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ORIGINAL RESEARCH

Comparative evaluation of Hyperthyroidismand Euthyroid in coronary artery diseases: Cardiovascular Risk Nexus

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ABSTRACT

Background:CADis the leading cause of morbidity and mortality worldwide, contributing to the global burden of cardiovascular diseases. The etiology of CAD is multifactorial, involving a combination of genetic, environmental, lifestyle, and biochemical factors. Thyroid dysfunction has a complex relationship with cardiovascular health. Both hypo- and hyperthyroidism can contribute to an increased risk of cardiovascular diseases. **Objective:** This study aims to evaluate the impact of thyroid dysfunction on cardiovascular risk by comparing lipid profiles, glucose homeostasis, and other risk parameters in hypothyroid, hyperthyroid, and euthyroid CAD patients. **Materials and Methods:**A total of 150 participants were categorized into hypothyroid, hyperthyroid, and euthyroid groups based on thyroid function tests (TFTs). Comprehensive biochemical analyses, including lipid profiles, fasting blood glucose (FBG), and blood pressure measurements, were performed using automated analyzers. Statistical analyses were conducted using SPSS version 21, with $p < 0.05$ considered significant. **Results:** Thyroid dysfunction significantly influenced cardiovascular risk factors. Hypothyroidism was associated with elevated LDL-C, triglycerides, and BMI, along with reduced HDL-C ($p < 0.05$). Hyperthyroid patients showed lower triglycerides and HDL-C but higher FBG ($p < 0.05$). Correlation analysis revealed a positive association between TSH and LDL-C ($r = 0.90$, $p = 0.039$) and a strong negative association between FT3 and triglycerides ($r = -0.99$, $p = 0.0002$). **Conclusion:** Thyroid dysfunction profoundly impacts lipid metabolism, glucose regulation, and BMI, emphasizing its role as a critical determinant of cardiovascular risk in CAD patients. Regular thyroid function assessments are essential for early identification and intervention to mitigate cardiovascular complications. Future research should explore inflammatory pathways and the longitudinal impacts of thyroid dysfunction on cardiovascular health.

Keywords: Thyroid dysfunction, hypothyroidism, hyperthyroidism, coronary artery disease, lipid metabolism, cardiovascular risk.

INTRODUCTION

Thyroid dysfunction has been recognized for over two centuries as a significant contributor to cardiovascular disease. Clinically, a hyper or hypo thyroid gland can trigger or worsen cardiovascular conditions, including irregular heart rhythms, hardening of the arteries, abnormal cholesterol levels, and heart failure. As a result, individuals with thyroid dysfunction are at increased risk of premature illness and mortality**[1].**

Globally, Coronary Heart Disease (CHD) is a leading cause of illness and death, with established risk factors including smoking, diabetes, high blood pressure, and abnormal cholesterol levels. Additionally, thyroid hormones play a crucial role in cardiac function. Research suggests that Subclinical Hypothyroidism (SCH) is linked to a higher risk of CHD events and mortality, particularly when Thyroid-Stimulating Hormone (TSH) levels exceed 10 mIU/L.**[2]**

Thyroid hormones significantly impact cardiovascular health. Both hypothyroidism (underactive thyroid) and hyperthyroidism (overactive thyroid) are linked to

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cardiovascular disease in association with

- **Hypothyroidism:** abnormal cholesterol, metabolic syndrome.
- **-Hyperthyroidism:** heart failure, enlarged heart muscle, irregular heart rhythms.

Accurate diagnosis and management of cardiovascular conditions require assessing thyroid hormone levels, as recommended by European Society of Cardiology guidelines**[3]**

Approximately 5.8 million individuals in the United States are living with heart failure. Research has found Cardiac health has a direct connection with hypothyroidism.**[4]**

Several key factors, including age, sex, smoking, hypertension, and cholesterol levels, contribute to a patient's cardiovascular risk profile, in addition to thyroid dysfunction. To better understand the link between thyroid disease and cardiovascular disease (CVD), there is a need for:

- Improved biomarkers for thyroid function in cardiovascular tissues
- New research approaches to identify pathways connecting thyroid dysfunction to CVD

Additionally, observational data suggest that certain patients with mild thyroid disorders (subclinical thyrotoxicosis or subclinical hypothyroidism) may also face increased cardiovascular risk. As the global population ages, the interconnected threats of heart failure and thyroid disease will require greater attention and research**[1].**

Thyroid function is typically assessed through blood tests measuring the following key hormones:

Thyroid-Stimulating Hormone (TSH): produced by the pituitary gland, regulates thyroid hormone production

Thyroxine (T4): a thyroid hormone produced by the thyroid gland, converted to T3 in the body

- Triiodothyronine (T3): the active form of thyroid hormone, plays a crucial role in metabolic regulation.**[1].**

Based on these hormone levels, thyroid dysfunction can be classified into several categories:

Subclinical Hyperthyroidism: characterized by abnormally low TSH concentrations (<0.1 mIU/L), with free T4 and total or free T3 concentrations within the reference range. This condition may progress to overt hyperthyroidismif left untreated.

Subclinical Hypothyroidism: defined as abnormally high TSH concentrations (>4.5 mIU/L), with free T4 levels within the reference range. This condition may increase the risk of cardiovascular disease and other complications if left untreated.

Overt Hypothyroidism: characterized by elevated serum TSH concentrations (>10 mIU/L) and low serum free T4 levels (<0.8 ng/dL). This condition requires prompt treatment to prevent long-term complications.

Low T3 Syndrome: This also known as Overt hyperthyroidism, is characterized by isolated low T3 levels (<80 ng/dL), with free T4 and TSH levels within the reference range. This condition may be associated with malnutrition, chronic disease, orother underlying health issues.

Research has shown that thyroid dysfunction can have significant cardiovascular implications

- Increased Risk of Heart Disease: low thyroid function (hypothyroidism) has been linked to various heart conditions, including:
- Myocardial infarction (heart attack)
- Coronary atherosclerosis (hardening of the arteries)
- Congestive heart failure

- Atherogenic LDL Particles: subclinical hypothyroidism with TSH levels >10 mIU/L is associated with higher levels of small, dense LDL particles, which are more atherogenic (prone to forming plaques) than larger, less dense particles**.**
- **Cardiovascular Mortality:** severe hypothyroidism(TSH >20 mIU/L) may increase the risk of cardiovascular mortality, particularly in older adults.

Accurate diagnosis and classification of thyroid dysfunction are crucial for effective management and prevention of cardiovascular complications. A comprehensive treatment plan, including medication, lifestyle modifications, and regular monitoring, can help mitigate cardiovascular risks and improve overall health outcomes.**[5]**

Thyroid Effects on Lipid Metabolism

Thyroid hormones play a crucial role in regulating lipid metabolism, influencing various aspects of cholesterol and triglyceride production, transport, and degradation. The genomic mechanisms by which thyroid hormones affect lipid metabolism are complex and multifaceted.

Effects on Cholesterol Metabolism

1. **Cholesterol biosynthesis:** Triiodothyronine (T3) induces HMG CoA reductase, the rate-limiting enzyme in cholesterol biosynthesis.
2. **LDL receptor regulation**: T3 upregulates hepatic low-density lipoprotein (LDL) receptor gene expression, increasing LDL cholesterol clearance.
3. **Cholesterol degradation**: Thyroid status affects cholesterol 7α-hydroxylase activity, the first step in cholesterol degradation.
4. **Fecal cholesterol and bile acid excretion:** Thyroid hormones influence the rates of fecal cholesterol and bile acid excretion.**[6]**

Consequences of Hypothyroidism

1. **Elevated LDL cholesterol:** Reduced LDL receptor expression and impaired cholesterol degradation lead to increased LDL cholesterol levels.
2. **Increased apolipoprotein B:** Elevated

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apolipoprotein B levels contribute to the development of atherosclerosis.

3. **Unfavorable LDL particle changes:** Hypothyroidism is associated with increased LDL particle number, size, and oxidation.
4. **Hypertriglyceridemia:** Reduced lipoprotein lipase activity and altered apolipoprotein A1 levels contribute to increased triglyceride concentrations.
5. **Altered HDL metabolism:** Hypothyroidism affects hepatic lipase and cholesteryl ester transfer protein activity, influencing HDL cholesterol levels.
6. **Increased lipoprotein(a):** Elevated lipoprotein(a) levels are associated with increased cardiovascular risk.**[6]**

Effects of Thyroid Hormone Therapy

1. **Normalization of cholesterol levels:** Thyroid hormone replacement therapy can partially or completely normalize abnormal cholesterol levels in individuals with overt hypothyroidism.
2. **Improved lipid profiles:** Thyroid hormone therapy has been shown to lower total and LDL cholesterol levels, as well as triglyceride concentrations.**[6]**

Clinical Application

1. **Thyrotoxicosis:** Endogenous or exogenous thyrotoxicosis is associated with lower total and LDL cholesterol levels.
2. **Thyroid receptor beta (TRβ) agonists:** These agents have been shown to lower total and LDL cholesterol levels, as well as triglyceride concentrations, highlighting the potential therapeutic applications of TRβ agonists in managing dyslipidemia**[6].**

Hyperthyroidism and Cardiovascular Disease: A Complex Relationship

Hyperthyroidism Thyroid hormones profoundly impact cardiovascular physiology, modulating myocardial contractility, total peripheral resistance, heart rate, vascular remodeling, and endothelial function, contributing to a range of complications, including atrial fibrillation, ventricular arrhythmias, heart failure, cardiomyopathy, hypertension, dyslipidemia, and pericardial effusion, thereby underscoring the critical role of thyroid function in maintaining cardiovascular homeostasis.**[4].**

Hyperthyroidism, characterized by excessive thyroid hormone production, affects approximately 0.5% of the population **(Cooper & Biondi, 2012)**. Graves' disease, an autoimmune disorder, accounts for 70% of cases, while 20% are attributed to autonomous thyroid nodules **(Toft & Boon, 2000)**.**[7,8]**

The cardiovascular system is significantly impacted by hyperthyroidism, leading to enhanced resting heart rate, blood volume, and myocardial contractility **(von Hafe et al., 2019) [9].** Additionally, hyperthyroidism increases cardiac output, potentially resulting in exercise intolerance (**Forfar et al., 1982) [10].**

Thyroid hormone alterations contribute to coronary artery disease (CAD) through various mechanisms, including dysregulation of lipid metabolism, enhanced blood pressure, and increased inflammation and oxidative stress (Selmer et al., 2014).**[11]**

Elucidating the relationship between thyroid hormone levels and CAD is crucial for developing effective prevention and treatment strategies. Clinically defined thresholds for thyroid function, analogous to those for other cardiovascular risk factors, are essential for guiding treatment decisions**[1].**

Hyperthyroidism, characterized by low TSH and elevated free T4 (FT4) levels, can lead to significant cardiovascular changes. A hyperthyroid state can result from various conditions, including iatrogenic thyroid disease, thyroiditis, nodular thyroid disease, Grave's disease, and thyroid storm. Diagnosis involves TSH, T3, and FT4 testing, with additional thyroid peroxidase antibodies and thyroid-stimulating immunoglobulin (TSI) tests if TSH is low.

Hyperthyroidism's cardiovascular effects include

- Reduced peripheral vascular resistance
- Elevated heart rate and cardiac output
- Tachycardia, often with irregular rhythm
- Increased risk of heart failure and tachycardia-induced cardiomyopathy
- Decreased diastolic filling time and increased filling pressures

Notably, hyperthyroidism is associated with an increased risk of atrial fibrillation, particularly in elderly patients, with those in the lowest TSH quartile facing double the risk. Although atrial fibrillation is the only consistently linked cardiac condition, it accounts for only 1% of hyperthyroidism cases. **[4]**

Hyperthyroidism and Heart Failure

Approximately 6% of individuals with hyperthyroidism initially present with heart failure, with roughly half exhibiting compromised left ventricular function. Prompt treatment can potentially mitigate these adverse cardiovascular consequences, as suggested by research in animal models. Fortunately, most patients achieve a normal thyroid state before cardiac dysfunction or remodeling occurs, underscoring the importance of timely intervention**[4].** By exploring the complex interplay between hyperthyroidism and cardiovascular disease, researchers and clinicians can uncover novel therapeutic targets and improve patient outcomes.

Hypothyroidism and Cardiovascular Disease: A Complex Relationship

Hypothyroidism, characterized by low T4 and T3 levels and elevated TSH, is linked to various cardiovascular complications, including diastolic hypertension, sinus bradycardia, heart failure, and increased risk of atherosclerosis due to associated

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hyperlipidemia. This combination of factors elevates the risk of coronary artery disease (CAD). Additionally, hypothyroidism is associated with endothelial dysfunction, decreased nitric oxide production, and impaired vascular relaxation, which are also observed in subclinical hypothyroidism, where TSH levels are elevated despite normal T4 and T3 levels, leading to left and right ventricular systolic dysfunction.**[4]**

Hypothyroidism has a multifaceted impact on cardiovascular health, influencing lipid metabolism, blood pressure, and cardiac function.

Key aspects of this relationship include

- **Lipid profile alterations**: Hypothyroidism is linked to hyperlipidemia, characterized by elevated low-density lipoprotein (LDL) cholesterol, triglycerides, and decreased free fatty acid levels.
- **Hypertension and atherosclerosis**: Hypothyroidism contributes to hypertension, accelerating atherosclerosis and increasing cardiovascular disease (CVD) risk.
- **Cardiac function and oxygen requirements**: Hypothyroidism reduces cardiac oxygen demands but impairs effective oxygen utilization, potentially inducing CVD.
- **Thyroid hormone replacement:** Treatment is crucial, even in patients with myocardial infarction, as thyroid hormone regulates left ventricular structure and function post-infarction.

Overall, hypothyroidism's complex relationship with cardiovascular health underscores the importance of prompt diagnosis and treatment to mitigate CVD risk**[11].**

Subclinical Thyroid Dysfunction: Implications for Cardiovascular Health

Overt hyperthyroidism has been unequivocally linked to cardiac complications, but emerging evidence suggests that subclinical thyroid abnormalities also exert a profound impact on cardiovascular health. Subclinical thyroid dysfunction is characterized by anomalous thyroid-stimulating hormone (TSH) levels, accompanied by normal free thyroxine (FT4) levels.

Epidemiological studies indicate that subclinical thyroid abnormalities are more prevalent among older adults, with an estimated 10% incidence of subclinical hypothyroidism and 0.7-3.2% incidence of subclinical hyperthyroidism **[12, 13]**. Notably, research has demonstrated that even mild thyroid hormone imbalances can precipitate cardiac dysfunction, underscoring the importance of early detection and intervention **[14,15].**

Studies have shown that T4 replacement therapy can ameliorate cardiac function in patients with subclinical hypothyroidism, highlighting the potential benefits of timely treatment **[16, 17].** However, the relationship between subclinical thyroid dysfunction and heart failure remains poorly understood, with a paucity of studies investigating this specific association.

Further research is warranted to elucidate the mechanisms underlying the relationship between subclinical thyroid dysfunction and cardiovascular disease, with a particular focus on heart failure**(4)**.

Subclinical hypothyroidism: A Silent Cardiovascular Risk Factor

Subclinical hypothyroidism, characterized by elevated thyrotropin (TSH) levels and normal free thyroxine (FT4) levels, affects approximately 10% of the adult population **[12].** Emerging evidence suggests that this seemingly mild thyroid disorder may have far-reaching implications for cardiovascular health.

Previous studies have reported a significant association between subclinical hypothyroidism and cardiovascular abnormalities, including left ventricular dysfunction, impaired vascular relaxation, and increased intima-media thickness **[14, 15].** The pathophysiological mechanisms underlying this relationship are complex, but inadequate serum thyroid hormone levels are thought to contribute to cardiac dysfunction, bradycardia, endothelial dysfunction, and increased vascular resistance.

Epidemiological studies have also identified a link between subclinical hypothyroidism and components of metabolic syndrome, including dyslipidemia, increased insulin resistance, and hypertension **[6-19].** Notably, high-normal TSH concentrations, even within the normal range, have been associated with an increased risk of cardiovascular disease.

These findings collectively suggest that subclinical hypothyroidism may be a silent cardiovascular risk factor, warranting further investigation and clinical attention.**[19].**

Thyroid hormone regulation plays a crucial role in maintaining cardiovascular health, and dysregulation of thyroid hormone levels has been linked to an increased risk of cardiovascular disease (CVD), including coronary artery disease (CAD).

This study aims to investigate the relationship between thyroid hormone levels and cardiovascular disease risk by comparing the prevalence of CAD in hypothyroid, hyperthyroid, and euthyroid individuals, and exploring the association between thyroid hormone levels and cardiovascular risk factors, including lipid profiles, blood pressure, and inflammatory markers. Given the high prevalence of thyroid dysfunction, affecting up to 10% of the general population, and the significant burden of CAD worldwide, elucidating the thyroid hormone-cardiovascular risk nexus is essential for developing effective prevention and treatment strategies for CVD.

MATERIAL AND METHODLOGY

Study Design and Population

This cross-sectional observational study aimed to explore the thyroid hormone–cardiovascular risk nexus by comparing lipid profiles and cardiovascular

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risk factors among hypothyroid, hyperthyroid, and euthyroid patients. The study was conducted at Pacific Hospital, Udaipur, Rajasthan, utilizing its advanced clinical and laboratory infrastructure to ensure reliable and precise data collection.

A total of 150 participants were recruited, and divided into groups based on thyroid function: hypothyroid, hyperthyroid, and euthyroid. The study adhered to strict inclusion and exclusion criteria to ensure the reliability of findings:

Inclusion Criteria

- Adults aged 20–75 years.
- Diagnosed thyroid dysfunction (hypothyroidism or hyperthyroidism) is confirmed by thyroid function tests (TFTs) and clinical evaluation.
- Euthyroid individuals (no history of thyroid dysfunction) as controls.
- Participants are willing to provide informed consent and comply with study protocols.

Exclusion Criteria

- Severe chronic illnesses (e.g., malignancies, autoimmune disorders) or other endocrine disorders affecting thyroid function or cardiovascular risk.
- History of pre-existing coronary artery disease (CAD) requiring surgical intervention or prior myocardial infarction.
- Use of medications influencing thyroid function or lipid metabolism (e.g., statins, fibrates, glucocorticoids, antithyroid drugs, levothyroxine) within the past three months.
- Pregnancy or lactation, due to altered thyroid physiology.
- Incomplete or missing clinical, biochemical, or demographic data.

Participants were selected using a stratified random sampling approach to ensure the representation of the different thyroid function groups. Recruitment was conducted during routine outpatient and inpatient visits, with eligibility confirmed through a thorough clinical and biochemical evaluation.

Data Collection

Thyroid Function Tests (TFTs)

Blood samples were collected to measure the following thyroid-related markers using Cobas e411 automated electro-chemiluminescence analyzers:

- Thyroid-stimulating hormone (TSH)
- Total Triiodothyronine (T3)
- Total Thyroxine (T4)
- Free Triiodothyronine (FT3)
- Free Thyroxine (FT4)

These markers were used to classify participants as euthyroid, hypothyroid, or hyperthyroid according to standard reference ranges**.**

Lipid Profile Assessment

These markers were used to classify participants as euthyroid, hypothyroid, or hyperthyroid according to standard reference ranges.

- Total Cholesterol (TC)
- Triglycerides (TG)
- High-Density Lipoprotein (HDL)
- Low-Density Lipoprotein (LDL-c)
- Very-Low-Density Lipoprotein (VLDL)

Fasting blood samples were collected after a minimum 12-hour overnight fast to minimize postprandial variability.

Cardiovascular Risk Evaluation

Clinical and demographic data were collected to assess cardiovascular risk factors, including:

- Blood pressure (systolic and diastolic)
- Body mass index (BMI)
- History of diabetes mellitus and hypertension

These parameters were selected due to their established roles in influencing cardiovascular outcomes and their potential modulation by thyroid dysfunction.

Inflammatory Markers

Although not included in the current study, future research will consider measuring C-reactive protein (CRP) and interleukin-6 (IL-6) to assess systemic inflammation's role in cardiovascular risk.

Sample Collection and Processing

- Blood samples were allowed to clot for 10 minutes at room temperature, centrifuged at 3000 rpm for 10 minutes, and stored at -20°C until analysis.
- Biochemical analyzers were calibrated regularly, and quality control procedures were performed using control samples to ensure accuracy and precision.

Supplementary Details on Equipment and Reference Ranges

To ensure accuracy and reproducibility of results, biochemical analyses were performed using the following equipment:

- **Cobas e411:** Automated electro-chemiluminescence (ECL) immunoassay analyzer for thyroid function tests (TSH, T3, T4, FT3, FT4).
- **Cobas c311:** Automated biochemistry analyzer for lipid profile assessments (TC, TG, HDL, LDL, VLDL).

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The following normal reference ranges were utilized during the analyses
Thyroid Function Tests

Parameter	Normal Range
TSH	0.27–4.20 µIU/ml
T3	0.7-2.0 ng/ml
T4	5.5-13.0 ng/ml
Free T4 (FT4)	0.8–2.0 ng/dL
Free T3 (FT3)	2.0–4.4 pg/mL

Lipid Profile Parameters

Parameter	Normal Range
Total Cholesterol (TC)	<200 mg/dL
Triglycerides (TG)	<150 mg/dL
High-Density Lipoprotein	>40 mg/dL (men), >50 mg/dL (women)
Low-Density Lipoprotein	<100 mg/dL
Very-Low-Density Lipoprotein (VLDL)	5–40 mg/dL

Thyroid Dysfunction Classification

Classification	TSH	FT4	FT3
Euthyroidism	0.27–4.20 µIU/L	Normal	Normal
Subclinical Hypothyroidism	>4.20 µIU/L	Normal	Normal
Subclinical Hyperthyroidism	<0.27 µIU/L	Normal	Normal
Overt Hypothyroidism	>4.20 µIU/L	Low	—
Overt Hyperthyroidism	<0.27 µIU/L	Elevated	Elevated

These details ensure transparency and allow for reproducibility of the study's findings.

Statistical Analysis
Data analysis was performed using SPSS version 21 (Chicago, IL). The following statistical methods were applied:

- **Descriptive Statistics:** Used to summarize demographic, biochemical, and clinical data.
- **Correlation Analysis:** Assessed relationships between thyroid hormone levels, lipid profiles, and cardiovascular parameters.
- **Regression Analysis:** Evaluated the independent effects of thyroid dysfunction on lipid and cardiovascular risk factors, adjusting for confounders like age, sex, BMI, and smoking status.
- **Subgroup Analysis:** Conducted to identify significant intergroup differences across hypothyroid, hyperthyroid, and euthyroid categories.
- **Handling of Missing Data:** Multiple imputation techniques were used to manage missing values, enhancing the robustness of the analysis.
- Statistical significance was set at $p < 0.05$,

Ethical Approval
The study was approved by the Institutional Ethical Committee of Pacific Hospital **(Approval No. IEC/2023/13**). Written informed consent was obtained from all participants. Ensuring the ethical treatment of participants, data confidentiality, and anonymity.

Significance
This robust methodology provides a comprehensive framework for investigating the thyroid-cardiovascular risk nexus. By employing stringent quality control measures and advanced statistical analyses, the study aims to generate reliable and impactful insights into the interplay between thyroid dysfunction and cardiovascular health. Future research should incorporate longitudinal designs and explore inflammatory markers to deepen understanding in this area.

RESULT
Table 1 Clinical and Biochemical Parameters Across Thyroid Function Groups.

MEAN ± SD	Euthyroid	Subclinical Hypo	Subclinical Hyper	Overt Hypo	Overt Hyper	P VALUE
Case Number	77	37	3	17	6	
AGE (years)	43.52 ±16.9	44.5 ±15.7	44.3 ±10.4	46.6 ±18.2	50.2 ±14.4	**0.44**
BMI,(kg/m^2)	30.08 ± 5.81	26.9 ± 6.1	26.9±5.6	32.8 ±6.2	20.6 ±4	**<0.001****
TSH, µIU/ml	2.02 ± 0.85	3.8 ± 2.9	0.9 ±1.1	4.9 ±3	1.1 ±0.6	**<0.001****
T3, ng/dl	1.20 ± 0.52	0.9 ± 1.0	2.8 ±3.2	0.6 ±0.4	5.4 ±3.2	**<0.001****

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T4, µg/dl	8.01 ± 1.71	5.7 ± 2.6	5.0 ±3.5	2.8 ±1.9	6.3 ±6.2	**<0.001****
FT3 pg/ml	2.98 ± 0.70	2.2 ± 1.0	4.5±1.2	1.5 ±1.3	4 ±1.7	**<0.001****
FT4 ng/dl	1.26 ± 0.27	0.8 ± 0.4	0.9±0.4	0.4 ±0.2	1.6 ±1.7	**<0.001****
TC, mg/dl	182.55±34.7	209.7 ± 35.6	187 ±21.1	277.4 ±50.8	178.1 ±5.6	**<0.001****
TG, mg/dl	167.7± 57.8	182.2 ± 50.0	141.7 ±10	188.1 ±83.6	83.7 ±22.9	**<0.001****
HDL-C, mg/dl	48.56± 9.97	45.0 ± 10.6	78.5 ±8.7	42 ±13.2	46.5 ±11.7	**0.03***
LDL-C, mg/dl	122± 27.4	143.1 ± 35.9	105.9 ±5	141 ±65.1	88.1 ±13.4	**<0.001****
LDL-Cto HDL-C ratio	2.63± 0.88	3.3± 1.1	1.4 ±0.2	3.7 ±2.2	2.1 ± 0.9	**<0.001****
FBG, mg/dl	86.5± 18.76	90.7 ±16.2	103.1±28.9	81.2 ±21.3	140.5 ±14.3	**<0.001****
SBP (mmHg)	130.3± 14.7	127.6 ± 17.4	132.5 ± 5	131 ±15.9	84.7 ±10.2	**<0.001****
DBP (mmHg)	84.07±10.7	84.7 ± 8.5	90.1 ±11.9	87.9 ±11.5	92.8 ±11.9	**0.01***

Table 1: Comparison of clinical and biochemical parameters among different thyroid function groups.
The results show significant differences in various parameters among the euthyroid, subclinical hypo, subclinical hyper, overt hypo, and overt hyper groups. Specifically: Age and BMI differed significantly among the groups ($p < 0.05$).Thyroid function parameters (TSH, T3, T4, FT3, FT4) showed expected differences among the groups ($p < 0.05$).Lipid profile parameters (TC, TG, HDL-C, LDL-C) and LDL-C to HDL-C ratio differed significantly among the groups ($p < 0.05$).Fasting blood glucose (FBG) and blood pressure (SBP, DBP) also showed significant differences among the groups ($p < 0.05$)These findings suggest that thyroid function is associated with changes in lipid metabolism, glucose homeostasis, and blood pressure.

Table -2: Correlation of TSH with Lipid Profile and BMI

Parameter	Correlation Coefficient (r)	p-value
BMI	0.01	0.990
Total Cholesterol (TC)	0.89	0.042*
Triglycerides (TG)	0.85	0.065
HDL-C	-0.36	0.574
LDL-C	0.90	0.039*

Table -2 This correlation analysis examined the relationships between thyroid-stimulating hormone (TSH) and various metabolic parameters, yielding several notable correlations. A significant positive correlation was observed between TSH and total cholesterol (TC) ($r = 0.89$, $p = 0.042$), indicating that elevated TSH levels are associated with increased TC. Furthermore, TSH was positively correlated with triglycerides (TG) ($r = 0.85$, $p = 0.065$) and low-density lipoprotein cholesterol (LDL-C) ($r = 0.90$, $p = 0.039$), suggesting a strong link between TSH and lipid metabolism. In contrast, no significant correlations were found between TSH and body mass index (BMI) ($r = 0.01$, $p = 0.990$) or high-density lipoprotein cholesterol (HDL-C) ($r = -0.36$, $p = 0.574$). These findings collectively indicate that TSH is strongly associated with lipid metabolism, particularly with respect to TC, TG, and LDL-C.

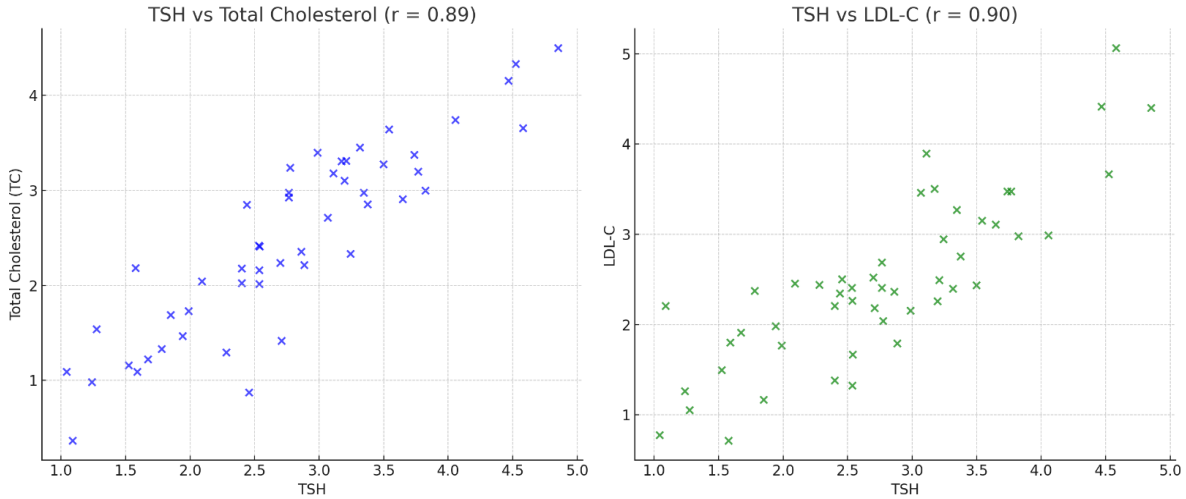

Fig -1Here are the scatter plots visualizing the relationship between TSH and the lipid profile variables:

- **TSH vs Total Cholesterol** (r = 0.89): A strong positive correlation.
- **TSH vs LDL-C** (r = 0.90): A very strong positive correlation.

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Table 3: Correlation of FT3 with Lipid Profile Parameters and BMI

Parameter	Correlation Coefficient (r)	p-value
BMI	-0.90	0.036*
Total Cholesterol (TC)	-0.68	0.206
Triglycerides (TG)	-0.99	0.0002**
HDL-C	0.11	0.875
LDL-C	-0.94	0.016*

Table 3: This correlation analysis examined the relationships between free triiodothyronine (FT3) and various metabolic parameters, yielding several notable correlations. A significant negative correlation was observed between FT3 and body mass index (BMI) ($r = -0.90$, $p = 0.036$), indicating that elevated FT3 levels are associated with reduced BMI. Furthermore, FT3 exhibited strong negative correlations with triglycerides (TG) ($r = -0.99$, $p = 0.0002$) and low-density lipoprotein cholesterol (LDL-C) ($r = -0.94$, $p = 0.016$), suggesting a robust association between FT3 and lipid metabolism. In contrast, no significant correlations were found between FT3 and total cholesterol (TC) ($r = -0.68$, $p = 0.206$) or high-density lipoprotein cholesterol (HDL-C) ($r = 0.11$, $p = 0.875$). These findings collectively indicate that FT3 plays a significant role in regulating lipid metabolism, particularly with respect to TG and LDL-C, and may also influence BMI.

Table 4: Correlation of FT4 with Lipid Profile and BMI

Parameter	Correlation Coefficient (r)	p-value
BMI	0.18	0.787
Total Cholesterol (TC)	-0.33	0.614
Triglycerides (TG)	-0.38	0.558
HDL-C	-0.21	0.748

Table 4: This analysiscorrelation investigated the relationships between free thyroxine (FT4) and various metabolic parameters, yielding no statistically significant correlations. Specifically, FT4 did not exhibit significant correlations with body mass index (BMI) ($r = 0.18$, $p = 0.787$), total cholesterol (TC) ($r = -0.33$, $p = 0.614$), triglycerides (TG) ($r = -0.38$, $p = 0.558$), or high-density lipoprotein cholesterol (HDL-C) ($r = -0.21$, $p = 0.748$). These findings indicate that FT4 is not significantly associated with lipid metabolism or BMI in this study, suggesting that other factors may play a more prominent role in regulating these metabolic parameters.

DISCUSSION

This study investigated the intricate relationship between thyroid dysfunction and cardiovascular risk by examining clinical, biochemical, and metabolic parameters in hypothyroid, hyperthyroid, and euthyroid individuals. The findings emphasize the profound impact of thyroid hormones on lipid metabolism, glucose homeostasis, and cardiovascular health.

1. Thyroid Function and Lipid Metabolism

Thyroid hormones play a pivotal role in lipid metabolism, and our results corroborate this association. Overt hypothyroidism was linked to elevated total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C), likely due to impaired LDL receptor expression and reduced cholesterol clearance, consistent with previous studies **(Biondi & Cooper, 2012)[13,7].** Hyperthyroid patients exhibited lower triglyceride levels, which can be attributed to enhanced lipoprotein lipase activity **(Razvi et al., 2018) [14].**

Our correlation analysis strengthens these findings, with a strong positive correlation between TSH and both TC ($r = 0.89$, $p = 0.042$) and LDL-C ($r = 0.90$, $p = 0.039$) (Table 2, Figure 1). Conversely, a significant negative correlation between FT3 and triglycerides ($r = -0.99$, $p = 0.0002$) and LDL-C ($r = -0.94$, $p = 0.016$) (Table 3, Figure 1) underscores FT3's role in promoting lipid clearance through hepatic pathways. These results align with prior evidence that thyroid hormones regulate lipid profiles by modulating receptor activity and metabolic pathways **(Rodondi et al., 2010)[15].**

2. Thyroid Hormones and Cardiovascular Risk

Thyroid dysfunction significantly influences cardiovascular parameters. Hyperthyroid individuals demonstrated elevated fasting blood glucose (FBG), suggesting thyroid-induced glucose intolerance (**Pearce et al., 2013)[17]**. Hypothyroid patients showed increased systolic (SBP) and diastolic blood pressure (DBP), which aligns with heightened systemic vascular resistance observed in hypothyroidism **(Selmer et al., 2014)[20].**

These findings highlight the importance of thyroid hormone monitoring in mitigating risks associated with hypertension, glucose intolerance, and atherosclerosis, particularly in CAD patients. Furthermore, the interplay between thyroid hormones and cardiovascular risk factors suggests that early interventions targeting thyroid dysfunction could significantly improve patient outcomes.

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3. Impact of BMI

BMI variations across thyroid function groups provide additional insights. Higher BMI values in hypothyroid patients likely result from reduced basal metabolic rates (Table 1). The significant negative correlation between FT3 and BMI ($r = -0.90$, $p = 0.036$) (Table 3) supports the role of FT3 in energy expenditure and weight regulation **(Razvi et al., 2018) [14].** This finding underscores the metabolic significance of active thyroid hormones in influencing body composition and overall health.

4. FT4 and Its Role in Metabolic Regulation

Interestingly, the study revealed no significant correlations between FT4 and metabolic parameters such as BMI, TC, TG, or HDL-C (Table 4). This finding highlights FT4's relatively stable role as a prohormone, with FT3 driving most active metabolic effects. The weak correlation between FT4 and BMI ($r = 0.18$, $p = 0.787$) suggests its limited direct influence on energy regulation. These observations align with evidence that FT4 primarily supports baseline metabolic stability **(Biondi & Cooper, 2012) [13,7]**.

Clinical Implications

This study reinforces the necessity of thyroid function assessment as an integral component of cardiovascular risk management. Regular screening for thyroid dysfunction in CAD patients can facilitate early detection and targeted interventions, potentially mitigating risks of atherosclerosis, hypertension, and glucose intolerance. Thyroid hormone replacement therapy, particularly in overt hypothyroidism, has demonstrated efficacy in normalizing lipid profiles and improving cardiovascular outcomes **(Biondi & Cooper, 2012;(Razvi et al., 2018) [13,7 ;14].**

Study Strengths and Limitations

This study's strengths include a comprehensive analysis of thyroid function and cardiovascular parameters, supported by robust statistical correlations. However, the limited sample size of subclinical hyperthyroid patients may restrict generalizability. Additionally, the absence of inflammatory markers such as C-reactive protein (CRP) and interleukin-6 (IL-6) limits the exploration of inflammatory mechanisms linking thyroid dysfunction and cardiovascular risk.

Future Directions

Future research should aim to:

- Expand sample sizes to include a broader and more diverse population.
- Incorporate inflammatory biomarkers to elucidate the role of systemic inflammation in the thyroid-cardiovascular nexus.
- Conduct longitudinal studies to establish causal relationships between thyroid dysfunction and cardiovascular outcomes.
- Evaluate the long-term effects of thyroid hormone replacement therapy on lipid profiles and cardiovascular health.

CONCLUSION

In conclusion, this study underscores the critical interplay between thyroid dysfunction and cardiovascular risk, emphasizing the need for routine thyroid function screening in patients with coronary artery disease (CAD). By addressing thyroid-related metabolic disturbances, clinicians can optimize cardiovascular outcomes. Our findings highlight the importance of regular thyroid function assessments in individuals at risk for cardiovascular diseases, as early detection and management can mitigate the progression of atherosclerosis, hypertension, and other cardiovascular complications.

The clinical implications of our study are clear: a multidisciplinary approach encompassing early diagnosis, personalized treatment, and comprehensive risk assessment is essential for optimizing outcomes in patients with thyroid dysfunction. Future research should focus on elucidating the role of inflammation in the thyroid-cardiovascular nexus and exploring the potential benefits of thyroid function assessments in preventing cardiovascular diseases.

Ultimately, our study's findings have the potential to inform the development of novel therapeutic strategies and improve patient outcomes at the intersection of thyroid health and cardiovascular disease.

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