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ORIGINAL RESEARCH

Evaluation of Clinical and Biochemical Cardiovascular Risk Factors in Patients with Subclinical Hypothyroidism at a Tertiary Centre

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ABSTRACT

Background: An estimated 42 million people in India are thought to be afflicted with thyroid abnormalities, which are among the most prevalent endocrine diseases in the world. The present study was conducted to assess cardiac risk factors in patients with subclinical hypothyroidism. **Materials & Methods:** A total of 140 subjects were recruited for the study, divided into two groups- Group I (Subclinical Hypothyroidism): 70 patients diagnosed with subclinical hypothyroidism, defined as elevated TSH levels (>4.8 µiu/ml) with normal free thyroxine (ft4) levels (0.8-2.0 ng/dl) and Group II (Euthyroid Control Group): 70 subjects with normal thyroid function, defined as TSH levels within the range of 0.5-4.8 µiu/ml and normal ft4 levels (0.8-2.0 ng/dl). **Results:** We found that Group I consisting of 28 males and 42 females, and Group II consisting of 30 males and 40 females (p = 0.721), showing no significant difference. We found that mean BMI was 27.5 ± 3.4 kg/m² and 25.8 ± 3.1 kg/m², WHR was 0.88±0.05 and 0.85±0.04, SBP was 128.4 ± 11.2 mmHg and 122.1 ± 10.8 mmHg and DBP was 84.2 ± 7.9 mmHg and 80.3 ± 7.6 mm Hg in group I and II respectively. We found that total cholesterol was 210.4 ± 35.2 mg/dL and 185.7 ± 30.6 mg/dLmg/dL, LDL-C was 135.6 ± 29.8 mg/dL and 112.8 ± 26.4 mg/dL, HDL-C was 44.3 ± 7.1 mg/dL and 48.5 ± 8.2 mg/dL and triglyceride was 162.7 ± 38.4 mg/dL and 48.5 ± 8.2 mg/dL in group I and group II respectively. Positive correlation between TSH and LDL cholesterol in present study because Pearson's correlation coefficient (r = 0.482). **Conclusion:** Heart risk variables such as blood pressure, lipid markers, and obesity indicators (BMI and WHR) are strongly correlated with subclinical hypothyroidism.

Keywords: Hypothyroidism, Triglyceride, Cholesterol, Body mass index

INTRODUCTION

An estimated 42 million people in India are thought to be afflicted with thyroid abnormalities, which are among the most prevalent endocrine diseases in the world.[1]

A high blood TSH value over the upper limit of normal in the presence of normal serum free thyroxine (fT4) levels and little to no hypothyroid symptoms is known as subclinical hypothyroidism.[2]

Given the possibility of developing into overt hypothyroidism and its correlation with lipid, cardiac, and other biochemical abnormalities that are becoming more well acknowledged, subclinical hypothyroidism, which has a high incidence rate (4–20%), is becoming more well-

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known.[3]

The incidence and prevalence of cardiovascular disease (CVD) have alarmingly increased globally since the turn of the twenty-first century, and India is not exempt from this trend.[4] Indeed, according to recent studies, CVDs cause more than 25% of all deaths in India.[5]

In order to reduce the increasing disease burden, researchers, stakeholders, and policymakers have refocused their efforts on identifying and managing the risk factors linked to CVDs. Numerous biochemical and clinical CVD risk factors have been found to date. Obesity is recognized as one of these that, apart from other cardiovascular risk factors, contribute to the development of CVD and CVD-related mortality.[6]

It is hypothesized that hypothyroidism's correlation with changed lipid profiles contributes to its cardiovascular problems. Because they control lipid synthesis, breakdown, and enzyme activity in the lipid metabolism pathways, thyroid hormones are important for lipid metabolism.[7] Although there is ample evidence linking overt hypothyroidism to CVD risk factors such as obesity, hypertension, and dyslipidemia, it is unclear whether subclinical hypothyroidism predisposes to CVD in a comparable way, and the precise relationship between subclinical hypothyroidism and CVD risk remains up for debate.[8]

AIM & OBJECTIVES

The present study was conducted to assess cardiac risk factors in patients with subclinical hypothyroidism.

MATERIAL & METHODS

Study Design

- **Type of Study:** Cross-sectional study
- **Study Setting:** Conducted at Department of Medicine, National Institute of Medical Science & Research, Jaipur, Rajasthan, India.
- **Study Duration:** January 2022 to April 2024
- **Sample Size:** 140 patients
- Informed written consent was secured from all patients before their inclusion in the study.

Ethical consideration

The study was approved by the research and ethical committee of the institutes.

Study Population

A total of 140 subjects were recruited for the study, divided into two groups:

- **Group I (Subclinical Hypothyroidism):** 70 patients diagnosed with subclinical hypothyroidism, defined as elevated TSH levels (>4.8 μIU/mL) with normal free thyroxine (fT4) levels (0.8-2.0 ng/dL).
- **Group II (Euthyroid Control Group):** 70 subjects with normal thyroid function, defined as TSH levels within the range of 0.5-4.8 μIU/mL and normal fT4 levels (0.8-2.0 ng/dL).

Inclusion Criteria

- Age ≥ 18 years.
- Patients diagnosed with subclinical hypothyroidism based on laboratory findings.
- Euthyroid individuals with normal thyroid profiles for the control group.

Exclusion Criteria

- Patients with overt hypothyroidism or hyperthyroidism.
- Individuals with known cardiac diseases, diabetes mellitus, hypertension, or any chronic illness.
- Patients on medications that may affect thyroid or cardiac function.
- Pregnant or lactating women.

Data Collection

Clinical and biochemical parameters were recorded for both groups. Clinical parameters included anthropometric measurements (body mass index, blood pressure) and medical history. Biochemical parameters included thyroid profile (TSH, fT4), lipid profile (total cholesterol, LDL, HDL, triglycerides), fasting blood glucose, and markers of cardiac risk such as high-sensitivity C-reactive protein (hs-CRP).

Laboratory Methods

- Thyroid function tests were performed using chemiluminescent immunoassay (CLIA).
- Lipid profile and fasting blood glucose were measured using automated analyzers following standard protocols.

STATISTICAL ANALYSIS

Data were analyzed using SPSS software. Continuous variables were expressed as mean ± standard deviation and compared using the independent t-test. Categorical variables were compared using the chi-square test. A p-value of <0.05 was considered statistically significant.

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RESULTS

Table 1: Demographic and Clinical Characteristics of Study Groups

Variable	Group I (Subclinical Hypothyroidism, n = 70)	Group II (Euthyroid, n = 70)	p-value
Age (years, Mean ± SD)	45.2 ± 8.6	43.7 ± 9.1	0.312
Gender (Male/Female)	28/42	30/40	0.721
Body Mass Index (kg/m²)	27.5 ± 3.4	25.8 ± 3.1	0.015*
WHR (Waist Hip Ratio)	0.88±0.05	0.85±0.04	0.018
Systolic BP (mmHg)	128.4 ± 11.2	122.1 ± 10.8	0.003*
Diastolic BP (mmHg)	84.2 ± 7.9	80.3 ± 7.6	0.011*

*Significant at $p < 0.05$

Table 1 presents the demographic and clinical characteristics of the participants in both groups. The mean age of patients with subclinical hypothyroidism (Group I) was 45.2 ± 8.6 years, while the control group (Group II) had a mean age of 43.7 ± 9.1 years. The difference in age between the two groups was not statistically significant ($p = 0.312$), indicating that both groups were comparable in terms of age distribution.

Gender distribution was similar in both groups, with Group I consisting of 28 males and 42 females, and Group II consisting of 30 males and 40 females ($p = 0.721$), showing no significant difference [Graph I].

The mean body mass index (BMI) of Group I was 27.5 ± 3.4 kg/m², which was significantly higher compared to 25.8 ± 3.1 kg/m² in Group II ($p = 0.015$). This indicates that patients with subclinical hypothyroidism had a higher BMI, which is a known risk factor for cardiovascular diseases.

Waist Hip Ratio was 0.88±0.05 and 0.85±0.04, the difference in WHR is small but significant ($p = 0.018$).

Systolic blood pressure (SBP) was significantly elevated in Group I (128.4 ± 11.2 mmHg) compared to Group II (122.1 ± 10.8 mmHg), with a p-value of 0.003. Similarly, diastolic blood pressure (DBP) was also higher in Group I (84.2 ± 7.9 mmHg) compared to Group II (80.3 ± 7.6 mmHg), with a p-value of 0.011. These results suggest that individuals with subclinical hypothyroidism exhibit elevated blood pressure levels, which may contribute to an increased risk of cardiovascular disease.

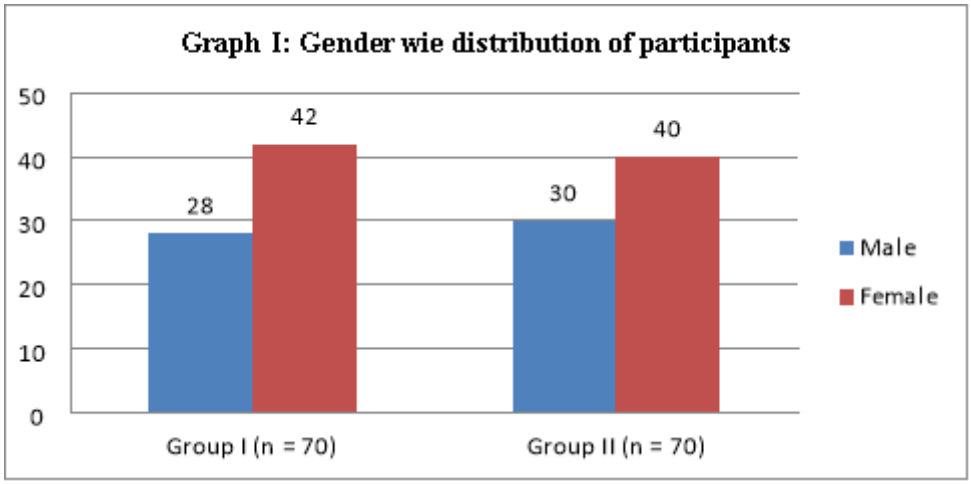

Table 2: Biochemical Parameters of Study Groups

Parameter	Group I (Subclinical Hypothyroidism, n = 70)	Group II (Euthyroid, n = 70)	p-value
TSH (µIU/mL)	6.8 ± 1.9	2.7 ± 0.9	<0.001*
fT4 (ng/dL)	1.2 ± 0.3	1.3 ± 0.2	0.058
Total Cholesterol (mg/dL)	210.4 ± 35.2	185.7 ± 30.6	<0.001*
LDL Cholesterol (mg/dL)	135.6 ± 29.8	112.8 ± 26.4	<0.001*
HDL Cholesterol (mg/dL)	44.3 ± 7.1	48.5 ± 8.2	0.005*

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Triglycerides (mg/dL)	162.7 ± 38.4	141.2 ± 35.6	0.001*
Fasting Blood Glucose (mg/dL)	96.4 ± 9.8	92.1 ± 8.6	0.017*
hs-CRP (mg/L)	3.1 ± 1.2	2.1 ± 0.9	<0.001*

*Significant at $p < 0.05$

Table 2 and graph II, presents the biochemical parameters of both groups, highlighting differences in thyroid function, lipid profile, and cardiac risk markers.

Thyroid-stimulating hormone (TSH) levels were significantly higher in Group I (6.8 ± 1.9 µIU/mL) compared to Group II (2.7 ± 0.9 µIU/mL), with a p-value of <0.001, confirming the diagnosis of subclinical hypothyroidism in Group I. Free thyroxine (fT4) levels were within the normal range in both groups, with no significant difference (p = 0.058).

In terms of lipid profile, total cholesterol levels were significantly higher in Group I (210.4 ± 35.2 mg/dL) compared to Group II (185.7 ± 30.6 mg/dL), with a p-value of <0.001. Low-density lipoprotein (LDL) cholesterol, often referred to as "bad cholesterol," was also elevated in Group I (135.6 ± 29.8 mg/dL) compared to Group II (112.8 ± 26.4 mg/dL), with a p-value of <0.001. Conversely, high-density lipoprotein (HDL) cholesterol, known as "good cholesterol," was lower in Group I (44.3 ± 7.1 mg/dL) compared to Group II (48.5 ± 8.2 mg/dL), with a p-value of 0.005. Triglyceride levels were also elevated in Group I (162.7 ± 38.4 mg/dL) compared to Group II (141.2 ± 35.6 mg/dL), with a p-value of 0.001. These findings indicate that individuals with subclinical hypothyroidism have an unfavorable lipid profile, which may increase their risk of developing cardiovascular diseases.

Fasting blood glucose levels were slightly higher in Group I (96.4 ± 9.8 mg/dL) compared to Group II (92.1 ± 8.6 mg/dL), with a p-value of 0.017, suggesting impaired glucose metabolism in patients with subclinical hypothyroidism.

High-sensitivity C-reactive protein (hs-CRP), a marker of systemic inflammation and an independent predictor of cardiovascular risk, was significantly elevated in Group I (3.1 ± 1.2 mg/L) compared to Group II (2.1 ± 0.9 mg/L), with a p-value of <0.001. This suggests that individuals with subclinical hypothyroidism exhibit a higher degree of systemic inflammation, which may contribute to their increased risk of cardiovascular events.

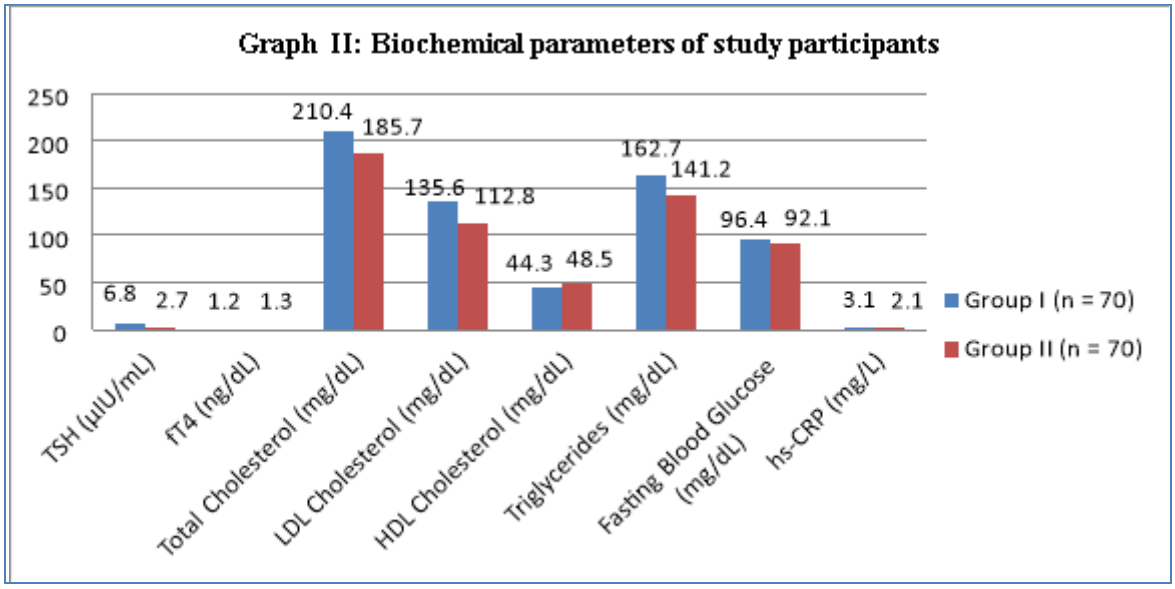

Table 3: Correlation Between LDL and TSH in Subclinical Hypothyroidism

Variable	LDL (mg/dL)
TSH (µIU/mL)	r = 0.482, p = 0.017

Pearson's correlation coefficient (r = 0.482): This indicates a moderate positive correlation between TSH levels and LDL cholesterol in patients with subclinical hypothyroidism. As TSH levels increase, LDL cholesterol also tends to increase. Significance (2-tailed, p = 0.017): Since the p-

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value is less than 0.05, the correlation is statistically significant, suggesting that the observed relationship is unlikely to have occurred by chance.

DISCUSSION

Because of its potential link to cardiovascular disease risk factors, subclinical hypothyroidism has attracted a lot of attention from researchers and doctors in recent years.[9] Although it is well established that overt hypothyroidism increases the risk of CVD, there is little, inconsistent, and contradictory information about the relationship between subclinical hypothyroidism and risk factors for CVD, such as blood pressure, obesity, and dyslipidemias.[10] The present study was conducted to assess cardiac risk factors in patients with subclinical hypothyroidism.

We found that Group I consisting of 28 males and 42 females, and Group II consisting of 30 males and 40 females (p = 0.721), showing no significant difference.

Kumar et al[11] investigated the association between subclinical hypothyroidism and cardiac risk factors such as obesity indicators {Body Mass Index (BMI) and Waist-hip Ratio (WHR)}, blood pressure, and lipid parameters.: Both groups had similar age distributions. However, there was a greater percentage of female patients in the subclinical hypothyroidism group (61%) compared to the euthyroid group (52%). As expected, TSH levels in the subclinical hypothyroidism group were significantly higher than in the euthyroid group. The subclinical hypothyroidism group recorded significantly higher mean values of BMI, Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), total cholesterol, and triglycerides, which were higher by 18%, 17%, 17%, 41%, and 16% compared to the euthyroid group, respectively. Other parameters like WHR and Low-Density Lipoprotein-Cholesterol (LDL-C) were found to be raised in subclinical hypothyroidism compared to the euthyroid group, while High-Density Lipoprotein-Cholesterol (HDL-C) levels were significantly lower by 16% in subclinical hypothyroidism.

We found that mean BMI was 27.5 ± 3.4 kg/m² and 25.8 ± 3.1 kg/m², WHR was 0.88±0.05 and 0.85±0.04, SBP was 128.4 ± 11.2 mmHg and 122.1 ± 10.8 mmHg and DBP was 84.2 ± 7.9 mmHg and 80.3 ± 7.6 mm Hg in group I and II respectively. This indicates that patients with subclinical hypothyroidism had a higher BMI, which is a known risk factor for cardiovascular diseases. The difference in Waist Hip Ratio is small but significant (p = 0.018).These results suggest that individuals with subclinical hypothyroidism exhibit elevated blood pressure levels, which may contribute to an increased risk of cardiovascular disease.

This finding aligns with previous studies indicating that SCH is associated with increased BMI and waist circumference, contributing to a higher risk of metabolic syndrome and cardiovascular diseases.[12]

John P. Walsh reported associations between subclinical thyroid dysfunction and increased blood pressure, highlighting the potential impact of thyroid hormone levels on cardiovascular health.[13]

In a study by Ejazet al[14], a total of 900 participants, of either gender and between the ages of 40 to 70 years, were enrolled in the study. Blood samples were sent to the laboratory to determine lipid and thyroid parameters. Participants were divided into two groups based on the presence of SCH. 179 (19.8%) participants had SCH. Total cholesterol (TC) and low-density lipoprotein (LDL) was significantly higher in participants with SCH compared to participants without SCH (228.41 ± 35.21 mg/dL vs. 171.21 ± 30.21 mg/dL; p-value: <0.00001) and (131.65 ± 28.22 mg/dL vs. 89.26 ± 18.52 mg/dL; p-value: <0.0001), respectively. This study found an increased incidence of dyslipidemias in patients with SCH. It is associated with elevated TC and LDL levels, which are risk factors for cardiovascular disease and mortality.

We found that total cholesterol was 210.4 ± 35.2 mg/dL and 185.7 ± 30.6 mg/dL, LDL-C was 135.6 ± 29.8 mg/dL and 112.8 ± 26.4 mg/dL, HDL-C was 44.3 ± 7.1 mg/dL and 48.5 ± 8.2 mg/dL and triglyceride was 162.7 ± 38.4 mg/dL and 48.5 ± 8.2 mg/dL in group I and group II respectively. There was positive correlation between LDL and TSH in subclinical hypothyroidism. These findings indicate that individuals with subclinical hypothyroidism have an unfavorable lipid profile, which may increase their risk of developing cardiovascular diseases.

Nicolas Rodondi found that the lipid profile alterations observed in SCH patients, characterized by higher total cholesterol, elevated LDL cholesterol, increased triglycerides, and lower HDL cholesterol levels, are well-documented. These dyslipidemic changes are attributed to decreased hepatic LDL receptor activity and reduced clearance of LDL particles, as well as alterations in lipid

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metabolism associated with thyroid hormone deficiencies.[15]

Khan et al.[16] found that the mean (SD) age was 46.0 (15.0) years for men and 58.7 (12.9) years for women, and 140 835 patients (73.9%) were female. Compared with individuals with a normal BMI (defined as a BMI of 18.5 to 24.9), lifetime risks for incident CVD were higher in middle-aged adults in the overweight and obese groups. Compared with normal weight, among middle-aged men and women, competing hazard ratios for incident CVD were 1.21 (95% CI, 1.14-1.28) and 1.32 (95% CI, 1.24-1.40), respectively, for overweight (BMI, 25.0-29.9), 1.67 (95% CI, 1.55-1.79) and 1.85 (95% CI, 1.72-1.99) for obesity (BMI, 30.0-39.9), and 3.14 (95% CI, 2.48-3.97) and 2.53 (95% CI, 2.20-2.91) for morbid obesity (BMI, ≥40.0). Higher BMI had the strongest association with incident heart failure among CVD subtypes. Average years lived with CVD were longer for middle-aged adults in the overweight and obese groups compared with adults in the normal BMI group. Similar patterns were observed in younger and older adults.

Positive correlation between TSH and LDL cholesterol in present study because Pearson's correlation coefficient (r = 0.482).This indicates a moderate positive correlation between TSH levels and LDL cholesterol in patients with subclinical hypothyroidism. As TSH levels increase, LDL cholesterol also tends to increase.

Sharma Kumar M reported a statistically significant positive correlation between serum TSH and LDL levels in SCH patients (r = 0.216, p = 0.03). This suggests that as TSH levels increase, LDL cholesterol levels also rise.[17]

S. Ashok Kumar found a statistically significant correlation between elevated TSH and increased LDL-C levels in SCH patients. The study reported that as TSH levels rose, there was a corresponding increase in LDL-C concentrations, highlighting the impact of thyroid function on lipid profiles.[18]

LIMITATIONS OF THE STUDY

- Small Sample Size: The sample size could become too small to detect meaningful differences.
- Lack of Long-Term Follow-Up
- Generalizability: This can limit the external validity of the study.
- Lack of Assessment of Symptoms or Clinical Outcomes
- No consideration of TPO antibodies or other thyroid antibodies: The study does not mention whether thyroid peroxidase (TPO) antibodies or other thyroid antibodies were measured. In patients with subclinical hypothyroidism, the presence of thyroid antibodies (such as anti-TPO antibodies) can provide more information regarding the etiology and potential progression of the condition, which might help to better stratify the subjects.

CONCLUSION

Authors found that Heart risk variables such as blood pressure, lipid markers, and obesity indicators (BMI and WHR) are strongly correlated with subclinical hypothyroidism. Overall, the findings of this study underscore that subclinical hypothyroidism is associated with various cardiovascular risk factors, including higher BMI, blood pressure, unfavorable lipid profiles, impaired glucose metabolism, and systemic inflammation. These factors collectively increase the cardiovascular risk in individuals with subclinical hypothyroidism, warranting attention in clinical practice for early detection and management to reduce the risk of cardiovascular events.

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