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SHORT COMMUINCATION article

Glycosylated hemoglobin in type 2 diabetic patients as a biomarker for predicting dyslipidemia

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Abstract: Type 2 diabetes mellites (T2DM) is a common complex disease with multiple factors contributing to its development and progression. Dyslipidemia refers to the abnormality of lipid metabolism, characterized by elevated levels of low-density lipoprotein (LDL), total cholesterol (TC), triglycerides (TG), and decreased levels of high-density lipoprotein (HDL). It is a major risk factor for cardiovascular disease in type 2 diabetic patients. This study aimed to evaluate the diagnostic value of glycosylated hemoglobin (HbA1c) and fasting blood glucose (FBG) in predicting the risk of developing diabetic dyslipidemia. 86 clinically diagnosed Libyan patients with type 2 diabetes mellitus (44 males: 42 females), 30 years and 70 years of age were engaged in this study. Levels of $HbA1_C$, blood glucose, TC, TG, LDL, and HDL were performed using a Lntegra Cobas 400+ analyzer. The findings showed that HbA1c exhibits a significant positive correlation with TC and TG with no significant correlation with LDL and HDL levels. Thus, this study suggests that HbA1c can be used as a potential dual marker of glycemic control and dyslipidemia in type 2 diabetes mellitus.

Introduction

Diabetes mellitus (DM) is a hereditary chronic metabolic disorder characterized by hyperglycemia due to defects in insulin production, insulin action, or both. Type 2 diabetes mellites (T2DM) is usually asymptomatic in its early stage and can be misdiagnosed for several years. This long-term metabolic condition resulted from a complicated interaction of genetic, environmental, and behavioral variables [1]. The International Diabetes Federation (IDF) reported that 537 million adults worldwide are living with DM and the number of DM patients is expected to rise to 783 million by 2045, and 352 million people are at risk of developing T2DM [2]. DM was also attributed to about 5.0% yearly mortality [3]. Dyslipidemia is one of the most common complications of uncontrolled hyperglycemia characterized by metabolic disorder [4]. It results from serum lipid abnormalities such as an increase in total cholesterol (TC), plasma triglyceride (TG), low-density lipoprotein (LDL), and decreased high-density lipoprotein (HDL) concentrations [5]. More importantly, it is a well-known risk factor for the development of cardiovascular disease (CVD) in patients with T2DM [6]. CVD is considered one of the most common causes of death among diabetic patients [7-9]. Patients with T2DM are four times as likely as healthy people to die from CVD [10]. Several factors predispose to abnormal lipid profile levels in the body including diet, smoking, physical inactivity, and obesity [11] in addition to

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other common illnesses such as biliary obstruction, T2DM, chronic kidney disease, high blood pressure, and CVD [12]. Lipid abnormalities are found to be a common risk factor for CVD, due to the raised LDL level [13]. Therefore, analyzing diabetic patients' lipid profiles is as crucial as glycated hemoglobin (HgA1c) management to be treated with the appropriate medication based on the type of illness [14].

The hemoglobin A1c (glycated hemoglobin, glycosylated hemoglobin, HbA1c, or A1c has been established as a gold standard to assess glycemic control, it also showed a crucial correlation with the lipid profile of patients with T2DM [15]. It is suggested that HbA1c could be utilized as a potential biomarker to predict dyslipidemia and CVD despite the conflicting results reported in some studies. For instance, a direct correlation was found between HbA1c and TC, TG, and LDL concentrations [16]. However, others reported no remarkable correlation between these lipid profile parameters and HbA1c except with TG [17]. Thus, this study tested the hypothesis that T2DM patients will exhibit abnormal levels of lipid profile parameters and HbA1c could be a useful indicator in predicting dyslipidemia. This study was designed to understand the pattern of dyslipidemia among T2DM Libyan patients and its association with $HbA1_C$. It also aimed to examine the impact of glycemic control on the lipid profile of T2DM patients and the importance of HbA1c as an indirect indicator of dyslipidemia.

Materials and methods

This cross-sectional observational study was conducted for diabetic Libyan patients (n= 86, 44 males and 42 females). The age of the adult patients ranged between 30 years and 70 years. This study was performed in the Western part of Libya from July 2023 to September 2023. All the patients were asked to fast for 8 to 12 hours before the blood sample collection. The excluded criteria were young patients of less than 25 years, patients with serious illnesses, pregnant women, and patients with known medical conditions that could affect the study.

Blood samples: Each participant provided a 5.0 ml venous blood sample, which was collected in EDTA tubes for testing $HbA1_C$, FBG, TC, TG, LDL, and HDL concentrations. The biochemical analysis was performed using a Lntegra Cobas 400+ analyzer.

Ethical approval: Based on medical research ethics, Sabratha University, Libya (SU: 02, 2023), an ethical approval was obtained. All patients were also informed about the study and a verbal agreement was reached.

Statistical analysis: All data is expressed as means and standard deviation (Mean±SD). The statistically significant difference between the groups was analyzed by one-way analysis of variance (one-way ANOVA). A statistical difference is significant at $^{*}p<0.05$ and $^{**}p<0.05$. A Pearson correlation coefficient was used to measure the relationship between variables.

Results

Eighty-six adult Libyan patients with T2DM were collected during the research period including 44 males and 42 females. The participant's characteristics were analyzed and compared according to gender (**Table 1**). The ratio of males exceeds the females, as the percentage of males was 51.2% compared to the female subjects (48.8%). Female patients had significantly higher values for HDL ($p<0.046$) than the male subjects.

This difference was statistically significant (**Table 2**). However, the concentrations of TC, TG, LDL, and $HbgA1_C$ showed no significant difference. In this study, the concentration of HbA1c exhibits a strong positive correlation with TG and TC levels, both results were highly statistically significant at a p-value of less than 0.01 **(Table 2)**. However, the correlation between the concentrations of $HbA1_C$, LDL, and HDL was not statistically significant.

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Table 1: Gender-wise comparison of Libyan patients' characteristics of type 2 diabetes mellitus

Gender / Parameter	**Male** (n=44)	**Female** (n=42)	*P*-value
Age (years)	31.8±9.9	53.8±10.5	0.237
HbA1c (%)	78.37±8.0	31.7±8.3	0.92
TC (mg/dl)	192.09±42.2	191.4±42.8	0.945
HDL (mg/dl)	42.4±9.2	50.0±23.9	0.046*
LDL (mg/dl)	123.6±34.4	129.5±31.1	0.405
TG (mg/dl)	203±104.6	179.6±85.2	0.262
FBG (mg/dl)	167.8±64.9	187.0±77.1	0.200

Table 2: The relationship between HbA1c and the lipoproteins

Parameter	**TG**	**LDL**	**HDL**	**TC**
HbA1c	**0.550	0.204	0.147	**0.283
P-value	0.000	0.060	0.176	0.008

Discussion

In the current study, we attempted to examine the potential correlation between HbA1c and lipid profile parameters in Libyan patients with T2DM. The present findings of lipid profile, FBG, and $HbA1_C$ supported that HbA1c can be used as a potential biomarker for predicting dyslipidemia in T2DM. The results indicated a strong positive correlation between HbA1c and both TC and TG concentrations in diabetic patients. These variables were consistent with the previous study conducted in 2017 which demonstrated a significant positive correlation between HbA1c and TG and TC concentrations [18]. A similar association was reported in another study which showed a positive relationship between HbA1c and TG concentration [19]. A substantial positive association between HbA1c and lipid profile parameters has been found in several studies. Thus, in study conducted in Iraq for instance exhibited a considerable correlation between TC, LDL, TG, and HbA1c concentrations [1, 6]. However, there was no correlation between HbA1c and lipid profile parameters except TG [20]. HbA1c has been linked to elevated TG levels suggesting that it may predict CVD and is a risk factor in T2DM. Insulin resistance is thought to be the root of dyslipidemia in patients with T2DM. Increasing hepatic secretion of very low-density lipoprotein (VLDL) is caused by both insufficient insulin secretion and function, which is mostly because of increasing substrate levels for TG synthesis [20]. On the other hand, we found no significant negative correlation between HDL and HbA1c concentrations as well as a non-significant positive correlation between LDL and HbA1c concentrations. These findings were consistent with a study that reported no correlation between these parameters [1]. Furthermore, another study was in agreement with the present findings in which a negative correlation was indicated [17]. On the other hand, studies have found a substantial correlation between HbA1c and LDL/HDL concentrations. In a study conducted in India, there was a crucial relationship between HDL, LDL, and HbA1c concentrations [21]. The levels of $HbA1_C$, FBG, TG, TC, and LDL concentrations in our study did not differ significantly between males and females. However, females exhibit significantly a higher level of HDL than in male subjects. Lifestyle changes such as diet, physical exercise, medication therapy, and obesity could contribute to this variation between genders. The difference between HbA1c, and lipid profile parameters particularly in the current study compared to other studies may be due to differences in population as well as the prevalence of dyslipidemia which may also be variable among populations. It is suggested that diabetic patients are recommended to join a fitness program for regular exercise and physical activity several times per week [22]. In Libya, family physicians should be aware of the relationship between HbA1c and hyperlipidemia in T2DM patients and check their patients' lipid profile and HbA1c at least twice a year to avoid complications [17].

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Conclusion: Glycosylated hemoglobin is a useful potential biomarker for predicting dyslipidemia in type 2 diabetes mellitus and could be used as a useful tool for treating patients. An educational program for diabetic Libyan patients should be conducted to monitor their lipid profile and avoid cardiovascular complications.

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Author declarations: The authors confirm that all relevant ethical guidelines have been followed and any necessary IRB and/or ethics committee approvals have been obtained.