A Study of LVIDd in Patients of Subclinical Thyroid Dysfunction with Heart Failure

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Abstract

**Background:** Approximately 1–2% of the adult population in developed countries has Heart Failure, with the prevalence rising to ≥10% among persons 70 years or more. Most of the molecular and cellular mechanisms responsible for the cardiovascular effects of thyroid hormone have been clarified. Thyroid hormones produce changes in cardiac inotropism (contractility) or diastolic relaxation (compliance), Heart Failure, Left Ventricular Internal Diameter at Diastole (LVIDd), is done at Baseline, 3 months and 6 months. **Results:** After comparing the thyroid profile and 2DEchocardiography findings in subclinical hypothyroidism of treated group after 6 months, there was increase in TSH and fall in FT4 (p < 0.001) with a significant decrease in Mitral A velocity and increase in E/A ratio in cases as compared to controls with treatment. **Conclusion:** There was improvement in EF, a decrease in LVIDd, increase in Mitral E velocity, decrease in Mitral A velocity and increase in E/A ratio in cases as compared to controls with treatment.

**Keywords:** Subclinical Hypothyroidism, LVIDd (Left Ventricular Internal Diameter at Diastole), Heart Failure, L-Thyroxine.

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**INTRODUCTION**

In nearly all regions of the world, Heart failure (HF) is both common and on the rise [2]. There are an estimated 23 million people with HF worldwide. In developed countries, the mean age of patients with heart failure is 75 years old. In developing countries, two to three percent of the population suffers from heart failure, but in those 70 to 80 years old, it occurs in 20-30 percent.

There are many ways to categorize heart failure:

- The side of the heart involved (left heart failure versus right heart failure). Right heart failure compromises pulmonary flow to the lungs. Left heart failure compromises aortic flow to the body and brain. Mixed presentations are common; left heart failure often leads to right heart failure in the long term.
- Whether the abnormality is due to insufficient contraction (systolic dysfunction), or due to insufficient relaxation of the heart (diastolic dysfunction), or to both.

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 diagnosis of HF-PEF (Preserved EF) is more difficult than the diagnosis of HF-REF (Reduced) because it is largely one of exclusion i.e. potential non-cardiac causes of the patient’s symptoms such as anemia or chronic lung disease must first be discounted. Usually these patients do not have a dilated heart and may have an increase in LV wall thickness and increased left atrial (LA) size. Most have evidence of diastolic dysfunction, which is generally accepted as the likely cause of HF in these patients hence the term ‘diastolic HF’ [2]. In patients with LV systolic dysfunction, the maladaptive changes occurring in surviving myocytes and extracellular matrix after myocardial injury (e.g. myocardial infarction) lead to pathological ‘remodelling’ of the ventricle with dilatation and
impaired contractility, one measure of which is a reduced EF. What characterizes untreated systolic dysfunction is progressive worsening of these changes over time, with increasing enlargement of the left ventricle and decline in EF, even though the patient may be symptomless initially.

Increased or reduced action of thyroid hormone on certain molecular pathways in the heart and vasculature causes relevant cardiovascular derangements [3]. Based on a series of studies, the panel determined that the reference range for serum TSH is 0.45 to 4.50 µIU per mL (0.45 to 4.50 mU per L) [4].

In recent decades, it has emerged that subclinical thyroid dysfunction may affect the cardiovascular system in the form of impaired LV diastolic function and subtle systolic dysfunction and an enhanced risk for atherosclerosis and myocardial infarction. It is becoming increasingly apparent that acute and chronic cardiovascular disease may alter thyroid hormone metabolism and contribute to more cardiovascular impairment.

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.

**MATERIAL 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 with all required investigations including routine blood investigations, lipid profile, blood sugar level and electrolytes, thyroid profile, ECG and 2D echocardiography were done for each patient.

**Exclusion Criteria:**
- Patients who are already diagnosed cases of hypothyroidism.
- Patients taking drugs which affect the thyroid function like amiodarone, lithium, interferon α, radio-iodine, interleukin-2, tyrosine kinase inhibitors.
- 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 was 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 Department of Medicine, Medical College, Amritsar. All data was recorded with patients in the left lateral position during end-expiration apnea.

A comparison was made of Thyroid Profile and Left ventricular internal diameter in diastole 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.

**OBSERVATIONS**

Two hundred (200) heart failure patients were taken up for study at Guru Nanak Dev Hospital, Govt. Medical College, Amritsar with maximum number of patients i.e. 81 (40%) were in age group 55-64 yr, (22%) patients of patients in age group of 55-64 yr, 114 (57%) patients were male and 86 (43%) patients were female.

Cases were given Levothyroxine and controls were not given in subclinical hypothyroid dysfunction. Thyroid profile and 2D Echocardiography findings were noted at baseline, 3 months and 6 months and compared in both groups.

The baseline mean TSH/FT3/FT4 in subclinical hypothyroidism (Table-1) cases were 9.20 µI/U/1.94 pg/ml/1.14ng/dl and in controls were 8.86 µI/U/2.32pg/ml/1.50ng/dl respectively. At 3 months, mean TSH/FT3/FT4 in subclinical hypothyroidism cases were 6.48µ I/U/2.01 pg/ml/1.37ng/dl and in controls were 8.99 µ 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 µ I/U/2.12 pg/ml/1.45ng/dl and in controls were 8.98µ I/U/2.17pg/ml/1.41ng/dl respectively.

| Table-1: Thyroid Profile in the Subclinical Hypothyroidism Group in Cases And Controls |
|--------------------------------------|-----------------|-----------------|-----------------|
|                                       | **Thyroid Function Tests** |                   |                   |
|                                       | **TSH µ I.U** (Mean±SD) | **FT3 pg/ml** (Mean±SD) | **FT4 ng/dl** (Mean±SD) |
| **BASELINE**                          | **3 MONTHS**      | **6 MONTHS**     |
| **Cases**                             | 9.20±3.03        | 1.94±0.59        | 1.14±0.36        |
| **Control**                           | 8.86±2.34        | 2.32±0.81        | 1.50±0.32        |

At Baseline, Left ventricular internal diameter at diastole was 5.88 cm/sec and 5.97 cm/sec in cases and controls respectively. At 3 months, Left ventricular internal diameter at diastole was 5.83 cm/sec in cases and controls respectively.
and 5.96 cm/sec in controls. At the end of 6 months, left ventricular internal diameter at diastole was 5.69 cm/sec in cases and was 5.97 cm/sec in controls.

**Table-1: Comparison of Thyroid Profile and 2d Echocardiography in Subclinical Hypothyroidism in Cases at Baseline, 3 Months & 6 Months of Treatment**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>At baseline (mean)</th>
<th>At 3 months (mean)</th>
<th>p' value</th>
<th>At 6 months (mean)</th>
<th>p' value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH (µ IU.)</td>
<td>9.2</td>
<td>6.4</td>
<td>0.000</td>
<td>4.16</td>
<td>0.000</td>
</tr>
<tr>
<td>FT3(pg/ml)</td>
<td>1.94</td>
<td>2.01</td>
<td>0.024</td>
<td>2.12</td>
<td>0.000</td>
</tr>
<tr>
<td>FT4(ng/dl)</td>
<td>1.14</td>
<td>1.37</td>
<td>0.000</td>
<td>1.45</td>
<td>0.000</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>43.00</td>
<td>46.08</td>
<td>0.001</td>
<td>48.92</td>
<td>0.006</td>
</tr>
<tr>
<td>LVIDd(cm)</td>
<td>5.88</td>
<td>5.83</td>
<td>0.626</td>
<td>5.69</td>
<td>0.195</td>
</tr>
<tr>
<td>Mital E (cm/sec)</td>
<td>66.75</td>
<td>71.25</td>
<td>0.035</td>
<td>73.67</td>
<td>0.085</td>
</tr>
<tr>
<td>Mital A (cm/sec)</td>
<td>83.00</td>
<td>79.58</td>
<td>0.084</td>
<td>75.17</td>
<td>0.028</td>
</tr>
<tr>
<td>E/A</td>
<td>0.95</td>
<td>0.93</td>
<td>0.917</td>
<td>1.02</td>
<td>0.450</td>
</tr>
</tbody>
</table>

p value ≤0.05 was taken as significant

**Graph-1: Comparison of Thyroid Profile and 2d Echocardiography in Subclinical Hypothyroidism in Cases at Baseline, 3 Months & 6 Months of Treatment**

**DISCUSSION**

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. Subclinical hypothyroidism (SH) is a common disorder with a prevalence from 1–10% of the adult population in most community studies.

In subclinical hypothyroidism cases, after comparing the thyroid profile and 2DEchocardiography findings, after 3 months and 6 months of treatment, there was a 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 0.000), LVEF improved from 43% to 48.92%(p 0.06) and LVIDd decreased from 5.88 to 5.69 cm.

The diastolic parameters depend upon cytosolic calcium concentration; modulated by sarcoplasmic reticulum. ATP dependent calcium [5]. Calcium transport is controlled by thyroid hormones [6]. Park M et al., also found greater progression of coronary angiographic lesion in hypothyroid patients with TSH level in the range seen in subclinical hypothyroidism compared with patients whose TSH levels were assiduously maintained in the normal range.

Among various proteins whose expression is modulated at transcriptional level, the most-extensively characterized are myosin heavy chains [7] and the sarcoplasmic reticulum protein involved in the regulation of intracellular calcium handling, namely, calcium activated ATPase and its inhibitory cofactor, phospholamban. In this regard, it has been extensively demonstrated that thyroid hormone upregulates expression of the sarcoplasmic reticulum calcium-activated ATPase and downregulates expression of phospholamban, thereby enhancing myocardial relaxation [8]. Indeed, the improved calcium reuptake during diastole may favorably affect myocardial contractility. In fact, the greater reduction in cytoplasmatic concentration of calcium at end-diastole increases the magnitude of the systolic transient of
calcium that, in turn, augments its availability for activation of tropo-myosin units.

In a study done by Karki P et al., [9] 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, 13 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.

Vitale and Brentaet [10] found out that the most-consistent cardiac abnormality recognized in Subclinical Hypothyroid patients was LV diastolic dysfunction, characterized by slowed myocardial relaxation and impaired early ventricular filling, both at rest and with exercise. Often, this is associated with a variable impairment in LV systolic function at rest.

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.

REFERENCES