

ORIGINAL ARTICLE

Hyperthyroidism And Cardiovascular Manifestations

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ABSTRACT

Introduction: Cardiac involvement in hyperthyroidism is of great prognostic importance as they can cause significant morbidity and mortality. The present study was undertaken to study the cardiac manifestations of hyperthyroidism, their correlation with thyroid hormone levels and the outcome with treatment.

Methodology: A descriptive, prospective study about cardiac manifestations of hyperthyroidism was conducted among 50 consecutive patients of hyperthyroidism attending medical OP or admitted in medicine wards, Department of Medicine, KIMS Medical College, Bhubaneswar during the period from December 2013 to November 2014.

Results: Mean age with hyperthyroidism in the study was 46.06 years. Majority of elderly patients with hyperthyroidism had MNG. The commonest presenting symptoms were heat intolerance and fatigue, followed by weight loss. Palpitation was the commonest cardiac symptom in hyperthyroidism (74%). Tachycardia (66%) was the most common cardiac sign noted.

Conclusion: Grave's disease was the commonest cause of hyperthyroidism. Treatment of hyperthyroidism reversed cardiac symptoms in majority of cases. Hyperthyroidism should be corrected or managed as soon as symptoms occur.

Keywords: Cardiac Manifestations, Hyperthyroidism, Thyroid Hormone Levels

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INTRODUCTION

Thyroid disorders constitute the second commonest endocrinological disorder in clinical practice after diabetes mellitus. Thyrotoxicosis is defined as the state of thyroid hormone excess. Hyperthyroidism denotes excessive thyroid function.¹ Cardiac involvement in hyperthyroidism is of great prognostic importance as they can cause significant morbidity and mortality. All the more they are potentially reversible also. Secondary complications like stroke can arise from atrial fibrillation. Cardiac problems resolve rapidly when hyperthyroidism is treated and thyroid hormone return to normal range.^{2,3} Early and prompt recognition of cardiac abnormalities and aggressive treatment prevents lot of complications of hyperthyroidism. Also, many a times, cardiac features are the presenting symptoms of hyperthyroidism. The present study was undertaken to study the cardiac manifestations of hyperthyroidism, their correlation with thyroid hormone levels and the outcome with treatment.^{4,5}

MATERIAL AND METHODS

A descriptive, prospective study about cardiac manifestations of hyperthyroidism was conducted among 50 consecutive patients of hyperthyroidism attending medical OP or admitted in medicine wards, Department of Medicine, KIMS Medical College, Bhubaneswar during the period from December 2013 to November 2014. Before the initiation of study, the protocol was approved by the Ethical Committee of KIMS Medical College, Bhubaneswar. In order to avoid any problem in the study and to guarantee full cooperation of the participants, Informed consent was obtained from the participants before their participation.

Procedure

Therapeutic strategies adopted in this study included drugs and surgery. One patient expired during the follow up due to refractory cardiac failure and three patients could not be reassessed. Forty-six patients were re evaluated after six months. Cardiac abnormalities assessed before and after treatment were Palpitation, Tachycardia, Atrial fibrillation, Systolic hypertension, Loud S1, ejection systolic murmur, pansystolic murmur, cardiac failure, cardiomegaly.

STATISTICAL ANALYSIS

Statistical analysis was conducted using SPSS version 17. Descriptive statistics is presented in tabular form.

RESULTS

Majority of the patients with hyperthyroidism were between 30 and 49 years old (62%). Mean age in the study was 46.06 years. Majority of elderly patients with hyperthyroidism had MNG. The patients were predominantly females. The male: female ratio was 1:2.57. The commonest presenting symptoms were heat intolerance and fatigue, followed by weight loss. Palpitation was the commonest cardiac symptom in hyperthyroidism (74%). Tachycardia (66%) was the most common cardiac sign noted. Atrial fibrillation was seen in 14% cases. Electro-cardiogram abnormalities were seen in three fourth of cases (76%), tachycardia being the commonest abnormality. One fourth (24%) of patients had cardiomegaly and nearly half of the patients (44%) had echocardiographic abnormalities. Hyperthyroidism per se is a risk factor for diastolic dysfunction in young patients. Valvular abnormalities were not common. Among the Valvular abnormalities, mitral regurgitation was the commonest one. Grave's disease was the commonest cause of hyperthyroidism, accounting for 50% cases. Atrial fibrillation was common in elderly patient with hyperthyroidism. 71.4% of patients with atrial fibrillation were above 60 years old. High T3 and low TSH levels correlated with the presence of atrial fibrillation. High T4 levels and low TSH levels were significantly associated with the presence of systolic hypertension. Age and severity of the disease is

the most important risk factors for atrial fibrillation in hyperthyroidism. Patients with multinodular goiter had severe disease as compared to hyperthyroidism due to other causes. MNG patients had a higher prevalence of atrial fibrillation. 85.7 % of patients with atrial fibrillation had MNG. Treatment of hyperthyroidism reverses the cardiac abnormalities in most of the cases. There was significant improvement clinically as well as in the ECG and echocardiographic abnormalities with treatment. Younger patients with atrial fibrillation had higher chance of reversing to sinus rhythm. Cardiac failure improved with treatment in all cases (Table-1). At follow up only 6% had cardiac symptoms compared to the 74% on presentation. Edema subsided with treatment in all cases. Treatment modality and etiology of hyperthyroidism did not have any impact on response to treatment. (Table-2).

Cardiac abnormality	At presentation	On follow up
Palpitation	74%	6%
Tachycardia	66%	12%
Atrial fibrillation	14%	4%
Systolic hypertension	32%	4%
Loud S1	15%	4%
Ejection systolic murmur	8%	4%
Pansystolic murmur	4%	6.5%
Cardiac failure	5%	0%
Cardiomegaly	24%	18%

Table-1: Cardiac abnormalities before and after treatment

DISCUSSION

The mean age of presentation was 46.06 years. 62% of patients were between 30 and 49 years. 56% of patients with Grave's disease and 61% of patients with MNG were in the age group between 30 and 49 years. This is comparable with the existing literature showing common occurrence of Grave's disease in the 20-50 age group¹. All patients with solitary nodule were between 30 and 39 years.⁶ Females outnumbered males in the current study. This is consistent with available literature.⁷ The male:female ratio in this study was 1.0:2.57. The male: female ratio was

Abnormality	At Presentation (%)	On follow up (%)
Diastolic dysfunction	26	10
Mitral regurgitation	16	02
Left ventricular hypertrophy	8	8
Pulmonary hypertension	6	2
Aortic regurgitation	4	2
Tricuspid regurgitation	4	0
Mitral valve prolapse	2	2

Table-2: Echo findings before and after treatment

1:3.8,1:2 and 1:1 in patients with Grave's disease, MNG and toxic adenoma respectively. A higher proportion of males were noted in this study. This may be due to the fact that females seek and get less medical attention in our country and may reflect a difference between the two sexes in availing medical care facilities. Literature shows a male: female ratio of 1:10 in patients with Grave's disease.⁷

Heat intolerance, fatigue and weight loss were the commonest presenting symptoms. In a previous Indian study on juvenile hyperthyroidism, the common symptoms observed at presentation were weight loss (82.1%), excessive sweating (78.6%), heat intolerance (76.8%), increased appetite (73.2%) and diarrhea (48.2%).⁸

Neurological abnormalities were seen in 80% cases. Tremor was the commonest neurological sign (74%), followed by hyperreflexia (36%). However, only 8% subjects reported tremor as a presenting symptom.¹

Thyroid ophthalmopathy was noted in 52% cases. Among Grave's disease patients, 84% had ophthalmopathy, comparable to the existing literature showing ophthalmopathy in 75% cases.

We noticed a slightly higher incidence of dermopathy (12%) as compared to the reported 5%.¹

Palpitation was the commonest cardiac symptom in our study, which was in concordance with the available literature. In our study, 74% patients had cardiac symptoms on presentation. 66% of our cases had tachycardia, 14% had atrial fibrillation and 32% had systolic hypertension. A widened pulse pressure was noted in 24% cases.

As per the literature, tachycardia is the commonest cardiac sign in hyperthyroidism. In a study of 880 patients of varying age, resting tachycardia was second only to goiter as the most common sign of hyperthyroidism.^{4,6} In our study, 14% patients had atrial fibrillation, which was comparable with the reported prevalence of 2-20%.^{1,9,10} Cardiovascular system examination showed abnormalities in 46% cases, the commonest being a loud S1. Among the murmurs an aortic ejection systolic murmur due to hyperdynamic circulation was the commonest one, seen in 16% cases. 10% cases had cardiac failure.

Electrocardiogram abnormalities were seen in 76% cases, tachycardia being the commonest abnormality. Atrial fibrillation was seen in 14% cases. Cardiomegaly was noted in chest X-ray in 24% cases. Echocardiographic abnormalities were seen in 44% cases. Diastolic dysfunction was noted in 26% cases. Valvular abnormalities were not common. Among the Valvular abnormalities, mitral regurgitation was the commonest one. Diastolic dysfunction was common in patients above 40 years and 38.4% of patients with diastolic dysfunction had associated hypertension. Advanced age and hypertension are risk factors for diastolic dysfunction. However none of the patients less than 40 years with diastolic dysfunction (6/13) had hypertension. Also 25% of our subjects of less than 40 years had diastolic dysfunction compared to the normal prevalence of 2-4% in the age group 25-35 years. So in the younger age groups, hyperthyroidism per se is an independent risk factor for diastolic dysfunction. Left atrial enlargement was seen in 42.8% (3/7) of cases with atrial fibrillation. All patients with left atrial enlargement were more than 60 years old. In a previous study analyzing the relationship between left atrial size and AF in hyperthyroidism, left atrial enlargement existed in 7% of patients younger than 40 years, in only 2% of those older than 40 without fibrillation, and in as many as 94% of those older than 40 year with AF.^{5,3}

Electrocardiogram abnormalities in our study were comparable with the available literature. We noticed less cardiomegaly and atrial fibrillation. This may be due to the fact that we had less number of elderly patients.^{9,10} Embolic episodes

were noted in none of our patients.

Grave's disease was the commonest cause of hyperthyroidism in our study. 50 % of our cases of hyperthyroidism were due to Grave's disease. This is slightly less compared to the reported incidence of 60-80%.¹ We had only very few cases of toxic adenoma. Since the numbers are too small and this is a hospital-based study, it is not appropriate to comment whether this reflects any regional epidemiological variation.¹¹

Atrial fibrillation was common in elderly patient with hyperthyroidism. 71.4% of patients with atrial fibrillation were above 60 years old. In the age group above 60 years, 62.5 % patients had atrial fibrillation.

In our study, it was observed that patients with severe disease had higher incidence of atrial fibrillation and systolic hypertension. Also it was observed that patients with multinodular goiter had severe disease as compared to hyperthyroidism due to other causes. Age and severity of disease were the important risk factors for atrial fibrillation in hyperthyroidism.¹²

MNG patients had a higher prevalence of atrial fibrillation. 85.7 % of patients with atrial fibrillation had MNG. Patients with multi nodular goiter, because of their old age, have an increased prevalence of AF. In a previous study prevalence of atrial fibrillation was 43% whereas it was only 10% in patients with Graves' disease.¹ MNG patients also had more systolic hypertension as compared to other etiologies.

With treatment there was significant reduction in cardiac abnormalities. Only two patients had persistent atrial fibrillation on follow up. Both of them were above 60 years old and had left atrial enlargement. Treatment of hyperthyroidism is frequently associated with reversion of atrial fibrillation to sinus rhythm. In one study, this occurred in 62 percent of 163 patients within 8 to 10 weeks after they returned to a euthyroid state. Seven patients had mild hyperthyroidism on follow up. There was significant reversal of echo findings on follow up with treatment. Diastolic dysfunction improvement was the most notable one. Left atrial enlargement persisted in all the three cases.

Treatment of hyperthyroidism reversed cardiac symptoms in majority of cases. In a previous study of 356 patients with cardiac involvement

with atrial fibrillation, angina or heart failure, over 90% had improvement in cardiac symptoms and signs after treatment.¹³⁻¹⁵

No statistically significant difference was noted between the two treatment groups with regard to response to treatment. No treatment modality was superior over the other and response to treatment was not dependent on the treatment modality adopted. No statistically significant correlation was noted between etiology of hyperthyroidism and treatment outcome. However, the numbers were too small to draw any significant conclusions.

CONCLUSION

In present study heat intolerance, fatigue and weight loss were the commonest presenting symptoms. Neurological abnormalities were seen in 80% cases. Thyroid ophthalmopathy was noted in 52% cases. Palpitation was the commonest cardiac symptom. Cardiovascular system examination showed abnormalities in 46% cases, the commonest being a loud S1.

Electrocardiogram abnormalities were seen in 76% cases, tachycardia being the commonest abnormality. Grave's disease was the commonest cause of hyperthyroidism. Treatment of hyperthyroidism reversed cardiac symptoms in majority of cases.

LIMITATIONS

This is a hospital based study conducted in a tertiary care center and so is not reflective of the patterns in the community. The study population was small. We had less number of elderly patients, probably because they seek and/or get less medical attention. Larger community based studies are needed to find out the exact prevalence of cardiac abnormalities and the clinico epidemiological patterns of hyperthyroidism in our region.

REFERENCES

1. Jameson JL, Weetman AP. Disorders of the thyroid gland –In: Harrison's Principles of Internal Medicine, 18th edition, vol 2; 2911-2939.

2. Klein I. Thyroid hormone and cardiovascular system. *Am J Med* 1990; 88:631-637.
3. Fazio S, Palmieri PA, Lombardi G, Biondi B. Effects of thyroid hormone on the cardiovascular system. *Recent Progress in Hormone Research* 2004 59:31-50.
4. Sandler G, Wilson GM. The nature and prognosis of heart disease in thyrotoxicosis. *Q J Med* 1959;28:247-269.
5. Summers VK, Surtees SJ. Thyrotoxicosis and heart disease. *Acta Med Scand* 1961; 169:661-671.
6. Glass CK, Holloway JM. Regulation of gene expression by the thyroid hormone receptor. *Biochim Biophys Acta* 1990; 1032:157-176.
7. Brent GA, Moore DD, Larsen PR. Thyroid hormone regulation of gene expression. *Annu Rev Physiol* 1991; 53:17-35.
8. Lazar MA. Thyroid hormone receptors: multiple forms, multiple possibilities. *Endocr Rev* 1993; 14:184-193.
9. Freedman LP. Anatomy of the steroid receptor zinc finger region. *Endocr Rev* 1992; 13:129-145.
10. Yen PM, Darling DS, Carter RL, Forgione M, Umeda PK, Chin WW. Triiodothyronine (T3) decreases binding to DNA by T3-receptor homodimers but not receptor-auxiliary protein heterodimers. *J Biol Chem* 1992; 267:3565-3568.
11. Refetoff S, Weiss RE, Usala SJ. The syndromes of resistance to thyroid hormone. *Endocr Rev* 1993; 14:348-399.
12. Schueler PA, Schwartz HL, Strait KA, Mariash CN, Oppenheimer JH. Binding of 3,5,3'-triiodothyronine (T3) and its analogs to the in vitro translational products of c-erbA protooncogenes: differences in the affinity of the alpha and beta forms for the acetic acid analog and failure of the human testis and kidney alpha-2 products to bind T3. *Mol Endocrinol* 1990; 4:227-234.
13. Katz D, Lazar MA. Dominant negative activity of an endogenous thyroid hormone receptor variant alpha 2 is due to competition for binding sites on target genes. *J Biol Chem* 1993; 268:20904-20910.
14. Strait KA, Schwartz HL, Perez-Castillo A, Oppenheimer JH. Relationship of c-erbA mRNA content to tissue triiodothyronine nuclear binding capacity and function in developing and adult rats. *J Biol Chem* 1990; 265:10514-10521.
15. Bradley DJ, Towle HC, Young WS III. Spatial and temporal expression of alpha and beta thyroid hormone receptor mRNAs, including the beta 2-subtype, in the developing mammalian nervous system. *J Neurosci* 1992; 12:2288-2302.