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A STUDY ON THE PREVELANCE OF LOW T3 SYNDROME IN HEART FAILURE WITH REDUCED EJECTION FRACTION AT NORTHERN RAILWAY CENTRAL HOSPITAL, NEW DELHI

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ABSTRACT

Background: Heart failure (HF) is associated with high morbidity and mortality and is often accompanied by endocrine abnormalities, including thyroid dysfunction. Low T3 syndrome (LT3S), defined by reduced free triiodothyronine (FT3) with normal thyroid stimulating hormone (TSH) and free thyroxine (FT4), has been linked to adverse outcomes in HF. This study aimed to determine the prevalence of low T3 syndrome in patients with heart failure with reduced ejection fraction (HFrEF) and its association with clinical outcomes.

Materials and Methods: This prospective observational study was conducted at Northern Railway Central Hospital, New Delhi over 18 months from July 2023 to December 2024. A total of 200 patients with HFrEF (LVEF <40%) were enrolled. Baseline clinical evaluation, thyroid function tests, and echocardiography were performed. Patients were categorized into low T3 syndrome and normal T3 groups and followed for six months to assess mortality, hospitalization, and major adverse cardiovascular events (MACE).

Results: The mean age was 64.95 ± 12.99 years and 57.5% were males. Low T3 syndrome was observed in 40% of patients. Mortality at six months was significantly higher in the low T3 group compared to the normal T3 group (52.5% vs 16.67%, $p<0.05$). Hospitalization rates were also higher in the low T3 group (71.25% vs 49.17%, $p<0.05$). However, no significant association was found between low T3 syndrome and individual cardiovascular events.

Conclusion: Low T3 syndrome is common in patients with HFrEF and is associated with increased mortality and hospitalization. Assessment of thyroid function may help identify high-risk patients.

Keywords: Heart failure, Low T3 syndrome, HFrEF, Thyroid dysfunction, Mortality.

INTRODUCTION

Heart failure (HF) is a complex clinical syndrome characterized by symptoms such as dyspnea, fatigue, and reduced exercise tolerance resulting from impaired ventricular filling or reduced cardiac output. It represents a major global health problem due to its high morbidity, mortality, and frequent hospitalizations. The one-year mortality rate in patients with chronic heart failure is approximately 7.2% with a hospitalization rate of 31.9%, while in patients hospitalized with acute heart failure these rates increase to 17.4% and 43.9%, respectively.[1] The burden of heart failure varies across populations. In India, the average age of patients admitted with heart failure is around 53 years, which is significantly younger compared to Western countries where the mean age exceeds 70 years.[2] Moreover, the in-hospital mortality rate among heart failure patients in India ranges from 10% to 30.8%, compared to 4–7% reported in Western populations.[3,4] Based on left ventricular ejection fraction (LVEF), heart failure is

classified into heart failure with preserved ejection fraction (HFpEF, LVEF >50%), heart failure with mid-range ejection fraction (HFmrEF, LVEF 41–49%), and heart failure with reduced ejection fraction (HFrEF, LVEF <40%).[5] Among these, HFrEF is associated with greater disease severity and poorer clinical outcomes. Thyroid hormone abnormalities have important effects on cardiovascular function. Both overt hyperthyroidism and hypothyroidism have been recognized as potential causes of heart failure due to their influence on myocardial contractility, heart rate, and vascular resistance.[6] Persistent subclinical thyroid dysfunction has also been associated with the development and progression of heart failure, even in individuals without underlying structural heart disease.[7] In addition to common comorbidities such as diabetes, hypertension, dyslipidemia, and renal disease, endocrine disorders—particularly thyroid dysfunction—can significantly affect the prognosis of patients with heart failure.[8] Low triiodothyronine (T3) syndrome (LT3S), a form of sick euthyroid syndrome, is the most common thyroid hormone alteration observed in patients with cardiac diseases. It occurs in approximately 20–30% of patients with chronic heart failure and is characterized by decreased free triiodothyronine (FT3) levels with normal free thyroxine (FT4) and thyroid-stimulating hormone (TSH) levels.[9] Reduced T3 levels have been associated with impaired myocardial function and adverse clinical outcomes, and some studies have suggested that T3 supplementation may improve survival in selected patients.[10] Because of the strong relationship between thyroid function and cardiovascular outcomes, major cardiology guidelines recommend routine evaluation of thyroid function in patients with heart failure.[11] Low T3 syndrome and subclinical hypothyroidism have also been reported following acute myocardial infarction and are associated with poorer prognosis, although the role of thyroid hormone supplementation in improving outcomes in such patients remains unclear.[12] Several studies have further demonstrated that low T3 syndrome is an independent predictor of all-cause mortality in heart failure, even after adjusting for conventional prognostic factors such as ejection fraction and natriuretic peptide levels.[13] At the cellular level, reduced T3 bioavailability in heart failure may result from tissue hypoxia and systemic inflammation, which impair deiodinase activity and increase the conversion of T3 into inactive metabolites.[14] Despite increasing recognition of thyroid dysfunction as an important prognostic factor in heart failure, data regarding the prevalence of Low T3 syndrome among patients with heart failure with reduced ejection fraction (HFrEF) in the Indian population remain limited. Therefore, the present study was conducted to assess the prevalence of Low T3 syndrome in patients with heart failure with reduced ejection fraction attending Northern Railway Central Hospital, New Delhi.

MATERIALS AND METHODS

This prospective observational single-centre study was conducted in the Department of Medicine at Northern Railway Central Hospital, New Delhi.All adult patients admitted with clinical features suggestive of heart failure and diagnosed with heart failure with reduced ejection fraction (HFrEF) (LVEF <40%) were enrolled prospectively. The study was conducted over a period of 18 months from July 2023 to December 2024.

Inclusion Criteria

Patients fulfilling the following criteria were included:

- Clinical features suggestive of heart failure (dyspnea, basal crepitations, bilateral pitting pedal edema, elevated JVP)
- Chest X-ray showing cardiomegaly (cardiothoracic ratio >0.5)
- Elevated NT-proBNP levels
- 2D echocardiography showing reduced LVEF <40%

Exclusion Criteria

Patients with the following conditions were excluded:

- Known hypothyroidism or hyperthyroidism
- Patients receiving amiodarone therapy
- Clinical evidence of sepsis
- History of CABG within the past three days
- Evidence of renal failure

Methodology: After obtaining approval from the Institutional Ethics Committee and written informed consent from participants, patients fulfilling the inclusion criteria were enrolled. Baseline clinical evaluation and laboratory investigations were performed. Thyroid function tests were done at study entry and patients were categorized into heart failure with Low T3 syndrome and heart failure with normal thyroid function.

All patients were followed for six months through monthly telephonic or physical follow-up, with at least two mandatory physical visits. Cardiovascular outcomes were assessed using Major Adverse Cardiovascular Events (MACE) five-point criteria, including myocardial infarction, stroke, cardiovascular death, unstable angina, and hospitalization for heart failure.

Laboratory and Echocardiographic Assessment: Baseline investigations included hemoglobin, total leukocyte count, platelet count, fasting and postprandial blood glucose, lipid profile, blood urea, serum creatinine, NT-proBNP, TSH, free T3, and free T4. Thyroid function tests were performed using chemiluminescence assay.

THYROID PROFILE	NORMAL RANGE
FREE T3	2.5 – 3.9 pg/ml
FREE T4	0.61-1.12 ng/dl
TSH	MALES AND NON-PREGNANT FEMALES: 0.38 to 5.33 uIU/ml
NT pro BNP levels normal value	>75 years - < 450 pg/ml <75 years - <125 pg/ml

Low T3 syndrome was defined as reduced free T3 with normal or low free T4 and TSH levels.

Two-dimensional Doppler echocardiography was performed for all patients. Left ventricular ejection fraction was calculated using the Simpson's biplane method recommended by the American Society of Echocardiography.

Parameters Assessed: Data were collected on demographic details (age, gender), clinical features, baseline comorbidities, thyroid profile, biochemical parameters, NT-proBNP levels, LVEF, and cardiovascular outcomes (MACE).

Statistical Analysis: Data were entered in Microsoft Excel and analyzed using SPSS version 25.0. Quantitative variables were expressed as mean ± standard deviation, while categorical variables were presented as frequency and percentages. The unpaired t-test was used to compare continuous variables and the Chi-square test was used for categorical variables. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 200 patients with heart failure with reduced ejection fraction were included in the study. The mean age of the study population was 64.95 ± 12.99 years, with a median age of 65 years and an age range of 36 to 89 years. Males constituted 115 (57.5%) of the study population, while 85 (42.5%) were females. The majority of patients belonged to the 61–70 years age group (39%), followed by 71–80 years (15.5%) and 81–90 years (15%) [Table 1]. The most common comorbidities observed among the study participants were hypertension (59.5%), diabetes mellitus (53%), and coronary artery disease (45%). Other comorbidities included obesity (12%), chronic obstructive pulmonary disease (11.5%), rheumatic heart disease (9%), congenital heart block (4%), atrial fibrillation (3%), cerebrovascular accident (2%), dyslipidemia (2%), and dilated cardiomyopathy (1%). The most common presenting symptom was shortness of breath (80.5%), followed by pedal edema (18%). Other symptoms included chest pain (3.5%), weakness on one side (1.5%), and palpitations (1%).

The mean left ventricular ejection fraction (LVEF) in the study population was 24.22 ± 8.18%, with a median of 20% and a range of 15% to 45%. Most patients (50.5%) had LVEF between 15–20%, while 27% had LVEF between 20–30%, and 22.5% had LVEF between 30–40%.The mean laboratory parameters recorded were as follows: mean haemoglobin 11.73 ± 1.66 g/dl, mean total leukocyte count 10.34 ± 2.10 $\times 10^3$ cells/mm^3, mean platelet count 2.46 ± 0.90 $\times 10^5$ cells/mm^3, mean fasting blood glucose 133.82 ± 43.29 mg/dl, and mean postprandial blood glucose 182.95 ± 70.54 mg/dl. Low T3 syndrome was observed in 80 patients (40%), while 120 patients (60%) had normal T3 levels. Among patients with low T3 syndrome, the mean TSH level was 1.88 ± 0.94 mU/L, mean T3 level was 1.42 ± 0.50 mcg/dl, and mean T4 level was 1.46 ± 0.55 mcg/dl. In the normal T3 group, the mean TSH level was 1.94 ± 0.98 mU/L, mean T3 level was 2.96 ± 0.29 mcg/dl, and mean T4 level was 1.45 ± 0.51 mcg/dl [Table 2]. At the end of six months of follow-up, 138 patients (69%) were alive, while 62 patients (31%) had died. A significantly higher proportion of patients in the low T3 syndrome group died during follow-up compared to the normal T3 group (52.5% vs 16.67%). This association was statistically significant (p = 0.001, Chi-square test). Hospitalization rates were significantly higher in patients with low T3 syndrome, with 71.25% experiencing more than one hospitalization compared to 49.17% in the normal T3 group (p = 0.001, Chi-square test) [Table 3]. Among the 62 patients who died in the study, 42 belonged to the low T3 syndrome group and 20 belonged to the normal T3 group. Within the low T3 syndrome group, the mean T3 level among patients who died was significantly lower compared to those who survived (1.36 ± 0.50 mcg/dl vs 1.45 ± 0.50 mcg/dl; p = 0.02).During the follow-up period, 23% of patients experienced myocardial infarction, 7% developed stroke, 40% had unstable angina, and 75% experienced heart failure events. Although a higher proportion of patients with low T3 syndrome experienced heart failure (80%) and stroke (10%), there was no statistically significant association between low T3 syndrome and major adverse cardiovascular events (p > 0.05).

Table 1: Baseline demographic and clinical characteristics of study population (n = 200)

Variable	Value
Mean age (years)	64.95 ± 12.99
Median age (years)	65
Age range (years)	36 – 89
Male	115 (57.5%)
Female	85 (42.5%)
Mean LVEF (%)	24.22 ± 8.18

Table 2: Prevalence of Low T3 syndrome and thyroid profile

Variable	Low T3 syndrome (n = 80)	Normal T3 (n = 120)
Prevalence	80 (40%)	120 (60%)
Mean TSH (mU/L)	1.88 ± 0.94	1.94 ± 0.98
Mean T3 (mcg/dl)	1.42 ± 0.50	2.96 ± 0.29
Mean T4 (mcg/dl)	1.46 ± 0.55	1.45 ± 0.51

Table 3: Association of Low T3 syndrome with mortality and hospitalization

Outcome	Low T3 syndrome (n = 80)	Normal T3 (n = 120)	p-value
Death at 6 months	42 (52.5%)	20 (16.67%)	0.001
Alive at 6 months	38 (47.5%)	100 (83.33%)	
Hospitalization >1 time	57 (71.25%)	59 (49.17%)	0.001
Hospitalization 0–1 time	23 (28.75%)	61 (50.83%)	

DISCUSSION

Heart failure (HF) continues to be a major cause of morbidity and mortality despite improvements in treatment. Thyroid hormone abnormalities have been increasingly recognized as important contributors to cardiovascular dysfunction and progression of heart failure. Both overt and subclinical thyroid dysfunction have been associated with the development and worsening of HF, and endocrine disorders such as thyroid abnormalities may significantly influence the prognosis of these patients.[6–8] Low T3 syndrome (LT3S), a form of sick euthyroid syndrome characterized by reduced free triiodothyronine (FT3) with normal free thyroxine (FT4) and thyroid stimulating hormone (TSH), is commonly observed in chronic HF and has been associated with poor outcomes.[9] Because of its prognostic importance, routine thyroid function assessment is recommended in patients with heart failure.[10,11] However, studies evaluating the prevalence and clinical significance of low T3 syndrome in Indian HF patients remain limited. In the present study, 200 patients with heart failure with reduced ejection fraction were evaluated. The mean age of the study population was 64.95 ± 12.99 years, and males constituted 57.5% of patients. Similar findings were reported by Iervasi et al., where the mean age was 66 ± 12 years and males accounted for 56% of the study population.[12,13] In the study by Kannan et al., the mean age was 57 years with 35% females,[8] while Sato et al. reported a mean age of 72.9 years with 53.3% males among patients with low FT3 syndrome.[14,15] These findings suggest that HF predominantly affects elderly individuals with a slight male predominance. Hypertension (59.5%), diabetes mellitus (53%), and coronary artery disease (45%) were the most common comorbidities observed in the present study. Comparable findings were reported by Iervasi et al., where hypertension was present in 48.6% and diabetes mellitus in 15.3% of patients.[13] Similarly, Kannan et al. reported hypertension in 62%, diabetes mellitus in 29%, and hyperlipidemia in 49% of patients.[8] Sato et al. also reported a high prevalence of hypertension (81.9%) and diabetes mellitus (48.6%) among HF patients with low FT3 levels.[15] These comorbidities are known to contribute to the development and progression of heart failure. The mean left ventricular ejection fraction in the present study was 24.22 ± 8.18%, indicating severe systolic dysfunction. In comparison, Kannan et al. reported a mean ejection fraction of 34% in their study population,[8] while Sato et al. also demonstrated reduced LVEF among patients with low FT3 syndrome.[15] The prevalence of low T3 syndrome in the present study was 40%. This finding is comparable to previous studies. Iervasi et al. reported low T3 syndrome in approximately 30% of HF patients,[13] while Sato et al. observed a prevalence of 35.2% among HF patients.[15] In contrast, Kannan et al. reported a lower prevalence of 14%.[8] Variations in prevalence may be attributed to differences in patient characteristics and severity of heart failure. Thyroid hormones play a key role in cardiovascular physiology by regulating myocardial contractility, heart rate, and systemic vascular resistance.[16,17] Reduced circulating T3 levels are mainly due to decreased activity of 5′-monodeiodinase, the enzyme responsible for conversion of T4 to T3 in peripheral tissues.[18,19] Although low T3 syndrome was previously considered an adaptive response to severe illness, increasing evidence suggests that reduced T3 levels may contribute to worsening cardiac function and adverse outcomes. In the present study, low T3 syndrome was significantly associated with increased mortality. At six months follow-up, mortality was significantly higher in the low T3 group compared with the normal T3 group (52.5% vs 16.67%, $p<0.05$). Similar findings were reported by Iervasi et al., where mortality was significantly higher among HF patients with low T3 syndrome compared with those with normal thyroid function.[13] Sato et al. also reported increased cardiac and all-cause mortality in HF patients with low FT3 levels.[15] Additionally, the present study showed that patients who died had significantly lower mean T3 levels compared to those who survived ($p=0.02$), suggesting that T3 levels may serve as a prognostic indicator. Low T3 syndrome was also associated with higher hospitalization rates in the present study, with significantly more patients experiencing repeated hospitalizations compared with those having normal T3 levels. This suggests that low T3 syndrome may reflect more severe disease and poorer clinical outcomes. During follow-up, major adverse cardiovascular events included heart failure episodes (75%), unstable angina (40%), myocardial infarction (23%), and stroke (7%). Although a higher proportion of low T3 patients experienced heart failure and stroke, the association was not statistically significant. Similar observations were reported by Kannan et al., where low T3 syndrome and subclinical hypothyroidism were associated with poorer outcomes including increased risk of ventricular assist device placement, cardiac transplantation, or death.[8] Furthermore, a meta-analysis including 41 studies demonstrated that low T3 syndrome is the most common thyroid abnormality in HF patients and is associated with

increased all-cause mortality, cardiac mortality, and major adverse cardiovascular events.[20]

Limitations: This study has certain limitations. It was a single-centre study, which may limit the generalizability of the findings. The sample size was relatively small and the follow-up period was limited to six months, which may not reflect long-term outcomes. Thyroid function tests were assessed only at baseline, and changes in thyroid hormone levels during follow-up were not evaluated. Additionally, as an observational study, a causal relationship between low T3 syndrome and adverse outcomes in heart failure cannot be established.

CONCLUSION

The present study demonstrated that low T3 syndrome is relatively common among patients with heart failure with reduced ejection fraction, with a prevalence of 40%. Patients with low T3 syndrome showed significantly higher mortality and hospitalization rates compared to those with normal T3 levels. These findings suggest that low T3 syndrome may serve as an important prognostic marker in patients with heart failure. Routine assessment of thyroid function in heart failure patients may help in early identification of high-risk individuals and improve clinical management. Further large-scale studies are required to clarify the potential therapeutic role of thyroid hormone modulation in this population.

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