Original Research Paper

Volume-9 | Issue-3 | March-2019 | PRINT ISSN - 2249-555X

General Medicine

ASSESSMENT OF LEFT VENTRICULAR FUNCTION IN NEWLY DIAGNOSED HYPERTHYROID PATIENTS BY ECHOCARDIOGRAPHY

Twinkle Gupta

Tejinder Talwar

Karun Bhatti* *Corresponding Author

Sahas Jindal

Anish Gupta

ABSTRACT **BACKGROUND:** Hyperthyroidism is one of the metabolic disorders that is associated with prominent cardiovascular changes in the form of marked reduction in peripheral vascular resistance and increased total blood volume and heart rate. Recent advances in Echocardiographic technology enable accurate non-invasive assessment of cardiac morphology and its haemodynamic parameters related to systolic or diastolic function. Therefore, Echocardiography can be used to assess morbidity in the hyperthyroid cases.
OBJECTIVES: To measure left ventricular function in newly diagnosed hyperthyroid patients and to correlate with that of euthyroid state.
METHODOLOGY: The study was conducted at MMIMSR, Mullana, Ambala. Fifty individuals were included in the study .Out of them, Twenty five were cases and twenty five were age and sex matched controls. The patients were taken both from OPD and indoor wards of department of Medicine. All patients were scrutinized and investigated as per the plan. All were subjected to evaluation by echocardiography.
RESULTS: In this study, significant high cardiac output state was observed with preserved systolic and diastolic function of the left ventricle in newly diagnosed hyperthyroidism
CONCLUSION: Echocardiography can be used as a sensitive tool to assess morbidity associated with hyperthyroidism.

KEYWORDS : Echocardiography, left ventricular function, hyperthyroidism.

INTRODUCTION

Almost two centuries ago, Caleb Parry, an English physician from bath, reported on the association between thyrotoxicosis and the cardiovascular system. As a result of over 60 years of clinical and basic science, it is clear that some of the most profound and characteristic symptoms and signs of thyrotoxicosis are those relating to the cardiovascular system.[1]Thyroid hormone causes a myriad of hemodynamic effects and all can be related directly or indirectly to the flow law. Thyroid hormones in addition to their direct effects on cardiovascular system also have indirect effects mediated through the autonomic nervous system, the renin-angiotensin aldosterone system (RAAS),vascular compliance, vasoreactivity and renal function.[2] In hyperthyroidism, there is hyperdynamic circulatory state because of marked fall in peripheral vascular resistance and increased total blood volume and heart rate. These cardiovascular changes can aggravate pre-existing cardiac disease or directly lead to thyrotoxic heart disease.

MATERIALS AND METHODS:

STUDY DESIGN

The study was conducted at M.M. Institute of Medical sciences and Research, Mullana, Ambala. Total fifty individuals were included in the study .Out of them, Twenty five were cases and twenty five were age and sex matched controls. The patients were taken from the outpatient department (OPD) and Indoor wards of the department of Medicine and Emergency Department.

These patients suspected to be suffering from hyperthyroidism on clinical evaluation and confirmed by serum TSH ,T_4 and T_3 levels estimation were taken for the study.

INCLUSION CRITERIA

Patients has to-

1. Be within the age range of 18-80 years.
2. Patients with newly diagnosed hyperthyroidism by T3, T4, TSH levels.

EXCLUSION CRITERIA

1. Patients with age <18 yrs and >80 yrs.
2. Patient with known primary cardiac disease including hypertension
3. Patients with anaemia, anxiety neurosis, acute psychiatric illness, Diabetes Mellitus or any endocrinal disorder.
4. Patients taking medication that could alter cardiac functions like amiodarone, beta blockers, calcium channel blockers,oestrogens,tam oxiphen,clofibrate,amphet amines,thyroid hormone therapy.
5. Iatrogenic.

METHODOLOGY

The study proforma included-

a) History: a detailed history regarding duration of illness, any treatment received and past history of illness was taken. Age and sex of the patient was noted.

b) General physical examination: a detailed general physical examination was done with special reference to pulse rate and character, blood pressure, Juglar venous pressure, presence of pallor.

c) Respiratory and cardiovascular examination: a thorough examination of chest and CVS was done with special reference to evidence of Congestive heart failure and special emphasis on heart sounds including murmurs.

THROID PROFILE

A combination of a low OR suppressed TSH concentration and a raised T3 and T4 concentration has diagnostic value for primary hyperthyroidism. In the present study, measurement of TSH, T3 and T4 will be done.

ELECTROCARDIOGRAM (ECG)

ECG was recorded in all the patients, in all the 12 standard leads, at a paper speed of 25mm per sec. Abnormalities on the ECG often provide the first evidence of cardiac dysfunction in patients in whom it is suspected. Diagnosis of tachycardia or cardiac rhythm disturbances or LVH was made using standard guidelines.

CHEST ROENTGENOGRAM

Posteroanterior films were obtained in all subjects. The following were noted:

- Cardiac Silhouette
- Pulmonary Vasculature and Parenchymal Changes.

ECHOCARDIOGRAPHY

Echocardiography was done in ECHO lab of cardiology unit in M.M.I.M.S.R. Echocardiography assessment was done by using model vivid-e Color Doppler echocardiography machine of GE make. Echocardiographic assessment was done in M-mode, two-dimensional and Doppler mode using colour flow mapping. Patients were examined in the left lateral and supine position in quiet respiration.

a) **M Mode Echocardiography**
b) Two Dimensional Echocardiography
Left Ventricular Indices were assessed and then were used to calculate Left Ventricular Mass by using the cube formula proposed by Devereux.

LV Mass = Myocardial Volume ×1.05g/cm³
=[{IVSd+LVIDd+LVPWd}³-(LVIDd)³]×1.05g/cm³.

c) Doppler Parameters Of Mitral Valve
a) E wave velocity
b) A wave velocity
c) E:A ratio
d) Deceleration time
e) IVRT

In this study, patients included in the study were treated as per the standard treatment schedule. The data obtained was analysed with appropriate statistical analysis tools at the end of the study and conclusive evidence was derived.

OBSERVATIONS:
1) GROUP 1- Newly diagnosed hyperthyroid patients (study group) GROUP 2- Normal population.
2) The mean age of studied patients was 36.80±11.86 in group 1 and 42.60±11.19 in group 2 and Male to Female ratio was 0.56:1.
3) The mean weight in group 1 was 47.88±4.40 as compared to 66.80 ± 13.40 in group 2.The difference is statistically significant (p<0.001).

The observations hence have been tabulated and presented as follows:

Table 1 showing Mean T_3 , T_4 and TSH values of the studied patients:

PARAMETER	GROUP 1(n=25)	GROUP 2(n=25)	p VALUE
T3(ng/ml)	3.33±1.85	1.09 ±0.38	<0.001
T4(µg/dl)	16.74±4.89	8.21± 2.12	<0.001
TSH(µIU/ml)	0.01 ±0.01	2.58± 1.58	<0.001

Table 2: Systemic arterial pressure distribution of the studied patients:

PARAMETER (mm Hg)	GROUP 1(n=25)	GROUP 2(n=25)	p Value
SBP	117.28± 11.34	115.52 ±9.94	0.562
DBP	65.92± 6.12	74.64 ±5.35	<0.001
PP	45.84 ± 7.32	40.88 ± 7.46	0.022
MAP	86.44 ± 8.49	88.16 ± 6.25	0.816

In group 1, diastolic blood pressure was significantly lower than group 2 and pulse pressure was significantly higher in group 1 than group 2.

Table 3 showing ECG changes in the studied patients:

	GROUP 1(n=25)	GROUP 2(n=25)	p VALUE
Sinus tachycardia	17(68%)	0	<0.001
Atrial fibrillation	1(4%)	0	
LVH	3(12%)	0	0.235

All subjects in group 2 showed no ECG abnormality whereas in group 1, Seventeen patients (68%) had sinus tachycardia, Three patients (12%) presented with left ventricular hypertrophy, Only one patient presented in atrial fibrillation with fast ventricular response (4%) ; remaining showed no rhythm disturbances.

No significant ST-T changes were observed in the hyperthyroid cases.

Table 4 showing Chest X Ray findings in the studied patients:

Cardiothoracic ratio	GROUP 1(n=25)	GROUP 2(n=25)	TOTAL	p Value
Increased	3(12%)	0	3(12%)	0.149
Normal	22(88%)	25(100%)	47(88%)	

In group 1, Three patients (12%) had increased cardiothoracic ratio. None in group 2 showed any increased cardiothoracic ratio. The difference was not statistically significant (p=0.149).

Pulmonary vasculature and Parenchymal findings in both group 1 and group 2 were almost similar, no significant differences were present.

LEFT VENTRICULAR FUNCTIONS:
SYSTOLIC PARAMETERS

Table 5 showing Left Ventricular dimensions of the studied patients:

DIMENSIONS(mm)	GROUP 1(n=25)	GROUP 2(n=25)	p Value
LVID(d)	42.56±0.77	40.02±4.43	0.007
LVID(s)	34.29±2.18	26.68±3.52	<0.001
IVS(d)	8.97 ± 0.85	8.39±0.95	0.029
IVS(s)	11.78 ±1.33	10.19±1.10	<0.001
LVPW(d)	9.16±0.79	8.70±0.80	0.039
LVPW(s)	11.95±1.71	10.51±1.11	0.001

In group 1, LVID(d), LVID(s), IVS(d),IVS(s), LVPW(d), LVPW(s) were significantly greater as compared to group 2 and statistically significant.

Table 6 showing Left Ventricular Volumes of the studied patients:

VOLUMES(ml)	GROUP 1(n=25)	GROUP 2(n=25)	p Value
EDV	85.69±7.53	76.24±3.99	<0.001
ESV	30.07 ± 4.04	25.08 ± 3.11	<0.001
SV	55.63 ± 6.29	51.32 ± 4.76	0.009

In group 1, EDV, ESV and SV were significantly higher as compared to group 2.

Table 7 showing Left Ventricular Indices of the studied patients :

LV INDEX (%)	GROUP 1(n=25)	GROUP 2(n=25)	p Value
EF	61.68 ±4.27	63.04 ±2.99	0.200
FS	33.36±4.20	32.06 ± 3.60	0.244

There was no statistically significant difference in Ejection fraction or fractional shortening in group 1 as compared to group 2.

Table 8 showing Left Ventricular Mass and LV Mass Index of the studied patients:

PARAMETER	GROUP 1(n=25)	GROUP 2(n=25)	p Value
LV Mass(gm)	111.56±21.93	113.28±23.44	0.738
LV Mass Index(gm/m²)	77.76±14.73	67.40±11.49	0.008

Left ventricular mass index was significantly higher in group 1 as compared to group 2.

DIASTOLIC PARAMETERS
Table 9 showing E wave, A wave and E/A ratio of the studied patients :

Clinical characteristics	GROUP 1(n=25)	GROUP 2(n=25)	p Value
E wave	87.62±14.81	79±3.35	0.007
A wave	66.14±15.06	57±2.45	0.004
E/A ratio	1.32±0.23	1.38±0.07	0.203

The E wave and A wave was statistically significant in group 1 as compared to group 2 but E/A ratio was not statistically significant.

Table 10 showing Deceleration time (DT) and Isovolumetric Relaxation Time (IVRT) of the studied patients :

PARAMETERS (msec)	GROUP 1(n=25)	GROUP 2(n=25)	p Value
DT	164.20±18.74	174.44±9.35	0.018
IVRT	88.08±6.28	88.44±6.09	0.838

The mean deceleration time was 164.20±18.74 msec in group 1 and 174.44 ±9.35 msec in group 2 .The difference was statistically significant (p=0.018). The mean Isovolumetric Relaxation Time(IVRT) was 88.08±6.28 msec in group 1 and 88.44±6.09 msec in group 2.The difference was not statistically significant(p=0.838).

Table 11 showing Haemodynamic Parameters of the studied patients :

PARAMETER	GROUP 1(n=25)	GROUP 2(n=25)	p Value
HR(bpm)	107.92± 9.06	80.40± 7.44	<0.001
CO(L/min)	5.98±0.83	4.11± 0.46	<0.001
CI(L/min/m²)	4.16±0.59	2.38 ± 0.39	<0.001

Mean Heart rate, Cardiac output and Cardiac index were significantly

raised in group 1 as compared to group 2.

RESULTS:

1) The mean age in group 1 was 36.80 ±11.86 years as compared to 42.60± 11.19 years in group 2.With majority of patients belonged to age of 31-40 years. Male to female ratio was 0.56:1.
2) Hyperthyroid subjects were leaner as compared to normal subjects and weight was statistically significant (47.88±4.40;p<0.001).
3) Cardiothoracic ratio was increased in Three hyperthyroid cases (12%) which was not statistically significant(p=0.149).No significant pulmonary vasculature and parenchymal changes were observed in the hyperthyroid cases.
4) On Electrocardiogram assessment, Sinus tachycardia was found in seventeen hyperthyroid cases only (68%) which was statistically significant (p<0.001) and LVH was present in three cases(12%).Only one patient presented in atrial fibrillation with fast ventricular response (4%). No significant ST-T changes in ECG were observed in the hyperthyroid cases.
5) The mean Systolic blood pressure was not statistically significant when compared to euthyroid subjects (p=0.562).The mean diastolic blood pressure was significantly lower in hyperthyroid patients when compared to euthyroid subjects (p<0.001).The mean pulse pressure was significantly higher in the hyperthyroid cases when compared to controls (p=0.022) .There was no statistically significant difference in mean arterial blood pressure between cases and controls.
6) On Echocardiography assessment, Left ventricular dimensions both in diastole and systole were statistically significant when compared with euthyroid subjects.
7) Left Ventricular mass was statistically not significant in cases when compared to controls (p=0.738) but Left ventricular mass index was statistically significant in hyperthyroid cases when compared with euthyroid subjects (p =0.008).
8) End diastolic volume (p<0.001), End systolic volume (p<0.001) and Stroke volume(p=0.009) in hyperthyroid cases were statistically significant when compared to euthyroid subjects.
9) Mean EF and FS were statistically not significant in patients of hyperthyroidism when compared with euthyroid subjects.
10) In diastolic parameters, E wave (p=0.007) and A wave (p=0.004) were statistically significant but their ratio was not statistically significant (p=0.203).
11) Mean DT in cases and control was 164.20±18.74 and 174.44 ±9.35 respectively which was statistically significant (p=0.018).
12) Mean IVRT in cases and control was 88.08±6.28 and88.44±6.09 respectively which was not statistically significant (p=0.838).
13) The mean heart rate in hyperthyroid cases was 107.92±9.06 and 80.40± 7.44 in controls.Mean Cardiac Output in hyperthyroid cases was 5.98 ± 0.83 and in controls was 4.11±0.46 .The difference was statistically significant (p<0.001).Cardiac Index was also statistically significant in cases as compared to controls(p<0.001).
14) No regional wall motion abnormality was seen in the hyperthyroid subjects.

DISCUSSION:

Hyperthyroidism can present with myriad cardiovascular changes. As a non invasive test, Echocardiography can play an important role in recognizing the cardiac pathology and dysfunction as well as to follow up their response to therapy.

[0]In our study, tachycardia was the most common finding on ECG seen in 68% of cases followed by atrial fibrillation seen in 4% of cases. In another study by Sonawale A et al, the most ECG abnormality was sinus tachycardia seen in 67% of patients followed by atrial fibrillation seen in 17.5% of patients.[3]In another study by Ansari SM et al, the incidence of atrial fibrillation in their study was 61.7%, around 29 patients had atrial fibrillation in their study.[4]

In a study by Yue WC et al, all patients had suppressed TSH(<0.03pmol/l) and elevated free T4(mean 66±4 pmol/l).[5]This was consistent with our study whereT3(p<0.001), T4 (p<0.001) and TSH levels (p<0.001)were statistically significant .

In our study, Systolic blood pressure was not statistically significant in our studies when compared to controls (p=0.562).However, Diastolic blood pressure was significantly lower when compared to controls(p<0.001). In another study by Marcisz C et al, the hyperthyroid subjects had increased systolic blood pressure and reduced diastolic blood pressure on comparison with controls.[6]In another study, Anakwue RC et al demonstrated there was no significant difference in blood pressure when cases were compared to controls.[7]

In our study, pulse pressure was statistically significant in hyperthyroid cases when compared with controls (p=0.022).In another study by Kandan V et al, 50% of the patients had widened pulse pressure which was consistent with our study.[8]

In our study, Mean arterial pressure was not statistically significant in hyperthyroid cases as compared to controls. However in a study by Merillon JP et al, mean arterial pressure was significantly lower in hyperthyroid patients as compared to euthyroid subjects.[9]

[1]In our study, the mean weight of the patients was 47.80±4.40 which was statistically significant when compared with controls. In another study by Anakwue RC et al, hyperthyroid patients were leaner with a mean of 56 which was statistically significant when compared with controls.[7]

In our study, LVH was present in only 12% of the hyperthyroid subjects which was not statistically significant (p=0.235).In another study by Dorr M et al, LVH was observed in 57.1% of the hyperthyroid subjects which was statistically significant(p<0.001).[10]

In our study, Cardiomegaly was not significant in hyperthyroid subjects when compared with control groups (p=0.159).In another study by Sonawale A et al, only 4 patients had cardiomegaly on Chest X ray which was not significant.[3]

In our study, Left ventricular diameter in systole and diastole were higher and statistically significant when compared with controls.In a study by Anakwue RC et al, LV end diastolic diameter was higher in cases than controls.[7]In a study by Mintz G et al, there was no significant difference between left ventricular internal dimensions both in systole and diastole between hyperthyroid subjects and control group.[11]In our study, Left ventricular posterior wall thickness was found to statistically significant in hyperthyroid when compared to the controls. In a similar study by Anakwue RC et al, posterior ventricular wall thickness was significantly higher in hyperthyroid patients than the control group.[7] Contrary to our study, Mintz G et al found no significant difference in the posterior wall thickness in between hyperthyroid subjects and control group.[11]In our study, Left ventricle Interventricular septal thickness was found to statistically significant in hyperthyroid when compared to the controls. In a similar study by Anakwue RC et al, IVS was significantly higher in hyperthyroid patients than the control group.[7]

In our study, End diastolic volume and End systolic volume were statistically significant when compared with euthyroid subjects. In a study by Merillon JP et al, left ventricular end diastolic and systolic volume were not statistically significant in hyperthyroid subjects when compared with controls.[9]In our study, Stroke volume was statistically significant in hyperthyroid cases when compared to controls. In another study by Marcisz C et al, the hyperthyroid subjects had augmented stroke volume when compared with euthyroid subjects.[6]

In our study, left ventricular mass was not found to be statistically significant when compared with controls. In a study by Marcisz C et al, left ventricular mass was found to be increased as compared to controls.[6]

However in our study, left ventricular mass index was found to be statistically significant. In a similar study by Dorr M et al, Overt hyperthyroidism was identified as an independent predictor for LVMI and was significantly increased in cases when compared with controls (p<0.05).[10]In another study by Anakwue RC et al, LVMI was significantly increased in hyperthyroid subjects than the normal subjects (p=0.05).[7]

In our study, ejection fraction was statistically not significant as compared to controls. Similar to our study, Pagsisihan DA et al demonstrated normal ejection fraction in their study.[12]

In our study, fractional shortening was not significant when compared with controls.In another study by Pagsisihan DA et al, Fractional shortening was normal in hyperthyroid cases as compared to

controls.[12]In contrast to our study Bond BR et al demonstrated increased indices of contractility including fractional shortening (21.4%) in hyperthyroid subjects compared to controls.[13]

Kahaly GJ et al in their study showed higher mitral E and A velocities were associated with a hyperthyroid state compared with euthyroid state.[14]This was consistent with our study.

In our study, E/A ratio was not statistically significant. In a similar study by Goyal V et al, E/A ratio was not statistically significant between cases and controls.[15]In contrast to our study, Pagsisihan DA et al in their study showed reduced E/A ratio implying left ventricular relaxation in the hyperthyroid subjects.[12]

In our study, deceleration time was found to be statistically significant when compared with controls. Similarly in a study by Kahaly GJ et al, a shorter deceleration time were associated with a hyperthyroid state when compared to euthyroid state.[14]

Rubler S et al in another study reported that IVRT in a group of patients with hyperthyroidism was not significantly different from the time interval measured in a group of normal patients.[16]This was consistent with our study. Mintz G et al in his study demonstrated shortened IVRT in a group of hyperthyroid patients ($p<0.005$) which normalized on attainment of euthyroid state.[11]

In our study, the mean heart rate was significantly higher in the hyperthyroid subjects than the controls. In a similar study by Merillon JP et al, heart rate were increased ($p<0.01$). [71] In a similar study by Merillon JP et al, cardiac output was increased in the hyperthyroid subjects ($p<0.01$).[9]This was consistent with our study. In our study, cardiac index was also found to be statistically significant in hyperthyroid cases when compared with controls. In a similar study by Lewis BS et al, increase in cardiac index was noted in a group of hyperthyroid patients which was statistically significant. [17]

In our study, no regional wall abnormality was detected in either cases or controls. Similarly no abnormalities in regional wall motion abnormality were detected in study of Forfar JC et al. [18]

CONCLUSION:

Hyperthyroidism represents hypermetabolism and is one of the most common causes of hyperdynamic circulatory state and by inducing vasodilatation or decreasing the peripheral vascular resistance, accelerating the heart rate and enhancing the ventricular contractility, thyroid hormone produces high output cardiac state.

The present study shows that there is marked increase in heart rate and stroke volume in newly diagnosed hyperthyroid subjects as compared to euthyroid subjects along with statistically significant increase in cardiac output and cardiac index. Left ventricular systolic and diastolic function are preserved with no significant ST-T changes or regional wall motion abnormality. Therefore, the study represents that Newly diagnosed hyperthyroidism is a high output cardiac state with normal left ventricle function.

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