

# Echocardiographic Changes in Overt and Subclinical Primary Hypothyroidism

Haridoss Sripriya Vasudevan<sup>1</sup>, J Jacinth Preethi<sup>2</sup>

Assistant Professor, Institute of Internal Medicine, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai, Tamil Nadu, India

## Abstract

**Background and Objectives:** Thyroid hormone is an important regulator of cardiac function and cardiovascular hemodynamics. The aim of this study was to assess the cardiovascular functions in primary overt and subclinical hypothyroid patients and to determine if there was a correlation between severity of disease and echocardiographic changes.

**Methodology:** A cross-sectional study was conducted in the Endocrinology Clinic of Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai. The study sample was grouped into mild, moderate, severe, and subclinical hypothyroid groups which were then compared by echocardiographic findings.

**Results:** A total of 84 patients were seen, from June 2013 to September 2013. Abnormal left ventricle posterior wall (LVPW) thickness and abnormal interventricular septal wall (IVSW) thickness were more frequently noted in those with clinical hypothyroidism (moderate and severe) as compared to those with subclinical hypothyroidism. Abnormal septal wall thickness was noted in 9 (69.23%) of moderately hypothyroid and 18 (72%) of severely hypothyroid patients, whereas this finding was noted in only 5 (16.66%) of the subclinical hypothyroid patients indicating significant differences between the groups. Diastolic dysfunction was also significantly more frequent in the moderate and severe hypothyroid group. On statistical analysis by one-way analysis of variance, it was found that LVPW (mm), IVSW (mm), and E/A ratio were significantly associated with the severity of hypothyroidism, while ejection fraction, fractional shortening, and LV internal diameter were not significantly different between groups.

**Conclusions:** The completely reversible nature of these cardiac complications being well known, this study aims at reassessing the need for early recognition, and more aggressive management aims at preventing the aforementioned complications.

**Key words:** Echocardiography, Hypothyroidism, Pericardial effusion, Septal wall thickness

## INTRODUCTION

Cardiac involvement in myxedema has been well known for a long time.<sup>[1]</sup> The cardiovascular findings of hypothyroidism are, however, more subtle. The cardiovascular system (CVS) manifestations of hypothyroidism include the following: (a) Reduced total intravascular volume, (b) reduced contractility, (c) reduced heart rate, (d) raised systemic vascular resistance (increased diastolic blood pressure), and (e) raised capillary permeability

(pericardial effusion), and the thyroid hormone is an important regulator of cardiac function and cardiovascular hemodynamics.<sup>[2]</sup> In hyperthyroidism, cardiac contractility and cardiac output are enhanced, and systemic vascular resistance is decreased, while in hypothyroidism, the opposite is true. Other changes observed in hypothyroid individuals include alteration in lipid profile values with increased cholesterol and low-density lipoproteins and electrocardiogram (ECG) changes such as bradycardia and low-voltage complexes.<sup>[3]</sup> Triiodothyronine (T<sub>3</sub>) mediates the expression of cardiac genes, inducing transcription of alpha-myosin heavy chain (MHC) and the sarcoplasmic reticulum calcium ATPase and negatively regulating expression of beta-MHC and phospholamban.<sup>[4]</sup> Santos *et al.* first reported reversible cardiomyopathy, manifested by asymmetric septal hypertrophy in untreated hypothyroid patients.<sup>[5]</sup> This finding was also described in children.<sup>[6]</sup> The increased thickness of interventricular septum (IVS)

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**Corresponding Author:** J Jacinth Preethi, Institute of Internal Medicine, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai - 3, Tamil Nadu, India. Mobil:+91-940019648. E-mail: jaci\_preeth@yahoo.com

and left ventricular posterior wall (LVPW) thickness were observed in untreated patients with hypothyroidism, and there is a correlation between severity of disease cardiac findings.<sup>[7]</sup> In the same study, such findings are also reported to be dependent on advancing age. It has also been postulated that long-standing hypothyroidism leads to reversible cardiomyopathy, manifested by both asymmetric septal hypertrophy and features of hypertrophic obstructive cardiomyopathy.<sup>[5]</sup> Pericardial effusion is seen in hypothyroidism, and this also appears to be dependent on the severity of the disease.<sup>[8]</sup> The cardiac changes noted in overt primary hypothyroidism are also observable in patients with subclinical hypothyroidism.<sup>[9]</sup> Patients with subclinical hypothyroidism thus manifest many of the same cardiovascular changes, but to a lesser degree than that which occurs in overt hypothyroidism. Subclinical hypothyroidism may thus be a potentially modifiable risk factor for cardiovascular disease and mortality.<sup>[10,11]</sup>

### Aim

This study was aimed to increase the understanding of cardiovascular changes in hypothyroidism in the Indian population to enable prevention, early diagnosis, and prompt intervention in both overt clinical and asymptomatic subclinical hypothyroidism.

## METHODOLOGY

The study design was a cross-sectional and it was conducted in the Endocrinology Clinic, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai, from June 2013 to September 2013. The study was approved by the Institutional Ethics Committee. A total of 84 patients with newly diagnosed drug naïve hypothyroidism were selected, of which 80 patients who fit the inclusion criteria of age >18 years of age, with subclinical hypothyroidism thyroid-stimulating hormone (TSH) >5.5  $\mu$  IU/ml with normal FT4 and FT3), or overt hypothyroidism were included. The clinically hypothyroid group was divided into three categories according to the level of TSH as follows: (i) Mild hypothyroidism (<20 m IU/ml), (ii) moderate hypothyroidism (20–50 m IU/ml), and (iii) severe hypothyroidism (>50 m IU/ml). 4 patients were excluded for various reasons (age <18 years, with known primary cardiac disease, and who were taking drugs that alter the cardiovascular functions such as amiodarone, beta blockers, and calcium channels blockers). A detailed questionnaire was used to elicit the symptoms of hypothyroidism. The patients were examined for signs of hypothyroidism, especially the examination of CVS. All the patients were evaluated for following parameters: Pulse rate, blood pressure, ECG, and echocardiography (chamber dimensions, diastolic function, systolic function,

wall motion abnormalities and pericardial effusion, LVPW thickness, and interventricular septal wall (IVSW) thickness). For categorical variables, Chi-square tests, and for continuous variables, analysis of variance (ANOVA) were used.  $P < 0.05$  were considered statistically significant. The data were analyzed using the Statistical Package for the Social Sciences (SPSS).

## RESULTS

Among the 80 patients included in our study, subclinical hypothyroid patients were the largest group with 30 patients (38%), followed by severe hypothyroidism with 25 cases (31%), moderate hypothyroidism with 13 cases (16%), and mild hypothyroidism with 12 cases (15%). The mean TSH in the mild hypothyroid group was 11.32 m IU/L, while among the moderate hypothyroid group, it was 33.43 m IU/L. The severe hypothyroid group had a mean TSH of 107.58 m IU/L.

Diastolic dysfunction was found in 1 (8.33%) patient in the mild hypothyroid group and in 2 (15.38%) of the moderately hypothyroid group. 9 (36%) patients of the severely hypothyroid group had diastolic dysfunction. In the subclinical hypothyroid group, the same was noted in 3 (10%) patients. This difference was not statistically significant.

On statistical analysis by one-way ANOVA it was found that LVPW thickness was significantly associated with the severity of hypothyroidism [Table 1]. Similarly, IVSW was also associated with severity of hypothyroidism [Table 2]. While ejection fraction (EF) %, fractional shortening (FS) %, and ventricular internal diameter (D) cm were not significantly associated, E/A was significantly associated with the severity of hypothyroidism [Table 3].

A multiple regression analysis was done with the dependent variable as IVSW thickness and LVPW thickness independently entering the significant items, including age and TSH as variable; it was found that only TSH continued to be statistically significant [Table 4].

Pericardial effusion was observed in 1 (8.33%) of the mild hypothyroid patients and also in 4 (30.76%) patients of the moderately hypothyroid group. 10 (40%) of the severely hypothyroid had the same. No pericardial thickening or constrictive physiology was made out [Table 5].

## DISCUSSION

In this study conducted in Indian population, we evaluated the cardiovascular function in newly detected primary overt

**Table 1: LVPW thickness**

Nature of hypothyroidism	Ventricular thickness		P value
	Normal (6–9 mm)	Abnormal (>9 mm)	
Subclinical (n=30)	28	2	<0.001
Clinical (n=50)			
Mild	11	1	0.0013
Moderate	7	6	
Severe	7	18	
Total	25	25	

LVPW: Left ventricle posterior wall

**Table 2: Interventricular septal thickness**

Nature of hypothyroidism	IVS thickness		P value
	Normal (6–9 mm)	Abnormal (>9 mm)	
Sub-clinical (n=30)	25	5	<0.001
Clinical (n=50)			
Mild	11	1	<0.001
Moderate	4	9	
Severe	7	18	
Total	22	28	

IVS: Interventricular septum

**Table 3: Comparison of the means of echo parameters**

Mean echo value	Severity of hypothyroidism				P value
	Subclinical	Mild	Moderate	Severe	
LVPW (mm)	8.49	8.74	9.23	10.54	<0.001
IVSW (mm)	8.74	8.75	9.20	10.42	<0.001
LVID (D) cm	4.44	4.50	4.41	4.77	0.071
EF (%)	62	63.08	61.61	61.6	0.897
FS (%)	36.06	37.41	34.30	31.4	0.099
E/A	1.50	1.69	1.62	1.25	<0.01

LVPW: Left ventricle posterior wall, IVSW: Interventricular septal wall, LVID: Left ventricular inner dimension, EF: Ejection fraction, FS: Fractional shortening

and subclinical hypothyroidism. Among the 80 patients included in our study, subclinical hypothyroid patients (38%) comprised the largest group. This indicates the need for efficient screening programs to identify this condition.

The prevalence of abnormal LVPW thickness increased as the severity of hypothyroidism increased. A significant association was found between the occurrence of increased LVPW thickness and the severity of disease. A similar relationship was also demonstrated for abnormal IVSW thickness. On comparing the occurrence of increased septal wall thickness with increasing severity of disease, it was found to be statistically significant. Rawat and Satyal in their study showed relatively increased thickness of IVS and LVPW when compared to the treated patients or control subjects.<sup>[7]</sup> However, on age group analysis, it was found that this difference was more marked in older patients. In our study, however, we found that although there was a trend of increasing wall thickness with age these changes

on multiple regression analysis with the dependent variable as IVSW thickness and LVPW thickness including age and TSH as variable, it was found that only TSH continued to be significant.

The cardiac chamber size was found to have a statistically insignificant association with hypothyroidism. This shows that the cardiac chamber size is not affected by hypothyroidism. Similar observations were also made by others (Verma *et al.*, 1996).<sup>[12]</sup> The LV systolic functions as measured by EF and FS were not statistically associated with the severity of hypothyroidism. No wall motion abnormalities or global hypokinesia was detected. In the study by Jagdish *et al.*, although FS and EF showed increase, it was statistically not significant.<sup>[13]</sup> Rawat and Satyal also showed no significant change in parameters of systolic function.<sup>[7]</sup>

In our study, diastolic dysfunction was found in 1 (8.33%) patient in the mild hypothyroid group, 2 (15.38%) of the moderately hypothyroid group, 9 (36%) patients of the severely hypothyroid group, and 3(10%) patients of the subclinical hypothyroid group which was significant. Similar findings of diastolic dysfunction were made by Biondi and Cooper, indicating an early diastolic dysfunction.<sup>[14]</sup> Pericardial effusion was observed to be more frequent in the severe and moderate group, but the difference between groups was not statistically significant perhaps because of the smaller sample size and prevalence of the finding. No pericardial thickening or constrictive physiology was made out unlike previous studies.<sup>[8]</sup>

The study was done on a sample of patients in the outpatient department. This makes the results of the study less generalizable to the overall population of hypothyroid patients. The sample size of 80 was relatively small to detect fine associations, especially in the presence of multiple confounding variables. The cross-sectional nature of the study makes it possible that the conclusions made may be unstable or that they may be reflective of a phenomenon particular to one phase of illness. The follow-up of the patients after replacement of thyroxine was not done due to several reasons. If done, it could have highlighted more on the reversibility of the cardiovascular changes.

## CONCLUSION

Increased IVSW and LVPW thicknesses along with diastolic dysfunction are some of the cardiac features of thyroid hypofunction. The subtle impairment of LV diastolic function even in subclinical hypothyroidism patients as shown in our study may justify the use of hormone replacement even without overt symptoms. An early diagnostic approach in patients with hypothyroidism will

**Table 4: Multiple regression analysis with dependent variable IVSW/LVPW and including age and severity of hypothyroidism**

Variables	Age		TSH	
	IVSW	LVPW	IVSW	LVPW
Coefficient	-0.0020	0.0151	0.0088	0.0191
SE	0.00895	0.0149	0.0022	0.0024
95% confidence interval	-0.0201-0.0160	-0.0149-0.0453	0.0045-0.0133	0.0143-0.0241
t ratio	0.5324	0.0152	9.9700	0.0192
P value	0.8186	0.0150	0.0002	0.0024

IVSW: Interventricular septal wall, LVPW: Left ventricle posterior wall, TSH: Thyroid-stimulating hormone, SE: Standard error

**Table 5: Pericardial involvement**

Pericardial pathology	Severity of hypothyroidism			
	Sub clinical	Mild	Moderate	Severe
Mild PE	1	1	2	2
Moderate PE	0	0	1	6
Large PE	0	0	1	2
Pericardial thickening	0	0	0	0
Constrictive physiology	0	0	0	0
Total	1	1	4	10

PE: Pulmonary embolism

surely diminish the extent of cardiac complication which accompanies it. Echocardiography is a useful non-invasive tool in assessing the response to replacement therapy.

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