

# A Study of LVEF in Patients of Subclinical Thyroid Dysfunction with Heart Failure.

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## ABSTRACT

**Background:** Heart failure is clinically defined as a syndrome caused by cardiac dysfunction generally resulting from myocardial muscle dysfunction or loss. Heart failure is a leading cause of hospitalization in people older than 65. Extensive evidence indicates that the cardiovascular system responds to the minimal but persistent changes in circulating thyroid hormone levels, which are typical of individuals with subclinical thyroid dysfunction. Subclinical hypothyroidism is associated with impaired LV diastolic function and subtle systolic dysfunction and an enhanced risk for atherosclerosis and myocardial infarction. **Methods:** A total of 200 patients between age group of 45 to 75 yrs, presenting in medical emergency and medical outdoor of Guru Nanak Dev Hospital, Government Medical College Amritsar with heart failure were studied. Comparison of Thyroid Profile and LVEF was done at Baseline, 3 months and 6 months. **Results:** The change in TSH, FT3, FT4, LVEF was significant at 3 months and 6 months as compared to baseline. Changes in FT4, LVEF, were significant at 3 months and 6 months, thus signifying progression of disease and worsening of cardiac functions. **Conclusion:** In treatment group in subclinical hypothyroidism patients, after comparing the thyroid profile and 2D Echocardiography after 6 months; TSH, LVEF both have shown improvement ( $p < 0.05$ ).

**Keywords:** Subclinical Hypothyroidism, LVEF, Heart Failure, L-Thyroxine.

## INTRODUCTION

Heart failure (HF) can be defined as an abnormality of cardiac structure or function leading to failure of the heart to deliver oxygen at a rate commensurate with the requirements of the metabolizing tissues, despite normal filling pressures or only at the expense of increased filling pressures.

There are many different ways to categorize heart failure, including: left heart failure versus right heart failure or whether the abnormality is due to insufficient contraction (systolic dysfunction), or due to insufficient relaxation of the heart (diastolic dysfunction) or to both.

The main terminology used to describe HF is historical and is based on measurement of LV ejection fraction (EF). Mathematically, EF is the stroke volume which is the end-diastolic volume minus the end-systolic volume divided by the end-diastolic volume. In patients with reduced

contraction and emptying of the left ventricle i.e. systolic dysfunction, stroke volume is maintained by an increase in end-diastolic volume because the left ventricle dilates, i.e. the heart ejects a smaller fraction of a larger volume. The more severe the systolic dysfunction, the more the EF is reduced from normal and, generally, the greater the end-diastolic and end-systolic volumes. The EF is considered important in HF, not only because of its prognostic importance but also because most clinical trials selected patients based upon EF.

In clinical practice, the ECG, Plasma BNP and Echo are the gold standard for HF patients. Plasma B-Type Natriuretic Peptide (BNP) is secreted by the heart,<sup>[1,2]</sup> and the plasma concentration is elevated in left ventricular hypertrophy or dysfunction (systolic or diastolic), and particularly in those with heart failure. Trans-thoracic Echocardiography is a simple,<sup>[3]</sup> safe, and effective method for assessing cardiac structure and function.

Increased or reduced action of thyroid hormone on certain molecular pathways in the heart and vasculature causes relevant cardiovascular derangements. Thyroid hormone may exert both genomic and nongenomic effects on cardiac myocytes. The genomic effects of thyroid hormone are mediated by the transcriptional activation or

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repression of specific target genes that encode both structural and functional proteins.<sup>[4]</sup> This process begins with the entry of triiodothyronine (T3), the biologically active thyroid hormone, into the cardiomyocyte through specific transport proteins located within the cell membrane.

The American Association of Clinical Endocrinologists and the Endocrine Society together defined subclinical hypothyroidism as "a serum TSH [thyroid-stimulating hormone] concentration above the statistically defined upper limit of the reference range when serum free T4 (FT4) concentration is within its reference range." Subclinical thyroid disease has been associated with systolic and diastolic cardiac dysfunction, and small studies have shown that thyroxine replacement improved measurements of cardiac function in subjects with subclinical hypothyroidism.<sup>[5]</sup>

In another study Biondini found out that the abnormalities of LV morphology and function promptly normalize with achievement of euthyroidism and are effectively attenuated by beta-blocking drugs.<sup>[6]</sup>

Because all cardiovascular abnormalities are reversed by restoration of euthyroidism ("subclinical hypothyroidism") or blunted by beta-blockade and L-thyroxine (L-T4) dose tailoring ("subclinical hyperthyroidism"), timely treatment is advisable in an attempt to avoid adverse cardiovascular effects.

### **Aims and Objectives**

Aims and Objectives of our study were

1. To study the correlation between subclinical thyroid dysfunction and heart failure.
2. To diagnose and treat the subclinical thyroid dysfunction at the earliest in heart failure.

### **MATERIALS AND METHODS**

A total of 200 patients between age group of 45 to 75 yrs, presenting in medical emergency and medical outdoor of Government Medical College Amritsar with heart failure were studied. The detailed history and systemic examination were carried out and findings were recorded on a proforma. All required investigations including routine blood investigations, thyroid profile, ECG and 2D-echocardiography were done for each patient.

### **Exclusion criteria**

1. Patients who are already diagnosed cases of hyperthyroidism and hypothyroidism.
2. Patients taking drugs which affect the thyroid function like amiodone, lithium, interferon  $\alpha$ , radio-iodine, interleukin-2, tyrosin kinase inhibitors.
3. Patients on levothyroxine.

The heart failure was defined by Framingham Criteria for CHF.

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 20 mIU/L. Normal Free T3 levels were taken as 1.42 to 4.2 pg/ml and normal Free T4 levels as 0.8 to 2 ng/dl. The M-Mode, 2D and Doppler Echocardiographic evaluations were performed with the patient in the left lateral position with a High frequency transducer interfaced with a Titanium Sonosite Machine, in the Department of Medicine.. All data was recorded with patients in the left lateral position during end-expiratory apnea.

Comparison of Thyroid Profile and LVEF was done at Baseline, 3 months and 6 months. Data generated from the study was analyzed according to standard statistical methods and p value less than 0.05 was taken as significant.

### **RESULTS**

Two hundred heart failure patients were taken up for study with maximum, i.e. 81 (40%) in age group 55-64 yr. followed by 75(37.5%) of 65-75yr. and 44 (22%) of 55-64 yr. 114 (57%) were males and 86 (43%) were females.

Out of all the 200 patients, subclinical hypothyroidism was present in 24 (12%) of cases and Overt hypothyroidism was present in 16 (8%). We divided our study group patients of subclinical hypothyroidism in cases and controls with equal no. of patients. Cases were given Levothyroxine and controls were not. Thyroid profile and 2D Echocardiography findings were noted at baseline, 3 months and 6 months and compared in both the groups. In the study group, 64 (32%) patients had diabetes mellitus type 2, 113 (56.5%) had HTN and IHD was present in 120 (60%) of patients.

**Table 1: Thyroid Profile In The Subclinical Hypothyroidism Group In Cases And Controls**

	Thyroid Function Tests		
	TSH $\mu$ I.U (Mean $\pm$ SD) baseline	FT3 pg/ml (Mean $\pm$ SD) 3 months	FT4 ng/dl (Mean $\pm$ SD) 6 months
Cases	9.20 $\pm$ 3.03	1.94 $\pm$ 0.59	1.14 $\pm$ 0.36
Control	8.86 $\pm$ 2.34	2.32 $\pm$ 0.81	1.50 $\pm$ 0.32

The baseline mean TSH/FT3/FT4 in subclinical hypothyroidism [Table 1] cases were 9.20  $\mu$  I.U/1.94 pg/ml/1.14ng/dl and in controls were 8.86  $\mu$  I.U/2.32pg/ml/1.50ng/dl respectively. At 3 months, mean TSH/FT3/FT4 in subclinical hypothyroidism cases were 6.48 $\mu$  I.U/2.01 pg/ml/1.37ng/dl and in controls were 8.99  $\mu$  I.U/2.23pg/ml/1.43ng/dl respectively.

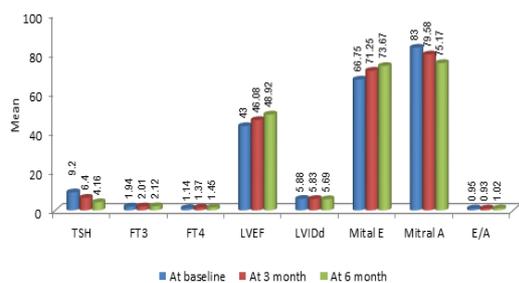
At the end of 6 months, mean TSH/FT3/FT4 in subclinical hypothyroidism cases were 4.16 $\mu$  I.U/2.12 pg/ml/1.45ng/dl and in controls were 8.98 $\mu$  I.U/2.17pg/ml/1.41ng/dl respectively.

The mean base line left ventricular ejection fraction in subclinical hypothyroidism cases was 43.42% and control was 44.17%. At 3 months, it was 46.08% in

cases and 43.58% in controls respectively. At the end of 6 months, it was 48.92% in cases and 43.25% in controls.

**Table 2: 2d Echocardiography (LVEF) In Subclinical Hypothyroidism in Cases and Controls.**

Subjects	LVEF (%) (mean±sd) Baseline	LVEF (%) (mean±sd) At 3 months	LVEF (%) (mean±sd) At 6 months
Cases	43.42±5.83	46.08±5.82	48.92±5.77
Controls	44.17±5.23	43.58±5.08	43.25±5.04



**Figure 1: Mean values comparing thyroid levels with LVEF.**

**Table 3: Significant Variables at 3&6 Months of Treatment.**

Parameter	At baseline (mean)	At 3 months (mean)	'p' value	At 6 months (mean)	'p' value
TSH (μ I.U.)	0.12	1.16	0.019	1.26	0.016
FT3(pg/ml)	2.13	1.93	0.151	1.86	0.235
FT4(ng/dl)	1.23	1.16	0.412	1.3	0.467
LVEF (%)	45.00	48.0	0.035	50	0.013

The change in TSH, FT3, FT4, LVEF was significant at 3 months and 6 months as compared to baseline. Changes in FT4, LVEF, were significant at 3 months and 6 months, thus signifying progression of disease and worsening of cardiac functions while rest of the parameter changes were not significant.

## DISCUSSION & CONCLUSION

The study was aimed to find the prevalence of subclinical thyroid dysfunction in patients of heart failure and to study the effect of treatment with Levothyroxine in subclinical hypothyroidism. In our study Out of all the 200 patients presenting with heart failure subclinical hypothyroidism and Overt hypothyroidism was present in 8%. In couple of studies done by Hollowell JG and Surks MI similar findings were observed.<sup>[7,8]</sup>

In the study group, diabetes mellitus type 2 was present in 32% of patients and hypertension was present in 56.5% of patients with underlying ischemic heart disease was present in 60% of patients. In subclinical hypothyroidism cases, after comparing the thyroid profile and 2DEchocardiography findings, after 3 months and 6

months of treatment, there was significant improvement in TSH from 9.2 to 4.16 (p 0.000), FT3 increased from 1.94 to 2.215 (p 0.000), FT4 increased from 1.94 to 2.215 (p 0.00). LVEF improved from 43% to 48.92% (p 0.06).

Our results were comparable with the study done by Mishra TK et al.<sup>[9]</sup> They found that the abnormalities of diastolic function are reversible one year after thyroxine therapy. The diastolic parameters depend upon cytosolic calcium concentration modulated by sarcoplasmic reticulum, ATP dependent calcium. Calcium transport is controlled by thyroid hormones.<sup>[10]</sup> A blunted increase in ejection fraction during exercise with clear improvement after thyroxine therapy was also reported by Forfar.

In a study done by Karki P,<sup>[11]</sup> revealed that the diastolic dysfunction was found in 15 (37.5%). Fourteen of them had impaired relaxation abnormality and only one patient had pseudonormal pattern. With replacement therapy,<sup>[13]</sup> reverted back to the normal whereas one having grade 2 diastolic dysfunction (pseudonormal pattern) reverted to grade 1. One patient who had grade 1 diastolic dysfunction (impaired relaxation) did not improve. The results were comparable with our study.

Though the results of our study were significant. It was a small study and information needs to be evaluated with larger studies in heart failure patients.

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