

Cardiovascular Changes in Hypothyroidism, a Tertiary Centre Study.

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ABSTRACT

Background: Among the commonly existing endocrine disorders found in India, Thyroid disease contributes fairly to the clinical scenario affecting around 9-15 % of the female population as well as the male population to a milder degree. Among the principal targets of the thyroid hormones is the cardiovascular system. The effects noted on the CVS are changes in the cardiac contractility, myocardial oxygen consumption, alterations in the systemic vascular resistance (SVR), decreased cardiac contractility leading to decreased cardiac output, increased rate of atherosclerosis and hence greater potential of CAD. Hypothyroidism also causes QT interval prolongation. Only few studies have been done in our country to assess these cardiovascular parameters in hypothyroid patients. Principally the thyroid hormone-T3, affects the heart with variations in cardiac gene expression principally mediated by T3. On 2D-ECHO mild Left Ventricular Diastolic Dysfunction (LVDD), mild concentric Left Ventricular Hypertrophy (LVH) with or without Left Ventricular Diastolic Dysfunction, mild mitral insufficiency or minimal pericardial effusion can be found. Since there does exist some evidence of a causal relationship, it is advisable to perform a basic cardiac work-up which should also include an echocardiogram to assess systolic and diastolic dysfunction as part of initial evaluation of the hypothyroid patients. Also to make note is the fact that persistent subclinical thyroid dysfunction may notably increase the cardiovascular disease risk ratio.

Keywords: Hypothyroidism, thyroid hormone, Cardiovascular system, Contractility, Atherosclerosis, Left ventricular diastolic dysfunction.

INTRODUCTION

Among the commonly existing endocrine disorders found in India, Thyroid disease contributes fairly to the clinical scenario. The burden is calculated to be enormous among women, affecting around 9-15 % of the female population as well as the male population to a milder degree.^[1] Thyroid hormones form an integral part of numerous systems of the body, with significant effects noted on the cardiovascular system.^[2]

The effects noted are changes in the cardiac contractility, myocardial oxygen consumption, cardiac output, blood pressure, and alterations in the systemic vascular resistance (SVR).^[2,3] In rhythm disturbances, hypothyroidism predisposes to ventricular dysrhythmias, while hyperthyroidism is notorious to cause atrial fibrillation.^[4] Among other effects of hypothyroidism on the CVS are increased SVR, decreased cardiac contractility which decreases cardiac output increases rate of atherosclerosis and hence greater potential of

CAD.^[4,5] Also hypothyroidism may cause prolongation of QT interval. Chances for having pericardial effusion rich in proteins is more.^[6] However, if the underlying thyroid disorder is recognized early and treated adequately, the CVS changes can be reversed in almost all cases. In almost 96% of the hypothyroid patients there is simultaneous presence of other atherosclerotic cardiovascular disease risk factors as well, leading additionally to an apparent increase in the risk of stroke.^[7,8] The various alterations in the cardiovascular system as mentioned above are widely known to be caused by decreased action of the thyroid hormone important organs such the heart, liver, and peripheral vasculature and therefore these changes can be adequately reversed with timely and adequate replacement of the thyroid hormone.^[9] As illustrated above, hypothyroidism has varied effects on the cardiovascular system which has been and continues to be studied extensively in the various clinical labyrinths across the world. However, only few studies have been done in our country to assess these cardiovascular parameters in hypothyroid patients.

Aim Of The Study

The study aims to highlight the covert effects of hypothyroidism on the cardiovascular system

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Objective

To study the occurrence of cardiovascular derangement in the Hypothyroid patients and establish a correlation, if any, between the various serum parameters being studied and use the information for better clinical approach.

MATERIALS AND METHODS**Study Setting**

The study will be conducted on 50 patients either attending or being admitted in the department of General Medicine, TMMC & RC, TMU , MORADABAD, U.P., INDIA, who meet the inclusion criteria during the study Period of one year.

Study Design

Type of the study: Observational Study.

Sample size and sampling methods

50 consecutive patients of Hypothyroidism were recruited.

Selection of Subjects

To be eligible for the study the patient will have to full fill all the following

Inclusion criteria

- All patients reporting to Medicine OPD at TMMCRC, Moradabad, with Hypothyroidism.

Exclusion criteria

- Patients < 18yrs
- Those who do not provide consent.
- Patients on treatment for cardiac ailments.
- Patients with known Hepatic and Renal dysfunction.
- Known diabetics.
- Pregnant women.

Outcome of the study was measured using appropriate statistical methods & was represented in the form of appropriate graphical forms at the end of study.

Study Plan

The data used for the study was recorded from the history, examination and investigations of the patients including the previous medical records.

Investigations

- CBC
- Serum thyroid profile
- Serum lipid profile
- Fasting Blood Glucose
- Post –Prandial Blood Glucose
- HbA1c
- SGOT, SGPT, Serum Bilirubin
- Serum Urea, Serum Creatinine, Urine protein
- ECG changes
- Chest radiography
- ECHO to study structural /functional changes in the heart

RESULTS

Table 1: Showing the distribution of the study population according to age and gender

		Frequency	Percent
Age groups	20-30 years	15	30.0%
	31-40 years	18	36.0%
	41-50 years	9	18.0%
	51-70 years	5	10.0%
	Above 70 years	3	6.0%
Sex	Female	38	76.0%
	Male	12	24.0%

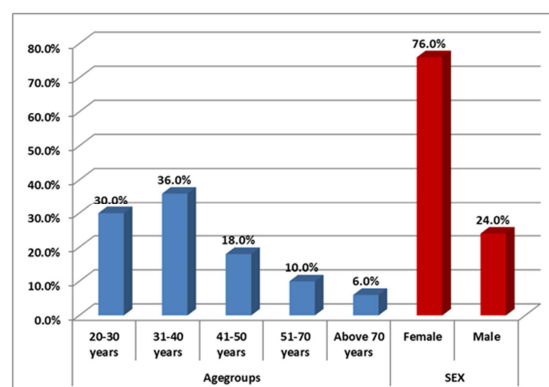


Figure 1: showing the distribution of the study population according to age and gender

Table 2: Showing mean HB (g/dL), TLC (cells/cmm), Fasting Blood Sugar (mg/dL), Post-prandial Blood Sugar (mg/dL) and HbA1c (%) among study population

	Minimum	Maximum	Mean	Std. Deviation
HB (g/dL)	6.00	16.50	10.87	2.87
TLC (cells/cmm)	3865.00	13220.00	8019.52	3062.23
Fasting Blood Sugar (mg/dL)	74.00	105.00	87.44	8.32
Post-prandial Blood Sugar (mg/dL)	97.00	151.00	114.86	12.84
HbA1c (%)	4.30	5.90	5.31	0.47

Table 3: Showing mean Total Bilirubin (mg/dL), SGPT (IU/L), Serum creatinine (mg/dL) and BMI (kg/m2) among study population

	Minimum	Maximum	Mean	Std. Deviation
Total Bilirubin (mg/dL)	0.40	0.90	0.52	0.11
SGPT (IU/L)	10.00	64.00	30.68	11.98
Serum creatinine (mg/dL)	0.53	1.20	0.80	0.19
BMI (kg/m2)	20.65	30.38	25.76	3.24

Table 4: Showing mean TSH (µIU/mL), T3 (ng/mL) and T4 (µg /dL) among study population

	Minimum	Maximum	Mean	Std. Deviation
TSH (µIU/mL)	6.48	360.00	23.58	50.17
T3 (ng/mL)	0.13	1.94	0.98	0.41
T4 (µg /dL)	3.31	13.28	6.52	1.88

Table 5: Showing mean Total Cholesterol (mg/dL), TG (mg/dL), LDL (mg/dL), HDL (mg/dL) and VLDL (mg/dL) among study population

	Minimum	Maximum	Mean	Std. Deviation
Total Cholesterol (mg/dL)	126.00	246.00	170.40	42.51
TG (mg/dL)	50.00	377.00	125.60	87.16
LDL (mg/dL)	67.00	168.00	114.78	25.85
HDL (mg/dL)	22.00	52.00	31.91	7.34
VLDL (mg/dL)	8.00	75.40	23.59	17.11

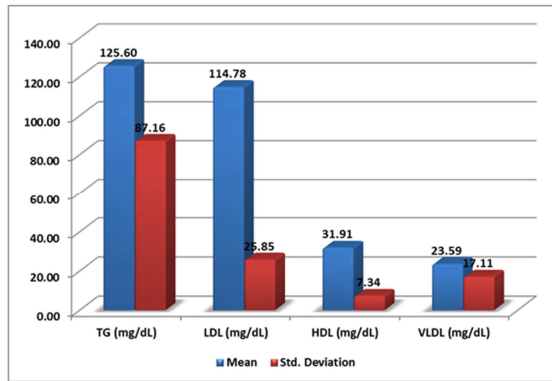


Figure 2: showing mean Total Cholesterol (mg/dL), TG (mg/dL), LDL (mg/dL), HDL (mg/dL) and VLDL (mg/dL) among study population

Table 6: showing the distribution of Normal Sinus Rhythm (NSR), NSR with Bradycardia and NSR with low voltage complexes among study population

	ECG	
	Frequency	Percent
Normal Sinus Rhythm (NSR)	31	62.0%
NSR with Bradycardia	3	6.0%
NSR with low voltage complexes	16	32.0%
Total	50	100.0%

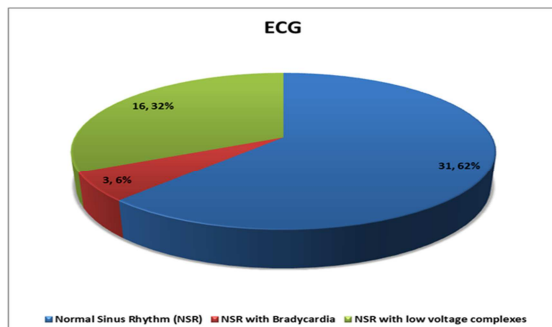


Figure 3: showing the distribution of Normal Sinus Rhythm (NSR), NSR with Bradycardia and NSR with low voltage complexes among study population

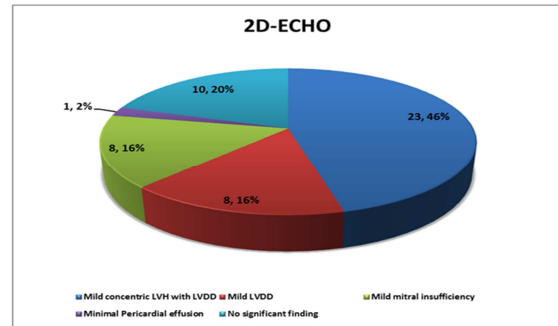


Figure 4: showing the distribution of 2D-ECHO findings among study population

DISCUSSION

Causes of Hypothyroidism^[12]

Primary	Autoimmune hypothyroidism: Hashimoto' thyroiditis, atrophic thyroiditis Iatrogenic: 131I treatment, sub-total or total thyroidectomy, external irradiation of neck for lymphoma or cancer Drugs: Iodine excess and amiodarone), lithium, anti-thyroid drugs, p-aminosalicylic acid, interferon-α and other cytokines, aminoglutethimide, sunitinib Congenital hypothyroidism: Absent or ectopic thyroid gland, TSH-R mutation iodine deficiency, Infiltrative disorders: Amyloidosis, sarcoidosis, hemochromatosis, scleroderma, cystinosis, Riedel's thyroiditis
Transient	Silent thyroiditis, including postpartum thyroiditis Sub-acute thyroiditis Withdrawal of thyroxine treatment in individuals with an intact thyroid After 131I treatment or subtotal thyroidectomy for Graves' disease
Secondary	Hypopituitarism: Tumours, pituitary surgery or irradiation, infiltrative disorders, genetic forms of combined pituitary hormone deficiencies Isolated TSH deficiency or inactivity Bexarotene treatment Hypothalamic disease: Tumours, trauma, infiltrative disorders, idiopathic

The signs and symptoms in decreasing order of frequency are as follows^[12]

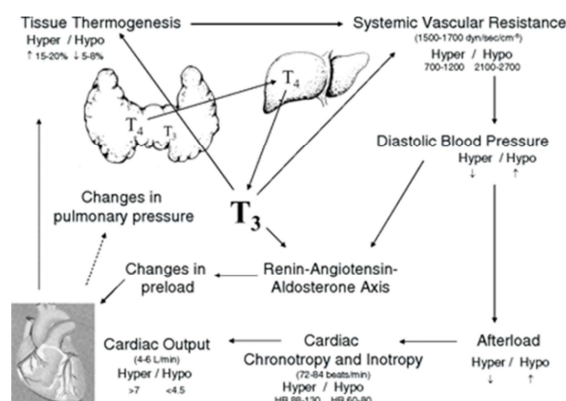
Symptoms	Signs
Tiredness, weakness	Dry coarse skin; cool peripheral extremities
Dry skin	Puffy face, hands and feet (Myxedema)
Feeling cold	Diffuse alopecia
Hair loss	Bradycardia
Constipation	Peripheral edema
Weight gain with poor appetite	Delayed tendon reflex relaxation
Dyspnea	Carpel tunnel syndrome
Hoarse voice	Serous cavity effusions
Menorrhagia Impaired hearing	

Hypothyroidism, refers to the less production of the thyroid hormone.^[10] Among its common presenting symptoms are poor ability to tolerate cold, tiredness, constipation, depression, and undue weight gain. Goitre, another common presentation of this disease group, is a condition in which the subject develops a globular swelling over the anterior aspect of the neck, which may also sometimes grow down behind

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the sternum.^[10] Hypothyroidism in pregnancy, if not treated adequately, can lead to a condition known as Cretinism, which is marked by mental retardation and poor physical growth of the baby.^[11]

Thyroid hormones affect the cardiovascular system in a number of ways. To begin with, hypothyroidism brings about a reduction in the resting heart rate, as opposed to tachycardia in a case of hyperthyroidism. Hypothyroidism further results in a reduced circulating volume as it causes a diminished cardiac output due to reduced ventricular contractility. Action of the thyroid hormones results in the activation of renin-angiotensin-aldosterone system (RAAS) activation, brought about by decreased resistance in the peripheral arterioles due their action on the vascular smooth muscles. RAAS activation further leads to increased renal sodium absorption. T3 also leads to an increased red cell mass, by stimulating erythropoietin synthesis. Thyroid hormones are also known to increase the sensitivity of the body tissues to the sympathetic system. Hence, hypothyroidism usually presents with a reduction in the cardiac output by almost 30% to 50%. However, it is interesting to point out here that the normal cardiovascular hemodynamics can be restored with the help of the treatment of hypothyroidism.^[13]



As can be seen from the diagram above, thyroid hormone, principally T3, affects the heart through a number of ways. Among other targets, the cardiac gene expression is significantly affected by thyroid hormone. As a result, majority of the cardiac manifestations of thyroid dysfunction are seen to be associated with variations in cardiac gene expression principally mediated by T3.^[14-17] Thyroid hormone has influence on genes, related to heart such as the sarcoplasmic reticulum Ca^{2+} -ATPase and its inhibitor-phospholamban, responsible for calcium uptake by sarcoplasmic reticulum during the diastole of the heart.^[18,19] Thyroid hormone's effect on the period of action potential is via genetic and non-genetic actions.^[20]

The inability of the smooth muscle cells of blood vessels to relax leads to increased vascular resistance, resulting in diastolic hypertension in almost 30% of the hypothyroid patients.^[21] This is

seen to be reversible in most patients with the initiation of the thyroid replacement therapy.^[22]

The development of hypercholesterolemia in a hypothyroid subject occurs via a number of mechanisms, including a decreased fractional clearance of LDL because of reduced expression of the LDL receptors in the liver. This reduced number of receptors is further complemented by a diminished receptor-activity.^[23-25] The metabolism of cholesterol into bile, mediated by an enzyme-cholesterol 7 α -hydroxylase, is negatively regulated by T3. This mechanism may be one of the principal reasons of increased serum cholesterol levels seen in hypothyroidism.^[25,26]

Subclinical hypothyroidism is a condition typically characterised by very low or decreased levels of TSH and normal levels of both T3 and T4.^[27] This subgroup of patients often remains asymptomatic. However, studies show that these patients are rather predisposed to the various cardiovascular manifestations.^[28]

In the absence of ample clinical evidence and well defined guidelines, there exists controversy around the treatment of subclinical hypothyroidism with thyroid replacement. The purpose of this study was to assess the various cardiovascular effects of hypothyroidism in the patients presenting to the Medicine department at TMMRC, Moradabad, U.P., India.

It becomes interesting to note here that the most recent ACC/AHA guidelines for the diagnosis and management of heart failure recommends the measurement of thyroid function in all patients with newly-diagnosed heart failure, as it represents a potentially reversible cause of cardiovascular disease. However, no specific recommendations have yet been made with regard to the management of subclinical hypothyroidism in heart failure patients.^[29]

Limitations Of The Study

Firstly, our study had a cross-sectional design, the data was collected at a single point of time, make it difficult, to be sure whether which happened first, the disturbance of thyroid hormones or the ECG changes. Second thing to consider would be the thyroid hormones that are mainly protein-bound and having little physiological effect. Therefore, the measurement of total T4 levels may not represent the actual level of free (active) T4. And lastly, the measuring of thyroid hormones and ECG was done only once. Repeated measurements may be needed to reduce measurement error and hence depict a better characterized association between thyroid-hormone status and various ECG changes in the future studies.

CONCLUSION

From the present study we can conclude that the cardiovascular features of thyroid disease, both signs as well as the presenting symptoms, are some of the

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most significant and clinically relevant findings that coexist with hypothyroidism, and that high levels of free T3 are associated with QTc prolongation. During clinical practice it should be borne in mind that sometimes signs and symptoms pertaining to the cardiovascular system may be the only manifestation of covert thyroid dysfunction. Also to make note is the fact that persistent subclinical thyroid dysfunction may notably increase the cardiovascular disease risk ratio. Since there does exist some evidence of a causal relationship, it is advisable to perform a basic cardiac work-up which should also include an echocardiogram to assess systolic and diastolic dysfunction as part of initial evaluation of the hypothyroid patients which can ultimately help to determine appropriateness of initiation of thyroxine replacement therapy.

Summary

There were 24.0% male and 76.0% female subjects with 30.0%) subjects in 20-30 years age group, 36.0% subjects in 31-40 years age group, 18.0% subjects in 41-50 years age group, 10.0% subjects in 51-70 years age group and 6.0% subjects in above 70 years age group.

The mean HB (g/dL) level of the study population was 10.87 ± 2.87 and TLC (cells/cmm) count was 8019.52 ± 3062.23 .

The mean Fasting Blood Sugar (mg/dL) was 87.44 ± 8.32 , Post-prandial Blood Sugar (mg/dL) was 114.86 ± 12.84 and HbA1c (%) level was 5.31 ± 0.47 .

The mean Total Bilirubin (mg/dL) was 0.52 ± 0.11 , SGPT (IU/L) was 30.68 ± 11.98 , Serum creatinine (mg/dL) was 0.80 ± 0.19 and BMI (kg/m²) was 25.76 ± 3.24 .

The mean TSH (μ IU/mL) was 23.58 ± 50.17 , T3 (ng/mL) was 0.98 ± 0.41 and T4 (μ g /dL) was 6.52 ± 1.88 .

The mean Total Cholesterol (mg/dL) level was 170.40 ± 42.51 , TG (mg/dL) was 125.60 ± 87.16 , LDL (mg/dL) was 114.78 ± 25.85 , HDL (mg/dL) level was 31.91 ± 7.34 and VLDL (mg/dL) level was 23.59 ± 17.11 .

The mean QTc (milliseconds) was 432.20 ± 27.14 among the study population.

Normal Sinus Rhythm (NSR) was reported among 62.0% subjects, NSR with Bradycardia among 6.0% subjects and NSR with low voltage complexes among 32.0% subjects on ECG.

On 2D-ECHO, Mild Left Ventricular Diastolic Dysfunction was found among 16.0% subjects, Mild concentric Left Ventricular Hypertrophy with Left Ventricular Diastolic Dysfunction was found among 16.0% subjects, Mild mitral insufficiency was found among 2.0% subject and Minimal Pericardial effusion was found among 20.0% subjects.

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