Original Article

# Frequency of Subclinical Hypothyroidism in Patients with Acute Decompensated Heart Failure

Subclinical Hypothyroidism with Heart Failure

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## ABSTRACT

**Objective:** To Determine the frequency of subclinical hypothyroidism in acute decompensated heart failure patients.
**Study Design:** Descriptive Cross-Sectional Study
**Place and Duration of Study:** This study was conducted at the Cardiology Department, DHQ Teaching Hospital, Bannu over a period of 12 months from August 2018 to July 2019.
**Materials and Methods:** One hundred and seventy-eight (n=178) adult patients above eighteen years of age admitted to cardiology department with acute decompensated heart failure (ADHF) were enrolled in the study. All the patients were evaluated for subclinical hypothyroidism (SH) through lab investigations and frequency of SH was estimated.
**Results:** A Total of 178 patients with ADHF were evaluated for SH, out of which 61.8% (n=110) were male and 38.2% (n=68) were females. Mean age of patients was 54.4±12.3 years. The mean TSH, Free T4 and LVEF (%) were 3.6± 2.91, 1.3±0.3 and 35.9±4.8, respectively. Subclinical hypothyroidism was present in 25.8% (n=46) of patients. The most frequent 28.9% (n=26) age group was 18-50 yrs. and majority of them were female 26.5% (n=18) patients. SH was more frequently 28.7% (n=39) found in patients having LVEF <35% with no statistical significance (p=0.12).
**Conclusion:** Subclinical hypothyroidism was frequently (almost 1/4$^{th}$) determined in patients admitted with acute decompensated heart failure. We recommend screening of all the patients presenting with ADHF on routine basis.
**Key Words:** Acute decompensated heart failure (ADHF), sub clinical hypothyroidism (SH)

**Citation of article: Shah S, Khan S, Khan MN, Mohammad R, Iqbal S, Khan MN. Frequency of Subclinical Hypothyroidism in Patients with Acute Decompensated Heart Failure. Med Forum 2021;32(8):91-95.**

## INTRODUCTION

Acute decompensated cardiac failure is a frequently observed phenomenon in patients presenting with acute respiratory embarrassment and characterized by sudden onset shortness of breath due to filling of pulmonary interstitial and alveolar spaces with fluid.[1] Thyroxine is a hormone produced by thyroid gland having a prominent role in controlling heart rate, systemic vascular resistance and contractility. Hyperactive functioning or hypoactive thyroid gland can lead to potentiation of heart failure (HF) manifestations.[2]

It has recently been reported that subclinical hypothyroidism is associated with atherosclerosis,[3] development of HF,[4] and cardiovascular death.[5] Though it is less symptomatic and not associated with mobility problems,[6] but seems to be associated with cardiac function, exercise capacity, and hemodynamic parameters. However, little is known about the clinical effect of sub-hypo on HF patients.

Hayashi T, et al observed 21% subclinical hypothyroidism in patients admitted with heart failure, 2% subclinical hyperthyroidism, and 35% had low-T3 syndrome. Furthermore, there was poor survival rate with escalated risk of cardiac events amongst subclinical hypothyroid patients.[7] Khan MA, et al reported 9.42% Subclinical hypothyroidism in Pakistan[8].

It was also observed in a study that levothyroxine replacement therapy in patients who do not have accompanying heart failure decreases systemic vascular resistance and mortality; increases cardiac contractile force and hence stroke volume.[9] However, the effect of subclinical hypothyroidism on heart failure prognosis is yet to be determined and whether treatment with thyroxine in SH having heart failure improves the

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Received: March, 2021
Accepted: May, 2021
Printed: August, 2021

prognosis is still controversial and needs further research.[10]

In a recent study, no benefit in terms of cardiac events, quality of life and mortality following levothyroxine therapy reported in elderly patients.[11] Frey et al. reported that about 4.6% heart failure patients had evidence of SH but treatment of subclinical hypothyroidism with thyroxin did not lessen cardiac hospitalization or death.[12]

Several studies have shown that subclinical hypothyroidism affects the prognosis in heart failure patients, and evidence is in favor of screening for subclinical hypothyroidism in these patients at presentation.[1,12]

Hence, our study is structured to estimate frequency of SH in patients presenting with ADHF in our local population. Currently, it is not suggested to perform routine screening for subclinical hypothyroidism in acute heart failure patients. If we find a frequent number of patients with SH in our ADHF population, screening of all the patients presenting with ADHF would be recommended on routine basis**.**

# MATERIALS AND METHODS

This is descriptive cross-sectional study conducted at cardiology department, DHQ Teaching Hospital, Bannu from 17th august 2018 to 16th July 2019. One hundred and seventy-eight (n=178) adult patients over 18 years of age admitted to cardiology department with acute decompensated heart failure were enrolled in the study. Sample size was calculated using WHO Sample Size Calculator taking 95% confidence interval. Non-probability Consecutive sampling technique was used. Patients included in the study were having acute decompensated heart failure aged 18 to 70 years and of both genders. Patients excluded from the study were those taking levothyroxine, amiodarone, anti-thyroid medication, patients with a history of radioiodine therapy, pregnant and lactating women.

Hospital ethics committee granted approval for the study. Informed written consent was obtained by all the participants. After enrollment, details of illness and demographic profile of the patients were recorded. Biochemical measurements (TSH and Serum free T4) were done at the time of presentation. The researcher maintained data quality and compliance to the study protocol conducted all the study procedures and data collection. All the obtained data was recorded on the Performa. Data was analyzed through SPSS version 19.0. The numerical data like age, BMI (calculated as defined in operational definitions), LVEF, TSH and FT4 were presented as mean and standard deviation while the categorical data like gender, comorbidities (hypertension, diabetes, dyslipidemia and atrial fibrillation) and subclinical hypothyroidism were expressed as frequency and percentage. Effect modifiers like age, gender, BMI (calculated as defined in operational definitions), comorbidities (hypertension, diabetes, dyslipidemia & atrial fibrillation) and LVEF were controlled by stratification. Post stratification chi square test was applied and *P*-value $\leq$ 0.05 considered as significant.

# RESULTS

A Total one hundred and seventy-eight (n=178) patients were evaluated as a diagnosed cases of acute decompensated heart failure (ADHF) for this study on predesign research proforma. Mean age was 54.4 ±12.3 (18 to 70) years. Male (61.8%) to female (38.2%) ratio was 1.6. The mean TSH, Free T4 and LVEF (%) were 3.6± 2.91, 1.3±0.3 and 35.9±4.8, respectively. Demographic, anthropometrics, clinical and laboratory parameters are tabulated in table 01.

**Table No.1: Distribution of demographic, anthropometric, clinical and laboratory parameters**

| Variables | Mean | Std. Deviation |
|---|---|---|
| **Age (years)** | 54.4 | 12.3 |
| **Lvef (%)** | 35.9 | 4.8 |
| **Height (meters)** | 1.8 | 0.1 |
| **Weight (kg)** | 74.1 | 10.3 |
| **Bmi (kg/m$^2$)** | 22. 5 | 4.1 |
| **Ft4 (ng/dl))** | 1.3 | 0.3 |
| **Tsh (miu/l))** | 3.6 | 2.9 |

Frequency of subclinical hypothyroidism was 25.8% (n=46) and the most frequent 28.9% (n=26) age group was 18-50 yrs. and majority of them were female 26.5% (n=18) patients. Sub clinical hypothyroidism was more frequently 28.7% (n=39) present with patients having LVEF <35% though it was not statistically significant (p=0.12) Frequency of age groups, baseline LVEF, BMI and subclinical hypothyroidism is illustrated in Figure 01. The most frequent risk factor for heart failure was HTN 26.4% (n=32). Frequency of Risk factors like hypertension, diabetes, dyslipidemia and atrial fibrillation are described in table 2.

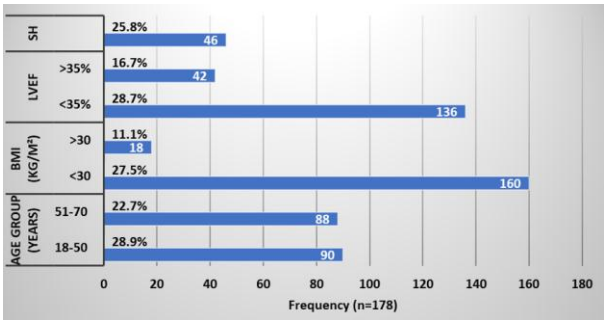


**Figure No.1: Frequency of age groups, BMI, LVEF and Subclinical hypothyroidism**

There was no statistical significant difference in frequency of SH across different effect modifiers (P>0.05 in all cases) as outlined in table 3.

Abbreviations; BMI: Body Mass Index, LVEF: Left Ventricular Ejection Fraction, SH: Subclinical hypothyroidism

**Table No.2: Frequency of different comorbidities and their stratification with Subclinical hypothyroidism**

| Comorbidities | | Subclinical hypothyroidism | | Total | P-value chi-Square |
|---|---|---|---|---|---|
| | | Present | Absent | | |
| Hypertension | Present | 32 | 14 | 46 | 0.789 |
| | | 26.4% | 24.6% | 25.8% | |
| | Absent | 89 | 43 | 132 | |
| | | 73.6% | 75.4% | 74.2% | |
| | Total | 121 | 57 | 178 | |
| | | 100.0% | 100.0% | 100.0% | |
| Diabetes | Present | 19 | 27 | 46 | 0.895 |
| | | 25.3% | 26.2% | 25.8% | |
| | Absent | 56 | 76 | 132 | |
| | | 74.7% | 73.8% | 74.2% | |
| | Total | 75 | 103 | 178 | |
| | | 100.0% | 100.0% | 100.0% | |
| Dyslipidemia | Present | 10 | 36 | 46 | 0.586 |
| | | 22.7% | 26.9% | 25.8% | |
| | Absent | 34 | 98 | 132 | |
| | | 77.3% | 73.1% | 74.2% | |
| | Total | 44 | 134 | 178 | |
| | | 100.0% | 100.0% | 100.0% | |
| Atrial fibrillation | Present | 27 | 19 | 46 | 0.750 |
| | | 25.0% | 27.1% | 25.8% | |
| | Absent | 81 | 51 | 132 | |
| | | 75.0% | 72.9% | 74.2% | |
| | Total | 108 | 70 | 178 | |
| | | 100.0% | 100.0% | 100.0% | |

**Table No.3: Subclinical hypothyroidism (stratification with respect to age, gender, BMI and LVEF)**

| Demographic, Anthropometrics, clinical parameter | | Subclinical Hypothyroidism | | Total | p-value chi-square |
|---|---|---|---|---|---|
| | | present | absent | | |
| Age Groups (years) | 18-50 (years) | 26 | 64 | 90 | 0.348 |
| | | 28.9% | 71.1% | 100.0% | |
| | 51-70 (years) | 20 | 68 | 88 | |
| | | 22.7% | 77.3% | 100.0% | |
| Gender | Male | 28 | 82 | 110 | 0.880 |
| | | 25.5% | 74.5% | 100.0% | |
| | Female | 18 | 50 | 68 | |
| | | 26.5% | 73.5% | 100% | |
| BMI | <30 kg/m$^2$ | 44 | 116 | 160 | 0.132 |
| | | 27.5% | 72.5% | 100% | |
| | >30 kg/m$^2$ | 02 | 16 | 18 | |
| | | 11.1% | 88.9% | 100% | |
| LVEF | <35% | 39 | 97 | 136 | 0.120 |
| | | 28.7% | 71.3% | 100% | |
| | >35% | 07 | 35 | 42 | |
| | | 16.7% | 83.3% | 100% | |

# DISCUSSION

Hypothyroidism is a commonly encountered clinical condition with variable prevalence.[13] Effect of thyroid hormones on heart contractility, coronary vessels and the prognosis of SH in heart failure patients has recently been a topic of discussion and research. Symptomatic SH patients suffer from reduced exercise tolerance, and delay in relaxation phase of left ventricle might gravely hamper filling phase of ventricle during exercise leading to left ventricular systolic dysfunction.[14] Several studies have also shown that subclinical hypothyroidism affects the prognosis in heart failure patients, and evidence is in favor of screening for subclinical hypothyroidism in these patients at presentation.[1,9] Our results showed that there were 25.8% (n=46/178) of patients in the study sample who were diagnosed with SH as per our operational definition. The most frequent 28.9% (n=26) age group was18-50 yrs with little female 26.5% (n=18) vs 25.5% (n=28), predominance thought insignificant (p=0.88).

There was no statistical significant difference in frequency of SH across different effect modifiers like gender, age, BMI, baseline LVEF and baseline comorbidities (P>0.05 in all cases).

Our results are similar with other studies on the subject**.** In a recent study, Hayashi T, et al assessed the prevalence and prognostic effect of subclinical hypothyroidism in acute decompensated cardiac failure patients. According to their findings, about 69% patients admitted with ADHF were euthyroid, 21% were having evidence of subclinical hypothyroidism and 35% had low T3 syndrome. Survival rate was reported as poor along with increased frequency of cardiovascular events.[10]

In a local study, Ullah A, et al found that about 3.98 % adult patients aged more than 15 years admitted with congestive heart failure had subclinical hypothyroidism with males affected predominantly and those with age < 60 years.[15]

According to a study conducted by Mahal S and her colleagues, exceptionally high percentage (51%) of patients admitted with ADHF had biochemical SH with history of repeated admissions in 31% of cases (P < .001). There was no significant increase in SH patients in terms of morbidity and mortality.[16] Although we did

not assess the effect of SH on patient's outcome in the present study due to time constraints, yet we suggest future studies in this direction. According to another study, 8.1% patients with ADHF suffered from subclinical hypothyroidism and 2.6% from subclinical hyperthyroidism.[17] Nanchen D, et al reported the occurrence of subclinical hypothyroidism in ADHF around 1.4%.[18]

Several studies have demonstrated that levothyroxine therapy in elderly patients with SH can improve left ventricular function and reduce the rate of hospitalizations in these patients.[19-23] We recommended further clinical trials to evaluate the role of levothyroxine in CHF patients on rate of hospitalizations and mortality in our population.

# CONCLUSION

Sub clinical hypothyroidism was frequently observed in patients admitted with acute decompensated heart failure.

**Recommendation:** We recommend further multicenter research trial to confirm it on large number of patients so that routine screening SH in patients presenting with ADHF could be suggested.

**Author's Contribution:**

| | |
|---|---|
| Concept & Design of Study: | Sadullah Shah |
| Drafting: | Samiullah Khan, Muhammad Niaz Khan |
| Data Analysis: | Raza Mohammad, Sunehra Iqbal, Muhammad Nadeem Khan |
| Revisiting Critically: | Sadullah Shah, Samiullah Khan |
| Final Approval of version: | Sadullah Shah |

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

# REFERENCES


1. Ware LB, Matthay MA. Clinical practice.Acute pulmonary edema. N Engl J Med 2005;353:2788-9.
2. Sato Y, Yoshihisa A, Kimishima Y, Kiko T, Watanabe S, Kanno Y. Subclinical hypothyroidism is associated with adverse prognosis in heart failure patients. Canadian J Cardiol 2018;34:80e87.
3. Bernadette Biondi, David S. Cooper, The Clinical Significance of Subclinical Thyroid Dysfunction. *Endocrine Reviews 2008;*29(1)76–131.
4. Gencer B, Collet TH, Virgini V, et al. Subclinical thyroid dysfunction and the risk of heart failure events: an individual participant data analysis from 6 prospective cohorts. Circulation 2012;126:1040-1049.
5. Tseng FY, Lin WY, Lin CC, et al. Subclinical hypothyroidism is associated with increased risk for all-cause and cardiovascular mortality in adults. J Am Coll Cardiol 2012; 60:730-737.
6. Simonsick EM, Newman AB, Ferrucci L, et al. Subclinical hypothyroidism and functional mobility in older adults. Arch Intern Med 2009;169:2011-2017.
7. Hayashi T, Kanzaki H, Funada A, Amaki M, Takahama H. Subclinical hypothyroidism is an independent predictor of adverse cardiovascular outcomes in patients with acute decompensated heart failure. ESC Heart Failure 2016;3:168–76.
8. Khan MA, Ahsan A, Rehman UL, Jabeen R, Saad Farouq F. Subclinical Hypothyroidism: Frequency, clinical presentations and treatment indications. Pak J Med Sci 2017;33(4):818–22.
9. Peeters RP. Subclinical hypothyroidism. N Engl J Med 2017;376:2556-65.
10. Chaker L, van den Berg ME, Niemeijer MN. Thyroid function and sudden cardiac death: a prospective population-based cohort study. Circulation 2016;134:713-22.
11. Stott DJ, Rodondi N, Kearney PM, Ford I, Westendorp RGJ, Mooijaart SP. Thyroid hormone therapy for older adults with subclinical hypothyroidism. N Engl J Med 2017;376:2534-44.
12. Frey A, Kroiss M, Berliner D. Prognostic impact of subclinical thyroid dysfunction in heart failure. Int J Cardiol 2013;168:300-5.
13. Udovcic M, Pena RH, Patham B, Tabatabai L, Kansara A. Hypothyroidism and the Heart. Methodist Debakey Cardiovasc J 2017;13:55-9.
14. Brenta G, Mutti LA, Schnitman M, Fretes O, Perrone A, Matute ML. Assessment of left ventricular diastolic function by radionuclide ventriculography at rest and exercise in subclinical hypothyroidism, and its response to L-thyroxine therapy. Am J Cardiol 2003;91:1327–30.
15. Ullah A. Subclinical hypothyroidism and hyperthyroidism in patients with congestive heart failure. Khyber Med Univ J 2013;5:137-40.
16. Mahal S, Datta S, Ravat V, Patel P, Saroha B, Patel RS. Does Subclinical Hypothyroidism Affect Hospitalization Outcomes and Mortality in Congestive Cardiac Failure Patients?. Cureus 2018;10:e2766.
17. Gencer B, Collet T, Virgini V, Bauer DC, Gussekloo J, Cappola AR, et al. Subclinical Thyroid Dysfunction and the Risk of Heart Failure Events An Individual Participant Data Analysis From 6 Prospective Cohorts. Circulation 2012;126:1040-9.
18. Nanchen D, Gussekloo J, Westendorp RG, Stott DJ, Jukema JW, Trompet S, et al. Subclinical thyroid dysfunction and the risk of heart failure in older persons at high cardiovascular risk. J Clin Endocrinol Metab 2012;97:852-61.

19. Monzani F, Di Bello V, Caraccio N, Bertini A, Giorgi D, Giusti C, et al. Effect of levothyroxine on cardiac function and structure in subclinical hypothyroidism: a double blind, placebo-controlled study. J Clin Endocrinol Metab 2001;86:1110-5.
20. Arem R, Rokey R, Kiefe C, Escalante DA, Rodriguez A. Cardiac systolic and diastolic function at rest and exercise in subclinical hypothyroidism: effect of thyroid hormone therapy. Thyroid 1996;6:397-402.
21. Brenta G, Mutti LA, Schnitman M, Fretes O, Perrone A, Matute ML. Assessment function by radionuclide ventriculography at rest and exercise in subclinical hypothyroidism, and its response to L-thyroxine therapy. Am J Cardiol 2003;91: 1327-30.
22. Oner FA, Yurdakul S, Oner E, Uzum AK, Erguney M. Evaluation of the effect of L-thyroxin therapy on cardiac functions by using novel tissue Doppler-derived indices in patients with subclinical hypothyroidism. Acta Cardiol 2011;66:47-55.
23. Biondi B, Palmieri EA, Lombardi G, Fazio S. Subclinical hypothyroidism and cardiac function. Thyroid 2002;12:505-10.