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Research Article

Glycemic Control Is Associated with Lipid Profile and Atherogenic Index of Plasma in Type 2 Diabetes Mellitus

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Background: Dyslipidemia is a common complication among type 2 diabetes mellitus (T2DM), and a major risk factor for cardiovascular events. This study aimed to investigate the association of glycemic control with lipid profile and atherogenic index of plasma (AIP) in patients with T2DM.
Methods: A total of 565 adult diabetic men were included in this cross-sectional study. Glycemic and lipid parameters were measured using an auto-analyzer with standard methods. Subjects were categorized into good (HbA1c < 7), inadequate (HbA1c 7-7.9), and poor (HbA1c ≥ 8). The association between glycemic control and lipid profile was evaluated using the analysis of variance and covariance.
Results: A significant association was found between poor glycemic control and total cholesterol, triglyceride, and AIP. Significance remained after adjustment for confounders. Results indicated no relationship between glycemic control and other lipid parameters before or after adjustment.
Conclusion: Findings from this study underlined the importance of glycemic control in T2DM patients for targeted interventions to prevent cardiovascular events. Further studies are needed to confirm these results.

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Introduction

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder, marked by hyperglycemia and insulin resistance. Dyslipidemia is a prevalent morbidity that affects individuals with T2DM [1]. The major hallmark of diabetic dyslipidemia is abnormal lipid levels in the bloodstream, including increased levels of low-density lipoprotein cholesterol (LDL) and triglyceride (TG), as well as decreased levels of high-density lipoprotein cholesterol (HDL). Insulin resistance, hyperinsulinemia, and increased production of very-low-density lipoprotein (VLDL) particles contribute to the pathophysiology of dyslipidemia, resulting in elevated circulating TG levels and decreased HDL levels [1][2]. T2DM patients have a higher risk of developing cardiovascular diseases (CVD), including micro and macrovascular complications. CVD is the leading cause of mortality in T2DM patients. Dyslipidemia can increase the risk of developing CVD and related complications, primarily through the progression of atherosclerosis [2][3].

Current evidence suggests that achieving proper glycemic control, in parallel with lifestyle modifications and medications, can also aid in managing dyslipidemia in T2DM patients. Studies have shown that lowering

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hemoglobin A1c (HbA1c) levels through glucose-lowering therapy and or insulin sensitizer agents is associated with favorable effects on lipid metabolism in patients with T2DM [4]. Studies have indicated that inadequate glycemic control is directly associated with TC and LDL levels. HbA1c is also well-established as a risk factor for atherosclerotic CVD and CVD-related mortality among T2DM patients [5][6]. Altogether, managing dyslipidemia in people with T2DM can be challenging due to multiple comorbidities and potential drug interactions [6]. Therefore, there is still limited evidence regarding the relationship between glycemic control status and components of dyslipidemia in patients with T2DM.

Objective

This study was conducted to investigate the association between glycemic control status and components of dyslipidemia among Iraqi patients with T2DM.

Methods

This cross-sectional study investigated the association between glycemic control and dyslipidemia in male Iraqi patients with T2DM. A total of 565 male patients aged 20 years and older were recruited from Medical City Hospital and the Specialized Center for Endocrinology and Diabetes-Al-Kindy Teaching Hospital. Patients who met the inclusion criteria (having a documented diagnosis of T2DM) were invited to participate in the study. The data are available in "Mendeley Data" (https://data.mendeley.com/datasets/wj9rwkp9c2/1) [7]. This study was conducted in accordance with the Declaration of Helsinki and was approved by the Committee on the Ethics of Medical Experiments of the Specialized Center for Endocrinology and Diabetes-Al-Kindy Teaching Hospital (Baghdad). Laboratory data including fasting blood lipids including TC, TG, LDL, and HDL levels were evaluated using auto-analyzer (Bckman 5800, USA), and reported as mmol/liter [8]. Additionally, the atherogenic index of plasma (AIP) values were calculated according to the following equation [9]: Log [TG/HDL]. Patients' glycemic control was assessed using hemoglobin A1c (HbA1c) levels, while inadequate and poor glycemic control were defined as HbA1c levels between 7-7.9%, and greater than 8%, respectively [10]. Data are expressed as mean and related standard deviation (SD). The one-way analysis of variance (ANOVA) was used to compare the mean values of blood lipids and AIP, among different glycemic control status groups (poor, inadequate, and good). Furthermore, we performed an analysis of covariance (ANCOVA) to adjust for potential confounding factors such as age, and body mass index (BMI). Statistical analyses were performed using SPSS version 23.0 (IBM Corp., NY, USA), and P-value < 0.05 was considered statistically significant.

Results

General characteristics of 565 study subjects are illustrated in Table 1. Overall mean and SD for Age, BMI, and HbA1c among study participants were 54.56 ± 8.27 years, 30.41 ± 4.39 kg/m^2, and 7.61 ± 1.39 %, respectively. According to the HbA1c categorization, 164 (29.03%) subjects had good glycemic control. 157 (27.79%) and 244 (43.19%) of total subjects had inadequate and poor glycemic control, respectively. We found a significant relationship between HbA1c categories with age (P < 0.001) and BMI (P = 0.03) of participants. Findings from lipid profile indicated higher levels in terms of TC (P < 0.001), TG (P = 0.002), and AIP (P = 0.02), in subjects with poor glycemic control. After adjustment for possible confounders (age and BMI), differences for TC (P = 0.001), TG (P = 0.005), and AIP (P = 0.03) remained significant. The relationship between glycemic control status with HDL and LDL, was not significant before adjustment nor after adjustment (P > 0.05) (Table 2).

Variables	Mean ± SD
Age (year)	54.56 ± 8.27
BMI (kg/m^2)	30.41 ± 4.39
HbA1c (%)	7.61 ± 1.39
TC (mmol/L)	4.87 ± 1.25
TG (mmol/L)	2.29 ± 1.10
HDL (mmol/L)	1.20 ± 0.60
LDL (mmol/L)	2.60 ± 1.04
AIP	0.26 ± 0.28

Table 1. General characteristics of study participants (N = 565) [a]

Abbreviations: BMI, Body Mass Index; HbA1c, Hemoglobin A1c; HDL, High-Density Lipoprotein; LDL, Low-Density Lipoprotein; TC, Total Cholesterol; TG, Triglyceride

[a] *Values are expressed as mean and ± SD*

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Variables	Good (N = 164)	Inadequate (N = 157)	Poor (N = 244)	P-value (ANOVA)	P-value (ANCOVA)[b]
HbA1c (%)	**< 7%**	**7 – 7.9 %**	**>= 8%**		
Age (years)	52.12 ± 8.74	54.99 ± 8.14	55.93 ± 7.67	**< 0.001**	-
BMI (kg/m^2)	29.81 ± 4.99	31.11 ± 4.51	30.38 ± 3.80	**0.03**	-
TC (mmol/L)	4.81 ± 1.26	4.59 ± 1.23	5.09 ± 1.22	**< 0.001**	**0.001**
TG (mmol/L)	2.08 ± 1.00	2.23 ± 1.10	2.46 ± 1.14	**0.002**	**0.005**
HDL (mmol/L)	1.23 ± 0.52	1.12 ± 0.35	1.24 ± 0.75	0.13	0.07
LDL (mmol/L)	2.69 ± 1.09	2.46 ± 0.93	2.63 ± 1.08	0.11	0.27
AIP	0.21 ± 0.27	0.27 ± 0.26	0.29 ± 0.28	**0.02**	**0.03**

Table 2. Comparison of lipid profile according to categories of glycemic control (HbA1c) [a]

Abbreviations: AIP, Atherogenic Index of Plasma; ANOVA, Analysis of Variance; ANCOVA, Analysis of Covariance; BMI, Body Mass Index; HbA1c, Hemoglobin A1c; HDL, High-Density Lipoprotein; LDL, Low-Density Lipoprotein; TC, Total Cholesterol; TG, Triglyceride

[a] *Values are expressed as mean and ± SD*

[b] *P–value obtained from ANCOVA after adjustment for age and BMI*

Discussion

Our results indicated that poor glycemic control was significantly associated with higher levels of TC, TG, and AIP. We also found a linear term for TC (p =0.01), TG (p =0.001), and AIP (p = 0.01), regarding glycemic control status.

Considering the growing trend of T2DM in Iraq during the last decade, monitoring and evaluating the diabetes-related morbidities is among important approaches for management policies [11].Recent data from Iraq, reported a considerable prevalence of dyslipidemia among diabetic cases (70.5 %), which reflects a great importance to aim lipid-controlling strategies in patients with T2DM [12]. A study in India was conducted to explore the association between HbA1c levels and lipid profile among 814 prediabetic and diabetic adults. Findings indicated that poor glycemic control (HbA1c ≥ 6.5%) was significantly associated with raised TG, but not TC, HDL, and LDL levels [13]. Another study among 140 Indonesian diabetic patients was also performed using the same purpose. Results of the study showed that patients with poor glycemic control (HbA1c > 7%) had increased TC and LDL levels and lower levels of HDL compared with good glycemic control (HbA1c ≤ 7%) group. They found no significant difference regarding TG levels between the groups [14]. Some findings from these studies are parallel with the current research; however, there are some considerations in respect of inconsistencies between studies. First, the criteria applied for categorization of glycemic control status were different. Second, the differences in the study population may lead to contradictory results. Overall, it can be hypothesized that inadequate or poor glycemic control is accompanied by dyslipidemia components among diabetic patients.

Previous research has shown that abnormal glucose homeostasis has a tight association with dyslipidemia. Diabetic dyslipidemia characterized by lipoprotein abnormalities, is a major clinical manifestation of glucose-lipid interaction which also known as “diabetes lipidus” [15][16]. Although, the underlying mechanisms related to lipid pathways in diabetes are not fully understood, the aberration of hepatic and non-hepatic lipases is probably responsible for the accumulation of TG-rich lipoproteins. In parallel, the lipolysis and oxidation of LDL result in small dense LDL formation. Moreover, insulin resistance may lead to the disruption in cholesterol scavenging and antioxidant activity of HDL particles [16][17]. These alterations shape a cluster of lipids and lipoproteins, which is potentially linked to cardiovascular diseases. Previous studies have underlined the causal role of dyslipidemia in the initiation and progression of cardiovascular

complications, including coronary heart disease, atherosclerosis, and stroke [6][18]. There are inconsistencies regarding the potential atherogenicity of dyslipidemia components. Hence, investigators have introduced AIP as a predictor of future atherosclerosis and related complications. Our findings, in parallel with previous studies, indicated a direct association between inadequate and poor glycemic control with AIP levels among diabetic patients [9].

Despite the advantages of this study (large sample size and using the optimal cut-off value of HbA1c), there are some limitations that should be noted. First, this study is conducted with a cross-sectional design, which does not support a causal inference. Authors affirm that time-series design might be preferable to overcome this type of bias. Moreover, the absence of possible confounders (e.g. dietary intakes, physical activity, and medications) may lead to analytic bias and probably misinterpretation of the findings. Furthermore, this study included only diabetic men; hence, generalizing the results to females or other conditions must be applied with caution.

Conclusion

According to our findings, increments in some lipid parameters (TC, TG) and AIP was found in diabetic patients with poor glycemic control. Regular monitoring of the lipid profile is recommended for T2DM patients.

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Statements and Declarations

Authors' contribution: M.D and M.N (conceptualization of the study); M.D and M.Gh (data analysis and interpreting of the results); M.D, M.N, and M.Gh (Finalizing the manuscript). All authors approved the final manuscript

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Declarations

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