

Study of Clinical Profile and Cardiac Dysfunction in Patients of Hyperthyroidism

¹Dr. Jayshree Awalekar, ²Dr.Ganesh Gore, ³Dr .C. D. Awalekar, ⁴Dr. Amit Pawale

Corresponding Author: Dr.Jayshree Awalekar, Department of Medicine Bharati Vidyapeeth Deemed to be University Medical College & Hospital,Sangli

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Introduction

Excess thyroid hormone typically causes systolic blood pressure to rise. Hyperthyroidism has been documented as a secondary cause of isolated systolic hypertension. Overt hyperthyroidism is common in the community, with the prevalence in iodine repleted areas reported to range from 0.5% to 3.9% in adults of all age groups and 11.8% in one study of the elderly, the prevalence may be higher in areas of iodine deficiency. The most common cause in the general population is the ingestion of exogenous T4 as replacement or suppressive therapy.^{9,10,13}

Hyperthyroidism increases heart rate (HR), myocardial contractility, Left Ventricular (LV) mass, ejection fraction & cardiac output(CO), The hemodynamic consequences of hyperthyroidism are due to the direct action of thyroid hormone on the heart and blood vessels^{1,2}.

Nongenomic actions target membrane ion channels and endothelial nitric oxide synthase, which serves to decrease Systemic Vascular resistance (SVR). Relaxation of vascular smooth muscle leads to decreased arterial resistance. The fall in SVR plays a central role in the

Cardiovascular Signs and Symptoms^{1,2}

Symptoms	Signs
Hyperactivity, irritability,	Tachycardia; atrial fibrillation in the elderly
Heat intolerance and sweating	Tremors Goitre
Palpitations	Warm, moist skin
Fatigue and weakness	Muscle weakness, proximal myopathy
Weight loss with increased appetite, Diarrhoea	Lid retraction or lag

hemodynamic changes that accompany hyperthyroidism, contributing to a further increase in HR, increase in systolic blood pressure, These result in an increase in cardiac output of up to 50-300%⁸ .Also there occurs improvement in diastolic relaxation so widening of pulse pressure is observed in hyperthyroid patients¹¹. All these factors contributes to an increase in LV End-diastolic volume (LVEDV)⁶.

The net result of increased preload and reduced afterload is translated into a significant increase in Stroke Volume (SV). Similarly, the increased HR & SV leads to a doubling or tripling of CO. The CO is much greater than it would be expected from the high levels of thyroid hormone and the increase in the body’s metabolic rate. Of the preceding factors, the increase in preload is mainly responsible for the increase in CO.

It predisposes to supraventricular and ventricular arrhythmias & atrial fibrillation(AF). Recent studies show pulmonary arterial hypertension(PAH) & systolic and diastolic dysfunction in hyperthyroidism.

Polyuria Oligomenorrhea, loss of libido	Gynecomastia
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Hemodynamic consequences of hyperthyroidism^{2,9}

❖ Peripheral vasodilatation.	❖ Reduction in renal perfusion.
❖ Reduction in peripheral resistances.	❖ Increase in myocardial contractility.
❖ Improvement in diastolic relaxation.	❖ Increase in ejection fraction.
❖ Increase in HR	❖ Increase in SV.
❖ Increase in cardiac output	❖ Increase in PAH

The vasodilatation and decrease in renal blood flow lead to a reduction in renal perfusion and activation of the renin-angiotensin system, which increases Na retention and blood volume.

The pathophysiological mechanisms of PHT (pulmonary hypertension) and/or right heart failure in thyrotoxicosis are not completely understood. High CO combined with elevated circulatory volume, determines an increased and rapid venous return to the right ventricle (RV). These factors lead to dilatation of RV, with pressure overload and augmentation of pulmonary arterial pressure (PAP)^{7,8}. PAH is characterized by a sustained augmentation of pulmonary arterial pressure with progressive increase of pulmonary vascular resistance, that leads to right ventricular failure and elevated mortality^{4,7,14}

Other authors suggested that the vasodilator effect of the thyroid hormone, which leads to reduced systemic vascular resistance (SVR), may not occur in the pulmonary vascular bed.

Hyperthyroidism & AF

AF occurs in 5% and 15% of patients with hyperthyroidism due to increased sympathetic stimulation. The majority of AF patients have an enlarged left atrium on echocardiography compared with less than 7% of hyperthyroid patients in sinus rhythm.^{3,11,12}

Hyperthyroidism and Angina pectoris

Because of the increase in cardiac oxygen consumption, due to a direct effect of T3 on cardiac muscle & or an increase in peripheral oxygen demand.^{1,11,13}

Hyperthyroidism and electrophysiological changes-

AF is common in hyperthyroidism, which may lead to heart failure and thromboembolisation which causes myocardial infarction, cerebrovascular accidents. Sinus tachycardia, nonspecific ST-T changes, bundle branch blocks are also observed.^{1,2,4}

Subclinical hyperthyroidism

Patients with subclinical hyperthyroidism have more subtle cardiac findings. These include small increases in HR and cardiac contractility, and increased risk of atrial fibrillation as compared with euthyroid subjects.

The isovolumic relaxation period was shorter in patients with subclinical hyperthyroidism than in control individuals and in patients with overt hyperthyroidism.^{12,13}

Aims: To study clinical profile ,Electrocardiographic changes & echocardiography in patients with hyperthyroidism.

Objective: To study clinical manifestations of hyperthyroidism.

To study cardiovascular manifestations of hyperthyroidism by electrocardiogram & echocardiography.

Material & Methods

Source of Data: Newly diagnosed cases of hyperthyroidism according Thyroid Function Tests (TFT) i.e.T3, T4, TSH levels, who fulfil inclusion and exclusion criteria from outpatients and in patients of Bharati Vidyapeeth Deemed University Medical College and Hospital at Sangli The Institutional Ethical committee approval was taken.

Inclusion Criteria

- Newly diagnosed cases of hyperthyroidism & subclinical hyperthyroidism of age 18-70 years.

Exclusion Criteria

- Known cases of Rheumatic valvular heart disease, ischemic heart disease, cardiomyopathy and congestive cardiac failure, COPD, Asthma. Pulmonary artery hypertension cases of secondary causes; Acute or chronic kidney disease; Patient already known case of thyroid dysfunction on treatment.
- **Sample Size**-30 patients **Sampling technique**-simple random sampling.

Study Methods

- Detail history and consent was obtained from the patient or by his/her relative.
- All the patients in the study were thoroughly examined and investigated with CBC, blood sugar level, blood urea, serum creatinine, thyroid function test, HIV, lipid profile, chest X-ray, ECG, 2D ECHO.

Normal values of TFT

Types	SI Unit	Conventional Units
serum T3 (triiodothyronine)	1.2 to 2.1 nmol/L	77-135 ng/dl
serum T4(Thyroxine)	70-151 nmol/L	5.4-11.7µg/dl
serum TSH	0.34-4.25 mlu/L	0.34-4.25µlu/ml

Interpretation of TFT-

TSH	T3	T4	Interpretation
Low	Normal	Normal	Subclinical Hyperthyroidism
Low	High Or Normal	High Or Normal	Hyperthyroidism

- Patients were imaged in left lateral and supine position using “GE healthcare Vivid S5 220-240V ~500VA 50/60HZ” echocardiography machine. Standard M mode, two dimensional data were taken.
- The recordings were done in end expiratory phase, and mean of three measurements on adjacent heart beats in a recording of adequate quality was used in the analyses. The conventional M mode, four chamber, two chamber views were used recommended by the American Society of Echocardiography.
- The M mode tracing was used to measure the LV end systolic and end diastolic diameters, interventricular septum thickness and posterior wall thickness. From these variables we calculated LV volume, cardiac output, ejection fraction.
- From four chamber view we measured the peak flow velocity in early diastole (E wave) and during atrial contraction (A wave). With these values, E/A ratios were determined, and diastolic dysfunction was calculated as E/A ratio <1.0

- Systolic dysfunction was measured by LV ejection fraction(LVEF)< 40%.
- PAH was measuring the pulmonary arterial pressure >25mmHg.
- Pericardial effusion measured in parasternal short and long axis view in systole by measuring the parasternal collection of fluid or blood. It was measured as, ECHO free space if <5mm called small effusion, if 5-10mm called moderate effusion and if >10mm called as large pericardial effusion.

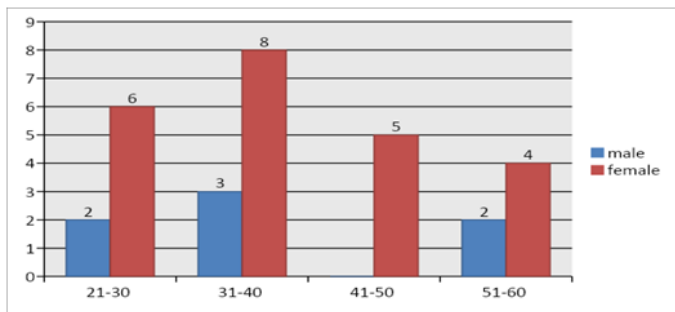
Statistical Analysis: Statistical analysis was done by using Microsoft Excel and SPSS-22. Proportions and percentage were obtained by z test. A standard error of difference between the two proportions was used.

Methods: Cross sectional study

Observations And Results

Table 1: Age & Sex Wise Distribution

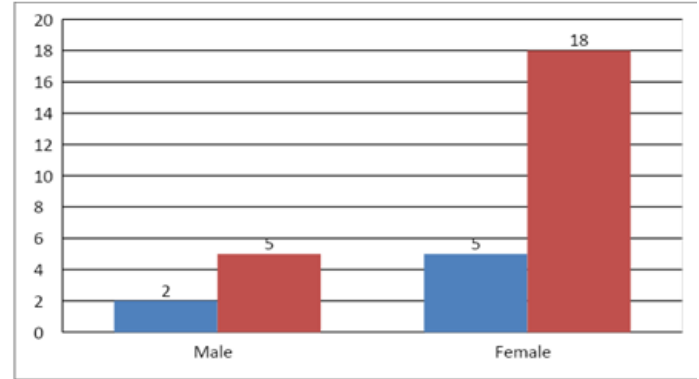
	Male	%	Female	%	Total	%
21-30	2	6.67	6	20	8	26.67
31-40	3	10	8	26.67	11	36.67
41-50	0	0	5	16.67	5	16.67
51-60	2	6.67	4	13.33	6	20



Our study shows, hyperthyroidism was common in females than males. Most are of 31-40 years age (36.67%), then 21-30 years (26.67%), 51-60 years (20%), 41-50 years (16.67%).

Table 2: Types of Hyperthyroidism

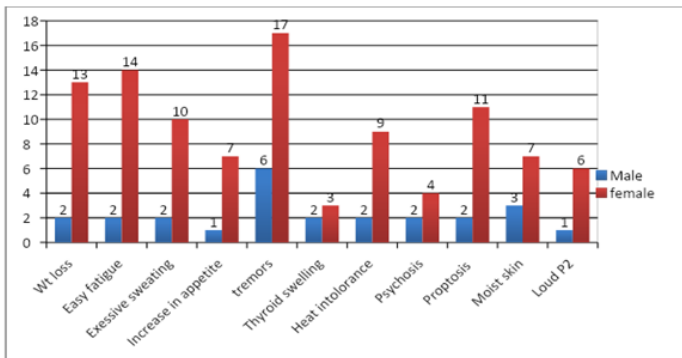
Types	Male	%	Female	%	Total	%
Subclinical hyperthyroidism	2	6.67	5	16.67	7	23.34
Overt hyperthyroidism	5	16.67	18	60	23	76.67



In present study the subclinical hyperthyroidism cases are 7 (23.33%) ,overt Hyperthyroidism are 23 (76.67%).

Table No. 3: Symptoms & Signs

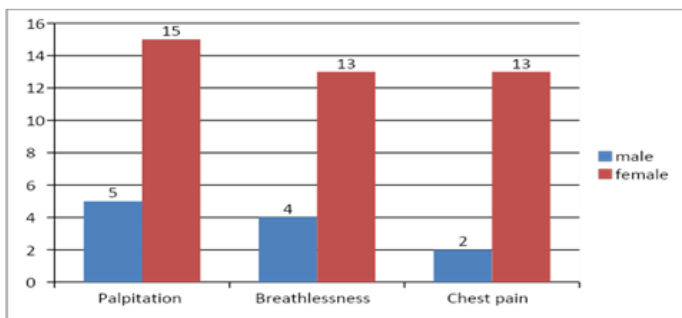
symptoms	Male	%	Female	%	total	%
Wt loss	2	6.67	13	43.33	15	50
Easy fatigue	2	6.67	14	46.67	16	53.34
Excessive sweating	2	6.67	10	33.33	12	40
Increase in appetite	1	3.33	7	23.33	8	26.66
tremors	6	20	17	56.66	23	76.66
Thyroid swelling	2	6.67	3	10	5	16.67
Heat intolerance	2	6.67	9	30	11	36.67
Psychosis	2	6.67	4	13.33	6	20
Proptosis	2	6.67	11	36.66	13	43.33
Moist skin	3	10	7	23.33	10	33.33
Loud P2	1	3.33	6	20	7	23.33



The commonest symptom was tremors in 23 cases (76.66%), followed by Easy Fatigue 16(53.34%), weight loss 15(50%), Excessive sweating 12 (40%), Heat tolerance 11(36.67%), Increase in appetite 8(26.66%), Psychosis 6 (20)% and Thyroid swelling in 5(16.67%), and signs like proptosis in about13(43.33%), moist skin 10 (33.33) and loud P2 in7(23.33%).

Table 4: Cardiovascular Symptoms

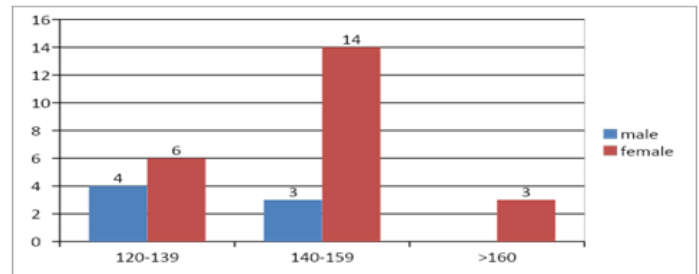
Symptoms	Male	%	Female	%	Total	%
Palpitation	5	16.67	15	50	20	66.67
Breathlessness	4	13.33	13	43.33	17	56.66
Chest pain	2	6.67	13	43.33	15	50



In present study commonest cardiovascular symptom is palpitations in 20 (66.67%) patients. Breathlessness in 17 (56.66%) and chest pain in 15(50%) patients.

Table 5: Systolic Blood Pressure

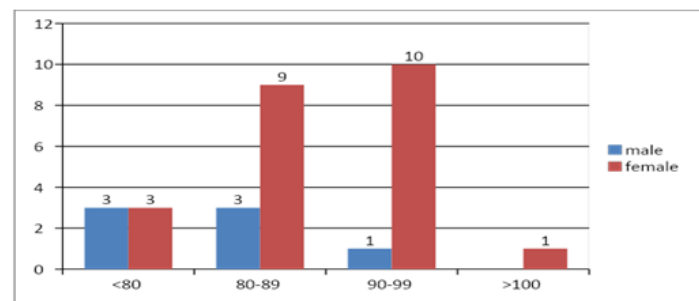
Blood pressure mm Hg	Male	%	Female	%	Total	%
120-139	4	13.33	6	20	10	33.33
140-159	3	10	14	46.67	17	56.67
>160	0	0	3	10	3	10



In present study the most of patients had systolic blood pressure present from range 140-159 mmHg in 17 (56.67%) patients followed by 120-139 mmHg in 10 (33.33%) patients , >160mmHg was in 3 (10%) patients.

Table 6 : Diastolic Blood Pressure

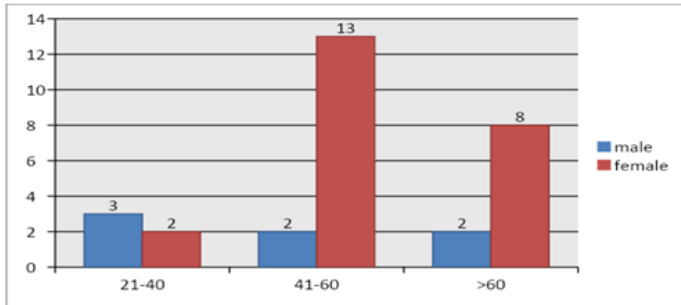
Blood pressure mmHg	Male	%	Female	%	Total	%
<80	3	10	3	10	6	20
80-89	3	10	9	30	12	40
90-99	1	3.33	10	33.33	11	36.67
>100	0	0	1	3.33	1	3.33



In present study most patients had diastolic blood pressure from range 80-89 mmHg 12 (40%) followed by 90-99 mmHg about 11(36.67%) ,<80 mmHg were 6 (20%) and >100 were 3.33%.

Table 7: Wide Pulse Pressure

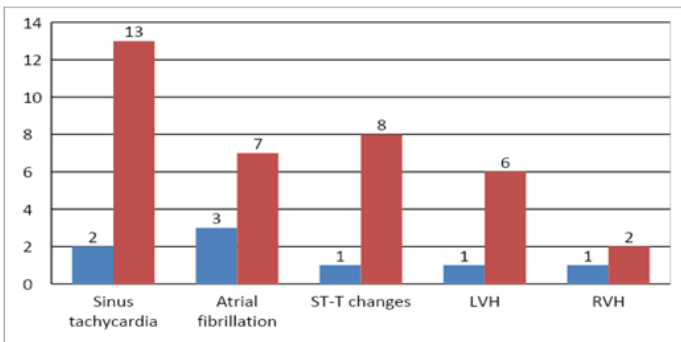
Pulse pressure mmHg	Male	%	Female	%	Total	%
21-40	3	10	2	6.67	5	16.67
41-60	2	6.67	13	43.33	15	50
>60	2	6.67	8	26.66	10	33.33



In present study , Pulse pressure of 21-40 mm Hg in (16.67%), 41-60mmhg (50%), and wide pulse pressure > 60mmHg present in 10(33.33%) patients.

Table 8 : ECG Changes

ECG Changes	Male	%	Female	%	Total	%
Sinus tachycardia	2	6.67	13	43.33	15	50
Atrial fibrillation	3	10	7	23.33	10	33.33
ST-T changes	1	3.33	8	26.67	9	30
LVH	1	3.33	6	20	7	23.33
RVH	1	3.33	2	6.67	3	10

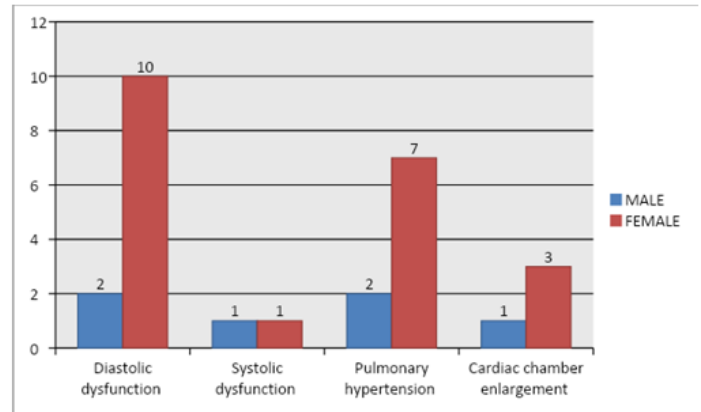


The most common ECG finding was sinus tachycardia in 15(50%) patients followed by Atrial fibrillation in 10

(33.33%), Non-specific ST-T changes in 9(30%),LVH in 7(23.33%), and RVH present in about3(10%) patients.

Table 9: ECHO Findings

ECHO	Male	%	Female	%	Total	%
Diastolic dysfunction	2	6.67	10	33.33	12	40
Systolic dysfunction	1	3.33	1	3.33	2	6.67
Pulmonary Arterial hypertension	2	6.67	7	23.33	9	30
Cardiac chamber enlargement	1	3.33	3	10	4	13.33



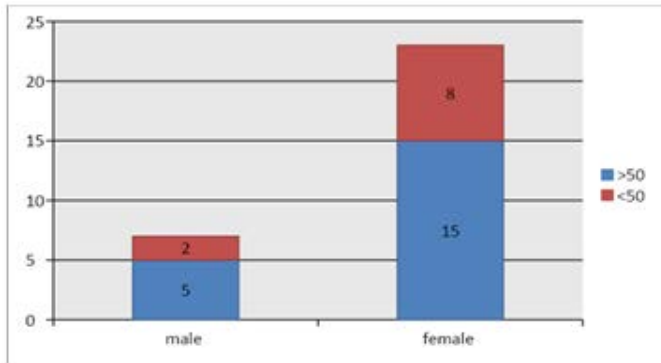
In present study, the most common cardiovascular manifestations found on ECHO was diastolic dysfunction in12 (40%) patients, PAH in 9(30%) patients, cardiac chamber enlargement in 4(13.33%) patients and systolic dysfunction in 2(6.67%) patients.

Echocardiography was abnormal in 16 patients, of which diastolic dysfunction was present in 12 (75%) patients which is significant than PAH systolic dysfunction & cardiac chamber enlargement. The PAH was present in 9 (56.25 %) out of 16 patients of abnormal echocardiography,which was significant than systolic dysfunction & cardiac chamber enlargement

The P value was z=2.59, p=0.009 for PAH

Table 10: LV Ejection Fraction

LVEF	Male	%	Female	%	Total	%
>50	5	16.67	15	50	20	66.67
<50	2	6.67	8	26.67	10	33.33



LVEF >50% present in 20(66.67%) patients and LVEF <50% present in 10(33.33%) patients, so LVEF >50% was significant than LVEF <50%.

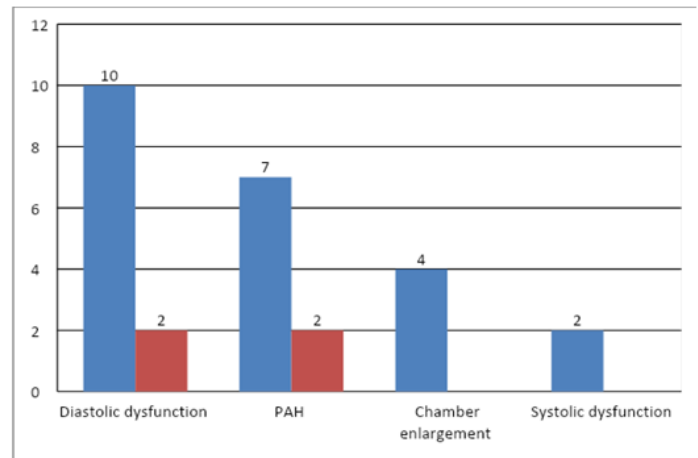
The p value was $z = 2.375$; $P = 0.018$.

Only 2 (6.67%) patients with LVEF <40% had systolic dysfunction.

Majority of patients had normal and/or increased LVEF.

Table 11: Types Of Hyperthyroidism & ECHO Findings

ECHO	Overt hyperthyroidism	%	Subclinical hyperthyroidism	%
	23		out of 7	
Diastolic dysfunction	10	43.48	2	28.57
PAH	7	30.43	2	28.57
Chamber enlargement	4	17.40	0	0
Systolic dysfunction	2	8.7	0	0



In present study there were 23 overt hyperthyroid and 7 subclinical hyperthyroid patients. In overt hyperthyroid diastolic dysfunction was a commonest finding present in 10(43.48%) patients, followed by PAH, chamber enlargement and systolic dysfunction.

In subclinical hyperthyroid patient had both diastolic dysfunction and PAH were in 2(28.57%) patients.

Discussion

Females were found to be more than male suffering from Hyperthyroidism. Female to male ratio was 3.13:1. Kandan V et al in their study had 60 % females. Vijaya K et al had 82 % patients were female. It shows that, prevalence of hyperthyroidism was more in females than male.

The peak incidence of Hyperthyroidism was observed in the age group of 31-40 years in 11(36.67%) patients, Vijaya K et al in their study found same age group incidence maximum⁴.

Subclinical hyperthyroidism found in 7(23.33%) patients while overt hyperthyroidism found in 23 (76.67%) patients. In present study, maximum number of patients suffering from overt Hyperthyroidism.

The commonest symptom found, was tremors in 23 (76.66%) cases, followed by Easy Fatigue 16 (53.34%), weight loss 15 (50%), Excessive sweating 12 (40%), Heat tolerance 11 (36.67%), Increased appetite 8 (26.66%), Psychosis in 6 (20%) and Thyroid swelling in 5 (16.67%).

In present study, patients had commonest signs was proptosis present in about 13 (43.33%) patients, moist skin in 10 (33.33%) and loud P2 in 7 (23.33%) patients.

The Singhal et al.¹⁰ had common symptoms of irritability, heat intolerance excessive sweating, palpitation, weight loss, increase appetite, tachycardia, fine tremors warm & moist skin, and proptosis serially. Vergara Villauz et al.^[16] reported palpitation 31 (56.4%), weight loss 21 (38.2%), tremors 22 (40%) excessive sweating 22 (40%), fatigue 16 (29.1%) shortness of breath (10.9%),

In this study the commonest cardiovascular symptom was palpitations in 20 (66.67%) patients followed by breathlessness in 17 (56.66%) and chest pain in 15 (50%) patients. The study done by Osman et al.¹¹ had palpitation in 73% followed by breathlessness 60% and chest pain in 25% patients. In Zarger et al.^[12] study palpitation was in 69.4% patients.

Most patients, in our study had systolic blood pressure (SBP.) ranged from 140-159 mmHg in 17 (56.67%) followed by 120-139 mmHg about 10 (33.33%) , >160mmHg was in 3 (10%). Most patients had diastolic blood pressure from range 80-89 mmHg 12 (40%) followed by 90-99 mmHg in 11(36.67%) ,<80 mmHg in 6 (20%) and >100 were 3.33%.

The wide pulse pressure (PP) present in 10 (33.33%) patients of our study. While it was 30% in Klein et al. study².

In present study the most common ECG finding was sinus tachycardia in 15 (50%) patients while study by Zarger et al.¹² was 63.5%. The prevalence of atrial fibrillation varies between 2% to 20%. The Atrial fibrillation present in 10 (33.33%) our patients, where as Zarger et al.^[12] study it was seen 8.9% & in Osman et al.¹¹ study it was found in 6% of patients. In Barsela et al.⁴ study 21% patients had atrial fibrillation.

Parameters	Our Study	Vidy a B et al. ¹² n=23	Kanda n V et al. ¹¹	Vijay a K et al. ⁴ n=50	Klei n et al. ²	Gupta et al. ^[13]
Palpitations		69%	78	92		
Tremors	76.6	30		88		
Weight loss	50			84		
Wide PP	33.33 %				30%	
Sinus tachycardia	15%	39%	42	68		
Atrial Fibrillation	33.33 %	26%	6%	8%		
Nonspecific ST-T Changes	30%	13%		8		14.6 %
LVH(ECG)	23.33 %	13%		10		
RVH(ECG)		8.7				10%
Systolic Dysfunction		21.7	18	18		
Diastolic Dysfunction		13				
PAH		8.7				

Non-specific ST-T changes present in 9 (30%) patients, while it was 2.9% in Zarger et al.^[12] study. The LV hypertrophy present in 7 (23.33%) patients while in Zarger et al.^[12] it was 5.4% and in Gupta et al.^[13] about 14.6% present. The RVH present in about 3(10%) patients.

Diastolic Dysfunction

On ECHO most common cardiovascular manifestation was found to be diastolic dysfunction which was present in 12 (40%) patients. The study was done by Yue et al¹⁵ the diastolic dysfunction was present in 17.9% patients. So

diastolic dysfunction was most commonest finding in this study.

	Our Study	Yue et al ¹⁵
Diastolic dysfunction	40 %	17.9

PAH (Pulmonary arterial pressure)-

In this study the second most finding noted on ECHO was pulmonary arterial hypertension (PAH) present in 9 (30%) patients. The study done by Marvisi et al.⁵ his finding of pulmonary hypertension was 35% and Merce et al.⁶ PAH was 41%. Arnigliato et al.⁷ it was 65% Jonathan H. Li.¹⁵ described a high prevalence of PAH about 24% , and Siu et al.⁸ it was 47%. Present study finding was similar to study of Marvisi et al.⁵ study & Jonathan H. Li¹⁵ study.

	Our Study	Marvisi et al. ⁵	Merce et al. ⁶	Arnigliato et al. ⁷	Jonathan H. Li. ¹⁵	Siu et al. ⁸
PAH %	30	35	41	65	24	47

(A) Cardiac Chamber Enlargement-

The third common finding on ECHO was cardiac chamber enlargement in 4 (13.33%) patients. While study done by Ansari et al.⁹ it was 19.1%

	Our Study	Ansari et al. ⁹
Chamber Enlargement	13.33	19.1

(B) Systolic Dysfunction-

Systolic dysfunction was present study in about 2(6.67%) patients while the study done by Ansari et al.⁹ it was 2.1%. In study done by Merce et al.⁶ his finding of systolic dysfunction was about 39%. So in this study finding of systolic dysfunction was similar to Ansari et al.⁹ study. Systolic dysfunction will be the late cardiac manifestation and for it LVEF <40%. As we taken newly detected cases

of thyroid disorders so patients suffering from systolic dysfunction were less.

	Our Study	Ansari et al. ⁹	Merce et al. ⁶
Systolic Dysfunction	6.67	2.1	39

The diastolic dysfunction was the commonest finding. The echocardiographies were abnormal in 16 patients and normal in 14 patients. The diastolic dysfunction was present in about 12(75%).

Diastolic dysfunction was significantly higher than PAH, cardiac enlargement and systolic dysfunction.

The second most common finding was pulmonary arterial hypertension which was present in 9 (56.25%) out of 16 abnormal echocardiography patients. P value was Z = 2.59, P = 0.009 p value was significant in this study significant than cardiac chamber enlargement and systolic dysfunction. The cardiac enlargement and systolic dysfunction were not significant findings.

Echocardiography, is the most important tool to detect earlier cardiovascular manifestations.

Conclusions

In present study total 30 patients were hyperthyroid. Females had high prevalence of thyroid disorders.

- Females were more than male
- Majority of patients in present study from the age group 31-40 years.
- In present study, majority of symptoms and signs in general examination were tremors, fatigue, proptosis, weight loss.
- In this study, cardiovascular symptoms palpitation, breathless and chest pain in which palpitation was most common.
- In present study, majority of patient had pulse pressure between 41-60mmhg.

- In present study, the commonest ECG finding was sinus tachycardia followed by non-specific ST-T changes, atrial Fibrillation and LV hypertrophy.
- In this study, on echocardiography diastolic dysfunction was the most common finding of hyperthyroidism. It was significantly higher than PAH, cardiac chamber enlargement and systolic dysfunction. Also there was high prevalence of pulmonary arterial hypertension in hyperthyroid patients than cardiac chamber enlargement and systolic dysfunction.
- In this study, majority of hyperthyroid patient had significant high LV ejection fraction.
- In this study, in subclinical hyperthyroid both diastolic dysfunction and PAH equally present in ECHO findings. The test of significance could not be applied due to less number of data for comparison.

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