International Journal of Research in Medical Sciences
Hiremath A et al. Int J Res Med Sci. 2024 Jun;12(6):1976-1981
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20241544

Original Research Article

An observational study of association of thyroid dysfunction and heart failure in a tertiary care centre

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Received: 29 March 2024
Revised: 06 May 2024
Accepted: 15 May 2024

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ABSTRACT

Background: Heart failure (HF) is becoming leading problem in world now a days. Thyroid hormone has been proven to influence physiologic functions of cardiovascular system in many ways. HF presents a clinical challenge, with thyroid dysfunction emerging as a significant comorbidity, affecting prognosis and management. Approximately 22% of patients with HF have been demonstrated to have thyroid dysfunction. Clinical studies were confirmed that the patients with sub-clinical hypothyroidism had high risk of cardiovascular disease due to increased low density lipoprotein, elevated homocystein, hypercoagulative blood. In this study, we aim to evaluate association between sub-clinical hypothyroidism and HF to know its clinical significance.
Methods: An observational study conducted over three months on 70 diagnosed HF patients admitted in tertiary care hospital, evaluating history, clinical profile and demographics, HF types, comorbidity, and screened for thyroid function.
Results: Thyroid dysfunction prevalence among HF patients was 27.14%, with subclinical hypothyroidism being most common. Treatment led to significant improvements in symptoms and cardiac function.
Conclusions: There is significant correlation between thyroid dysfunction and HF with Subclinical hypothyroidism can be independent risk factor for HF. Timely and early recognition and management of thyroid dysfunction in HF patients are crucial for prognosis enhancement. Early intervention holds promise for improved outcomes in HF management.

Keywords: HF, Thyroid dysfunction, Observational study, Prognosis, Treatment outcomes

INTRODUCTION

According to European society of cardiology (ECS), HF is a clinical syndrome with symptoms and/or signs caused by structural and/or functional cardiac abnormality and corroborated by elevated natriuretic peptide (NT pro BNP) levels. It is rapidly growing in developed and developing countries with major cause of morbidity and mortality worldwide.[1]

In recent years prevalence of thyroid dysfunction is increased in patients of HF.[2] Epidemiological studies have also found an association between thyroid dysfunction and dyslipidemia, increased insulin resistance, and hypertension-components of metabolic syndrome, increased heart rate, systolic dysfunction of left ventricle, endothelial dysfunction, oxidative stress, increased vascular stiffness leading to HF which signifies that thyroid dysfunction is a well-established independent but modifiable risk factor for HF.[3] In this sub-clinical hypothyroidism is more common than other thyroid dysfunction. Sub-clinical hypothyroidism with TSH ≥10 mIU/L are associated with high morbidity and mortality among HF patients.[4] This study aims in studying correlation of thyroid dysfunction and HF and its impact on outcome and improvement with treatment.

Aim

Aim of the study was to study the association of thyroid dysfunction and HF and its outcomes.

Objectives

Objectives were to study thyroid dysfunction in diagnosed HF patients, to study association of thyroid dysfunction and HF and to study outcomes of HF after treating underlying thyroid dysfunction.

METHODS

Study site

It was an observational study, conducted at medicine OPD, wards and ICU in RCSM GMC and CPR hospital Kolhapur (Tertiary care hospital).

Study period

Study carried out for 3 months (From January 2023 to March 2023).

Study population

Diagnosed HF patients were included in study sample size 70 patients.

All 70 patients of diagnosed HF were evaluated in terms of demographic characteristics, cause and kind of HF and screened for thyroid dysfunction with help of thyroid function test. Based on results, effects and association between thyroid dysfunction and HF were studied and compared using t test, chi square tests as appropriate. Patients in this study group were matched for age, sex and other co morbidities.

Inclusion criteria

Patients of both sexes diagnosed as HF except congenital heart disease/ valvular heart disease and patient willing to participate in the study were included.

Exclusion criteria

Patients not willing to participate in study, patients who were receiving concurrent treatment with drugs contributing to thyroid dysfunction lithium, amiodarone, sulphonylureas, glucocorticoids, etc.) and patients on treatment of thyroid disorder were excluded from study.

Statistical analysis

Done using IBM SPSS version 20.0 Null hypotheses were formed for each variable and tested with the z scores to find p values and a $p<0.05$ was considered to be statistically significant. Informed verbal consent was taken.

RESULTS

As shown in Table 1, among 70 patients mean age of presentation was 60±11 years with male predominance that is 41 (58.57%) patients. Mean BMI among study population was 28.7 kg/m^2.

Table 1: Demographic characteristics of patients in this study population.

Variables	N (%)
No. of patients	70
Age (in years), mean (SD)	60±11
Male patients	41 (58.57)
Female patients	29 (41.42)
BMI, mean (kg/m^2)	28.7

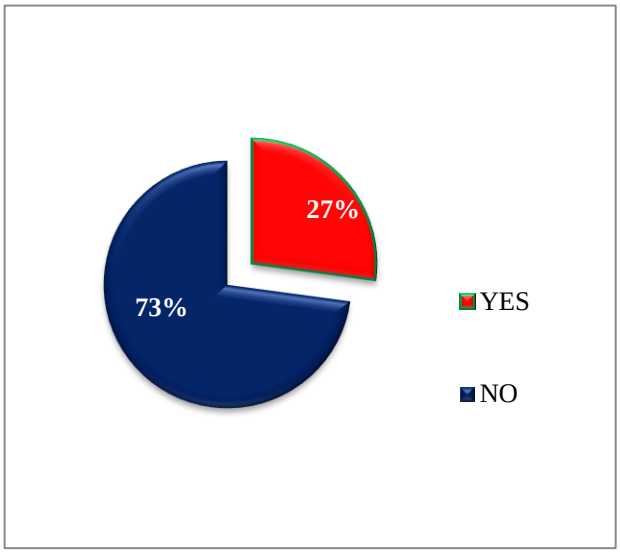

Figure 1: Number of patients with thyroid dysfunction.

As mentioned in Figure 1, among total 70 patients with HF, 27% (19) patients had thyroid dysfunction

Table 2: Frequency of types of thyroid dysfunction among study population.

Types of thyroid dysfunction	N (%)
Subclinical hypothyroidism	8
Overt hypothyroidism	5
Low T3	2
Overt hyperthyroidism	4
Subclinical hyperthyroidism	-
Total	19 (27.14)

As per Table 2, out of 19 patients with thyroid dysfunction, most of patients had sub-clinical hypothyroidism (8) followed by over hypothyroidism, overt hyperthyroidism.

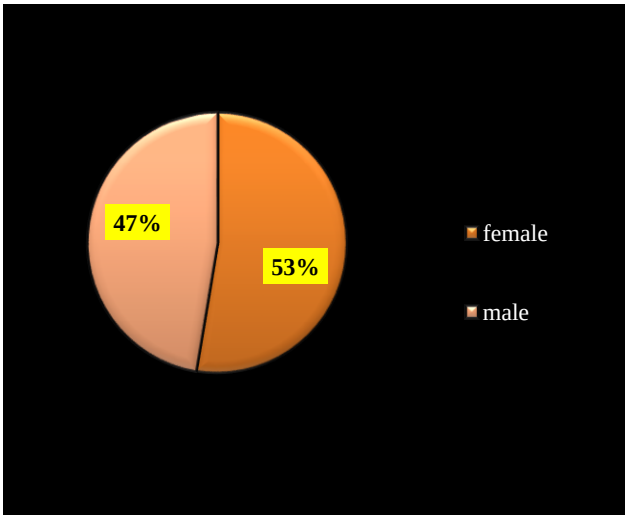

Figure 2: Distribution according to gender in patients with thyroid dysfunction.

As seen in Figure 2, there was female predominance in patients with thyroid dysfunction as compared to patients with euthyroid in this study population.

Table 3: Comorbidities in patients in this study population, (n=70).

Comorbidity	N (%)
Dyslipidaemia	37 (52.86)
Hypertension	34 (48.57)
IHD	26 (37.14)
Diabetes mellites	21 (30)

As per Table 3, among 70 patients, dyslipidaemia was most common comorbidity (37 patients that is 52.86%) followed by hypertension (34 patients that is 48.57%), IHD (37.14%), diabetes mellites (30%). Confounding factors were ruled out by matching in these study group.

As per above Table 4, which shows that low T3 syndrome has highest morbidity and mortality followed by sub-clinical hypothyroidism.

As mentioned in above Figure 3, mean TSH, FT3 and FT4 were more in patients with thyroid dysfunction as compared to euthyroid group.

As per Figure 4, among 70 patients, patients with thyroid dysfunction had more prevalence of HFrEF (58%) as compared to euthyroid group (47%). Also, patients with NYHA class 2 and 3 were more common in thyroid dysfunction group (52.6%) than euthyroid (39.1%). Diastolic dysfunction was common (36.84%) in patients with thyroid dysfunction as compared to euthyroid in which systolic dysfunction was common (84.31%).

In this study, occurrence of thyroid dysfunction among 70 patients of HF was 27.14% (19/70) mean age was 60.82±11.1 years.

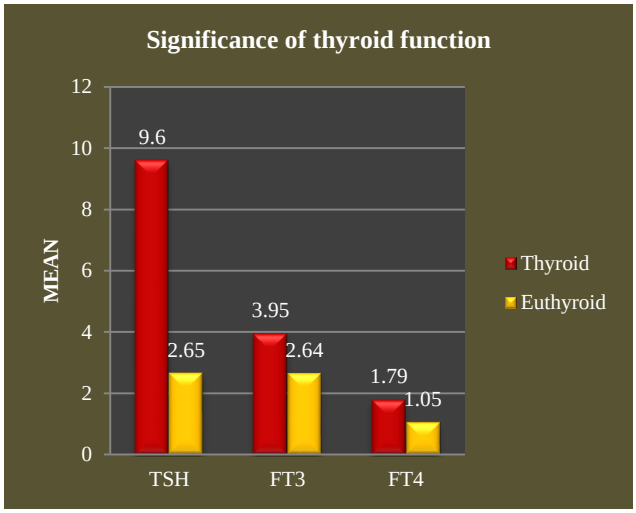

Figure 3: Comparison of thyroid profile in patients in this study population among thyroid and euthyroid patients.

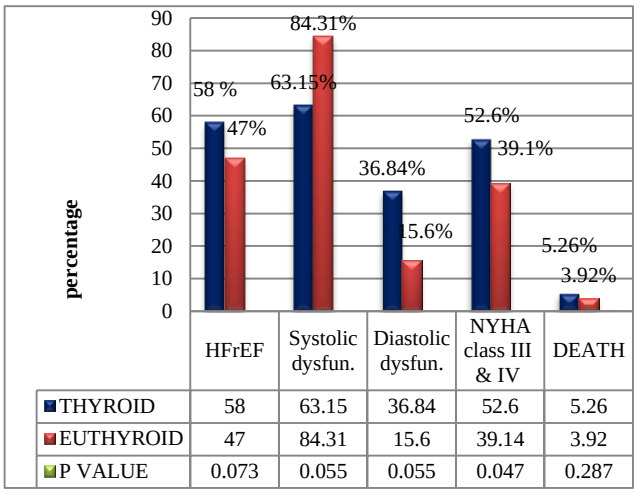

Figure 4: Complications among thyroid and euthyroid patients in this this study population.

Regarding gender distribution there is male predominance (58.57%) in total HF patients and female predominance (52.64%) in patients with thyroid dysfunction and HF patients.

Most of patients had subclinical hypothyroidism (11.4%) followed by overt hypothyroidism (7.12%) followed by overt hyperthyroidism and low T3. Among these, patients with TSH ≥7 and low T3 had increased morbidity.

Most of the patients had HFrEF (50%) and NYHA class III/IV (42.85%). Also, the percentage of HFrEF (58%) and NYHA class III, IV (52.6%) and mean NT pro-BNP (3195.105) is greater among patients with thyroid dysfunction as compared to euthyroid and total patients.

Compared with HFpEF patients with euthyroidism, those with Subclinical hypothyroidism had increased levels of NT pro BNP that is 3195.105 and 2252.96 respectively.

Table 4: Clinical and demographic presentation of patients among different types of thyroid dysfunction.

Parameters	Subclinical hypothyroidism	Overt hypothyroidism	Low t3	Overt hyperthyroidism
N	8	5	2	4
Mean age (in years)	60	61	69	60
Sex (M:F)	3:5	3:2	1:1	1:3
Symptoms	2/8 (25%)	5/5 (100%)	1/2 (50%)	4/4 (100%)
Mean EF	38%	38%	30%	41.2%
NYHA class III, IV	4/8 (50%)	2/5 (40%)	2/2 (100%)	2/4 (50%)
>1 admissions	2/8 (25%)	-	1/2 (50%)	-
Death	-	-	1	-

Table 5: Comparison between patients with thyroid dysfunction and euthyroid patients in this study population.

Parameter	Thyroid disorder, n=19 (%)	Euthyroid, n=51 (%)	Total, n=70 (%)	P value
Age (Mean±SD) (in years)	60.2±10.05	61.05±11.55	60.82±11.1	0.7784
Gender				
Male	9 (47.36)	32 (62.74)	41/70 (58.5)	0.2454
Female	10 (52.64)	19 (37.26)	29/70 (41.2)	
BMI (Mean ± SD)	28.2±3.32	26.8±1.30	27.19±2.12	0.0135
TSH (Mean ± SD)	9.66±9.01	2.65±1.27	4.54±5.6	0.000001
FT3 (Mean ± SD)	3.95±4.25	2.64±0.55	2.99±2.29	0.0326
FT4 (Mean ± SD)	1.79±2.19	1.05±0.21	1.26±1.18	0.0196
EF (Mean ± SD)	36.57±8	40.8±9.88	39.7±9.55	0.09385
HFrEF	11 (58)	24 (47.07)	35 (50)	
HFMrEF, HFPrEF	8 (32.6)	27 (52.9)	35 (49.9)	
NTpro BNP	3195.105	2252.96	2724.032	
Systolic dysfunction	12 (63.15)	43 (84.31)	56 (80)	0.05507
Diastolic dysfunction	7 (36.8)	8 (15.6)	14 (20)	
NYHA class I and II	9 (47.3)	31 (60.31)	40 (57.1)	
NYHA class III and IV	10 (52.6)	20 (39.1)	30 (42.8)	0.472
H/o >1 admission	3/19 (15)	6/51 (11.76)	9	
Death	1 (5.26)	2 (3.92)	3 (4.28)	0.2875

Diastolic dysfunction was common among the patients of HF as compared to systolic dysfunction in HF with euthyroid patients.

Outcome of these patients improved after treating the underlying thyroid dysfunction.

Treatment

Emergency management of HF. Treatment of underlying thyroid dysfunction in all the patients regardless of symptoms except in low T3 patients. Among the 19 patients, 8 patients came for follow up after 3 months, improvement is seen in terms of symptoms, heart rate, ejection fraction, Nt pro BNP levels after treatment of thyroid dysfunction.

DISCUSSION

Current global prevalence of HF is almost 65 million cases with 29% mod, 19% intermediate and 51% were severe HF. In recent years prevalence of thyroid dysfunction is increased in patients of HF.[5]

Euthyroidism was defined as a TSH level of 0.45 to 4.49 mIU/L. Subclinical hypothyroidism as a TSH level of 4.5 to 19.9 mIU/l with normal FT4 and T3 levels with or without symptoms. Subclinical hypothyroidism was subdivided into 3 groups: TSH of 4.5 to 6.9, 7.0 to 9.9, and 10.0 to 19.9 mIU/l. Overt hypothyroidism is increased TSH and low FT4. Low T3 syndrome-euthyroid sick syndrome/ Non thyroidal illness syndrome- decreased TT3 and hyperthyroid-low TSH and increased T3 and/ or T4.[6]

There are multiple mechanisms through which thyroid hormones affect cardiovascular function. Thyroid hormones bind to thyroid hormone receptor-α in cardiac myocytes to regulate gene expression. Specific effects include upregulation of myosin heavy chain-α and downregulation of myosin heavy chain-β to affect the contractile apparatus, regulation of calcium cycling through induction of SERCA2a and downregulation of

phospholamban, and enhancement of adrenergic responsiveness through upregulation of the β1-adrenergic receptor. Interestingly, the absence of thyroid hormone also affects transcription of thyroid hormone-responsive genes, because of repression of these genes by thyroid hormone receptor when ligand is absent.[7]

In addition, thyroid hormones exert multiple nongenomic effects on the cardiomyocyte by directly binding to specific targets, including ion channels on cell and mitochondrial membranes. Thyroid hormones stimulate vasodilation through increasing nitric oxide production in vascular smooth muscle and calcium reuptake in arterioles, leading to decreased coronary vascular tone and decreased systemic vascular resistance.[8] In total, thyroid hormone deficiency causes decreased contractility, increased systemic vascular resistance, and bradycardia, whereas thyroid hormone excess causes increased contractility, increased blood volume from activation of the renin-angiotensin-aldosterone axis, pulmonary hypertension, and tachycardia. Our data indicate that thyroid function is a key prognostic indicator in patients with preexisting HF.[9]

In the study, the relationship between thyroid dysfunction and HF was explored, providing valuable insights into how thyroid health can impact cardiac function. This investigation found that approximately 27% of HF patients exhibited thyroid dysfunction, primarily subclinical (42.11%) and overt hypothyroidism. This correlates with study done by Mohamud et al in which there was also subclinical hypothyroidism was more common (33.3%) among thyroid dysfunction.[10]

These forms of thyroid dysfunction were associated with increased morbidity, particularly in the presence of elevated TSH and low T3.[11]

Patients with HF and thyroid dysfunction experienced worse cardiac outcomes compared to euthyroid patients. This was evidenced by higher NT-proBNP levels, more frequent occurrences of HF with reduced ejection fraction (HFrEF), and an increased prevalence of NYHA class III/IV. This correlates with study done by Yadav et al where also patients with thyroid dysfunction had more morbidity in terms of HF, NT pro BNP levels, NYHA grading.[11,12]

Subclinical hypothyroidism, the most common form of thyroid dysfunction, presented notable risks for HF patients. Low T3 syndrome was linked to the highest rates of morbidity and mortality among the different types of thyroid dysfunction. The data indicates that treating thyroid dysfunction in HF patients can improve clinical outcomes.[13]

These findings align with existing literature suggesting that thyroid hormones play a critical role in cardiovascular function. For instance, thyroxine (T4) and triiodothyronine (T3) have been shown to influence cardiac contractility, heart rate, and blood pressure Klein and Danzi.[14] Consequently, disruptions in thyroid function may exacerbate HF progression.[15]

Limitations

It is important to note that these observations are based on small sample size and may not be generalized to large population.

CONCLUSION

This study suggests that thyroid dysfunction is a heterogeneous entity with varying risk of HF. The study underscores the need for routine thyroid function screening in HF patients. It supports the potential benefits of early intervention and treatment of thyroid dysfunction to manage HF more effectively. Integrating thyroid management into HF care protocols may improve patient outcomes. Significance lies in timely recognition of thyroid dysfunction and must be mandatory because prognosis of HF improves with early detection and appropriate treatment of underlying thyroid dysfunction.

ACKNOWLEDGEMENTS

Authors would like to thank to all teaching and non-teaching staff of department of medicine in RCSM GMC and CPR hospital Kolhapur for encouraging me to do this research.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Hiremath A, Barge V, Bafna V, Paritekar A. An observational study of association of thyroid dysfunction and heart failure in a tertiary care centre. Int J Res Med Sci 2024;12:1976-81.