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Integrated Evaluation of Thyroid Function, Lipid Profile, Inflammation, and Oxidative Stress in Patients with Hypothyroidism

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Abstract

Background: Hypothyroidism is associated with metabolic abnormalities that extend beyond thyroid hormone deficiency and may contribute to increased cardiovascular risk. **Objective:** To evaluate thyroid function tests, lipid profile parameters, high-sensitivity C-reactive protein (hs-CRP), and oxidative stress markers in patients with hypothyroidism compared with healthy controls, and to analyze their interrelationships. **Methods**: This cross-sectional analytical study included 500 participants (250 newly diagnosed hypothyroid patients and 250 age- and sex-matched healthy controls). Fasting blood samples were analyzed for thyroid hormones (TSH, free T3, free T4), lipid profile (total cholesterol, triglycerides, HDL-C, LDL-C), apolipoproteins (Apo-A1, Apo-B), lipoprotein(a), hs-CRP, and oxidative stress markers (malondialdehyde and total antioxidant capacity). Statistical analysis was performed using Student's *t*-test and Pearson's correlation. **Results:** BMI was significantly higher in hypothyroid patients ($p < 0.001$). TSH levels were markedly elevated, with reduced thyroid hormone levels ($p < 0.001$). Hypothyroid patients demonstrated significantly increased total cholesterol, triglycerides, LDL-C, Apo-B, and lipoprotein(a), with decreased HDL-C and Apo-A1 ($p < 0.001$). Malondialdehyde levels were elevated and total antioxidant capacity reduced ($p < 0.001$). Elevated hs-CRP levels were significantly more prevalent in hypothyroid subjects. TSH showed significant positive correlations with malondialdehyde and lipoprotein(a), and a negative correlation with Apo-A1. **Conclusion:** Hypothyroidism is strongly associated with dyslipidemia, oxidative stress, and systemic inflammation, suggesting an integrated metabolic disturbance with potential cardiovascular implications.

Key words: TSH, T3, T4, CRP, HDL, LDL, ApoA1

Introduction

Hypothyroidism is among the most prevalent endocrine disorders encountered in routine clinical practice. It is characterized by inadequate synthesis and secretion of the thyroid hormones triiodothyronine (T3) and thyroxine (T4), typically accompanied by a compensatory elevation in thyroid-stimulating hormone (TSH). Epidemiological data indicate that approximately 4–10% of the general population is affected, with a higher prevalence observed in women and in advancing age groups [1,2]. While the clinical presentation often includes fatigue, weight gain, constipation, dry skin, and cold intolerance, the systemic impact of thyroid hormone deficiency extends well beyond these overt symptoms. Given the central role of thyroid hormones in regulating basal metabolic rate, lipid metabolism, mitochondrial function, and cellular redox balance, their deficiency results in widespread metabolic and biochemical disturbances.

Dyslipidemia represents one of the most consistently documented metabolic consequences of hypothyroidism. Thyroid hormones regulate hepatic lipid metabolism by enhancing the expression of low-density lipoprotein (LDL) receptors and facilitating cholesterol clearance from circulation. In the setting of reduced hormone levels, this regulatory mechanism is impaired, leading to elevations in total cholesterol (TC) and LDL cholesterol (LDL-C) [3]. Both overt and subclinical hypothyroidism have been associated with adverse lipid profiles, thereby contributing to an increased risk of cardiovascular morbidity [4]. In addition to elevated LDL-C, alterations in triglycerides (TG) and high-density lipoprotein cholesterol (HDL-C) further accentuate the atherogenic milieu, even in individuals with mild thyroid dysfunction.

Beyond lipid abnormalities, accumulating evidence indicates that hypothyroidism is accompanied by a state of chronic low-grade inflammation. Increased circulating levels of inflammatory biomarkers, including C-reactive protein (CRP), interleukin-6 (IL-6), and tumour necrosis factor-alpha (TNF-α), have been observed in affected patients [5]. Persistent inflammatory activation may impair endothelial function, promote vascular stiffness, and accelerate atherosclerotic progression, thereby compounding the cardiovascular risk associated with dyslipidemia.

Oxidative stress has also emerged as a significant component of the pathophysiological spectrum of hypothyroidism. Thyroid hormones influence mitochondrial oxidative phosphorylation and modulate endogenous antioxidant systems. A decline in hormone levels may reduce the activity of key antioxidant enzymes—such as superoxide dismutase (SOD), catalase, and glutathione peroxidase (GPx)—while simultaneously increasing lipid peroxidation products, including malondialdehyde (MDA) [6,7]. The resulting imbalance between reactive oxygen species generation and antioxidant defence mechanisms may contribute to cellular injury and may interact synergistically with inflammatory pathways.

Collectively, disturbances in thyroid hormone levels, lipid metabolism, inflammatory mediators, and oxidative stress parameters appear to represent interconnected aspects of a broader metabolic dysfunction in hypothyroidism. An integrated biochemical evaluation of these domains may offer a more comprehensive understanding of disease severity and associated cardiovascular risk.

Therefore, the present study aims to assess the interrelationship between thyroid function tests, lipid profile parameters, inflammatory markers, and oxidative stress indices in patients with hypothyroidism, underscoring the relevance of a multidimensional approach in clinical assessment and risk stratification.

Materials and Methods

This cross-sectional study, approved by the Institutional Ethics Committee, involved participants aged 18 to 60. The case group comprised newly diagnosed, untreated hypothyroidism patients with elevated serum TSH and either low (overt) or normal (subclinical) free T4 levels. The control group included age- and sex-matched healthy individuals with normal thyroid function.

Individuals with diabetes, hypertension, chronic kidney or liver disease, cardiovascular disorders, inflammation, pregnancy, and those on thyroid hormones, lipid-lowering drugs, or antioxidants were excluded to minimize confounding effects.

Blood samples were collected after an overnight fast and analysed for:

- Thyroid function tests (TSH, free T3, free T4) via chemiluminescent immunoassay.
- Lipid profile (total cholesterol, triglycerides, HDL cholesterol) through enzymatic colourimetric methods; LDL was calculated.
- High-sensitivity C-reactive protein (hs-CRP) as an inflammatory marker using immunoturbidimetric methods.
- Oxidative stress markers (MDA, SOD, catalase, GPx) were assessed by spectrophotometric methods.

Statistical Analysis

Data were expressed as mean ± standard deviation, with differences analysed using Student's t-test and Pearson's correlation for relationships between hormone levels and other parameters. A p-value under 0.05 was deemed significant.

Results

Demographic Characteristics

The control group's mean age was 53.5 ± 7.9 years, while the hypothyroid group was 52.9 ± 5.5 years, with no significant age difference ($t = 0.99$, $p > 0.05$). The control group's mean BMI was 24.2 ± 2.3 kg/m², compared to 27.4 ± 4.5 kg/m² in the hypothyroid group, a highly significant difference ($t = -10.02$, $p < 0.001$). Mean systolic blood pressure was 119 ± 26.3 mmHg for the control group and 123 ± 32.2 mmHg for the hypothyroid group, with no significant difference ($t = -1.53$, $p > 0.05$). Mean diastolic blood pressure was 90.3 ± 14.9 mmHg in the control group and 92.7 ± 19.4 mmHg in the hypothyroid group, with no significant difference ($t = -1.56$, $p > 0.05$). (Table 1)

Table 1: Demographic characteristics of the study population across different groups

Parameters	Control group (n=250)	Hypothyroid group (n=250)	T Test	P-value
Age (Years)	53.5 ± 7.9	52.9 ± 5.5	0.99	>0.05
BMI (kg/mt^2)	24.2 ± 2.3	27.4 ± 4.5	-10.02	<0.001

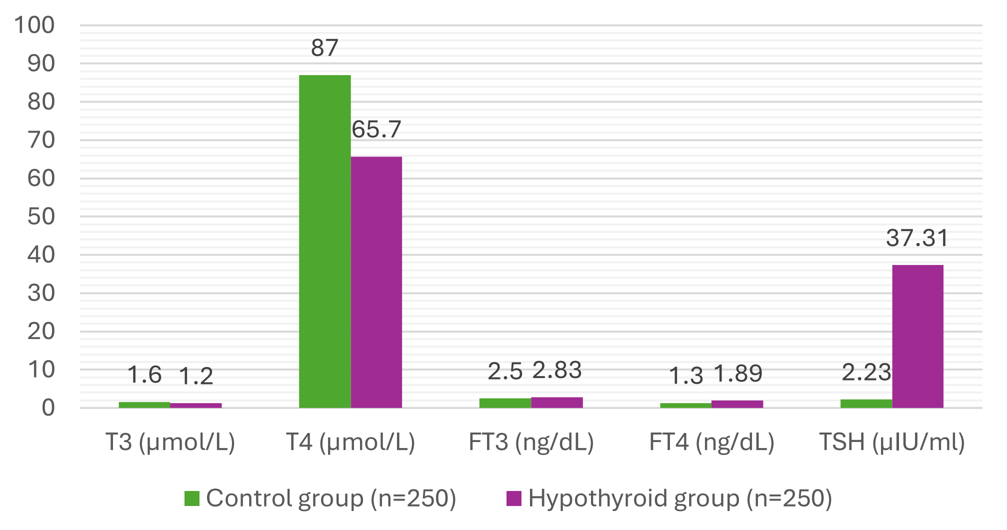
Systolic Pressure (mm of Hg)	119 ± 26.3	123 ± 32.2	-1.53	>0.05
Diastolic Pressure (mm of Hg)	90.3 ± 14.9	92.7 ± 19.4	-1.56	>0.05

Thyroid Function

In this study, the mean serum triiodothyronine (T3) level was significantly lower in the hypothyroid group, measuring 1.2 ± 0.1 µmol/L, compared to the control group, which had a mean level of 1.6 ± 0.56 µmol/L ($p < 0.001$). Similarly, the mean thyroxine (T4) level was reduced in the hypothyroid group at 65.7 ± 23.4 µmol/L, in contrast to the control group's 87 ± 33.2 µmol/L ($p < 0.001$).

Conversely, the hypothyroid group exhibited a higher mean free triiodothyronine (FT3) level of 2.83 ± 0.17 ng/dL compared to the control group's 2.5 ± 0.8 ng/dL ($p < 0.001$). The mean free thyroxine (FT4) level was also elevated in the hypothyroid group, reaching 1.89 ± 0.61 ng/dL, versus 1.3 ± 0.4 ng/dL in the control group ($p < 0.001$). Finally, the thyroid-stimulating hormone (TSH) level was considerably higher in the hypothyroid group, with a mean of 37.31 ± 17.3 µIU/mL, compared to the control group's level of 2.23 ± 0.50 µIU/mL ($p < 0.001$). (Figure 1)

Graph 1: Baseline thyroid function test parameters among the different study populations



Lipid Profile Alterations

Hypothyroid patients had significantly higher total cholesterol (TC) at 215.8 ± 16.8 mg/dL compared to controls at 133.3 ± 6.4 mg/dL ($p < 0.001$). Triglyceride (TAG) levels were also elevated (214.1 ± 20.4 mg/dL vs. 141.3 ± 3.2 mg/dL, $p < 0.001$).

High-density lipoprotein (HDL) levels dropped from 47.31 ± 4.5 mg/dL in controls to 36.1 ± 3.93 mg/dL in hypothyroid subjects ($p < 0.001$). Low-density lipoprotein (LDL) was higher in the hypothyroid group (121.7 ± 19.2 mg/dL) vs. controls (57 ± 2.3 mg/dL) ($p < 0.001$).

Apolipoprotein A1 (Apo-A1) was lower in hypothyroid patients (78.2 ± 21.3 mg/dL) compared to controls (97.7 ± 35.1 mg/dL) ($p < 0.001$). Apolipoprotein B (Apo-B) was also elevated (141 ± 33.6 mg/dL vs. 77 ± 22.7 mg/dL, $p < 0.001$).

Overall, hypothyroid patients showed a more atherogenic lipid profile, with higher TC, TAG, LDL, and Apo-B, and lower HDL and Apo-A1 levels. (Table 2)

Table 2: Baseline lipid profile parameters among the different study populations

Parameters	Control group (n=250)	Hypothyroid group (n=250)	p-value
TC (mg/dL)	133.3±6.4	215.8±16.8	**<0.001**
TAG (mg/dL)	141.3±3.2	214.1±20.4	**<0.001**
HDL (mg/dL)	47.31±4.5	36.1±3.93	**<0.001**
LDL (mg/dL)	57 ± 2.3	121.7±19.2	**<0.001**
Apo-a1 (mg/dL)	97.7± 35.1	78.2 ± 21.3	**<0.001**
Lipo-a (mg/dL)	23.7 ± 2.9	41.5 ± 11.9	**<0.001**
Apo-B (mg/dL)	77 ± 22.7	141 ± 33.6	**<0.001**

Oxidative Stress Parameters

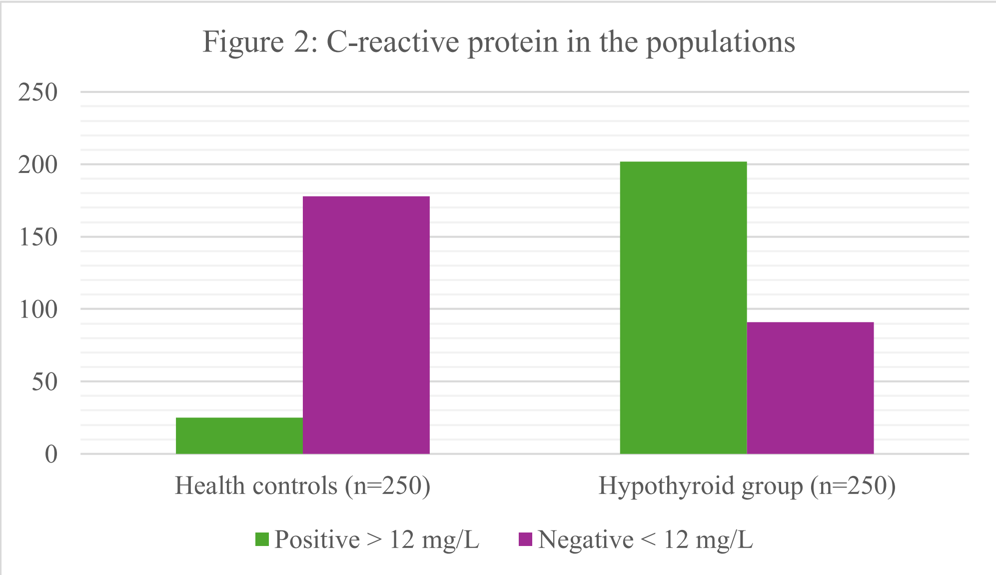
In the control group, the mean total antioxidant capacity (TAC) was 8.9 ± 6.3 µmol/dL, significantly lower at 6.7 ± 5.3 µmol/dL in the hypothyroid group ($p < 0.001$). The mean malondialdehyde (MDA) level was 4.5 ± 1.2 nmol/mL in controls, elevated to 7.2 ± 2.5 nmol/mL in hypothyroid patients ($p < 0.001$). However, the mean nitric oxide (NO) level did not show a significant difference, with 11.8 ± 3.8 µmol/L in the control group and 12.8 ± 7.5 µmol/L in the hypothyroid group ($p > 0.05$). (Table 3)

Table 3: Baseline oxidative stress parameters among the different study populations

Parameters	Control group (n=250)	Hypothyroid group (n=250)	P-value
TAC (µmol/dL)	8.9 ± 6.3	6.7 ± 5.3	<0.001
MDA (nmol/mL)	4.5 ± 1.2	7.2 ± 2.5	<0.001
NO (µmol/L)	11.8 ± 3.8	12.8 ± 7.5	>0.05

Inflammatory Marker

In a study of healthy controls (n = 250), 25 individuals had hs-CRP levels above 12 mg/L (positive), while 178 were below that threshold (negative). In contrast, among individuals with hypothyroidism (n = 250), 202 tested positive for elevated hs-CRP, with only 91 below the threshold. This indicates a significantly higher prevalence of elevated hs-CRP levels in the hypothyroid group, suggesting a greater inflammatory burden in these patients. (Figure 2)



Correlation Analysis in the hypothyroid group

In the hypothyroid group, TSH showed a significant positive correlation with malondialdehyde and lipoprotein(a), and a significant negative correlation with apolipoprotein A1 (p < 0.001 for all), indicating a close association between thyroid dysfunction, oxidative stress, and atherogenic lipid markers."

These findings demonstrate a direct association between thyroid dysfunction and atherogenic oxidative changes. (**Table 4**)

Table 4: Pearson correlation in the Hypothyroidism group (n=250)

Variables	TSH
MDA	r^2= 0.234
Apo-A1	r^2= -0.376
Lipo-A	r^2= 0.523

Discussion

The present study demonstrates that hypothyroidism is associated with significant metabolic disturbances extending beyond thyroid hormone deficiency. Elevated TSH levels with altered T3 and T4 concentrations confirmed biochemical hypothyroidism, consistent with established clinical patterns [1,2]. Patients with hypothyroidism also exhibited a significantly higher BMI, reflecting the known role of thyroid hormones in regulating basal metabolic rate and energy expenditure [3]. Although blood pressure did not differ significantly between groups, the metabolic profile observed suggests potential long-term cardiovascular implications.

A prominent finding was the presence of marked dyslipidemia in hypothyroid patients. Total cholesterol, triglycerides, LDL cholesterol, Apo-B, and lipoprotein(a) were significantly increased, whereas HDL cholesterol and Apo-A1 were reduced. Thyroid hormones regulate hepatic LDL receptor activity and cholesterol clearance; thus, hormone deficiency contributes to elevated circulating LDL levels [9]. Similar lipid abnormalities have been documented in both overt and subclinical hypothyroidism [4]. The concurrent rise in Apo-B and Lp(a), along with reduced Apo-A1, indicates both quantitative and qualitative atherogenic changes, reinforcing the heightened cardiovascular risk in this population.

The study further identified significant oxidative imbalance, as evidenced by increased malondialdehyde levels and reduced total antioxidant capacity. Thyroid hormones influence mitochondrial oxidative phosphorylation and redox regulation; their deficiency may enhance reactive oxygen species generation and lipid peroxidation [6,7]. Interestingly, nitric oxide levels were not significantly altered, suggesting that lipid peroxidation rather than nitric oxide bioavailability may predominate in early oxidative alterations.

A substantially higher prevalence of elevated hs-CRP levels was observed in hypothyroid patients, indicating low-grade systemic inflammation. hs-CRP is a well-established marker of cardiovascular risk, and its elevation in hypothyroidism has been previously reported [5]. The coexistence of dyslipidemia, oxidative stress, and inflammation suggests interrelated pathogenic mechanisms contributing to vascular dysfunction.

Correlation analysis revealed significant positive associations between TSH and malondialdehyde as well as lipoprotein(a), and a negative association with Apo-A1. These findings indicate that increasing severity of thyroid dysfunction parallels worsening oxidative stress and atherogenic lipid alterations. The strong association between TSH and Lp(a), a largely genetically determined lipoprotein, warrants further mechanistic investigation.

Clinical Implications

These findings underscore the importance of comprehensive metabolic assessment in hypothyroid patients. While thyroid hormone replacement remains fundamental, evaluation of lipid abnormalities, inflammatory markers, and oxidative stress parameters may improve cardiovascular risk stratification and guide more individualized management strategies.

Conclusion

The findings of this study indicate a significant association between hypothyroidism and dyslipidemia, oxidative stress, and systemic inflammation. Patients with hypothyroidism display a distinctly atherogenic lipid profile, characterized by elevated levels of total cholesterol, triglycerides, LDL cholesterol, Apo-B, and Lp(a), along with decreased HDL cholesterol and Apo-A1 levels.

Elevated malondialdehyde levels and diminished antioxidant capacity suggest increased oxidative stress, while higher hs-CRP levels indicate chronic inflammatory activation. The significant correlations observed between TSH and both oxidative and atherogenic lipid markers underscore the close interrelationship between thyroid dysfunction and cardiovascular risk factors.

These findings reinforce the notion that hypothyroidism constitutes a complex metabolic state with potential cardiovascular implications. A comprehensive evaluation of thyroid function, lipid parameters, inflammatory markers, and oxidative stress indices may offer deeper insights into the disease burden and facilitate more effective clinical management strategies.

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