



STUDY ON PREVALENCE AND SIGNIFICANCE OF LOW FT3 SYNDROME IN CHRONIC HEART FAILURE

Cardiology

B. Mounica

P.G.

**Karodi Murali
Krishna**

Associate Professor of Cardiology

ABSTRACT

Introduction: The pathophysiology of the cardiovascular system is significantly influenced by thyroid hormones. Low-FT3 (triiodothyronine) syndrome refers to a change in thyroid function in heart failure patients. **Objectives:** Assess the prevalence of low FT3 syndrome in chronic heart failure and to assess the correlation of thyroid hormones with the severity of chronic heart failure. **Methods:** Free FT3, T4, thyroid stimulating hormone (TSH), echocardiographic parameters, New York Heart Association (NYHA) score, and brain natriuretic peptide (BNP) levels were examined in 100 patients. **Results:** There was a strong association between Free FT3 levels and NYHA class. FT3 levels had significant negative correlations with Left atrium (LA) size, End-diastolic diameter (EDD), and BNP and statistically significant positive correlations with Ejection fraction (EF). **Conclusion:** The current study concluded that low FT3 syndrome was more common. There was a significant inverse relationship between FT3 levels and BNP levels.

KEYWORDS

BNP, low FT3 syndrome, echocardiographic characteristics, chronic heart failure, and NYHA score.

INTRODUCTION

The cardiovascular system's pathophysiology is significantly influenced by thyroid hormones.^{1,2} Majority (80%) of active form of FT3 is produced from conversion of pro T4.³ Clinical and experimental research has demonstrated that 3 FT3 is crucial for altering heart rate, contractions, and peripheral vascular resistance. By binding to particular nuclear receptors that optimise the genes in charge of the structure and function of cardiac proteins, FT3's action is modified.⁴ Thyroid hormone effects left ventricular contractions, heart rate, peripheral resistance, and diastolic functions, and on some occasions hypothyroidism can lead to heart failure. Low cardiac output can be brought on by slowed heartbeat, decreased myocardial contractility, or increased peripheral resistance.^{5,6} Hypertrophy of left ventricle, abnormal relaxation, and decreased heart rate can cause delay in filling of left ventricle. When metabolic demand is more than cardiac output it may lead to heart failure.⁷⁻⁹ Patients with known cardiac disease are more prone for heart failure.⁴ Low FT3 levels in circulation are caused by decreased 5' monodeiodinase enzyme activity, which converts T4 to FT3.^{10,11}

Aims and Objectives of the study

1. To assess the prevalence of low FT3 syndrome in patients with chronic heart failure.
2. To assess the correlation between levels of thyroid hormones and severity of chronic heart failure and BNP levels.

MATERIALS & METHODS

Type of design: Observational study.

Source of data:

Using a simple random sampling method, 100 patients were selected and admitted into cardiology wards in a tertiary care hospital in Andhra Pradesh from January 2018 to January 2021.

Sample size:

Considering the prevalence of low FT3 syndrome as 30% (Levarsi et al.)¹² with 95% C.I. allowable error of 10%, loss to follow up of 20% by using, $n = Z^2 p(1-p)/d^2$, $n = 87.2$, rounded off to 100.

Inclusion criteria:

Chronic heart failure patients between 30 and 80 years aged.

Exclusion criteria:

Known hypothyroid patients on thyroxine, Patients on amiodarone, on anti-thyroid drugs, Patients with Chronic kidney and liver disease, and sepsis.

Method of Data collection:

100 chronic heart failure patients were studied for fT3, fT4, TSH, NYHA scoring, echocardiographic parameters, i.e., EF, left ventricular end-diastolic diameter (LVEDD), diastolic dysfunction

and LA size, BNP levels. Patients were followed at regular monthly intervals for three months. The study was carried out with wide preference to human research ethical principles (such as the Declaration of Helsinki) and after receiving approval from the institutional ethical committee and the patients' informed consent.

Statistical Analysis:

Data tabulation was done using Microsoft excel 2013 and analysis using SPSS 25. Quantitative data were expressed in mean and standard deviation, and qualitative data in frequencies and percentages. Statistical tests such as ANOVA, and Pearson correlation coefficient were used to find a significant association. A p-value of <0.05 was considered to be statistically significant.

OBSERVATIONS & RESULTS

In the present study, the mean age of the study participants was 56.07 ± 12.31 . The majority, i.e., 30%, belonged to the 56-65 age group, and 4% were seen in the 25-35 years age group. Gender distribution showed 56% males and 44% females. Distribution based on Body mass index (BMI) showed 61% were in the 25-29.9 kg/m² category. The mean BMI in the present study was 26.65 ± 2.67 .

As per table 1, based on EF, 54% had EF <30 , and 10% had EF between 40-49. The mean EF in the present study was 30.53 ± 6.37 . According to NYHA class, the majority (49%) belonged to NYHA Class IV, and 1% was seen in NYHA Class I. Based on diagnosis, DCMP (64%), ICMP with mild LV dysfunction (1%), ICMP with moderate LV dysfunction (4%), ICMP with severe LV dysfunction (30%), and in 1% of cases Refractory Heart Failure was observed. Diastolic dysfunction showed 37% grade 1 dysfunction, 26% grade 2 dysfunction, 13% grade 4 dysfunction, and 11% had grade 3 dysfunction.

According to table 2, the mean LA size was 46 ± 4.39 , and the mean EDD was 60 ± 7.45 . The mean TSH was 2.92 ± 0.75 , the mean fT3 was 0.76 ± 0.33 , and the mean fT4 was 12 ± 1.23 .

Table 3 showed a significant association was observed between and fT3 with NYHA class, and Diastolic dysfunction. A statistically non-significant association was observed between diagnosis and fT3 levels.

FT3 levels had significant positive correlation with EF, whereas it had negative correlation with the remaining others i.e., LA size, EDD, and BNP (Table 4, fig 1, and 2).

DISCUSSION:

Low thyroid hormone, especially low serum FT3, is a common finding in patients with conditions other than hypothyroidism, such as cardiac problems. Despite the lack of clarity regarding the pathophysiology, it is thought that adaptive mechanisms play a part.¹⁰ However, a direct link was shown between low levels of FT3 and a poor prognosis in

cardiac patients, based on the knowledge of FT3's effects on the heart and blood arteries.

Prevalence of low FT3 syndrome:

In the present study, the prevalence of low FT3 syndrome was higher (42%), while it was 30% in Lervasi et al.¹² study, 20.6% in Zargar et al.¹³ study, and 18% in the study by Opasich et al.¹⁴

Age:

In the present study, the mean age of the study participants was 56.07 ± 12.31 , which was similar to Ascheim et al.¹⁵ (67 ± 11.2 years), Lervasi et al.¹² (66 ± 12 years).

Gender:

In this study, 56% were males, and 44% were females, which was similar to Lervasi et al.¹², while more number of males (75.38%) were seen in the study by Ascheim et al.¹⁵

EF:

A statistically significant association between EF and T3 levels was found in this study. Patients with lower mean ejection fraction values exhibited lower total T3 values overall. Similar study findings were reported by Kozdag et al.¹⁶, where Low FT3 syndrome had a lower ejection fraction.

NYHA class:

In the present study, the majority (49%) belonged to NYHA Class IV, and a significant negative correlation was reported with FT3 values, i.e., the higher the NYHA class, the lower the FT3 values. Similar results were observed in a study by Saurav S et al.¹⁷, which showed a rising trend in low FT3 prevalence as the CHF stage rose.

Diastolic dysfunction:

In this study, the majority (37%) had grade 1 dysfunction, and 11% had grade 3 dysfunction. The mean LA size was 46 ± 4.39 , and the mean EDD was 60 ± 7.45 . This study observed a significant negative correlation between Diastolic dysfunction and FT3 levels, i.e., FT3 levels reduce as the dysfunction grade is higher.

A Study by Pingtore et al.¹⁸ reported that age, male, NYHA class, Diastolic dysfunction, and Ejection fraction were considered predictors for low FT3 levels and mortality. Shilpa D et al.¹⁹ reported that patients with LVEF <30% had suppressed serum FT3, whereas none of the patients with LVEF >60% had suppressed FT3. All (n=4, 100%) the patients with cardiogenic shock had low FT3 levels.

According to Lymvaivos et al.²⁰, FT3 levels gradually returned to baseline levels in participants whose LVEF had altered by less than 50% after six months, but not in those whose LVEF had increased by more than 50%.

Echocardiographic parameters:

In the present study, the mean LA diameter was 46 ± 4.39 with a negative correlation, which was similar to Kozdag et al.¹⁶ In this study, mean EF and EDD were 30.53 ± 6.37 , 29 ± 10 , respectively, while similar findings were noted in Kozdag et al. study¹⁶ also.

BNP levels and Ft3:

BNP levels and FT3 levels were found to be negatively correlated in the current study, with a significant P value.

CONCLUSION

In comparison to other investigations, the current study discovered a higher prevalence of low T3 syndrome. There was a significant inverse relationship between FT3 levels and BNP levels. Patients with lower EF were far more likely to experience low FT3 syndrome. EF and BNP levels both functioned as outcome predictors.

Declaration of Conflicting Interests

Authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Funding

Authors received no financial support for the research, authorship and/or publication of this article.

REFERENCES

- Polikar R, Burger AG, Scherrer U, et al. The thyroid and the heart. *Circulation*. 1993 May; 87(5): 1435–41.

- Klein I, Ojamaa K. Mechanism of disease: thyroid hormone and the cardiovascular system. *N Engl J Med*. 2001; 344: 501–509.
- Pilo A, Lervasi G, Vitek F, et al. Thyroidal and peripheral production of 3,5,3'-triiodothyronine in humans by multicompartmental analysis. *Am J Physiol*. 1990; 258: E715–E726.
- Danzi S, Klein I. Thyroid hormone and the cardiovascular system. *Minerva Endocrinol*. 2004; 29: 139–50.
- Franklyn JA, Gammage MD, Ramsden DB, et al. Thyroid status in patients after acute myocardial infarction. *Clin Sci (Colch)*. 1984 Dec; 67(6): 585–590.
- Wiersinga WM, Lie KI, Toubler JL. Thyroid hormones in acute myocardial infarction. *Clin Endocrinol*. 1981; 14: 367–374.
- Klemperer JD, Klein I, Gomez M, et al. Thyroid hormone treatment after coronary artery bypass surgery. *N Engl J Med*. 1995 Dec 7; 333(23): 1522–27.
- Murzi B, Lervasi G, Masini S, et al. Thyroid hormones homeostasis in pediatric patients during and after cardiopulmonary by-pass. *Ann Thorac Surg*. 1995 Feb; 59(2): 481–85.
- Holland FW, Brown PS, Weintraub BD. Cardiopulmonary bypass and thyroid function: a "euthyroid sick syndrome." *Ann Thorac Surg*. 1991; 52: 46–50.
- Utiger RD. Altered thyroid function in nonthyroidal illness and surgery: to treat or not to treat? *N Engl J Med*. 1995; 333: 1562–63.
- Chopra IJ. Euthyroid sick syndrome: is it a misnomer? *J Clin Endocrinol Metab*. 1997; 82: 329–334.
- Lervasi G, Pingitore A, Patrizia L, et al. Low-FT3 Syndrome. *Circulation*. 2003 Feb 11; 107(5): 708–13.
- Zargar A H, Ganie M A, Masoodi S R, et al. Prevalence and pattern of sick euthyroid syndrome in acute and chronic non-thyroidal illness—its relationship with severity and outcome of the disorder.. Pattern and prevalence of sick euthyroid syndrome in this part of the world. *J Assoc Physicians India*. 2004 Jan; 52: 27–31.
- Opasich C, Pacini F, Ambrosino N, et al. Sick euthyroid syndrome in patients with moderate-to-severe chronic heart failure. *European Heart Journal*. 1996 Dec; 17(12): 1860–6.
- Ascheim DD, Hryniewicz K. Thyroid hormone metabolism in patients with congestive heart failure: the low triiodothyronine state. *Thyroid*. 2002 Jun; 12(6): 511–5.
- Kozdag G, Ural D, vural A, et al. Relation between free triiodothyronine/free thyroxine ratio, echocardiographic parameters and mortality in dilated cardiomyopathy. *European Journal Of Heart Failure*. 2005 Jan; 7(1): 113–8.
- Saurav S, Singh A, A.Debnath, et al. Prevalence of Low FT3 syndrome and its association with severity in patients of Chronic heart failure: A hospital based study. *The Journal of the Association of Physicians of India*. 2014 Feb 20; 8(1): 251–57.
- Pingtore A, Landi P, Taddei M C, et al. Triiodothyronine levels for risk stratification of patients with chronic heart failure. *Am. J. Med*. 2005 Feb; 118(2): 132–6.
- Shilpa D, Walvi U. Sick Euthyroid Syndrome In Acute Myocardial Infarction Sick Euthyroid Syndrome In Acute Myocardial Infarction And Its Correlation With Left Ventricular Function. *N/MS*. 2014; 3(1): 7–13.
- Lymvaivos I, Mourouzis I, Xinaris C, et al. Thyroid hormone and recovery of cardiac function in patients with acute myocardial infarction: A strong association ? *Eur J Endocrinol*. 2011; 165(1): 107–114.