

## Research Article

# Study of LV functions in patients of subclinical hypothyroidism in patients coming to rural medical college of Sub-Himalayan region of India

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## ABSTRACT

**Background:** Subclinical hypothyroidism (SCH) is a common disorder and has been implicated in increased cardiovascular morbidity and mortality. Therefore, it is important to study the effect of SCH on cardiac morphology and function. Thus, present study titled "Study of LV functions in patients of subclinical hypothyroidism in patients coming to rural medical of sub-Himalayan region of India" was conducted in the department of medicine, Rajinder Prasad government medical Tanda over a period of three years from December, 2010 to November, 2013 to study left ventricular function in subclinical hypothyroidism.

**Methods:** The study was conducted in the department of medicine, Rajinder Prasad government medical Tanda over a period of three years from December, 2010 to November, 2013 to study left ventricular function in subclinical hypothyroidism. The data was analysed using computer software Epi-info version 6.0 and SPSS version 12.0 for Windows. Descriptive characteristics were presented as percentages for quantitative variables including measurement of thyroid hormones and ejection fraction. Mean and standard deviation were reported.

**Results:** Diastolic parameters were markedly altered, mainly isovolumic relaxation time, which was increased and reduction of E/A wave ratio (<1). Systolic function parameters were within normal range. 155 patients had diastolic dysfunction with E/A wave <1.45 patients were not affected and they had E/A wave >1.

**Conclusions:** Implication for echocardiography in SCH patients observed were that early recognition of silent diastolic dysfunction can be done. We can institute L-thyroxine therapy which has been found to reverse diastolic dysfunction of heart along with improvement in lipid levels, decreased systemic vascular resistance, diastolic hypertension and coagulation profile. SCH, invariably affects heart and sooner or later and leads to diastolic dysfunction. Early recognition by echocardiography and then treatment with L-thyroxine is indicated.

**Keywords:** Subclinical hypothyroidism, LV functions

## INTRODUCTION

Subclinical hypothyroidism (SCH) is a disorder characterized by normal serum T<sub>3</sub> and T<sub>4</sub> value with serum TSH levels >5 µIU (Evered et al.,<sup>1</sup> 1972). Hypothyroidism is a common disorder, with prevalence ranging from 1 to 10% among the adult population, in

most community studies. Its prevalence is up to 20% in women aged over 60 years (Gharib et al.,<sup>2</sup> 2005).

In view of minor thyroid hormone secretion impairment, it is predictable that metabolic and organ function indices of subclinical hypothyroidism will show only marginal alterations. Nevertheless, such changes may be clinically

relevant when they target organs over a period of several years. In particular, cardiovascular system is very sensitive to the effects of thyroid hormone on it (Bengal et al.,<sup>3</sup> 2000). As with overt hypothyroidism, SCH may also be associated with an increased risk of cardiovascular disease, congestive heart failure and possible all-cause mortality (Hak et al.,<sup>4</sup> 2000). Studies have revealed that over a period of time diastolic dysfunction of heart has been observed and this dysfunction is reversible if early L-thyroxine replacement therapy is given (Biondi et al.,<sup>5</sup> 1999).

Recent data suggest that SCH should not be considered a mere laboratory abnormality and may represent a well-defined, often clinically relevant disease characterized by thyroid hormone production that is persistently insufficient to maintain euthyroidism (Pinchera,<sup>6</sup> 2005). Cardiovascular system is an important target of thyroid hormone action (Biondi and Klein,<sup>7</sup> 2004) and is sensitive to slight variations in circulating thyroid hormone levels). An early event in SCH-related cardiomyopathy, evaluated by Doppler echocardiography, is the impairment of diastolic function (Biondi et al., 2002b).<sup>8</sup> The diastolic dysfunction is caused by the reduced activity of sarcoplasmic reticulum  $Ca^{2+}$ -ATPase which controls the efficient concentration of calcium in the cytoplasm within the sarcoplasmic reticulum during diastole (Biondi et al.,<sup>9</sup> 2002a). Both diastolic and systolic functions during exercise are also impaired in SCH. Monzani et al.<sup>10</sup> (2001) also reported diminished diastolic function by echocardiographic parameters in patients with SCH. To assess diastolic dysfunction in SCH, Doppler echocardiography has been used to estimate the degree of myocardial impairment in SCH. It has been found that there is significant prolongation of the isovolumic relaxation time, increased A-wave, and reduced early diastolic mitral flow velocity/late diastolic mitral flow velocity ratio. Also, systemic vascular resistance was significantly increased. All these parameters reverted to normal, when patients were put on L-thyroxine replacement therapy for six months (Biondi et al.,<sup>5</sup> 1999). High blood pressure, mainly diastolic hypertension, has been documented in 20% of SCH patients compared with 3.4% in healthy euthyroid controls (Luboshitzky et al.,<sup>11</sup> 2002). Keeping in view that this disease and its pattern has been recently identified, a lot of research its going on in this direction, for a disease which is still virgin.

Subclinical hypothyroidism is a common disorder and has been implicated in increased cardiovascular morbidity and mortality. Therefore, it is important to study the effect of SCH on cardiac morphology and function. Thus, present study titled "Study of left ventricular function in subclinical hypothyroidism" was conducted in the department of medicine, Rajinder Prasad government medical Tanda over a period of three years from December, 2010 to November, 2013 to study left ventricular function in subclinical hypothyroidism.

**Aims and objectives:** To study left ventricular function in subclinical hypothyroidism.

## METHODS

The present study was conducted in patients diagnosed as subclinical hypothyroidism (SCH) in Medicine OPDs of government medical college hospital, Tanda over a period of 3 year from December, 2010 to November, 2013. Subjects diagnosed as SCH, having TSH >5  $\mu$ IU and normal  $T_3$  and  $T_4$  concentration were taken up for study. Detailed history and clinical examination of the subjects was performed.  $T_3$ ,  $T_4$  and TSH were performed in endocrine laboratory of the RPGMC, Tanda by radio-immunoassay. Each patient underwent Doppler echocardiography, using Phillips 2-D colour Doppler machine. Standard Doppler echocardiography was performed with subjects in partial left decubitus using Phillips 2-D colour Doppler machine. M-mode quantitative analysis was performed according to the American society of echocardiography in parasternal long axis view. Endocardial fractional shortening was calculated as the percent change in LV internal dimensions between systole and diastole. Doppler velocity of LV systolic outflow track was performed by placing the sample volume close to the aortic valve. Similarly, all valve Doppler velocities were calculated according to the American Society of Echocardiography and LV parameters with systolic and diastolic function were performed. Various recognized parameters like EDV, ESV, EF, EPSS, E-wave, A-wave was calculated.

Cardiac output (liters per minute) was calculated as SV (milliliters) x heart rate (beats per minute). Pulsed Doppler LV inflow recording was performed in an apical four-chamber view by placing the sample volume at the tip level. Early (E) and atrial peak velocities (meter per second) and their ratio, E-wave deceleration time (milliseconds), isovolumic relaxation time (IVRT; milliseconds; the time interval between systolic output flow and transmitral E-wave onset, by placing the ample volume between outflow track and the mitral valve) was measured as indexes of LV global diastolic dysfunction.

## RESULTS

In our study 124 females and 36 males having SCH were studied, with females forming the bulk of the patients i.e. 72.5% as compared to the 22.5% male into. Majority of the patients fell into age group of 31-40 years. 54.8% females were in the 31-40 years age group as compared to 88.8% males. 38.7% females had BMI in the range of 25-29.99  $kg/m^2$  as compared to 33.3% in male group. We observed a mean of  $26.30 \pm 3.98$   $kg/m^2$ . 56.6% females had TSH in 5-10 microIU range as compared to 22.2% males with mean of  $10.47 \pm 1.37$  microIU. Gender wise parameters of echo are given in Table 1.

**Table 1: Demographic characteristics of study population.**

Echo parameter	Male No. (%)	Female No. (%)	Total No.
<b>IVS(d) (mm)</b>			
6.5-8.0	28 (77.8)	108 (87.1)	136
>8.0	8 (22.2)	16 (12.9)	24
<b>IVS(s) (mm)</b>			
9-9.5	4 (12)	88 (70.9)	92
>9.5	32 (88)	36 (29.1)	68
<b>LVID(d) (mm)</b>			
40-40.99	16 (44.4)	96 (77.7)	112
≥50	20 (55.6)	28 (22.3)	48
<b>LVID(s) (mm)</b>			
30-33	8 (22)	84 (67.7)	92
≥34	28 (78)	40 (32.2)	88
<b>LVPW(d) (mm)</b>			
6-7	20 (55.6)	92 (74.2)	112
>7	16 (44.4)	32 (25.8)	48
<b>LVPW(s) (mm)</b>			
7-8	8 (22.3)	48 (38.7)	56
≥9	28 (77.7)	56 (61.7)	104
<b>EF (%)</b>			
50-60	20 (55.6)	92 (74.2)	112
61-70	16 (44.4)	32 (25.8)	48
<b>Stroke volume (ml)</b>			
60-70	4 (11.1)	68 (54.8)	72
>70	32 (88.9)	56 (45.2)	88
<b>Cardiac output (l/m)</b>			
<55.5	16 (44.5)	84 (67.7)	100
≥55.5	20 (55.5)	40 (32.3)	60
<b>E/A ratio</b>			
≤0.99	32 (88.8)	96 (74.2)	124
>0.99	4 (11.1)	32 (25.8)	36
<b>DeT (ms)</b>			
≤200	4 (11.1)	32 (25.8)	36
>200	32 (88.8)	96 (74.2)	124
<b>IVRT (ms)</b>			
<99.9	4 (11.1)	36 (29.1)	40
≥100	32 (25.8)	88 (70.9)	120
<b>La size (mm)</b>			
<3.99	20 (55.6)	92 (74.2)	112
≥4	16 (44.4)	32 (25.8)	48
<b>FS (%)</b>			
22-28	8 (22)	100 (80.6)	108
>28	28 (78)	24 (19.1)	52

IVS(d): Interventricular septum in diastole, IVS(s): Interventricular septum in systole, LVID(d): Left ventricular internal dimension in diastole, LVID(s): Left ventricular internal dimension in systole, LVPW(d): Left ventricular posterior in diastole, LVPW(s): Left ventricular posterior in systole, EF: Ejection fraction, DeT: Deceleration time, IVRT: Isovolumic relaxation time LA: Left atrium, FS: Fractional shortening

## DISCUSSION

The present study titled “Study of LV functions in patients of subclinical hypothyroidism in patients coming to rural medical of sub-Himalayan region of India” was conducted in the RPGMC, Tanda, over a period of one year from December, 2010 to November, 2013. 200 patients, 155 females and 45 males were randomly selected and inducted in the study, and the results so obtained were analyzed statistically.

The youngest patient was 28 years old female and oldest 45 year old female. Majority of patients belonged to 31-50 years age group i.e. 125 patients, followed by 20-30 years age group, having 12 patients. The observed mean was  $34.17 \pm 4.71$  years, comparable with the study of Akcakoyum et al. (2009).

Fifteen patients had BMI in the range of 25-29.99 kg/m<sup>2</sup> and 14 patients had BMI in the range of 18 -24.99 kg/m<sup>2</sup>. Least BMI observed was 20.7 kg/ m<sup>2</sup> and the highest was 36 kg/ m<sup>2</sup>. Mean BMI was  $26.30 \pm 3.98$  kg/ m<sup>2</sup>. So tilt toward previous study of Akcakoyum et al. (2009). In the study, patients having TSH >5 µIU and normal T<sub>3</sub> and T<sub>4</sub> with or without clinical features were studied. 100 patients had TSH in 5-10 µIU range and other 100 had it in >10 µIU range. Majority of females i.e. 90 had TSH in 5-10 µIU range. Mean TSH was  $10.47 \pm 1.37$  µIU.

Increase in TSH in many studies has been reported to affect cardiac function, especially diastolic function. Though the dysfunction is mild but is significant when it takes place over a long period of time. Among diastolic function parameters studied with tissue Doppler echocardiography, LVID (d) (mm) was having dimension in lower range, as also LVID (s) (mm) parameter, which implied impaired relaxation of left ventricle. While Tseng et al.<sup>12</sup> (1989) found that the isovolumic contraction time, the projection period and the ratio of pre-ejection to period to LV ejection time were normal in patients with SCH. Galderisi et al.<sup>13</sup> (2004) studied patients with overt hypothyroidism, and Mao et al. (2004) studied patients with congenital hypothyroidism. They reported a decrease in early diastolic velocity of annulus and early/late diastolic velocity ratio and an increase in precontraction time and relaxation.

Turhan S et al.<sup>14</sup> (2006) reported that precontraction and relaxation time were significantly higher in patients with SCH, as was found in our study. Foldes et al.<sup>15</sup> (1987) found a lower ejection fraction and slightly decreased fractional shortening in patient of SCH, which was consistent with our study. Feldman et al.<sup>16</sup> (198) found in their study that subclinical hypothyroidism leads to an impairment of the isovolumic relaxation time and filling of the left ventricle, and to an impairment of the myocardial contractility, decrease of stroke volume and ejection fraction. This finding was consistent with our study.

Mishra et al.<sup>17</sup> (2005) found that Deceleration Time (DT) and isovolumic relaxation time (IVRT) was significantly prolonged in subclinical hypothyroidism patients. The E/A ratio were also significantly reduced. These findings were consistent with our study. Akcakoyum et al. (2009). Found in their study that longitudinal diastolic function reserve index was significantly lower in patients with SCH. While Bell et al.<sup>18</sup> (1985) showed by radionuclide ventriculography that patients with SCH had normal ejection fraction at rest. Akcakoyun et al. (2009) found in their study that longitudinal diastolic function reserve index was significantly lower in SCH patients. Biondi et al. (1999) found that there was no abnormality in LV morphology and mass in patients with SCH and their echocardiographic parameters were almost normal in range. This was consistent with our study.

Doppler derived indices of left ventricular diastolic filling showed clear abnormalities of myocardial relaxation, as indicated by significant prolongation of the isovolumic relaxation time, and significant reduction of the early diastolic mitral flow velocity/late diastolic mitral flow velocity (E/A ratio), mainly accounted for increased A-wave of mitral flow velocity. Increased IVRT and decrease in E/A ratio was significant and these results were in favor that diastolic dysfunction of left ventricle was seen in 155 patients out of 200 studied patients. Cardiac status of 5 male and 40 females was not affected by SCH and they had E/A ratio >1 and isovolumic relaxation time <100 ms. Systolic function parameters in our study were almost normal.

SCH is a very common disorder. Its prevalence keeps on increasing with advancing age. More females are affected than males (3:1). The predominant clinical complaints of patients are tiredness, cold intolerance, constipation and weight gain. In SCH patients TSH is >5  $\mu$ IU, with low normal T<sub>3</sub> and T<sub>4</sub>. Heart is the most important organ affected by increase in TSH. As in our study we found that increase in TSH is associated with diastolic dysfunction of left ventricle.

## CONCLUSIONS

The present study was carried out on 200 patients of SCH who had TSH >5  $\mu$ IU and T<sub>3</sub>, T<sub>4</sub> values in low normal range. Study was conducted to ascertain left ventricular function of heart. In the study 155 were females and 45 were males.

- The age of patients varied from 26 to 45 years. The youngest patient was 26 years old and oldest 46 years old, both females.
- The highest number of patients were in the 31 to 40 years age group, followed by 20 to 30 years age group.

- In the present study, commonest complaint was tiredness (n=28), followed by cold intolerance (n=19) and constipation (n=16).
- ECG findings in all the patients were within normal limits.
- We studied left ventricular function using pulsed tissue Doppler echocardiography.
- Systolic as well as diastolic parameters were studied. The result was that diastolic parameters were markedly altered, mainly isovolumic relaxation time, which was increased and reduction of E/A wave ratio (<1). Systolic function parameters were within normal range.
- 155 patients had diastolic dysfunction with E/A wave <1.
- 45 patients were not affected and they had E/A wave >1.
- Implication for echocardiography in SCH patients observed were that early recognition of silent diastolic dysfunction can be done. We can institute L-thyroxine therapy which has been found to reverse diastolic dysfunction of heart along with improvement in lipid levels, decreased systemic vascular resistance, diastolic hypertension and coagulation profile.

To conclude, we can say that SCH, invariably affects heart and sooner or later and leads to diastolic dysfunction. Early recognition by echocardiography and then treatment with L-thyroxine is indicated. Though L-thyroxine replacement therapy induction is controversial, but it should be indicated as more and more studies favor its use in SCH.

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