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Original Research

To evaluate role of glycosylated haemoglobin as a biomarker in dyslipidemia and atherogenicity in type 2 diabetes mellitus

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ABSTRACT:

Aim: To evaluate role of glycosylated haemoglobin as a biomarker in dyslipidemia and atherogenicity in type 2 diabetes mellitus. **Methods:** This research was carried out at the Department of Medicine. This research included 130 diagnosed instances of type 2 diabetes in people aged 19 to 68. The patients were separated into two groups based on their glycated haemoglobin levels. After at least 6 hours of fasting, venous blood samples from all subjects were collected and analysed for fasting plasma glucose (FPG), 2 hours post prandial glucose levels (2hPG), serum total cholesterol (TC), triglycerides (TG), HDL-C, Very low density lipoprotein cholesterol (VLDL-C), and LDL-C using standard methods. The atherogenic index of plasma (AIP) was determined using the base 10 logarithm of the TG/HDL-C ratio. **Results:** There were 60 men and 70 females among the 130 cases investigated. The majority of patients were between the ages of 55-65. FBG, TC, TG,VLDL-C, LDL-C, HbA1c, AIP, ratios of TC/HDL-C and LDL-C/HDL-C are higher in patients with HbA1c more than 7%, whereas HDL-C levels are lower in individuals with HbA1c less than 7%, and these differences are highly significant. Dylipidemia was the most prevalent characteristic in the lipid profile of patients with HbA1c levels more than 7%. HbA1c had a direct and substantial connection with FBG and 2Hpg. It also indicates a direct and very significant relationship between HbA1c and TC, TG, LDL-C, TC/HDL-C, LDL-C/HDL-C, and AIP, as well as an inverse relationship between HbA1c and HDL. Patients with HbA1c >7% were more prone to cardiovascular risk because their AIP levels were in the high risk category, i.e. AIP > 0.22, and the connection was highly significant, demonstrating that glycemic management greatly adds to the future risk of cardiovascular issues. The lipid characteristics of individuals with HbA1c <7% were normal, while the AIP levels remained in the danger category. **Conclusion:** The current research concludes that individuals with poor glycemic control have an atherogenic lipid profile, and Glycated haemoglobin predicts dyslipidemia and atherogenicity.

Keywords: lipid profile, type 2 diabetes, glycosylated haemoglobin, glycemic management, plasma atherogenic index

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INTRODUCTION

Diabetes Mellitus is responsible for around 5% of all fatalities each year.[1] Type 2 diabetes mellitus (DM) is a well-known risk factor for the development of cardiovascular disease (CVD), cerebrovascular accidents (CVA), and peripheral vascular disorders, according to epidemiological research. [2] Diabetic dyslipidemia, the leading cause of micro and macrovascular complications, is characterised by elevated plasma triglyceride (TG), low-density lipoprotein (LDL), and apolipoprotein B concentrations, as well as decreased high-density lipoprotein cholesterol (HDL-C) concentrations. Dyslipidemia is a well-known and controllable risk factor that, if detected early, may result in the implementation of aggressive cardiovascular preventative measures. [3]

In Type 2 diabetes, relative insulin deficiency and decreased adiponectin cause a decrease in lipoprotein lipase activity, resulting in high levels of low-density lipoprotein (LDL), triglycerides, and low levels of high-density lipoprotein (HDL) (HDL). Qualitative LDL defects, such as atherogenic, glycated, or oxidised LDL, are also seen in Type 2 diabetes, increasing the risk of atherogenesis. [4]

Glycosylated haemoglobin (HbA1c) is a common glycemic status marker. When glycated haemoglobin (HbA1c) was first discovered in diabetic patients, it

was referred to as an unusual haemoglobin. Following that discovery, an International Expert Committee recommendation that was later adopted by WHO established HbA1c as an objective measure of glycemic control and a validated relationship between A1C and average glucose across a range of diabetes types and patient populations (International Expert Committee, 2009; World Health Organisation, 2011). HbA1c has been proposed as a dual marker for glycemic control and a risk factor for coronary artery disease (CAD). [5] According to the American Diabetes Association (ADA), each 1% increase in HbA1c increases the risk of diabetes-related mortality by 25%. Each percentage point rise in HbA1c is also associated with a 35% increase in the risk of microvascular complications and an 18% increase in the risk of myocardial infarction (fatal and non-fatal). Blood glucose reduction or management may reduce the lipid risk factor for cardiovascular disease. [5] There is evidence of a link between poor glycemic management and dyslipidemia advancement. [6] The most common consequence of diabetes is atherosclerosis, which damages major arterial beds and causes a variety of metabolic problems. Intensive glycemic control indicates that blood glucose and glycohaemoglobin (HbA1c) levels are normal or near normal, regardless of how simple or complicated the treatment plan is. A substantial relationship has been discovered between lipid profile and CAD. The Framingham research found a linear increase in CAD risk with increasing TC levels from 180 mg to 400 mg. The research discovered that those with HDL cholesterol levels less than 35 mg/dl are eight times more likely to develop CAD than those with HDL cholesterol levels more than 65 mg/dl. [7] The Lipid Research Clinics Coronary Primary Prevention Trial revealed that a 1% decrease in TC lowered the risk of CAD by 2%. [8] According to the Helsinki heart research, a 12% increase in HDL cholesterol and an 11% decrease in LDL cholesterol were both associated with a 34% decrease in CAD. The purpose of this research was to determine the significance of HbA1c in predicting diabetes dyslipidemia and atherogenecity.

METHODS

After receiving clearance from the protocol review committee and the institutional ethics committee, this research was carried out at the Department of Medicine. There were 130 confirmed instances of type 2 diabetes in people aged 19 to 68 years old who went to the diabetic OPD and were admitted to the medical wards. The research excluded patients with issues such as retinopathy, nephropathy, a history of heart disease, hepatic diseases, or any other chronic condition. The patients were split into two groups based on their glycated haemoglobin (HbA1c) levels; excellent glycemic control was defined as HbA1c <7.0 percent (53mmol/mol) and poor glycemic control as HbA1c>7.0 percent (> 53mmol/mol). After at least 6 hours of fasting, [9] venous blood samples from each participant were obtained and analysed for fasting plasma glucose (FPG), 2 hours post prandial glucose levels (2hPG), serum total cholesterol (TC), and triglycerides (TG) using a kit-based approach on an autoanalyser XL-640 Erba. The kit calculated HDL-C using the precipitation method[10] & Frieldwald's formula[11] was used to determine VLDL-C and LDL-C, which is VLDL-C = TG/5 where TG is less than 400 mg/dl and LDL-C was calculated as: TC - (HDL-C+ VLDL-C). The Ion Exchange Resin Method was used to compute HbA1c. The atherogenic index of plasma (AIP) was determined using the base 10 logarithm of the TG/HDL-C ratio. [12] The National Cholesterol Education Programme (NCEP) Adult Treatment Panel III (ATP III) guideline was used to determine blood lipid reference levels. According to NCEP-ATPIII recommendations, hypercholesterolemia is characterised as TC more than 200 mg/dl, high LDL-C greater than 100 mg/dl, hypertriglyceridemia greater than 150 mg/dl, and low HDL-C less than 40 mg/dl. Dyslipidemia was described as having one or more abnormal serum lipid concentrations. [13]

STATISTICAL ANALYSIS

Demographic and lipid data were provided as mean standard deviation. Actual numbers and percentages were used to represent categorical variables. The unpaired t-test was used to compare demographic and lipid factors. The chi-square test was used to compare categorical variables. Statistical significance was defined as a P value of <0.05.

RESULTS

There were 60 men and 70 women among the 130 cases investigated. The majority of patients were between the ages of 55 and 65. Table 1 compares the examined parameters in the excellent and poor glycemic control groups. FBG, TC, TG,VLDL-C, LDL-C, HbA1c, AIP, ratios of TC/HDL-C and LDL-C/HDL-C are higher in patients with HbA1c more than 7%, whereas HDL-C levels are lower in individuals with HbA1c less than 7%, and these differences are highly significant. Dylipidemia was the most prevalent characteristic in the lipid profile of patients with HbA1c levels more than 7%. This demonstrates the critical importance of glycemic management in reducing the future risk of cardiovascular disease, which may be attributed to an atherogenic lipid profile.

Table 1: Lipid parameter in normal and Glycated haemoglobin patients

Parameters	Glycated haemoglobin		p-value
	≤ 7.0%	>7.0%	
Age in years	49.27± 7.37	57.65± 6.88	highly significant
FPG	158.77 ±39.24	190.14 ±46.13	highly significant
2hPG	212.77 ±61.28	251.09± 55.22	highly significant
VLDL-C	31.04± 4.87	44.02± 9.12	highly significant
HDL-C	54.68± 11.22	48.15± 6.68	highly significant
TC	174.79± 23.87	224.87± 42.48	highly significant
TG	150.12± 32.24	224.29± 51.21	highly significant
TC/HDL-C	3.39 ±0.53	4.88± 1.48	highly significant
LDL-C/HDL- C	1.67± 0.43	2.79 ±116	highly significant
LDL-C	87.87± 16.25	131.24± 38.88	highly significant
AIP	0.37± 0.11	0.58± 0.19	highly significant

P <0.001- highly significant

Table 2 reveals a direct and substantial association between HbA1c and FBG and 2hPG. It also indicates a direct and very significant relationship between HbA1c and TC, TG, LDL-C, TC/HDL-C, LDL-C/HDL-C, and AIP, as well as an inverse relationship between HbA1c and HDL.

Table 2: Correlation of HbA1c with FBG, 2hPG and lipid parameters

Parameters	r-value	p-value
FPG	0.48	highly significant
2hPG	0.39	highly significant
VLDL-C	0.68	highly significant
HDL-C	-0.36	highly significant
TC	0.65	highly significant
TG	0.69	highly significant
TC/HDL-C	0.67	highly significant
LDL/HDL-C	0.57	highly significant
LDL-C	0.55	highly significant
AIP	0.70	highly significant

P < 0.001- highly significant

Table 3: Association of AIP and HbA1c

AIP	≤7	>7	p-value
<0.11 (low risk)	0	3	0.019
0.11 -0.22(Intermediate risk)	3	0	
>0.22 (High risk)	22	102	

p< 0.05 - S (significant

Table 3 shows that patients with HbA1c >7% were more prone to cardiovascular risk because their AIP levels were in the high risk group, i.e. AIP > 0.22, and the association was highly significant, demonstrating that glycemic control significantly contributes to the future risk of cardiovascular problems. The lipid characteristics of individuals with HbA1c< 7% were normal, while the AIP levels remained in the danger category.

DISCUSSION

Elevated HbA1c, in addition to dyslipidemia, is now recognised as a separate risk factor for CVD in both with and without diabetes. In the diabetic population, the estimated risk of CVD increases by 18% for every 1% rise in absolute HbA1c levels. Even in non-diabetic instances with normal HbA1c levels, a positive connection between HbA1c and CVD has been observed. [14] In addition, insulin insufficiency lowers hepatic lipase activity, and various additional processes in the synthesis of physiologically active lipoprotein lipase may be changed in DM. [15] A number of human investigations utilising tracer kinetics have shown that type 2 diabetes increases liver synthesis of apolipoprotein B (apoB), the primary protein component of VLDL and LDL. Enhanced fatty acid release from fat cells is caused by increased lipolysis in adipocytes as a consequence of inadequate insulinization. The increase in fatty acid transport to the liver that results, which is a typical aberration in insulin-resistant diabetes, may produce an increase in VLDL production. [16]. A second regulating mechanism might be insulin's direct influence on the synthesis of apoB and other proteins involved in the breakdown of circulating lipoproteins in the liver. Insulin directly increased the degradation of newly synthesised apoB in some studies. [17] As a result, insulin shortage or hepatic insulin resistance may enhance apoB secretion, raising LDL-C and VLDL-C levels. Previous

research has shown a direct and strong association between HbA1c and FBG, 2hPG. [18,19] Khan HA et al. discovered comparable relationships between HbA1c and TC, TG, LDL-C, and HDL-C. [20] We also discovered a direct and substantial relationship between HbA1c and AIP, TC/HDL-C, and LDL-C/HDL-C ratio. As a result, patients with higher HbA1c values had more severe dyslipidemia. Because excessive HbA1c levels and dyslipidemia are independent risk factors for cardiovascular disease, diabetic individuals with elevated HbA1c and dyslipidemia are considered to be at high risk for cardiovascular disease. Improving glycemic management in diabetes may lower the risk of cardiovascular events. In our investigation, individuals with HbA1c >7% were more prone to cardiovascular risk because their AIP levels were in the high risk category, i.e. AIP > 0.22, and the link was very significant, demonstrating that glycemic management greatly adds to the future risk of cardiovascular issues. According to Dobiasova et al.[21], persons with type 2 diabetes who have poor glycemic control had the greatest AIP. Dobiasova et al. discovered a greater FERHDL in diabetics compared to nondiabetics. [21] We believe that even if the lipid profile seems to be within normal limits, the AIP levels when computed may be in the high risk range, emphasising the need of calculating this simple ratio every time a lipid profile is requested. As a result, AIP represents the intricate metabolic interactions that occur throughout the whole lipoprotein complex.[21]

Furthermore, as compared to nondiabetic controls, they are more likely to have a preponderance of tiny, dense LDL particles.[22] All of these characteristics point to AIP being a useful measure for plasma atherogenicity and cardiovascular risk in type 2 diabetic patients. Earlier research focused on total cholesterol and HDL-C levels to minimise the risk of CVD, while triglyceride levels were overlooked as a risk factor. Since Gaziano et al. revealed that "the ratio of triglycerides to HDL was a robust predictor of myocardial infarction[23]," several discoveries about the link between HDL-C and TGs have been produced. Tan et al.[12] compared the findings of AIP analysis to those of another study's TG/HDL-C ratio analysis. [24] AIP's P values were consistently lower than those of TG/HDLC. Although an unmistakable independent, negative link between HDL-C and cardiovascular risk has been established, the impact of TGs to cardiovascular risk has been underappreciated. This might be attributed to the considerable variability of plasma TG concentrations (which reduces the statistical significance of evaluations), a lack of knowledge about the involvement of TGs in biochemical pathways, or the never-ending search for an atherogenic marker that is independent of other lipids. In actuality, every therapeutic hypolipidemic intervention causes larger or smaller alterations in the plasma lipid and apoprotein spectrum, including changes in lipoprotein particle sizes and changes in cholesterol esterification and lipolytic rates. [25]

CONCLUSION

According to the findings of this research, individuals with poor glycemic control have an atherogenic lipid profile, and Glycated haemoglobin predicts dyslipidemia and atherogenicity. The atherogenic index of plasma is an independent metric that has a strong correlation with cardiovascular risk. This metric is simple to compute every time a lipid profile is requested, allowing the patient's cardiovascular risk to be analysed.

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