

The progressive Role of Dyslipidemia and Inflammation in Type 2 Diabetes in Iraqi Patients

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KEYWORDS

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ABSTRACT

Type II diabetes is a complex metabolic disorder that raises the risk of dyslipidemia and obesity. Inflammation is the primary factor in the pathogenesis of this disease and coincides with metabolic dyslipidemia. This work aims to predict the role of dyslipidemia and inflammatory markers in development type II DM by evaluating the levels of lipid profile, TNF-R2, systemic immune inflammatory index (SII) and related biochemical factors in patients with type 2 diabetes. Thirty samples were obtained from diabetic patients and 30 samples from non-diabetic individuals as a control. D10 apparatus (BIO-RAD, USA) used to measure hemoglobin A1c HbA1c, Enzymatic and colorimetric method used to measure biochemical parameter, ELISA technique used to estimate the TNF-R2 levels, and Complete Blood Count determine to calculate SII by the formula (neutrophil *platelet / lymphocyte count) . The results showed significant increase in most of lipid profile levels in patients than control except HDL has the verse results. Also, the results showed that HbA1C was significantly increased in patient compared to healthy group. Furthermore, TNF-R2 and SII appeared higher significant values in patients than control. Furthermore, the results indicated positive correlation between HbA1C and lipid profile (TC, TGs, VLDL and LDL), TNF-R2, SII, and BMI. It can be concluded that dyslipidemia and both TNF-R2 and SII inflammatory parameters have a cardinal role in the development of T2DM and can be served as early diagnostic factors to detect disease progression.

1. Introduction

Diabetes is a metabolic disorder of the endocrine system. It occurs due to absolute or relative insulin deficiency [1-2]. Diabetic patients are at greater risk of developing dyslipidemia, high blood pressure, and obesity [2]. Type II Diabetes often leads to diabetic dyslipidemia characterized by high triglycerides, low HDL, and atherogenic LDL particles, significantly increasing cardiovascular disease risk [3]. Diabetic dyslipidemia is a group of interconnected metabolic abnormalities of plasma lipids and lipoprotein, especially dyslipidemia associated with resistance to insulin, visceral obesity, and liver fatty content [4]. It is common in patients with type 2 diabetes mellitus (T2DM) and is considered an essential factor linked with cardiovascular disease [5,6]. Systemic inflammation is often observed in T2D concurrent with metabolic dyslipidemia [7]. Tumor necrosis factor- α (TNF- α) is an inflammatory cytokine that participates in a number of signaling pathways that due to program cell death (apoptosis) and inflammatory processes, through interaction with two types of transmembrane receptors: "tumor necrosis factor receptor (TNFR) 1 and TNFR2" [8]. The mortality of type 2 diabetes patients is associated with soluble tumor necrosis factor receptor 2 (sTNFR2) levels in circulation [9]. Previous data indicated that pro-inflammatory cytokines like TNF- α were contributed in the lipid disorder severity, and some of them may significantly influence the progression of lipid metabolism in obesity, hyperlipoproteinemia, and type 2 diabetes [10]. Furthermore, elevated levels of TNFRs in patients with type 2 diabetes have been considered very strong predictors of subsequent progression to ESRD in patients with and without proteinuria [11]. Based on the above, the current data designed to determine the relationship between lipid disorders, inflammation, and type 2 diabetes and their role in prognosis and helping to predict diabetes patients in the city of Nassiriya.

2. Patients And Methods

A. Subjects

The study included 30 diabetic patients of both sexes who visited the Diabetes and Endocrinology

Center in Thi_Qar between October 20, 2023 and February 20, 2024. In addition to 30 healthy people. Their age ranged from (37-83). Diagnosis of the condition depends on biochemical examination. In addition clinical features (depend on physician diagnosis) toconfirming the diagnosis.

B. Methods

The 5 ml blood samples were collected by using Ethylene diaminetetraacetic acid (EDTA) tube to measured (HbA1c, CBC) and tubes of serum separation involve a clot activator and inert gel to separate the serum to measure (biochemical variables), then clear collected serum stored at -20°C until the time of use to estimate TNF-R2. HbA1c test performed by D10 apparatus (BIO-RAD, USA), TNF-R2 levels were determined using the Sandwich-ELISA Sun Long (China) and catalog NO: SL3063Hu, Complete Blood Count by Blood coulter device from the Chain Company Mindray. Biochemical parameter (RBS test, Lipid Profile) measurement by used Enzymatic and colorimetric method supplied by Bio Labo Company and the formula (neutrophil *platelet / lymphocyte count) used to calculate SII.

C. Statistical Analysis

Results were presented as mean $\pm$ standard deviation (SD). The P values ≤ 0.05 were considered as significant . T-test , chi-square, and Pearson correlation coefficient were used to test the difference and the relationship between parameters .

3. Results and Discussion

The description of the investigated groups according to sex is shown in Figure (1). This study included 60 individuals classified into two categories the first one patients category that included thirty person suffering from type II DM [17 male and 13 female] and the second were healthy people as a control that included 30 individuals [15 male and15 female] .

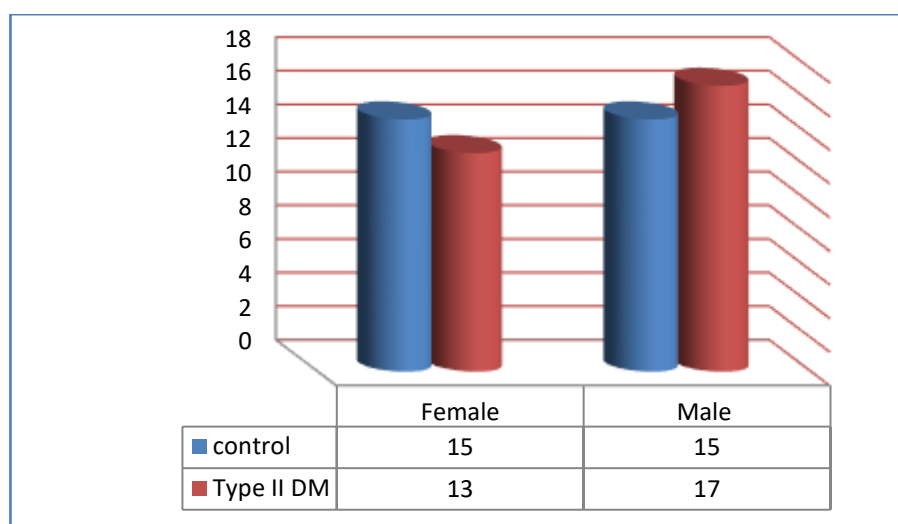


Figure 1. Distribution of Type 2 DM Patients and control according to sex

In the current study, the maximum percentage of patient groups was found within the age group (56-65) years, and the minimum percentage of patient group in the age group of 36-45 years Table (2). Other incidences of patient cases and healthy were also distribution within the age group as listed in Table (2).

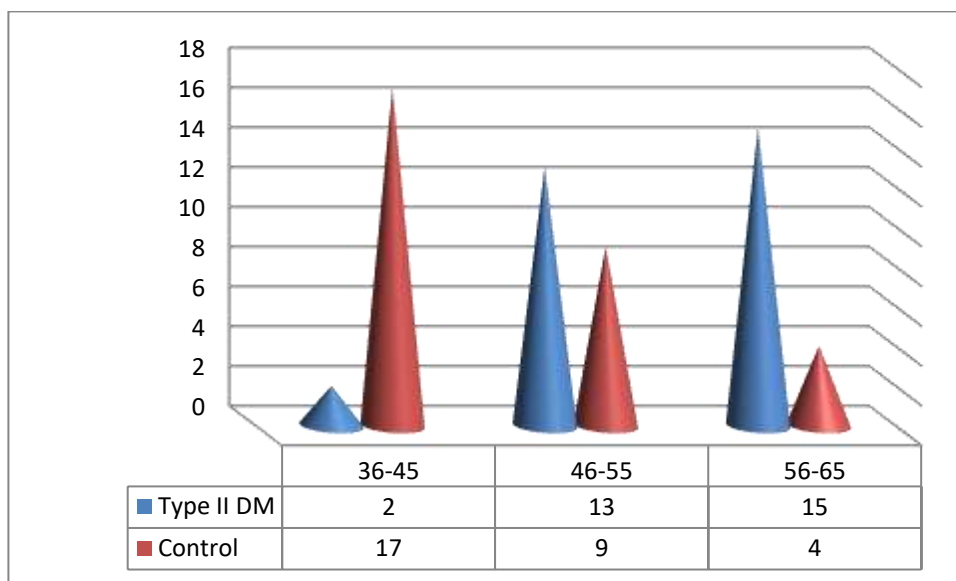


Figure 2. Distribution of Type 2 Diabetes Mellitus Patients Based on Age

Table 1 lists the results of some biochemical parameters like (RBS mg/dL, HbA1c%) eGFR and lipid profile in patients and control. RBS and HbA1c values recorded significantly elevated levels with a significant difference ($p=0.01^{**}$) in patients compared to healthy subjects, and the lipid profile indicated significant increases in triglycerides TC mg/dL, total cholesterol TGs (mg/dL), low-density lipoprotein. LDL (mg/dL) and very-low-density lipoprotein (VLDL) (mg/dL) in the patient group compared to the control group, while HDL (mg/dL) showed significantly lower levels in the patient group compared to the control group Table 1 .

Table 1: Biochemical assessments for T2DM and control subjects

Parameters	Mean± SD Patients	Mean± SD Control	T test	P value
TC	175.766±40.01	79.8±15.153	11.264	0.01^{**}
TGs	182.7±46.057	152.633±23.205	3.193	0.01^{**}
HDL	45.4±8.8	51.3±8.9	-2.5	0.014^{**}
LDL	102.11±37.4	85.41±23.5	2.096	0.04[*]
VLDL	35.2±17.1	15.9±3.03	6.04	0.01^{**}
RBS	216.4±99.2	102.7±20.3	6.15	0.01^{**}
HbA1c	8.6± 2.03	4.9±0.43	9.4	0.01^{**}
eGFR	84.97±15.6	118.1±15.8	-8.13	0.01^{**}

Furthermore, Table 1 displays the results for glomerular filtration rate (eGFR) (ml/min/m²) in both groups of patients and healthy subjects, where the patient group showed significant reduce in eGFR in comparison to healthy group, and this decrease was offset by higher levels of lipids profile in patients Table 1. On the other hand, TNF-R2 and the novel inflammatory biomarker SII were used to estimate systemic inflammation. The results demonstrated an increase in TNF-R2 and SII values in patients compared to control with a high significant difference Table 2.

Table (2): TNF- α and SII values in serum of patient and healthy subjects.

Groups	No.	TNF-R2 Mean± S.D. pg/ml	SII
Healthy	30	9.736 ± 2.399	270.48± 63.27
DM Type II	30	32.027±7.978	385.89±60.07
P value	0.00 ^{**}		0.00 ^{**}

Regarding to the correlation between some parameters in this study the Table 3 shows the relation between dyslipidemia and inflammation parameters in type II DM by detecting the correlation between lipid profile and inflammatory markers.

Table 3: Person correlation between some parameters in study

Person		TNF-R	SII	HbA1c	TC	TGs	HDL	LDL
BMI	r	0.371	0.247	0.098	0.207	0.198	-0.316	0.158
	p. value	0.044*	0.189	0.608	0.273	0.294	0.089	0.403
TNF-R	r		0.211	0.009	0.243	0.003	-0.138	0.031
	p. value		0.262	0.963	0.195	0.988	0.466	0.871
SII	r			0.351	0.059	0.051	-0.027	0.177
	p. value			0.057	0.765	0.79	0.88	0.35
HbA1C	r				0.332	0.266	-0.071	0.212
	p. value				0.073	0.156	0.708	0.26
TC	r					0.45	-0.368	0.916
	p. value					0.013*	0.04*	0.0*
TGs	r						-0.352	0.102
	p. value						0.05	0.59
HDL	r							-0.333
	p. value							0.072

The findings of this study revealed linked between dyslipidemia and inflammation in type II DM may be leads to nephropathy diabetes. The results indicated that men are more common in this study compare to women, these results in line with previous local study that found men were more than women [2].The maximum number of patients was found within the age group (56-65) years, and this result consents with the fact that people have more chance to suffering from DM in four and five decay of age .

This study revealed a significant increase in all levels of TG, TC, LDL, and VLDL lipids among T2DM patients compared to controls, with the exception of HDL, which showed lower levels in patients compared to healthy controls. These results were in agreement with Al-Shehri, who found that patients with T2DM had an increase in the average values of TC,TG, and LDLcompared to the control group. Meanwhile, the average value of HDL decreased significantly in patients with T2DM compared to the control group [12] . The data of another study indicated that there were statistically significant differences in HbA1c values and lipid profile values between T2DM patients and controls [2] .

Regarding to glomerular filtration rate (eGFR) (ml/min/m2) results the patient group showed significant decrease in eGFR compared to the control group, and this decrease was offset by higher values of lipids profile and inflammatory markers in patients Table 1and Table 2 .These results indicate a relationship between dyslipidemia and inflammation in type 2 DM, which may lead to diabetic nephropathy. The results of a local study showed that patients with T2DM had increased values of lipid profile and HbA1C and found that there was a relationship between T2DM and kidney function parameters, as patients with T2D had raised values of creatinine and urea., which are an indicator of glomerular filtration rate [13] .

Increased total cholesterol in diabetic patients compared to control. It may be attributed to decreased muscle activity or suppression catabolism of cholesterol [14]. While high triglyceride levels in diabetics could be due to reduce levels of insulin, which leads to high blood sugar and the secretion of fatty acids from adipose tissue. where fatty acids are mobilized in adipose tissue for energy purposes, and the excess fatty acids accumulate in the liver to convert it into triglycerides [15]. On the other hand, the results demonstrated an increase in TNF-R2 and SII values in patients compared to control with a high significant difference Table 2. Elevated values of circulating soluble TNFR2 are related with mortality in T2DM patients [9]. Previous study findings by Saeed *et al.* referred that an elevated serum level of TNF α in T2DM patients linked with develop and predict the pathogenesis of T2DM [16]. Also, previous data showed that higher SII values were related with a greater potential of developing T2DM [17].

According to analysis of the Pearson correlation of between studied parameters the results indicated that HbA1c appeared a significant positive correlation with lipid profile (TC, TG, VLDL and LDL), BMI, RBS, TNF-R2 and SII Table 2, While the results showed a negative correlation between HbA1c and HDL ($r = -0.071$, $P = 0.708$). The same findings were indicated by Iraqi study [2] and Turkey study [18], where these results showed that patients with T2DM have elevated levels of HbA1c, which may be related to dyslipidemia, so it may be a good prognostic factor for dyslipidemia in patients with T2DM. Furthermore, HbA1c shows a positive correlation with BMI, TNF-R2, and SII. Chen and Fang data indicated that both high BMI and abnormal lipid levels have a significant roles in complications that related to diabetes, also they found high BMI is combined with an increased risk of dyslipidemia in type 2 diabetes patients, especially when be associated with a family history of dyslipidemia [19]. Another study focused on obesity as a major risk factor for diabetes, with a direct relationship between body mass index and high blood sugar levels [20]. Alzamil study indicated that TNF- α is can produced by adipocytes and inflammatory cells in response to chronic inflammation and that it is associated with concurrent obesity and Type II DM and is associated with HbA1c [21]. Published data suggest that a high SII value is associated with a high probability of developing T2DM [17].

4. Conclusion

According to these results, it can be concluded that dyslipidemia and both TNF-R2 and SII inflammatory parameters have an essential role in the development of T2DM and can be considered as early diagnostic factors to detect disease progression.

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