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### Key Words

Hypothyroidism, ECG changes, ECHO

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**Received:** 20 September 2021

**Accepted:** 22 November 2021

**Published:** 14 December 2021

**Citation:** M. Murali Krishna and Shaik Hussain Basha, 2021. A Study of Cardiovascular Manifestations in Newly Diagnosed Hypothyroidism Patients. Res. J. Med. Sci., 15: 126-130, doi: 10.36478/makrjms.2021.126.130

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## A Study of Cardiovascular Manifestations in Newly Diagnosed Hypothyroidism Patients

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### ABSTRACT

Cardiac abnormalities associated with hypothyroidism attracted a great deal of investigational effort. There are only a few studies done in our country to assess CVS parameters in hypothyroid patients. Hypothyroidism causes reversible cardiac dysfunction. This study is aimed at studying the cardiac manifestations of hypothyroidism by ECG and ECHO. Thus, reassessing the need for treatment even in the milder forms of the disease. Data for this study were collected from 50 new patients of hypothyroidism. They were clinically evaluated and underwent relevant investigations, including thyroid profile estimation, cardiac evaluation using ECG and 2D ECHO. The majority of patients were between the age groups of 31-40, with the mean age being 36.26 years. There was an overall female preponderance over all age groups with a mean age of 36.26 years. The female population constituted about 76% of the total. The most common symptoms were weight gain, lethargy, dry skin and hoarseness of voice. On general examination, the most common findings were weight gain and dry skin found in around 76% and 64% of patients, respectively. Goiter was found in 10% of patients. On systemic examination, diminished heart sound is found in 28% of patients and cardiomegaly in 8%. CNS examination revealed delayed ankle jerk in 40%. Lipid analysis showed an increase of TC, LDL, VLDL, TGL and a decrease of HDL. Normal ECG is found in 30% of patients. Bradycardia is the most common finding seen in 20 patients counting for 40%. Low voltage complexes are seen in 34% of patients. ECHO findings. Echo findings are normal in 40% cases. Pericardial effusion is the next common finding seen in 14 cases accounting for 28%. Diastolic dysfunction is seen in 26% of the total, 18% of them being mild dysfunction. Moderate diastolic dysfunction in 4%, Severe diastolic dysfunction is seen in 2%. Among 50 new cases of hypothyroidism, pericardial effusion was found in 28% of patients. Diastolic dysfunction was seen in 26% of patients. Thus any unexplained pericardial effusion should be screened for hypothyroidism.

## INTRODUCTION

Thyroid hormones affect almost all nucleated cells and are essential for normal growth and energy metabolism. Thyroid dysfunction is common readily recognizable and easy to treat, but it can have significant adverse effects when undiagnosed or untreated. Despite an increased understanding of thyroid disease and the availability of reliable laboratory tests to assess thyroid hormones, cases of severe thyroid dysfunction still occur occasionally. Hypothyroidism and hyperthyroidism commonly arise from pathological processes within the thyroid gland (primary thyroid disease), although in rare cases, they arise from disorders of the hypothalamus or pituitary (central hypothyroidism) or from peripheral causes, such as struma ovarii, or functional thyroid cancer metastases<sup>[1]</sup>. In iodine-replete populations, thyroid dysfunction is most commonly due to thyroid autoimmunity. Both iodine deficiency and excess can result in hypothyroidism as well as hyperthyroidism<sup>[1]</sup>. Hypothyroidism is characterized by a broad clinical spectrum, ranging from an overt state of myxedema, end-organ effects and the multisystem failure to an asymptomatic or subclinical condition with normal levels of thyroxine and triiodothyronine and slightly elevated levels of serum thyrotropin<sup>[2]</sup>. The prevalence of hypothyroidism in the developed world is about 4-5%<sup>[3]</sup>. Subclinical hypothyroidism prevalence in the developed world is about 4-15%<sup>[3]</sup>. According to the National Family Health Survey 2015-16 India Factsheet, Households using iodized salt in the Urban area (96.5%), Rural area (91.4%)<sup>[4]</sup>. It has long been recognized that some of the most common and characteristic signs and symptoms of thyroid disease are those caused by the effects of thyroid hormone on the heart and cardiovascular system. Hyperthyroidism and hypothyroidism cause changes in cardiac contractility, myocardial oxygen intake, cardiac production, blood pressure and systemic vascular resistance (SVR)<sup>[5]</sup>. Though it is widely known that hyperthyroidism sometimes leads to atrial fibrillation, it is not so well recognized that hypothyroidism might predispose to rhythm disturbances. In almost all of these cases, cardiovascular changes are reversible when the underlying thyroid disorder is identified and treated<sup>[6]</sup>. Overt hypothyroidism affects 3% of the female population and is associated with increased SVR, decreased cardiac contractility and cardiac output and accelerated atherosclerosis and coronary artery disease<sup>[7]</sup>. Changes in blood pressure, changes in lipid metabolism, decreased cardiac contractility, and increased SVR associated with hypothyroidism are caused by reduced action of thyroid hormones on multiple organs, such as the heart and peripheral vasculature, liver and are potentially reversible with thyroid replacement hormone<sup>[8]</sup>. The present study was conducted to study the cardiac manifestations of

Hypothyroidism among newly diagnosed hypothyroid patients by ECG and ECHO who attended the Outpatient and Inpatients of Department of General Medicine, Fathima Institute of Medical Sciences, Kadapa during the study period. The study helps in reassessing the need for early recognition and more aggressive management of disease and also aid in preventing complications.

## MATERIALS AND METHODS

**Study Area:** Department of General Medicine, Fathima Institute of Medical Sciences, Kadapa, A.P.

**Study Population:** Patients attending to the medical outpatient department and wards during the period.

**Sample Size:** 50 patients.

### Inclusion Criteria:

- Hypothyroid patients.
- Newly diagnosed patients.
- Detected hypothyroid patients, not on treatment.

### Exclusion Criteria:

- Patients with known cardiac disease,
- Patients with COPD, severe anemia, diabetes mellitus or any other endocrinal disorder,
- Patients who are taking medications that alter the thyroid function like beta-blockers, lithium, OCP's, steroids and alcohol.

**Data Collection:** The present study was cross-sectional study conducted in Department of General Medicine, Fathima Institute of Medical Sciences, Kadapa, 50 new cases of hypothyroidism were selected for the study. After taking informed consent, a detailed history was obtained, followed by a thorough clinical examination to assess clinical severity and complications.

### Investigations were Carried Out:

- T3, T4, TSH.
- Haemoglobin, TC, DC, ESR.
- RBS.
- Urine routine-sugar.
- -albumin.
- -microscopy.
- Blood urea.
- Serum creatinine.
- Lipid profile.
- A standard 12 lead ECG and 2decho.

The data was analyzed using SPSS software version 16. Quantitative and Qualitative variables were expressed in terms of Descriptive statistics like (mean±standard deviation), frequencies and percentages. Each data variable was correlated with other variables where ever required using a non-parametric statistic, i.e., chi-square analysis with various outcomes that were

noted in the study. P-value <0.05 was considered statistically significant in this study.

## RESULTS AND DISCUSSIONS

In the present study, mean age of the study population was  $36.26 \pm 9.58$ . Among the study population, the majority, i.e., 44% belonged to 31-40 years age group, followed by 28% in 21-30 years age group, 20% in 41-50 years age group, 8% in 51-60 years age group. In the present study, the majority were female, i.e., 76% and males were 24%. In the study, the mean age among males was  $36.25 \pm 8.92$  and the mean age among females was  $36.26 \pm 9.90$ . Majority of the study population belonged to age groups of 31-40 years. In the present study, among the study population Weight gain(74%), Lethargy(64%), Hoarseness of voice(52%), Dry skin(64%), Constipation(50%), Breathlessness (30%), Cold intolerance(50%), Menstrual symptoms (40%), Depression(26%). In our study, the Body mass index was calculated. BMI of  $>25\text{kg/m}^2$  was observed among 76% of the said population. Out of these, 64% were overweight and 12% were obese. In our study, 64% had dry skin on examination, 26% had pallor, 20% with edema, 10% with goiter. 44% had a pulse rate  $<60/\text{min}$  and the mean pulse rate calculated to be  $66.6 \pm 11.73$ . Mean SBP  $127.8 \pm 16.22\text{mmHg}$ , Mean DBP was  $84.24 \pm 9.43\text{mmHg}$ .

**Table 1: Systemic Examination**

Systemic examination	Findings	Frequency	Percentage
Cardiovascular	Cardiomegaly	4	8%
	Diminished heart sounds	14	28%
	Normal	32	64%
	Delayed Ankle jerk	20	40%
CNS	Normal	30	60%

In our study, systemic examination findings were cardiomegaly (8%), Diminished heart sounds (28%), Delayed ankle jerk (40%).

**Table 2: Descriptive Statistics**

	Minimum	Maximum	Mean	SD
Hb	7.3	14.2	11.546	2.0
BUN	16	44	25.86	6.5
Creatinine	0.75	1.4	1.027	0.17
RBS	75	110	94.42	10.11
Total Cholesterol	162	300	188.92	19.79
HDL	25	50	35.28	6.49
LDL	70	170	113.78	22.78
VLDL	22	49	34.28	6.25
Triglycerides	176	230	204.32	12.82

**Table 3: Severity of Hypothyroidism**

Severity of Hypothyroidism	Levels of TSH in $\mu\text{I}$	Frequency	Percentage
Mild	10-20 $\mu\text{I}$	17	34%
Moderate	20-50 $\mu\text{I}$	22	44%
Severe	$>50 \mu\text{I}$	11	22%
Total		50	100%

In our study, the severity of Hypothyroidism was categorized into mild, moderate, severe, based on TSH levels. 44% had Moderate Hypothyroidism, 34% with mild, 22% with severe Hypothyroidism based on TSH levels.

**ECG Changes:** In our study, 40% had Bradycardia, 34% with Low voltage complex, 26% with ST-T changes, 10% with Right Bundle Branch Block, 6% with Left Bundle Branch Block.

**ECHO Changes:** In the present study, 30% had normal ECHO findings, 28% with pericardial effusion, 8% with systolic dysfunction, 18% with Mild Diastolic Dysfunction, 4% with moderate diastolic dysfunction, 2% with severe Diastolic Dysfunction.

### Severity of Hypothyroidism and Pericardial Effusion:

In the present study, among 14 cases with pericardial effusion on ECHO, 2 cases with mild hypothyroidism based on TSH levels, 5 cases with moderate hypothyroidism and 7 cases with severe hypothyroidism.

The cardiovascular signs and symptoms of thyroid disease are the most profound and clinically relevant findings that be associated with both hyperthyroidism and hypothyroidism. The importance of the early identification of the effects of thyroid disease on the heart also derives from the examination that restoration of normal thyroid function most often reverses the abnormal cardiovascular hemodynamics. In almost all of these cases, cardiovascular changes are quite reversible when the underlying thyroid disorder is recognized and treated. Thyroid disease is quite common. Current estimates indicate that it affects as many as 9-15% of the adult female population and a lesser percentage of adult males. This gender-specific prevalence almost definitely results from the underlying autoimmune mechanism for the most common forms of thyroid disease, which consist of both Graves' and Hashimoto's disease. However, with advancing age, particularly beyond the eighth decade of life, the incidence of disease in males rises to be equal to that of females. The study helps in reassessing the need for early recognition and more aggressive management of disease and also aid in preventing complications. In the present study, mean age of the study population was  $36.26 \pm 9.58$ . Among the study population, the majority, i.e., 44% belonged to 31-40 years age group, followed by 28% in 21-30 years age group, 20% in 41-50 years age group, 8% in 51-60 years age group. In the present study, the majority were female, i.e., 76% and males were 24%. In the present study, mean age among males was  $36.25 \pm 8.92$  and the mean age among females was  $36.26 \pm 9.90$ . The majority of age groups in the study population were 31-40 years. In the present study, among the study population Weight gain(74%), Lethargy(64%), Hoarseness of voice (52%), Dry skin(64%), Constipation (50%), Breathlessness (30%), Cold intolerance (50%), Menstrual symptoms(40%), Depression (26%). Elshafie in their study reported that the majority of symptoms were vague and not specific to a particular disease.

Fatigue, the most common symptom, accounted for 25%, followed by constipation, which accounted for 20%. Rare symptoms such as dysarthria and dysphagia, hoarse voice, sleep apnea, all of which were localized to the oropharynx, were observed in one patient. These symptoms could not be explained as the patient had no goiter. Clinical and radiological investigations were carried out to exclude other possible neurological causes. Another rare presenting symptom was edema (swelling of the lower limbs), which was observed in another patient. Twenty-four patients (10 hypothyroid patients plus 14 subclinical hypothyroid patients) were asymptomatic, accounting for 38% of patients with hypothyroidism. Seven patients had one symptom only and that was either constipation or fatigue. Three patients had two symptoms. Three had three symptoms and one patient had four symptoms. Four patients had one sign of hypothyroidism only, either dry skin or the presence of a goiter. Only one patient had two signs. The remaining patients with hypothyroidism, i.e., 25 out of 30, had no signs. The 38 patients having subclinical hypothyroidism were asymptomatic and had no signs. Some classical signs of hypothyroidism include hoarseness of voice, hair loss, bradycardia and confusion were uncommon. All patients showed the normal blood count and erythrocyte sedimentation rate (ESR), with normal biochemical findings. In our study, 64% had dry skin on examination, 26% had pallor, 20% with edema, 10% with goiter. 44% had a pulse rate <60/min and the mean pulse rate calculated to be  $66.6 \pm 11.73$ . Mean SBP  $127.8 \pm 16.22$  mmHg, Mean DBP was  $84.24 \pm 9.43$  mmHg. In our study, the severity of Hypothyroidism was categorized into mild, moderate, severe, based on TSH levels. 44% had Moderate Hypothyroidism, 34% with mild, 22% with severe Hypothyroidism based on TSH levels. Overt hypothyroidism is linked with accelerated atherosclerosis and an elevated risk of coronary artery disease (CAD). While some of the above effects may be explained by a higher prevalence of hypertension and dyslipidemia in patients with hypothyroidism, not all individuals with hypothyroidism have abnormal blood pressure or lipid profiles. Also, studies showed an increased risk of all-cause mortality and cardiovascular events<sup>55</sup> in patients with hypothyroidism, even after adjusting for the presence of cardiovascular risk factors, implicating other factors in their elevated risk<sup>[9-11]</sup>.

**ECG Changes:** In our study, 40% had Bradycardia, 34% with Low voltage complex, 26% with ST-T changes, 10% with Right Bundle Branch Block, 6% with Left Bundle Branch Block. Thyroid hormones have a substantial effect on the heart and cardiovascular system. The most common clinical signs include narrowed pulse pressure, diastolic hypertension, low cardiac output, reduced EF impaired diastolic function

and bradycardia. Overt hypothyroidism is correlated with accelerated atherosclerosis and CAD due to hypercholesterolemia and diastolic hypertension. In hyperthyroid, AF, sinus tachycardia, wide pulse pressure, dyspnoea on exertion, exercise intolerance are common. Increased LV mass owing to sustained volume overload with resultant cardiac work occurs in hyperthyroid. It may trigger ST-T ECG changes due to LV strain. Plasma lipids (TC and LDL cholesterol) may be lowered in hyperthyroidism and this is responsible for the anti-atherogenic effect and there is a less chance of accelerated atherosclerosis and CAD. Most of the previous studies that investigated the relationship of thyroid dysfunction with QTc interval as both prolonged and shorter QTc intervals have been associated with sudden cardiac death and complex ventricular arrhythmias. The consensus from previous smaller studies is that both hyperthyroidism and hypothyroidism are associated with prolongation of the QTc interval<sup>[12,13]</sup>. In the present study, 30% had normal ECHO findings, 28% with pericardial effusion, 8% with systolic dysfunction, 18% with Mild Diastolic Dysfunction, 4% with moderate diastolic dysfunction, 2% with severe Diastolic Dysfunction. Qari<sup>[14]</sup> in their study, ECHO findings were 70% had dilated cardiomyopathy and 30% were afflicted with pericardial effusion. As for patients with subclinical hypothyroidism, 40% were afflicted with cardiomyopathy and 60% had pericardial effusion. In the present study, among 14 cases with pericardial effusion on ECHO, 2 cases with mild hypothyroidism based on TSH levels, 5 cases with moderate hypothyroidism and 7 cases with severe hypothyroidism. Hypothyroidism causes pericardial effusion through enhanced permeability of the epicardial vessels and decreased lymphatic drainage of albumin, resulting in the accumulation of fluid in the pericardial space. Interestingly, autoimmunity does not play a significant role in the pathophysiology and a majority of effusions are asymptomatic due to slow fluid accumulation. Kabadi<sup>[15]</sup> in their study reported that the incidence of pericardial effusion was only 3-6%, depending on the inclusion of one or both subjects, an extremely infrequent occurrence when compared with that of previous studies. Moreover, the occurrence of pericardial effusion in hypothyroidism appears to be dependent on the severity of the disease. Thus pericardial effusion may be a frequent manifestation in myxedema, an advanced severe stage, as previously found, but a rare association of hypothyroidism, an early mild stage, because of the timeliness with which the latter condition is nowadays detected.

## CONCLUSION

Pericardial effusion is the most common abnormal finding in ECHO, which emphasizes that any

unexplained pericardial effusion should be screened for hypothyroidism. This study also shows that diastolic dysfunction is also a common cardiological abnormality found among newly diagnosed hypothyroidism. Treatment of hypothyroidism with levothyroxine may have a beneficial impact on several parameters of cardiac dysfunction, like left ventricular diastolic and systolic dysfunction, including subclinical hypothyroidism, especially in younger individuals.

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