ASSESSMENT OF LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IN SUB-CLINICAL HYPOTHYROIDISM

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ABSTRACT

Background: Adverse cardiovascular effect of hypothyroidism has been identified in many studies. Early identification of patients with sub-clinical hypothyroidism may lead to early treatment and thereby favourable effect on cardiovascular morbidity and mortality.

Objectives: To find out the association of sub clinical hypothyroidism and left ventricular dysfunction and also to find out relationship between systolic and diastolic dysfunction in these patients.

Material and Methods: A total 30 cases of sub clinical hypothyroidism along with 15 age sex matched healthy control subjects were included in study. Serum TSH, T₄, T₃ hormone level was measured and those who were found to have sub-clinical hypothyroidism underwent for 2D Echo. Results: Significant reduction in peak early filling velocity [PE] (p<0.001) and early filling time velocity integral [EI] (p<0.001). Ratio of early and late peak velocities (PE/PA) (p<0.001), ratio of time velocity integral of early and atrial filling [EI/Al] (p<0.001) and ratio of the early peak to average velocity [PE/M] (p<0.001) were also reduced. Mean EF was 54.9±5.55 as compared to 55.7±3.46 of control subjects with a T value of 0.48, however there was significant diastolic dysfunction in case of hypothyroid patients [mean EI/Al = 1.35 ± 0.53] as compared to control group subjects [mean EI/Al = 2.11 ± 0.26] with a T value of 5.22. Conclusion: Sub-clinical hypothyroidism showed significant diastolic dysfunction in the absence of significant impairment of systolic function.

Key words: Subclinical hypothyroidism, Diastolic, EF.

1. INTRODUCTION

The cardiac manifestation in sub clinical hypothyroidism are of mainly systolic dysfunction (1). Because of adverse cardiovascular effect of hypothyroidism has been identified in many studies. Most of the studies focused on systolic/ diastolic dysfunction in hypothyroidism (2, 3, 4, 5, 6). Early identification of patients with sub-clinical hypothyroidism may lead to early treatment and thereby favourable effect on cardiovascular morbidity and mortality. So in order to know the effect of sub-clinical hypothyroidism on LV diastolic functions we have designed the present study.

2. OBJECTIVES

- To find out the association of sub clinical hypothyroidism and left ventricular dysfunction.
- To find out relationship between systolic and diastolic function in these patients.

3. MATERIAL AND METHODS

The study was conducted in the Non-invasive cardiology laboratory of SMS Medical College and Hospital, Jaipur, India. A total 30 cases of sub clinical hypothyroidism along with 15 age sex matched healthy control subjects were included in study. Only those cases in which sub clinical hypothyroidism was diagnosed on the basis of standard criteria were included in the study. All the conditions (Age > 70 years, HR >100 b/m, conditions causing LV hypertrophy, conditions rendering myocardium stiff eg. hemachromatosis, amyloidosis, alcoholism, diabetes mellitus, sarcoidosis and other infiltrative disease, treating overt hypothyroidism, presence of any chronic medical and surgical condition which may independently effect the left ventricular function adversely) influencing the left ventricular function were excluded. Serum TSH, T₄, T₃ hormone level was measured and those who were found to have sub-clinical hypothyroidism underwent for 2D Echo. Written consent of the patients was taken. The study was approved by local ethical committee.

4. RESULTS

The mean age of patients were 46.9±6.92, while for control it was 47.4±5.96 years. Among 30 cases studied female patients were 76.66% and male were 23.33%. 27 (90%) cases were had no sign of hypothyroidism and but 1 (3.3%) had dull expression and 1 had sparse hair and 3 (10%) were associated with prolonged relaxation of achilis tendon reflex. None of the patient had ECG abnormality. 26 (86.66%) were had no dislipidemia, 4 (13.3%) cases were associated with increased total cholesterol and 2 (6.6%) cases were associated with increased triglyceride level (Table 1). On Doppler evaluation exhibit highly significant reduction in peak early filling velocity (PE) (p<0.001)
and early filling time velocity integral (Ei) (p<0.001). Ratio of early and late peak velocities (PE/PA) (p<0.001), ratio of time velocity integral of early and atrial filling (Ei/Ai) (p<0.001) and ratio of the early peak to average velocity (PE/M) (p<0.001) were also reduced. Mean EF was 54.9± 5.5 as compared to 55.7 ± 3.46 of control subjects with a T value of 0.48 (not significant) however there was significant diastolic dysfunction in case of hypothyroid patients (mean Ei/Ai = 1.35 ± 0.33) as compared to control group subjects (mean Ei/Ai = 2.11 ± 0.26) with a T value of 5.22 (highly significant statistically) (Table 2).

5. DISCUSSION

In this study sub-clinical hypothyroid patients on Doppler evaluation exhibit highly significant reduction in peak early filling velocity (PE) (p<0.001) and early filling time velocity integral (Ei) (p<0.001). These findings are significantly suggestive of reduced early diastolic filling in sub-clinical hypothyroid patients. On the other hand ratio of early and late peak velocities (PE/PA) (p<0.001), ratio of time velocity integral of early and atrial filling (Ei/Ai) (p<0.001) and ratio of the early peak to average velocity (PE/M) (p<0.001) were also reduced highly significantly suggesting augmented atrial contribution to diastolic filling and reduced relative importance of early diastolic filling or in other words impaired left ventricular diastolic function. Also one third filling fraction was significantly reduced and percentage atrial contribution to filling was increased in these patients as compared to control population again signifying augmented atrial contribution and reduced early diastolic filling or in other words presence of diastolic dysfunction. However peak atrial velocity (PA), mean filling velocity (M) and time velocity integral of atrial filling (Ai) were not significantly different from control population. It must be realized that reduction in early filling in absence of augmented of atrial filing indicates only early and mild diseases, but in our case reduction in early filling was accompanied by augmentation of atrial filling indicating significant diastolic dysfunction. Bireta G. et al (2003) (7) studied left ventricular diastolic function by radionuclide ventriculography at rest and exercise in sub-clinical hypothyroidism and found significant difference between time to peak filling rate TPFR at rest and after treatment. Diastolic function was impared in sub-clinical hypothyroid function both at rest and during exercise and returns to normal value after L-T4 therapy. Yazici M. et al (2004) (8), were investigated the effects of thyroxine therapy on cardiac function in patients with sub-clinical hypothyroidism and Index of Myocardial Performance (IMP) in the evaluation of left ventricular function and found there is impairment of left ventricular diastolic function both in sub-clinical and overt hypothyroidism, by thyroxine therapy the dysfunction was recovered in sub-clinical hypothyroidism but not in overt hypothyroidism. Biondi B. et al. (1999) (9) was studied left ventricular diastolic function by 2D echo and showed no abnormalities of left ventricular morphology and a slight, but not significant reduction in the systolic function in the patient group in contrast, Doppler derived indices of diastolic function showed significant prolongation.

### Table 1. Characteristics of the study population

| Characteristic                        | Patients | Controls |
|--------------------------------------|----------|----------|
| Mean Age* (± SD) Years               | 46.9 ± 6.92 | 47.4 ± 5.96 |
| Sex                                  | 7 (23.3) | 5 [33.3] |
| Female                               | 23 (76.6) | 10 (66.6) |
| Symptoms/Signs:                      |          |          |
| Lethargy                             | 3 (10)   |          |
| Constipation                         | 3 (10)   |          |
| Cold intolerance                     | 1 (3.3)  |          |
| Menstrual disorder                   | 3 (10)   |          |
| Decreased appetite                   | 2 (6.6)  |          |
| Increase in weight                   | 3 (10)   |          |
| Dull expressionless face             | 1 (3.3)  |          |
| Sparse hair                          | 1 (3.3)  |          |
| Prolonged relaxation of deep tendon reflex | 3 (10)   |          |

### Table 2. Comparison of Left Ventricular Diastolic and Systolic Function in Control Subjects and Sub-Clinical Hypothyroid Patients

| Indices of LV function | Control | Patient | t   | P    |
|------------------------|---------|---------|-----|------|
| LV Diastolic Function  |         |         |     |      |
| 1. PE (mean ± SD)      | 0.66 ± 0.08 | 0.50 ± 0.10 | -4.55 | <0.001 |
| 2. PA (mean ± SD)      | 0.53 ± 0.09 | 0.52 ± 0.10 | -0.05 |       |
| 3. M (mean ± SD)       | 0.31 ± 0.07 | 0.32 ± 0.08 | 0.32 |       |
| 4. Ei (mean ± SD)      | 7.52 ± 1.60 | 4.20 ± 0.78 | -6.19 | <0.001 |
| 5. Ai (mean ± SD)      | 3.61 ± 0.78 | 3.49 ± 1.47 | -0.29 |       |
| 6. Ti (mean ± SD)      | 13.15 ± 2.90 | 9.79 ± 2.37 | -3.15 | <0.01  |
| 7. %AC (mean ± SD)     | 27.57 ± 2.83 | 35.55 ± 10.27 | 3.23 | <0.01  |
| 8. 1/3 FF (mean ± SD)  | 47.01 ± 4.17 | 38.23 ± 6.66 | -4.41 | <0.001 |
| 9. P %T (mean ± SD)    | 0.11 ± 0.01 | 0.08 ± 0.03 | -2.78 | <0.01  |
| 10. Time E (mean ± SD) | 0.10 ± 0.02 | 0.08 ± 0.01 | -3.04 | <0.01  |
| 11. PE/PA (mean ± SD)  | 1.27 ± 0.14 | 0.99 ± 0.24 | -3.87 | <0.001 |
| 12. PE/M (mean ± SD)   | 2.27 ± 0.35 | 1.65 ± 0.41 | -4.29 | <0.001 |
| Ei/Ai (mean ± SD)      | 2.11 ± 0.26 | 1.35 ± 0.53 | -5.22 | <0.001 |

| LV Systolic function    |         |         |     |      |
|------------------------|---------|---------|-----|------|
| 1. EF (mean ± SD)       | 55.7 ± 3.46 | 54.9 ± 5.55 | -0.48 |       |
tion of isovolumic relaxation time (p <0.001), increase a wave (55 +/- 13 v/s 48 +/- 9cms/ sec, P <0.05), and re-
duced early diastolic mitral flow ve-
locity/late diastolic mitral flow ve-
locity ratio (1.4 +/- 0.3 v/s. 1.7 +/- 0.3
p<0.001). These findings indicate
that sub-clinical hypothyroidism
strongly affects diastolic function.
R. Verma et al. (1996) (10) done echo-
cardiography study on both sub-
clinical and overt hypothyroidism
and found both are associated with
cardiovascular alteration both struc-
tural and functional. IVS and LVPW
thickness are markedly affected, as
well as there is impairment of left
ventricular function more in dias-
tole. A. Gupta et. al (1996) (11), found
that the diastolic dysfunction is
present in both sub-clinical and over
hypothyroidism while pericardial ef-
fusion is seen only in overt hypothy-
roidism and mean serum cholesterol is
significantly raised in oth sub-clin-
ical and overt hypothyroidism with
respect to control group. Similar
results presented by B&H authors
(12, 13).

Systolic v/s diastolic dysfunc-
tion:
The role of altered diastolic func-
tion in patients with impaired sys-
tolic function has yet to be clearly de-
ined, but may also be quite impor-
tant. Primary diastolic dysfunction
in the absence of systolic dysfunc-
tion is an important, increasingly recog-
nized condition. In this study
Mean EF of sub-clinical hypothyroid
patients in this study was 54.9:  5.55
as compared to 55.7 ± 3.46 of control
subjects with a T value of 0.48 (not
significant) however there was sig-
nificant diastolic dysfunction in case
of hypothyroid patients (mean Ei/Ai
= 1.35 ± 0.53) as compared to control
group subjects (mean Ei/Al = 2.11 ±
0.26) with a T value of 5.22 (highly
significant statistically) (Table 2),
and hence sub-clinical hypothyroid pa-
tients showed significant diastolic
dysfunction in the absence of signifi-
cant impairment of systolic function
as shown by Ejection Fraction.

6. CONCLUSION
In our study Sub-clinical hypo-
thyroidism showed significant dia-
stolic dysfunction in the absence of
significant impairment of systolic
function as shown by Ejection Frac-
tion.

Conflict of interest: none declared.

REFERENCES
1. Bionadi B, Klein I, et al. Hypothy-
roidism as a risk factor for cardio-
vascular disease. Endocrine. 2004
24(1); 1-13.
2. William F Crowely Chester Ridg-
way et at. Non invasive evaluation of
cardiac function in hypothyroidism.
New England Journal. 1977 296:1-6.
3. Bough EW, Crowley WF. et al.
Myocardial function in hypothy-
roidism. Arc Intern Med. 1978; 138:
1476-1480.
4. Farfar JC, Muir AL, Toft AD. Left
ventricular function in hypothy-
roidism response to exercise and
beta-adrenoceptor blockade. Br
Heart J. 1982; 48: 278-284.
5. O’Malley S, Peterson A, Mc
Cullough FD, Rosenthal et al. Re-
versible abnormalities of myocar-
dial relaxation in hypothyroidism.
J Clin Endocrinol Metab. 1985; 61:
269-272.
6. Shenoy MM, Goldman JM. Amer-
ican Journ Of Med Sciences. 1987;
294:1-9
7. Brenta G, Multi LA, Schnitonan M.
et al. Assessment of left ventricular
diastolic function by radionuclit-
de ventriculography at rest and ex-
ercise in sub-clinical hypothyroid-
ism and its response to L thyrox-
in therapy. Am J Cardiol. 2003; 91:
1327-1330.
8. Yazici M, Gorgulu S, Sertbas Y. et
at. Effects of T4 therapy on cardiac
function in patients with sub-clini-
cal hypothyroidism index of myo-
cardial performance in the evalua-
tion of left ventricular function. Int
J Cardiol. 2004; 95: 133-143.
9. Bionadi B, Klein I. et al. Hyperthy-
roidism as a risk factor for cardio-
vascular disease. Endocrine. 2004;
24:1-13.
10. Verma R, Jain AK, Ghose T. Heart
in hypothyroidism - an echocardio-
graphic study. JAPI. 1996; 44: 390-
392.
11. Gupta A, Sinha RSK et al. Echocar-
diographic changes and alterations
in lipid profile in cases of sub-clin-
cal and overt hypothyroidism. JA-
Pl. 1996; 44(8): 390-392.
12. Bilic-Komarica E, Beciragic A,
Junuzovic Dz. Effects of Treatment
with L-thyroxin on Glucose Reg-
ulation in Patients with Subclini-
cal Hypothyroidism. Med Arh. 2012
Dec; 66(6): 364-368. doi: 10.5455/
medarh.2012.66.364-368.
13. Bilic-Komarica E, Beciragic A,
Junuzovic Dz. The Importance of
HbA1c Control in Patients with
Subclinical Hypothyroidism. Mat
Soc Med.  2012 Dec; 24(4): 212-219.
doi: 10.5455/ msm.2012.24.212-219.