

Original Research Article

Clinical profile of thyrotoxicosis and related cardiovascular morbidities among patients attending endocrine outpatient department in a tertiary care centre

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ABSTRACT

Background: Thyroid disorders are common in India. Symptoms and signs of thyrotoxicosis are nonspecific. Graves disease is an autoimmune condition and is the most common cause of thyrotoxicosis. Cardiovascular system is frequently affected in thyroid disorders but there is not much data on prevalence of thyrotoxicosis and related cardiovascular morbidities in central India. Objectives of study the clinical profile of patients with thyrotoxicosis and outline the related cardiovascular manifestations in a tertiary care center. Design-over a period of nine months a descriptive cross sectional study was conducted in a tertiary health care center.

Methods: A total of 150 patients with thyrotoxicosis were studied. Patients with known diagnosis of thyrotoxicosis and newly diagnosed cases were included. The participants were investigated for thyroid profile, Electrocardiogram, Complete blood count, serum electrolytes and kidney function test.

Results: Out of 150 patients of thyrotoxicosis, 87 (58 %) were diagnosed with Graves's disease. Hypertension was observed in 78 (52 %) of participants. Atrial fibrillation was found in 18 (12%) and sinus tachycardia in 53 (35.33 %) of the participants.

Conclusion: Grave's disease is the commonest cause of thyrotoxicosis. Hypertension, sinus tachycardia and Atrial Fibrillation are the common cardiovascular diseases observed to be associated with thyrotoxicosis.

Keywords: Atrial fibrillation, Cardiovascular system, Graves' disease, Thyrotoxicosis

INTRODUCTION

Thyroid diseases contribute to a major burden of endocrine problems in India. According to recent studies, about 300 million people are suffering from thyroid disease worldwide with India contributing to 42 million of them.¹ The prevalence of thyroid disorders depends on age, sex and geographical factors.^{2,3} Hyperthyroidism is the most common cause of thyroid dysfunction in areas with mild to moderate iodine deficiency.^{3,4} Though the

exact prevalence of hyperthyroidism is not available in India, an epidemiological study conducted in Cochin showed the prevalence of overt hyperthyroidism to be 1.3%.⁵ Thyrotoxicosis is defined as state of thyroid hormone excess and the most common cause is Graves's disease. It is more common in women as compared to men.⁶ Grave's disease is the most common etiology of thyrotoxicosis, followed by toxic multi-nodular goiter and toxic adenoma. Other causes include thyroiditis, sub-acute thyroiditis, gestational hyperthyroidism and drug

induced thyrotoxicosis (example amiodarone).⁶⁻⁸ Studies have shown a genetic predisposition to Graves's disease.⁷

Patients can present with a wide range of symptoms which include irritability, sweating, heat intolerance, palpitations, fatigue, anxiety and breathlessness.⁹ The signs include tachycardia, tremors, moist skin, goiter, eye signs and rarely dermatopathy.⁹ These manifestations are nonspecific and vary depending on age, sex, disease duration and etiology.⁵

Patients with thyrotoxicosis also have various degrees of cardiovascular involvement. These include heart failure, arrhythmias including atrial fibrillation and atrial flutter.¹⁰ Cardiovascular manifestations are due to direct cellular effects of thyroid hormones on the heart and indirect effects due to interaction with sympathetic nervous system and changes in peripheral vascular smooth muscle cells.¹¹ Available literature reveals association between thyrotoxicosis and cardiovascular diseases.^{10,11} Our center being in central India; gets many patients from surrounding states. Also, many patients of thyrotoxicosis attending our tertiary care endocrine clinic present with symptoms suggestive of cardiovascular involvement. However there is no published study on thyrotoxicosis from tertiary health care institute for Central India. Therefore this study was planned with the objective to assess the clinical profile of thyrotoxicosis and outline the cardiovascular effects of thyrotoxicosis in a tertiary care center.

METHODS

This descriptive study was conducted in the endocrine clinic at the tertiary care center (Government Medical College and Super- specialty Hospital, Nagpur Maharashtra, India). Permission from institutional ethics committee was obtained before initiation of the study. Study was conducted from July 2018 to March 2019 (9 months). All patients attending the endocrine clinic constituted the study population.

Inclusion criteria

A known diagnosis of thyrotoxicosis, new patients with clinical history suggestive of thyrotoxicosis and a serum TSH < 0.3mU/L.

Exclusion criteria

Patients with known heart disease (Ischemic Heart Disease, valvular heart disease), pre-existing hypertension (Blood Pressure \geq 140/90 mm Hg or on antihypertensive drugs before the onset of thyrotoxicosis), pregnant patients, diabetic patients (fasting blood glucose >126 mg/dl) and with proven thyroid malignancy.

On an average, 100 patients of various endocrine disorders register to this clinic on a weekly basis.

Purposive convenient sampling technique was adopted for enrolling subjects in the study. Out of 3600 patients, 150 patients were enrolled. A predesigned and pre-tested study tool was adopted in this study for collection of data. Data was collected by interview technique, clinical examination and review of laboratory records. After obtaining the written informed consent, details about socio-demographic characteristics of study participants, detailed history about thyroid symptoms (weight loss, palpitations, tremors, neck swelling, pain over anterior aspect of neck, breathlessness, anxiety, and easy fatigue), general examination, thyroid gland examination, cardiovascular examination and investigations were done. T3, T4, TSH were analyzed by chemiluminescence based assay platform. Electrocardiogram (ECG) was done for assessment of cardiovascular morbidities. Fasting and post lunch blood glucose levels were assessed. Complete Blood Count (CBC), serum electrolytes, Technetium 99 scan was also done wherever indicated. Sinus tachycardia was defined as heart rate >100 beats per minute; atrial fibrillation was defined as absent p waves and irregular heart rate.¹⁰

Statistical analysis

Data was entered and analyzed in EPI INFO 2007 software. Proportions were calculated for all the categorical variables. Means and standard deviations (SD) were calculated for numerical variables. All the proportions were expressed along with 95% confidence interval. Chi square test was applied and p-value <0.05 was considered significant.

RESULTS

Total 150 patients with history and clinical features suggestive of thyrotoxicosis were enrolled in the study. Out of them, 72% belonged to age less than 50 years. After excluding three subjects of younger age groups <15 years, the mean \pm SD age was 41.96 \pm 13.52 years. 33 (22%) were male and 117 (78%) were female. All these patients were thoroughly evaluated and following observations were noted:

The baseline characteristics of the study population are given in Table 1.

Twenty six percent (39) patients were from urban area as compared to 74% (111) from rural. Wide pulse pressure (systolic blood pressure - diastolic blood pressure >40 mm Hg) was found in 82% (123) of the participants. The most common cause of thyrotoxicosis was Grave's disease- 58% (87) followed by thyroiditis- 28 19.33% (28). Toxic multi-nodular goiter was found in 15.33% (24) whereas toxic adenoma in 7.33% (11) of the participants.

Table 2 shows cardiovascular morbidities of thyrotoxicosis. 52% (78) participants were found to be hypertensive. It was seen in 65.5% (57) patients with

Grave's disease, 56.52% (13) patients with MNG and 36.36% (4) patients with toxic adenoma. Proportionately smaller number, 13.7% (4) patients with thyroiditis had hypertension. Sinus tachycardia (ST) was observed in 51

cases (34%); most of them (47.12%) had Grave's disease. Atrial fibrillation (AF) was observed in 18 (12%) patients and most of them 12 (13.7%) had Grave's disease.

Table 1: Demographic and clinical profile of participants (n=150).

Parameter	Number	Percentage	Grave's disease	Thyroiditis	MNG	Toxic adenoma
Age						
<30	29	19.33 %	17	3	8	1
31-40	42	28 %	27	11	6	4
41-50	37	24.66 %	18	5	3	5
51-60	27	18 %	16	7	3	1
>60	15	10 %	9	3	3	0
Gender						
Male	33	22 %	20	7	4	2
Female	117	78 %	67	22	19	9
Residence						
Rural	111	74 %	66	22	14	9
Urban	39	26 %	21	7	9	2
Complaints						
Weight loss	72	48 %	58 (38.66 %)	3(2 %)	5(3.3 %)	6(4 %)
Palpitations	60	40 %	58 (38.66 %)	8(5.3 %)	8(5.3 %)	6(4 %)
Neck swelling	33	22 %	38 (25.33 %)	3(2 %)	17(11.3 %)	4(2.6 %)
Anxiety	21	14 %	38 (25.33 %)	4(2.6 %)	3(2 %)	1(0.6 %)
Tremors	38	25.33 %	9(6 %)	3(2 %)	6(4 %)	2(1.3 %)
Pain over neck	26	17.33 %	13(8.6 %)	26(17.3 %)	0(0 %)	0(0 %)
Breathlessness	16	10.66 %	27(18 %)	3(2 %)	6(4 %)	2 (1.3 %)
Easy fatigue	24	16 %	0(0%) 5(3.3 %) 15(10 %)	1(0.6 %)	5(3.3 %)	3 (2 %)

Table 2: Cardiovascular morbidities and thyroid conditions.

Cardiac morbidities	Thyroid conditions				Total N=150
	Graves (n= 87)	Thyroiditis (n= 28)	MNG (n= 24)	Toxic adenoma (n= 11)	
Hypertension					
Present	57 (65.5%)	4 (13.7%)	13 (56.52%)	4 (36.36%)	78 (52%)
Absent	30 (34.4%)	25 (86.20%)	10 (43.47%)	7 (63.63%)	72 (48%)
Atrial fibrillation					
Present	12 (13.7%)	1 (3.4%)	3 (10%)	2 (18.18%)	18 (12%)
Absent	75 (86.2%)	28 (96.5%)	20(86.95%)	9 (81.81%)	132 (88%)
Sinus tachycardia					
Present	41 (47.12%)	2 (6.89%)	7 (30.43%)	3 (27.27%)	53 (35.33%)
absent	46 (52.87%)	27 (93.10%)	16 (69.56%)	8 (72.72%)	97 (64.66%)

Table 3 demonstrates electrocardiographic changes according to the age group and gender. Rate of sinus tachycardia was not significantly different between different age groups (p value 0.455). The rate of atrial fibrillation was significantly higher in age group of 31-40 years (p value < 0.0001). Rates of sinus tachycardia and

atrial fibrillation were not significantly different between male and female patients.

Table 4 demonstrates that TSH levels of 0.01 were found to be associated with sinus tachycardia (p < 0.0134) (Kruskal Wallis ANOVA test for non-parametric data).

Mean age in participants with Grave's disease was 42.1 years, in thyroiditis it was 45 years, in MNG it was 40.46 whereas in toxic adenoma it was 39.91 years.

Table 5 depicts association between atrial fibrillation and thyroiditis, Grave's disease, MNG and toxic adenoma.

Table 3: Electrocardiographic changes according to age group and gender.

Parameters	Sinus tachycardia		Atrial Fibrillation		Total	
	Yes	No	Yes	No		
Age (in years)	<30	13 (44.82%)	16 (55.17%)	1 (3.4%)	28 (96.5%)	29
	31-40	16 (38.09%)	26 (61.90%)	14 (33.33%)	28 (66.66%)	42
	41-50	9 (24.32%)	28 (75.67%)	2 (5.4%)	35 (94.5%)	37
	51-60	9 (33.33%)	18 (66.66%)	1 (3.7%)	26 (96.29%)	27
	>60	6 (40%)	9 (60%)	0 (0%)	15 (100%)	15
p value	0.455		<0.0001			
Gender	Male	13 (24.52%)	20 (20.61%)	3 (16.66%)	30 (22.72%)	33
	Female	40 (75.47%)	77 (79.38%)	15 (83.33%)	102 (77.27%)	117
p value	0.581		0.560			

Table 4: Electrocardiogram and thyroid profile.

ECG features	Thyroid profile		
	T3 (normal 86- 187 ng/dl)	T4 (normal 5-12 mcg/dl)	TSH (normal 0.3-5mU/L)
Normal	307.86±128.59*	21.28±14.02	0.066±0.075
	284.5(2.02-784)**	20(4-130)	0.05(0.005-0.37)
Sinus tachycardia	330.96±176.99	27.40±37.69	0.043±0.052
	288(3.92 -1000)	19.81 (12.2-220)	0.01(0.001-0.32)
Atrial fibrillation	304.69 ±80.34	21.37±7.72	0.059±0.10
	297.1(197-534)	21.31(11.4-46.12)	0.02(0.005-0.450)
Kw statistics***	0.209	0.141	8.629
p value	0.9909	0.9319	0.0134

*indicates Mean±SD **indicates median and range *** indicates Kruskal wallis

T3 indicates triiodothyronine.

T4 indicates thyroxine.

TSH indicates thyroid stimulating hormone.

ECG indicates electrocardiogram.

Table 5: atrial fibrillation in Grave's disease, multinodular goiter and toxic adenoma and thyroiditis.

Atrial fibrillation	Graves, MNG*, toxic adenoma	Thyroiditis
Present	17	1
Absent	104	28
p value	0.115	

*indicates multinodular goiter.

DISCUSSION

Thyroid hormones play a major role in the metabolic regulation of the body.¹² Thus it is imperative that any abnormalities in it will affect multiple organs. Thyroid diseases including thyrotoxicosis hamper the quality of life.¹³ Due to the advances in treatment options; there is a perception that thyrotoxicosis is a reversible condition with no long term sequelae. But evidence suggests that

there may be adverse outcomes. Long-term follow-up studies have shown increased mortality from cardiovascular events.¹⁴ Thus; early detection may help in preventing morbidity and improve quality of life.

High circulating levels of free thyroxine and triiodothyronine result in thyrotoxicosis.¹⁵ When thyrotoxicosis is associated with thyroid gland over activity, hyperthyroidism occurs. But thyrotoxicosis can occur without hyperthyroidism, when stored thyroid hormones are released from damage to thyroid gland (sub-acute thyroiditis, amiodarone induced thyroiditis) or when excess thyroid hormones are consumed.¹⁵⁻¹⁷ Grave's disease accounts for most cases of thyrotoxicosis.¹⁸ It is a systemic autoimmune disease characterized by formation of thyroid stimulating receptor antibodies. (TRAb).¹⁹

Thyroid hormones increase rate and force of systolic contraction (positive chronotropic and inotropic effect) and decrease the systemic vascular resistance.²⁰ As a

result, thyrotoxicosis increases systolic blood pressure and heart rate and widens the pulse pressure.²¹ Thyrotoxic heart disease refers to cardiovascular effects of Graves' disease. It can manifest as sinus tachycardia, supraventricular premature contractions, atrial fibrillation, arterial hypertension, cardiomyopathy and heart failure.²²

To assess the clinical profile of thyrotoxicosis and study its effects on cardiovascular system, we performed a cross sectional study in a tertiary care center. Technetium 99 scan was used to establish the etiology of thyrotoxicosis. Clinical examination and electrocardiogram was done to assess the cardiovascular manifestations.

Our study had 78% female and 22% male study participants. A study done by Banzal et al, reported female contribution to be 65%.²³ This observation could be due to gender wise difference in the number of patients visiting our hospital. In our study, maximum percentage of patients (24.67%) belonged to age group of 41-50 years. A study conducted by Hashmi et al, demonstrated 24% patients in this age group.²⁴

Graves' disease was the commonest cause of thyrotoxicosis (58%) followed by thyroiditis (18.67%). Multi nodular goiter was observed in 16% of the participants whereas toxic adenoma was seen in 7.34%. A study conducted by Shetty et al also revealed Graves' disease as the commonest cause of thyrotoxicosis.¹⁰

Weight loss (38.66%) and palpitations (25.33%) were predominant symptoms in participants with Grave's disease; those with thyroiditis had neck pain as the most common symptom (17.3%). Multi nodular goiter had neck swelling as the commonest symptom (11.3%) whereas weight loss (4%) and palpitations (4%) were predominant symptoms in participants with toxic adenoma.

In the present study atrial fibrillation was found to be present in 12% of the study population. The prevalence of atrial fibrillation in the study conducted by Zarger et al, was 8.9%.²⁵ The study conducted by Dhadke et al, reported the prevalence of atrial fibrillation as 11.4%.²⁶ In our study, atrial fibrillation was observed in 13.7% in Graves's disease, 3.4% in thyroiditis, 10% in MNG and 18.18% in toxic adenoma. The study conducted by Zarger et al, reported the presence of atrial fibrillation in 4.6% patients with Grave's disease, 14.8% with MNG and no patients with thyroiditis had atrial fibrillation.²⁵ The decreased prevalence of atrial fibrillation in patients with thyroiditis can be explained by acute and self-resolving nature of the disease. The rate of atrial fibrillation was significantly high (p value <0.0001) in patients of age 31-40. A similar result was seen in study conducted by Baladi et al where rate of atrial fibrillation was higher (p value <0.02) in above 30 years of age patients.²⁷

This study reports that tachycardia was observed in 47.12% of patients with Graves's disease. A similar study conducted by Shetty et al reported 61.3% of patients with Grave's disease having tachycardia.¹⁰

Mean age in participants with Grave's disease was 42.1 years, in thyroiditis it was 45 years, in MNG it was 40.46 whereas in toxic adenoma it was 39.91 years. The study conducted by Shetty et al revealed mean age in Grave's disease to be 43.49 years, in thyroiditis as 48.8 years and in MNG as 46.9 years.¹⁰

Hypertension was observed in 52% (78) of participants. Most of them belonged to the age group of 31-40 years. A study conducted by Prisant et al reported hypertension to be significantly higher in age group of 20-49 years.²⁸

Strength of this study

- This is the first study of its kind in a tertiary care hospital in central India.
- Population based study.
- Etiologies and cardiovascular complications of thyrotoxicosis are highlighted.

There are some Limitations of this study. Due to cost constraints, thyroid Technetium scan could not be done in all participants. Also, this is single center study.

CONCLUSION

Patients with thyrotoxicosis should be examined and evaluated thoroughly since they have various degrees of cardiovascular involvement. The most common cause of thyrotoxicosis was Grave's disease. Hypertension, sinus tachycardia and atrial fibrillation were common cardiac comorbidities.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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