Open Access https://www.jparathyroid.com

Journal of Parathyroid Disease

Journal of Parathyroid Disease 2026,14, e13325

DOI:10.34172/jpd.13325

Original

Serum interleukin-37 as a potential modulator of dyslipidemia in newly diagnosed hypothyroid patients with insulin resistance; a prospective cross-sectional study

Bashair Talib Jassim[1*], **Raid M. H. Al-Salih**[1]

Abstract

Introduction: Hypothyroidism is frequently accompanied by insulin resistance and an unfavorable lipid profile, which may increase cardiometabolic risk. Interleukin-37 (IL-37) is an anti-inflammatory cytokine with proposed roles in immune and metabolic regulation; however, its relationship with dyslipidemia in hypothyroid patients with insulin resistance remains insufficiently understood.

Objectives: study examines the association between circulating IL-37 concentrations and lipid-profile parameters in this population.

Materials and Methods: This prospective cross-sectional study was conducted between December 2024 and August 2025 among 25 newly diagnosed adults with hypothyroidism and insulin resistance recruited from two hospitals in Thi-Qar Governorate, Iraq. Demographic and clinical data were collected, and fasting blood samples were analyzed for thyroid function, insulin resistance, serum IL-37, and lipid-profile parameters, including triglycerides (TG), total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and very-low-density lipoprotein cholesterol (VLDL-C). Associations between circulating IL-37 levels and lipid parameters were examined using Pearson correlation and linear regression analyses, with multivariable models adjusted for age, sex, and body mass index (BMI).

Results: Twenty-five newly diagnosed patients with hypothyroidism and insulin resistance were included; 60% were women, and the mean age was 36.5 years. Circulating IL-37 concentrations were positively correlated with TG, total cholesterol, LDL-C, and VLDL-C, whereas an inverse correlation was observed with HDL-C. In linear regression analyses, IL-37 was significantly associated with all lipid-profile parameters in unadjusted models. After adjustment for demographic characteristics, the positive associations with TG, total cholesterol, LDL-C, and VLDL-C remained significant; however, the association with HDL-C was no longer statistically significant.

Conclusion: In newly diagnosed patients with hypothyroidism and insulin resistance, higher circulating IL-37 levels were associated with an adverse lipid profile. These findings suggest that IL-37 may reflect the inflammatory–metabolic disturbance underlying dyslipidemia and potentially heightened cardiovascular risk in this clinically vulnerable population.

Keywords: Interleukin-37, Hypothyroidism, Insulin resistance, Lipid profile, Dyslipidemias

Please cite this paper as: Jassim BT, Al-Salih RMH. Serum interleukin-37 as a potential modulator of dyslipidemia in newly diagnosed hypothyroid patients with insulin resistance; a prospective cross-sectional study. J Parathyr Dis. 2026;14:e13325. doi:10.34172/jpd.13325.

Introduction

Hypothyroidism is a common thyroid disorder and represents an important endocrine health concern; a local study in Nasiriya City reported hypothyroidism as more prevalent than hyperthyroidism (1). A well-documented metabolic consequence of this condition is dyslipidemia, manifesting primarily as elevated total cholesterol, low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG) (2). The underlying pathophysiology involves thyroid hormone-mediated regulation of cholesterol biosynthesis, hepatic LDL receptor expression, cholesterol clearance, and reverse cholesterol transport; when these processes are impaired in hypothyroid states, atherogenic lipid accumulation ensues (2,3). Beyond its direct lipid effects, hypothyroidism has been increasingly recognized as a contributor to insulin resistance, with both overt and subclinical forms associated with impaired glucose homeostasis and elevated insulin levels in multiple population-based analyses (4,5). The TSH itself has been proposed to independently perturb metabolic pathways, including hepatic endoplasmic reticulum stress through the IRE1α/XBP-1 signaling cascade, which may further compound insulin resistance in affected individuals (5). Collectively, newly diagnosed hypothyroid patients represent a clinically significant population in whom the interplay of dyslipidemia and insulin resistance warrants systematic investigation.

Interleukin-37 (IL-37) is a pleiotropic anti-

Received: 18 May 2026, **Revised:** 14 Aug. 2026, **Accepted:** 23 Aug. 2026, **ePublished:** 2 Sep. 2026

[1]Department of Chemistry, College of Science, University of Thi-Qar, Thi-Qar, Iraq

***Corresponding author:** Bashair Talib Jassim, Email: Bashaar.jasim@utq.edu.iq

Implication for health policy/practice/research/medical education

This study evaluated the relationship between circulating interleukin-37 (IL-37) and lipid-profile parameters in newly diagnosed patients with hypothyroidism and insulin resistance. Higher IL-37 concentrations were associated with increased triglycerides (TG), total cholesterol, low-density lipoprotein cholesterol (LDL-C), and very-low-density lipoprotein cholesterol (VLDL-C), while an inverse relationship was observed with high-density lipoprotein cholesterol (HDL-C). After adjustment for age, sex, and body mass index (BMI), the associations of IL-37 with TG and atherogenic cholesterol fractions remained significant, whereas the association with HDL-C was no longer significant.

inflammatory cytokine belonging to the IL-1 superfamily that has garnered substantial research interest for its broad immunosuppressive properties; unlike most members of this family, IL-37 dampens innate and adaptive immune activation through dual signaling: intracellularly via the Smad3 pathway and extracellularly through ligation of the IL-18 receptor alpha, thereby suppressing the production of multiple pro-inflammatory mediators (6). Experimental studies have established a direct link between IL-37 and metabolic homeostasis; in murine models of obesity-associated metabolic syndrome, IL-37 treatment significantly reduced adipose tissue inflammation, lowered plasma insulin, improved glucose tolerance, and decreased pro-inflammatory cytokine secretion from cultured adipose tissue (7). In human studies, serum IL-37 levels have been found to be inversely correlated with the presence and severity of metabolic syndrome components, including dyslipidemia, hyperglycemia, and visceral adiposity, suggesting that reduced IL-37 signaling may contribute to the low-grade systemic inflammation that drives metabolic deterioration (8). More recently, elevated IL-37 has been identified as a discriminating immunometabolic biomarker in patients with metabolic syndrome, with its serum levels demonstrating good diagnostic accuracy by receiver operating characteristic analysis (9).

Emerging evidence points toward a specific role for IL-37 in thyroid-related pathology. Serum IL-37 concentrations have been reported to be significantly elevated in patients with Hashimoto's thyroiditis and were found to correlate positively with oxidative stress markers, suggesting that this cytokine is upregulated as a counter-regulatory response to thyroid autoimmune inflammation (10). Similarly, a study of workers with thyroid hormonal perturbations demonstrated that elevated TSH was associated with significantly raised circulating IL-37, reinforcing the concept that thyroid dysfunction and IL-37 dysregulation are physiologically linked (11). Despite these observations, no study to date has specifically examined the relationship between serum IL-37 and dyslipidemia in hypothyroid patients who simultaneously exhibit insulin resistance, a high-risk metabolic phenotype defined by the co-occurrence of lipid abnormalities and impaired insulin sensitivity. This prospective cross-sectional study was therefore designed to evaluate whether serum IL-37 serves as a potential modulator of dyslipidemia in newly diagnosed hypothyroid patients with insulin resistance, aiming to clarify its immunometabolic role in this clinically vulnerable population.

Objectives

This study aimed to investigate the association between circulating IL-37 concentrations and lipid-profile parameters in newly diagnosed patients with hypothyroidism and insulin resistance, and to determine whether these associations remain independent or not.

Materials and Methods

Study design and participants

This prospective cross-sectional study was conducted from December 2024 through August 2025 at Al-Nasiriya general hospital and Bint Al-Huda maternity hospital in Thi-Qar governorate, Iraq. Laboratory analyses were carried out in the biochemistry laboratory, college of science, university of Thi-Qar. The study enrolled 25 newly diagnosed patients with hypothyroidism and insulin resistance who attended the participating hospitals during the study period and met the predefined eligibility criteria.

Inclusion and exclusion criteria

Eligible participants were adults with newly diagnosed hypothyroidism and insulin resistance who attended the participating study sites during the recruitment period and provided written informed consent. Hypothyroidism was identified using thyroid-function tests, including an elevated TSH and decreased thyroxine (T4) concentration, and insulin resistance was determined using the HOMA-IR index. Individuals were not included if they had previously received thyroid-hormone replacement or medications that could alter glucose metabolism, insulin sensitivity, inflammatory status, or lipid concentrations. Patients with incomplete clinical or laboratory data were excluded.

Data collection

Written informed consent was obtained from all participants before enrollment. Demographic and relevant clinical information, including age, sex, and body mass index (BMI), was collected through participant interviews using a structured data-collection form. Venous blood samples were obtained under standard aseptic conditions for measurement of TSH, T4, fasting insulin and glucose, serum IL-37 concentrations, and lipid-profile parameters, including TG, total cholesterol, LDL-C, high-density lipoprotein cholesterol (HDL-C), and very-low-density lipoprotein cholesterol (VLDL-C). Each participant was assigned a study code to maintain the confidentiality of personal information.

Insulin resistance definition

Insulin resistance was estimated using the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR), a fasting, indirect measure based on the physiological relationship between circulating glucose and insulin. Fasting blood glucose and fasting serum insulin were measured from the same blood sample after an overnight fast, usually 8–12 hours. HOMA-IR is then calculated as:

$$\text{HOMA} - \text{IR} = \frac{Fasting\ insulin\ (\mu U/mL) \times Fasting\ glucose\ (mmol/L)}{22.5}$$

Higher HOMA-IR values indicate lower insulin sensitivity and, therefore, greater insulin resistance (12-14).

Hypothyroidism definition

Newly diagnosed hypothyroidism is a condition caused by impaired hormone production within the thyroid gland itself, resulting in insufficient circulating thyroid hormones, particularly T4. The diagnosis of overt primary hypothyroidism is typically established by an elevated serum TSH level above the normal range together with a free T4 concentration below the laboratory reference range (15,16).

Blood sample collection

Approximately 5 mL of venous blood was collected from each male and female participant by standard venipuncture into serum separator tubes containing a gel clot activator. Samples were allowed to clot at room temperature and were subsequently centrifuged at 3,000 × g for 10 minutes to obtain serum. The separated serum was carefully aliquoted and either analyzed immediately for biochemical parameters or stored at −20 °C until further analysis.

Measurement of serological biomarkers

Serum IL-37 concentrations were quantified using a commercial human IL-37 sandwich enzyme-linked immunosorbent assay (ELISA) kit (SunLong Biotech Co., Ltd., Hangzhou, China; Cat. No. SL2231Hu) in accordance with the manufacturer's instructions. Absorbance was measured at 450 nm, and IL-37 concentrations were calculated from the corresponding standard curve. The assay had a detection range of 2–150 pg/mL, a minimum detectable concentration of 0.5 pg/mL, and intra-assay and inter-assay coefficients of variation of less than 10% and 12%, respectively. Serum samples were stored at −20 °C until analysis. Serum insulin concentrations were measured using the Elecsys® Insulin electrochemiluminescence immunoassay (ECLIA), and serum TSH concentrations were determined using the Elecsys® TSH assay (Roche Diagnostics, Germany). Fasting serum glucose, total cholesterol, TG, and HDL-C were measured using automated enzymatic methods with commercial kits supplied by Roche Diagnostics. The VLDL-C was estimated by dividing serum TG concentration by 5, and LDL-C was calculated by subtracting HDL-C and VLDL-C from total cholesterol (17).

Outcome measurement

Measured outcomes included serum IL-37 concentration and lipid-profile parameters, comprising TG, total cholesterol, LDL-C, HDL-C, and VLDL-C. The primary outcome was assessing the correlation between circulating IL-37 levels and lipid profile parameters, assessed using Pearson correlation and linear regression analyses.

Statistical analysis

Data were analyzed using IBM SPSS Statistics version 27 (IBM Corp., Armonk, NY, USA). The Shapiro–Wilk test was applied to assess the normality of continuous variables. Categorical variables were summarized as frequencies and percentages, whereas normally distributed continuous variables were presented as mean ± standard deviation. Pearson's correlation coefficient was used to examine the associations between circulating IL-37 concentrations and lipid-profile parameters. Simple linear regression analyses were then conducted to evaluate unadjusted associations, followed by multivariable linear regression models adjusted for age, sex, and BMI. All statistical tests were two-sided, and a *P* value below 0.05 was considered statistically significant.

Results

This study included 25 participants (60% female) with a mean age of 36.52 ± 12.25 years and a mean BMI of 26.22 ± 2.18 kg/m. The mean TSH and T4 concentrations were 14.19 ± 2.34 μIU/mL and 8.67 ± 1.84 pmol/L, while the mean HOMA-IR was 11.49 ± 2.41. Serum IL-37 levels averaged 100.8 ± 19.32 pg/mL. Regarding the lipid profile, mean TG and total cholesterol concentrations were 175.04 ± 16.14 mg/dL and 218.20 ± 18.12 mg/dL, respectively. Mean LDL-C, HDL-C, and VLDL-C levels were 148.79 ± 19.01 mg/dL, 34.40 ± 6.01 mg/dL, and 35.01 ± 3.22 mg/dL, respectively (Table 1).

The results indicated that circulating IL-37 levels showed significant positive correlations with TG, total cholesterol, LDL-C, and VLDL-C concentrations, indicating that higher IL-37 levels were associated with a less favorable atherogenic lipid profile. In contrast, IL-37 was significantly and inversely correlated with HDL-C, suggesting lower HDL-C concentrations among participants with higher circulating IL-37 levels. No statistically significant correlations were observed between IL-37 levels and either age or BMI (Table 2).

In unadjusted linear regression analyses, higher circulating IL-37 levels were significantly associated with higher TG, total cholesterol, LDL-C, and VLDL-C concentrations, whereas an inverse association was observed with HDL-C. These associations remained statistically significant after adjustment for age, sex,

Table 1. Demographic, clinical, and lipid profile characteristics of participants

Demographic characteristics		
Gender	Male	10 (40)
	Female	15 (60)
Age (year)		36.52 ± 12.25
BMI (kg/m²)		26.22 ± 2.18
Clinical data and lipid profile		
TSH (μIU/mL)		14.19 ± 2.34
Free T4 (pmol/L)		8.67 ± 1.84
HOMA-IR		11.49 ± 2.41
IL-37 (pg/mL)		100.8 ± 19.32
TG (mg/dL)		175.04 ± 16.14
Cholesterol (mg/dL)		218.2 ± 18.12
LDL-C (mg/dL)		148.79 ± 19.01
HDL-C (mg/dL)		34.40 ± 6.01
VLDL-C (mg/dL)		35.01 ± 3.22

Qualitative and quantitative variables were reported as N (%) and Mean ± SD.

BMI: Body mass index, TSH: Thyroid-stimulating hormone, T4: Thyroxine, HOMA-IR: Homeostatic model assessment of insulin resistance, IL-37: Interleukin-37, TG: Triglycerides, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, VLDL-C: Very-low-density lipoprotein cholesterol.

and BMI for all lipid profile parameters except HDL-C, indicating that the relationship between IL-37 and an unfavorable lipid profile was independent of these demographic and anthropometric factors. Overall, elevated circulating IL-37 was associated with higher atherogenic lipid fractions and lower HDL-C levels (Table 3).

Discussion

This prospective cross-sectional study examined the relationship between circulating IL-37 concentrations and lipid-profile parameters in 25 newly diagnosed Iraqi adults with hypothyroidism and insulin resistance. The central finding was that IL-37 levels were positively correlated with TG, total cholesterol, LDL-C, and VLDL-C, while an inverse relationship was observed with HDL-C. In adjusted linear regression analyses controlling for age, sex, and BMI, the positive associations of IL-37 with TG, total cholesterol, LDL-C, and VLDL-C remained statistically significant, whereas the inverse association with HDL-C did not retain significance after adjustment. These findings are internally consistent and reflect a coherent pattern of IL-37 elevation in a setting of established atherogenic dyslipidemia, a pattern that aligns with the broader premise that IL-37 is upregulated in states of chronic metabolic inflammation (2,3). The study contributes to an emerging body of evidence pointing toward a possible relationship between IL-37 and lipid dysregulation in endocrine-metabolic disorders, a connection that has received little direct empirical attention in hypothyroid populations.

The positive associations observed between IL-37 and the atherogenic lipid fractions, TG, total cholesterol, LDL-C, and VLDL-C, are noteworthy, particularly given that these associations survived adjustment for key confounders. Hypothyroidism is well established as a cause of atherogenic dyslipidemia through impaired thyroid hormone–dependent regulation of cholesterol biosynthesis, reduced hepatic LDL receptor expression, and diminished reverse cholesterol transport, collectively resulting in elevated circulating cholesterol and triglyceride levels (2, 3). A systematic review and meta-analysis by Treister-Goltzman et al encompassing 35 studies confirmed that even mild subclinical hypothyroidism is associated with significantly higher total cholesterol, LDL-C, and TG alongside lower HDL-C compared with euthyroid controls, underscoring the atherogenic lipid burden inherent to thyroid hypofunction (18). The role of insulin resistance compounds this dyslipidemia further: in the setting of impaired insulin signaling, hepatic VLDL production is enhanced, lipolysis from adipose tissue is increased, and LDL particles tend to become smaller and denser, all of which amplify the atherogenic lipid phenotype seen in the present cohort (4). The independent persistence of IL-37 associations with TG, total cholesterol, LDL-C, and VLDL-C after demographic adjustment suggests that the IL-37–lipid relationship in this population is not simply mediated by age, sex, or

Table 2. Correlations of circulating IL-37 levels with lipid-profile parameters

Variables	IL-37 (pg/mL)			
	r	95% CI		*P* value*
		Lower	Upper	
Demographic characteristics				
Age (year)	-0.048	-0.435	354	0.850
BMI (kg/m²)	0.205	-0.207	0.555	0.325
Lipid profile parameters				
TG (mg/dL)	0.400	0.006	0.687	0.047
Cholesterol (mg/dL)	0.458	0.077	0.726	0.021
LDL-C (mg/dL)	0.498	0.128	0.746	0.011
HDL-C (mg/dL)	-0.407	-0.691	-0.014	0.043
VLDL-C (mg/dL)	0.391	0.005	0.697	0.046

IL-37: Interleukin-37, BMI: Body mass index, TG: Triglycerides, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, VLDL-C: Very-low-density lipoprotein cholesterol, R: Pearson correlation, CI: Confidence interval. *Pearson correlation coefficient .

Table 3. Linear regression analysis of the association between circulating IL-37 and lipid-profile parameters

Dependent variables		IL-37 (pg/mL) as independent variable			
		B	95% CI		*P* value
			Lower	Upper	
Unadjusted	TG (mg/dL)	0.335	0.004	0.665	0.046
	Cholesterol (mg/dL)	0.430	0.070	0.790	0.021
	LDL-C (mg/dL)	0.490	0.122	0.858	0.011
	HDL-C (mg/dL)	-0.127	-0.249	-0.004	0.043
	VLDL-C (mg/dL)	0.067	0.001	0.133	0.047
Adjusted*	TG (mg/dL)	0.411	0.046	0.776	0.028
	Cholesterol (mg/dL)	0.498	0.127	0.868	0.011
	LDL-C (mg/dL)	0.526	0.132	0.921	0.012
	HDL-C (mg/dL)	-0.111	0.114	-0.250	0.029
	VLDL-C (mg/dL)	0.082	0.009	0.155	0.030

IL-37: Interleukin-37, TG: Triglycerides, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, VLDL-C: Very-low-density lipoprotein cholesterol, CI: Confidence interval, B: Unstandardized coefficients. *Adjusted for age, gender, and BMI.

BMI but may instead reflect a genuine immunometabolic interaction; in line with this, prior evidence from human metabolic syndrome studies demonstrated that serum IL-37 was significantly associated with dyslipidemia-related metabolic syndrome components, with IL-37 emerging as an immunometabolic biomarker with good diagnostic accuracy by receiver operating characteristic analysis (8,9).

The finding of elevated IL-37 in association with adverse lipid parameters in this cohort raises an important interpretive question: whether raised IL-37 reflects a causal contributor to dyslipidemia or, more plausibly, a counter-regulatory immunological response to the ongoing inflammatory–metabolic disturbance characteristic of hypothyroidism with insulin resistance. IL-37 is an anti-inflammatory cytokine that broadly suppresses innate immune activation through dual intracellular and extracellular signaling pathways, and elevated circulating IL-37 has been consistently documented in conditions of active inflammation and metabolic dysfunction, suggesting that its upregulation is largely reactive rather than pathogenic (6). In experimental models of metabolic syndrome, IL-37 administration led to reduced adipose tissue inflammation, lowered plasma insulin, improved glucose tolerance, and suppressed production of pro-inflammatory cytokines including TNF-α and IL-1β from adipose tissue, implying that IL-37 acts as a brake on the inflammatory processes that underlie insulin resistance and lipid dysregulation (7). From this perspective, the higher IL-37 levels observed in patients with worse lipid profiles in the present study may represent a biological attempt to counteract the intensifying inflammatory milieu rather than a driver of the lipid abnormalities per se. Supporting this concept, Abdel-Moneim et al found that IL-37 levels were inversely correlated with the accumulation of metabolic syndrome components in Egyptian patients, with the most metabolically impaired group showing the lowest IL-37, a pattern compatible with insufficient counter-regulatory capacity (8). By contrast, the present finding of higher IL-37 in the more dyslipidemic patients could reflect an earlier or more active counter-regulatory phase in this relatively young cohort (mean age 36.5 years), where the immune system is still mounting a meaningful anti-inflammatory response despite metabolic deterioration (9).

The inverse correlation between IL-37 and HDL-C in unadjusted analyses is clinically meaningful, given that low HDL-C is a well-recognized component of the atherogenic lipid triad in both hypothyroidism and insulin resistance (4,18). However, this association did not remain statistically significant after adjustment for age, sex, and BMI, suggesting that the IL-37–HDL-C relationship may be substantially confounded by demographic and anthropometric variables, particularly sex and BMI, both of which are known independent determinants of HDL-C concentrations (18). The finding that women comprised 60% of the cohort is relevant in this context, as sex-related hormonal and metabolic influences on HDL metabolism may have introduced variance that attenuated the IL-37 signal for this specific lipid fraction (4). With respect to the thyroid-specific context, the current findings complement prior observations in thyroid disease; Ruggeri et al reported significantly elevated serum IL-37 in patients with Hashimoto's thyroiditis that correlated with oxidative stress parameters, suggesting that autoimmune and inflammatory thyroid pathology actively stimulates IL-37 production as a protective response (10). Moreover, Ali et al demonstrated that workers with elevated TSH exhibited significantly higher circulating IL-37 compared with controls, reinforcing the notion that thyroid hormonal perturbations and IL-37 dysregulation are physiologically linked, with TSH elevation potentially serving as a stimulus for IL-37 upregulation (11). Taken together with the present findings, there appears to be a consistent thread connecting thyroid dysfunction, systemic inflammation, and IL-37 elevation across both autoimmune and non-autoimmune thyroid disease contexts.

Beyond its associations with lipid fractions, the

elevation of IL-37 in this cohort of hypothyroid, insulin-resistant patients may carry broader cardiovascular significance. Endothelial dysfunction is a recognized early step in atherogenesis, and IL-37 has been demonstrated to suppress the toll-like receptor-2 (TLR2)-nuclear transcription factor-κB (NF-κB)-intercellular adhesion molecule-1 (ICAM-1) inflammatory signaling cascade in human coronary artery endothelial cells, suggesting a potentially atheroprotective role for this cytokine at the vascular level (19). In ApoE-deficient murine models of atherosclerosis, exogenous IL-37 reduced atherosclerotic plaque size, decreased macrophage and pro-inflammatory T-lymphocyte infiltration, and promoted regulatory T-cell responses—collectively suggesting that IL-37 may limit atherogenic progression even when lipid levels are unfavorable (20). Dysregulation of lipid metabolism in the context of hypothyroidism is further substantiated by epidemiological data showing that subclinical hypothyroidism, even without overt hormonal deficiency, is associated with unfavorable lipid alterations including elevated TG, reduced HDL-C, and an increased LDL/HDL ratio that together portend early atherogenic risk (21). Furthermore, thyroid dysfunction has been frequently co-identified in patients with metabolic syndrome: a large Pan-India cross-sectional study found hypothyroidism to be the most prevalent thyroid disorder among patients with metabolic syndrome, with affected individuals exhibiting reduced HDL-C, elevated HOMA-IR, and raised TG, a lipid and insulin resistance profile closely mirroring that of the present cohort (22).

Furthermore, evidence from an Iraqi population has demonstrated the coexistence of insulin resistance with adverse biochemical and lipid alterations, as Al-Fayyadh et al reported significantly higher HOMA-IR and lipid-profile parameters in patients with type 2 diabetes compared with healthy controls (23). The IL-37's emerging role in modulating fatty acid metabolism, as shown in a study where IL-37 restored carnitine palmitoyl-transferase 1A (CPT1A)-mediated fatty acid oxidation in diabetic kidney disease, hints at potential metabolic-lipid regulatory functions for this cytokine that extend beyond pure inflammation suppression and warrant further investigation in endocrine-metabolic settings (24).

In summary, this prospective cross-sectional study provides evidence that circulating IL-37 concentrations are significantly and positively associated with an atherogenic lipid profile, specifically elevated TG, total cholesterol, LDL-C, and VLDL-C, in newly diagnosed patients with hypothyroidism and concurrent insulin resistance, with these associations remaining significant after adjustment for age, sex, and BMI. The inverse correlation with HDL-C observed in unadjusted analyses did not persist after demographic adjustment, suggesting that confounding by sex and BMI may account for part of this relationship. Collectively, the findings indicate that IL-37 may serve as a biomarker reflecting the inflammatory–metabolic disturbance that underlies dyslipidemia in this clinically vulnerable population, rather than as a direct mediator of lipid abnormalities, consistent with its established role as a counter-regulatory anti-inflammatory cytokine that is upregulated in states of metabolic and inflammatory stress. These findings align with and extend prior evidence linking IL-37 to metabolic syndrome components and thyroid immune pathology. Given the heightened cardiovascular risk that accompanies the convergence of hypothyroidism, insulin resistance, and dyslipidemia, and the potential atheroprotective functions attributed to IL-37 at the vascular level, future longitudinal studies with larger, more diverse cohorts are warranted to establish causal directionality, evaluate the influence of thyroid hormone replacement on IL-37 dynamics, and determine whether this cytokine holds clinical value as a therapeutic target or prognostic indicator in endocrine-metabolic disease.

Conclusion

These findings suggest that circulating IL-37 is closely linked to an adverse lipid profile in newly diagnosed patients with hypothyroidism and insulin resistance, with independent associations observed for TG, total cholesterol, LDL-C, and VLDL-C after accounting for age, sex, and BMI. The loss of significance for HDL-C after adjustment indicates that this particular association may be more influenced by demographic factors than the other lipid parameters. Collectively, these results point to IL-37 as a potential inflammatory marker of dyslipidemia and, by extension, cardiovascular risk in this patient population, warranting further investigation in larger, longitudinal studies to clarify its mechanistic role and clinical utility.

Limitations of the study

First, the cross-sectional design prevents any causal inference; the data establish association but cannot determine whether elevated IL-37 precedes, accompanies, or follows the development of dyslipidemia in this population. Second, the sample size of 25 participants is modest, which reduces statistical power and may limit the generalizability of the findings, particularly for the HDL-C association that lost significance after adjustment. Third, the study was restricted to newly diagnosed hypothyroid patients with confirmed insulin resistance recruited from a single geographic region in Iraq, which may constrain external validity to other ethnic, environmental, or clinical populations. Fourth, single time-point measurements of both IL-37 and lipid parameters do not capture the longitudinal dynamics of these markers, and it remains unknown how IL-37 levels might evolve following initiation of thyroid hormone replacement therapy. Fifth, the regression models were adjusted for age, sex, and BMI only; other potential confounders, such as dietary habits, physical activity level, comorbid conditions, medication

use, and duration of untreated hypothyroidism, were not accounted for, and residual confounding cannot be excluded. Finally, the biological directionality of the IL-37–lipid relationship remains unclear from this design, and mechanistic studies using experimental models or longitudinal designs with repeated measurements are needed to clarify whether IL-37 serves primarily as a biomarker of metabolic inflammatory burden or as a functional mediator in lipid regulation.

Acknowledgments

The authors sincerely thank all participants for their time and cooperation. We also acknowledge the staff of Al-Nasiriya General Hospital and Bint Al-Huda Maternity Hospital, Thi-Qar Governorate, Iraq, for their assistance with participant recruitment and sample collection. Special appreciation is extended to the personnel of the Biochemistry Laboratory, College of Science, University of Thi-Qar, for their valuable technical support during laboratory analyses.

Authors' contribution

Conceptualization: Both authors.
Data curation: Bashair Talib Jassim.
Formal analysis: Raid M. H. Al-Salih.
Investigation: Raid M. H. Al-Salih.
Methodology: Raid M. H. Al-Salih.
Project management: Bashair Talib Jassim.
Supervision: Both authors.
Validation: Bashair Talib Jassim.
Writing–original draft: Both authors.
Writing–reviewing and editing: Both authors.

Conflicts of interest

The authors declare that they have no competing interests.

Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declaration of generative artificial intelligence (AI) and AI-assisted technologies in the writing process

During the preparation of this manuscript, the authors used generative artificial intelligence (Perplexity) and AI-assisted writing tools (Grammarly) to assist with drafting, language editing, and refinement of grammar and style. All content generated by these tools was subsequently critically reviewed, revised, and validated by the authors, who take full responsibility for the accuracy, integrity, and originality of the work.

Ethical issues

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki. The research protocol was reviewed and approved by the Research Committee of the Training and Human Development Center, Thi-Qar Health Directorate, Ministry of Health, Iraq (approval number: 2024/299; registration date: 18 December 2024). Official administrative permission was also issued to facilitate the implementation of the study in the relevant institutions of the Thi-Qar Health Directorate, including Al-Nasiriya Teaching Hospital and Bint Al-Huda Teaching Hospital. In addition, informed consent was obtained from all participants before participation and blood sample collection, as approved within the institutional research approval process. The authors confirm that all ethical issues, including plagiarism, data fabrication, and double publication, have been fully observed.

Funding/Support

This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

References

1. Zoori A, Mousa H. Prevalence of thyroid disorders in Nasiriya City, Iraq. University of Thi-Qar Journal of Science. 2023;10:122-7.
2. Su X, Peng H, Chen X, Wu X, Wang B. Hyperlipidemia and hypothyroidism. Clin Chim Acta. 2022;527:61-70. doi: 10.1016/j.cca.2022.01.006.
3. Su X, Chen X, Peng H, Song J, Wang B, Wu X. Novel insights into the pathological development of dyslipidemia in patients with hypothyroidism. Bosn J Basic Med Sci. 2022;22:326-339. doi: 10.17305/bjbms.2021.6606.
4. Choi YM, Kim MK, Kwak MK, Kim D, Hong EG. Association between thyroid hormones and insulin resistance indices based on the Korean National Health and Nutrition Examination Survey. Sci Rep. 2021;11:21738. doi: 10.1038/s41598-021-01101-z.
5. Xu C, Zhou L, Wu K, Li Y, Xu J, Jiang D, et al. Abnormal Glucose Metabolism and Insulin Resistance Are Induced via the IRE1α/XBP-1 Pathway in Subclinical Hypothyroidism. Front Endocrinol (Lausanne). 2019;10:303. doi: 10.3389/fendo.2019.00303.
6. Bai J, Li Y, Li M, Tan S, Wu D. IL-37 As a Potential Biotherapeutics of Inflammatory Diseases. Curr Drug Targets. 2020;21:855-863. doi: 10.2174/1389450121666200429114926.
7. Ballak DB, Li S, Cavalli G, Stahl JL, Tengesdal IW, van Diepen JA, et al. Interleukin-37 treatment of mice with metabolic syndrome improves insulin sensitivity and reduces pro-inflammatory cytokine production in adipose tissue. J Biol Chem. 2018;293:14224-14236. doi: 10.1074/jbc.RA118.003698.
8. Abdel-Moneim A, Mahmoud R, Allam G, Mahmoud B. Relationship between Cytokines and Metabolic Syndrome Components: Role of Pancreatic-Derived Factor, Interleukin-37, and Tumor Necrosis Factor-α in Metabolic Syndrome Patients. Indian J Clin Biochem. 2024;39:37-46. doi: 10.1007/s12291-022-01079-z.
9. Keskin L, Kiran TR, Erdem M, İnceoğlu F. Interleukin-37 and interleukin-39 as novel immunometabolic biomarkers in metabolic syndrome: A cross-sectional study. Medicine (Baltimore). 2026;105:e48515. doi: 10.1097/MD.0000000000048515.
10. Ruggeri RM, Cristani M, Vicchio TM, Alibrandi A, Giovinazzo S, Saija A, et al. Increased serum interleukin-37 (IL-37) levels correlate with oxidative stress parameters in Hashimoto's thyroiditis. J Endocrinol Invest. 2019;42:199-205. doi: 10.1007/s40618-018-0903-3.
11. Ali IN, Baqer NN, Jawad HG. Association between shift work and levels of thyroid hormones and interleukin-37. Endocr Regul. 2025;59:227-235. doi: 10.2478/enr-2025-0026.
12. Muniyappa R, Madan R, Varghese RT. Assessing Insulin Sensitivity and Resistance in Humans. In: Feingold KR, Adler RA, Ahmed SF, Anawalt B, Blackman MR, Chrousos G, et al, eds. Endotext. South Dartmouth (MA): MDText.com, Inc.; October 16, 2024.
13. Gutch M, Kumar S, Razi SM, Gupta KK, Gupta A. Assessment of insulin sensitivity/resistance. Indian J Endocrinol Metab. 2015;19:160-4. doi: 10.4103/2230-8210.146874.
14. Song Y, Manson JE, Tinker L, Howard BV, Kuller LH, Nathan L, et al. Insulin sensitivity and insulin secretion determined by homeostasis model assessment and risk of diabetes in a multiethnic cohort of women: the Women's Health Initiative Observational Study. Diabetes Care. 2007;30:1747-52. doi:

10.2337/dc07-0358.
15. Patil N, Rehman A, Anastasopoulou C, Jialal I. Hypothyroidism. Treasure Island (FL): StatPearls Publishing LLC.; 2026.
16. Chaker L, Razvi S, Bensenor IM, Azizi F, Pearce EN, Peeters RP. Hypothyroidism. Nat Rev Dis Primers. 2022;8:30.
17. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem. 1972;18:499-502.
18. Treister-Goltzman Y, Yarza S, Peleg R. Lipid profile in mild subclinical hypothyroidism: systematic review and meta-analysis. Minerva Endocrinol (Torino). 2021;46:428-440. doi: 10.23736/S2724-6507.20.03197-1.
19. Yan X, Xie B, Wu G, Hu J, Wang D, Cai X, et al. Interleukin-37: The Effect of Anti-Inflammatory Response in Human Coronary Artery Endothelial Cells. Mediators Inflamm. 20192019:2650590. doi: 10.1155/2019/2650590.
20. Ji Q, Meng K, Yu K, Huang S, Huang Y, Min X, et al. Exogenous interleukin 37 ameliorates atherosclerosis via inducing the Treg response in ApoE-deficient mice. Sci Rep. 2017;7:3310. doi: 10.1038/s41598-017-02987-4.
21. Mawlood MS. The unseen impact of subclinical hypothyroidism on lipid profile and cardiovascular risk. Biochem Biophys Rep. 2026;46:102605. doi: 10.1016/j.bbrep.2026.102605.
22. Deshmukh V, Farishta F, Bhole M. Thyroid Dysfunction in Patients with Metabolic Syndrome: A Cross-Sectional, Epidemiological, Pan-India Study. Int J Endocrinol. 2018;2018:2930251. doi: 10.1155/2018/2930251.
23. Al-Fayyadh MSM, Ismael KH, Al-Saady AJ. Study of insulin resistance, cortisol hormone and some biochemical parameters in Iraqi type 2 diabetic patients. University of Thi-Qar Journal of Science. 2023;10:68-72.
24. Xiong L, He T, Liu C, Qin S, Xiao T, Xin W, et al. IL-37 Ameliorates Renal Fibrosis by Restoring CPT1A-Mediated Fatty Acid Oxidation in Diabetic Kidney Disease. Kidney Dis (Basel). 2023;9:104-117. doi: 10.1159/000529460.