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Aberrations of Serum Lipid Profile in Type 2 Diabetes Mellitus Patients: A Case Control Study

Srikrishna Paul¹, Hrishikesh Mishra¹, Manish Kumar Sahu¹, Amit Thakur², Prashant Nigam^{1*}

¹Dept. of Biochemistry, Chhattisgarh Institute of Medical Sciences, Bilaspur

²Dept. of Medicine, Chhattisgarh Institute of Medical Sciences, Bilaspur

*Corresponding Author Address for correspondence: Associate Professor & Head, Dept. of Biochemistry, Chhattisgarh Institute of Medical Sciences, Bilaspur, C.G., Pin code: 495001, India, Email: nigam.prashant866@gmail.com

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Abstract

Background: Type 2 Diabetes mellitus is associated with significant morbidity and mortality. Aberrant serum triglyceride, LDL, HDL cholesterol levels may increase the risk for cardiovascular disease and stroke in these patients. **Aim:** Present study was aimed at finding correlation between the severity of diabetes mellitus represented by glycemic parameters and serum lipid profile i.e., serum triglyceride, total cholesterol, LDL, HDL and VLDL cholesterol. **Materials and Methods:** The study included randomly selected 100 newly diagnosed adult T2DM patients (age 52.14 ± 14.5 years) and 100 healthy individuals (age 51.12 ± 17.7 years) as cases and controls respectively. History taking and general examination of participants was done, followed by collection blood samples in clot activator and EDTA vacutainer tubes as required for fasting and postprandial blood glucose, lipid profile and HbA1c. Two tail independent t-test was done to compare the variables between cases and controls, considering P value <0.05 as statistically significant. **Results:** FBG, PPBG and HbA1c were found to be significantly higher in cases as compared to controls. Serum triglyceride, total cholesterol, LDL-C, VLDL-C were found to be significantly elevated, while HDL-C was found to be significantly decreased among the cases as compared to controls. Serum triglyceride and VLDL-C showed a significant positive correlation with HbA1c. **Conclusion:** Type 2 diabetes mellitus is associated with dyslipidemia which is positively correlated glycemic status. Thus, proper glycemic control and early detection and management of dyslipidemia may play a significant role in preventing cardiovascular morbidity and mortality in T2DM patients.

Key words: Type 2 diabetes mellitus, serum lipid profile, dyslipidemia, HbA1c

INTRODUCTION:

Diabetes mellitus is one of the most challenging health problems worldwide. The most prevalent type of diabetes is type 2 diabetes mellitus (T2DM) which is characterized by combination of resistance to insulin action and inadequate insulin secretion or both. ^[1] Prevalence of T2DM is rising on a global scale. India also has experienced an alarming rise in its prevalence during the past few years. It is estimated that in India 77 million adults have T2DM, more commonly in metropolitan areas than in rural areas. It is estimated that about 25 million adults in India are prediabetic. ^[2]

T2DM is associated with significant morbidity and mortality due to disease related complications including cardiovascular disease, stroke, peripheral vascular disease, nephropathy, neuropathy, retinopathy etc. High levels of insulin in response to insulin resistance in T2DM, can promote synthesis and storage of triglycerides in liver and adipose tissue. Further, metabolism of lipoproteins is affected which can lead to aberrant LDL, HDL cholesterol levels in these patients. Aberrant triglyceride, LDL, HDL cholesterol levels are considered as independent risk factors for cardiovascular disease and stroke. ^[3,4,5] Several studies have shown that adequate and sustained control of blood glucose levels, blood pressure and blood lipid levels can prevent or delay disease-related complications in T2DM patients. Thus, the present study was aimed at finding correlation between the severity of diabetes mellitus represented by glycemic parameters and risk of cardiovascular disease and stroke represented by serum lipid profile i.e., serum triglyceride, total cholesterol, LDL, HDL and VLDL cholesterol.

MATERIALS AND METHODS:

The study was conducted at OPD of CIMS Bilaspur, Chhattisgarh, India, in compliance with the declaration of Helsinki after due approval of Institutional Ethics Committee, vide Order No 251/C.I.M.S/ I.E.C/2022, Bilaspur, dated 20/12/2022. Participants were recruited after getting their informed consent. Sample size was calculated using Epi Info 1.4.3 (Fleiss with CC) considering two-sided confidence interval as 95, power as 90%, ratio of controls to cases as 1, hypothetical proportion of controls with exposure as 40, hypothetical proportion of cases with exposure as 62.5 and least extreme odds ratio to be detected as 2.5. The study included randomly selected 100 newly diagnosed adult T2DM patients (age 52.14 ± 14.5 years) and 100 healthy individuals (age 51.12 ± 17.7 years) as cases and controls respectively. T2DM patients were defined according to American Diabetes Association as having HbA1c $\geq 6.5\%$ or fasting blood glucose ≥ 126 mg/dl and insulin resistance by HOMA-IR values >1.9 . HOMA-IR is calculated by using the following formula:

$$\text{HOMA-IR} = \text{fasting glucose (mg/dl)} \times \text{fasting insulin (mIU/ml)} / 405.$$

The homeostasis model of insulin resistance (HOMA-IR) was developed by Matthews et al. (1985), and is widely used method for the estimation of insulin resistance. ^[6,7] Cases were further divided into three groups into good, moderate and poor glycemic control as HbA1c $< 8\%$, 8-10%,

>10% respectively. Individuals with acute/chronic complications of diabetes mellitus, pulmonary disease, thyroid disease, pregnancy, lactation and history of alcohol abuse were excluded from the study.

History taking and general examination of participants was done, followed by collection blood samples. Five ml of blood samples were collected in clot activator and EDTA vacutainer tubes as required after overnight fasting of 8 hours and 2 hours after having complete regular meal. Assessed glycemic parameters included fasting blood glucose (FBG), postprandial blood glucose (PPBG) and HbA1c. Similarly, serum lipid profile was assessed including fasting serum triglyceride, total cholesterol, high density lipoprotein- cholesterol (HDL- C), low density lipoprotein- cholesterol (LDL- C), and very low density lipoprotein- cholesterol (VLDL-C) levels. All laboratory parameters were estimated spectrophotometrically following manufacturer's guidelines on fully automated ILAB 650 clinical chemistry analyzer (Instrumentation Laboratory, USA).

Statistical analysis was done using Microsoft Excel 2019 and IBM SPSS v22.0. All descriptive parameters were reported as mean $\pm$ SD. Two tail independent t-test was done to compare the variables between cases and controls, considering P value less than 0.05 as statistically significant. Similarly, two tail Welch's t test was done to compare the serum lipid profile parameters among cases having good, moderate and poor glycemic control considering P value less than 0.05 as statistically significant. Correlation analysis was done to find inter-relationship between glycemic status and serum lipid profile of cases.

RESULTS:

Glycemic parameters including FBG, PPBG and HbA1c were found to be significantly higher in cases as compared to controls as shown in Table 1.

Table 1. Glycemic Parameters among Cases and Controls

Glycemic Parameters	Cases	Controls	P value
Fasting Blood glucose	159.15 $\pm$ 26.2	87.59 $\pm$ 11.5	<0.001
Post-prandial Blood glucose	228.87 $\pm$ 38.1	124.29 $\pm$ 8.4	<0.001
HbA1c	7.68 $\pm$ 0.9	4.71 $\pm$ 0.8	<0.001

Cases and controls were divided into seven subgroups based on their age by dividing them in groups each with a range of 10 years as shown in Table 2. Highest number of newly diagnosed T2DM patients was found in age group of 41-50 years followed by 51-60 years. Extreme age groups 21-30 years and >80 years had least number of cases. HbA1c considered as a benchmark of glycemic control, was assessed among all cases. A total of 76 cases showed good glycemic control (HbA1c <8%) across all the age groups. Similarly, 20 and 4 patients showed moderate and poor glycemic control respectively. Thus, majority of the cases across all the age groups showed good to moderate glycemic control. No significant difference was observed between male and females cases in glycemic parameters.

Table 2. Glycemic Parameters According to Age Interval Among Cases

S no.	Age interval (years)	Number of Controls	Cases			
			Number of Cases	Good Glycemic Control N (%)	Moderate Glycemic Control N (%)	Poor Glycemic Control N (%)
1.	21-30	15	5	5 (100)	0 (0)	0 (0)
2.	31-40	13	17	13 (76.47)	2 (11.76)	2 (11.76)
3.	41-50	25	27	21 (77.78)	6 (22.22)	0 (0)
4.	51-60	18	23	18 (78.26)	5 (21.74)	0 (0)
5.	61-70	14	17	12 (70.59)	4 (23.53)	1 (5.88)
6.	71-80	10	8	4 (50)	3 (37.5)	1 (12.5)
7.	80- 90	5	3	3 (100)	0 (0)	0 (0)
Total		100	100	76 (76)	20 (20)	4 (4)

Among serum lipid profile parameters, triglyceride, total cholesterol, LDL- C, VLDL- C were found to be significantly elevated ($p < 0.05$) among the cases as compared to controls. On the other hand, HDL- C was found to be significantly decreased ($p < 0.05$) among the cases as compared to controls as shown in Table 3.

Table 3. Comparison of the Lipid parameters among Cases and Controls

Lipid Parameters	Cases (Mean $\pm$ SD)	Controls (Mean $\pm$ SD)	P- Value
Total Cholesterol	214.55 $\pm$ 64.2	158.1 $\pm$ 22.7	< 0.001
Triglyceride	189.7 $\pm$ 76.4	109.63 $\pm$ 20.3	< 0.001
LDL- C	97.17 $\pm$ 23.2	45.33 $\pm$ 14.7	< 0.001
HDL-C	41.51 $\pm$ 11.1	47.6 $\pm$ 15.8	< 0.001
VLDL- C	37.96 $\pm$ 15.2	21.9 $\pm$ 4.1	< 0.001

Similarly, Serum lipid profile parameters were assessed by dividing cases according to gender and status of glycemic control. All the lipid parameters were found to be higher in female cases but the difference was found to be statistically significant in serum triglycerides and VLDL-C only as shown in Table 4. Serum triglyceride and VLDL- C showed a trend of increasing values from good to poor glycemic control as shown in table 5. But none of the serum lipid profile parameters showed statistically significant difference (<0.05) among good, moderate and poor glycemic control groups.

Table 4. Comparison of the Lipid parameters among males and females in Cases

Lipid Parameters	Male	Female	P Value
Total Cholesterol	200.54 $\pm$ 68.55	222.09 $\pm$ 60.99	0.11
Triglyceride	169.14 $\pm$ 77.85	200.88 $\pm$ 73.89	0.04
LDL- C	96.83 $\pm$ 25.73	97.35 $\pm$ 22.04	0.91
HDL-C	38.77 $\pm$ 12.90	42.98 $\pm$ 9.89	0.07
VLDL- C	33.82 $\pm$ 15.57	40.17 $\pm$ 14.78	0.04

Table 5. Mean $\pm$ SD of Lipid parameters according to degree of glycemic control

	Glycemic Control		
Lipid Parameters	Good	Moderate	Poor
Total Cholesterol	218.74 ± 63.3	200.1 ± 65.6	207.25 ± 82.6
Triglyceride	185.22 ± 78.1	197.2 ± 75.5	239.0 ± 54.9
LDL- C	97.14 ± 23.5	99.8 ± 23.3	84.5 ± 19.7
HDL-C	41.71 ± 11.6	39.65± 8.9	47.0± 12.90
VLDL- C	37.06 ± 15.6	39.44 ± 14.5	47.8 ± 10.9

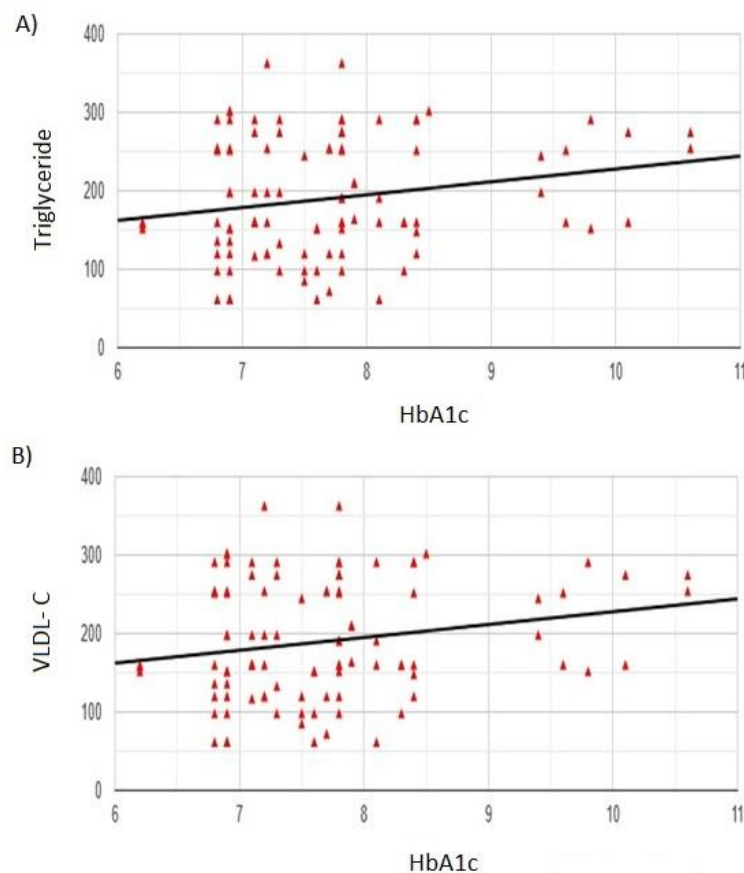
Further, among cases, serum triglyceride and VLDL showed a significant positive correlation with HbA1c ($r = 0.198$ and $p = 0.049$). Total cholesterol and HDL- C showed weak negative correlation while LDL-C showed no correlation with glycemic parameters as shown in Table 6.

Table 6. Correlation and significance of Glycemic and Lipid Parameters

		Fasting Blood glucose	Post Prandial Blood glucose	HbA1c
Total Cholesterol	Pearson Correlation	0.042	0.007	-0.152
	P value	0.675	0.941	0.131
Triglyceride	Pearson Correlation	0.005	0.161	0.198
	P value	0.957	0.110	0.049
LDL- C	Pearson Correlation	0.054	-0.108	0.000
	P value	0.595	0.286	1.000
HDL-C	Pearson Correlation	-0.031	0.043	-0.004
	P value	0.759	0.668	0.965
VLDL-C	Pearson Correlation	0.005	0.161	0.198

	P value	0.962	0.110	0.049
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Figure 1. Correlation Plot between A) Serum Triglyceride and HbA1c, B) Serum VLDL and HbA1c



DISCUSSION:

Glycemic parameters FBG, PPBG and HbA1c are known to be increased in diabetes mellitus and known to serve as essential biomarker for diagnosis and management. FBG itself has been reported to be modestly and nonlinearly associated with risk of cardiovascular disease even in nondiabetics (Sarwar N et al 2010).^[8] Another study has concluded that FBG is positively related to risk of stroke with non-linear dose-response relationship. Lowest incidence was reduced to minimum with FBG level of 70-100 mg/dL (Shi H et al 2021).^[9] Elevated PPBG can indicate inadequate glucose control and predict future complications. High PPBG levels are associated with an increased risk of cardiovascular diseases and other diabetes-related complications, such as

retinopathy and nephropathy. PPBG has been reported to have stronger association as compared to FBG with risk for cardiovascular disease (Cavalot F et al 2006).^[10] Similarly, HbA1c indicates the average blood glucose levels over the preceding 2-3 months, is used as a long-term indicator of glycemic control in diabetes mellitus patients. It is considered as a gold standard marker for diagnosing diabetes mellitus and monitoring the efficacy of treatment. American Diabetes Association recommends maintaining HbA1c levels below 7% for most adults with diabetes to minimize microvascular and macrovascular complications.^[11] Considering the integral association with diagnosis and pathogenesis of complications of T2DM, these markers were included in our study to differentiate cases and controls and correlate with serum lipid profile parameters.

Lipid abnormalities in patients with diabetes, often termed as diabetic dyslipidemia are common in people with T2DM and prediabetes. Several studies have reported occurrence of dyslipidemia characterized by high total cholesterol, high triglycerides, LDL- C and increased levels of small dense LDL particles among diabetes mellitus patients. LDL- C levels may be moderately increased or normal. In our study significant dyslipidemia was found in cases as compared to controls, that is consistent with previous reports. Total cholesterol, triglyceride, LDL- C, and VLDL-C were found to be significantly elevated among the cases as compared to controls. HDL- C was found to be significantly decreased among the cases as compared to controls. Interestingly, values of all serum lipid profile parameters were found to higher among female cases as compared to males as previously reported in a hospital-based study (Thekra Almaqati et al. 2022).^[12]

Although there was no significant difference between lipid profiles of diabetic patients having good, moderate and poor glycemic control; values of serum triglyceride and VLDL-C showed a significant positive correlation with HbA1c.

Similar findings have been previously reported by (Sushil Kumar et al 2022)^[13] where hyperglycemia-induced dyslipidemia, raised triglyceride and VLDL were the most common findings. Similarly combined lipid abnormalities were more commonly seen as compared to a single abnormality in the lipid profile. Furthermore, (Mithal et al 2014)^[14] reported a cross sectional study on prevalence of dyslipidemia in adult Indian diabetic patients among 5400 patients with T2DM which revealed that dyslipidemia control in Indian T2DM patients is very poor with almost half of them not reaching their LDL -C goal. So, dyslipidemia being one of the main risk

factors for cardiovascular disease in T2DM patients there is a need to treat dyslipidemia aggressively to reduce risk of future cardiovascular disease events.

CONCLUSION :

The dyslipidemia seen in type 2 diabetes mellitus is associated with high levels of triglycerides, LDL- C, VLDL- C and HDL-C. Serum triglyceride and VLDL-C have a significant positive correlation with HbA1c. Alteration in glycemic parameters and dyslipidemia and are have a positive association. Thus, proper glycemic control and early detection and management of dyslipidemia may prevent cardiovascular morbidity and mortality in T2DM patients.

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