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A Study on Lipid Profile in Type 2 Diabetes Mellitus and its Association with Glycemic Control at a Tertiary Care Hospital in Himachal Pradesh

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Abstract **Original Research Article**

Diabetes Mellitus (DM) denotes a group of metabolic disorders resulting from a multifaceted interaction of genetic and environmental factors that share the phenotype of hyperglycemia which when uncontrolled results in impaired lipid metabolism leading to an array of cardiovascular, cerebrovascular and other complication. International Diabetes Federation (IDF) estimates the global prevalence of diabetes to increase from 7.5% in 2019 to 8.0% in 2030 and 8.6% in 2045 with India ranking 2nd in top 10 countries with most number of people with diabetes contributing significantly to global disease burden. The present study was carried out with the aim of determining the increase in abnormal lipid profile among cases of diabetes compared to apparently healthy controls and to determine the presence or absence of association between abnormal blood glucose and dyslipidemia. The study comprised of 202 cases of type 2 diabetes mellitus (T2DM) and 202 apparently healthy controls all of whom underwent laboratory investigation using venous blood sampling to determine their serum glycated haemoglobin (HbA1c), Fasting blood sugar (FBS), Random blood sugar (RBS), total cholesterol (TC), triglycerides (TG), high density lipoprotein (HDL), low density lipoprotein (LDL), and very low density lipoprotein (VLDL). The prevalence of abnormal lipid profile was greater in cases compared to controls with a significant correlation between poor glycemic control and dyslipidemia. This finding clearly indicates that patients with diabetes have a greater prevalence of dyslipidemia which had adverse effects on end organs especially the heat and brain. Thus optimal glycemic control is essential to control lipid dysfunction in diabetics hence leading to decreased morbidity.

Keywords: Type 2 Diabetes Mellitus, Dyslipidemia, Glycated Haemoglobin, Fasting Blood Sugar (FBS), Random Blood Sugar (RBS), Total Cholesterol (TC), Triglycerides (TG), High Density Lipoprotein (HDL), Low Density Lipoprotein (LDL), And Very Low Density Lipoprotein (VLDL).

INTRODUCTION

Diabetes Mellitus (DM) is a term used to describe a group of metabolic disorders caused by a complex interaction of genetic and environmental factors [1]. The phenotype of hyperglycemia is caused by varying degrees of insulin resistance, impaired insulin secretion, decreased glucose utilisation, or increased glucose production. Secondary pathophysiological alterations in numerous organs, such as the eyes, kidneys, nerves, heart, blood vessels, and brain, are caused by the metabolic dysregulation associated with DM, posing a significant burden on the patient with DM and the health-care system [2].

Diabetes is a significant contributor to the worldwide illness burden. Since the earliest estimates by the International Diabetes Federation, its prevalence has nearly tripled. India is ranked second among the top ten countries with the highest number of diabetics [3]. According to the District Level Household and Facility Survey-4 (DLHS-4) conducted by the International Institute for Population Sciences (IIPS) as the nodal agency, designated by the Ministry of Health & Family Welfare, Government of India, the prevalence of diabetes mellitus (DM) was 7% in men and 9% in women aged 18 and above in Himachal Pradesh in 2012-2013 [4].

Chronic problems are more likely when hyperglycemia lasts longer, and they usually appear in the second decade of hyperglycemia [5]. In diabetes mellitus, cardiovascular disease (CVD) is the leading cause of morbidity and mortality [6]. In the diabetic population, each 1 percent increase in absolute glycated haemoglobin (HbA1c) levels increases the predicted risk of CVD by 18% [7]. Furthermore, it has been claimed that lowering HbA1c levels by 0.2 percent can

reduce mortality by 10% [8]. The level of HbA1c is used to assess diabetes patients' glycemic management over the past two to three months. In order to avoid diabetes complications, glycemic management with a lower HbA1c level is critical [9].

The patient's glycemic control has a substantial impact on serum lipid levels, and dyslipidemia is commonly seen in persons with diabetes who have poor glycemic control [10]. Dyslipidemia is a condition of lipoprotein metabolism that includes lipoprotein overproduction or deficiency, and it is defined as an important component of the metabolic syndrome in type 2 diabetes mellitus. Hypertriglyceridemia and low levels of high-density lipoprotein (HDL) cholesterol are the most obvious changes, but there are also abnormalities in the structure of lipoprotein particles [11].

The tiny, dense form of low-density lipoprotein (LDL) cholesterol is the most common type among diabetics. Because small LDL particles can more easily enter and create stronger bonds to the artery wall, creating atherosclerotic plaque and promoting atherosclerosis, they are more atherogenic than large LDL particles [12]. Diabetic patients with high HbA1c levels and dyslipidemia are regarded to be at a very high risk for cardiovascular disease [13]. As a result, the goal of this study was to examine the lipid profile in the blood of patients with type 2 diabetes and its relationship to HbA1c levels. There have been very few studies in Himachal Pradesh to study the impact of lipid dysfunction contributing to morbidity associated with diabetes. Hence this study was carried out at a tertiary care centre in Himachal Pradesh as most of the people suffering from diabetes in the aforementioned region visit this hospital.

MATERIAL AND METHODS

The present study was undertaken in the Department of Medicine in collaboration with the Department of Biochemistry at Maharishi Markandeshwar Medical College and Hospital, Kumarhatti, Solan. The study design was Analytical, Observational, Retrospective, Case-control. It included patients visiting outpatient department and those admitted to the hospital suffering from T2DM (both already known cases and newly diagnosed cases) and controls not suffering from Diabetes Mellitus. The sample size comprised of 202 cases and 202 controls.

A standardized interview was conducted on all cases and controls to gather demographic variables and possible risk factors. Documentation of sociodemographic details (age, sex, height, weight, bmi), duration of diabetes, level of education, smoking status, history of alcohol abuse family history of T2DM or dementia, cardiovascular history, medication history was done using a pretested pro forma. All cases and controls were explained the procedure and objectives of the study in detail following which an informed consent was obtained.

Laboratory testing was done to obtain the subjects' Fasting/Random Blood Sugar, Hemoglobin A1c and Lipid Profile. In addition to these all the tests required for patient care including but not limited to complete blood count, liver function tests, renal function tests, thyroid profile, x-ray chest , electrocardiogram were done. The blood samples were collected by standard collection technique using all aseptic precautions. The sample was stored and sent to laboratory for investigations in accordance with standard guidelines. The assessment of HbA1c was done using Siemens Dimension RxL Max Fully Automated Analyser. The evaluation was done with human whole blood samples sent to laboratory for investigations as soon as possible. Glycosylated Hemoglobin was measured using Ion Exchange Resin method for invitro diagnosis.

Descriptive statistics was performed on all the relevant demographic and clinical parameters. Pearson's correlation coefficient method was used for testing of numeric variables with each other. Differences in means of continuous variables between cases and controls were tested by student's t test. Permission for conducting the study was obtained from institutional ethical committee.

RESULTS

Total Number of Cases of T2DM included in the present study was 202; out of which 97 were males and 105 were females. The age of patients ranged from 30 to 65 years with a mean of 52.4 ± 8.3 years. The height of patients ranged from 148 to 182 centimetres with a mean of 163.2 ± 7.4 centimetres. The weight of patients ranged from 47.8 to 93.5 kilograms with a mean of 69.7 ± 9.3 kilograms. According to Revised Consensus Body Mass Indices Guidelines for India, none were underweight (BMI < 18.5 kg/m^2), 30 had normal or lean BMI (18.5-22.9 kg/m^2), 45 were overweight (23.0-24.9 kg/m^2) and 127 were obese (>=25 kg/m^2). Out of 202 cases, 22 patients had history of consumption of alcoholic beverages and 31 patients had history of smoking. 39 patients had a history of diabetes mellitus in family. Duration of Diabetes in cases was 7.4 ± 3.8 years. HbA1c in cases was 9.4 ± 2.2 %. FBS in cases had a mean of 206.6 ± 88.4 mg/dl. RBS in cases had a mean of 314.1 ± 112.4 mg/dl. Total Cholesterol in cases had a mean of 190.9 ± 56.9 mg/dl. Triglycerides in cases had a mean of 180.9 ± 145.5 mg/dl. HDL in cases had a mean of 39.7 ± 14.1 mg/dl. LDL in cases had a mean of 134.2 ± 42.9 mg/dl. VLDL in cases had a mean of 35.2 ± 24.6 mg/dl.

Descriptive Statistics of Cases

	Mean	Std. Deviation	Minimum	Maximum
AGE	52.4	8.3	30	65
HEIGHT	163.2	7.4	148	182
WEIGHT	69.7	9.3	47.8	93.5
BMI	26.2	3.1	19.2	36.5
DURATION OF DM	7.4	3.8	1	20
HbA1c	9.4	2.2	5.8	15
FBS	206.6	88.4	57	524
RBS	314.1	112.4	122	723
TOTAL CHOLESTEROL	190.9	56.9	118	405
TRIGLYCERIDES	180.9	145.5	49	1538
HDL	39.7	14.1	11	79
LDL	134.2	42.9	84	317
VLDL	35.2	24.6	8	307

Pearson's correlation test was performed to study the significance of correlation of HbA1c levels with total cholesterol, triglycerides, HDL, LDL, and VLDL Significant correlation was observed between HbA1c and total cholesterol as well as HbA1c and LDL.

		Total Cholesterol	Triglycerides	HDL	LDL	VLDL
HbA1c	Pearson's r	0.181	0.107	-0.052	0.151	0.082
	p-value	0.01	0.129	0.462	0.032	0.246

Total Number of Controls was 202 out of which 111 were males and 91 were females. The age of controls ranged from 30 to 65 years with a mean of 51.4 ± 8.2 years. The height of controls ranged from 150 to 176 centimetres with a mean of 162.4 ± 7.2 centimetres. The weight of controls ranged from 51.4 to 86.4 kilograms with a mean of 64.5 ± 7.4 kilograms. According to Revised Consensus Body Mass Indices Guidelines for India, none were underweight (BMI < 18.5 kg/m^2), 41 had normal or lean BMI (18.5-22.9 kg/m^2), 99 were overweight (23.0-24.9 kg/m^2) and 62 were obese (>=25 kg/m^2). Out of 202 controls, 34 had history of consumption of alcoholic beverages and 32 had history of smoking. 21 controls had a history of diabetes mellitus in family. HbA1c in controls was 5.5 ± 0.4 %. FBS in controls was 90.6 ± 8.6 mg/dl. RBS in controls was 117.1 ± 7.7 mg/dl. Total Cholesterol in controls was 166.2 ± 32.6 mg/dl. Triglycerides in controls was 132.2 ± 38.3 mg/dl. HDL in controls was 46.7 ± 12.5 mg/dl. LDL in controls was 148.8 ± 32.3 mg/dl. VLDL in controls was 25.8 ± 9.8 mg/dl.

Descriptive Statistics of Controls

	Mean	Std. Deviation	Minimum	Maximum
AGE	51.4	8.2	30	65
HEIGHT	162.4	7.2	150	176
WEIGHT	64.5	7.4	51.4	86.4
BMI	24.4	1.9	20.1	31.3
HbA1c	5.5	0.4	4.1	6.2
FBS	90.6	8.6	2	105
RBS	117.1	7.7	101	135
TOTAL CHOLESTEROL	166.2	32.6	18	284
TRIGLYCERIDES	132.2	38.3	65	286
HDL	46.7	12.5	25	68
LDL	148.8	32.3	81	206
VLDL	25.8	9.8	10	57

Independent Student's t test was performed to analyse the statistical significance of the difference in mean values of continuous variables between the case group and control group. There was significant difference in the values of weight, BMI, HbA1c, FBS, RBS, total cholesterol, triglycerides, HDL, LDL, and VLDL between cases and controls.

Independent t test

	T	Df	P	Mean Difference	SE Difference
AGE	-1.233	402	0.218	-1.015	0.823
HEIGHT	-1.138	402	0.256	-0.827	0.726
WEIGHT	-6.203	402	< 0.001	-5.201	0.839
BMI	-6.935	402	< 0.001	-1.741	0.251
HbA1c	-24.384	402	< 0.001	-3.888	0.159
FBS	-18.549	402	< 0.001	-115.96	6.252
RBS	-24.85	402	< 0.001	-197.069	7.93
TOTAL CHOLESTEROL	-5.361	402	< 0.001	-24.738	4.614
TRIGLYCERIDES	-4.594	402	< 0.001	-48.624	10.584
HDL	5.247	402	< 0.001	6.96	1.327
LDL	3.854	402	< 0.001	14.564	3.779
VLDL	-5.051	402	< 0.001	-9.411	1.863

DISCUSSION

Diabetes is a global concern, with rates of incidence rising quickly in both developing and developed countries. Hemoglobin A1c is not only a good indication of long-term glycemic management, but it also has a good correlation with the risk of long-term diabetic complications. In people with type 2 diabetes, cardiovascular disease is the leading cause of death. It all starts with atherosclerosis, a condition in which atherogenic plaque builds up inside arteries. Dyslipidemia is strongly linked to atherosclerosis in clinical studies, and up to 97 percent of diabetic individuals have dyslipidemia [14]. The severity of dyslipidemia increases in patients with a higher HbA1c number, according to Khan and colleagues [15]. The goal of this study was to investigate the glycemic status of patients with type 2 diabetes and its relationship to serum lipid markers.

In their investigation, Rashid and Haider discovered that in patients with good glycemic control, serum levels of TC, TAG, and LDLcholesterol were much lower, while HDL-cholesterol was significantly higher [16]. All lipid fractions were disturbed in patients with uncontrolled type 2 diabetes mellitus in a similar retrospective cohort investigation [17]. Aboola-Abu from Nigeria came up with similar findings, emphasising the importance of effective glycemic management and dyslipidemia control in delaying atherosclerosis and preventing coronary heart disease [18]. In a comparable study by Al-Alawi, serum HDL-cholesterol concentrations were greater in female patients than in male patients [19].

Samantha and colleagues discovered that male patients were slightly older than female patients in their study. Male patients had greater glucose, TC, TAG, LDL-cholesterol, and HDL-cholesterol concentrations in their blood, but there was no statistically significant difference [20]. Because estrogens affect lipid metabolism, women of younger ages have lower serum TC levels than men. Furthermore, women are more conscious than men, and they may devote more time and effort to maintaining a healthy lifestyle and preventing sickness. According to studies, women develop cardiovascular disease 7–10 years later than males [21].

The size of LDL-cholesterol particles, rather than the quantitative calculation of blood levels, is crucial in determining the risk of developing vascular problems in type 2 diabetes mellitus. The TAG/HDL-cholesterol ratio, which is a reliable, indirect, and practicable marker of LDL-cholesterol particle size, can be used to quantify LDL-cholesterol particle size [22]. Even if blood LDL-cholesterol levels are low, greater TAG/HDL-cholesterol ratios have been linked to an increased risk of cardiovascular events [23]. Previous research has shown that glycemic management has a significant impact on serum lipid profile levels and atherosclerosis in diabetic patients [24]. In these patients, early detection of dyslipidemia can be employed as a preventive measure against the development of CVD.

The results of our study were similar to other studies showing increased lipid dysfunction in individuals with type 2 diabetes compared to apparently healthy controls and a significant association was found between glycemic control and severity of lipid dysfunction. This warrants optimized glycemic targets to prevent dyslipidemia and hence decrease the resultant complications and morbidity linked to dyslipidemia in diabetes.

CONCLUSION

The present study showed greater lipid dysfunction in diabetics than non diabetics and statistically significant association between HbA1c and lipid profile, thus suggesting that, in addition to being a glycemic management metric, HbA1c is linked with dyslipidemia in patients with type 2 diabetes mellitus. Improving glycemic management may improve the serum lipid profile, lowering the risk of cardiovascular events in this group of patients. The magnitude of dyslipidaemia in type 2 diabetes mellitus patients is highlighted in this study. Diabetics are more likely to have dyslipidaemia, and those with poorly controlled

diabetes are more likely to have it. As a result, lipid profiles should be performed annually in all diabetic patients, and all patients should be adequately treated with drugs, dietary, and lifestyle changes to achieve target values of HbA1C < 7, as well as target values of TC < 200 mg/dl, TG < 150 mg/dl, LDL-C < 100 mg/dl, and HDL-C > 40 mg/dl in males and > 50 mg/dl in females.

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