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Evaluation of Lipid Profile in Pregnancy and Patients with Gestational Diabetes Mellitus in North Indian Population

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ABSTRACT

Background: Significant alterations in maternal lipid metabolism occur during pregnancy**.** gestational diabetes mellitus (GDM) is the most commonly seen metabolic disorder during pregnancy. The association between dyslipidemia and GDM is unclear.

Methods: The study population was from pregnant women attending the antenatal clinic of Department of Obstetrics and Gynecology, Lok Nayak Hospital, Delhi. Ethical clearance was granted by the ethical committee of the institute. Patients who attended the clinic at or before 28 weeks of gestation and were willing to participate were included in the study and venous sample was taken for lipid profile in fasting state. Lipid levels were compared in GDM and non GDM patients.

Findings: Total 936 patients were recruited in the study and out of these 64 patients were diagnosed as GDM. The mean values of total serum cholesterol, triglyceride (TG) and high-density lipoprotein (HDL) cholesterol were 194.89±35.96 mg/dl, 170.96±46.69 mg/dl and 50.1±7.16 mg/dl respectively in all pregnant patients. The levels of total serum cholesterol and triglycerides were significantly higher in patients with GDM than in patients without GDM ($p<0.001$), whereas the difference in HDL cholesterol was not significant between two groups.

Interpretation: Triglyceride levels are raised in all pregnant patients. Total cholesterol and triglyceride levels a significantly raised in GDM patients in comparison to non GDM patients.

KEYWORDS: Gestational diabetes mellitus (GDM), total cholesterol (TC), high density lipoprotein (HDL), triglyceride (TG), glucose tolerance test (GTT)

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INTRODUCTION

Pregnancy causes profound variations in maternal lipid metabolism(1).The mechanism whereby pregnancy induces hyperlipidemia has not been fully elucidated. The complementary and opposing actions of the individual pregnancy hormones and their changing concentrations during pregnancy would be expected to lead to pronounced alterations in lipoprotein metabolism as gestation progresses(2) .

Gestational diabetes mellitus (GDM) is the most prevalent metabolic disorder during pregnancy affecting up to 25% of pregnancies in some countries(3). Previous studies have suggested an association between disordered glucose and lipid metabolism in the development of GDM, although results have been inconsistent and previously published meta-analysis studies summarized the association between dyslipidemia with the occurrence of GDM(4, 5). The exact relationship between maternal plasma lipid metabolism and GDM is still unclear but recent studies underscore the fact that GDM induces a state of dyslipidemia consistent with insulin resistance. The goal of the study was to find the average lipid levels in the pregnant patients in second trimester and to compare the lipid levels in pregnant non GDM and GDM patients.

METHODOLOGY

The study population was from pregnant women attending the antenatal clinic of Department of Obstetrics and Gynecology, Lok Nayak Hospital, Delhi. Ethical clearance was granted by the ethical committee of the institute. Patients who attended the clinic at or before 28 weeks of gestation and were willing to participate were included in the study. Known diabetics were excluded. All patients underwent glucose tolerance test (GTT) with 75 grams of glucose between 24 to 28 weeks of gestation. The subjects were advised an unrestricted diet three days prior. A fasting venous sample was taken after overnight fasting of 8 to 14 hours. A solution containing 75 grams of glucose was given to all subjects and two samples were taken at hourly interval. Plasma glucose estimation was done by hexokinase method on autoanalyzer Cobas C501. The cut-offs used for GTT was as per International Association of Diabetes and Pregnancy Study Groups Recommendations on the Diagnosis and Classification of Hyperglycaemia in Pregnancy (IADPSG)2010 criteria (i.e., one or more abnormal plasma venous glucose values $\geq$ fasting, 92 mg/dl; 1 h, 180 mg/dl; or 2 h, 153 mg/dl)(6). While taking fasting sample for GTT 2ml of venous blood sample for lipid profile also taken in plain vacutainer. Serum Cholesterol, HDL-Cholesterol were analyzed on AU480 biochemistry autoanalyzer by cholesterol oxidase peroxidase (CHOD-POD) method. Triglycerides were analyzed on AU480 biochemistry autoanalyzer by glycerol-3-phosphate (GPO)-peroxidase (POD) method. Total cholesterol, triglyceride and HDL values were obtained in all the patients and compared among normal patients and GDM patients.

Data analysis was done by using SPSS. Chi square test and fisher exact test were applied to categorical variables, whereas student t test was applied to analyse quantitative variables. Probability of 5% for the level of significance was used.

Results

A total 936 were recruited in the study and were therefore included for final analysis of the results. Total cholesterol, triglyceride (TG) and high-density lipoprotein (HDL) were also measured in all the patients. The mean value of cholesterol level was 194.89$\pm$35.96 mg/dl. More than half i.e. 51.8% had cholesterol between 160-200 mg/dl and only 8.4% had more than 250 mg/dl out of total population. The mean value of triglyceride in total population was 170.96$\pm$46.69 mg/dl and 64.6% of total population had TG levels between 150 to 199 mg/dl. The mean HDL level was 50.1$\pm$7.16 mg/dl and 87.8% of total population had HDL between 40-60 mg/dl

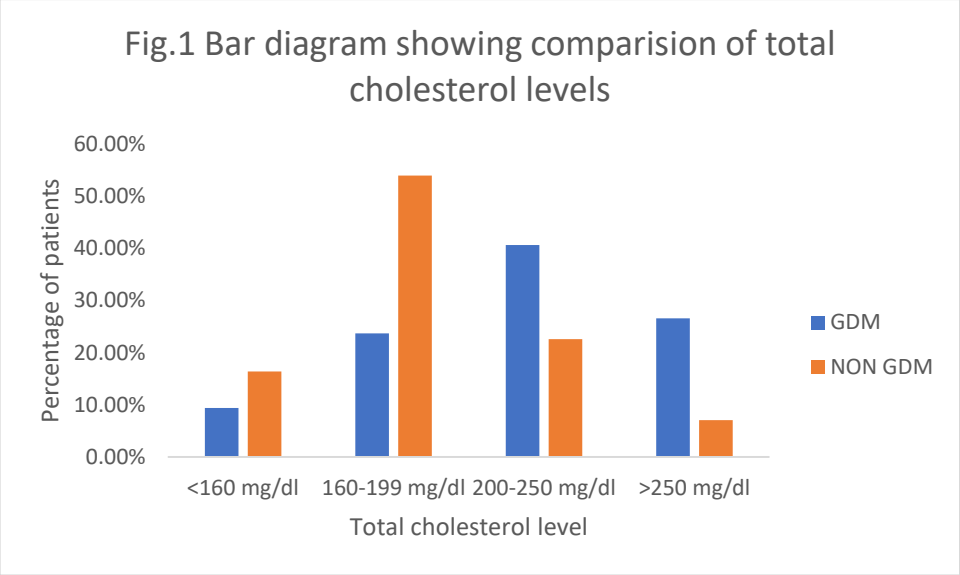
Table 1. Distribution of cholesterol, triglyceride and HDL in total population

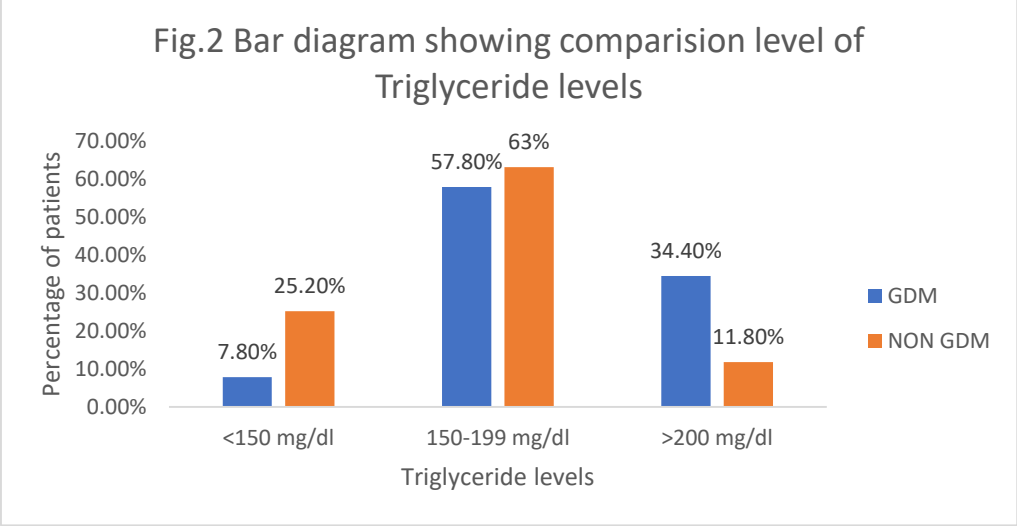
Cholesterol (mg/dl)	**Number (n=936)**
<160	149(15.9%)
160-199	485(51.8%)
200-249	223(23.8%)
>250	79(8.4%)
Triglyceride (mg/dl)	
<150	225(24.0%)
150-199	586(62.6%)
>200	125(13.4%)
High density lipid (mg/dl)	
<40	63(6.7%)
40-59	822(87.8%)
>60	51(5.4%)

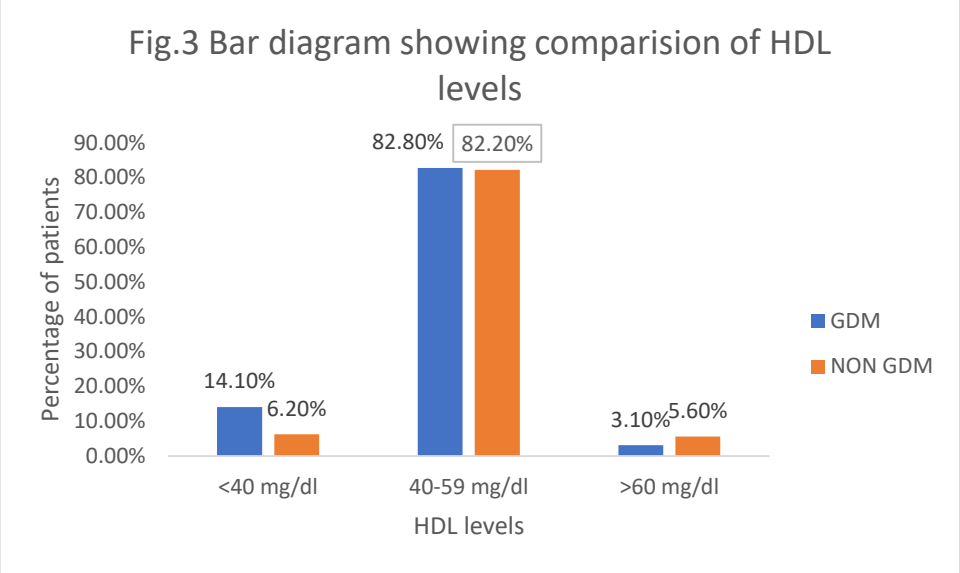
Out of total 936 patients 872 patients had normal GTT whereas 64 patients had abnormal GTT and were diagnose with GDM. The mean age of GDM patients was 27.1±3.9 years and non GDM patients was 24.7±3.5 years. The mean cholesterol levels in GDM and non GDM were 221.9$\pm$43.6 mg/dl and 192.9$\pm$34.5 mg/dl respectively. The mean triglyceride levels in GDM and non GDM were 187.8$\pm$33.9 mg/dl and 169.7$\pm$47.3 mg/dl respectively. The difference in cholesterol and triglyceride in patients with and without GDM was statistically significant with p value <0.001, whereas difference in HDL was not significant between two groups. Chi square test was used to calculate p value in table 2

Table 2. Distribution of cholesterol, triglyceride and HDL in GDM and non-GDM group

Cholesterol (mg/dl)	GDM n=64(%)	Non-GDM n=872(%)	p value
<160	6(9.4)	143(16.4)	**<0.001**
160-199	15(23.7)	470(53.9)	
200-249	26(40.6)	197(22.6)	
>250	17(26.6)	62(7.1)	
Triglyceride (mg/dl)			
<150	5(7.8)	220(25.2)	**<0.001**
150-199	37(57.8)	549(63)	
>200	22(34.4)	103(11.8)	
HDL (mg/dl)			
<40	9(14.1)	54(6.2)	0.08
40-59	53(82.8)	769(82.2)	
>60	2(3.1)	49(5.6)	







DISCUSSION

This study spanning one and half years was conducted on 936 pregnant women recruited at or before 28 weeks. 32.2% of total patients had high total cholesterol levels but 100% pregnant patients had high triglyceride levels as per NCEP ATPIII guidelines(7). The mean value of serum cholesterol was 194.89 ± 35.96 mg/dl. The mean value of triglyceride in the total population was 170.96±46.69 mg/dl. These levels are comparable with previous studies(8-10).

In present study, the levels of serum cholesterol and triglyceride were significantly ($p<0.001$) higher in patients of GDM, as compared to non GDM patients, whereas the difference in HDL levels between two groups was not significantly different ($p=0.08$). In a recent large retrospective cohort study from China, the GDM group showed higher TG concentrations and lower HDL-C concentrations throughout pregnancy. However, there were no significant differences in TC and LDL concentrations, between the GDM and non GDM group(11). In another recently published small study from Bangladesh, there were no significant difference in lipid levels between GDM and non GDM(12).

It is well known that during pregnancy, a series of profound metabolic adaptations occur to favor and ensure fetal development and maternal survival. As a result, maternal plasma triglyceride (TG) concentrations rise significantly, 2 to 4fold, in uncomplicated late gestation and revert to pre-pregnancy levels after delivery(13, 14). Maternal accumulation of fat depots and hyperlipidemia are the two principal changes in lipid metabolism that occur during pregnancy(15). Estrogen seems to be responsible for most of the alterations in lipoprotein metabolism during pregnancy, but its actions are complemented and opposed by the other pregnancy hormones and in late pregnancy by increasing insulin resistance. Estrogens can increase the concentration of plasma triglyceride by stimulating hepatic production of the triglyceride-rich very low density lipoproteins (VLDL) and by inhibition of hepatic and adipose tissue lipoprotein lipases(16). The role of progesterone in pregnancy associated hyperlipidemia is questionable. Effect of progesterone is to favor storage of depot fat in adipose and breast tissue and to partially reduce the hypertriglyceridemic action of estrogens(17). In late pregnancy rising concentrations of prolactin inhibit adipose tissue lipoprotein lipase activity resulting in a rise in the concentration of plasma triglyceride. HPL has lipolytic activity which may increase substrate supply of free fatty acids for the increased maternal hepatic VLDL production. The hypertriglyceridemia in late pregnancy may be further enhanced by hyperinsulinemia due to insulin resistance which is known to be associated with higher concentrations of triglyceride. During pregnancy, women with GDM have higher serum triglycerides concentrations but lower LDL levels than do normal pregnant women(18) however we have not compared LDL levels in present study.

There is scarcity of studies in literature comparing lipid levels in women with and without gestational diabetes. Although many studies suggest that women with GDM have increased levels of triglycerides, LDL-C and total cholesterol and lower levels of HDL-C, these findings are generally inconsistent. Among these outcomes, TGs was the most significant, with most of the included studies reporting higher TG levels in women with GDM. Our study shows that triglycerides are significantly elevated among GDM women compared with women without GDM. These findings supports biological likelihood linking hyperglycemia and dyslipidemia. Hypertriglyceridemia may underlie the insulin resistance due to its adverse effect on insulin sensitivity and beta cell function(19).

Hyperglycemia and dyslipidemia, as a result can cause endothelial dysfunction of the fetoplacental vasculature and promote the development of fetal aortic atherosclerosis(20). Our finding of consistent elevations in triglyceride levels pregnancy in women with GDM compared with non GDM is important as hypertriglyceridemia is thought to be one of the key drivers of fetal macrosomia(21). It is unclear as to whether hyperlipidemia and hypertriglyceridemia occur

exclusively later in pregnancy after the manifestation of GDM or if the dyslipidemia exists before the manifestation of insulin resistance. Various meta-analysis studies have established that triglycerides are elevated early in pregnancy with the greatest difference in levels between women with and without GDM occurring during the second trimester when GDM is traditionally diagnosed(4, 5).

CONCLUSION

Pregnancy leads to marked changes in the lipid profile. TGs are most significantly elevated in all pregnant patients while one third patients had raised TC. Patients with GDM had significantly higher TGs and TC levels whereas HDL levels were comparable in both groups.

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