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Relationships among asprosin, leptin, and other biomarkers in diabetic patients with hypothyroidism or hyperthyroidism

Mohammed H. Shaheed [1], Shaimaa Imad Ali [1*], Nawar F. Razooqi [1], Qutban Ibrahim Hasan [1], Husam Salman [1], Alaa Hussein J. AL-Qaisi [1]

[1]Department of Chemistry, College of Science, Al-Nahrain University, Jadriya, Baghdad, Iraq

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Corresponding author
Shaimaa Imad Ali
shaimaa.emad@nahrainuniv.edu.iq

ABSTRACT

Thyroid disorders and diabetes mellitus frequently occur and disrupt metabolic balance. Vitamin D, leptin, and asprosin contribute to metabolic regulation, and alterations in lipid profiles can further complicate this condition. To investigate relationships among asprosin, leptin, and other biomarkers in diabetic patients with hypothyroidism or hyperthyroidism, a cross-sectional study was conducted with 130 participants divided into three groups: diabetes with hypothyroidism (n = 50), diabetes with hyperthyroidism (n = 50), and diabetes with normal thyroid function (n = 30). Participants were recruited from Al-Yarmouk Hospital in Baghdad, Iraq, between July 2024 and May 2025. Thyroid hormone levels (TSH, free T3, free T4) and vitamin D were measured using an enzyme-linked fluorescence assay. Lipid profile and HbA1c levels were assessed using a spectrophotometer. Levels of asprosin and leptin were determined by enzyme-linked immunosorbent assay. Patients with hypothyroidism showed significantly higher leptin and asprosin levels and lower vitamin D compared with the other groups. Hypothyroid diabetics also had less favorable lipid profiles, including increased LDL and total cholesterol. Free T3 showed negative correlations with total cholesterol and positive correlations with HbA1c and vitamin D. Triglycerides and BMI showed positive correlations with TSH.

Thyroid dysfunction significantly affects metabolic markers in diabetes. Hypothyroidism is associated with increased asprosin and leptin. Monitoring these markers may improve management.

Keywords: *Asprosin, Diabetes mellitus, Leptin, Thyroid Dysfunction, Vitamin D*

1 INTRODUCTION

Among the most prevalent endocrinopathies seen in routine clinical practice are diabetes mellitus and thyroid disorders (TD), which commonly coexist. Patients with type 2 diabetes have a higher prevalence of TD than people without the disease; in Kathmandu, Nepal, the prevalence is 27.94% [1]. The pathophysiological relationship between type 2 diabetes and thyroid disease is explained by the interplay of several metabolic, genetic, and hormonal disturbances [2]. Diabetes affects thyroid hormone action by altering thyroid-stimulating hormone (TSH) levels and reducing peripheral tissue conversion of thyroxine (T4) to triiodothyronine (T3). Furthermore, some diabetic patients with normal thyroid function may develop thyroid disease as a result of chronic hyperglycemia [3]. Type 2 diabetics experience fluctuating insulin resistance and decreased insulin production, which leads to hyperglycemia. Thyroid disease, however, might also be influenced by persistent hyperglycemia over time [4]. Patients with diabetes are more likely to develop thyroid dysfunction, with hypothyroidism being the most common condition, compared with those without

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metabolic disease. Studies have shown that the prevalence of thyroid hormone abnormalities varies among patients with type 2 diabetes [5]. Because untreated thyroid dysfunction can alter metabolic regulation in patients with diabetes and increase the risk of cardiovascular disease, diagnosing and treating thyroid disorders in these patients may improve glycemic control, reduce cardiovascular disease risk, and promote overall health and well-being [6].

Thyroid hormones influence growth, development, and metabolic processes in humans, and several essential functions are affected by thyroid dysfunction. Thyroid disorders alter the structure and function of the thyroid gland and may be benign or cancerous. Thyroid disease is believed to account for 30%–40% of all endocrine disorders and has the second-highest incidence after diabetes mellitus; thyroid illness is also described as the most common type of endocrine disorder [7]. About 5% of people suffer from hypothyroidism, and another 5% of cases are undiagnosed. Primary hypothyroidism affects 99% of patients. In regions with a significant iodine supply, the most common cause of thyroid failure is Hashimoto's disease, also referred to as chronic autoimmune thyroiditis [8].

Patients with newborn progeroid syndrome (NPS), a rare genetic condition marked by extreme leanness and lack of appetite, as well as low calorie intake and low energy expenditure, were found to have the asprosin hormone, which regulates glucose homeostasis. These patients are also underweight in certain areas of their bodies. A distinct metabolic dysregulation involving partial lipodystrophy and a decrease in plasma insulin, while preserving normal blood sugar levels, results from cleavage of asprosin from the C-terminal of profibrillin (encoded by FBN1) [9]. After being released, asprosin travels to the liver and activates the olfactory G-protein-coupled receptor OR4M1. Through an unidentified receptor, it crosses the blood-brain barrier to activate hypothalamic neurons that regulate hunger [10]. On the other hand, those who are overweight or obese may have plasma asprosin concentrations that are up to four times higher than those of people with a healthy body mass index (BMI). This association between asprosin and body composition, which is thought to be driven by asprosin's effects on hunger, makes asprosin a crucial target for controlling energy balance and, in turn, disease in people with diabetes or obesity [11].

Leptin is secreted primarily by adipose tissue and functions as a vital hormone in regulating energy balance. Leptin deficiency is associated with weight gain, increased food consumption, and adipose tissue accumulation [12]. Leptin's effects on improving glucose homeostasis are mediated either directly or indirectly by several target tissues, such as skeletal muscle, liver, the central nervous system, and the pancreas. Research indicated that subjects with diabetes have higher leptin levels than controls. In addition, insulin levels, insulin sensitivity, age, sex, body mass index, central adiposity, and antidiabetes therapy are all variables that influence leptin levels [13].

The vitamin D family comprises sterols with hormone-like functions. The active ingredient, calcitriol (1,25-diOH-D3), binds to intracellular receptor proteins. Vitamin D is known as the "Sunshine vitamin" because it is produced in the Malpighian layer of the epidermis by photolysis of 7-dehydrocholesterol, aided by exposure to UV light [14]. Low vitamin D levels are known risk factors for diseases such as diabetes, multiple sclerosis, Crohn's disease, and rheumatoid arthritis, and they have been linked to several autoimmune diseases. While vitamin D nuclear receptors (DVR) are present in many cancers, including breast, prostate, colon, thyroid carcinoma, and leukemia, observational studies have connected vitamin D deficiency to diabetes [15].

2 MATERIALS AND METHODS

2.1 Sample collection

Eight milliliters of venous blood were collected from each participant after an overnight fast using sterile plastic syringes. The study was conducted at Yarmouk Teaching Hospital in Baghdad between December 2024 and February 2025 and included 130 Iraqi participants aged 30-65 years, divided into three groups: diabetes with hypothyroidism (n = 50), diabetes with hyperthyroidism (n = 50), and diabetes with normal thyroid function (n = 30). Blood samples were allowed to clot at room temperature for 30 min in gel separator tubes, then centrifuged at 3000 rpm for 5 min to separate the serum. Serum was used to measure fasting serum glucose (FSG), HbA1c, and lipid profile (total cholesterol, triglycerides, HDL-C, and LDL-C) using an automated chemistry analyzer (Mindray BS-240, China). Thyroid hormones (TSH, free T3, and free T4) were analyzed by enzyme-linked fluorescent assay (ELFA) using VIDAS$^{@}$ kits (bioMérieux, France) with detection ranges of 0.01–100 µIU/mL for TSH, 1.0-20.0 pmol/L for free T3, and 2.0-100.0 pmol/L for free T4. Serum levels of asprosin, leptin, and vitamin D (25(OH)D) were measured using commercial ELISA kits: asprosin (Cloud-Clone Corp., China) with a detection range of 0.156-10 ng/mL, leptin (DRG Instruments GmbH, Germany) with a detection range of 0.2-100 ng/mL, and vitamin D (Elabscience, USA) with a detection range of 4-100 ng/mL. Serum aliquots for ELISA were stored at -20 °C until analysis. Anthropometric measurements included age and body mass index (BMI), calculated as weight in kilograms divided by height in meters squared (kg/m^2).

2.1.1 Inclusion criteria

Adults aged 30-65 years with a confirmed diagnosis of type 2 diabetes mellitus (T2DM) and a disorder in thyroid function tests.

2.1.2 Exclusion criteria

Patients with previously diagnosed thyroid disorders, those taking medications known to affect thyroid function (e.g., amiodarone, corticosteroids), pregnant women, and patients with acute infections, chronic inflammatory or autoimmune diseases. These criteria were applied to ensure sample homogeneity, minimize confounding, and enhance reproducibility.

2.2 Anthropometric assessment

Body mass index (BMI) was classified into three categories: normal weight (BMI < 25 kg/m^2), overweight (BMI 25-30 kg/m^2), and obesity (BMI> 30 kg/m^2). The waist-to-hip ratio (WHR) was calculated by dividing the waist circumference (measured in cm) by the hip circumference (measured in cm).

2.3 Statistical analysis

Statistical analysis was carried out using Statistical Analysis for Social Sciences (SPSS) (ver. 29). For both categorical and numerical variables, the mean and standard deviation were used. ANOVA was used to determine whether differences between variables were significant. The relationship between the parameter and disease was assessed using ROC analysis, with a significance level set at $p < 0.05$.

3 RESULT AND DISCUSSION

3.1 Demographic and clinical parameters (glucose and lipid profile)

As shown in Table 1, the mean age of participants did not differ significantly among the three groups ($p = 0.347$), suggesting that age is not a confounding factor in the observed metabolic variations. However, BMI was significantly higher in the diabetes with hypothyroidism group (34.1 ± 1.12 kg/m^2) compared with the euthyroid (26.4 ± 2.42 kg/m^2) and hyperthyroid groups (22.7 ± 2.31 kg/m^2) ($p < 0.001$). This finding aligns with the well-established association between hypothyroidism and weight gain due to reduced metabolic rate. The duration of diabetes was significantly longer in the hypothyroid group (12.7 ± 2.91 years) compared with the hyperthyroid group (9.4 ± 2.48 years) ($p < 0.045$), suggesting that prolonged diabetes duration may contribute to the development of hypothyroidism.

Fasting blood sugar (FBS) and HbA1C% were significantly elevated in the hypothyroid group (177.41 ± 20.36 mg/dL and 8.51 ± 1.85%) compared with the hyperthyroid (160.47 ± 20.85 mg/dL and 7.50 ± 0.99%) and euthyroid (169.43 ± 20.11 mg/dL and 7.96 ± 1.29%) groups ($p < 0.001$). These findings suggest that hypothyroidism worsens glycemic control, potentially through insulin resistance and decreased glucose metabolism. Conversely, hyperthyroidism was associated with lower FBS and HbA1C, likely due to increased glucose turnover and utilization.

A significant dyslipidemia pattern was observed in the hypothyroid group, characterized by elevated total cholesterol (TC), triglycerides (TG), and LDL-C levels (TC: 225.4 ± 13.4 mg/dL; TG: 170.41 ± 10.22 mg/dL; LDL-C: 144.11 ± 9.87 mg/dL) compared with the euthyroid and hyperthyroid groups ($p < 0.003$, $p < 0.006$, and $p < 0.003$, respectively). In addition, HDL-C levels were significantly lower in the hypothyroid (40.27 ± 3.28 mg/dL) and euthyroid (37.40 ± 3.78 mg/dL) groups compared with the hyperthyroid group (46.1 ± 3.69 mg/dL) ($p < 0.011$), further contributing to an atherogenic lipid profile. In contrast, the hyperthyroid group exhibited a more favorable lipid profile, with lower TC, TG, and LDL-C levels and higher HDL-C levels, reinforcing the lipid-lowering effects of thyroid hormones. These findings highlight the crucial role of thyroid function in lipid metabolism and underscore the increased cardiovascular risk associated with hypothyroid diabetes.

3.2 Metabolic markers (asprosin, leptin, and vitamin D)

As shown in Table 2, significant variations in metabolic and endocrine markers were observed across the three groups. Asprosin levels were highest in the hypothyroid group (50.4 ± 4.11 ng/mL) compared with the hyperthyroid (41.07 ± 5.42 ng/mL) and euthyroid (33.1 ± 3.47 ng/mL) groups ($p < 0.008$), suggesting a potential link between hypothyroidism and increased asprosin secretion, which is known to stimulate hepatic glucose production and insulin resistance.

Table 1 Demographic and Clinical Parameters between study groups

Markers	**Diabetes with Hypothyroidism** (N = 50)	**Diabetes with Hyperthyroidism** (N = 50)	**Diabetes with Euthyroid** (**N = 30**)	**p-value**
Age (year)	59.4 ± 7.1^{a}	55.3 ± 6.63^{a}	50.4 ± 6.90^{a}	0.3470
BMI (kg/m^2)	34.1 ± 1.12^{a}	22.7 ± 2.31^{b}	26.4 ± 2.42^{c}	<. 001
Duration of disease (Year)	12.7 ± 2.91^{d}	9.4 ± 2.48^{b}	11.6 ± 2.76^{c}	<. 045
FBS (mg/dL)	177.41 ± 20.36^{a}	160.47 ± 20.85^{b}	169.43 ± 20.11^{c}	<. 001
HbAlC%	8.51 ± 1.85^{a}	7.50 ± 0.99^{b}	7.96 ± 1.29^{b}	<. 001
TC (mg/dL)	225.4 ± 13.4^{a}	180.42 ± 11.7^{b}	205.13 ± 10.45^{c}	<. 003
TG (mg/dL)	170.41 ± 10.22^{a}	130.68 ± 11.32^{b}	150.17 ± 12.33^{c}	<. 006
HDL-C (mg/dL)	40.27 ± 3.28^{a}	46.1 ± 3.69^{a}	37.40 ± 3.78^{c}	<. 011
LDL-C (mg/dL)	144.11 ± 9.87^{a}	111.44 ± 9.72^{b}	120.39 ± 10.10^{b}	<. 003

Leptin levels followed a similar trend and were significantly higher in the hypothyroid group (29.41 ± 3.84 ng/mL) compared with the hyperthyroid (17.48 ± 3.12 ng/mL) and euthyroid (23.67 ± 3.24 ng/mL) groups ($p < 0.004$), indicating an influence of thyroid dysfunction on adipose tissue regulation and energy metabolism.

Conversely, vitamin D levels were lowest in the hypothyroid group (15.79 ± 2.68 ng/mL) and highest in the euthyroid group (20.65 ± 2.77 ng/mL) ($p < 0.035$), suggesting an inverse relationship between hypothyroidism and vitamin D status, potentially due to impaired synthesis and metabolism. Thyroid function markers demonstrated expected patterns: TSH levels were significantly elevated in the hypothyroid group (8.7 ± 1.45 µIU/mL) and suppressed in the hyperthyroid group (0.33 ± 0.91 µIU/mL) compared with the euthyroid group (3.1 ± 0.75 µIU/mL) ($p < 0.001$). In addition, free T3 and free T4 levels were highest in the hyperthyroid group (6.5 ± 0.91 pg/mL and 2.4 ± 0.29 ng/dL, respectively) and lowest in the hypothyroid group (2.5 ± 0.35 pg/mL and 0.81 ± 0.98 ng/dL, respectively) ($p < 0.001$).

These findings reinforce the intricate relationship between thyroid dysfunction, metabolic regulation, and endocrine homeostasis, highlighting the potential impact of hypothyroidism on insulin resistance, lipid metabolism, and vitamin D deficiency, whereas hyperthyroidism appears to enhance metabolic levels.

3.3 Correlation analysis

As shown in Table 3, in patients with diabetes and hypothyroidism, both asprosin and leptin showed significant correlations with multiple metabolic and hormonal markers ($p \leq 0.05$).

Table 2 Asprosin, leptin, and thyroid hormones between the study groups

Markers	**Diabetes with Hypothyroidism** (**N = 50**)	**Diabetes with Hyperthyroidism** (**N = 50**)	**Diabetes with Euthyroid** (N = 30)	**p-value**
Asprosin (ng/mL)	50.4 ± 4.11^{a}	41.07 ± 5.42^{b}	33.1 ± 3.47^{bc}	<. 008
Leptin(ng/mL)	29.41 ± 3.84^{a}	17.48 ± 3.12^{b}	23.67 ± 3.24^{ba}	<. 004
Vita. D (ng/mL)	15.79 ± 2.68^{a}	18.19 ± 3.62^{b}	20.65 ± 2.77^{bc}	<. 035
TSH (μ IU/mL)	8.7 ± 1.45^{a}	3.33 ± 0.91^{b}	3.1 ± 0.75^{b}	<. 001
Free T3 (pg/mL)	2.5 ± 0.35^{a}	6.5 ± 0.91^{b}	4.4 ± 0.30^{ab}	<. 001
Free T4 (ng/dL)	0.98 ± 0.18^{a}	2.4 ± 0.22^{b}	1.2 ± 0.20^{ab}	<. 001

Asprosin was negatively correlated with vitamin D ($r = -0.48$), free T3 ($r = -0.65$), free T4 ($r = -0.59$), and HDL-C ($r = -0.45$), and positively correlated with TSH ($r = 0.72$), total cholesterol ($r = 0.55$), triglycerides ($r = 0.60$), and LDL-C ($r = 0.58$). Leptin demonstrated a similar pattern, showing negative correlations with vitamin D ($r = -0.50$), free T3 ($r = -0.60$), free T4 ($r = -0.57$), and HDL-C ($r = -0.48$), and positive correlations with TSH ($r = 0.63$), total cholesterol ($r = 0.58$), triglycerides ($r = 0.62$), and LDL-C ($r = 0.59$). These findings suggest a strong association between elevated adipokines and altered thyroid and lipid parameters in this subgroup.

Table 4 shows that in patients with diabetes and hyperthyroidism, asprosin and leptin showed moderate but significant correlations with several metabolic and thyroid parameters. Asprosin was positively correlated with TSH ($r = 0.52$), total cholesterol ($r = 0.42$), triglycerides ($r = 0.50$), and LDL-C ($r = 0.48$), and negatively correlated with free T3 ($r = -0.55$) and free T4 ($r = -0.53$) ($p \leq 0.05$ for all). However, its correlations with vitamin D ($r = -0.29$) and HDL-C ($r = -0.36$) were not statistically significant. Leptin showed a similar pattern, with positive associations with TSH ($r = 0.48$), total cholesterol ($r = 0.45$), triglycerides ($r = 0.51$), and LDL-C ($r = 0.50$), and negative associations with free T3 ($r = -0.50$) and free T4 ($r = -0.49$) ($p \leq 0.05$). Like asprosin, leptin's negative correlations with vitamin D ($r = -0.40$) and HDL-C ($r = -0.39$) did not reach statistical significance. These findings suggest that, although attenuated compared with the hypothyroid group, adipokines remain significantly linked to lipid and thyroid parameters in hyperthyroid diabetic patients.

In diabetic patients with normal thyroid function (euthyroid), both asprosin and leptin remained significantly associated with several metabolic and hormonal markers, as shown in Table 5. Asprosin was significantly positively correlated with TSH ($r = 0.58$), total cholesterol ($r =$

0.45), triglycerides (r = 0.49), and LDL-C (r = 0.47), and negatively correlated with free T3 (r = -0.59) and free T4 (r = -0.55) ($p \leq 0.05$). However, its correlations with vitamin D (r = -0.28) and HDL-C (r = -0.39) were not statistically significant. Leptin showed significant positive correlations with TSH (r = 0.52), total cholesterol (r = 0.47), triglycerides (r = 0.50), and LDL-C (r = 0.48), and negative correlations with free T3 (r = -0.53), free T4 (r = -0.51), and HDL-C (r = -0.41) ($p \leq 0.05$). Leptin also showed a statistically significant inverse correlation with vitamin D (r = -0.42; $p \leq 0.05$). These results suggest that, even in the absence of overt thyroid dysfunction, adipokines such as asprosin and leptin remain strongly linked to lipid and thyroid-related metabolic markers in individuals with diabetes. The correlation patterns suggest a metabolic profile closer to normal thyroid function but with persistent adipokine involvement. Overall, these results emphasize that thyroid dysfunction in diabetic patients modulates the association between adipokines, vitamin D, and lipid metabolism markers, which may affect metabolic homeostasis and disease progression.

Table 3 Correlation Analysis in Diabetes with Hypothyroidism

Markers	**Asprosin (ng/mL)**		**Leptin (ng/mL)**	
	R	**P- value**	**R**	**P- value**
Vitamin D (**ng/mL**)	-0.48	≤ 0.05	-0.50	≤ 0.05
TSH (**μIU/mL**)	0.72	≤ 0.05	0.63	≤ 0.05
Free T3 (pg/mL)	-0.65	≤ 0.05	-0.60	≤ 0.05
Free T4 (ng/dL)	-0.59	≤ 0.05	-0.57	≤ 0.05
TC (mg/dL)	0.55	≤ 0.05	0.58	≤ 0.05
TG (mg/dL)	0.60	≤ 0.05	0.62	≤ 0.05
LDL-C (mg/dL)	0.58	≤ 0.05	0.59	≤ 0.05
HDL-C (mg/dL)	-0.45	≤ 0.05	-0.48	≤ 0.05

3.4 ROC analysis

The ROC curve analyses demonstrated that both asprosin and leptin have excellent diagnostic performance in distinguishing between the studied groups. For asprosin, the area under the curve (AUC) was 0.95, with an optimal cut-off value of 43.15, indicating a very high ability to correctly classify individuals. Similarly, leptin showed an AUC of 0.94, with a cut-off value of 23.24, also reflecting outstanding discriminatory power. These findings suggest that both biomarkers could serve as reliable indicators for the condition under investigation, as shown in Figures 1 and 2.

Table 4 Correlation Analysis in Diabetes with Hyperthyroidism

Markers	**Asprosin(ng/mL)**		**Leptin (ng/mL)**	
	R	**P- value**	**R**	**P - value**
Vitamin D (ng/mL)	-0.29	NS	-0.40	NS
TSH (**μIU/mL)**	0.52	≤ 0.05	0.48	≤ 0.05
Free T3 (pg/mL)	-0.55	≤ 0.05	-0.50	≤ 0.05
Free T4 (ng/dL)	-0.53	≤ 0.05	-0.49	≤ 0.05
TC (mg/dL)	0.42	≤ 0.05	0.45	≤ 0.05
TG (mg/dL)	0.50	≤ 0.05	0.51	≤ 0.05
LDL-C (mg/dL)	0.48	≤ 0.05	0.50	≤ 0.05
HDL-C (mg/dL)	-0.36	NS	-0.39	NS

Table 5 Correlations in Diabetes with Euthyroid

Markers	**Asprosin (ng/mL)**		**Leptin (ng/mL)**	
	R	**P-value**	**R**	**P-value**
Vitamin D (ng/mL)	-0.28	NS	-0.42	≤ 0.05
TSH (**μIU/mL**)	0.58	≤ 0.05	0.52	≤ 0.05
Free T3 (pg/mL)	-0.59	≤ 0.05	-0.53	≤ 0.05
Free T4 (ng/dL)	-0.55	≤ 0.05	-0.51	≤ 0.05
TC (mg/dL)	0.45	≤ 0.05	0.47	≤ 0.05
TG (mg/dL)	0.49	≤ 0.05	0.50	≤ 0.05
LDL-C (mg/dL)	0.47	≤ 0.05	0.48	≤ 0.05
HDL-C (mg/dL)	-0.39	NS	-0.41	≤ 0.05

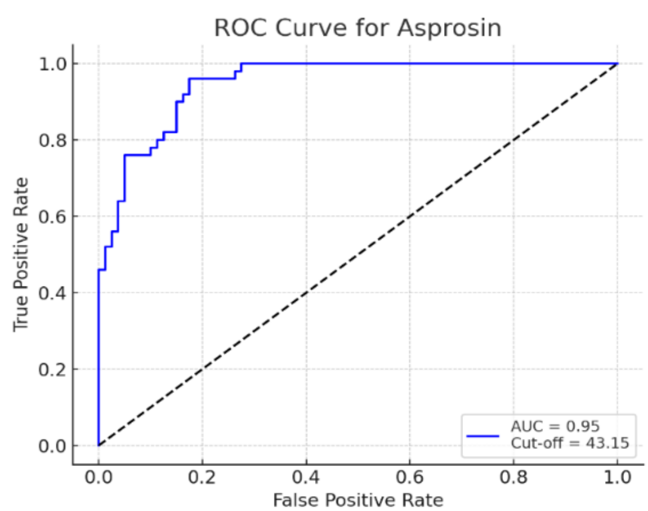

Fig. 1 ROC Curve for Asprosin in Differentiating Diabetic Patients with Hypothyroidism

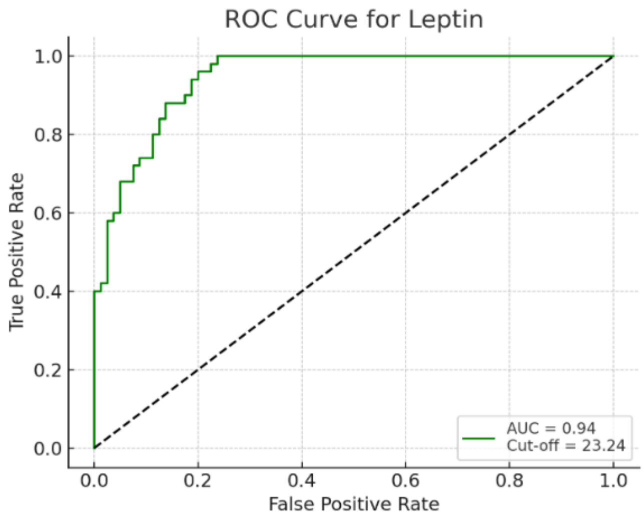

Fig. 2 ROC Curve for Leptin in Differentiating Diabetic Patients with Hypothyroidism

These results suggest that, even in the absence of overt thyroid dysfunction, adipokines such as asprosin and leptin remain strongly linked to lipid- and thyroid-related metabolic markers in people with diabetes. The observed pattern suggests a metabolic profile closer to normal thyroid function but with persistent adipokine involvement. Overall, these findings align with established physiological mechanisms and offer valuable insights into the complex relationship among thyroid function, adipokines, and lipid metabolism in diabetes. The inverse relationship between free T3 and total cholesterol supports the well-known role of thyroid hormones in promoting cholesterol clearance and lipid processing, which helps lower cholesterol levels. Conversely, the positive correlations between TSH and lipid measures, such as triglycerides and LDL-C, as well as with BMI, reflect the metabolic imbalance often observed in hypothyroidism, in which reduced lipid clearance and increased fat accumulation raise cardiovascular risk. These correlations underscore the hormonal and metabolic interactions that influence disease progression and highlight the importance of monitoring thyroid health and adipokine levels as indicators of metabolic complications in diabetic patients.

This study explored the relationship between thyroid dysfunction and metabolic parameters in patients with type 2 diabetes mellitus (T2DM). Our findings revealed significant associations between thyroid status and several biochemical markers, including HbA1c, lipid profile, and BMI. These observations are consistent with previous studies suggesting that altered thyroid function can affect glycemic control and lipid metabolism in individuals with diabetes. However, the cross-sectional nature of this study is a notable limitation. Because the data were collected at a single time point, causality between thyroid dysfunction and the observed metabolic changes cannot be established. Future longitudinal studies are needed to determine whether thyroid abnormalities precede or result from metabolic disturbances in patients with T2DM. In addition, we acknowledge the smaller sample size in the control group (diabetic patients with normal thyroid function) compared with the other groups. This was due to the relatively lower prevalence of euthyroidism among patients with T2DM during the recruitment period. Despite this imbalance, a post hoc power analysis confirmed that the sample size provided sufficient statistical power (>80%) to detect significant differences among groups. This information has been incorporated into the Statistical Analysis section. Nonetheless, this sample size discrepancy remains a potential limitation that may affect the generalizability of the findings.

Overall, this study adds to the growing body of evidence supporting the interplay between thyroid function and metabolic control in patients with diabetes. Our findings underscore the importance of routine thyroid screening in T2DM management and highlight the need for future research with stronger causal designs. In contrast to diabetes with hyperthyroidism and euthyroid status, our results show that diabetes with hypothyroidism is linked to a significantly higher BMI, poorer glycemic control, and a more atherogenic lipid profile. These findings are consistent with earlier studies showing that hypothyroidism causes weight gain by altering lipid metabolism and lowering metabolic rate [16]. Furthermore, previous studies reporting that thyroid hormones affect glucose metabolism and that hypothyroidism is associated with increased insulin resistance and reduced glucose utilization are supported by the higher fasting blood sugar (FBS) and HbA1c levels observed in hypothyroid patients [17]. Lower HDL-C levels and higher levels of cholesterol, triglycerides (TG), and low-density lipoprotein cholesterol (LDL-C) are among the lipid profile abnormalities in hypothyroid diabetic patients, supporting prior studies linking hypothyroidism to dyslipidemia. According to Bradley et al. [17], the main reasons for altered lipid metabolism in hypothyroidism include decreased hepatic LDL receptor activity, reduced lipoprotein clearance, and altered cholesterol synthesis. Patients with diabetes who also had hyperthyroidism, in contrast, had higher lipid levels, a lower BMI, and better glycemic control. This is consistent with evidence suggesting that increased thyroid hormone levels enhance lipid catabolism, increase energy expenditure, and improve insulin sensitivity, thereby lowering the risk of dyslipidemia and hyperglycemia, as reported by Guerri, Giulia, et al. [18].

With a focus on adipokines (asprosin and leptin), vitamin D levels, and thyroid hormones, the present study assessed metabolic and hormonal variations among diabetic patients with thyroid disorders. The results indicate interactions between thyroid status and metabolic regulation, demonstrated by significant differences in these markers among hypothyroid, hyperthyroid, and euthyroid diabetic groups. According to our findings, diabetic patients with hypothyroidism had higher asprosin levels than those with hyperthyroidism and euthyroid status. Asprosin, a glucogenic protein secreted by adipose tissue in response to fasting, significantly influences hepatic glucose production and insulin resistance. Elevated asprosin levels in hypothyroid patients align with findings by Liu, Lifei, et al. [19], who reported increased asprosin levels in insulin-resistant states, suggesting that hypothyroidism exacerbates insulin resistance and glucose dysregulation.

In addition, leptin levels followed a similar pattern, with significantly higher values in the hypothyroid group compared with hyperthyroid and euthyroid diabetic patients. This finding is consistent with previous studies associating hypothyroidism with increased leptin secretion due to reduced metabolic clearance and greater fat mass [20]. Conversely, hyperthyroid diabetic patients demonstrated lower leptin levels, likely due to an enhanced metabolic rate and reduced adipose tissue. The study also reported significant differences in vitamin D levels among the three groups: hypothyroid diabetic patients had the lowest levels, hyperthyroid patients had intermediate levels, and euthyroid individuals had the highest levels. These findings are consistent with increasing evidence linking vitamin D deficiency to hypothyroidism [21]. Lower vitamin D levels in hypothyroid individuals may be associated with chronic inflammation, altered calcium metabolism, and impaired hepatic hydroxylation of vitamin D. In patients with diabetes, especially those with thyroid dysfunction, this finding underscores the importance of routine vitamin D monitoring.

As expected, thyroid-stimulating hormone (TSH) levels were significantly suppressed in hyperthyroid individuals and significantly elevated in hypothyroid diabetic patients, providing evidence of altered thyroid function in these groups. Furthermore, consistent with established endocrine pathophysiology, free triiodothyronine (T3) and free thyroxine (T4) levels were significantly higher in hyperthyroid individuals and significantly lower in hypothyroid patients, as reported by Eski, Mehmet Tahir, et al. [22]. The metabolic, endocrine, and lipid parameters in diabetic patients with different thyroid function states were correlated in this study. The relationships observed highlight intricate interactions among thyroid hormones, adipokines, vitamin D levels, and lipid metabolism, providing insight into metabolic changes in diabetic patients with thyroid dysfunction. Asprosin, a newly discovered fasting-induced glucogenic adipokine, showed strong positive correlations with leptin, total cholesterol (TC), triglycerides (TG), and LDL-C. These results are consistent with earlier findings that asprosin promotes lipid accumulation and dyslipidemia by increasing hepatic glucose production and contributing to insulin resistance [23]. In addition, asprosin showed significant negative correlations with free T3 and free T4 and a strong positive correlation with TSH, indicating reciprocal regulation between asprosin and thyroid hormones. The metabolic consequences of hypothyroidism, where decreased energy expenditure and insulin resistance may result in elevated circulating asprosin levels, are consistent with the observed inverse relationship with thyroid hormones.

TSH showed a strong positive correlation with leptin, an important modulator of energy homeostasis and adiposity, while free T3 and free T4 showed inverse correlations. These results are consistent with those of Keikhaei, N., and Heidari, Z. [24], who found that increased adipose tissue mass and decreased metabolic clearance in hypothyroidism are linked to elevated leptin levels. Leptin's role in lipid dysregulation was further supported by its positive correlations with TC, TG, and LDL-C. These findings indicate that leptin may contribute to the pathophysiology of obesity-associated insulin resistance, which is worsened in hypothyroid diabetic patients. Vitamin D status exhibited a significant inverse correlation with TSH and leptin, suggesting a potential link between thyroid dysfunction, adiposity, and vitamin D deficiency. These results are consistent with studies reporting lower vitamin D levels in hypothyroid and obese individuals due to reduced sun exposure, altered vitamin D metabolism, and chronic inflammation [25]. In addition, vitamin D was positively associated with HDL-C, reinforcing its protective role in lipid homeostasis and cardiovascular health. The lack of significant associations between vitamin D and other lipid markers suggests that its effects are primarily mediated by anti-inflammatory and insulin-sensitizing properties rather than by direct lipid-lowering mechanisms.

As anticipated, TSH demonstrated strong positive correlations with TC, TG, and LDL-C, supporting the well-established role of hypothyroidism in promoting dyslipidemia through reduced hepatic LDL receptor activity and impaired lipid clearance, as reported by Taylor et al. [8]. Conversely, free T3 and free T4 exhibited negative correlations with these lipid markers, emphasizing the lipid-lowering effects of thyroid hormones through enhanced fatty acid oxidation and cholesterol metabolism. Interestingly, HDL-C had a negative correlation with TSH and a positive correlation with free T3, suggesting that thyroid hormones may help maintain healthier lipid profiles. These findings further support the inclusion of thyroid function screening in evaluations of lipid disorders, particularly in diabetic populations.

The observed elevation of asprosin and leptin levels in hypothyroid diabetic patients aligns with known metabolic derangements associated with thyroid hormone deficiency. Asprosin, a fasting-induced adipokine, stimulates hepatic glucose production and is implicated in insulin resistance, both of which are exacerbated in hypothyroid states due to reduced metabolic rate and impaired glucose utilization. Liu et al. [26] demonstrated that elevated asprosin levels correlate with increased HOMA-IR, supporting its role in deteriorating insulin sensitivity. Our findings reinforce this, as hypothyroid diabetics in our study exhibited significantly higher fasting glucose and HbA1c levels in conjunction with elevated asprosin, suggesting that thyroid hormone deficiency may amplify asprosin's diabetogenic effects.

Similarly, leptin, a hormone involved in appetite regulation and energy expenditure, is known to increase in hypothyroid patients due to greater fat mass and diminished metabolic clearance. Previous studies by Keikhaei et al. [27] reported a strong positive correlation between TSH and leptin, which we also observed. Leptin resistance, a common consequence of chronic hyperleptinemia, may further contribute to the insulin-resistant phenotype in hypothyroid diabetics. Moreover, elevated leptin levels have been associated with pro-inflammatory states, which may aggravate metabolic dysfunction. Together, the rise in both asprosin and leptin suggests a hormonal milieu favoring insulin resistance, dysregulated lipid metabolism, and increased cardiovascular risk in hypothyroid diabetics. These observations highlight the need for integrated monitoring of adipokines and thyroid status in metabolic disease management and call for further mechanistic studies to delineate causal relationships.

4 CONCLUSION

The findings of this study suggest that thyroid dysfunction in individuals with type 2 diabetes is associated with significant alterations in metabolic markers, including elevated asprosin and leptin levels, dyslipidemia, and reduced vitamin D levels. These associations may contribute to worsening insulin resistance and cardiovascular risk in this population. However, given the study's cross-sectional, observational design, causal relationships cannot be definitively established. The observed correlations underscore the potential clinical value of monitoring thyroid function and adipokine levels in diabetic patients, especially those with unexplained dyslipidemia or metabolic irregularities. These results also suggest a possible role for vitamin D optimization as an adjunct strategy for managing thyroid-related metabolic disturbances. Future research should focus on longitudinal and interventional studies to examine the causal mechanisms underlying these relationships and better understand the underlying pathophysiological mechanisms. Investigating targeted therapeutic approaches that modulate adipokines and thyroid function could offer promising avenues to improve metabolic control and reduce cardiovascular complications in diabetic patients.

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Author contributions

S.I. designed the study; M.H. conducted experiments; N.F. and A.H. analyzed the data; Q.I., H.S., and S.I. wrote the manuscript.

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Conflict of interest

The authors declare no competing interests.

Consent to publish

N/A

Ethical approval

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