21°C until ready to use.

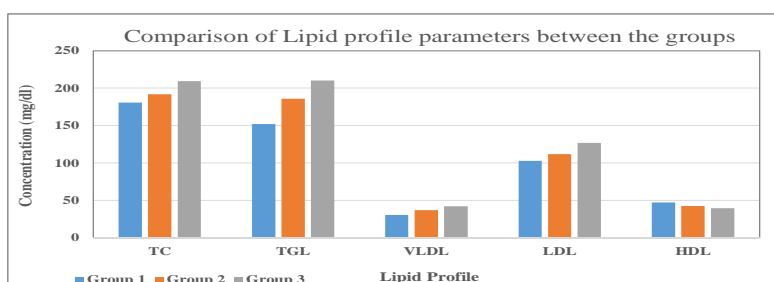
#### Analysis of samples

Samples were brought to room temperature and allowed to thaw before analysis. Total cholesterol and triglycerides were estimated by enzymatic methods [11], [12]. HDL-Cholesterol (HDL-C) was estimated by phosphotungstic acid precipitation followed by enzymatic analysis in supernatant fraction [13] and LDL-Cholesterol (LDL-C) was determined by using Friedewald's equation [14] according to which  $LDL\ cholesterol = Total\ cholesterol - (HDL\ cholesterol + VLDL\ cholesterol)$ . VLDL cholesterol (VLDL-C) was calculated as 1/5 of Triglycerides.

## Results

**Table 1: Distribution of subjects according to diabetic status**

Group	Number of Subjects	Diabetic Status
1	45	Non-Diabetic pregnant women
2	30	GDM women
3	15	Pregnant type 2 DM women



**Table 2: Comparison of lipid profile parameters between the groups**

Lipid profile	Groups	Mean	Standard deviation	ANOVA F	Significance (P value)
Total cholesterol (TC)	1	180.7	10.8	30.7	< 0.05*
	2	191.8	14.6		
	3	209.2	12.3		
Triglycerides (TGL)	1	151.9	10.5	116.1	< 0.05*
	2	185.7	17		
	3	210.4	16.6		
Very Low Density Lipoprotein (VLDL)	1	30.3	2.1	114.3	< 0.05*
	2	37.1	3.5		
	3	42.2	3.5		
Low Density Lipoprotein (LDL)	1	102.8	8	31	< 0.05*
	2	112.0	12.8		
	3	126.5	10.8		
High Density Lipoprotein (HDL)	1	47.1	3.7	19.1	< 0.05*
	2	42.7	5.9		
	3	39.6	2.5		

\* - Significance

The mean Total cholesterol levels were found to be significantly higher in women with GDM ( $191.8 \pm 14.6$  mg/dl) and type 2 DM women ( $209.2 \pm 12.3$  mg/dl) compared to controls ( $180.7 \pm 10.8$  mg/dl). Similarly, Serum triglycerides (TGL) were significantly higher in women with GDM ( $185.7 \pm 17$  mg/dl) and type 2 DM women ( $210.4 \pm 16.6$  mg/dl) as compared with controls ( $151.9 \pm 10.5$  mg/dl). Such a significance was also seen in the case of VLDL and LDL, with the mean VLDL being ( $37.1 \pm 3.5$  mg/dl) in GDM, ( $42.2 \pm 3.5$  mg/dl) in type 2 DM and the mean LDL being ( $112 \pm 12.8$  mg/dl) in GDM and ( $126.5 \pm 10.8$  mg/dl) in type 2 DM, which were significantly higher than the controls. In contrast, HDL cholesterol was significantly elevated in controls ( $47.1 \pm 3.7$  mg/dl), compared to GDM ( $42.7 \pm 5.9$  mg/dl) and type 2 DM women ( $39.6 \pm 2.5$  mg/dl).

**Table 3: Relationship between maternal age and lipid profile**

Group	Correlation of maternal age with				
	TC	TGL	VLDL	LDL	HDL
	P Value	P Value	P Value	P Value	P Value
1	0.02*	0.12	0.09	0.29	0.05
2	0.90	0.78	0.76	0.61	0.38
3	0.21	0.36	0.40	0.29	0.49

\* - Significance

No significant correlation was found between the maternal age and the lipid profile parameters except for the Total Cholesterol value which increased with maternal age in the control group alone.

## Discussion

Women with GDM and type 2 DM 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 diabetic pregnancy. 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 [15]. The plasma lipid and lipoprotein changes in diabetic pregnancy have been studied by many researchers [16],[17]. This study was designed to observe the changes in lipid profile in

normal pregnancy (Group-1), GDM women (Group-2) and type 2 DM women (Group-3).

Hyperlipidemia is a common feature in normal pregnancy and consists primarily of an increase in triglycerides with smaller rises in cholesterol [18]. Total cholesterol was studied in normal and GDM pregnancies by de Arcos [19] and results reported to show a trend towards being higher in GDM women. Recently, Schaefer-Graf et al. [20] found that maternal serum triglyceride levels significantly correlated with abnormal fetal growth in women with gestational diabetes mellitus. In our study results, there was a significant elevation of total serum cholesterol in groups-2 and 3 when compared to group-1. LDL-cholesterol and VLDL-cholesterol levels are also elevated usually in pregnancy along with other lipids. A study done in 1982 by Hollingsworth [21] depicts changes in LDL-cholesterol where GDM patients failed to demonstrate a rise with pregnancy. Study results of de Arcos [19] showed non-significant rise in LDL and VLDL-cholesterol in GDM patients when compared to normal pregnancy. Montelongo [18] reported significant increase in LDL-cholesterol in GDM groups in comparison to normal pregnancies. Our results are in agreement with the results of Montelongo [18] where significant difference was seen in LDL values among the groups. There is some evidence that not only TGL and Total cholesterol, but even the concentration of HDL-cholesterol is increased in pregnant women. Hollingsworth studied HDL-cholesterol levels in GDM women and values were found to be lower than in normal pregnancy. Our results showed significantly lower values in diabetic pregnancy compared to normal pregnancy, actual values being  $(47.1 \pm 3.7)$ ,  $(42.7 \pm 5.9)$  and  $(39.6 \pm 2.5)$  mg/dl in groups-1, 2 and 3 respectively. From above results, it seems that diabetic subjects have lower HDL-cholesterol values which do not increase even under the influence of hyperlipidemia of pregnancy.

From our study it is evident that all the parameters of lipid profile except for HDL cholesterol is elevated in gestational diabetes and type 2 DM in pregnancy than in controls. So, dietary modifications and appropriate treatment might reduce the fetal and maternal morbidity and mortality in a diabetic pregnancy.

## Conclusion

In the present study, Total Cholesterol, Serum Triglycerides, VLDL and LDL levels were significantly elevated in GDM and pregnant type 2 DM women

when compared to normal pregnant women. On the contrary, HDL cholesterol was found to be significantly elevated in controls. Therefore, our study shows that the lipid profile in a diabetic pregnancy alters in such a manner that could be harmful to the fetus. Extended studies are required to see the effect of these alterations on fetus. Early diagnosis and treatment of diabetic pregnancy will reduce the severity of complications associated with this condition.

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