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EVALUATION OF CARDIOVASCULAR PARAMETERS IN SUBJECTS WITH ALTERED THYROID STATUS IN A TERTIARY CARE HOSPITAL IN KOLKATA

Physiology

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ABSTRACT

Thyroid problems are widespread around the world, and they are quite prevalent in India as well. Thyroid disease is expected to affect 42 million people in India, according to estimates from multiple studies on the ailment. . The thyroid hormone regulates and controls a number of the body's metabolic processes. As a result, thyroid disorders impact every organ, with the heart being especially vulnerable. Pulse, BP indicate the condition. Thyroid hormones have the ability to influence the heart's electrophysiologic and inotropic functions as well as alter the risk of atherosclerosis. It is well known that thyroid hormone affects lipid mobilisation and metabolism regulation. Serum levels of lipoprotein A, triglycerides, apolipoprotein-B, total cholesterol, and LDL are all higher in individuals with overt hypothyroidism. It is hospital based Cross sectional, Descriptive type of observational study done with a sample size of 120 collected from OPD over a period of one year. Patient of any sex 18 to 60 years with altered thyroid status, following our inclusion criteria attending OPD included in this study. The statistical analysis done in SPSS 25.0 excel STAT. Participants had a mean age of 48.94±13.46 years , with mean weight 61.25±12.29 kg, and BMI averaging 77.68±15.34 kg/meter2. Lipid profiles displayed varied readings with mean Total Cholesterol 41.19±19.75mg/dl, Triglyceride 114.97±68.75 mg/dl . The heart rate mean was 81.29±13.87 . There exists a weak correlation between FT4 and P wave duration (r=0.25). Moderate correlation between Total Cholesterol, Triglyceride and LDL cholesterol with BMI (r=0.53), (0.49) and (r=0.57)was found. In this study,it was found that there was weak positive correlation between value of FT4 and HDL. In the present study there were a significant positive correlation between VLDL and TSH levels. This is similar to the other previous studies. In our study there were weak positive correlation exist between Heart rate (HR; beats per min) and TSH levels .

KEYWORDS

Thyroid Disorder, Electrophysiology, Lipid Profile

INTRODUCTION

Normal growth tissue differentiation and metabolism depend on thyroid hormones. Triiodothyronine (T3), tetraiodothyronine, or thyroxin (T4) are the hormones that the thyroid gland produces. Clinical and experimental data indicate that even small changes in thyroid hormone concentrations,[1,3] as in low triiodothyronine syndrome and subclinical hypothyroidism or hyperthyroidism, negatively impact the cardiovascular system. Thyroid hormones plays an important role in maintaining cardiovascular homeostasis. Dyslipidaemia, endothelial dysfunction, variations in blood pressure, and the direct impact of thyroid hormones on the myocardium are a few possible processes that could link the two disorders. Thyroid hormone (TH) receptors are found in the heart and vascular tissue, and minute variations in TH concentration can affect the cardiovascular system's (CV) physiology. Endothelial dysfunction, blood pressure variations, cardiac systolic and diastolic dysfunction, and dyslipidaemia are the possible processes that connect CV illness with thyroid dysfunction.[2] Subclinical thyroid dysfunction (STD) presents as subclinical hypothyroidism (SHypo) or subclinical hyperthyroidism (SHyper). Increased risk of cardiovascular disease (CVD) and death is associated with it. It is characterised by abnormal serum thyrotropin (TSH) and normal free thyroid hormones . pressure, heart rhythm, vascular resistance, and cardiac contractility. [8,9] .It is commonly known that practically every cell and organ in the body is impacted by thyroid hormones, particularly Thyroid hormones have non-genomic and inherited effects and are important for heart function. Thus, it is expected that the regulation of heart function and circulatory haemodynamics will be significantly altered by both excess and deficit of thyroid hormone. [4] Blood pressure, vascular resistance, cardiac output, cardiac contractility, and rhythm abnormalities can all be attributed to thyroid dysfunction, which is explained by the cellular mechanisms of thyroid hormone action on the heart and circulatory system. [5,6] The vascularity, contractility, and electrophysiology of the heart are influenced by thyroid hormones. Subclinical hypothyroidism, or SH, is linked to an increased risk of coronary heart disease (CHD), particularly in those under the age of 65.[7]. The molecular mechanism of thyroid hormone action on the heart are explained by different cardiac function .

These tissues have thyroid hormone receptors, therefore even minute variations in thyroid hormone can have an impact on blood T3.[10,11,12,13,14,15,16]

Mechanism of Thyroid Hormone Action on Heart

By influencing a few molecular pathways in the heart, TH modifies cardiac characteristics. One possible mechanism of action is by direct transcriptional impact on both specific and nonspecific cardiac genes (genomic influence); an other mechanism involves nongenomic action on the plasma membrane, mitochondria, and sarcoplasmic reticulum. Because T3 and T4 are lipophilic, they can readily diffuse through the cytoplasmic membrane of cardiomy. [17,18,19,20] Lipophilic T3 penetrates the nucleus and attaches itself to inactive thyroid hormone receptors (THRs), turning them into activated forms that either heterodimerise or homodimerize with the 9-cis retinoic acid receptor. The resulting complex then binds to the enhancer region of target genes and recognises one of several DNA consensus sequences as well as the thyroid response elements (TRE). Transcription starts when a protein complex binds to the response elements and activates the target gene's promoter. Many cardiac genes, including myosin heavy chain α (MHC-α), SERCA, Na-K-ATPase, β-adrenergic receptor, cardiac troponin I, and atrial natriuretic peptide, have been identified as candidates for transcriptional activation by thyroid hormone. On the other side, some genes, such as myosin heavy chain β (MHC-β), have suppressed transcription . [21,22,23,24]

Heart Failure and the Role of Thyroid Hormone

Heart loses some blood-pumping ability with age. Heart failure (HF) causes from the added stress of health conditions, medical disorders etc. Although HF can be caused by a single risk factor, the risk is significantly increased when many risk factors are present. HF is a phenomenon that arises from many illnesses that injure the heart; it is not a sickness in and of itself. Individuals with many medical conditions are at an increased risk of getting heart failure. These ailments include: (i) coronary artery disease (myocardial infarction, ventricular remodelling, and arthrosclerosis); (ii) heart muscle disease (hypertrophic cardiomyopathy, dilated cardiomyopathy, inflammation, or myocarditis); (iii) atypical heart valves; (iv) congenital heart disease ; and (v) hypertension. [25,26]

Coronary Artery Disease

The heart muscle beats continuously, requires a steady flow of nutrients and oxygen, which the blood provides via the coronary

arteries for proper function. The arterial disease known as coronary artery disease is brought on by a buildup of arethromatous plaque in the arteries that feed blood to the heart. Numerous known risk factors for coronary heart disease include high blood pressure, high cholesterol, diabetes, positive family history, smoking, obesity, and inactivity. Nevertheless, these variables only partially account for cardiovascular disease.[27,28]

Atherosclerosis

The complicated process of atherosclerosis involves the growth of cellular components in the arterial wall as well as the deposition of plasma lipoproteins. This long-term inflammatory disease progresses in phases, starting with fatty streak lesions that are primarily made up of foam cells that are macrophages derived from lipid-engorged monocytes. Eventually, these lesions develop into complex plaques that have a fibrous cap covering a core of necrotic and lipid-filled cell debris. These plaques serve as a barrier to blood flow through the arteries and have the potential to cause clinical events, especially in situations when thrombus development and plaque rupture are encouraged.[29,30] Although they are not mirror images, hyperthyroidism and hypothyroidism represent opposing clinical states. Increased oxidative metabolism and significantly lower plasma levels of lipids and lipoproteins are hallmarks of hyperthyroidism. Polysaturated fatty acid content, or arachidonic acid content, is elevated in hyperthyroidism and has been linked to an increase in LPx. Conversely, owing of the metabolic repression brought on by lower thyroid hormone, hypothyroidism is characterised by diminished oxidative metabolism and noticeably elevated levels of lipid and lipoprotein plasma. Furthermore, hypothyroid patients show elevated LPx (defined as a much bigger LDL content in the lipid peroxides and a higher oxidation rate) in comparison to individuals with normal cholesterol levels. The absence of TH causes β-carotene conversion to Vitamin E to be blocked, which explains the marked decrease in Vitamin E content and increase in β-carotene levels compared to normal patients. The higher than normal LDL oxidation in hypothyroid patients can be explained by this potential prooxidant activity caused by elevated β-carotene LDL content and ineffective antioxidant protection. Patients with hypothyroidism also experience hypercholestemia, which is brought on by a decrease in both receptor activity and the fractional clearance of LDL by a smaller number of LDL receptors.[31]

Myocardial Infarction

One of the main conditions linked to coronary artery disease is myocardial infarction. An unstable mixture of lipids and white blood cells (particularly macrophages) in the artery wall, known as an atherosclerotic plaque, ruptures and blocks a coronary artery, cutting off blood flow to a portion of the heart. This condition is known as MI. If the resultant ischaemia and oxygen deprivation are not addressed in a timely manner, the myocardium may suffer harm or even die (infarction). [32]

Cellular Effects of Thyroid Hormone on the Cardiovascular System

Thyroid hormone may affect cardiac myocytes in both genetic and nongenomic ways. The transcriptional activation or repression of particular target genes that encode both structural and functional proteins mediates the genomic effects of thyroid hormone. Triiodothyronine (T3), the physiologically active thyroid hormone, enters the cardiomyocyte through certain transport proteins found in the cell membrane to initiate this process. Thus yet, there is no convincing proof that cardiomyocytes convert thyroxine (T4) to T3 in a way that is significant to biology.

Once inside the cardiomyocyte, T3 travels to the nucleus where it binds with either nuclear receptor α1 (a transcriptional activator) or α2 (a transcriptional repressor). The thyroid hormone-receptor complex can bind (nuclear receptor α-1) or release (nuclear receptor α-2) specific DNA sequences known as thyroid-responsive elements when T3 occupies these receptors along with recruited cofactors. These elements then act as cis- or trans-regulators to alter the rate of transcription of particular target genes.[33,34,35]

Thyroid Function in Cardiovascular Disorders

There is a reciprocal interaction between the cardiovascular system and thyroid function. Thyroid hormone metabolism may be affected by both acute and chronic cardiovascular diseases, according to a body of research. Serum thyroid hormone concentrations fall and reverse-T3 levels rise in individuals with chronic heart failure; the amount of these changes reflects the degree of functional impairment determined by the New York Heart Association classification. Circulating T3 levels in individuals following coronary aortic bypass or cardiopulmonary bypass surgery decrease dramatically in the aftermath.[36,37]

Numerous lines of evidence imply that patients' abnormal thyroid status may affect the expression of genes related to the heart and worsen heart function.[38]

Subclinical Hypothyroidism and Lipids

Elevated levels of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and apolipoprotein B (ApoB) have been linked to clinical hypothyroidism. These all factors increase the risk of coronary artery disease significantly . The 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) enzyme's activity and rate of degradation are regulated by thyroid hormone through the production of the SREBP-2 gene, a transcription factor that positively affects the function of the LDL receptor. Thus, increasing the expression of LDL receptors in the liver and peripheral tissues, as well as upregulating the activity of lipoprotein metabolism and reverse cholesterol transport-related enzymes such as hepatic lipase, lipoprotein lipase, and cholesterol ester transport protein (CETP) and lecithin-cholesterol acyltransferase LCAT , are the primary ways that thyroid hormone influences lipids. Nevertheless, the effectiveness of thyroid function and/or the severity of thyroid malfunction determine these effects. Triglyceride (TG) metabolism appears to be disrupted primarily by thyroid hormone influence on LPL, whereas changes in HL activity tend to modify cholesterol metabolism in thyroid dysfunction.[39,40]

As a result, after adjusting for age and body mass index (BMI), patients with recently diagnosed SCH showed a substantial increase in TGs and LDL-C and low HDL-cholesterol compared with the control group.The TSH-positive women showed a noteworthy elevation in small dense LDL particles (LDL particles) that are linked to a higher atherogenic score. However, in addition to the correlation between SCH and hyperlipidaemia, there is evidence of a relationship between lipids and free thyroxine (FT4) levels within the normal reference range. Furthermore, low normal FT4 levels were significantly linked to increased insulin resistance, indicating a higher risk of cardiovascular disease in individuals with low normal thyroid function.[41]

Aims And Objective

Primary Objective: To evaluate Clinical cardiovascular parameters and Electrocardiographic (ECG changes) in altered Thyroid status.

Secondary Objective: To determine association between cardiovascular parameters with hormone levels (Thyroid stimulating hormone-TSH, Free Thyroxin- FT4).

METHODOLOGY & PARTICIPANT

It is a descriptive type of observational study which is cross sectional in design conducted in the Department of Physiology, from among patients of altered thyroid function, attending the General Medicine OPD of Calcutta National Medical College & Hospital, Kolkata over a period of 1 year. Every patient with altered thyroid function, a 12-lead ECG study had done in the Department of Physiology, Calcutta National Medical College & Hospital, and other investigations like Lipid Profile, Fasting Blood Sugar, Thyroid Profile etc. done in the Dept. of Biochemistry. Calcutta National Medical College & Hospital, Kolkata, West Bengal, India.

Patient of any sex 18 to 60 years with altered thyroid status, attending OPD(General Medicine) of CNMC&H were the participant. We had chosen every 3rd patient of each OPD by systemic random sampling.

The study conducted over a period of one year. Patient of any sex age group 18 to 60years attending Medicine OPD enlisted as case for the study after taking their consent a) Question asked on the basis of pretested questionnaires, b) General survey and relevant clinical examination to be done, c) Blood sample collected for evaluating relevant biochemical parameters and haematological parameters. d) ECG done in all patients with altered thyroid status in the dept. of Physiology, CNMC&H.

It was a hospital based study with a sample size of 120 (n=120). All

continuous variables was expressed as mean (standard deviation). Collected data was presented in Microsoft office excel 2007. Data analysis was done by obtaining data collected and sorting them and analysis using SPSS version 25.0.

Inclusion criteria:

Patients who are voluntarily agree to participate in the study and fulfil following criteria was included in the study.

1. Newly diagnosed patient with deranged thyroid profile either hyper or hypo.
2. Detected patient either not on treatment or Patient on treatment for less than 4 months.
3. Age group specified above (18 to 60years).

Exclusion Criteria:

1. Patient with known cardiac disease.
2. Patients with COPD, Severe anaemia, Diabetes Mellitus or any other Endocrine disorder.
3. Severe and terminally ill patient.
4. Patients who are on drugs like beta blockers, OCP, Steroid, Amiodarone etc. which affect electrophysiology of the heart.
5. Patients who have undergone thyroid surgery.
6. Patients who have renal dysfunction.

Subjects were instructed to report in the morning hours(8-9 am) :

- 10-12 hours fasting
- 8 hours sound sleep
- No vigorous or exhaustive activity in previous 24 hours.
- The identity of patients were not revealed.

Ethical Clearance:

Ethical clearance was obtained from Institutional Ethics Committee.

Funding Of The Study:

There was no financial burden for the patients.

Conflict Of Interest:

There was no conflict of interest with regard to conducting the study.

Observation , Results & Statistical Analysis:

All together 120 subjects participated in the study. There were 93 females and 27 males(fig:1). Females were mostly 31-40years of age group. Males were mostly between the age group of 51-60years. The distribution of subjects by age is shown in (fig:2). On examination it was found that 48 patients were suffering from hypothyroid and were suffering from hyperthyroidism. 62 patients i.e. 50.67% of total subjects had become euthyroid due to ongoing treatment (fig:3).

All continuous variables was expressed as mean (standard deviation). Collected data was presented in Microsoft office excel 2007. Data analysis was done by obtaining data collected and sorting them and analysis using SPSS version 25.0.

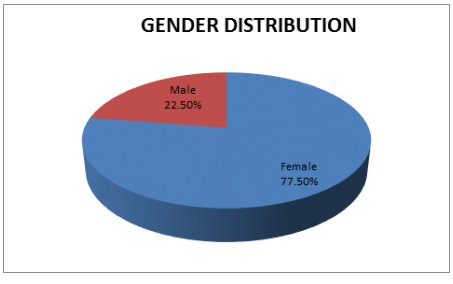

Fig:1

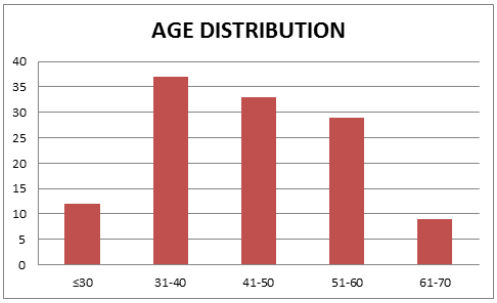

Fig:2

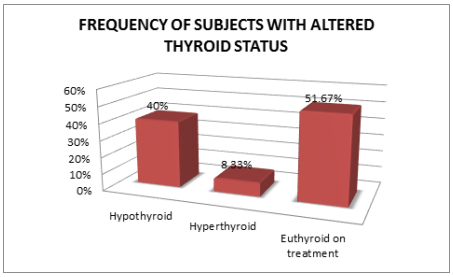

Fig:3

Table: 1. Descriptive Data of Subjects (n=120)

Parameters	Mean ± Standard Deviation(SD)
Weight in Kg	58.07 ± 9.169
Height in meters	1.5307 ±.06236
BMI(wt. in Kg/meter^2)	24.81143 ± 3.86053

Table: 2. Variation of Pulse Rate (Beats/ min), n= 120

	Number (n)	Mean ± SD
PulseRate	120	80.8500 ±11.3283

Table 3: Distribution of FT4 &TSH, n=120

	Number (n)	Mean ± SD
FT4 (ng/dl)	120	1.0050 ±.2745
TSH (mIU/L)	120	7.4814 ±14.2123

Table: 4, Distribution of Lipid profile (mg/dL), n=120

	Number (n)	Mean ± SD
T CHOL	120	155.0000 ± 42.5384
TG	120	118.8917 ±52.8661
HDL	120	38.9750 ±8.3530
LDL	120	110.1758 ±24.4372
VLDL	120	28.6017 ±5.4586

Table: 5. Distribution of ECG Parameters, n= 120

	Number (n)	Mean ± SD
ECG P-Wave (duration in ms)	120	93.3833 ±9.2457
QRS COMPLEX (ms)	120	82.3500 ±9.4154
QT INT(ms)	120	371.3333 ±61.4794
Heart Rate(HR) (beats per min)	120	81.6083 ±11.7239

Table: 6. Correlation: TCHOL(mg/dL), STG(mg/dL), HDL(mg/dL), TSH(mlU/mL), FT4(ng/dl) Cell Contents Pearson correlation P-Value

	TCHOL(mg/dL)	STG(mg/dL)	HDL(mg/dL)	FT4(ng/dl)
STG(mg/dL)	0.522			
	0.000			
HDL(mg/dL)	0.582	0.255		
	0.000	0.005		
FT4(ng/dl)	0.098	0.087	0.255	
	0.285	0.343	0.005	
TSH(mlU/mL)	0.154	0.036	0.133	-0.016
	0.093	0.695	0.147	0.861

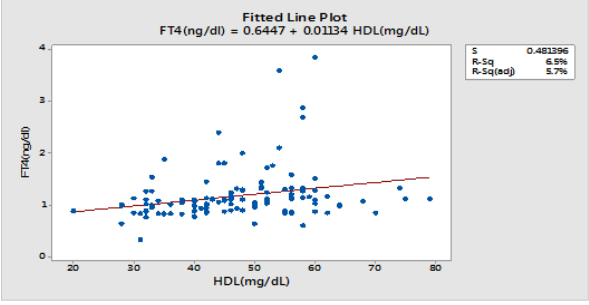

Fig:4

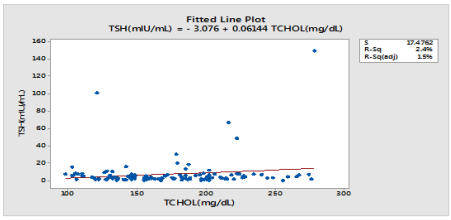

Fig:5

Interpretation:

HDL: Since p-value of the coefficients of HDL is significant at 10% or 5% level in the regression of HDL & FT4, and correlation between HDL & FT4 also significant at 10% or 5% level, it could be concluded that HDL has a good impact in variation of Ft4.

TCHOL: Since p-value of the coefficients of TCHOL is insignificant at 10% or 5% level in the regression of TCHOL & TSH, and correlation between TCHOL & TSH also insignificant at 10% or 5% level, it could be concluded that TCHOL has no impact in variation of TSH.

Table: 7.Correlation: LDL(mg/dL), VLDL(mg/dL), ECG(Duration of PWAVE in ms),FT4(ng/dl),TSH(mlU/mL)

Correlations Cell Contents Pearson correlation P-Value

	LDL(mg/dL)	VLDL(mg/dL)	ECG(PWAVE duration in ms)	FT4(ng/dl)
VLDL(mg/dL)	0.018			
	0.841			
ECG(PWAVE)	0.003	0.023		
	0.974	0.802		
FT4(ng/dl)	-0.111	0.088	0.032	
	0.228	0.338	0.730	
TSH(mlU/mL)	0.035	0.419	-0.006	-0.016
	0.703	0.000	0.951	0.861

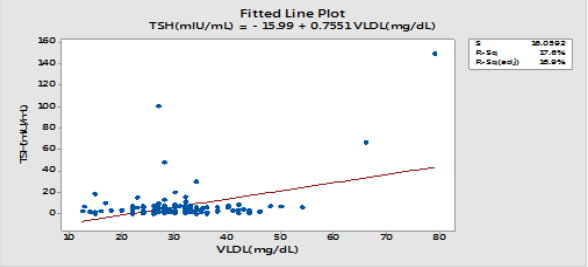

Fig:6

Interpretation:

VLDL: Since p-value of the coefficients of VLDL is significant at 10% or 5% level in the regression of VLDL & TSH, and correlation between VLDL & TSH also significant at 10% or 5% level, it could be concluded that VLDL has a good impact in variation of TSH.

Table: 8. Correlation: QRS COMPLEX(ms), QT_INT(ms), HR/min, FT4(ng/dl), TSH(mlU/mL)

Correlations Cell Contents Pearson correlation P-Value

	QRSCOMPL(ms)	QT_INT	HR/min	FT4(ng/dl)
QT_INT	0.212			
	0.020			
HR/min	-0.099	-0.133		
	0.281	0.149		
FT4(ng/dl)	-0.136	0.091	-0.031	
	0.138	0.324	0.740	
TSH(mlU/mL)	0.041	0.068	0.294	-0.016
	0.658	0.462	0.001	0.861

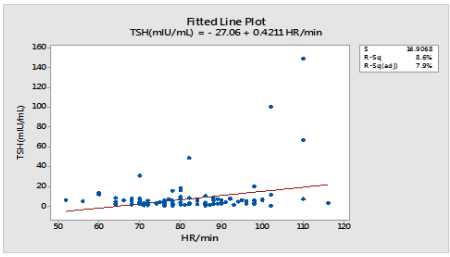

Fig:7

Interpretation:

HR/min: Since p-value of the coefficients of HR/min is significant at 10% or 5% level in the regression of HR/min & TSH, and correlation between HR/min & TSH also significant at 10% or 5% level, it could be concluded that HR/min has a good impact in variation of TSH.

DISCUSSION:

The present cross sectional study was conducted to categorise the patients into Hypothyroidism and Hyperthyroidism and also to evaluate the cardiovascular parameters with thyroid dysfunction state. In our study the total 120 subjects were included. Based on FT4 and TSH results the subjects were classified into hypothyroidism (40%), hyperthyroidism (8.33%) and euthyroid on treatment (not more than 4 month) (51.67%). This was because most patients included in the study had been under treatment for last 3-4 months.

In our study, incidence of hypothyroidism was higher than hyperthyroidism.This is similar to the other study. There is a significant gender disparity among the participants, with females constituting 77.5% and males 22.5%. So the study highlighted hypothyroidism was more common than hyperthyroidism and females were more commonly affected with thyroid dysfunction than males. This is similar to the another studies.[42,43]

In this study we found correlation between FT4 (free thyroxin) and HDL (high density Lipoprotein) [figure] showing FT4 in Y-axis and HDL in X-axis. It was found that there was weak positive correlation between value of FT4 and HDL. This is similar to the findings obtained by other studies.[44]

In the present study there were a significant positive correlation between VLDL and TSH levels. This is similar to the other previous studies. [45,46]

In our study there were weak positive correlation exist between Heart rate (HR; beats per min) and TSH levels . There were no definite correlation between Heart rate and TSH level found in other studies.[47]

CONCLUSION:

- This study highlights the relationship between cardiovascular health and thyroid function.
- Though certain correlations have been found, the study emphasises the intricacy of these associations and the necessity of more investigation to completely comprehend the causes and consequences of thyroid hormone fluctuations on cardiovascular consequences.
- The results imply that vigilant monitoring of thyroid hormone levels and related cardiovascular parameters may be essential for controlling cardiovascular risk.

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