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FULL PAPER

The role of Irisin level hormone and some biochemical parameters in Iraqi diabetic type 2 with hypothyroidism

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The study aimed to determine the values of the created serum irisin, which plays in hypothyroid patients with type 2 diabetes. In this research, based on the inclusion and exclusion criteria, a total of 60 patients with type 2 diabetes patients with hypothyroidism were chosen as the case group, with a 1:1 ratio which was determined based on the patients' inclusion rate. The adults in the age range of 30 to 60 were included in this cohort, which was formed at the Medical City/ Baghdad Teaching Hospital. A control group of 60 healthy volunteers of the same gender and age served as the study's control group. The clinical data was collected on the participants to determine their medical history, hemoglobin (HbA1c), serum hormones T3, T4, TSH, serum AST, ALT, and serum lipids. An enzyme-linked immunosorbent test was used to measure the amount of irisin of the blood (ELISA). The data was analyzed using SPSS 23.0 software and compared between both groups. In total, the single factor analysis revealed that the level of irisin in the T2DM with the hypothyroidism group was significantly greater than in the control group (14.445±3.008 ng/mL vs. 4.121±0.308 ng/mL). The T2DM with hypothyroidism group had higher levels of HbA1c, serum hormone TSH, serum AST, ALT, total cholesterol (TC), and triglyceride (TG) than the control group. The blood irisin levels were greater in the T2DM with Hypothyroidism group than in the control group.

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KEYWORDS

Irisin; diabetes mellitus type 2 with hypothyroidism.

Introduction

Diabetes mellitus (DM) is a chronic endocrine disease defined by hyperglycemia, which occurs as a result of the inadequate pancreatic insulin output or insulin sensitivity throughout the body, or both [1]. Thyroid hormones are important regulators of the basal metabolic rate and thermogenesis, which are both likely to be influenced by irisin. Irisin could also be interfering with thyroid function. Thyroid hormones communicate via the central and peripheral channels that impact energy consumption [2]. Irisin is one of the newest myokines described by [3,4,5] and secreted by cardiomyocytes as well as a small amount is further distributed in adipose tissue, brain, liver, spleen, testis, and other tissue [6]. The kidney, liver, and lung also contain irisin in low levels [7]. Likewise, it is present in human cerebrospinal fluid (CSF), although its role in the brain is largely unknown [8]. Thyroid hormones have a considerable impact on the metabolic status of the human body; they can regulate both obligatory and facultative thermogenesis and

have an impact on the cardiovascular system. Because thyroid hormones and irisin have similar physiological functions and potential linkages, it is fair to infer that serum irisin levels may be impacted in thyroid dysfunction circumstances [9]. Thyroid hormone was discovered to be capable of generating browning of white fat via thyroid hormone receptors (TRs), which was followed by an increase in uncoupling protein 1 synthesis (UCP1). Furthermore, numerous investigations have discovered that irisin has a significant influence on metabolism by stimulating browning of subcutaneous white adipocytes via increased UCP1 expression, which leads to increase oxygen consumption and thermogenesis [2,10]. While a few studies have been conducted to investigate the association between circulating irisin and low thyroid hormone levels in hypothyroid individuals, the results have been mixed, with no unambiguous conclusions [11]. It is likely that irisin levels change based on the thyrometabolic state, depending on how irisin and thyroid hormones interact. One of the studies was especially useful because it used multiple thyroid models in both sedentary and active conditions. Doubtless, further research on irisin physiology, particularly its physiological modulation, is needed in the near future. Despite its significance related to the oxidative stress, serum irisin was not connected to TSH, skeletal muscle mass, or metabolic variables such blood glucose or lipids [12]. The aim of our study is to demonstrate a link between irisin levels and thyroid hormone levels.

Materials and methods

Subjects

A total of 60 patients T2DM with hypothyroidism were chosen as the study group ranging in the age range of 30 to 60 years. All subjects (47.6±9.191years old) were recruited from a single neighborhood in the Medical City / Baghdad Teaching Hospital, and all were supplied by verbal informed consent. The healthy cohort members of the same sex and age were randomly chosen as the control group in a 1:1 ratio (47.16±10.48 years old). The control group did not have diabetes, hypertension, hyperlipidemia, or obesity. The Research Ethics Committee at our hospital approved this project.

Collection of clinical data

The physical examination data of all individuals were acquired. Their general condition, medical history, height, and weight were all reported. The following formula was used to calculate body mass index (BMI): Body mass index (BMI) = body weight (kg) divided by height (m^2) squared (kg/m^2). The peripheral blood was collected from each subject's cubical vein in the early morning (fasting and without exercise for more than 8 hours). Some were used to measure hemoglobin (HbA1c), serum hormones T3, T4, TSH, serum AST, ALT, and blood lipids (the total cholesterol (CHOL), and triglyceride (TG)). The serum samples were further maintained at room temperature for 2 hours before centrifugation to reduce the adhesion between red blood cells and serum, and also decrease the hemolysis incidence during centrifugation. The upper serum was put in an eppendorf (EP) tube and stored at -8 °C in a freezer for irisin level testing.

Detection of serum irisin level by enzyme-linked immunosorbent assay (ELISA)

A human ELISA kit (Sandwich) obtained from Sino Best Biological Technology Co., Ltd. was used to determine serum irisin levels. Human irisin has been proven to be particularly sensitive to this kit. The sensitivity was measured at 0.1 ng/mL.

Statistical analysis

For data analysis, SPSS 23.0 statistical software was employed. The mean standard

deviation was used to calculate data (SD). To do univariate analysis, T-tests were used in order to examine the continuous variables; P≤ 0.05 was considered statistically significant [13].

Results and discussion

The levels of irisin and clinical indices in the T2DM and control groups were compared. The irisin level in T2DM with hypothyroidism was greater than in the control group (14.445±3.008 ng/mL vs. 4.121±0.308 ng/mL, respectively) and the difference was statistically significant. The T2DM group had significantly higher HbA1C, serum hormone T3, T4, TSH, serum AST, ALT, total cholesterol (TC), and triglyceride (TG) levels than the control group (P ≤0.05 for each comparison) (Table 1).

TABLE 1 The comparison of Irisin level and clinical indices between T2DMwith hypothyroidism group

Groups	NO. of Diabetes & hypothyroidism	NO. of Control	P-value
Irisin (ng/mL)	14.445±3.008	4.121±0.308	0.000 (H. S)
HbA1c (%)	8.347±1.820	5.773±0.509	0.000 (H. S)
T3 ng/ml	0.974±0.240	1.154±0.244	0.000 (H. S)
T4 ng/ml	7.465±2.229	8.316±1.323	0.012 (S)
TSH µIU/ml	10.088±4.260	2.031±0.883	0.000 (H. S)
AST mg/dl	29.145±9.267	27.2±8.1006	0.223 (N.S)
ALT mg/dl	28.481±9.319	27.4± 4.134	0.000 (H. S)
TC (mmol/L)	173.05±34.508	156.03±45.167	0.022 (S)
TG (mmol/L)	144.933±51.132	120.616±46.937	0.000 (H. S)

S = significant difference (P ≤ 0.05), H.S = high significant difference (P ≤ 0.001), N.S = non significant difference (P ≥ 0.05).

The most significant roles of irisin include browning of white adipocytes [14]. Although this function is believed to be the main factor controlling the release of irisin, the other studies found that this relationship is not consistent. Moreover, the other factors were found to influence both FNDC5 expression and irisin secretion such as obesity, drugs, lipid profile, and diseases [15].

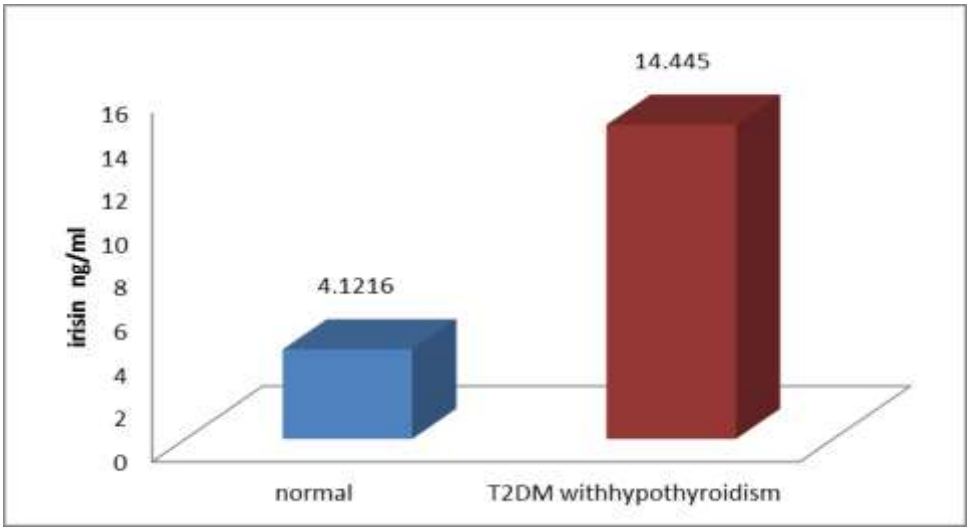

FIGURE 1 The comparison between different groups related to irisin

In the current investigation, we discovered that circulating irisin levels were considerably higher in T2DM with hypothyroidism participants than in the non-diabetic controls, as displayed in Figure 1. In this study, there was a positive relationship between irisin and HbA1C, as well as a positive relationship between irisin and AST and AIT. Despite a favorable relationship between serum irisin and total cholesterol, there was a negative relationship between irisin and TG, T3, T4, and TSH (Table 2).

TABLE 2 Correlation of irisin level between T2DM with hypothyroidism patient and all parameters study

No	Factor	r	p-value	Interpretation
1	HbA1c	0.175	0.180(N.S)	Weak positive correlation
2	T3	-0.233	0.073(N.S)	Weak negative correlation
3	T4	-0.027	0.840(N.S)	Weak negative correlation
4	TSH	-0.244	0.061(N.S)	Weak negative correlation
5	AST	0.234	0.072(N.S)	Weak positive correlation
6	ALT	0.321	0.012(S)	Weak positive correlation
7	TC	0.066	0.617(N.S)	Weak positive correlation
8	TG	-0.172	0.189(N.S)	Weak negative correlation

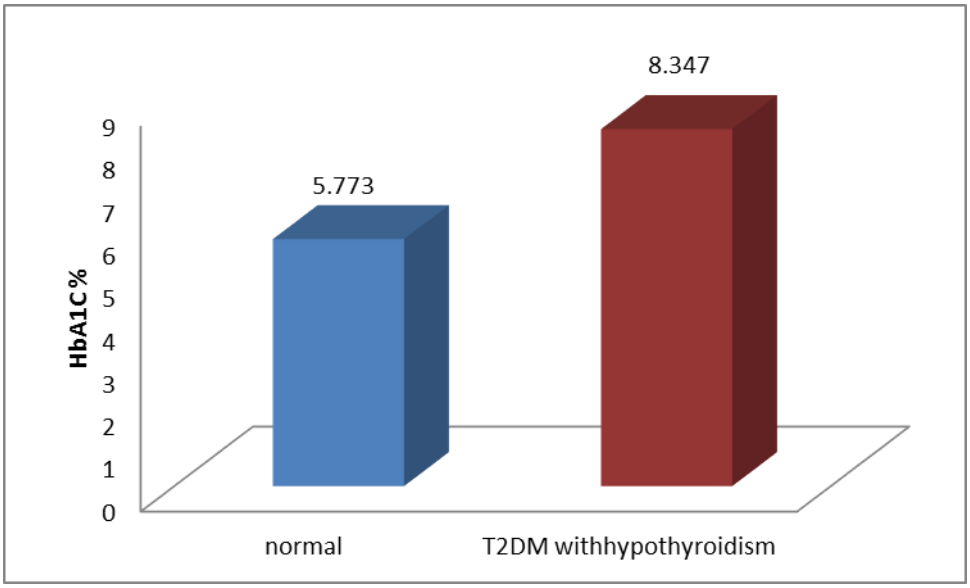

FIGURE 2 The comparison between different groups related to HbA1C

As illustrated in Figure 2, it is visible that HbA1C is higher in hypothyroidism patients and diabetics compared to the controls. The HbA1c results in this study are further consistent with the findings of a study conducted in [16] which found that the level of glycated haemoglobin was considerably greater in patients with T2DM who had thyroid issues. The increase in HbA1c levels in this study indicates that persons with diabetes have impaired blood glucose management. Furthermore, this study agreed with [17] when hypothyroidism was compared to the controls, there was a substantial increase in HbA1c values. Thyroid hormones are insulin antagonists which indirectly influence insulin activity.

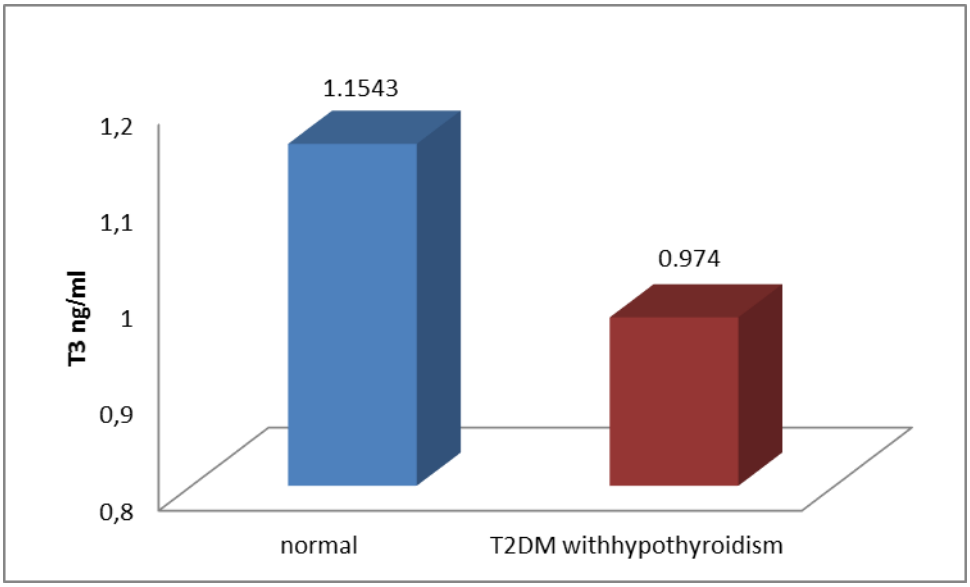

FIGURE 3 The comparison between different groups related to T3

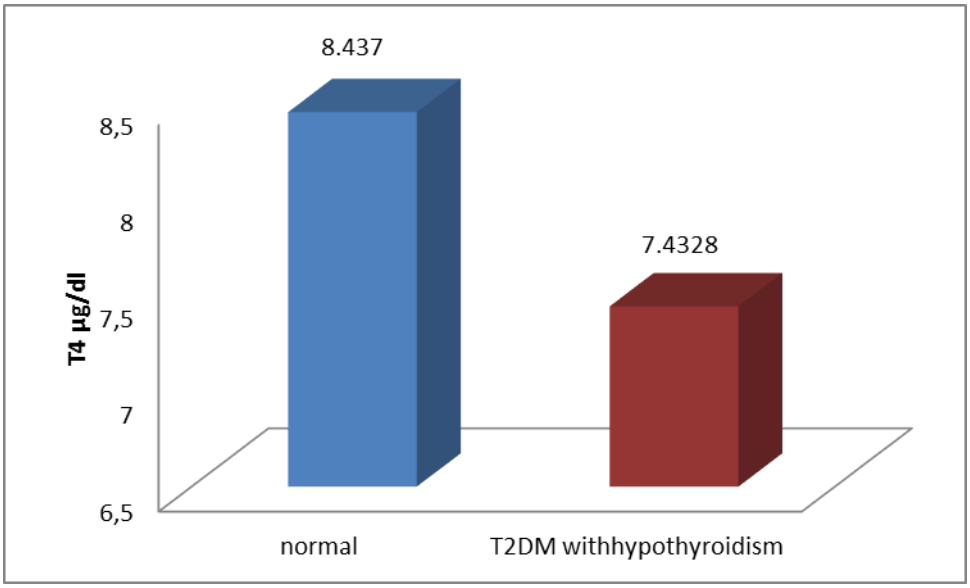

FIGURE 4 The comparison between different groups related to T4

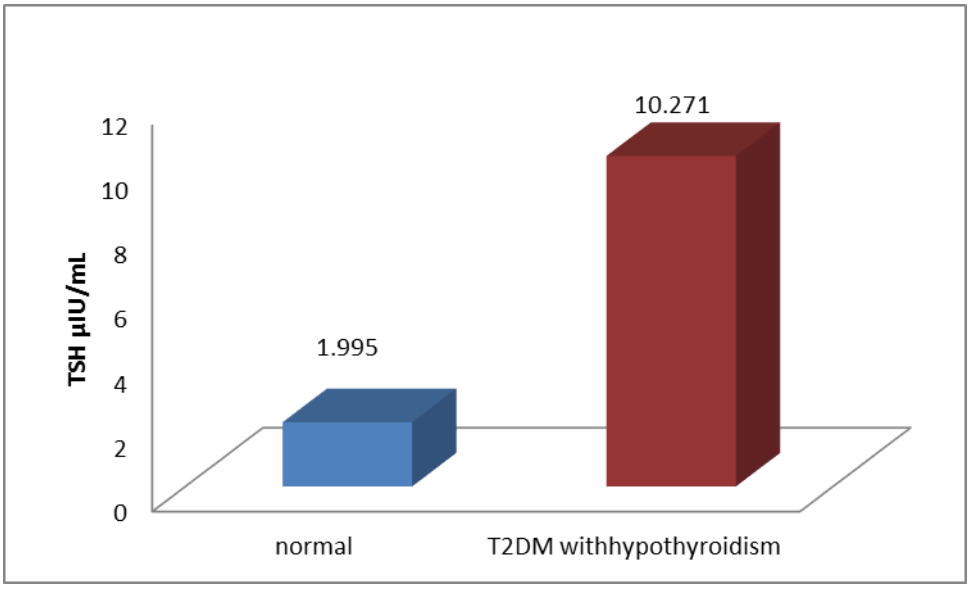

FIGURE 5 The comparison between different groups related to TSH

It is not unusual for patients with hypothyroidism to have lower T3 and T4 levels than those who are normal, as depicted in Figures 3 and 4. Based on the glycemic condition of the studied diabetics, the existence of both high and low levels of thyroid hormones in diabetics can be attributed to change TRH production and release [18]. Thyroid hormone levels in diabetes people may be altered due to treatment. Insulin is an anabolic hormone that raises T4 levels while decreasing T3 levels by preventing hepatic conversion of T3 to T4. This finding is consistent with the previous research by [19]. The findings of this study revealed an increase in TSH levels and a decrease in T3 and T4 levels in diabetics with hypothyroidism compared to the healthy control groups and all of these hormones have implications on glucose homeostasis regulation [20]. Through our study, the higher levels in patients with diabetes and hypothyroidism were vivid, as demonstrated in Figure 5.

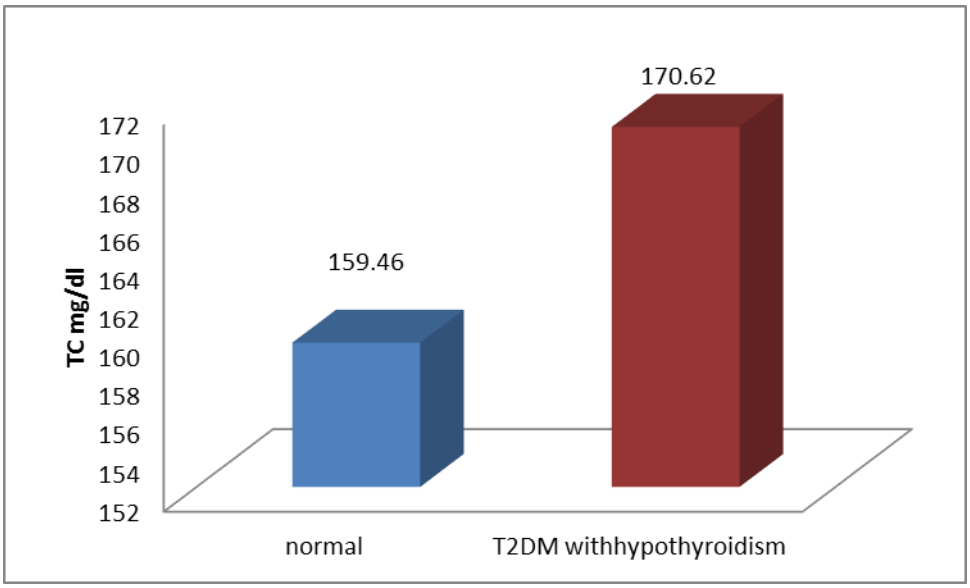

FIGURE 6 The comparison between different groups related to (TC) total cholesterol

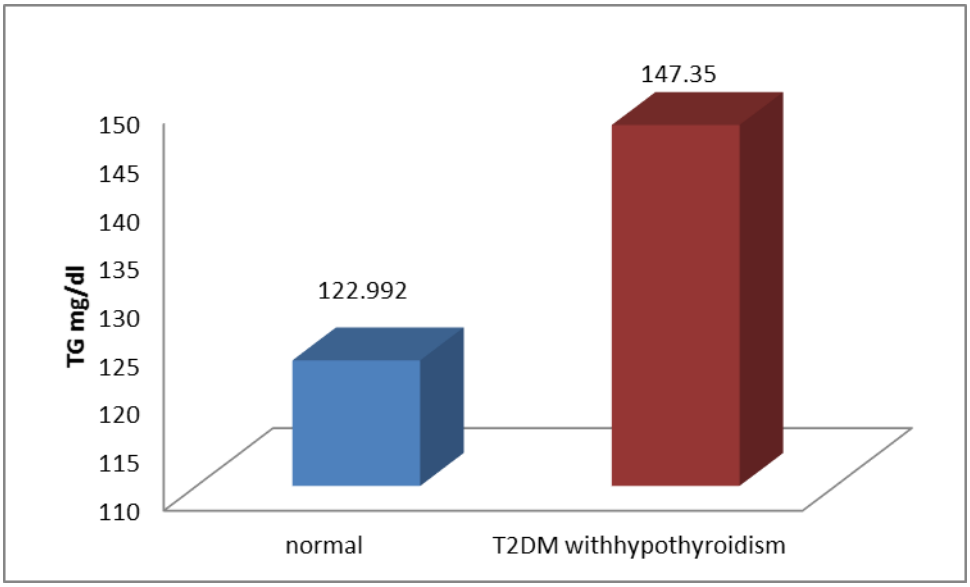

FIGURE 7 The comparison between different groups related to (TG) triglyceride

Thyroid hormones further increase lipoprotein lipase, which catabolizes hepatic lipase and TG-rich lipoproteins. Furthermore, in overt hypothyroidism, there is a decrease in lipoprotein lipase activity, which reduces clearance of TG-rich lipoproteins. As a result, the overt hypothyroid individuals may have elevated TG concentrations [21]. The umbrella diabetes with hypothyroidism group can be observed in Figures 6 and 7 that they have higher total cholesterol and T.G, and because this group are under the umbrella of metabolic syndrome in comparison to the normal population. Regarding the faulty metabolism, hypothyroidism, and diabetes are more prevalent than in the general population. Diabetes and thyroid disorders are linked to dyslipidemia, and many patients with these diseases have uncontrolled dislipidemia. The current study's findings were consistent with those of [22]. They discovered that the mean total (TC) levels in hypothyroidism were higher than in controls. The current study findings matched with those of [23], who discovered significantly higher TG values in hypothyroidism patients compared to the normal thyroid group.

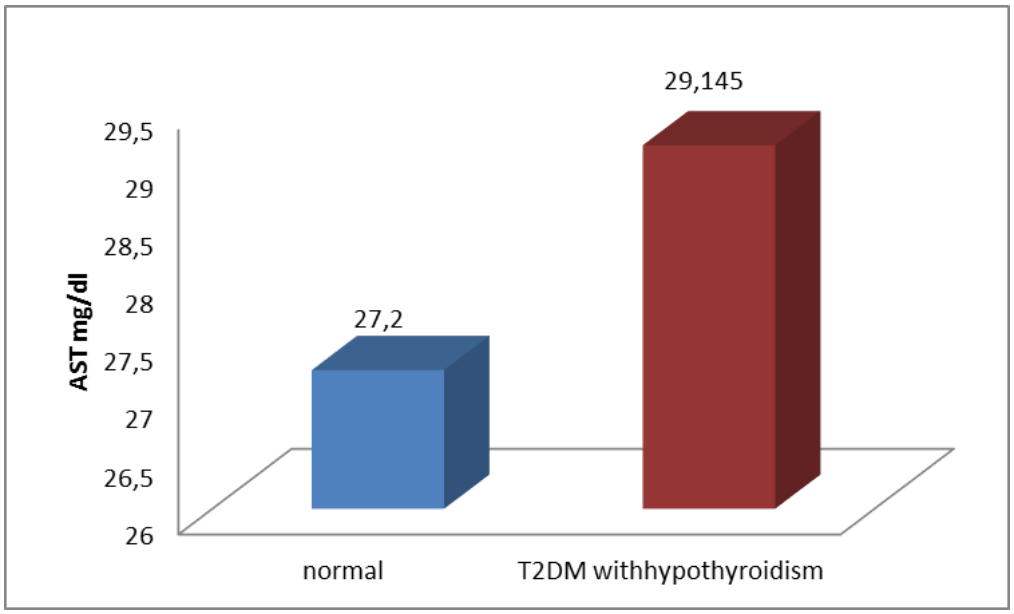

FIGURE 8 The comparison between different groups related to AST

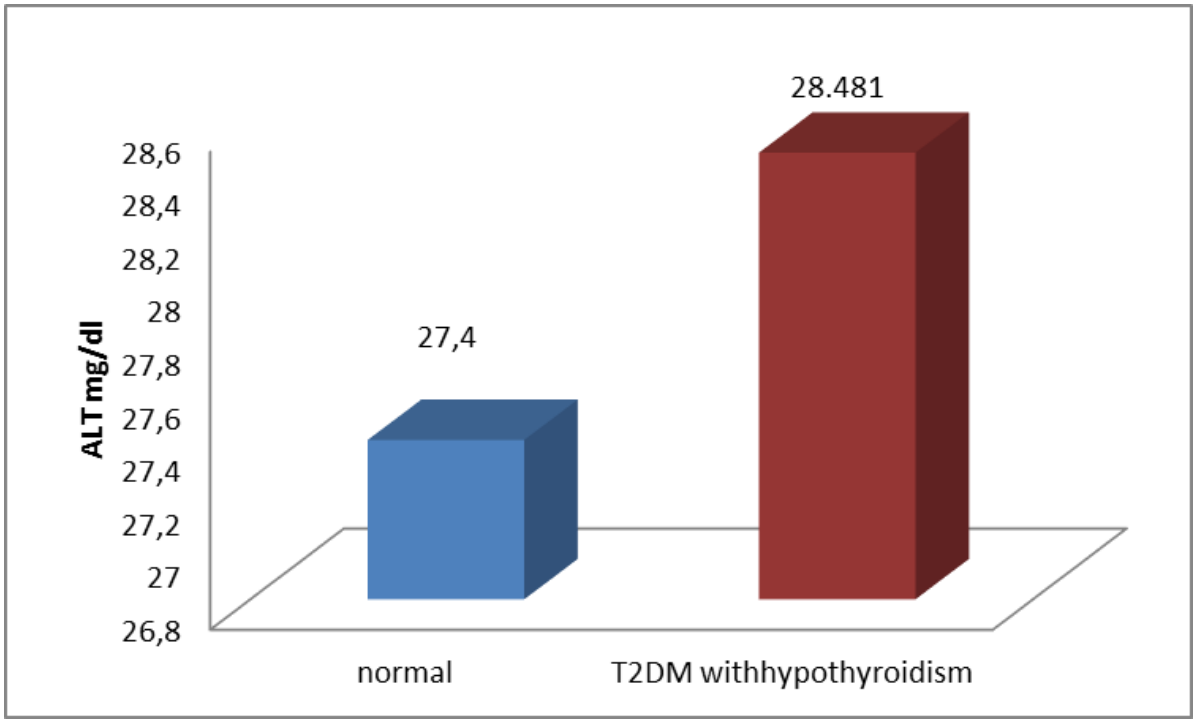

FIGURE 9 The comparison between different groups related to ALT

In the current investigation, we discovered that circulating AST, ALT levels were considerably higher in T2DM with hypothyroidism participants than in non-diabetic controls, as displayed in Figures 8 and 9. This finding further agrees with a study according to [24]. Moreover, serum ALT and AST levels were used to assess liver function in the current investigation. When individuals with metabolic syndrome and type 2 diabetes mellitus were compared to the controls, the serum ALT and AST levels were found to be considerably higher.

Conclusion

1. Type 2 diabetes mellitus can be affected by the degree of hypothyroidism.
2. The serum irisin level was noticeable increased in T2DM patients with hypothyroidism compared to controls.
3. The level of (TSH) increases in patient with hypothyroidism.
4. Both (T3 and T4) decrease in patient T2DM with hypothyroidism compared to the controls.
5. The level of (HBA1C) increases in patient T2DM with hypothyroidism compared to the controls.
6. The level of (AST and ALT) increases in patient T2DM with hypothyroidism compared with those with controls.
7. The serum TC and TG increased significantly in T2DM patients with hypothyroidism compared to the controls.

Suggestions for future studies

1- Evaluation the potential role of irisin based pharmacotherapies.
2- Assessment of the role of serum irisin in T1DM.
3- Study the irisin level in T2DM with and without hypothroidism in the age range of 60 and above.

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