Journal of Cardiovascular Disease Research

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 08, 2022

ORIGINAL RESEARCH

Clinical and Subclinical Hyperthyroidism and its Cardiovascular Manifestation

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Received: 19 September, 2022 Accepted: 23 October, 2022

Abstract

Background: Patients with hyperthyroidism present a morbid life. The quality of life is low. Under this setting, understanding the clinical profile of these patients helps to improve their quality of life by the physician.

Objectives: To study various cardiac manifestations in overt hyperthyroidism and subclinical hyperthyroidism.

Methods: A total of 46 consecutive unselected patients with overt and subclinical hyperthyroidism were recruited. Institutional Ethics Committee permission was obtained and informed consent was taken from each and every patient. All had a structured cardiovascular history and examination, including measurements of blood pressure (BP) and pulse rate. All had resting 12-lead electrocardiogram and 2D-ECHO. Data was entered and analyzed.

Results: In Hyperthyroidism out of 46. In patients population female preponderance was seen with male to female ratio being 4.5:5. Palpitation was the most common cardiovascular symptom , present in thirty two (70%) cases followed by Dyspnea and Chest pain. Atrial fibrillation was the predominant ECG finding in the present study, 19 patients out of 46 patients of hyperthyroidism followed by Sinus Tachycardia (35%), RAD (15%), RVHi (17%) and ST Changes (13%)

2D-Echocardiographic analysis showed Pulmonary Hypertension in 10 (22%) cases and Chamber Enlargement in 12 (26%) cases followed by Systolic Dysfunction (21.7%), Diastolic Dysfunction and Regurgitant Lesion chiefly MR & TR in a isolate case.

Conclusion: In conclusion, thyroid disorder is a frequent disease, affecting more women than men. Thyroid hormones have essential effects on the cardiovascular system. Imbalance of their levels leads to disturbance in the homeostasis of the cardiovascular system. Serious cardiac complications such as congestive heart failure, atrial fibrillation, and angina pectoris may arise in thyroid disorder patients importantly, most of these deleterious hormone-mediated cardiovascular effects can be reversed or managed with the proper regulation or blockade of these hormones. Therefore, it is important for both endocrinologists and cardiolo-

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gists to apply a global approach in the assessment of such patients and to improve the prognosis of severe cardiac complications in overt / subclinical hyper-thyroid dysfunction.
Keywords: hyperthyroid, cardiovascular system,

Introduction

It has long been acknowledged that some of the most distinguishing and common signs and symptoms of thyroid disorder are those that result from the effects of thyroid hormone on the heart and cardiovascular system.[1]Thyroid hormone has a direct effect on the heart and peripheral vascular system. The hormone increases myocardial contractility and heart rate and cause peripheral vasodilation which increases the cardiac output.[2]Recent studies shows that 300 million people in the world are affected from thyroid disorders and among them about 42 million people resides in India with women being more commonly affected (Nimmy NJ *et al.,* 2012).[3]

The heart is an organ which is very sensitive to the action of thyroid hormones and quantifiable changes in cardiac performance are identified with small variations in serum concentration of thyroid hormone.[4]

Atrial arrhythmias, reduction in exercise tolerance, and congestive cardiac failure have been reported in cases of hyperthyroidism and are more common in older patients.[4] Hyperthyroidism results in rise in mortality from increased incidence of circulatory diseases and dysrhythmias. Incidence of cerebral embolism is more in hyperthyroid patients with atrial fibrillation, especially in the elderly and anticoagulation is indicated in them

Hemodynamic consequences of hyperthyroidism[5]

- Peripheral vasodilation.
- Reduction in renal perfusion.
- Reduction in peripheral resistances.
- Increase in myocardial contractility.
- Improvement in diastolic relaxation.
- Increase in heart rate.
- Increase in stroke volume.
- Increase in cardiac output.

The characteristic tachycardia is caused by a combination of more rapid diastolic depolarization and shortening of the action potential of the sinoatrial cells. The refractory period of the atrial cells is also shortened. LV systolic function is consistently increased at rest in hyperthyroid patients and the rate of LV chamber relaxation and LV filling is increased. The hyperthyroid cardiovascular system has a reduced functional reserve.[6]

Material and Methods

Patients diagnosed to have hyperthyroidism according fT3, fT4, TSH levels. A cross sectional study consisting of 46 cases of hyper-thyroid dysfunction was undertaken to study the cardiac manifestations by ECG and ECHO.

Inclusion Criteria

1. Patients who were diagnosed to have hyperthyroidism by fT3, fT4 and TSH levels.
2. Patients who were diagnosed to have hypothyroidism by fT3, fT4 and TSH levels.

Exclusion Criteria

1. Unwilling patient,
2. Smokers,
3. Previous radioactive iodine therapy

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4. Thyroidectomy,
5. External radiation
6. Consumption of drugs known to cause SCH
7. Primary or Secondary dyslipidemia, diabeties mellitus, renal and hepatic failure, or other systemic diseases were excluded from the studies
8. Patient on antiarrythmic drug

Methods

All patients who were willing to participate were evaluated with written Performa. Age, gender, symptoms with duration, signs with duration and other atypical presentations were documented. All patients had underwent a physical examination and following diagnostic test

1. Thyroid function test estimation- On the bases of Thyroid Function Test (fT3/fT4/TSH) patient were diagnosed with hyper-thyroid disorder.
2. Arterial Pulse rate Recording
3. Basal Metabolic Index
4. BLOOD PRESSURE Recording
5. Complete Blood Count
6. Lipid Profile Estimation
7. Chest X RAY
8. ECG
9. 2-D Echo Study

Data collection and statistical analysis

The data regarding history, clinical examination, routine and special investigations of study cases entered in pretested proforma and observations were tabulated.

Statistical software namely SPSS 17.0 was used for the analysis of data Mean values of the findings were compared among and between groups. Analysis of variance (ANOVA) test and Unpaired 't' test were done to assess the significance among the groups and between groups respectively. Pearson correlation coefficient test was done to evaluate the correlation of biochemical parameters with the severity of Thyroid disorder. 'p' values <0.05 were considered significant. Microsoft word and excel have been used to generate graphs, tables and descriptive statistics.

Observation and Result

Age Group	No. of cases of hyperthyroidism	Gender			
		Male		Female	
		No. of Patients	Percent	No. of Patients	Percent
20-40	16	6	28.6	10	40.0
41-60	21	12	57.1	9	36.0
Above 60	9	3	14.3	6	24.0
Total	46	21	100.0	25	100.0
P value for Chi –square test =0.351					

Table 1: Age and gender wise distribution of cases of Hyper-Thyroidism

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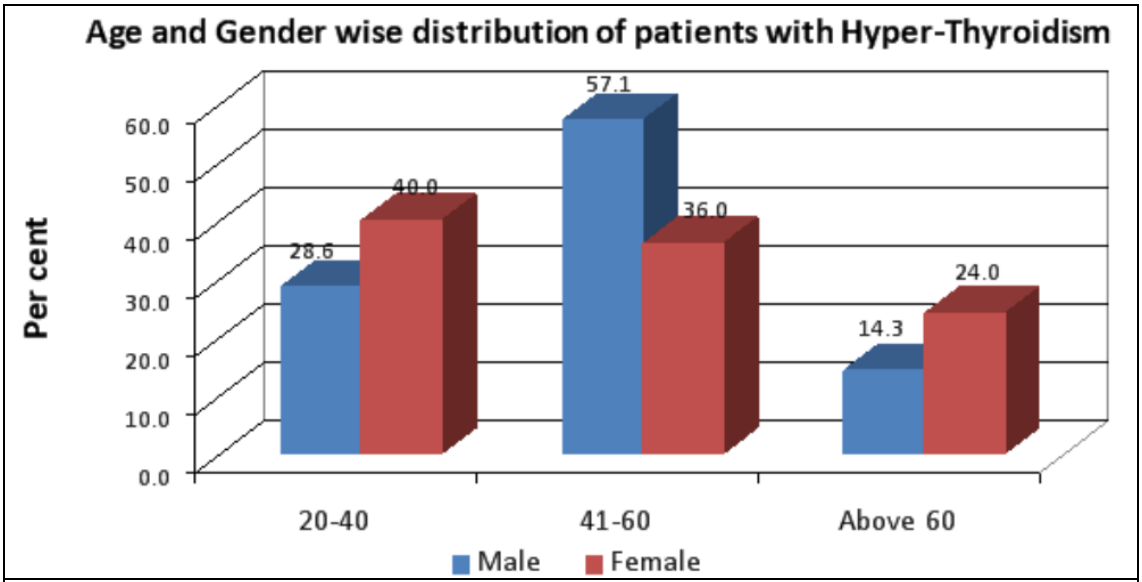

Figure 1

Figure1: In the present study, maximum twenty one (45.6%) cases were in the fourth and fifth decade. Maximum twelve (57.1%) were males in fourth and fifth decade while ten 40(%) female second and third decade and nine (36%) in fourth and fifth decade. female to male ratio was (ratio 5 : 4.5) mean age with SD was 47.9 +/- 14.5 yrs.

Age Group	Thyroid state				Total
	Overt hyper		Subclinical hyper		
	No. of Patients	Percentage	No. of Patients	Percent	
20-40	10	27.0	6	66.7	16
41-60	19	51.4	2	22.2	21
Above 60	8	21.6	1	11.1	9
Total	37	100.0	9	100.0	46

Table 2: Age wise distribution of the Overt and Subclinical Hyperthyroid Cases n=46

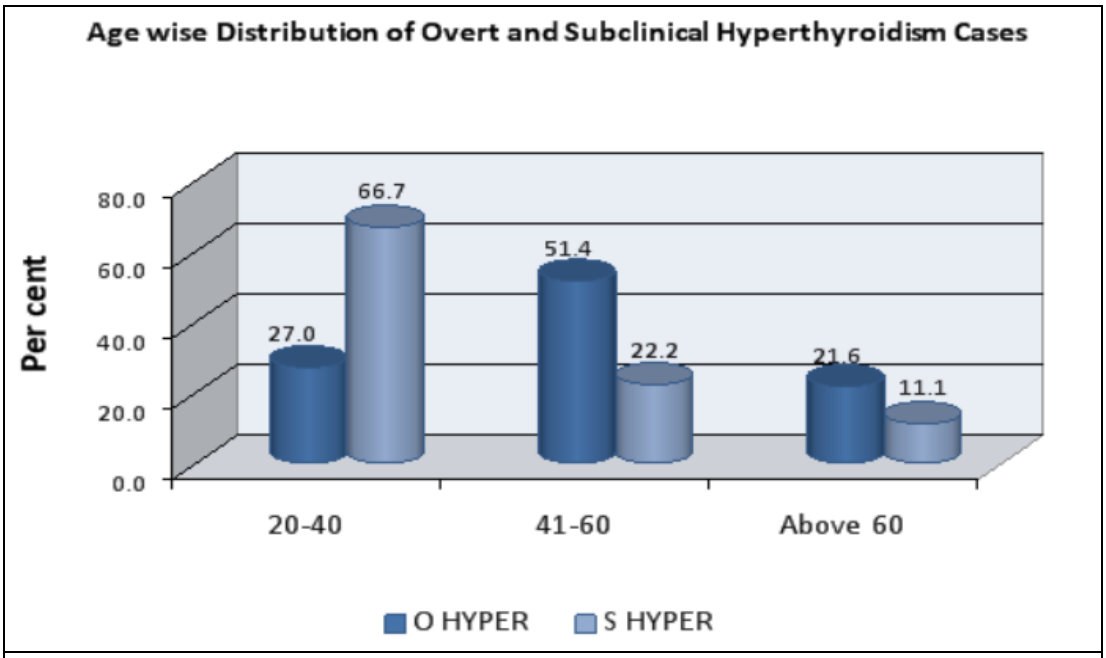

Figure 2

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Figure 2: In present study, It was observed that Overt Hyperthyroidism was present in thirty seven (80.44%) cases while Subclinical Hyperthyroidism was present in only nine (19.56%) cases. Overt hyperthyroidism was more common in fourth and fifth decade which were nineteen cases (51.4%) while Subclinical Hyperthyroidism was more common in age group of 20-40 yrs of age which were six cases (66.7%).

Sex	Thyroid state				Total
	O hyper		S hyper		
	No. of Patients	Percent	No. of Patients	Percent	
Male	20	54	1	11.1	21
Female	17	46	8	88.9	25
Total	37	100.0	9	100.0	46
P value for Chi –square test =0.020					

Table 3: Gender wise incidence of Overt and Subclinical Hyperthyroidism n=46

Symptoms	Males		Females		Total No of Patients =46 i.e. 100%
	No. of Patients	Percent	No. of Patients	Percent	
Weight loss	18	85.71	12	48.00	65.2%
Excessive sweating	11	52.38	9	36.00	43.5%
Tremors	9	42.86	9	36.00	39.1%
Diarrhea	9	42.86	3	12.00	26%
Heat intolerance	8	38.10	6	24.00	30.4%
Increased appetite	8	38.10	10	40.00	39%
Decreased sleep	12	57.14	8	32.00	43.4%
Thyroid swelling	4	19.05	6	24.00	22%
Easy fatigue	10	47.62	17	68.00	57%
Oligomenorrhoea	0	0.00	8	32.00	17%

Table 4: Distribution of Patients According to Symptoms in Hyperthyroidism n=46

Symptoms	Males		Females		Total No of Patients		p-value foe Chi Square test
	No. of Patients	Percent	No. of Patients	Percent	No. Of patient	Percent	
Breathlessness	8	38.10	6	24.00	14	30.4	0.301
Palpitation	19	90.48	22	69	32	70	0.005
Chest Pain	0	0.00	2	8.00	2	4	0.185

Table 5: Distribution of Patients According to Cardiovascular Symptoms *n=46*

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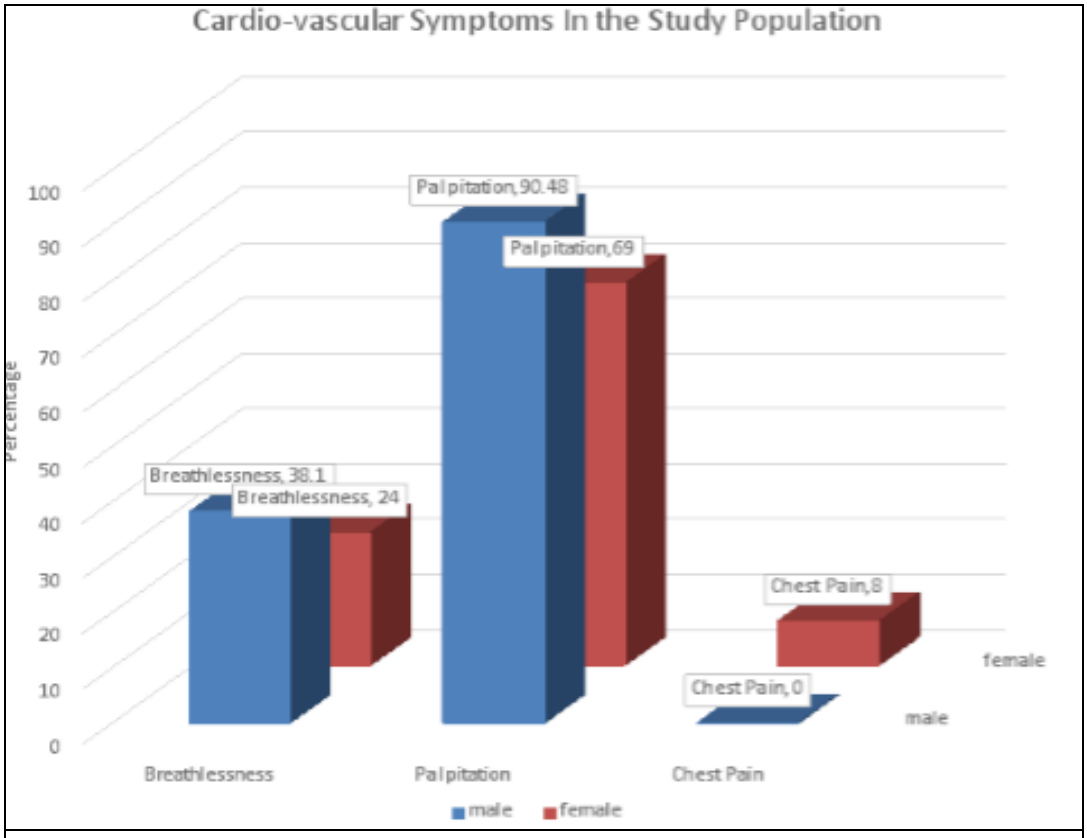

Figure 3

Figure 3: In the present study, Palpitation was the most common cardiovascular symptom which was present in thirty-two cases (70%) out of which twenty-two female and nineteen males had it. Breathless was the second most common symptom which was present in fourteen (30.4%) cases followed by chest pain which was present in two cases(4%).

Symptoms	Males		Females		Total No. Of Patients		p-value foe Chi Square test
	No. of Patients	Per cent	No. of Patients	Per cent	No. of patients	Percent	
Pallor	6	28.57	4	16.00	10	21.7	0.303
PretibialMyx-Edema	3	14.29	4	16.00	7	15.2	0.872
Eye Sign	12	57.14	1	4.00	13	28.2	0.000
Most Skin	9	42.86	6	24.00	15	32.6	0.174
Goiter	3	14.29	5	20.00	8	17.3	0.611

Table 6: Distribution of Patients According to General Physical Examination n=46

Symptoms	Males		Females		Total	
	No. of Patients	Percent	No. of Patients	Percent	No. of patients	Percent
Loud P2	6	28.5	3	12	9	19.5
Cardiomegaly	9	42.8	4	13	13	26
Varying heart Sound	13	62	6	24	19	41.3
Total	21	100	25	100	46	100

Table 7: Distribution of Patients According to Cardiovascular Exam and Sex n=46

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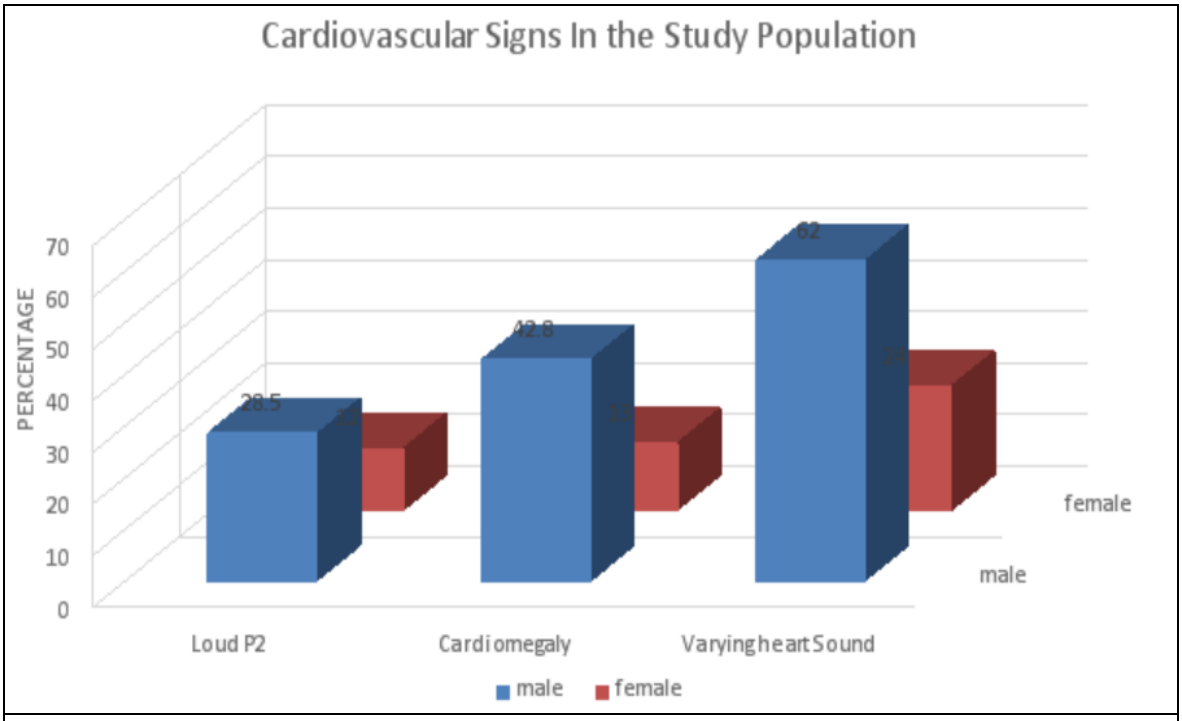

Figure 4

Figure 4: In the present study, on CVS Examination it was seen that nineteen (41.3%) patients had variable heart sound which included thirteen (62%) male and six (24%) female, followed thirteen (26%) had Cardiomegaly and nine (19.5%) had Loud P2

Symptoms	Males		Females		Total	
	No. of Patients	Percent	No. of Patients	Percent	No. Of Patients	Percentage
Normal_ ECG	2	10%	9	36%	11	24%
Sinus tachycardia	5	24%	10	40%	16	35%
Atrial fibrillation	13	62%	6	24%	19	41%
ST changes	2	10%	4	16%	6	13%
RVH	6	29%	2	8%	8	17%
LVH	3	14%	1	4%	4	9%
Ectopic	0	0%	0	0%	0	0%
LAD	2	10%	2	8%	4	9%
LBBB	0	0%	0	0%	0	0%
RBBB	4	19%	0	0%	4	9%
RAD	6	29%	1	4%	7	15%

Table 8: Distribution of Patients According to ECG Changes n=46

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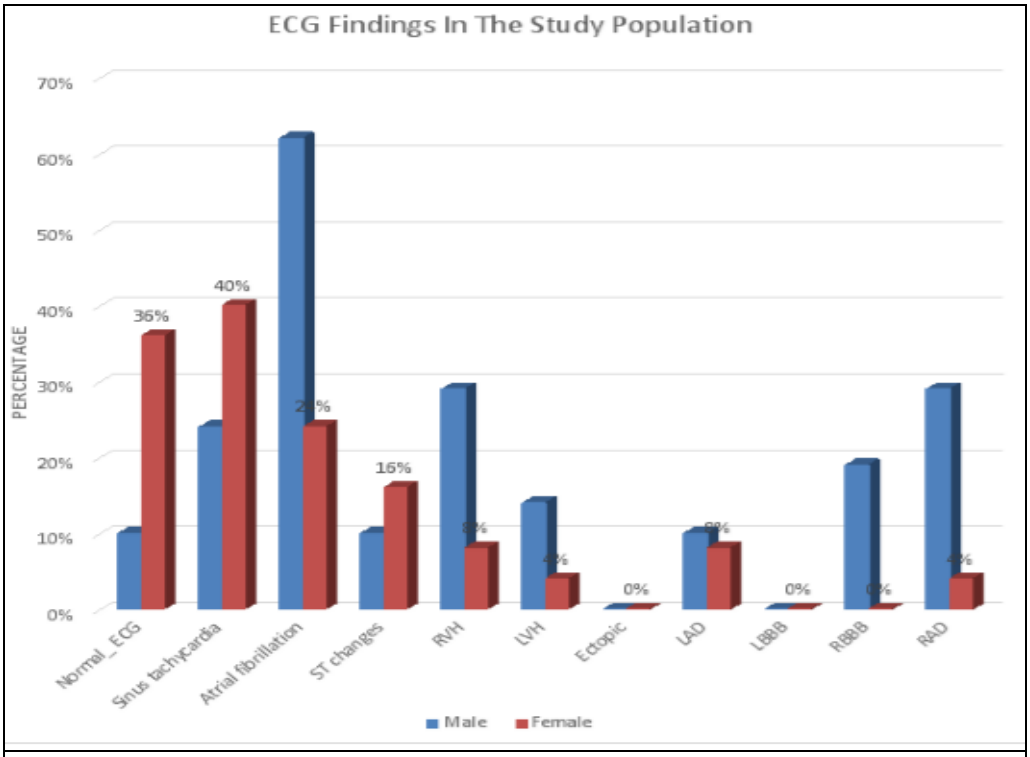

Figure 5

Figure 5: In the present study, Atrial Fibrillation was found to be most prevalent ECG finding which was present in nineteen (41%) patients which constitute six females and thirteen males, followed by Sinus Tachycardia which was present in sixteen (35%) cases. Other important ECG findings were RAD in seven (15%) patients, RVH in eight (17%) patients and ST Changes in six (13%) cases.

Findings	Males		Females		Total	
	No. of Patients	Percent	No. of Patients	Percent	No. of Patients	Percent
Normal echocardiography	11	52%	17	68%	28	61%
Systolic dysfunction	7	33.3%	3	12%	10	21.7
Diastolic dysfunction	2	10%	4	16%	6	13%
Chamber enlargement	9	43%	3	12%	12	26%
Regurgitant lesion	2	10%	2	8%	4	9%
Pulmonary Hypertension	6	29%	4	16%	10	22%

Table 9 : Distribution of Patients According to ECHO CHANGES n=46

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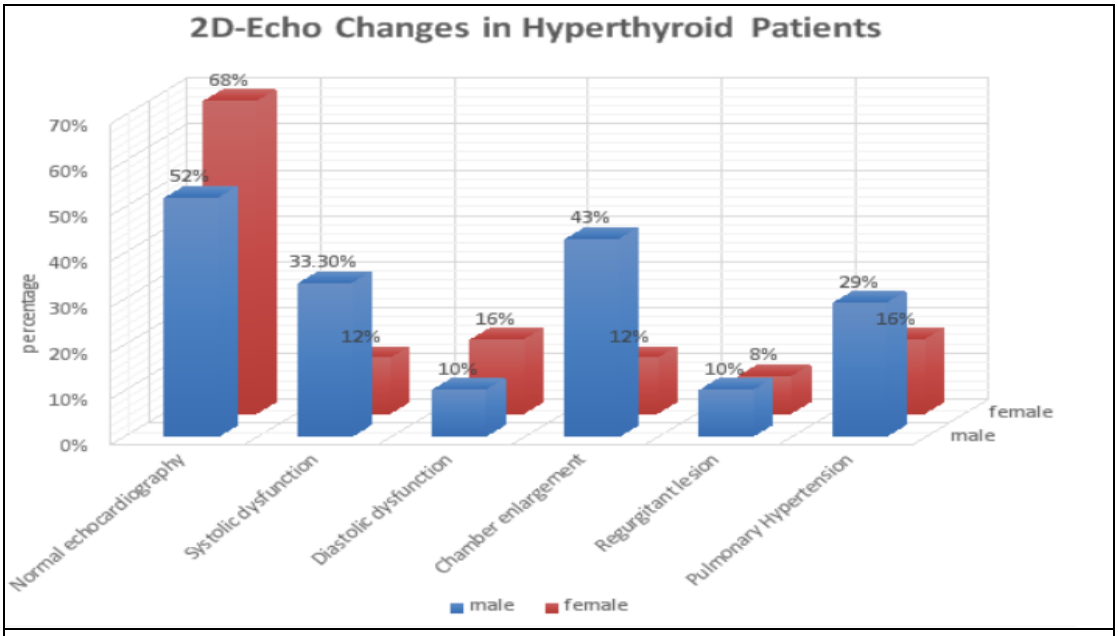

Figure 6

Figure 6: In the present study, by means of 2D-ECHO studies of Hyper-thyroid patients it was evident that twenty-eight (61%) patients had Normal Echo Study which included eleven (52%) males and seventeen (68%) females, was followed by Pulmonary Hypertension in ten (22%) cases with six males and four females, Chamber Enlargement in twelve (26%) cases which constituted nine males and three females. Other important finding were Systolic Dysfunction in ten (21.7%) cases, Diastolic Dysfunction and Regurgitant Lesion chiefly MR & TR.

	Male		Female		Total	
Ejection Fraction	**No. of Patients**	**Percentage**	**No. of Patients**	**Percentage**	**No. Patients**	**Percentage**
Less than 60%	4	19%	2	8%	6	13%
More than 60%	17	81%	23	92%	40	87%

Table 10: Ejection Fraction In The Cases Of Hyperthyroidism n=46

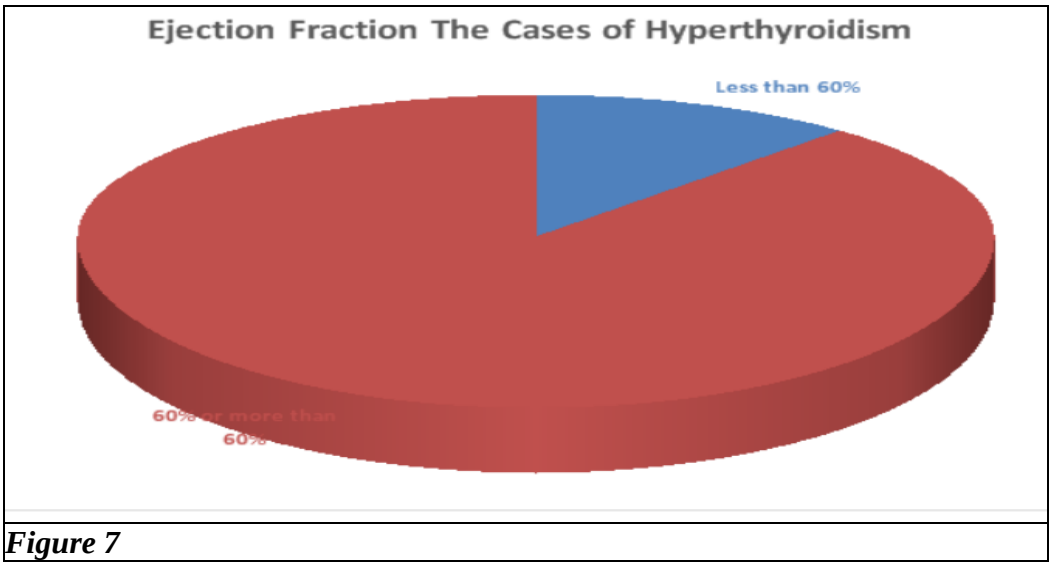

Figure 7

Figure 7: Ejection fraction was 60% or more than 60% in fourty (87%) patients of the total cases which included seventeen (81%) males and twenty-three (92%) females of Hyperthyroidism while only six patients had ejection fraction of less than 60%

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Discussion

During the last three decades, numerous clinical studies have shown that thyroid diseases are associated with an increased risk for manifestations of coronary artery disease (CAD) as well as higher rates of cardiac events, cardiovascular disease (CVD)-related death, and all-cause mortality. Those patients who already have existing CVD, disorders of the thyroid gland can worsen old cardiac symptoms or cause new ones [7]

In the present study, the age of the patients ranged from 22-70 years, the peak incidence of the disease was seen in the fourth and fifth decade of life, which was twenty one (45.6%) patients from the total of 46 patients of Hyper-Thyroidism which included twelve (57.1%) males and nine (36%) females. However in the age group 20-40 yrs. there were sixteen (34.7%) patients which constituted ten (40%) female patients and six (28.6%) male patients. the mean age of the patients was 47.9 yrs. +/- 14.5 yrs. With female is to male ratio 5:4.5.

Kandan et al (2016) [8] also observed peak incidence in the fourth and fifth decade of the life being twenty five (50%) patients from the total of fifty patient which included fifteen females and ten males, followed by the age group of about 20-40 years which had a total of twenty two (44%) patients. The female is to male ratio was 3:2. Though the female predominance was more pronounced in this study but still the result were in-coherence with our study.

In present study, weight loss and easy fatigability was the most prevalent symptom i.e.in forty six (65.2%) cases and twenty seven (57%) case respectively followed by decreased sleep, excessive sweating, increased appetite, heat intolerance and tremors. Other symptoms study were thyroid swelling and diarrhea. Female patient with Hyperthyroidism can also present with Oligo-menorrhea

Balki et al, [9]also observed that most prevalent general symptoms were weight loss and easy fatigability i.e. seventeen (76%) patients and thirteen (65%) patients respectively, study conducted by Kandan et al<2016> and Boelert et al (2010) [10] also reflected similar results which were in congruent to our study.

In the present study, Palpitation was the most common cardiovascular symptom which was present in thirty-two cases (70%) out of which twenty-two female and nineteen males had it. Dyspnea was the second most common symptom which was present in fourteen (30.4%) cases followed by chest pain which was present in two cases(4%).

Ali L et al (2015),[11]observed palpitation in 80% of the patient with hyperthyroidism while in the study conducted by Balki et alpalpitation and dyspnea was present in 69.6% and 39.4% respectively. Kandan et al had the similar findings which were in-coherent with our study.

Atrial fibrillation was found to be the predominant ECG finding in our study which was present in nineteen patients from the total of 46 patients of hyperthyroidism followed by Sinus Tachycardia which was present in sixteen (35%) cases, Other important ECG findings were RAD in seven (15%) patients, RVH in eight (17%) patients and ST Changes in six (13%) cases which in comparison to the study conducted by Osman et al [12], which observed twenty four patients with hyperthyroidism had atrial fibrillation and twenty six patients had abnormal cardiac axis while seven patients had RBBB.

In a similar study conducted by Kandan et al 28% patients had atrial fibrillation which was slightly higher than our study and 10% of patient from the study group of fifty patient had RBBB. In the study by Barsela S et al[13] 21% of patients had atrial fibrillation, while 8.9% in that of Zarg et al [14] 28% patients in this study had atrial fibrillation.

In the present study, pulmonary hypertension was seen in ten (22%) patients compared to the study conducted by Kandan et al only 8% patients had pulmonary hypertension while a similar study conducted by Sui et al[15] on pateints of hyperthyroidism 47% patients had pulmonary hypertension.

Atrial fibrillation was seen nineteen patients in our study this may the reason for the presence high incidence of systolic dysfunction in our study population with hyperthyroid disease

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however in the study conducted by Mercei J et al only 3% patients of hyperthyroidism had systolic dysfunction however study conducted kandan et al there were a total of 18% patient with systolic dysfunction which was in agreement with our study in which systolic dysfuction was present in 21.7% patients of Hyperthyroidism.

Regurgitant lesions were seen in 23% of the patients in the study by Merce et al while in the present study 9% of the patients had the same which was similar to the results observed by Kandan et al which had 6% patients of regurgitant lesion.

Anakwue et al<40>, Impaired diastolic dysfunction was found in at least 28% of the thyrotoxicosis patients,similarlySmit et al[16] in the Netherlands showed in a randomized placebo-controlled study that reversible diastolic dysfunction can occur after long-term exogenous subclinical hyperthyroidism while in our study six (13%) patients had diastolic dysfunction.

Conclusion

In conclusion, thyroid disorder is a frequent disease, affecting more women than men. Thyroid hormones have essential effects on the cardiovascular system. Imbalance of their levels leads to disturbance in the homeostasis of the cardiovascular system. Since the heart is a target to many of the genomic and non-genomic actions of thyroid hormone, most patients with Thyroid disorder demonstrate hemodynamic and cardiovascular manifestations of this disease. Serious cardiac complications such as pericardial effusion, congestive heart failure, atrial fibrillation, and angina pectoris may arise in thyroid disorder patients importantly, most of these deleterious hormone-mediated cardiovascular effects can be reversed or managed with the proper regulation or blockade of these hormones. Therefore, it is important for both endocrinologists and cardiologists to apply a global approach in the assessment of such patients and to improve the prognosis of severe cardiac complications in overt / subclinical thyroid dysfunction.

Limitations of this study

1. Sample size was small.
2. Duration of the study was limited
3. Patients could not be followed up to look for the resolution of cardiac changes after achievement of euthyroid state.

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