

A Study of Cardiovascular Manifestations in Hyperthyroid Patient**Pramod R. Jha¹, Sachin Gadiya², Jayant Mayavanshi^{3*}**¹Professor, Department of Medicine, SBKS MI & RC, Sumandeep Vidyapeeth, Vadodara, Gujarat, India²Resident Doctor, Department of Medicine, SBKS MI & RC, Sumandeep Vidyapeeth, Vadodara, Gujarat, India³Assistant Professor, Department of Medicine, SBKS MI & RC, Sumandeep Vidyapeeth, Vadodara, Gujarat, India

Received: 25-08-2023 / Revised: 28-09-2023 / Accepted: 30-10-2023

Corresponding author: Dr. Jayant Mayavanshi

Conflict of interest: Nil

Abstract:**Background:** Hyperthyroidism is a vastly prevalent endocrine disorder with wide array of symptoms and signs with multi system involvement. One of the most critical systems involved is the cardiovascular system.**Objectives:** With an aim to study prevalence of cardiovascular manifestation in hyperthyroid patients. The objectives to study cardiovascular symptoms and signs, ECG changes, 2 D ECHO in hyperthyroid patients and correlation between duration of hyperthyroidism and severity of cardiovascular manifestation.**Methodology:** This cross-sectional study was carried out in 55 patients with hyperthyroidism in the Department of General Medicine, SBKS MIRC, Sumandeep Vidyapeeth over a span of one and half year. Detailed evaluation was done through clinical examination, ECG and 2D echocardiography. Statistical data analysis was made based on frequency distribution, mean, standard deviation and association of cardiovascular involvement in hyperthyroidism was evaluated.**Results:** Among 55 patients with hyperthyroidism, palpitation was the most common cardiac symptom found to be present in about 78% of patients. Other cardiac symptoms were breathlessness and chest pain, present in 31% and 14.5% of patients respectively. Tachycardia was the most common cardiac sign present (80%). About 32% patients had hypertension; and atrial fibrillation was present in 20% patients. Electrocardiogram abnormalities noted was sinus tachycardia present in 67% patients and was the commonest ECG abnormality. Atrial fibrillation(20%), LVH (10.9%), ST T changes (7%), RBBB (5.4%), RVH (3.6%) were other electrocardiogram abnormalities noted. On Echocardiography; systolic dysfunction (16.3%), chamber enlargement (14.5%), diastolic dysfunction, mitral regurgitation, mitral valve prolapse were the abnormalities present in decreasing order of frequency. Hyperthyroid patients having cardiac symptoms had significantly low levels of TSH than patients who did not have cardiac symptoms.**Conclusion:** Hyperthyroid patients present clinically with various nonspecific signs and symptoms which are difficult to attribute to cardiovascular involvement. Hence, a high index of suspicion is the key for early diagnosis of cardiovascular involvement in hyperthyroidism. So, early and frequent evaluation by ECG and 2D echocardiography is crucial to assess the patients for cardiovascular changes so that prior interventions could be performed to improve the clinical outcomes.**Keywords:** Hyperthyroidism, Cardiovascular System, Electrocardiography, 2D Echocardiography.This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.**Introduction**

Thyroid means (Greek thyreos means shield, plus eidos, form). The thyroid gland is one of the largest endocrine glands. Thyroid hormone exerts wide spectrum physiological, biochemical effects on all organs. Hyperthyroidism is a condition in which the thyroid gland functions excessively. Thyrotoxicosis is defined as the state of thyroid hormone excess and causes cardiac, neurological, ophthalmological, dermatological, gastrointestinal, endocrinological symptoms and signs. The clinical presentation depends on the duration of disease, age of patient and hormone level in blood. [1]

Heart is mainly affected as T3, T4 has major effects on the cardiovascular function and hemodynamics produce after significant derangement in function. The main changes are increases in heart rate, cardiac contractility, systolic and mean pulmonary artery pressure, cardiac output, diastolic relaxation, and myocardial oxygen consumption reductions in systemic vascular resistance and diastolic pressure. [2] Cardiovascular symptoms and signs are common in patients with hyperthyroidism. [3] They include tachycardia, palpitations, hyperdynamic precordium, systolic hypertension with widened

pulse pressure, exertional dyspnea, angina like chest pain. Hyperthyroidism is also associated with an increased risk of atrial fibrillation, heart failure, pulmonary hypertension, and angina. [4] the most prevalent cardiac consequence of hyperthyroidism is atrial fibrillation. In hyperthyroidism patients cardiac involvement is of great prognostic importance and causes significant morbidity and mortality.

All the more affected patients are potentially reversible also with early diagnosis and appropriate treatment. Secondary complications like cerebral stroke can be associated arise from atrial fibrillation. Cardiac problems resolve rapidly, when hyperthyroidism is treated with anti-thyroid drugs and thyroid hormone return to normal level. An individual susceptibility to excess thyroid hormone is an important factor determining the clinical manifestations, there may be most of genetic and regional variations can occur. Hence a study of local population is needed. The present study was undertaken because of study of the cardiac manifestations like symptoms and signs of hyperthyroidism and their correlation with thyroid hormone levels.

Materials and Methods

Study site: This study was carried out at Department of General Medicine Dhiraj Hospital SBKS and MIRC, Sumandeep Vidyapeeth, Pipariya, Vadodara.

Type of study: cross sectional study

Sample size: Minimum 50 patients and maximum as many possible.

$$n = \frac{NZ^2P(1 - P)}{d^2(N - 1) + Z^2 P(1 - P)}$$

P= 0.08, N=100

n = Sample size with finite population correction

N = Population size

Z = 1.96 [Z statistic for level of confidence]

P = Expected prevalence d = 5% precision

Study Period: Study was carried out over period of eighteen months from approval date by institutional ethics committee.

Inclusion criteria:

- All patients with hyperthyroidism above 18 years of age, both newly diagnosed and previously known cases.
- Hyperthyroid was defined as Serum TSH <0.39 mIU/mL Serum FT4 > 2 ng/dl Serum FT3 > 3.8 pg/ml

Exclusion criteria:

- Patients not giving consent.
- Known case of any cardiac disorder.

Data collection and analysis:

- Data collection and analysis was carried out in the medicine department at SBKS and MIRC after approval from the institutional ethics committee.
- The study was carried out over a period of one and half year.
- 55 patients with all selection criteria were included in the study after obtaining the informed consent.
- Detailed history was taken regarding the demographic profile, anthropometric measurements and BMI (body mass index)
- General and systemic examination were done in all patients.
- Routine biochemical investigations like Complete Blood Picture, RBS, Renal Function Tests were done.
- For thyroid function tests- 3 ml of early morning fasting samples containing plain clotted blood were collected and sent for FT3, FT4, TSH estimation. The hormone estimation is done by IMMUNO ASSAY-ELFA (ENZYME LINKED FLUORESCENT ASSAY). Instrument used was Meglumi 800. Time taken is 40mins.
- Standard 12 Lead ECG by BPL Cardiart genx3 was taken and 2D Echocardiography by GE VIVID S6 was done to evaluate cardiovascular involvement.
- Chest x ray was done to evaluate cardiomegaly, horizontal width of the heart divided by the widest internal diameter of the thorax) above 0.5 is considered as cardiomegaly.
- Then findings were entered into CRI (case record information)
- Results were analyzed applying the appropriate statistical methods like Descriptive statistics and formulae to know the prevalence of CVS involvement.

Statistical Methods:

- Categorical data was presented as frequency and percentage and continuous data as mean and standard deviation.
- Statistical analysis was done by using descriptive and inferential statistics using Chi Square test and software used in the analysis were SPSS version 17.0 and Graph Pad Prism version 6.0. p<0.05 is considered as level of significance.

Results

Table 1: Cardiac symptoms in hyperthyroid patients

Cardiac symptoms	No. of patients(n)	Percentage (%)
Palpitations	43	78.18
Breathlessness	17	30.91
Chest pain	8	14.55

In present study, palpitation was the most common symptom found, present in about 78% of patients. Other cardiac symptom was breathlessness and chest pain present in 31% and 14.5% of patients respectively, **Table 1**.

Table 2: Cardiac signs in hyperthyroid patients

Cardiac SIGNS	No. of patients(n)	Percentage (%)
Tachycardia	44	80
Wide Pulse pressure	21	38.18
Systemic hypertension	18	32.73

Tachycardia was present in 44 patients (80%), 11 patients (20%) wide pulse pressure, 18(32%) patients had hypertension, **Table 2**.

Table 3: Correlation of cardiac symptoms with duration of illness

Cardiac symptoms	Duration of illness Frequency (Percentage)			Total
	≤6 months	7 - 12 months	> 12 months	
Palpitation	11 (25.58%)	23 (53.49%)	9 (20.93%)	43
chest pain	2 (25%)	2 (25%)	4 (50%)	8
Breathlessness	4 (23.53%)	8 (47.06%)	5 (29.41%)	17

From **Table 3**, it is seen that in patient having palpitation, 25.5% patients had hyperthyroidism for less than 6 months, 53.4% for 7 to 12 months and 20.9% for more than 12 months. In patient having chest pain, 25% patients had hyperthyroidism for less than 6 months, 25% for 7 to 12 months and 50% for more than 12 months. And in patient presenting with breathlessness, 23.5% patients had hyperthyroidism for less than 6 months, 47% for 7 to 12 months and 29.4% for more than 12 months.

Table 4: ECG abnormalities in hyperthyroid patients

ECG Abnormality	No. of patients(n)	Percentage (%)
Sinus tachycardia	37	67.27
Atrial Fibrillation	11	20.00
LVH	6	10.91
ST T changes	4	7.27
RBBB	3	5.45
RVH	2	3.64

Abnormal ECG findings were observed in 81 % cases. The commonest abnormality in ECG was sinus tachycardia found in 37(67.2%) patients. Other abnormalities were, AF in 20% (11), LVH in 10.9% (6), ST T changes in 7.3% (4), RBBB in 5.4% (3) and RVH in 3.6% (2). Out of 11 patients with AF, 3 patients had controlled heart rate, **Table 4**.

Table 5: Chest X-ray Abnormality in hyperthyroid patients

X-Ray	No. of patients(n)	Percentage (%)
Normal	47	85.45
Cardiomegaly	8	14.55
Total	55	100

Chest X-ray was normal in 47 patients while 8 patients (14.5%) had cardiomegaly, **Table 5**.

Table 6: ECHO abnormalities in hyperthyroid patients

Abnormality	No. of patients(n)	Percentage (%)
Systolic dysfunction	9	16.36
Chamber enlargement	8	14.55
Diastolic dysfunction	7	12.73
Mitral regurgitation	2	3.64
Mitral valve prolapse	2	3.64

Echocardiographic abnormalities were noted in 50.9% of patients. 16 % of patients had systolic dysfunction and this was the commonest echocardiographic finding observed; followed by chamber enlargement in 8 patients (14.5%), diastolic dysfunction ion observed in 7 patients (12.7%), mitral valve prolapse and mitral regurgitation found in 2 patients each (3.6%), **Table 6**.

Table 7: Correlation of thyroid profile in hyperthyroid patients with abnormal ECG and normal ECG

	ECG Abnormality		Normal ECG		p value
	Mean	SD	Mean	SD	
Mean Sr. TSH	0.25	0.19	0.28	0.16	P=0.6596
Mean FT3	3.9	2.11	3.70	2.38	P=0.5207
Mean FT4	4.10	2.00	3.92	2.03	P=0.5409

In patients having abnormalities on echocardiography, it is observed that, mean TSH was 0.25+0.19, while mean FT3 and FT4 were 3.9+2.11 and 4.1+2.0, respectively. In patients with normal ECG, mean TSH was 0.28+0.16, while mean FT3 and FT4 were 3.72+2.38 and 3.92+2.03, respectively. The mean difference in the two groups was statistically not significant, **Table 7**.

Table 8: Correlation of thyroid profile in hyperthyroid patients with abnormal Echo and normal Echo

	Echo Abnormality		No Echo Abnormality		p value
	Mean	SD	Mean	SD	
Mean Sr. TSH	0.08	0.16	0.24	0.16	P = 0.0010
Mean FT3	6.50	1.92	4.72	2.40	P = 0.0083
Mean FT4	6.52	2.23	4.39	1.88	P = 0.0005

In patients having abnormalities on echocardiography, it is observed that, mean TSH was 0.08+0.16, while mean FT3 and FT4 were 6.5+1.92 and 6.52+2.23, respectively. In patients with normal Echo, mean TSH was 0.24+0.16, while mean FT3 and FT4 were 4.72+2.4 and 4.39+1.88, respectively. The mean difference in the two groups was statistically significant, **Table 8**.

Table 9: Correlation of thyroid profile with Ejection Fraction (EF)

	Ejection Fraction (EF) %		
	<40	40-50	>50
Mean FT3	8.01	8.88	4.89
Mean FT4	6.80	7.43	4.81
Mean TSH	0.08	0.02	0.21

In patients with preserved ejection fraction (>50%), the mean Sr. FT3 was 4.89, FT4 4.81 and mean TSH 0.21. In patients with mid-range ejection fraction (40-50%), the mean Sr. FT3 was 8.88, FT4 7.43 and mean TSH 0.02. In patients with reduced ejection fraction (<40%), the mean Sr. FT3 was 8.01, FT4 6.80 and mean TSH 0.08. The difference between these groups is significant with p value of 0.026, **Table 9**.

Discussion

Thyroid hormones play an important role in various metabolic functions in the body and thus thyroid disorders affect each and every organ, of which heart is principally sensitive to its effects. It exerts multiple actions on cardiovascular system and can present with myriad of symptoms and signs. It has been recognized that some of the most characteristic signs and symptoms of thyroid disorders are those that are consequences from the actions of thyroid hormone on the heart and cardiovascular system.

In hyperthyroid state, the hormone causes increase in heart rate, myocardial contractility, and increase in cardiac output by dilating peripheral arteries and produces many other changes in the heart. The objective of this study is to assess the cardiovascular changes in hyperthyroid patients. Cardiac symptoms seen in hyperthyroidism are either due to the effect of

increased sympathoadrenal activity or due to the direct effect of thyroid hormones on the heart.

In present study, palpitation was most common cardiac symptoms present in 78.18% of patients, breathlessness in 30% and chest pain 14%. This result is comparable with study by Kandan V et al [5]. In studies by Khurana et al [6] and Klein et al [2] breathlessness was higher than our study. Frequency of chest pain was higher in present study than other studies. In present study tachycardia, was most common sign which was present in 80% of patients. This result was comparable with study by Kandan V et al [5] in which 82% patients had tachycardia, and in study by Khurana et al [6] 72% patient had tachycardia but differed from study by Klein et al [7] in which it was present in 95%. 32% of patient had Systemic hypertension while around 40% of patient had hypertension in studies by Kandan et al and Khurana et al. 39% of patient had wide pulse pressure higher frequencies were noted in studies by Kandan V et al and Khurana et al being 50% and 75% respectively.

Electrocardiogram abnormalities were seen in 81% of patients. Sinus tachycardia was found in 67.2% patients which were 46% in study by Kandan V et al [5] and 39% study by Khurana et al [6]. Atrial fibrillation was seen in 20% of patient which was comparable to study by Khurana et al who reported 22% prevalence in

atrial fibrillation; however prevalence of atrial fibrillation in study by Kandan V et al [5] is more 28% and less in study by Klein et al [2] 15%. In hyperthyroid patient prevalence of atrial fibrillation varies between 2-20% [7]. Out of 20% patients with atrial fibrillation 5.4% patients had controlled heart rate. Intraventricular conduction disturbances like RBBB was detected on 5.45% without any associated heart disease of other etiology, similar to study by Khurana et al [6] where 4% patients had RBBB, however 10% patients had RBBB in study by Kandan V et al [5]. LVH was present in 10% patients whereas in Kandan V et al it was present in 8% of patients. Similar to study by Kandan V et al ST-T changes was present in 7.2% of patients in our study. In present study, echocardiographic finding was comparable with study by Kandan V et al such that systolic dysfunction was present in 16.3% and 18% respectively, which was higher than study by Khurana et al. Diastolic dysfunction found in 12% in both studies; whereas chamber enlargement was higher in study by Kandan V et al, 18% vs 14.5% in our study and also regurgitant lesion present in 6% vs 3.6% patient had in our study. Cardiomegaly was observed on Chest X Ray (PA view) in 14% and figures were almost similar to the study by Kandan V et al [5] in 12% patients.

Mean TSH in patients having abnormal ECG were compared to those patients having normal ECG; and the mean TSH in first group was on lower side but the difference in the two group was not significant (0.25 ± 0.19 vs 0.28 ± 0.16 , $p=0.65$). Mean FT3 and FT4 in patients with abnormal ECG was high than patients with normal ECG but the difference was statistically not significant. Mean TSH in patients having abnormal Echo were compared to those patients having normal Echo; and mean TSH in first group was significantly low and the difference between the two group was significant (0.08 ± 0.16 vs 0.24 ± 0.16 , $p=0.005$). Mean FT3 and FT4 in patients with abnormal Echo was high than patients with normal Echo and the difference was statistically significant.

On comparing mean TSH, mean FT3, mean FT4 of patients with normal ejection fraction to the mean TSH of patients with midrange and reduced ejection fraction it was observed that, the mean TSH was significantly low in patients having midrange and reduced ejection fraction than those patients with normal ejection fraction while the mean FT3, FT4 was significantly high in patients with midrange and reduced ejection fraction than patients with normal ejection fraction.

Thus, it was noted that in patients having cardiovascular abnormalities the thyroid profile was more deranged than patients without cardiac abnormalities except for ECG abnormalities.

Maximum patient (89%) in the study had normal ejection fraction ($>50\%$), while only 9% had mid-range ejection fraction and 1.8% had reduced ejection fraction. Maximum patient persisted to have normal ejection fraction even with increasing duration of hyperthyroidism.

This study showed that 12% of patients of hyperthyroidism developed heart failure. The prevalence of heart failure in our study was higher than study done by Chung Wah siu et al [7] who stated prevalence in his study of about 6%. In present study atrial fibrillation was coexistent in 70% patients of heart failure as compared to 94% of coexistent atrial fibrillation present in study by Chung Wah siu et al, concluding atrial fibrillation to be an independent predictor for development of heart failure. The study by Chung Wah siu et al also stated that heart failure developed in longstanding untreated hyperthyroidism and similar observation was made in our study that maximum patients who developed heart failure had hyperthyroidism for more than 12 months.

Conclusion

Hyperthyroidism is a common thyroid problem which has many effects on almost all organ systems in the body. Cardiovascular effects are the very common, and generally they cause the main complaints leading the patient to come to hospital. The common cardiovascular symptoms were palpitations, breathlessness, chest pain and cardiovascular signs were tachycardia, hypertension and wide pulse pressure. Electrocardiographic changes observed were sinus tachycardia, atrial fibrillation, LVH, RBBB, RVH. Echocardiographic findings in hyperthyroidism were systolic dysfunction, diastolic dysfunction, chamber enlargement, mitral regurgitation and mitral valve prolapse. Prevalence of cardiovascular abnormalities is higher in patients with deranged thyroid profile. As a result, early detection of hyperthyroidism in patients will certainly reduce the severity of cardiac problems that often accompany these conditions.

References

1. Jameson JL. Harrison's principles of internal medicine. McGraw-Hill Education, 2018.
2. Klein I, Ojamaa K. Thyroid hormone and the cardiovascular system. *New England Journal of Medicine*. 2001 Feb 15; 344(7):501-9.
3. Osman F, Franklyn JA, Holder RL, Sheppard MC, Gammage MD. Cardiovascular manifestations of hyperthyroidism before and after antithyroid therapy: a matched case-control study. *Journal of the American College of Cardiology*. 2007 Jan 2; 49(1):71-81.
4. Iglesias P, Acosta M, Sánchez R, Fernández-Reyes MJ, Mon C, Díez JJ. Ambulatory

- blood pressure monitoring in patients with hyperthyroidism before and after control of thyroid function. *Clinical endocrinology*. 2005 Jul; 63(1):66-72.
5. Sathyamurthy P. Cardiovascular manifestations in hyperthyroidism. *International Journal of Research in Medical Sciences*. 2016 Jul; 4(7):3032
 6. Khurana NK, Kumar S, Kumar S, Kumar P, Rizwan A. Frequency of Cardiovascular Manifestation in Patients With Hyperthyroidism. *Cureus*. 2021 Jan; 13(1).
 7. Siu CW, Yeung CY, Lau CP, Kung AW, Tse HF. Incidence, clinical characteristics and outcome of congestive heart failure as the initial presentation in patients with primary hyperthyroidism. *Heart*. 2007 Apr 1; 93(4):483-7.