Leptin and other Biochemical Investigations in the Serum of Type 2 Diabetes Mellitus Patients

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Abstract: Type 2 diabetes mellitus (T2DM) is a chronic metabolic disease characterized by hyperglycemia and insulin resistance, and serious health consequences can be developed from T2DM such as in the eye (diabetic retinopathy), the renal (diabetic nephropathy), the cardiovascular system (hypertension), etc. Leptin is one of the regulators that released by the adipose tissue, which involved in mediating inflammatory processes, and related to oxidative stress. This article was made to examine the level of leptin in T2DM patients and its association with lipid profile and glycaemia status in T2DM patients. Also, the possibility of using leptin in the prognosis of T2DM was investigated. The study was included 60 T2DM patients and 30 normal glycemic non-diabetic control. The results have shown a significant high levels of serum leptin, glucose, HbA1c, triglycerides, and cholesterol in T2DM patients with significant low level of high-density lipoprotein, when compared to control. Leptin has shown to be involved in the pathophysiology of type 2 diabetes mellitus. The T2DM patients were contained a significant high levels of leptin in their serum compared to the normal glycemic people without T2DM disease. Furthermore, leptin was correlated significantly with the percentage of HbA1c in T2DM patients, which indicates a major part of influence between leptin and insulin resistance development in T2DM patients. Moreover, lipids were altered significantly in T2DM patients, but the results have revealed no significant involvement of leptin with this alteration. Based on these findings, we suggest the use of leptin in the prognosis of risks in T2DM patients.

Keywords: T2DM, leptin, HbA1c, lipid profile.

1. Introduction

T2DM (type 2 diabetes mellitus) is a chronic metabolic disorder with an increasing global prevalence [1]. T2DM (non-insulin dependent diabetes) is the most common type of diabetes, including hyperglycemia, insulin resistance, and insulin insufficiency [2]. T2DM [3, 4] is caused by the interaction of genetic, environmental, and behavioral risk factors. People with T2DM are more prone to a wide range of short- and long-term issues, which can lead to premature death. Patients with T2DM have a higher risk of morbidity as well as mortality because of the disease's prevalence, gradual onset, and late detection, particularly in resource-poor developing countries like Africa [5].

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T2DM is defined by aberrant glucose, lipid, as well as protein metabolism, which can be caused by insulin resistance, reduced insulin production, or a combination of the two. Among the three major types of diabetes, T2DM is substantially more popular than type 1 diabetes mellitus (T1DM) or gestational diabetes (accounting for more than 90% of all cases) [6]. Overt hyperglycemia comes before prediabetes [7, 8], a high-risk syndrome that predisposes people to T2DM. Symptoms of prediabetes include impaired fasting glucose (IFG), impaired glucose tolerance (IGT), and high glycated hemoglobin A1c (HbA1c) values [9, 10]. Individuals with IFG levels have higher-than-normal fasting plasma glucose levels but do not meet the diagnostic criteria for diabetes. IGT is defined by muscular insulin resistance as well as delayed (second-phase) insulin release after a meal, whereas IFG is defined with hepatic insulin resistance as well as delayed (first-phase) insulin release [8].
Leptin is largely produced by adipocytes and released in a diurnal pulsatile manner from small vesicles within adipocytes, with greater rates in the evening as well as early morning. Although leptin secretion is unaffected by its mRNA regulation [11], increased leptin mRNA transcription is required to maintain steady rates of leptin secretion as well as avoid rapid depletion of leptin vesicle reserves [12]. Leptin circulates in the serum in the both free as well as bound forms after it is secreted [13]. Obesity has been linked to changes in adiponectin as well as leptin levels [14-16]. Adiponectin as well as leptin level in T2DM patients are more linked with the obesity as well as less with the xdiabetes, according to a recent study by our group [17]. In fact, increased adiponectin levels have been linked to a decreased risk of T2DM [18]. This article was made to examine the level of leptin in T2DM patients as well as its association with lipid profile also glycaemia status in T2DM patients. Also, the possibility of using leptin in the prognosis of T2DM was investigated.

2. Materials and Methods

2.1. Patients

The T2DM patients were documented in the consultancy of Al-Yarmook Teaching Hospital (Baghdad, Iraq). They were informed about the standard criteria of the research and agreed to become a volunteers in this work. 60 patients with T2DM were selected for the study from January to April 2022, and controlled with 30 healthy volunteered people. The subjects were in equal gender distribution in each group.

2.2. Methods

The T2DM patients and healthy control people were donated a vein blood. The blood then centrifuged in a medical centrifuge (4000 rpm for 10 minutes), and the serum was kept in a deep freezing at -20 °C to be analyzed for glucose, triglycerides (TGs), cholesterol, and HDL in a spectrophotometric method (Apel PD-303, Japan) by using commercial kits from Linear, Spain. The level of glycated hemoglobin was determined in the blood by cobas c111, while the level of leptin was determined by using sandwich ELISA kit from My BioSource (USA).

2.3. Statistics

The data were processed statistically on the computer by a program from IBM called SPSS version 26.0, for mean comparisons in an independent sample t-test, and the relationship between leptin and other parameters were calculated according to the Pearson correlation. At last, the sensitivity of leptin as diagnostic markers for T2DM disease was determined by the receiver operating characteristic (ROC) curve through calculating the area under a curve (AUC).

3. Results

The characteristics of the volunteered people are contained in Table 1. Age was shown non-significant (P>0.05) differences between the T2DM patients (44.95±10.21 year) and control people (43.60±9.69 year). Also, the body mass index (BMI) was significantly higher (P>0.05) in T2DM patients (26.71±2.67 kg/m^2) in the comparison to the control people (23.97±1.83 kg/m^2). Glucose was significantly elevated in the serum of T2DM patients (207.53±21.64 mg/dL) compared to control people (99.10±5.30 mg/dL). Furthermore, the HbA1c level was also significantly higher in T2DM (8.74±0.92 %) compared to control (5.48±0.42 %).

Table 1: Volunteered people characteristics.

Parameter	**T2DM**	**Control**	***P*-value**
N	60	30	-
Age (year)	43.60±9.69	44.95±10.21	0.534
BMI (kg.m^{-2})	23.97±1.83	26.71±2.67	0.0001
Glucose (mg/dL)	99.10±5.30	207.53±21.64	0.0001
HbA1c (%)	5.48±0.42	8.74±0.92	0.0001
Leptin (ng/mL)	4.82±2.66	15.46±3.89	0.0001
TGs (mg/dL)	103.73±14.97	173.82±39.81	0.0001
Cholesterol (mg/dL)	150.47±17.04	166.60±24.36	0.0001
HDL (mg/dL)	54.77±16.14	39.10±7.13	0.0001

Table 2: Correlation of leptin in T2DM patients.

Parameter	**Leptin (ng/mL)**	
	r	*p*-value
Age (year)	-0.062	0.637
BMI (kg.m^{-2})	0.084	0.525
Glucose (mg/dl)	0.192	0.142
HbA1c (%)	0.619	0.0001
TGs (mg/dl)	-0.199	0.128
Cholesterol (mg/dl)	-0.015	0.128
HDL (mg/dl)	0.071	0.591

The levels of leptin were significantly (P<0.05) elevated in serum of T2DM patients (15.46±3.89 ng/mL) compared to the serum of control people (4.82±2.66 ng/mL). Also, the levels of TGs were significantly (P<0.05) increased in serum of T2DM patients

(173.82±39.81 mg/dl) compared to the serum of healthy control (103.73±14.97 mg/dl). Cholesterol level was significantly elevated in T2DM patients (166.60±24.36 mg/dl) compared to control (150.47±17.04 mg/dl). While, the levels of HDL was significantly (P<0.05) lower in serum of T2DM patients (39.10±7.13 mg/dl) compared to the serum of control people (54.77±16.14 mg/dl).

The results have shown significant positive association between leptin and glycated hemoglobin in the blood of T2DM patients, as shown in Table 2.

The ROC curve of leptin has indicated the usefulness of this biomarker in the diagnosis of T2DM disease. Leptin has shown excellent sensitivity (AUC = 0.989, P<0.0001) in the diagnosis of T2DM patients comparing to the healthy controls, as shown in Figure 1.

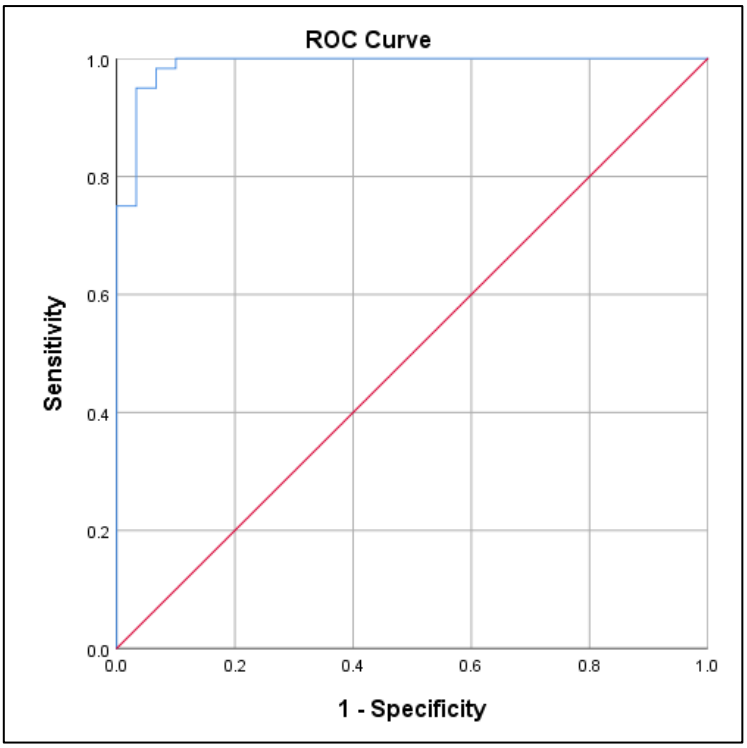

Figure 1: The ROC curve of leptin in the diagnosis of T2DM disease.

4. Discussion

The study was involved the examination of leptin levels between T2DM patients and control, as investigated the relationship of leptin with glycemic profile, and lipid profile in these patients. Leptin level was significantly elevated in the serum of T2DM patients. Moonishaa *et al.* have reported a significant increase in the level of serum leptin in T2DM patients. The researchers concluded that hyperleptinemia, which reflects leptin resistance, play a key role in a development of insulin resistance in obese T2DM patients, forming leptin a potential biomarker [19]. Another agreement was found with the study of Coimbra *et al.* who reported a significant higher levels of leptin in T2DM elder patients compared to non-diabetic elders [20]. Katsiki *et al.* have linked the elevated levels of leptin in T2DM patients to the increase of cardiovascular complications [21]. Sari *et al.* have reported that serum leptin level in

T2DM is associated with the onset of several health consequences including, obesity, dyslipidemia, hypertension, and metabolic diseases [22].
T2DM patients have shown significant alterations in the levels of lipid profile parameters. Ozder has reported that poor glycemic controlled T2DM patients have shown significant higher levels of TGs and cholesterol, with significant low level of HDL [23]. Other studies were reported similar results [24-26]. Furthermore, leptin was not associated with lipid profile in T2DM patients, nevertheless, In T2DM patients, there was a substantial correlation between leptin as well as HbA1c percentage. This association may indicate a role of leptin in the development of insulin resistance or Vis versa.

5. Conclusions

Leptin has shown to be involved in the pathophysiology of type 2 diabetes mellitus. The T2DM patients were contained a significant high levels of leptin in their serum compared to the normal glycemic people without T2DM disease. Furthermore, leptin was correlated significantly with percentage of HbA1c in T2DM patient, which indicates a major part of influence between leptin and insulin resistance development in T2DM patients. Moreover, lipids were altered significantly in T2DM patients, but the results have revealed no significant involvement of leptin with this alteration. Based on these findings, we suggest the use of leptin in prognosis of risks in T2DM patient.

6. Highlights

The study found high levels of leptin, glucose, HbA1c, triglycerides, and cholesterol in T2DM patients. Leptin was significantly correlated with HbA1c, indicating its involvement in insulin resistance development. Leptin may be useful in the prognosis of T2DM risks.

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