



Levels of Serum IL-34 and Lipid profile in Type 2 Diabetes Mellitus Patients

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ABSTRACT

Diabetes mellitus type 2 (T2DM) is a growing global health issue that is inextricably related to the obesity epidemic. Because of hyperglycemia and individual components of the insulin resistance (metabolic) syndrome, people with T2DM are at a significant risk for both microvascular and macrovascular consequences. Environmental (fat, a poor diet, and physical inactivity, for example) and hereditary variables also contribute to the many pathophysiological disruptions that cause impaired glucose homeostasis in T2DM. Several studies have been conducted to investigate the role of dyslipidaemia in the macrovascular complications of diabetes. The current investigation's purpose was to determine the prevalence, pattern, and the link between IL-34 and dyslipidemia in T2DM patients. This study involves sixty T2DM patients. 30 people who appear to be in good health served as the control. Both the patients and the controls are the same age and BMI. Lipid abnormalities were discovered in this research. T2DM is distinguished by a high frequency of dyslipidaemia. An increase in poor lipids causes a variety of problems, including cardiovascular disease (CVD). Inflammation causes the proinflammatory cytokine IL-34, which is more prevalent in T2DM patients. Abnormal lipids and IL-34 can be factors in cardiovascular disease.

Keywords: *IL-34, lipid profile, Inflammation, cardiovascular problems*

INTRODUCTION

Diabetes mellitus type 2 (T2DM) Hyperglycemia is a chronic metabolic condition defined by unusually high blood glucose levels (Demir et al., 2021).. It is caused by the body's inefficient utilization of insulin combined with a gradual progressive loss of pancreatic β -cells (WHO, 2018). Age, a family history of diabetes, high blood pressure, high triglyceride levels, heart disease, or stroke are the main causes (Jian et al., 2021). T2DM in all its forms has been rapidly increasing worldwide especially in Arabic world. The Kingdom of Saudi Arabia has the highest prevalence of T2DM (31.6%), while Somalia has the lowest (3.9%).

(2017) (Meo SA et al.). Depending on WHO the prevalence of T2DM from 8.5% to 13.9% (WHO 2018). Over time, diabetes can have an impact on any organ or system of the body, resulting in various complications. The two most common types of diseases are microvascular and macrovascular. The former relates to long-term conditions that affect small blood vessels, such as retinopathy, nephropathy, and neuropathy. However, cerebrovascular disease, peripheral vascular disease, and ischemic heart disease are all macrovascular disorders (Graves LE et al., 2020). Glycated hemoglobin (HbA1c) reflects the average amount of glucose accumulated in the blood over the last 2–3 months and has direct

relationships with diabetes and future risk of complications (Islam, M.S et al.,2020). Intervention trials have shown a somewhat modest relationship between glycemic control and CVD risk. where, an HbA1c reduction of 0.9% was associated with a 14% reduction in the MI risk (Mellbin LG et al.,2019). Insulin resistance is commonly associated with the development of T2DM and CVD (James et al 2021). Dyslipidemia is described as the presence of abnormal blood concentrations of one or more of the following: Triglycerides, total cholesterol, low-density lipoprotein cholesterol (LDL), and high-density lipoprotein cholesterol (HDL) (AL-Bahrani et al.,2022). IL-34 was found to be positively and strongly connected not simply with adiposity metrics (such as BMI and abdominal fat areas), but also with insulin resistance and chronic inflammatory markers (Lin H et al 2008).

CHEMICALS AND METHODS

Subject

Patients: The current study included 60 Arab Iraqi patients with T2DM, 27 of whom were men and 33 of whom were women. They were 57.1± 8.81 years old on average, and their BMI was 29.04 ± 4.42 (kg/m²). Fasting blood glucose (FBG) was 266.24 mg/dl., and the HbA1c level was 8.72%. The "Al-Najaf Hospital" in the Iraqi city of Najaf registered these patients between September 2022 and January 2023. Clinical signs, symptoms, and biochemical testing were used for each patient to determine their diagnosis of diabetes mellitus. The current study excluded

patients with any illnesses, inflammation, or cardiac problems.

Controls

Thirty individuals, 13 men and 17 women, who appeared to be in good health, were selected. They were around the same age as the patients, and their average BMI was 28.45 ±5.43. How FBG operates. The means of FBG and HbA1c were 98.33±5.6 mg/dl, 5.54±0.59, respectively. Any individual was suffering from a chronic, systemic diseases and anemic were excluded.

Biochemical Research

Based on medical history, current medication use, or both, diabetes was discovered and diagnosed in accordance with American Diabetes Association (ADA) criteria (ADA, 2016). An HbA1c of 6.5% or an FBG of less than 126 mg/dl (or 7.1 mmol/L) were used to define T2DM (ADA, 2016). Self-reported hypertension is presently treated with antihypertensive medication. The World Health Organization classifies body mass index (BMI). The measures of height and weight were taken in accordance with WHO standards, and the BMI was calculated using the formula (height/weight) (kg/m²). Healthy adults had a BMI between 18 and 25, whereas obese people were defined as having a BMI more than 30 kg/m². Each patient gave consent control person. The blood was divided using two gel tubes and two anticoagulant tubes. The blood in the gel tube was centrifuged for 5 minutes at 3000 Xg to separate the serum, which was then placed into brand-new, disposable tubes after 15 minutes at room temperature for clotting.

Instruments for Experimentation

TABLE 1: Laboratory equipment.

| Instruments | Company | Origin |
|------------------------|-----------|---------|
| Centrifuge | Hettich | Germany |
| Deep freezer | Hitachi | Japan |
| ELIA Microplate reader | BioTek | USA |
| Gel tube made of glass | Q.L.lab | China |
| Micropipette | Dragon | China |
| Refrigerator | Hitachi | Japan |
| Spectrophotometer | Spetra721 | Taiwan |
| Water bath | Hettich | Germany |

Chemicals

TABLE 2: shows the chemicals and kits.

| Type of Kits | Company/Country |
|---------------|-----------------|
| Blood Glucose | Spinreact/Spain |
| CRP | LTD/Britain |
| HbA1c | BT LAB/ China |
| HDL-c | Biolabo/ France |
| Triglyceride | Biolabo/ France |
| T.cholesterol | Biolabo/ France |
| IL-34 | Biolabo/ France |

Statistical

A pupil T- test was used to estimate variations in scale variables between individual orders, and a contingency table analysis(2- test) was performed to examine connections between nominal variables. The p- value arrestment for statistical significance for all 2- tagged tests was set at 0.05. Using IBM SPSS Windows interpretation 26, 2017, all statistical analyses

were carried out. Results and Discussion
1- Comparison Between T2DM and Control

RESULTS AND DISCUSSION

1-Lipid profile

Table 3 shows the results of lipid profile variables in T2DM patients and healthy controls.

TABLE 3: Lipid profile parameters in healthy as well as the T2DM patients:\

| Parameters | (60) Patients Mean±SD | (30)Controls Mean±SD | p-value |
|--------------------------------------|--------------------------|----------------------|---------|
| TC mg/dl | 286.85±42.43 | 159.06±2.32 | <0.0001 |
| TG mg/dl | 248.13±45.68 | 151.31±23.57 | <0.0001 |
| HDL-c mg/dl | 46.49±7.31 | 41.73±5.8 | 0.0001 |
| VLDL-c mg/dl | 49.73±9.24 | 30.37±4.83 | <0.0001 |
| LDL-c mg/dl | 191.86±36.13 | 88.34±13.48 | <0.0001 |
| TG/HDL | 5.72±1.57 | 3.86±0.64 | <0.0001 |
| TyG mg ² /dl ² | 10.28±0.39 | 8.90±0.28 | <0.0001 |
| GHR | 5.61±1.57 | 3.75±0.67 | <0.0001 |

TC stands for total cholesterol, while TG stands for triglyceride. HDL-c stands for high density lipoprotein cholesterol, VLDL-c stands for very low density lipoprotein cholesterol, and LDL-c stands for low density lipoprotein cholesterol, TyG: triglyceride-glucose index and GHR: fasting blood glucose/high-density lipoprotein cholesterol ratio.

There was a significant increase in serum TC, TG, HDL-c, VLDL-c, LDL-c, TG/HDL and TyG in T2DM patients are compared with controls. Diabetic dyslipidemia is frequently characterized by high TC, high TG, low HDL cholesterol, and an increase in LDL (Santos-Gallego CG et al., 2014). Because of the interdependence between carbs and lipid metabolism in diabetes, several factors can alter blood lipid levels. As a result, any disruption in

glucose metabolism leads to disruption in lipid metabolism, and vice versa. Insulin resistance is the primary defect in the majority of T2DM patients (Haffner SM et al., 2000). It is now widely acknowledged that dyslipidemia is linked to type 2 diabetes. Patients with T2DM frequently have atherogenic dyslipidemia and obesity, which raises their risk of coronary artery disease. Elevated TG, low LDL-C, and TG/HDL, a measure of tiny dense LDL particle, have all

been linked to the development of cardiovascular disease in diabetes (Dobiášová M et al., 2001). Although most cases of dyslipidemia have a hereditary basis, environmental factors such as nutrition, exercise, and smoking behaviors can also play a part in the disease's development and progression. LDL cholesterol is atherogenic, and it is associated with an increased risk of atherosclerosis and its consequences (Garvey WT et al., 2003). Diabetic patients with comorbid (but often undiagnosed) dyslipidemia are easy targets for cardiovascular disease. Patients with T2DM frequently have an atherogenic lipid profile, which raises their risk of cardiovascular disease (CVD) significantly when compared to people without diabetes. It has been demonstrated that early management to regulate circulating lipids reduces cardiovascular problems and mortality. Adults with diabetes are two to four times more likely than adults without diabetes to die from cardiac disease (American cardiac Association, 2019). The HDL level is substantially and independently connected with cardiovascular disease, although the association is inverted, with lower HDL levels being an essential indicator of cardiovascular illness and higher levels of HDL guarding against coronary heart disease. These observations led to the conclusion that HDL plays a role as an acceptor of cellular free cholesterol, it plays a function in

reverse cholesterol transfer. Diabetes dyslipidemia is distinguished by hypertriglyceridemia and low HDL values (Jedda et al., 2021). Hypertriglyceridemia predisposes patients to life-threatening consequences such as diabetic ketoacidosis and coronary artery disease (Oh, R. and Lanier et al., 2007). Diabetes, which is more common in diabetics than in non-diabetics, causes an increase in VLDL triglycerides (Aljabri et al., 2016). However, lipid profiles and related ratios such as (FBG/HDL-C) ratios which called glucose , HDL ratio (GHR) Various studies have been conducted to assess their usefulness in determining the severity and mortality of diseases (Guo Q. Q et al.,2020). According to research The TyG index was an excellent predictor of insulin resistance as well as glycemic management. According to Fernando et al., the TyG index was found to be significantly related to HOMA-IR and the euglycemic-hyperinsulinemic clamp test for identifying insulin resistance (Guerrero-Romero F et al.,2010).

1-2-Interlukine-34

Serum levels of IL-34 are significantly higher ($p=0.0156$) in T2DM patients than controls.

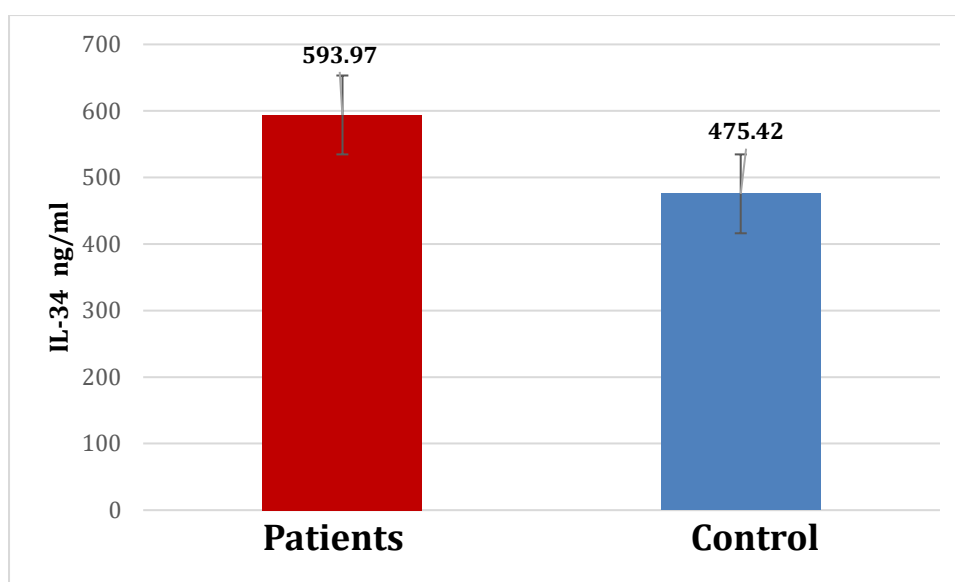


FIGURE 1: IL-34 levels in T2DM patients and controls.

Many pro-inflammatory cytokines such as IL-34 have been linked to an increased risk of T2DM via increasing insulin resistance (Hu FB et al 2004). IL-34 is expressed in adipose tissue, and its circulating level has been found to be considerably higher in obese patients (Chang et al 2014). Inflammation and insulin resistance are widespread in a variety of chronic conditions, including type 2 diabetes (Piya MK et al.,2013). Chronic low-grade systemic inflammation is a major contributor to T2DM progression and the development of micro- and macrovascular problems (Seijkens T et al., 2013). Low-grade systemic inflammation is also thought to play a role in insulin resistance, T2DM, steatosis, and cardiovascular disease (Piya MK et al.,2013). Another study on pregnant diabetes mellitus women discovered that In either maternal or cord blood from gestational diabetes mellitus patients, IL-34 concentrations were positively associated with blood glucose levels and insulin resistance (Piao C et al.,2019). Mouse pancreatic β -cells exposed to high glucose levels produced more IL-34, which inhibited insulin release (Mostafa et al.,2021).

CONCLUSION

Increase lipids in T2DM causes many complications such as CVD. IL-34 is a pro-inflammatory cytokine. Elevated this interleukin in patients with T2DM may indicate that patients have a risk of inflammation. Dyslipidemia and inflammation leading to many complications such as CVD.

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