

## Study of cardiovascular manifestations in subclinical hypothyroidism

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**How to citation this article:** Jayshankar Prasad Gupta, Kumar Sandeepan, Ram Raj Ravi, “Study of cardiovascular manifestations in subclinical hypothyroidism”, IJMACR- June - 2023, Volume – 6, Issue - 3, P. No. 311 – 316.

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**Type of Publication:** Original Research Article

**Conflicts of Interest:** Nil

### Abstract

**Introduction:** Subclinical hypothyroidism is characterized by elevated levels of thyroid-stimulating hormone (TSH), while thyroxine (T4) and tri-iodothyronine (T3) levels remain within the normal range for the general population. It is widely recognized that hypothyroidism has negative effects on the cardiovascular system, which can be effectively treated with levothyroxine therapy. Recent studies have also demonstrated similar cardiovascular changes in individuals with subclinical hypothyroidism. However, there is currently insufficient evidence to support the use of levothyroxine treatment in subclinical hypothyroidism as beneficial, as it is in cases of hypothyroidism. Thus, the purpose of this study is to reinforce the existing evidence regarding this matter.

**Aim and objective:** To examine the cardiovascular alterations observed in individuals with subclinical hypothyroidism, establish the correlation between these

changes and subclinical hypothyroidism, and understand the advantages of early detection and treatment in reducing these cardiovascular modifications.

**Materials and methods:** Over a span of one year and nine months, from April 2021 to December 2022, a total of 50 cases with subclinical hypothyroidism who visited the outpatient departments of General Medicine and Endocrinology at Patna Medical College and Hospital in Patna were enrolled in this research study.

**Results:** Of the 50 cases, 34(68%) were of the age group 41-50 years; 39(88%) were females. The mean value for height(cm), weight(kg), waist(cm), hip(cm), waist hip ratio & BMI (kg/m<sup>2</sup>) were 157.94±5.25, 55.8±6.42, 103.65±20.89, 96.68±2.16, 1.13±0.16, 26.43±2.97 respectively. The mean systolic and diastolic blood pressure were 139.42±9.20mmhg and 88.32±8.14mmhg. The mean total cholesterol, Triglyceride, HDL, LDL were 158.60±21.97mg/dl, 180.20±38.69mg/dl, 47.00±7.90mg/dl, 75.56±21.43 mg/dl.

Electrocardiographic study showed strong positive statistically significant correlation between TSH and qtc interval; and 2D echocardiographic study showed statistically significant positive correlation between TSH with interventricular septal wall thickness and left ventricular posterior wall thickness.

**Conclusion:** Subclinical hypothyroidism is seen to be associated with hypertension, higher BMI, and thickened interventricular septal wall and left ventricular posterior wall thickness which are risk factors for cardiovascular disease.

**Keywords:** Hypertension, BMI, interventricular septal thickness, QTc interval.

### **Introduction:**

Hypothyroidism is usually a progressive disease that impacts the entirety of bodily functions. As the heart is the main target of thyroid hormone activity, hypothyroidism may precipitate or aggravate heart failure, influencing heart rate and blood pressure (bp) while increasing cardiovascular (cv) stiffness and cardiomegaly.<sup>[1,2]</sup> overt hypothyroidism (oh) is therefore associated with heightened cv morbidity and mortality.<sup>[3]</sup>

Subclinical hypothyroidism (sch) is defined as a condition characterized by elevated serum thyroid-stimulating hormone (tsh) concentrations (tsh: >4.5 mu/l), while circulating thyroxine (t4) and triiodothyronine (t3) levels remain within the population reference range.<sup>[4]</sup> the incidence of sch varies between 4 and 20 % depending upon the gender (females are more prone), age (older than 65) and population studied.<sup>[5,6]</sup>

Besides the classic risk factors for cv disease (cvd), i.e., hypercholesterolemia and diastolic hypertension, some newer risk factors such as a disrupted coagulability and insulin resistance have recently been evaluated.<sup>[8]</sup>

The cardiovascular system has recently become an important topic of research. Studies have shown subclinical hypothyroidism caused cardiovascular changes like impaired systolic and diastolic dysfunction can be reversed by easily available levothyroxine therapy.<sup>[9]</sup>

Although there is high prevalence of subclinical hypothyroidism among global<sup>[10]</sup> as well as indian population,<sup>[11]</sup> the evidence supporting screening for this disorder and the benefits and risks of its treatment remain controversial.<sup>[12]</sup>

Therefore, screening is not recommended commonly, and even if detected as subclinical hypothyroidism, treatment is not commonly advised. There are only a few studies done in our country have been conducted assessing cardiovascular changes in subclinical hypothyroidism.

Therefore, this study was undertaken to reiterate the need to consider subclinical hypothyroidism as a cause for cardiovascular disease, and thus the levothyroxine therapy for reversing and halting the same.

### **Aims and objective**

- 1.to study the cardiovascular changes seen in patients with subclinical hypothyroidism
- 2.to establish a relationship between these changes and subclinical hypothyroidism.
- 3.to know the benefits of early diagnosis and correction of subclinical hypothyroidism in minimizing cardiovascular effects.

### **Materials and methods**

**Place of study:** Patna medical college and hospital, Patna.

**Source of data:** patients attending the outpatient department (OPD) of department of general medicine and department of endocrinology.

**Study duration:** April 2021 to December 2022 sample size: 50

**Type of study:** cross sectional observational study.

**Study population:** those who were presenting in the department of general medicine with clinical sign and symptoms of hypothyroidism were enrolled for the study.

**Sample size:** after evaluation of subclinical hypothyroidism cases a total 50 patients were taken according to inclusion and exclusion criteria.

**Inclusion criteria**

1. Age – above 18 years
  2. Serum TSH level –
    - a) 2.5 mIU/ml to 4.0 mIU/ml with Positive Anti-TPO antibody.
    - b) 4.0 mIU/ml to 10.0 mIU/L with or without Positive Anti-TPO antibody.
- Serum free T4 – within normal range.

**Exclusion Criteria:**

- Hypertension, Diabetes Mellitus, Hypertension  
Renal Disorders, Valvular Heart Diseases  
Any drugs that can cause Subclinical hypothyroidism and affect lipid metabolism.  
Alcoholic, Drug Abuse, Smokers  
Diseases of respiratory system

**Data Collection:** History regarding symptoms of subclinical hypothyroidism along with cardiovascular symptoms was recorded. A detailed clinical examination was performed, and findings were recorded. Selected patients were investigated as per investigations mentioned below.

**Methodology**

Following the acquisition of ethical approval from the institutional ethics committee at Patna Medical College and Hospital, as well as obtaining written informed

consent from the participating patients, they were enrolled in the study. A concise history, a thorough clinical assessment was conducted to document the measurements of systolic and diastolic blood pressure, heart rate, height, weight, and waist circumference. A blood sample was collected from each patient and sent to the laboratory for routine blood work, which also included tests for TSH, fT3, fT4, anti-TPO Ab, and fasting lipid profile. Additionally, electrocardiographic, and echocardiographic findings were documented for each patient. Once the data was gathered from each patient, it was analyzed using the SPSS 23.0 software package. The Pearson correlation coefficient was employed to assess the correlation between various parameters, with a p-value of less than 0.05 being deemed statistically significant.

**Results**

The majority of individuals, 34 cases (68.0%), are in the age group of 41-50. The remaining 12 cases, (24.0%) belong to the age group of 51-60 years respectively. The mean age was 46.44 years.

Female cases were predominantly higher than male cases, female were 88% and male were 22% respectively. The Male & Female ratio was 1: 3.54.

The mean weight was 55.80 kg. Waist circumference was 103.65 cm, the mean hip circumference was 98.68 cm. Waist-to-hip ratio for the individuals was 1.13 & the mean body mass index (BMI) was 26.43(kg/m<sup>2</sup>), respectively.

The mean systolic blood pressure among the study population was 139.42±9.20 mmHg, diastolic blood pressure 88.32±8.14 mmHg & Heart rate was 76.00±2.04 respectively.

The mean level of Total Cholesterol among study population was 158.60±21.97 (mg/dl), mean level of

Triglyceride was  $180.50 \pm 38.69$  (mg/dl), HDL was  $47.00 \pm 7.90$  (mg/dl), LDL was  $75.56 \pm 21.43$  (mg/dl) and VLDL was  $36.04 \pm 7.73$  respectively.

Electrocardiographic findings among the study population. The PR interval, representing the time between atrial depolarization and ventricular depolarization, has a mean value of  $137.14 \pm 7.27$  milliseconds. The QRS interval, which represents ventricular depolarization, has a mean value of  $83.18 \pm 3.31$  milliseconds. The qtc interval, a corrected measure of ventricular depolarization and repolarization, has a mean value of  $409.98 \pm 6.78$  milliseconds. Finally, the QRS axis, indicating the overall direction of ventricular depolarization, has a mean value of  $61.34 \pm 4.96$  degrees.

The left ventricular posterior wall thickness (LVPW) has a mean value of  $8.06 \pm 0.97$  millimeters. The interventricular septal wall thickness (IVSW) has a mean

value of  $9.19 \pm 0.92$  millimeters. The left ventricular internal dimension (LVID) in the diastole has a mean value of  $4.34 \pm 0.17$  centimeters. The ejection fraction (EF), which indicates the percentage of blood pumped out of the left ventricle with each contraction, has a mean value of  $60.78 \pm 4.24$  %. The fractional shortening (FS), representing the percentage of change in left ventricular dimension during systole, has a mean value of  $30.82 \pm 3.49$  %. Finally, the ratio of early (E) to late (A) ventricular filling velocities (E/A ratio) has a mean value of  $1.64 \pm 0.17$ .

In terms of TSH vs SBP, DBP & BMI (Body Mass Index), there is a strong positive correlation with a *r* value of 0.677. This indicates that higher TSH levels are associated with higher SBP, DBP & BMI values. The *p*-value for this correlation is  $<0.0001$ , indicating that the correlation is statistically significant.

Table 1: Correlations Of anthropometric parameters with TSH

		TSH ( $\mu$ IU/L)	Hight (cm)	Weight (Kg)	Waist (cm)	Hip (cm)	BMI (kg/cm <sup>2</sup> )
TSH ( $\mu$ IU/L)	Pearson Correlation	1	-.122	.633**	.349*	-.213	.640**
	P Value		.398	<0.0001	.013	.138	<0.0001
	No of cases	50	50	50	50	50	50

Table 2: Correlation of SBP, DBP, FBS, HbA1C

		TSH ( $\mu$ IU/L)	SBP (mmHg)	DBP (mmHg)	FBS (mg/dl)	HbA1C (%)
TSH ( $\mu$ IU/L)	Pearson Correlation	1	.677**	.704**	.706**	-.229
	P Value		<0.0001	<0.0001	<0.0001	.110
	No of cases	50	50	50	50	50

Higher TSH levels are associated with higher levels of total cholesterol, triglycerides, LDL, and VLDL, as well as lower levels of HDL. The *P* value is  $<.05$ .

Regarding TSH and QTc interval, there is a very strong positive correlation with a coefficient of 0.908. The *p*-

value of 0.000 indicates that this correlation is statistically significant.

		TSH	HR	PR interval	QRS interval	QTc interval	QRS axis
TSH	Pearson Correlation	1	-.083	.091	.226	.908**	.030
	P value		.565	.531	.114	.000	.838
	No of cases	50	50	50	50	50	50

For TSH and LVPW (Left Ventricular Posterior Wall thickness), there is a very strong positive correlation with a coefficient of 0.935. The p-value of <0.0001 indicates that this correlation is statistically significant.

Regarding TSH and IVSW (Interventricular Septal Wall thickness), there is a very strong positive correlation with a coefficient of 0.867. The p-value of <0.000 suggests that this correlation is statistically significant.

		TSH	LVPW	IVSW	LVIDD	EF	FS	EA
TSH	Pearson Correlation	1	.935**	.867**	-.181	-.139	.044	-.870**
	P value		<0.0001	<0.0001	.208	.336	.761	<0.0001
	No of cases	50	50	50	50	50	50	50

**Discussion**

There have been studies done in past which has established association of subclinical hypothyroidism with cardiovascular changes which changes which can be stopped or reversed easily with levothyroxine therapy but there are not enough evidences to support this.

In our study, we observed that the cases had elevated systolic and diastolic blood pressure as well as BMI, and these factors exhibited a strong positive correlation with tsh levels. It is important to note that higher blood pressure (systolic and diastolic) and BMI are well-established risk factors for cardiovascular diseases.<sup>[13]</sup> additionally, our research revealed a significant positive correlation of tsh levels with interventricular septal wall thickness, left ventricular posterior wall thickness, and qtc interval. An increased interventricular septal wall thickness <sup>[14]</sup> is associated with a higher incidence of coronary heart disease, while a prolonged QTc interval renders the heart more susceptible to ventricular

arrhythmias.<sup>[15]</sup> therefore, based on our study findings, individuals with subclinical hypothyroidism are at an elevated risk of developing cardiovascular diseases.

Nevertheless, our research encountered specific constraints. Initially, the number of participants in our study was limited, resulting in a small sample size. Additionally, our study followed a cross-sectional design, meaning that cases were assessed only at a single moment in time, without any subsequent follow-up. Consequently, we lacked follow up data regarding observed changes and the established correlations, which would have provided further support for our findings.

**Conclusions**

Subclinical hypothyroidism has the potential to induce alterations in the cardiovascular system or increase an individual's vulnerability to cardiovascular disease. If these modifications and connections are firmly established, it is possible to prevent or even reverse many of these effects using easily accessible

levothyroxine therapy. Consequently, there is a necessity for additional prospective studies and randomized controlled trials (RCTS) to support these findings.

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