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RELATIONSHIP BETWEEN THYROID DYSFUNCTION, OXIDATIVE STRESS, AND ATHEROGENIC LIPID MARKERS: A COMPARATIVE STUDY

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ABSTRACT

Background:
Thyroid dysfunction, particularly hypothyroidism, is associated with metabolic disturbances that may increase cardiovascular risk. Altered thyroid hormone levels influence lipid metabolism, oxidative balance, and inflammatory pathways. This study aimed to evaluate the relationship between thyroid dysfunction, oxidative stress, and atherogenic lipid markers in comparison with healthy individuals.

Methods:
This comparative cross-sectional study included 500 participants divided into two groups: hypothyroid patients (n = 250) and age- and sex-matched euthyroid controls (n = 250). Thyroid function tests (TSH, fT3, fT4), lipid profile parameters, apolipoproteins, lipoprotein(a), oxidative stress markers (malondialdehyde [MDA], total antioxidant capacity [TAC]), nitric oxide (NO), and CRP were assessed. Intergroup comparisons were performed using Student's *t*-test, and Pearson's correlation analysis was used to evaluate associations between TSH and biochemical variables.

Results:
Hypothyroid patients exhibited significantly higher BMI ($p < 0.001$) and a markedly atherogenic lipid profile, characterized by elevated total cholesterol, triglycerides, LDL-C, lipoprotein(a), and Apo-B, along with reduced HDL-C and Apo-A1 ($p < 0.001$). Total antioxidant capacity was significantly reduced, while MDA levels were elevated in the hypothyroid group ($p < 0.001$), indicating increased oxidative stress. A greater proportion of hypothyroid patients demonstrated elevated hs-CRP levels, reflecting heightened inflammatory status. Correlation analysis revealed significant associations between TSH and oxidative as well as atherogenic lipid markers in the hypothyroid group.

Conclusion:
Hypothyroidism is associated with dyslipidemia, oxidative stress, and systemic inflammation, suggesting an integrated mechanism contributing to increased cardiovascular risk. Comprehensive metabolic and inflammatory assessment may be essential in the clinical management of patients with thyroid dysfunction.

Key words: TFT, MDA, TAC, CRP

Introduction

Thyroid dysfunction remains a significant global health concern because of its high prevalence and its broad metabolic consequences. Hypothyroidism, including both overt and subclinical forms, is particularly common in women and older adults and often presents with nonspecific symptoms. Thyroid hormones—triiodothyronine (T3) and thyroxine (T4)—are essential regulators of basal metabolic rate, mitochondrial bioenergetics, lipid turnover, and cellular redox balance. Consequently, alterations in thyroid status may induce systemic metabolic changes that extend beyond endocrine dysregulation. [1]

Dyslipidemia is one of the most consistently documented biochemical abnormalities in hypothyroidism. Thyroid hormones modulate hepatic cholesterol synthesis, lipoprotein metabolism, and low-density lipoprotein (LDL) receptor expression. Reduced thyroid hormone availability impairs LDL receptor–mediated clearance, resulting in elevated total cholesterol and LDL cholesterol concentrations. In addition, increased triglycerides, apolipoprotein B (Apo-B), and lipoprotein(a) [Lp(a)], along with reduced high-density lipoprotein cholesterol (HDL-C) and apolipoprotein A1 (Apo-A1), contribute to a pro-atherogenic lipid profile. Recent large-scale analyses and guideline updates continue to emphasize the association between altered thyroid function and adverse lipid patterns, even within the subclinical range [2-4].

Oxidative stress has emerged as an important mechanistic link between thyroid dysfunction and cardiovascular risk. Thyroid hormones influence mitochondrial oxidative phosphorylation and regulate endogenous antioxidant systems. In hypothyroid states, altered mitochondrial activity may increase the production of reactive oxygen species (ROS), leading to lipid peroxidation and oxidative modification of circulating lipoproteins. Elevated malondialdehyde (MDA) levels and reduced antioxidant capacity have been reported in patients with hypothyroidism, suggesting an imbalance between oxidant generation and antioxidant defense [5,6]. Oxidized LDL particles exhibit enhanced atherogenicity through increased macrophage uptake and foam cell formation.

The interaction between oxidative stress and atherogenic lipid markers is clinically significant. Oxidative modification of lipoproteins promotes endothelial dysfunction and vascular inflammation, key steps in atherogenesis. Contemporary cardiovascular–endocrine research highlights the integrated influence of thyroid hormone status on lipid composition, inflammatory pathways, and oxidative susceptibility of lipoproteins [7,8].

Despite growing recognition of these interconnected processes, comprehensive studies evaluating thyroid function, oxidative stress indices, and atherogenic lipid markers simultaneously remain limited. A comparative and integrative assessment of these parameters may enhance understanding of the metabolic and cardiovascular implications of thyroid dysfunction.

Therefore, the present study aims to investigate the relationship between thyroid dysfunction, oxidative stress, and atherogenic lipid markers, and to examine their interrelationships in comparison with healthy individuals.

Materials and Methods

This comparative cross-sectional study was conducted at a tertiary care teaching hospital following approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants prior to enrollment.

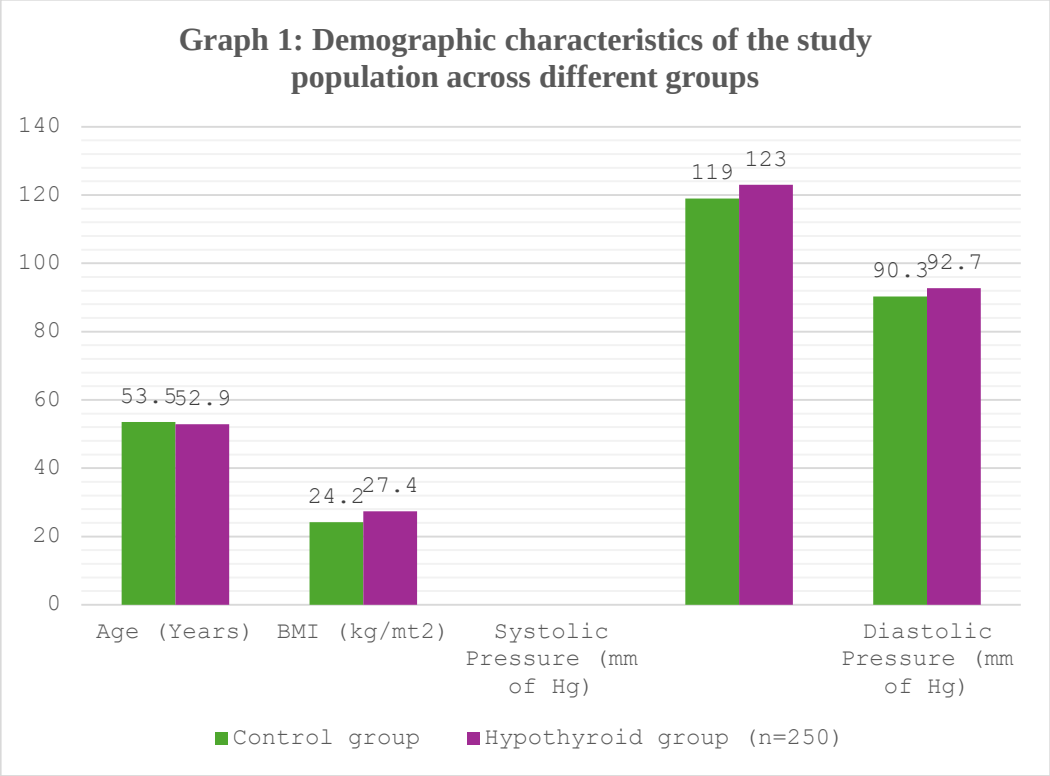
A total of 500 subjects were included and categorised into two groups: patients with thyroid dysfunction (overt or subclinical hypothyroidism) and age- and sex-matched healthy controls with normal thyroid function. Hypothyroidism was defined as elevated serum thyroid-stimulating hormone (TSH) levels with reduced (overt) or normal (subclinical) free thyroxine (fT4). Individuals with diabetes mellitus, hypertension, cardiovascular disease, renal or hepatic disorders, inflammatory conditions, pregnancy, or those receiving thyroid hormone therapy, lipid-lowering agents, or antioxidant supplements were excluded to minimize confounding factors.

Anthropometric measurements, including height, weight, and body mass index (BMI), were recorded. Blood pressure was measured after adequate rest using a standardized sphygmomanometer.

After an overnight fast of 8–12 hours, venous blood samples were collected under aseptic conditions. Serum was separated by centrifugation and analysed for thyroid function tests (TSH, free triiodothyronine [fT3], and fT4) using chemiluminescent immunoassay. Lipid parameters, including total cholesterol, triglycerides, and high-density lipoprotein cholesterol (HDL-C), were estimated by enzymatic colorimetric methods, and low-density lipoprotein cholesterol (LDL-C) was calculated using the Friedewald formula. Apolipoprotein A1 (Apo-A1), Apolipoprotein B (Apo-B), and lipoprotein(a) [Lp(a)] were measured using immunoassay techniques.
Oxidative stress was assessed by estimating malondialdehyde (MDA) using the thiobarbituric acid reactive substances method and total antioxidant capacity (TAC) using spectrophotometric assays.
Statistical analysis was performed using SPSS version 16. Data were expressed as mean ± standard deviation. Intergroup comparisons were made using Student's *t*-test, and Pearson's correlation was applied to assess associations between TSH and biochemical parameters. A p-value < 0.05 was considered statistically significant.

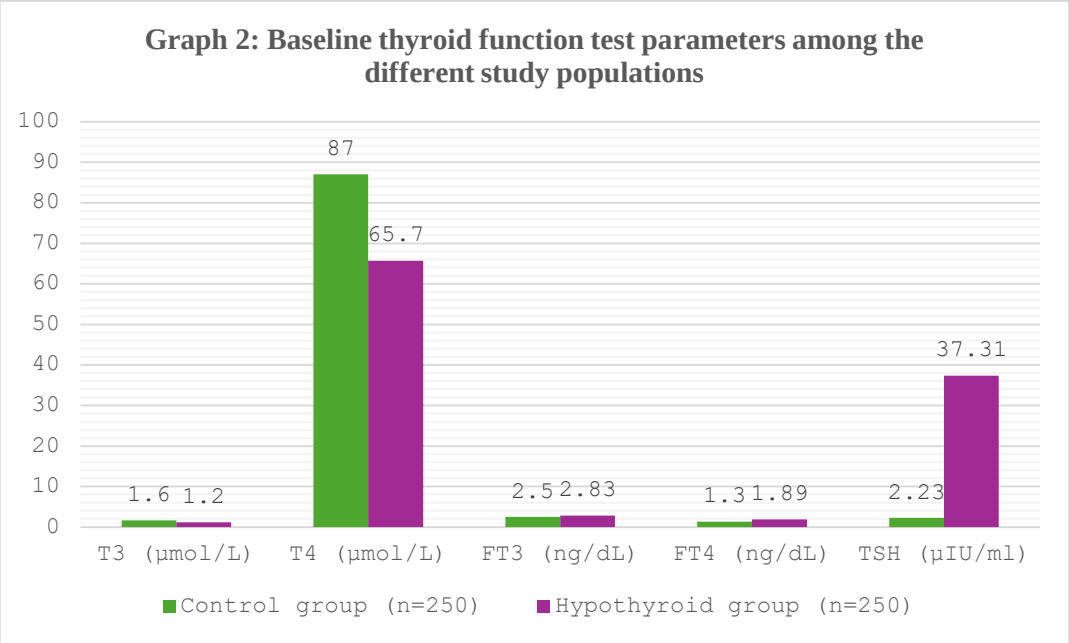
Results

The average age was similar in both groups, with no significant difference between controls (53.5 ± 7.9 years) and hypothyroid participants (52.9 ± 5.5 years).
Body mass index was noticeably higher in the hypothyroid group (27.4 ± 4.5 kg/m²) compared to the control group (24.2 ± 2.3 kg/m²), and this difference was highly significant ($p < 0.001$).
Systolic and diastolic blood pressure values were slightly higher in the hypothyroid group; however, these differences were not statistically significant ($p > 0.05$). (Graph 1)



Thyroid Function

Patients with hypothyroidism showed a clearly unfavourable lipid pattern compared to controls. Total cholesterol and triglyceride levels were significantly higher ($p < 0.001$). LDL, lipoprotein(a), and Apo-B were also markedly elevated in the hypothyroid group ($p < 0.001$).
In contrast, protective markers such as HDL and Apo-A1 were significantly lower among hypothyroid patients ($p < 0.001$).
Overall, hypothyroidism was associated with a distinctly more atherogenic lipid profile. (Graph 2)



Lipid Profile Alterations

Patients with hypothyroidism demonstrated significantly higher levels of total cholesterol and triglycerides compared to controls ($p < 0.001$). LDL, lipoprotein(a), and Apo-B were also markedly elevated, while protective markers such as HDL and Apo-A1 were significantly reduced ($p < 0.001$). Overall, hypothyroidism was associated with a distinctly more atherogenic lipid profile compared to healthy individuals. (Table 1)

Table 1: lipid profile parameters among the Control & Hypothyroid groups

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

The mean total antioxidant capacity (TAC) was significantly lower in the hypothyroid group compared to the control group ($p < 0.001$), indicating a reduced antioxidant defense. Additionally, malondialdehyde (MDA), a marker of lipid peroxidation, was notably elevated in individuals with hypothyroidism ($p < 0.001$), signifying increased oxidative stress. Although nitric oxide (NO) levels were marginally higher in the hypothyroid group, this difference was not statistically significant ($p > 0.05$). (Table 2)

Table 2: Oxidative stress parameters among the Control & Hypothyroid group

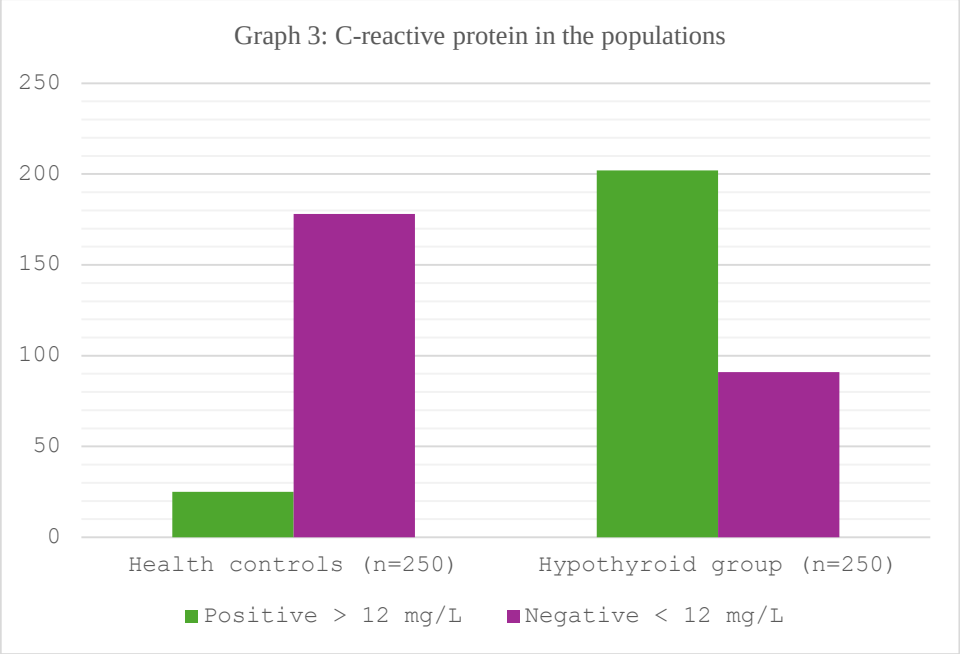
Parameters	Control group (n=250)	Hypothyroid group (n=250)	P-value
TAC (µmol/dL)	8.9 ± 6.3	6.7 ± 5.3	<0.001
MDA (nmol/mL)	4.5 ± 1.2	7.2 ± 2.5	<0.001
NO (µmol/L)	11.8 ± 3.8	12.8 ± 7.5	>0.05

Inflammatory Marker

In the control group (n = 250), 25 participants exhibited CRP levels above 12 mg/L, while the majority had values below this threshold.

In contrast, a substantially higher proportion of individuals in the hypothyroid group (n = 250) demonstrated elevated CRP levels (>12 mg/L), indicating a greater frequency of positive inflammatory status.

Overall, elevated CRP was markedly more prevalent among hypothyroid patients, reflecting an increased inflammatory burden in this population. (Graph 3)



Correlation Analysis

In the control group (n = 250), TSH showed a moderate positive correlation with BMI and total cholesterol, and a strong positive correlation with systolic blood pressure. HDL demonstrated a strong negative correlation with TSH, while MDA showed a moderate inverse association. No significant correlations were found between thyroid parameters and Apo-A1, Apo-B, Lp(a), or hs-CRP.

In the hypothyroid group, TSH was significantly positively correlated with MDA and lipoprotein(a) and negatively correlated with Apo-A1 ($p < 0.001$), indicating a clear association between thyroid dysfunction, oxidative stress, and atherogenic lipid alterations. (Table 3)

Table 3: Correlation analysis among the study parameters across different groups of the study population

Table 3b: 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
Apo-B	
hs-CRP	
TC	
HDL	
Sys BP	
BMI	

Table 3a: Pearson correlation in the control group (n=250)		
Variables	TSH	T4
BMI	r^2= 0.287	
Sys BP	r^2= 0.752	
TC	r^2= 0.365	r^2= 0.185
HDL	r^2= -0.645	
MDA	r^2= -0.375	
Apo-A1		
Lipo-A1		
Apo-B		
hs-CRP		

DISCUSSION

The present study examined the relationship between thyroid dysfunction, lipid abnormalities, oxidative stress, and inflammation in hypothyroid patients compared with healthy controls. The findings demonstrate significant metabolic and oxidative disturbances associated with hypothyroidism, consistent with previously reported Indian data.

Age distribution was comparable between groups, minimising age-related confounding and supporting appropriate matching, as similarly reported by Kumar et al. [9] and Tiruwa and Rathore [10].

Body mass index was significantly higher in hypothyroid patients ($p < 0.001$), reflecting increased adiposity associated with reduced basal metabolic rate and altered lipid metabolism. Comparable findings have been reported by Mahato et al. [11] and Kumar et al. [9].

No significant differences were observed in systolic or diastolic blood pressure, aligning with findings by Handhal et al. [12], suggesting that blood pressure changes may not be universal in hypothyroidism.

As expected, hypothyroid subjects exhibited elevated TSH and reduced total T3 and T4 levels ($p < 0.001$), confirming biochemical thyroid dysfunction [9,13].

A distinctly atherogenic lipid profile was observed, characterized by increased total cholesterol, triglycerides, LDL-C, Lp(a), and Apo-B, along with reduced HDL-C and Apo-A1 ($p < 0.001$). These findings agree with studies by Mahato et al. [11], Kumar et al. [9], and Lee et al. [14]. The lipid alterations likely reflect impaired LDL receptor activity and reduced cholesterol clearance secondary to thyroid hormone deficiency.

Hypothyroid patients demonstrated reduced total antioxidant capacity and elevated malondialdehyde levels, indicating enhanced oxidative stress. Similar patterns have been reported by Kale [15] and Petrulea et al. [16].

Nitric oxide levels did not differ significantly, consistent with observations by Kumar et al. [17].

A higher prevalence of elevated hs-CRP in the hypothyroid group suggests chronic low-grade inflammation, supporting findings from Tuzcu et al. [18], Kumar et al. [9], and Vinod et al. [19].

In euthyroid controls, TSH correlated with BMI, blood pressure, lipid parameters, and oxidative markers, suggesting that even subtle variations within the normal range may influence metabolic status, as noted by Lee et al. [14].

In hypothyroid patients, TSH showed significant associations with malondialdehyde, Lp(a), and Apo-A1, reinforcing the interrelationship between thyroid dysfunction, oxidative stress, and atherogenic lipid changes [11,12].

Overall Interpretation: The present findings align closely with existing literature and confirm that hypothyroidism is associated with dyslipidemia, oxidative stress, and systemic inflammation. These interrelated alterations may contribute to increased cardiovascular risk, underscoring the need for comprehensive metabolic evaluation and early risk stratification in patients with thyroid dysfunction.

Conclusion

This study highlights that thyroid dysfunction, particularly hypothyroidism, is associated with notable disturbances in lipid metabolism, oxidative status, and inflammatory activity. Individuals with hypothyroidism demonstrated a more atherogenic lipid pattern, diminished antioxidant capacity, increased lipid peroxidation, and a greater frequency of elevated inflammatory markers when compared with healthy controls.

The findings emphasise the close interplay between thyroid hormone imbalance, altered lipid regulation, oxidative stress, and vascular inflammation. Significant associations between TSH levels and both oxidative and atherogenic markers further indicate that thyroid dysfunction may contribute meaningfully to cardiovascular risk.

These observations suggest that early detection of metabolic and inflammatory abnormalities, along with comprehensive risk evaluation, may support timely management and potentially reduce long-term cardiovascular complications in patients with hypothyroidism.

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