Original Article

Fasting Lipid Profile in Pregnant Patients as a Predictor of Gestational Diabetes Mellitus

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ABSTRACT

Objective: To predict the risk of developing gestational diabetes mellitus (GDM) in early pregnancy by comparing the fasting lipid profile in pregnant patients with or without gestational diabetes during the second trimester of pregnancy.

Methodology: It was a cross-sectional study that was conducted in the Department of Gynecology & Obstetrics, Sharif Medical City Hospital, Lahore for six months from January to June 2021. A total of 385 patients were enrolled in the study. Out of 385 patients, 210(54.5%) women were with gestational diabetes mellitus (group A) and 175(45.5%) were without GDM (group B). A fasting lipid profile was performed by taking blood samples of patients. All samples were assessed for levels of total cholesterol (TC), triglyceride (TG) concentrations, low-density lipoproteins (LDL), and high-density lipoproteins (HDL).

Results: The mean age of the patients was 27.5±4.2 (group A) and 26.7±4.2 years (group B), respectively. The body mass index (BMI) was 29.4±3.6 in group A versus 25±3.5 in group B. The mean lipid profile in group A versus group B was; TC (177.1±21.3 versus 136.5±29.6, p <0.001), TG (186.3±23.9 versus 131.1±30.4, p <0.001), LDL (140.3±19 versus 96.3±23.1, p <0.001), and HDL (40.9±4.6 versus 44.3±23.9, p=0.044).

Conclusion: Hyperlipidemia is associated with GDM and identifies the need to evaluate maternal lipid profile in women with gestational diabetes mellitus during the antenatal period.

Keywords: *Gestational diabetes. Cholesterol. Triglyceride.*

INTRODUCTION

Gestational diabetes mellitus is the most common medical disorder which affects 14% of pregnancies worldwide. An epidemiological transition towards sedentary lifestyle changes due to urbanization predisposes females not only to an increased prevalence of type 2 diabetes mellitus but also to GDM. Gestational diabetes mellitus is significantly prevalent in the South Asian region, however, in Pakistan, it mostly remains unnoticed. According to some studies conducted at small scale, the prevalence in Pakistan ranges from 3.3-8%.[1] Gestational diabetes mellitus is not only associated with adverse fetomaternal outcomes but also with long-term risk of type 2 diabetes mellitus, hyperlipidemia particularly obesity-associated GDM, cardiovascular disease (CVD) in the mother, and also diabetes mellitus and CVD in the child as well.[2] The major factors predisposing to this disorder include advanced maternal age, obesity, family history of diabetes, westernized diet, ethnicity, personal history of GDM, and diabetes mellitus. The major pathological dysfunction of this disorder is pancreatic β-cell disorder and or resistance to insulin which is directly or indirectly linked to predisposing factors as well.[2]

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Physiologically, in normal pregnancy insulin resistance and lipid metabolism is altered, beginning at 24 to 28 weeks of gestation and this progresses in all trimesters. The major change observed is in triglycerides and cholesterol levels. Maternal physiological hyper-cholesterolemia is the mother's adaptive response to meet the growing cholesterol demand of the fetus during pregnancy. Gestational diabetes mellitus is also associated with both maternal and fetal adverse outcomes. The rate of pregnancy-induced hypertension, cesarean delivery, and macrosomia is high in patients with GDM.[3]

Dyslipidemia is a medical disorder which is characterized by high levels of low-density lipoproteins and triglycerides and low levels of high-density lipoproteins.[4] Cholesterol and low-density lipoprotein have a positive correlation with other hormones like thyroid stimulating hormone.[5] Serum lipid levels have also shown some correlation with raised blood pressure, especially in nulliparous women. In these women, lipid levels were found to be raised in patients with preeclampsia and eclampsia. Neonatal body weight is also positively correlated with maternal triglycerides level. Both fetal lipids and fetal growth are well predicted by maternal lipids in pregnancies with controlled diabetes.[6]

The rationale of our study was to compare the fasting mean lipid profile levels in pregnant females during their second trimester of pregnancy presenting with or without gestational diabetes. In routine, the lipid profile of females with hypertensive disorders is checked and cured if found deranged. But in pregnant females with GDM, work on lipid profile is scarcely studied. There is not much local evidence available in this regard.

Furthermore, the literature review highlights the ambiguity in understanding the relationship between the lipid profile of females with or without GDM. So, this study was conducted to confirm whether the lipid profile was deranged with GDM in patients of Pakistan. This study will help in early screening of lipid profile of GDM patients for their early detection, prevention, and timely management to prevent a bad obstetrical outcom.

METHODOLOGY

It was a cross-sectional study conducted at Sharif Medical City Hospital (SMCH), Lahore in the Department of Gynaecology & Obstetrics for six months from January to June 2021. Ethical approval was taken from the ethical committee. The sampling technique was non-probability consecutive sampling. A sample size of 385 cases was calculated by the WHO sample size calculator.

All females in the Outpatient Department (OPD) of SMCH between 18-40 years of age with parity of <5 and 24 to 32 weeks of gestation were included in this study. Pregnant females with hypertension [blood pressure (BP) ≥140/90 mmHg], diabetes [glycosylated hemoglobin (HbA1c) >6.5], patients on anti-hyperglycemic medication, obese females (BMI >35 kg/m^2), and females on lipid-lowering drugs or using statins before conception (on medical record) were excluded. Informed consent was taken from all patients. The demographic profile i.e., name, maternal age, and gestational age were noted. An oral glucose tolerance test (75 g OGTT) was done to diagnose gestational diabetes. It was diagnosed on the basis of a fasting plasma glucose level ≥5.6 mmol/L or 2-hour plasma glucose level of ≥7.8 mmol/L.[7] A venous blood sample was obtained under aseptic measures for a fasting lipid profile. All samples were sent to the laboratory for assessment of fasting lipid profile. Levels of total cholesterol, triglyceride concentrations, low-density lipoproteins, and high-density lipoproteins were noted. All the information was noted on a proforma. Reference range for total cholesterol was <200 mg/dL, triglycerides <150 mg/dL, LDL <130 mg/dL, and HDL between 35-55 mg/dL.[8]

STATISTICAL ANALYSIS

Statistical Package for the Social Sciences (SPSS) version 21 was used for data analysis. Quantitative variables like levels of TC, TG, LDL, and HDL along with maternal age and gestational age were presented as means and standard deviations (SD). Frequency and percentages were calculated for patients with GDM. The mean TC, TG, LDL, and HDL of both groups were compared by using an independent t-test. A p-value ≤0.05 was considered as significant. Data was stratified on the basis of age, gestational age, BMI, and parity.

RESULTS

Out of these 385 patients, 210(54.5%) were with GDM (group A) and 175(45.5%) were without GDM (group B). The mean age of the subjects in group A was 27.5±4.2 years and 26.7±4.2 years in group B. The mean gestational age was 27.8±2.2 weeks in group A and 27.6±2.1 weeks in group B, with a mean BMI of 29.4±3.6 in group A and 25±3.5 in group B.

Table 1 shows that group A patients had significantly elevated levels of TC, TG, and LDL as compared to group B patients. However, HDL levels were found to be lower in group A as compared to group B.

Stratification was done with regard to age, gestational age, BMI, and parity for TC, TG, LDL, and HDL. In group A, TC, TG, and LDL levels were significantly high as compared to patients in group B, when the data was stratified on the basis of gestational age (24-28 weeks & 29-32 weeks), age of the enrolled patients (18-30 years & 31-40 years), BMI (BMI <25 kg/m^2 & BMI ≥25 kg/m^2), and parity of the patient (primigravida & multigravida). However, HDL levels were found to be lower in group A (Table 2).

Table 1: Comparison of Lipid Profile in Pregnant Patients with and without Gestational Diabetes Mellitus

Lipid Profile	Groups		t-value	p-value
	Group A with GDM (Mean±SD)	Group B without GDM (Mean±SD)		
Total Cholesterol (mg/dL)	177.1±21.3	136.5±29.6	15.572	<0.001*
Triglycerides (mg/dL)	186.3±23.9	131.1±30.4	19.882	<0.001*
Low-Density Lipoprotein (mg/dL)	140.3±19	96.3±23.1	20.457	<0.001*
High-Density Lipoprotein (mg/dL)	40.9±4.6	44.3±23.9	-2.019	0.044*

**Significant p-value*

Table 2: Stratification for Age, Gestational Age, BMI, and Parity with regard to TC, TG, LDL, and HDL

Variables			Groups	Mean±SD	p-value
Age (Years)	18-30	TC (mg/dL)	Group A	176.5±21	<0.001*
			Group B	135.1±28.8	
		TG (mg/dL)	Group A	185.3±24.1	<0.001*
			Group B	130.9±30.4	
		LDL (mg/dL)	Group A	142.5±19.1	<0.001*
			Group B	96±22.8	
		HDL (mg/dL)	Group A	41.1±4.5	0.067
			Group B	44.8±25.6	
	31-40	TC (mg/dL)	Group A	179.3±22.3	<0.001*
			Group B	146.7±33.7	
		TG (mg/dL)	Group A	190.3±22.9	<0.001*
			Group B	133±30.9	
		LDL (mg/dL)	Group A	131.8±16.1	<0.001*
			Group B	98.7±25.4	
		HDL (mg/dL)	Group A	40.4±4.9	0.472
			Group B	41.3±4	
Gestational Age (Weeks)	24-28	TC (mg/dL)	Group A	175.6±20.8	<0.001*
			Group B	137.6±30.2	
		TG (mg/dL)	Group A	184.9±23.4	<0.001*
			Group B	130.1±31.5	
		LDL (mg/dL)	Group A	142.1±18.1	<0.001*
			Group B	96.4±23.9	
		HDL (mg/dL)	Group A	41.2±4.9	0.101
			Group B	45.4±29.2	
	29-32	TC (mg/dL)	Group A	179.9±21.9	<0.001*
			Group B	134.4±28.6	
		TG (mg/dL)	Group A	189±24.7	<0.001*
			Group B	133.2±28.4	
		LDL (mg/dL)	Group A	136.9±20.1	<0.001*
			Group B	96.2±21.7	
		HDL (mg/dL)	Group A	40.4±4	0.013*
			Group B	42.2±4.3	
BMI (kg/m^2)	<25	TC (mg/dL)	Group A	170.8±22.8	<0.001*
			Group B	131.8±27.7	
		TG (mg/dL)	Group A	179.9±25.9	<0.001*
			Group B	127.8±27.3	
		LDL (mg/dL)	Group A	140.6±13.9	<0.001*
			Group B	95.7±21.7	
		HDL (mg/dL)	Group A	40.3±4.2	0.421
			Group B	45±30.5	
	≥25	TC (mg/dL)	Group A	178±20.9	<0.001*
			Group B	143.7±31.2	
		TG (mg/dL)	Group A	187.3±23.5	<0.001*
			Group B	136.2±34.1	
		LDL (mg/dL)	Group A	140.2±19.6	<0.001*
			Group B	97.3±25.1	
		HDL (mg/dL)	Group A	41.0±4.7	0.002*
			Group B	43.3±6.4	
Primigravida		TC (mg/dL)	Group A	178.2±19	<0.001*
			Group B	143.7±29.5	
		TG (mg/dL)	Group A	188.2±27.2	<0.001*
			Group B	131.9±30.1	
		LDL (mg/dL)	Group A	144.5±19.5	<0.001*
			Group B	98.5±22.6	
		HDL (mg/dL)	Group A	41.7±3.8	0.179
			Group B	42.8±3.8	
Multigravida		TC (mg/dL)	Group A	176.8±21.9	<0.001*
			Group B	134.4±29.5	
		TG (mg/dL)	Group A	185.8±23	<0.001*
			Group B	130.9±30.6	
		LDL (mg/dL)	Group A	139±18.7	<0.001*
			Group B	95.7±23.3	
		HDL (mg/dL)	Group A	40.7±4.8	0.061
			Group B	44.8±27.1	

**Significant p-value*

DISCUSSION

In pregnant patients, metabolic changes occur throughout the pregnancy. In the first and second trimesters of pregnancy, lipogenesis occurs which leads to fat deposition, and during the last part of pregnancy, lipolysis is increased which leads to a drop in maternal fat stores.[9]

Even though the cause and aetiology of GDM is not yet clear, it somehow has similar pathophysiology as of type 2 diabetes. Because of the failure of pancreatic β-cells, both GDM and type 2 diabetes exhibit insulin resistance and deficient insulin production. Hyperlipidemia is associated with pregnancy-related complications in mothers and babies of these mothers showed high risk of atherosclerosis.[10] Another study indicated that the risk of GDM & hyperlipidemia was positively associated with maternal central obesity.[11]

In a study by Zhai et al., the association of hyper-lipidemia & type 2 DM was observed. They concluded that glycemic control in type 2 diabetics was lower in patients with hyperlipidemia.[12]

Our study shows that in early pregnancy females with GDM have significantly elevated levels of TC, TG, and LDL, however, HDL levels were found to be lower as compared to women without GDM. After adjusting for potential confounders, we find that lean or obese women with higher TG concentrations are at an increased risk of developing GDM while lean women with high HDL were protected. Regarding total cholesterol and LDL levels, the results of our study are not consistent with Farsangi et al., who showed no change in the levels of TC and LDL in pregnant patients with GDM.[13]

Similar to our study, Asif et al. found that TC levels are higher in patients with GDM as compared to the controls.[14] Some case-control studies report an association between increased risk of GDM with higher TG concentration.[15] One of the South Asian studies also showed the altered selected lipid profile in patients with GDM. The study showed higher levels of triglycerides and lower levels of HDL in patients with GDM as compared to the control group.[16] However, Layton et al., exhibited no positive correlation between GDM and high lipid levels in pregnant patients.[17]

The association of metformin and insulin treatment on maternal serum lipid levels in patients with GDM was observed in another study. Their study showed that the levels of TG are higher in patients who were treated with metformin and insulin, and the increase was more in metformin-treated patients. More than 50% of patients were given metformin and the rise of total triglycerides was found to be one mmol/lit from the baseline value. The rise of 0.6 mmol/lit of total triglycerides from the baseline value was observed in patients who were given insulin.[18]

Closer investigations reveal that many reasons might have contributed to these conflicting results including but not limited to different study designs, the basis of sampling and final sample size, differences in population features, cofounders, and different diagnostic criteria for GDM. A recent study by Wang et al. found that the lipid profile was dramatically different between patients with gestational diabetes mellitus and the control group. They found that the maternal TG, TC, LDL concentration, and the ratio of TG/LDL have been increased progressively throughout the pregnancy, however, HDL concentration showed a slight decrease in the third trimester. The study did not find any significant difference between the concentration of TC and LDL in all three trimesters in the GDM group and the control group.[19]

A study in Iran observed a relationship between dyslipidemia, gestational diabetes mellitus, and other maternal and neonatal outcomes. A significant relationship was found between hyperlipidemia and gestational diabetes mellitus, preeclampsia, cholestasis of pregnancy, and macrosomia. According to this study, dyslipidemia increases the chances of gestational diabetes mellitus by 4.1 folds.[20] The relationship between dyslipidemia and gestational diabetes was also studied in another research which showed that a lower level of plasma HDL was the most current lipid disorder followed by a high level of plasma TG in patients with gestational diabetes. Plasma HDL levels were found to be significantly decreased in patients who used insulin for the control of blood sugar as compared to the patients who did not use insulin.[21]

CONCLUSION

Gestational diabetes mellitus is evidently associated with hyperlipidemia as evidenced by the significantly elevated total cholesterol, LDL, and triglyceride concentrations in pregnant patients with GDM. In early pregnancy, females with GDM have significantly elevated levels of TC, TG, and LDL. Therefore, fasting blood lipids should be considered in women during pregnancy for better antenatal care.

LIMITATIONS & RECOMMENDATIONS

This study was conducted at a single hospital therefore, the diversity of the population lacks. A multi-centered study having adequate diversity in population characteristics can give more comprehensive results.

It is recommended that a fasting lipid profile should be done in the first trimester as it can help predict the risk of developing GDM at an early pregnancy stage.

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