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Original Research Article

A Study to Assess Cardiovascular Risk Factors in Subclinical Hypothyroidism in Tertiary Medical Centre

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Abstract

Introduction: The TSH increase in SCH is typically between more than 5 and within 10 Iu/ml, while individuals with a TSH over 10 Iu/ml tend to have lower free T4 levels and may exhibit typical hypothyroid symptoms. According to several research and current therapeutic recommendations, individuals with subclinical hypothyroidism have a greater risk of cardiovascular disease (CVD) and all-cause death than those with euthyroidism.

Aim and Objective: To evaluate patients with subclinical hypothyroidism's cardiovascular risk by looking at their lipid profiles, homocysteine levels, C-reactive protein levels, and platelet counts.

Materials and Methods: From June 2021 to June 2022, this descriptive longitudinal study was carried out at the government medical college in Saharanpur. 40 newly diagnosed subclinical hypothyroid female patients between the ages of 30 and 60, with 40 like aged and gender patients. Study subjects were recruited as per inclusion and exclusion criteria. The key factor used to diagnose SCH was a somewhat elevated TSH level (10 IU/ml) with a normal free T4 level.

Result: The mean total cholesterol was 194.71±58.34, their mean LDL was 119.42±24.01, their mean HDL was 46.06.14, their mean TGL was 135.6937.99, their mean homocystine level was 13.818.05, and their mean CRP level was 6.924.40. The research subjects' mean TSH was 5.143.11, whereas the mean free T3 was 0.340.29 and the mean free T4 was 1.030.14.

Conclusions: Based on the study's findings, we can say that people with subclinical thyroid abnormalities are more likely to be overweight, have pre-hypertension, have dyslipidemia, and have higher CRP. Due to these changed parameters in the subclinically hypothyroid female participants, it may result in the development of cardiovascular risk.

Keywords: SCH, TSH, Hypertension, LDL.

Introduction

When thyroxine (T4) and triiodothyronine (T3) levels are normal and hypothyroid symptoms are either limited or nonexistent, a condition known as subclinical hypothyroidism is present. The term subclinical hypothyroidism (SCH) was first used in the early 1970s, at the same time as blood TSH tests were available. Subclinical hypothyroidism is sometimes referred to as preclinical hypothyroidism, decreased thyroid reserve, and moderate thyroid insufficiency [1].

SCH patients normally have a TSH rise between 5 and 10 Iu/ml; however, those with a TSH over 10 Iu/ml have lower free T4 levels and may have typical hypothyroid symptoms. A thyroid gland disease called primary hypothyroidism can either be asymptomatic or evident. Defects in the brain or pituitary gland are frequently the cause of secondary hypothyroidism [2].

Undoubtedly, each person has a unique, genetically determined set point for their hypothalamic-pituitary-thyroid axis. According to a Danish twin study, heritability explained 64% of the variation in TSH (95% CI: 57-70%), 65% of the variation in FT4 (95% CI: 58-71%), and 64% of the variation in FT3 (95% CI: 57-70%). FT4 plays the most significant part in regulating TSH secretion. It has been questioned whether the regulation mechanism actually works as a log-linear relationship between TSH and FT4. Mathematical models predict that the relationship is best illustrated by two overlapping sigmoid curves, with TSH levels being greater in men and the elderly. The signs of thyroid dysfunction are vague, though, and include fatigue, melancholy, dyslipidemia, weight gain, and constipation. More serious symptoms include pericardial effusion and myxedema. Hypothyroid subjects seldom report the whole constellation of symptoms, but usually describe tiredness, cramps, weakness, and myalgia [3].

Numerous epidemiological studies have discovered a link between dyslipidemia, elevated insulin resistance, and hypertension, all of which are symptoms of metabolic syndrome, and subclinical hypothyroidism or high-normal TSH concentrations (i.e., serum TSH concentrations at the upper end of the normal range) [4].

The link between subclinical hypothyroidism, cardiovascular disease (CVD), and mortality remains unclear despite these processes and data suggesting the possible impact of elevated TSH on heart metabolism. Latest patient-by-patient meta-analysis by the Thyroid Study. Thyroid hormone replacement medication shouldn't be often given to those with subclinical hypothyroidism, according to current clinical recommendations. The importance of taking into account variations in the normal range of TSH when assessing long-term negative health outcomes is highlighted by some recent studies that indicate even high-normal TSH concentrations are linked to an increased risk of cardiovascular disease (CVD) and mortality in the US general population or in adults with chronic kidney disease. We conducted this analysis to ascertain the relationship between subclinical hypothyroidism and cardiovascular disease with the aforementioned background in mind.

Aim and Objectives

To assess the Cardiovascular Risk in subclinical hypothyroidism by analyzingthe levels of Lipid profile, Homocysteine, C Reactive Protein and Platelet count in participants with subclinical hypothyroidism in comparison to Euthyroid control group.

Materials and Methods

This Descriptive longitudinal study was conducted at government medical college Saharanpur during June 2021 to June 2022, Forty newly diagnosed Subclinical

hypothyroid female patients in theage group of 30 – 60 years and forty sex and age matched Euthyroid healthy controls were included in the study according to the inclusion and exclusion criteria mentioned below. Diagnosis of SCH was based mainly on the mild elevation of TSH level (≤ 10μIU/ml) with normal free T_4 level. Study subjects were recruited on the basis of following inclusion and exclusion criteria

Inclusion criteria:

Newly diagnosed individuals with SCH based on TSH value between >5 to 10 IU/ml and with normal free T4 value.

Exclusion criteria:

1. Hyperthyroidism
2. Hypothyroidism
3. Diabetes Mellitus
4. Polycystic Ovary Syndrome
5. Hypertension
6. Other serious medical conditions
7. Subjects those who were taking the drugs, which can cause SCH and affect lipid metabolism.

Institutional ethical permission were taken, each participant gave a written informed consent to participate, after knowing the nature of the study.

All participants gave blood samples for the assessment of biochemical parameters after a 12-hour overnight fast. To separate the serum, the samples were immediately centrifuged for 5 minutes at 3000 rpm. Before their evaluation, the samples were kept at a temperature of 20 degrees Celsius. Thyroid profile testing using ECLIA and ELISA for free T3, free T4, and TSH, respectively. The CHOD-PAP technique was used to determine the lipid profile. Immunoassay was used to test homocysteine (Hcy). C-Reactive Protein was examined using immunoturbidimetry. The Coulter method was used to calculate the platelet count. Using a Stadiometer, the subjects' height and weight were determined. Heavy apparel and shoes were taken off before height and weight were recorded. A crucial and simple way to assess central obesity is by measuring waist circumference. Among south Asian ethnic groups, the ideal waist size is less than 90 cm for men and fewer than 80 cm for women. At the halfway between the bottom border of the least perceptible rib and the top of the iliac crest, at the conclusion of normal expiration, the waist circumference was measured using a standard, non-elastic measuring tape, to the closest 0.5cm. The patient was told to stand tall with their feet together and their arms by their sides. Around the highest protuberance of the buttocks, the hip circumference was measured using a standard measuring tape held parallel to the floor. Body Mass Index was calculated using the Quetlet method. It is calculated by dividing the patient's height in meters by the square of their weight in kilos.

BMI equals Wt in kg/Ht in m2.

Calculating the ratio of waist circumference to hip circumference in cm allowed researchers to establish the waist-to-hip ratio (Standard approach).

WC/HC = WHR

After five minutes of rest, the blood pressure was taken in a quiet, comfortable environment with the feet flat on the floor. The participants were positioned with their backs against the chair and were instructed to keep their arms at heart level while being supported at the elbows. The cuff was knotted 2.5 cm above the cubital fossa. A mercury Sphygmomanometer was used to palpate the blood pressure and take the reading. At a rate of 2 to 4 millimetres of mercury per second, the cuff was deflated. Phase I of the Korotokoff phenomenon was understood as representing systolic blood pressure, and phase IV as representing diastolic blood pressure.

Statistical Analysis

Data from the study were entered into Microsoft Excel spreadsheet and examined using SPSS software. Every piece of information was presented as Mean Standard Deviation, and its normalcy was evaluated. A Student's t-test was used to compare the mean values of the control and patient groups in order to ascertain statistical significance. The two variables' connection was calculated using Pearson's Correlation Coefficient.

Result

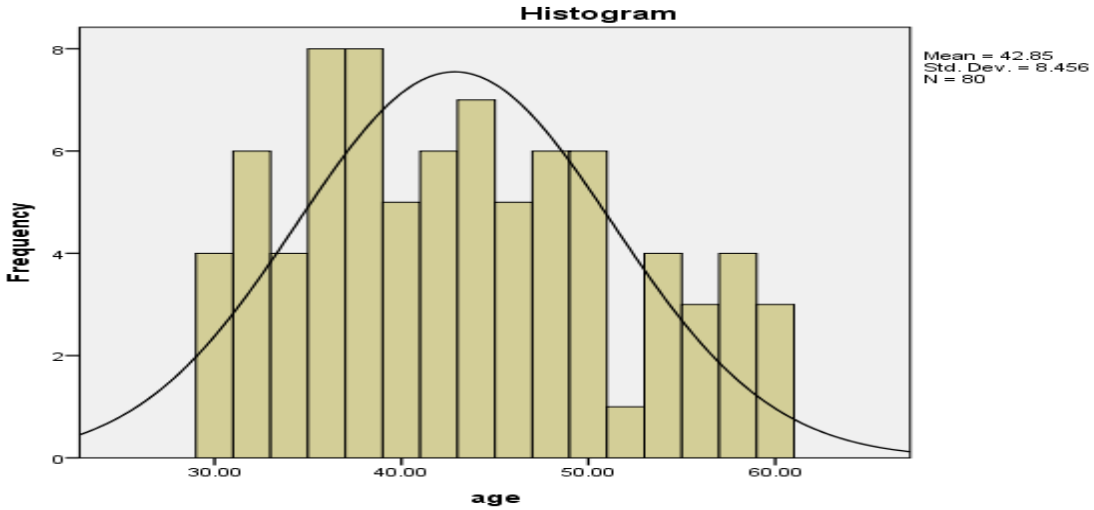

Figure 1: Distribution of study subjects as per age

Figure 1 shows Distribution of study subjects as per age, The mean age of the study subjects was 42.85 yrs with SD- 8.45 yrs

Table 1: The mean anthropometric measurement of study subjects

	N	Mean	Std. Deviation	Std. Error Mean
BMI	80	24.9913	2.89875	.32409
WHR	80	0.8452	0.06183	.00691
SBP	80	121.7500	14.57021	1.62900
DBP	80	78.3500	8.85195	.98968

Table 1 shows The mean anthropometric measurement of study subjects, The mean BMI of study subjects was 24.99±2.89, The mean waist hip ratio of study subject was 0.84±0.06, The mean systolic BP was 121.75±14.57 whereas mean diastolic BP was 78.35±8.85

Table 2: Mean Thyroid profile of the study subjects

	N	Mean	Std. Deviation	Std. Error Mean
FREE T3 ng/dl	80	0.3420	0.29376	0.03284
fREE T4 ng/dl	80	1.0264	0.13938	0.01558
TSH IU/ML	80	5.1391	3.10834	0.34752

Table 2 shows Mean Thyroid profile of the study subjects, The mean free T3 was 0.34±0.29 whereas the mean Free T4 was 1.03±0.14, mean TSH of the study subjects was 5.14±3.11

Table 3: The mean value of different lipid profile parameter and CRP value

	N	Mean	Std. Deviation	Std. Error Mean
T CHOL	80	194.7125	58.33778	6.52236
LDL	80	119.4250	24.00885	2.68427
HDL	80	46.0000	6.13766	0.68621
TGL	80	135.6875	37.98654	4.24702
H.CYS mol/l	80	13.8063	8.04634	0.89961
CRP mg/dl	80	6.9250	4.40016	0.49195
PT (lac)	80	3.7950	1.19640	0.13376

Table 3 shows the mean value of different lipid profile parameter and CRP value, The mean total cholesterol was 194.71±58.34, mean LDL was 119.42±24.01, The mean HDL was 46.0±6.14, The mean TGL of the study subjects 135.69±37.99, The mean homocystine level was 13.81±8.05, the CRP level was 6.92±4.40.

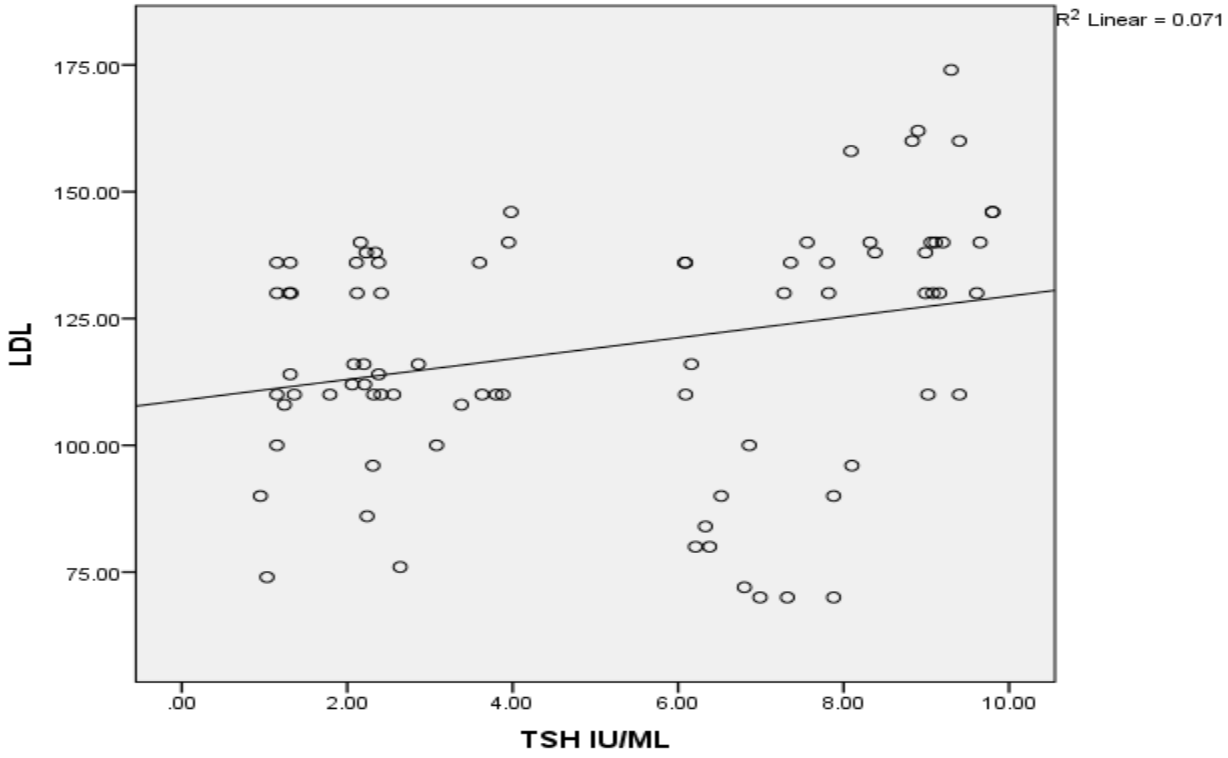

Figure 2: Associations of TSH with LDL

Fig 2 shows Associations of TSH with LDL, on applying regression analysis there is mild association of LDL with TSH with R square 0.071.

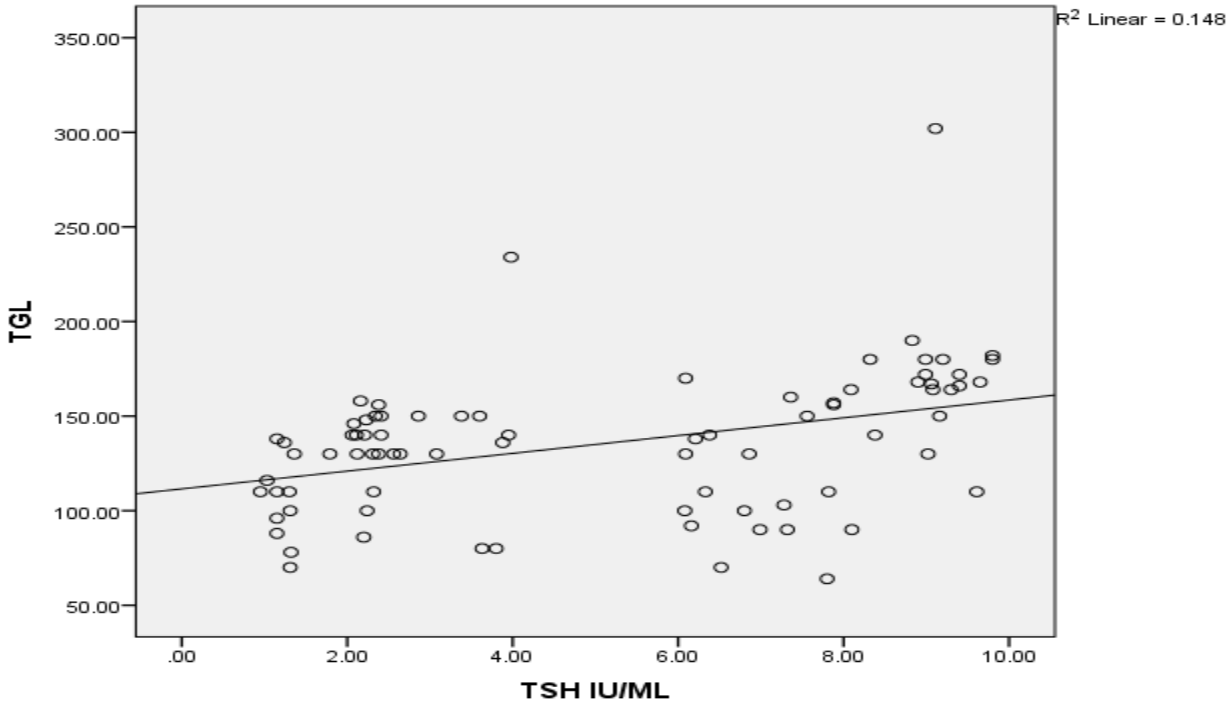

Figure 3: Association of TSH with TGL

Figure 3: shows Association of TSH with TGL, on applying regression analysis there is mild association with TGL and TSH in the study subjects.

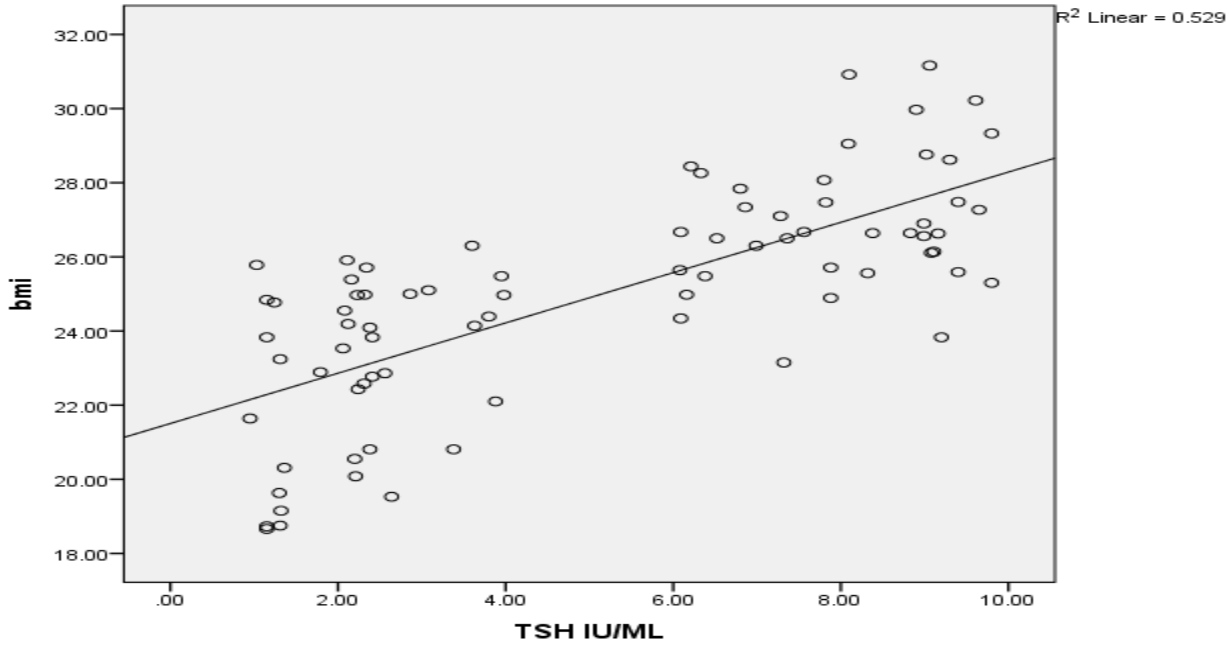

Figure 4: Association of TSH with BMI of the study subjects

Figure 4: Association of TSH with BMI of the study subjects, on applying regression analysis there is moderate association between TSH and BMI.

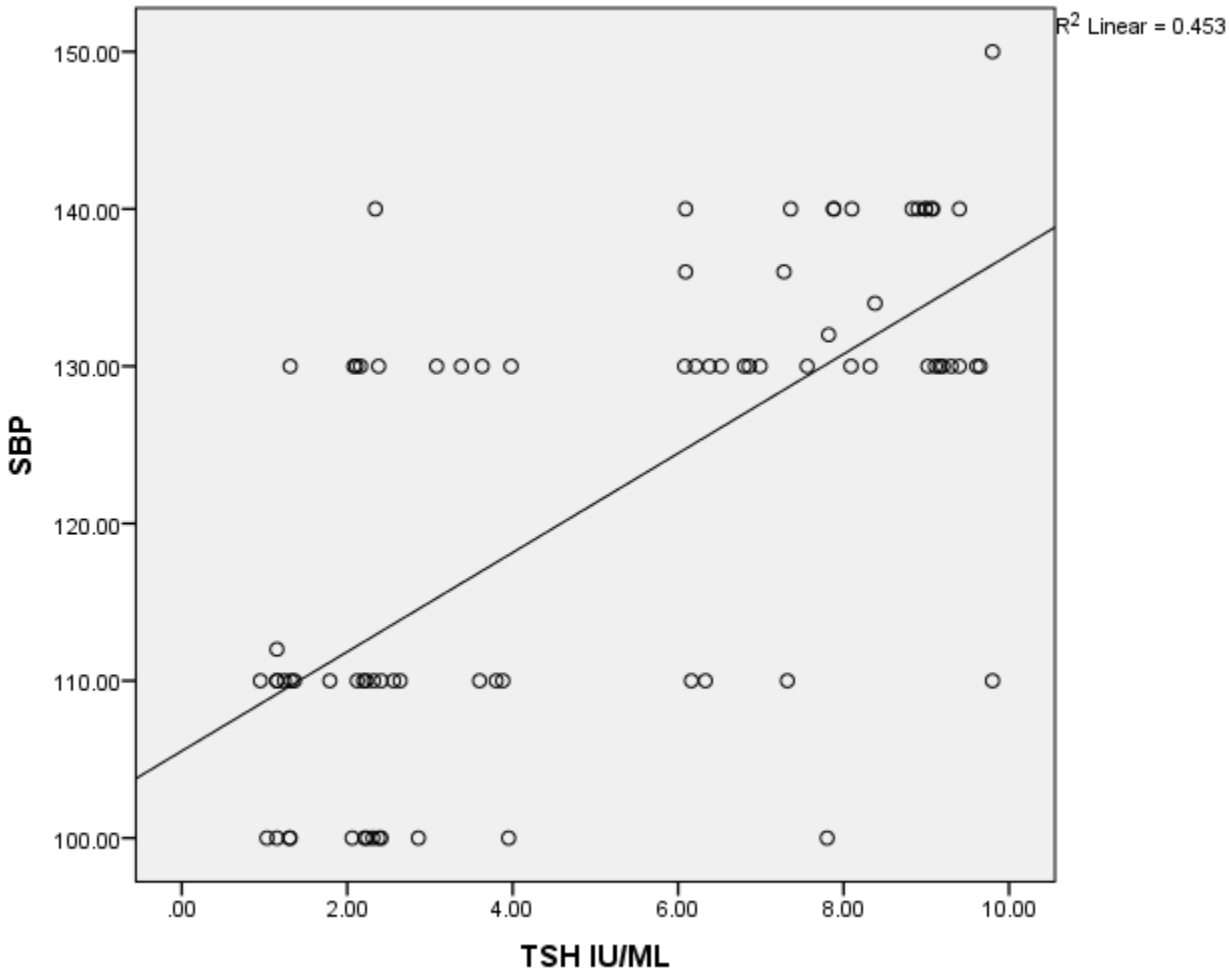

Figure 5: Association of TSH with BMI of the study subjects

Figure 5 shows Association of TSH with BMI of the study subjects, on applying regression analysis there is moderate analysis with R square 0.453.

Discussion

The two types of hypothyroidism are common among the elderly, especially in women. Subclinical hypothyroidism is linked to cardiovascular abnormalities and a higher risk of atherosclerosis because it has a lipid profile that is more likely to cause atherosclerosis when there is hypertension present. A rise in C-reactive protein, homocysteine, and coagulation markers are additional possible atherogenic factors linked to subclinical hypothyroidism. Our study is supported by the observation of comparable circulatory anomalies in SCH, albeit on a more minor scale.

In this study, euthyroid study subjects and patients of subclinical hypothyroidism were assessed for body composition parameters like BMI and WHR as well as for biochemical parameters including homocysteine, lipid profile, and CRP, an inflammatory marker, and platelet count, a

coagulation indicator. All research participants had their blood pressure measured, including systolic and diastolic readings. The outcomes of the case group and the control group were contrasted with all collected findings.

The study's findings showed that participants with TSH levels over 5.0 IU/L had higher BMI and WHR values than those with lower TSH levels. These findings corroborated a large population investigation that found a strong positive connection and correlation between TSH and BMI.

Blood vessel stiffness and left ventricular diastolic dysfunction have both been connected to hypothyroidism. Log N-terminal prohormone of brain natriuretic peptide (NT-proBNP), cardio-ankle vascular index (CAVI), and C-reactive protein (CRP) were found to be elevated in SCH in a cross-sectional study that looked at the relationship between thyroid hormone level and left ventricular diastolic function and 83 untreated SCH patients [6]. Hence, high logNT-proBNP may be linked to elevated CAVI in SCH patients, and this condition may be a risk factor for CV events linked to arterial stiffness and left ventricular diastolic dysfunction. Particularly in people with moderate to high CV risk scores, SCH may potentially be a risk factor for coronary artery calcification (CAC) [7]. As a result, it was discovered that the CAC score (CACS) was higher in SCH patients than in controls (Cntr versus SCH; p=0.045). The chance of CACS >100 was independently correlated with male gender, age >55, and the presence of SCH in a multivariate analysis.

According to the current study, there is a rise in blood pressure in subclinical hypothyroidism instances. SCH may increase the risk of hypertension, according to Liu *et al* [8], contrary to the findings of Duan *et al* [9] and Walsh *et al* [10], who showed no connection between SCH and an increase in blood pressure. Similar to the findings of Bjorn o. et al [11], our investigation revealed a positive and linear relationship between TSH within the reference range and systolic and diastolic blood pressure. It is still unclear if a changed lipid profile in SCH, particularly in those with serum TSH values less than 10 IU/mL, has therapeutic importance. The link between overt hypothyroidism, accelerated atherosclerosis, and a higher risk of cardiovascular disease has been shown in several research. The data supporting a link between subclinical hypothyroidism and an increased risk of cardiovascular disease, however, seems to be weak.

The frequency of arteriosclerosis or hyperlipidemia was shown to be higher in subclinical hypothyroidism with thyroid peroxidase antibodies, according to a Rotterdam investigation.

In this study, individuals with subclinical hypothyroidism had substantially higher total cholesterol and triglyceride levels than healthy controls ($p< 0.0001$ and $p <0.038$, respectively). Despite the fact that patients had greater levels of low density lipoprotein cholesterol than controls, this difference was not statistically significant. In contrast, patients' levels of high density lipoprotein cholesterol decreased statistically significantly (p 0.0001) when compared to controls. As a result, the dyslipidemia found in the current study was equivalent to that seen in studies showing a beneficial relationship between SCH and high TC, TG. In contrast to earlier studies, ours discovered a link between SCH and high TC levels. BMI, WHR, TC, TGL, homocysteine, CRP, platelet count, and diastolic blood pressure were all substantially elevated in the current research, while LDL-C levels were not ($p > 0.05$). Also, SCH patients' lower HDL-C levels compared to controls showed a significant p value (p0.000), which was in line with Erem *et al* findings [12].

This study focused on the connection between SCH and cardiovascular risk factors, which help to cause a variety of detrimental health effects. This study will help in understanding the prevalence and cardiovascular risk factors of subclinical hypothyroidism, as well as in concentrating attention on these aspects, to help in the prevention of cardiovascular disease in our community.

Conclusions

On the basis of findings of this study we can conclude that subclinical thyroid abnormality patients are associated with Overweight, Prehypertension, dyslipidemia, increased CRP. It can lead to development of cardiovascular risk that may occur due to these altered parameters in the subclinical hypothyroid female subjects. The study also showed an increasing prevalence of hypertension with increasing Body mass Index (BMI).

Source of support: Nil

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