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Evaluation Of the Thyroid Function Test in Cardiac Failure Patients: A Cross-Sectional Study

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ABSTRACT

Background: The cardiovascular system is influenced by thyroid hormones. Hyperthyroidism can result in atrial arrhythmias, hypertension, and cardiac failure; hypothyroidism can cause hyperlipidemia and ventricular arrhythmias. However, these disorders can usually be reversed by addressing the underlying thyroid problem. We looked into the relationship between thyroid levels within the reference range and heart failure.

Methodology: A descriptive, cross-sectional study was conducted on 100 heart failure patients of age greater than 18 years, New York Heart Association (NYHA) II-IV. The demographic details were collected, and Serum TSH, free T3, and free T4 were investigated.

Data were analyzed by standard statistical software.

Results: Out of 100 patients, 64 were males and 36 were females, with a mean age of 42.97 ± 11.07 years. Forty-eight patients belonged to NYHA class II, 30 patients to class III, and 22 patients to class IV. The majority of the patients (51) had an ejection fraction of 31-35%. Low T3 syndrome was seen in 49 patients, followed by subclinical hypothyroidism in 17 patients. The majority (68.1%) of the NYHA class IV patients had TSH levels of >4.2mcIU/ml. Free T3 and free T4 levels were within the reference range in all classes of patients. In patients with a lower ejection fraction (<30%), 56% of patients had a TSH level of 0.4-4.2 mIU/mL.

Conclusion: In patients with pre-existing heart failure, subclinical hypothyroidism with TSH ≥ 4.2 mIU/L and isolated low T3 levels are associated with poor prognosis. Furthermore, studies are required to explore the therapeutic effects of T4 and T3 administration in heart failure.

Keywords: Cardiac failure, Thyroid disorders, Thyroid hormones, Low T3 syndrome, Subclinical hypothyroidism.

INTRODUCTION

Heart failure (HF) is one of the prominent causes of morbidity and mortality worldwide.[1] According to the present American College of Cardiology Foundation (ACCF) and American Heart Association (AHA) standards, HF is a complicated clinical syndrome brought on by a functional or structural impairment of blood ejection or ventricular filling, which in turn causes the classic clinical signs of exhaustion and dyspnea, as well as rales and edema symptoms.[2] Globally, HF has significant rates of morbidity and mortality. It is more prevalent in senior citizens.[3]

By directly influencing the heart, the conduction system, and the peripheral vasculature, thyroid hormone plays a critical role in controlling cardiovascular activities.[4] While an excess of thyroid hormone can cause atrial arrhythmias, a shortage can lead to hyperlipidemia and ventricular arrhythmias.[5] Heart failure and hypertension may result from these disorders.[6] However, these cardiac irregularities can usually be reversed with appropriate treatment for the underlying thyroid problem.[7] Indians are prone to thyroid disorders. Roughly 42 million people are living in India with thyroid disorders.[8]

Heart function is significantly impacted by both hereditary and non-genomic influences of thyroid hormones.[9] Thyroid hormones control the genes for SERCA, phospholamban, α-myosin heavy chain, and β-myosin heavy chain in heart.[10] Non-genomic tasks include regulating several ion channels, including the Ca2+ channels in cardiac myocytes.[11] Thyroid hormone deficiency results in lower contractility, increased systemic vascular resistance, and bradycardia, while excess thyroid hormone produces tachycardia, increased blood volume from activation of the renin-angiotensin-aldosterone axis, and enhanced contractility.[12]

No thorough research has been done to examine the role of thyroid hormone abnormalities in aggravating heart failure in the outpatient setting, despite the American Heart Association's recommendations to assess thyroid function in all heart failure patients. Hence, the present study was conducted with the aim of exploring the association between thyroid hormone and heart failure.

MATERIALS AND METHODS

The present study was conducted in the Department of Medicine at Bapuji Hospital and Chitagiri Government Hospital, affiliated with JJM Medical College, Davangere.

Study design and source: This is a cross-sectional study. Heart failure patients admitted to the wards of the General Medicine Department or the cardiology ICU and wards were enrolled in the present study. This one-year eight eight-month study was done from November 2017 to July 2019 in the Department of Medicine, JJM Medical College and Hospital.

Inclusion criteria: Patients in the age group of 18-80 years, either gender, with heart failure who belonged New York Heart Association (NYHA) classification II- IV, and patients with heart failure with reduced ejection fraction < 40% were included in the study.

Exclusion criteria: patients below 18years, Heart failure patients who belonged to the NYHA classification I and had left ventricular ejection fraction >40% were excluded from the study. A small number of participants taking medications interfering with thyroid function tests -Methimazole/Propylthiouracil & Liothyronine, Thyroid hormone extract, Lithium/ Chronic Intravenous Dobutamine are excluded.

Prior to the commencement, the ethical clearance was obtained from Institutional Ethics Committee, JJM medical college, Davangere
All the patients fulfilling selection criteria were explained about the nature of study and a written informed consent was obtained before enrollment.

Sample size: A total of 100 heart failure patients were enrolled in the study.

Sampling procedure: Based on the convenience Sample method, the sample size was calculated using the following formula

$$n = 4 p q / d^2$$

Where, p = Prevalence
q = 100-p (%)
d = Absolute error considered as 10%
Considering the above formula, the sample size was calculated as 100 patients.
Every consecutive patient fulfilling the selection criteria was enrolled.

Method of collection of data: Demographic data, such as age and sex, were recorded. Patients were interviewed for chief complaints, and a physical examination was done. These findings were recorded on a predesigned and pretested Performa.

The selected patients underwent the investigations such as an Electrocardiogram, 2D Echocardiography, and thyroid function test.

Statistical analysis: The data obtained were coded and entered into a Microsoft Excel Worksheet. The categorical data were expressed as rates, ratios, and proportions, and comparison was done using the chi-square test. The continuous data were expressed as mean ± standard deviation (SD), and comparison was done using an independent sample t-test. A probability value (p-value) of less than or equal to 0.05 was considered statistically significant.

RESULTS

Out of 100 patients, the majority of them were in the age group of 51 to 60 years (26%), followed by 20% between 41-50 years, 18% between 61-70 years, 18% between 71 -80 years,11% between 81-90 years, and 6% between 31-40 years. The mean age of the study population was 42.97 ± 11.07 years. Out of 100 patients, 64 were males and 36 patients were females, accounting a ratio of male to female 2.1:1. The Majority of the patients had co-morbidities like diabetes mellitus (38),

myocardial infarction (37), and hypertension (36). Forty-eight patients belonged to NYHA class II, 30 patients to class III, and 22 patients to class IV. The majority of the patients (51) had an ejection fraction of 31-35% **(table 1)**.

Table 1: Demographic characteristics of patients

S.No	Parameter	Number of patients
1	**Age in years**	
	20-30	1
	31-40	6
	41-50	20
	51-60	26
	61-70	18
	71-80	18
	81-90	11
2	**Gender**	
	Male	64
	Female	36
3	**Comorbidities**	
	Diabetes Mellitus	38
	Chronic Kidney Disease	13
	Myocardial Infarction	37
	Tuberculosis	6
	Hypertension	36
4	**Habits**	
	Alcohol	36
	Smoking	40
5	**NYHA CLASS**	
	II	48
	III	30
	IV	22
6	**Body Mass Index**	
	< 18.5	1
	18.5- 24.9	37
	25-24.9	50
	> 30	12
7	**Ejection fraction (%)**	
	≤ 30	25
	31 - 35	51
	36 -40	24

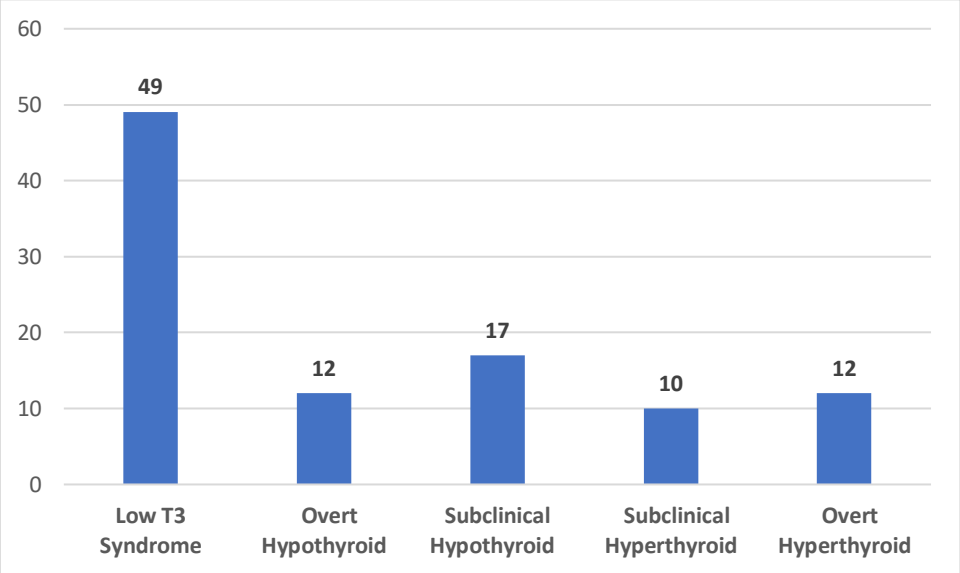

Figure 1: Thyroid diseases among the patients.

Low T3 syndrome was seen in 49 patients, followed by overt hypothyroid in 12 patients, subclinical hypothyroidism in 17patients, Subclinical hyperthyroidism in 10 patients, and overt hyperthyroid in 12 patients **(figure 1)**.

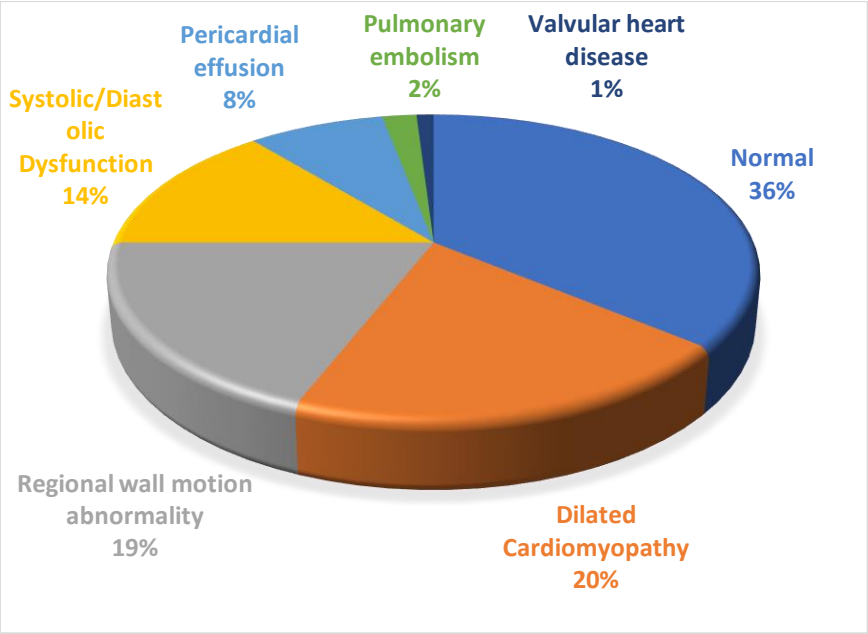

Figure 2: Cardiac manifestations based on 2D Echo

The 2D echo of the included patients showed that dilated cardiomyopathy (20%) was very common, followed by regional wall motion abnormality (19%), systolic/diastolic dysfunction (14%), pericardial effusion (8%) **(Figure 2)**.

Table 2: Association between TSH, Free T3, Free T4, and NYHA grade

Parameters	NYHA Class			Chi-square p-value
	II (n=48)	III (n=30)	IV (22)	
TSH (mcIU/ml) 0.4-4.2 >4.2	40 8	26 4	7 15	<0.001
Free T3(ng/ml) < 1.71 1.71 - 3.71 > 3.71	11 37 0	9 20 1	7 15 0	0.516
Free T4 (mcg/dl) < 0.7 0.7- 1.48 > 1.48	3 39 6	2 24 4	1 13 8	0.167

The 83.3%, 77% and 81.25% of the patients from NYHA class II showed TSH levels of 04-4.2mcIU/ml, free T3 level of 1.71-3.71ng/ml, free T4 level of 0.7-1.48mcg/dl, respectively. The positive association was observed between TSH levels (0.4-4.2) and NYHA class, with a statistically significant p-value of <0.001.

The 86.6%, 66.6% and 80% of the patients from NYHA class III showed TSH levels of 04-4.2mcIU/ml, free T3 level of 1.71-3.71ng/ml, free T4 level of 0.7-1.48mcg/dl, respectively.

Around, 68.1%, 68.1% and 43.3% of the patients from NYHA class IV showed TSH levels >4.2mcIU/ml, free T3 level of 1.71-3.71ng/ml, free T4 level of 0.7-1.48mcg/dl, respectively **(Table 2).**

Table 3: Association between ejection fraction and TSH, T3, T4

Parameters	Ejection fraction (%)			Chi-square p-value
	<30 (n=25)	31-35 (n=51)	36-40 (n=24)	
TSH (mcIU/ml) 0.4-4.2 >4.2	14 11	39 12	20 4	0.07
Free T3(ng/ml) < 1.71 1.71 - 3.71 > 3.71	6 19 0	16 34 1	5 19 0	0.704
Free T4 (mcg/dl) < 0.7 0.7- 1.48 > 1.48	1 21 3	3 38 10	2 17 5	0.848

In patients with a lower ejection fraction (<30%), 56% of patients had a TSH level of 0.4-4.2 mIU/mL, and 44% of patients had a TSH level of> 4.2 mIU/mL. And the majority of them had Free T3 level of 1.71-3.71 (76%), Free T4 level of 0.7-1.48mcg/dl (84%). Among 51 patients with an ejection fraction of 31-35%, 76.4% of them had a TSH level of 0.4-4.2 mIU/mL, 66.6% of them had a Free T3 level of 1.71-3.71, and 74.5% of them had a Free T4 level of 0.7-1.48mcg/dl . Among 24 patients with an ejection fraction of 36-40%, 83.3% of them had a TSH level of 0.4-4.2 mIU/mL, 79.1% of them had a Free T3 level of 1.71-3.71, and 70.8% of them had a Free T4 level of 0.7-1.48mcg/dl. There was no statistically significant association between the ejection fraction and thyroid profile **(Table 3)**.

DISCUSSION

Thyroid hormone production is regulated by the pituitary gland, which produces TSH to stimulate the thyroid to make thyroid hormone when thyroid hormone levels are low.[13] Thyroid hormone feeds back to reduce TSH production and preserve a unique pituitary-thyroid set point in the thyroid axis, which functions as a traditional negative feedback loop.[14] The goal of the current study was to ascertain the prevalence of thyroid conditions among heart failure patients at a Davanagere tertiary care hospital.

Among 100 patients, dilated cardiomyopathy (20%) was the most prevalent condition in the 2D echo, followed by regional wall motion abnormality (19%), systolic/diastolic dysfunction (14%), and pericardial effusion (8%). Various studies done by **Rhee CM et al, Iervasi G** et al and **Pingitore et al** similar cardiac abnormalities were observed with varying percentage related to cardiac abnormalities.[15,16,17]

In the present study, Low T3 syndrome was seen in 49 patients, followed by overt hypothyroid in 12 patients, subclinical hypothyroidism in 17patients, Subclinical hyperthyroidism in 10 patients, and overt hyperthyroid in 12 patients. Similar results were seen in a study carried out by **Soham Biswas** et al, with 68% of patients having euthyroid, followed by 15% of subclinical hypothyroidism.[18]

According to a study by **Unnikrishnan**, the prevalence of these thyroid conditions was higher in the study population than in the general Indian population (10.95% overt hypothyroid, 0.67% overt hyperthyroid, 8.02% subclinical hypothyroid, and 1.27% subclinical hyperthyroid). [19]

Low T3 levels have been linked to problems in myocardial perfusion and metabolism as well as myocardial fibrosis in heart failure patients. Twenty to thirty percent of heart failure patients have the low T3 syndrome, which is characterized by low T3 levels with TSH and FT4 levels in the reference range.[20] In our study, 49% of participants had low T3 syndrome. Low T3 syndrome was found to be independently linked to increased all-cause mortality in studies involving hospitalized heart failure patients. This connection is validated in outpatients with chronic heart failure by similar research.[21]

In the current study, we found that TSH, free T3, and free T4 levels were almost normal (euthyroid profile) in the majority of patients, irrespective of NYHA classes and the ejection fraction percentage. A similar study was done by **Kannan et al** on heart failure patients in the USA in which majority of patients had NYHA class II (45%) or III (32%) symptoms. In that study, 74% of the HF patients were euthyroid, 5% had subclinical hypothyroidism, 5% had subclinical hyperthyroidism, 1% had overt hyperthyroidism and less than 1% had overt hypothyroidism. [22]

There are certain limitations to our investigation. The study was cross-sectional. Therefore, it was unable to determine the risk that thyroid conditions pose for the development of HF. The results may not be broadly applicable because the study participants were chosen from among the hospital's patients. The primary goal of the descriptive study design was to determine the prevalence of different thyroid dysfunctions; the importance of other comorbidities in the development and course of HF was not investigated.

CONCLUSION

In comparison to hyperthyroidism, hypothyroidism was about five times more common among the patients overall. Only, hypothyroidism was identified in NYHA class II HF patients, with subclinical cases predominating over overt ones. As the severity of HF worsened, thyroid issues became more common. Therefore, in patients with suspected heart failure, thyroid function must always be assessed. Early detection and treatment of thyroid disorders may reduce morbidity and death from heart failure because thyroid hormone abnormalities have a significant impact on cardiac structure and function. It is necessary to assess the HF patients' results following thyroid dysfunction repair.

Author contribution

All the authors were involved in study concept and design, literature search, data acquisition, analysis, interpretation of results, manuscript preparation, and manuscript editing.

Consent form declaration

Informed consent from all the participants was taken.

Ethical clearance

Institutional ethical committee clearance (ref. No: JJMMC/IEC/SY/28-2017) was obtained.

Conflict of interest

Authors declare no conflicts of interest.

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