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Association of HbA1c with serum lipid profile in patients withType 2 Diabetes Mellitus: A Comparative cross-sectional Study

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Abstract
Background*: Diabetes mellitus (DM) is considered to be one of the most pervasive non-communicable disease. Diabetic patients with accompanied dyslipidaemia are soft targets of cardiovascular deaths. Glycated haemoglobin (HbA1c) which is chemically linked to sugar and it is considered a gold-standard measure of chronic glycaemia in diabetic patients. Changes in lipid profile is also well related with severity of DM as adjudged by HbA1c.*
Aims and objectives: *To investigate the association of serum lipids with Glycated Haemoglobin in type 2DM patients.*
Materials and Methods: *A cross-sectional study was conducted among the patients with a history of type 2 Diabetes mellitus for the past 10 years who were attending diabetic clinic at MES Medical College and hospital, Perinthalmanna, Malappuram district, Kerala. Anthropometric measures, blood pressure, fasting serum blood glucose (FBPS), postprandial blood glucose (PPBS), HbA1c, fasting serum lipids (total cholesterol, T-Chol triglycerides, TG, low density lipoprotein (LDL-C) and high-density lipoprotein cholesterol (HDL-C) were registered for both cases and controls.*
Results: *FBS, PPBS, HbA1C were significantly high in case group. LDL, CHOL, TG were high in case as compared to control group, HDL is significantly low compared to control group. HbA1C /LDL, HbA1C /HDL, HbA1C /CHOL statistically strongly significant results in patients when compared to controls. HbA1c is significantly associated with lipid profile of diabetic patients.*
Conclusion*: Type 2DM patients are more prone to dyslipidaemia. Hence HbA1c can be considered as an indirect predictor for dyslipidaemia in addition to as a biomarker for glycaemic control*
Key words*: Association, HbA1c, lipid profile, Type2 DM*

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I. Introduction

Diabetes mellitus (DM) is manifested as a heterogeneous group of metabolic disorders. It is characterized by high blood sugar over a period of long time with interruptions of carbohydrate, fat and protein metabolism due to either being short in insulin discharge or lessened sensitivity of tissues to insulin.[1]Across the globe, DM is considered to be one of the most pervasive non-communicable disease. The numbers of diabetic victims have mounted worldwide and its extensiveness has been escalating more rapidly in middle and low-income nations.[2]Miserably, our nation leads the globe with the maximum numbers of diabetic sufferers and is often referred to as the diabetes capital of the world.[3]

Long-term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels are the sequale of chronic hyperglycaemia. Lipid abnormalities in patients with diabetesare often phrased as "diabetic dyslipidaemia" and are typically characterized by high total cholesterol (T-Chol), high triglycerides (TG), low high density lipoprotein cholesterol (HDL-C) and increased levels of small dense LDL particles. Low density lipoprotein cholesterol (LDL-C) levels may be moderately increased or normal.[1]

Diabetic patients with accompanied (but often unnoticed) dyslipidaemia are soft targets of cardiovascular deaths. Patients with type 2DM often exhibit an atherogenic lipid profile, which greatly increases their risk of CVD compared with people without diabetes. Around 50% of people with diabetes die of cardiovascular disease (primarily heart disease and stroke).[4]Diabetes (type 2DM) and related cardiovascular complications are major public health challenges worldwide. Individuals with type 2DM have two- to four-fold

increased risk of coronary artery disease (CAD), the leading cause of death among people with type2 DM.[5]Dyslipidemia and hypertension are major modifiable risk factors for type 2DM and related CAD, which account for more than 87% of disability in low and middle-income countries.

HbA1C

Glycated haemoglobin (HbA1C) is a form of haemoglobin which is chemically connected to a sugar and it is considered a gold-standard measure of chronic glycaemia in diabetic patients. It was studied that HbA1c was a better CHD predictor than fasting or 2-h glucose**.** HbA1c was strongly associated with atherosclerosis as measured by carotid IMT (intima-media thickness**)**. The ADA recommends measurement of HbA1c in patients with both type 1 and 2 diabetes, first to document the degree of glycaemic control, then as part of continuing care**.** Changes in lipid profile is also well related with severity of DM as adjudged by HbA1c.[6]Lipid abnormalities are common in people with Type 2 DM and prediabetes but the pattern of the different lipids may vary between ethnic groups, economic levels, and access to health care. Hence, this study was undertaken to investigate the association of serum lipids with glycated Haemoglobin in type 2DM patients.

II. Materials And Methods

Data were obtained from the subjects with history of type 2 Diabetes mellitus for the past 10 years (including male and female) who were attending diabetic clinic at MES Medical College and hospital, Perinthalmanna, Malappuram district, Kerala. A patient based cross-sectional study was conducted from December 2020 to May 2021. Patients including both individuals who were willing to participate with an age limit of 30-55, without any serious illness such as liver diseases, kidney diseases, endocrine diseases and malignancy were included for this study. All the subjects were matched according to the age and sex. Healthy subjects with an age limit of 30-55 without any clinical evidence of major diseases based on the baseline investigations were selected as controls. Written informed consent were obtained from each subject. Anthropometric measurements like, blood pressure, fasting serum blood glucose (FBPS), postprandial blood glucose (PPBS), HbA1c, fasting serum lipids (total cholesterol, T-Chol triglycerides, TG, low density lipoprotein (LDL-C) and high-density lipoprotein cholesterol (HDL-C) were registered.

Sampling Procedure

To determine the required sample size

$$n = \frac{r+1}{r} \frac{SD^2 (Z\beta + Z\alpha/2)^2}{d^2}$$

SD – Taken from previous studies, d = Expected mean difference between case and control

r = ratio of case and control, Z (α/2) =1.96 (5 % alpha error), Zβ = 0.84 (20% beta error)

SD – 0.65, d = 0.29, r = 2, Z (α/2) =1.96 (5 % alpha error),Zβ = 0.84 (20% beta error

Sample Collection:

Anthropometric measurements – Age, Sex, Body Mass Index (BMI), Waist Hip ratio (WHR) and blood pressure were registered. 5ml of venous blood with overnight fasting were collected in the next morning (before breakfast) for blood sugar estimation and serum lipid profile. Fasting blood sample for serum separation was collected in a clot activator tube under aseptic conditions and serum was separated. Fasting blood glucose, and Lipid Profile, were estimated using J &J Vitros 5.1FS autoanalyzer and HbA1c using whole blood were analyzed using – Immunoturbidimetric method.

Ethical Approval

The protocol was approved by Ethical Review Committee of MES Medical College on 10 October 2019 with IEC No.IEC/MES/09/2019). Research participation, confidentiality, and consent were followed as per Helsinki declaration, with local adaptation to allow both verbal and written instructions.

Statistical Analysis:

Data were examined by using the Statistical Package of Social Sciences (SPSS-IBM) version 22.0. Descriptive statistics were computed for the variables. Unpaired t test was used to establish the association between variables 'P' value was less than 0.05 was used to indicate statistical significance.

III. Results

Demographic details of the cases and controls were shown in Table 1. Statistically significant difference was obtained for the anthropometric measurements such as systolic, diastolic blood pressure, BMI and WHR among two groups (P <0.05). Variations in FBS, PPBS & HbA1c levels among cases and controls

were depicted in Table 2.There is increase in all three parameters in cases compared to controls which wasstatistically significant ($p<0.05$).

Table 1: Demographic details of cases and controls

Variables	Cases	Controls	P value
Age	48.66±6.57	47.27 ± 2.42	0.06
Males	45	55	0.183
Females	45	35	
Body Mass Index	24.99 ±4.54	23.81±2.675	<0.05*
Waste Hip Ratio	0.91±0.002	0.89±0.005	<0.05*
SBP	128± 16.5	113.11± 8.02	<0.05*
DBP	82.7± 8.8	73.66 ± 6.94	<0.05*

***Denotes statistical significance**

Table 2: Distribution of diabetic parameters among cases and controls

Diabetic Parameters	Cases	Controls	P value
FBS	166.9±51.9	85.32 ±8.4	<0.05*
PPBS	216.25±69.1	114.34±12.33	<0.05*
HbA1C	7.91±2.14	5.13± 0.244	<0.05*

***Denotes statistical significance**

Table 3 described the results of lipid profile levels of cases and control group. Statistically significant increase in TG, LDL, VLDL & cholesterol levels were seen in cases compared to controls, whereas HDL showed a statistical decrease among cases. The association between HDL, LDL, and Chol with HbA1c was depicted in Table 4. HbA1c / HDL, HbA1c /LDL and HbA1c / Chol ratios were significantly higher in cases when compared to controls.

Table 3: Distribution of lipid parameters among cases and controls

Lipid Parameters	Cases	Controls	P value
Total Cholesterol	200.73±28.09	172.4±19	<0.05*
Triglyceride	141.4±47.6	116.34 ±34.3	<0.05*
HDL	36.98±4.51	39.34 ± 2.9	<0.05*
LDL	129.2±27.3	109.6 ±19.6	<0.05*
VLDL	27.7±8.04	23.34 ±6.68	<0.05*

***Denotes statistical significance**

Table 4: Association of HbA1C with T-Chol, HDL,LDL among cases and control

Parameters	Cases	Controls	P value
HbA1c/CHOL	0.04±0.13	0.03±0.003	<0.05*
HbA1c/HDL	0.21±.06	0.13±0.01	<0.05*
HbA1c/LDL	0.06±0.02	0.04±0.007	<0.05*

***Denotes statistical significance**

IV. Discussion

Patients with diabetes have been evidently recognized with arising complications due to the continuous hyperglycaemia through numerous mechanisms like dyslipidaemia, platelet activation, and altered endothelial metabolism.[7, 8] Both lipid profile and diabetes have been shown to be the vital forecasters for metabolic disorders including dyslipidaemia, hypertension and cardiovascular ailments.[9]Blood lipid levels are modifiable risk factors for coronary heart diseases (CHDs). Being hydrophobic in nature, cholesterol, cholesterol esters, triglycerides and phospholipids are transported to the other tissues in the form of lipoproteins. Major classes of lipoproteins are chylomicrons (CM), LDL and HDL, named by the site of their assembly and type of lipid and apoprotein they have. Excess fatty acids (FA) in the liver are converted into triacylglycerol which along with phospholipids, free and esterified cholesterol are packaged to VLDL along with a variety of apoproteins. While travelling through the peripheral tissues, triacylglycerol content is hydrolysed with the help of lipoprotein lipase (LPL) into FA and VLDL remnants. VLDL remnants through further hydrolysis of triglyceride contents give rise to intermediate density lipoproteins (IDL) and LDL. LDL having apoB100 apo protein component is the major cholesterol carrier in peripheral circulation. Elevated plasma levels of these non HDL lipoproteins are major CHD risk factors.[10]Dyslipidaemia as a metabolic irregularity is recurrently connected with diabetes mellitus.[11]

In current work, significantly elevated mean serum levels of total cholesterol, triglycerides and LDL cholesterol were figured out in patients with diabetes, which are well-identified threat causes for cardiovascular diseases. The prevalence rates for high total cholesterol, very high LDL-C and low HDL-C were seen in the diabetic subjects.

HbA1c is done to monitor the control of blood glucose in diabetes mellitus. Several studies have shown the positive correlation of HbA1c with duration of DM and as a strong predictor of risk (cardiovascular diseases) for diabetes complications. According to a study conducted by Palem SP [12] Type 2 diabetic patients with high level of Hb1Ac were at a higher risk of developing cardiovascular diseases in future. The results of the study conducted by Hussain et al [13] proved that HbA1c can also be used as a predictor of dyslipidaemia and thus early diagnosis of dyslipidaemia can be used as a preventive measure for the development of CVD in patients with Type 2DM. In this present study, we had found a statistically significant increase in TC, LDL TG and decrease in HDL among the diabetic patients which was in accordance with the study conducted by Ali et al.[14] where Diabetic individuals had high level of TC, TG, LDL, VLDL and low level of HDL in comparison to non-diabetic and normal control individuals. We have observed a significant difference in HbA1c / HDL, HbA1c /LDL and HbA1c / Chol ratios which was in line with study conducted by Patil et al.[15]A study by Elizabeth et.al.[16] observed that LDL and HDL cholesterol were significantly associated with HbA1c. HDL cholesterol was inversely associated with HbA1c whereas LDL cholesterol was positively associated with HbA1c in diagnosed diabetic patients. This finding was similar to the results obtained in our study where HDL level was significantly lower and LDL was higher in cases.

Elevated blood glucose level combined with dyslipidaemia increases atherosclerosis-related inflammation and makes it more extensive. A larger extent of coronary artery calcification in asymptomatic patients with newly-diagnosed Type 2DM has been demonstrated. Dyslipidaemia is not only an important risk for macrovascular complications ,studies have also observed the association of dyslipidaemia with microvascular complications related to Type 2DM namely diabetic retinopathy, diabetic nephropathy and diabetic neuropathy.[17] HbA1c is widely acknowledged as a key and more accurate criterion for determining the severity of DM over fasting glucose levels.HbA1c levels offer more advantage by providing a stable index of long-term glycaemic status, which is related to two to three months of average glucose concentration in plasma. Elevated HbA1c levels are notably linked to severe coronary artery atherosclerosis. The American Diabetes Association, in its recent position statement, stated that lowering HbA1c may be associated with a reduction in the microvascular, neuropathic, and possibly macrovascular complications of DM.[18] The HbA1c value <7.0% reduced the risk of cardiovascular diseases and value >7.0% leads to dyslipidaemia to the patients**.** Controlling the glycaemic levels may significantly decrease the risk of cardiovascular diseases in diabetes. Brinke et al.[19] has reported thatlowering HbA1c in type 2 diabetics decreases the absolute risk of developing CHD by 5-17%, as well as decreasing all-cause mortality by 6-15%.

V. Conclusion

It was concluded that type 2DM patients were more prone to dyslipidaemia. HbA1c can be considered as an indirect predictor for dyslipidaemia in addition to as a biomarker for glycaemic control. Thus this present study suggested theimportance of glycaemic control in prevention of cardiovascular diseases in type 2 diabetes**.**

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