****

**PREVALENCE OF CARDIOVASCULAR MANIFESTATIONS IN THYROTOXICOSIS**

Research Submitted to department of medicine /college of medicine /AL-NAHRAIN University as a part of M.B.Ch.B graduation requirement.

**DONE BY: AYA SAAD ABDUL-EMMA**

**SUPERVISOR: MAHMOOD SHAKIR ALZAIDY**

**Dedicated**

**To**

**MY Beloved family and the many friends who supported me on this journey and encouraged me to believe in myself. Thank you.**

**Acknowledgement**

**I would like to express my deepest gratitude to my supervisor associate professor MAHMOOD SHAKIR ALZAIDY for his unwavering support, collegiality and mentorship throughout this project.**

**ABSTRACT**

**Background:** It is well known that thyroid hormone directly affects the heart and peripheral vascular system. In hyperthyroidism, cardiovascular manifestations are frequent findings: atrial arrhythmias, limitations in exercise tolerance, and congestive heart failure were reported to occur more common in older patients as a result of hyperthyroidism. Cardiovascular signs of hyperthyroidism include tachycardia, widened pulse pressure, marked increase in cardiac output with impaired cardiovascular and respiratory exercise capacity. Most of the cardiac abnormalities return to normal once a euthyroid state has been achieved in a majority of patients. There are very few studies which address the most important cardiovascular manifestations of hyperthyroidism.

**AIM:**The aim was to study the prevalence of various cardiac manifestations in newly diagnosed thyrotoxicosis.

**Methods:** This cross sectional study was doneat MADINAT AL-IMMAMIAN ALKADYMIAN TEACHING HOSPITAL, BAGHDAD, IRAQ,from October 2017 to February 2018. This studyincluded 25 patients with newly diagnosed to have thyrotoxicosis based on T3, T4 and TSH levels. They were 3 males and 22 females with age ranging from 20 to 70 years,they were chosen randomly out of the attendants of the outpatient department of endocrinology and diabetes at AL-IMMAMIAN ALKADYMIAN TEACHING HOSPITAL. Those patients have no previous history of cardiovascular diseases. Patients were informed about the study and their approval to participate was taken. All the patients underwent clinical evaluation, measurement of blood pressure, clinical examination of precordium, basic laboratory tests T4, T3 and TSH and radiological variables were studied in these patients. ECG and 2D ECHO were performed in these patients to analyze the presence of any cardiac manifestations.

For the purpose of the study , questionnaire formula was prepared ,it contained information about the patients age ,gender ,BMI , clinical symptoms of hyperthyroidism , hypertension, previous history of IHD , ECG and ECHO STUDY findings.

**Results and discussion:** In this study females (88%) were more than males (12%), commonest cardiovascular symptoms were palpitation (92%), followed by dyspnoea (28%) and chest pain (16%). The commonest cardio vascular signs were found to be tachycardia (92%), widened pulse pressure (76%). The commonest ECG finding was found to be Sinus tachycardia (52%) followed by atrial fibrillation (12%), Systolic dysfunction and chamber enlargement (12%) were the commonest echo findings.

**Conclusions:** This study shows that cardiovascular manifestations are quite common and varied in hyperthyroidism which are to be looked for in the management.

Introduction

Thyroid hormones have a profound effect on numerous metabolic processes, virtually in all tissues and hence every tissue in the body gets affected to a greater or lesser extent in thyroid hormone disturbances, the heart being particularly sensitive to its effect. Thyroid hormone directly affects the heart and peripheral vascular system. The hormone causes increase in heart rate, myocardial ionotropy and increases the cardiac output by dilating the peripheral arteries [1]. In hyperthyroidism, cardiovascular manifestations are frequent findings. Hyperthyroidism can produce changes in blood pressure, myocardial oxygen consumption, cardiac contractility, cardiac output and systemic vascular resistance [2]. Atrial arrhythmias, limitations in exercise tolerance, and congestive heart failure were reported to occur more common in older patients as a result of hyperthyroidism [3]. Hyperthyroidism results in excessive mortality from increased incidence of circulatory diseases and dysarrhythmias [4]. Incidence of cerebral embolism is common in the hyperthyroid patients with atrial fibrillation, especially in the elderly group and anticoagulation was indicated in them. Numerous studies have shown that treatment of hyperthyroidism results in conversion to sinus rhythm in up to two-third of patients. Drugs like beta-blockers help to reduce left ventricular hypertrophy and atrial and ventricular arrhythmias in patients with hyperthyroidism [5].

**Thyrotoxicosis:** Thyrotoxicosis describes a constellation of clinical features arising from elevated circulating levels of thyroid hormone.

The most common causes are Graves’ disease, multi nodular goitre and autonomously functioning thyroid nodules (toxic adenoma)[17].

## Hemodynamic effects of thyroid hormones

 Hemodynamic effects of thyroid hormones are generally non-genomic and faster, by direct effects on heart and blood vessels. In the peripheral vascular system, the rapid use of oxygen, increased production of metabolic end products and relaxation of arterial smooth muscle fibers by thyroid hormone cause peripheral vasodilatation [[7](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3832836/#CIT0024)]. This fall in peripheral vascular resistance (PVR) plays the central role in all hemodynamic changes caused by thyroid hormones [[15](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3832836/#CIT0060)]. Decreased PVR causes an increase in heart rate, a selective increase in blood flow of some organs (skin, skeletal muscles, heart), and a fall in diastolic pressure with consequent widening of pulse pressure. Vasodilatation without an increase in renal blood flow causes a reduction in renal perfusion and activation of the renin-angiotensin system that causes sodium retention and increased blood volume [[6](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3832836/#CIT0061)]. In addition, thyroid hormones regulate erythropoietin secretion and increased red cell mass may also contribute to the blood volume increase [[13](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3832836/#CIT0062)]. Improved diastolic relaxation and increased blood volume increased left ventricular end-diastolic volume (LVEDV). Reduced PVR and increased LVEDV means increased preload and decreased after load; thus the stroke volume increases. Increased stroke volume and increased heart rate lead to doubling or tripling of cardiac output, which cannot be solely explained by an increased metabolic rate of the body [[12](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3832836/#CIT0063)]. The importance of the contribution of decreased systemic vascular resistance to the increase in systemic blood flow in patients with hyperthyroidism is evidenced by studies in which the administration of arterial vasoconstrictors, atropine and phenylephrine, decreased peripheral blood flow and cardiac output by 34% in patients with hyperthyroidism but not in normal subjects [14].

Clinical manifestations of thyrotoxicosis : cardiovascular signs and symptoms are common in patients with hyperthyroidism [8], and in some patients these symptoms predominate. They include:

-tachycardia at rest, during sleep and exaggerated during exercises.

-palpitations, due to both tachycardia and more forceful cardiac contractility.

-hype dynamic precordium indicative of the increase in cardiac contractility.

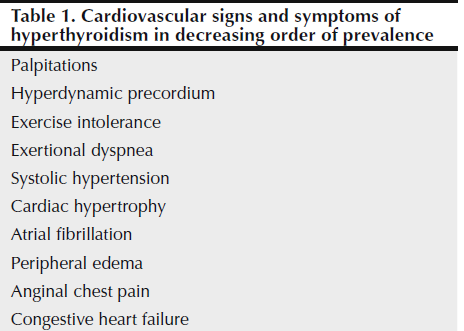
-systolic hypertension with widened pulse pressure [9].

-exertional dyspnea which is more due to respiratory and skeletal weakness than cardiac dysfunction.

-angina like chest pain ,with EKG findings suggested of myocardial ischemia, which can occur especially in women , this appear to be the result of coronary vasospasm and responds to orally administered calcium channel blockers.

-increased in left ventricular mass index and left ventricular hypertrophy [10, 11].

-hyperthyroidism also increased risk of atrial fibrillations, heart failure, pulmonary hypertension and angina

[18]

*Atrial fibrillation in thyrotoxicosis:* Atrial fibrillation occurs in about 10% of patients withthyrotoxicosis. The incidence increases with age so thatalmost half of all males with thyrotoxicosis over the age of 60 are affected. Moreover, subclinicalthyrotoxicosisis a risk factor for atrial fibrillation.Characteristically, the ventricular rate is littleinfluenced by digoxin, but responds to the addition ofa -blocker. Thromboembolic vascular complicationsare particularly common in thyrotoxic atrial fibrillationso that anticoagulation with warfarin is required.

**AIM OF THE STUDY:**

* TO evaluate the cardiovascular manifestations of thyrotoxicosis.

**Patients and methods:**

This study was doneat MADINAT AL-IMMAMIAN ALKADYMIAN TEACHING HOSPITAL, BAGHDAD, IRAQ,from October 2017 to February 2018. This is a cross sectional studyincluded 25 patients with newly diagnosed to have thyrotoxicosis based on T3, T4 and TSH levels, who fulfilled the inclusion criteria and exclusion criteria. They were 3 males and 22 females with age ranging from 20 to 70 years,they were chosen randomly out of the attendants of the outpatient department of endocrinology and diabetes at AL-IMMAMIAN ALKADYMIAN TEACHING HOSPITAL. Those patients have no previous history of cardiovascular diseases. Patients were informed about the study and their approval to participate was taken. All the patients underwent clinical evaluation, measurement of blood pressure, clinical examination of precordium, basic laboratory tests T4, T3 and TSH and radiological variables were studied in these patients.

ECG and ECHO were performed in these patients to analyze the presence of any cardiac manifestations.

For the purpose of the study , questionnaire formula was prepared ,it contained information about the patients age ,gender ,BMI , clinical symptoms of hyperthyroidism , hypertension, previous history of IHD , ECG and ECHO STUDY findings.

***Inclusion criteria***

- All patients with overt hyperthyroidism of grave’s disease, toxic adenoma, multinodular goiter etiology

- All patients with subclinical hyperthyroidism of grave’s disease, toxic adenoma, multinodular goiter etiology

***Exclusion criteria:***

*-patients with previous history of cardiovascular diseases.*

*-Patients with relapse attack of thyrotoxicosis*

*-patients undergo thyroid surgery*

***Statistical analysis***

The collected data of the 25 patients was statistically analyzed with SPSS 23.0 version. To describe about the data descriptive statistics frequency analysis, percentage analysis, cross tabulation were used for categorical variables .

**RESULTS:**

In this study of 25 patients of hyperthyroid, twenty two females (88%) and 3 males (12%) were involved with age ranging from 20 to 70 years and body mass index from 18.33\_29.07 as seen in Table 1 , 2 and figure 1.

In this study out of the total patients, 92% of the patients had palpitations, 28% presented with exertional dyspnea, 16% presented with chest pain as seen in Table 3, 4, 5.out of the total patients , 4% have pedal edema as seen in Table 6.

In this study about 32% of the patients had heart rate ranging between 80-100 and about 68% had above 100 (Table 7). 16% of the patients had SBP of less than 120, 48% had SBP ranging between 120 to 139. 32% had SBP ranging between 140 to 159. And about 4% had above 159 (Table 8).

In this study about 52% of the patients had DBP of less than or equal to 80. 48% had DBP ranging between 80-89 and about 4% had between 90-99 (Table 9). Among the 25 patients studied 2 patients of which 2females and no males had a pulse pressure ranging from 21-40. 25 patients including 18 females and 1 male had between 41-60. And about 4 patients had above 60 (Table 10).

In this present study the commonest ECG findings were found to be Sinus tachycardia (52%), atrial fibrillation (12%) as seen in (Table 11).

In this study, echocardiographic evaluation showed systolic dysfunction in 12% of patients and chamber enlargement in 12% of patients, followed by diastolic dysfunction in 4%, and pulmonary hypertension in 4% of patients (Table 12).

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Table1 : age and gender distribution among thyrotoxic patients | | | | | |
|  | | | gender | | Total |
| female | male |
| Age | up to 40 years | Count | 15 | 0 | 15 |
| % of Total | 60.0% | 0.0% | 60.0% |
| 41\_60 years | Count | 6 | 1 | 7 |
| % of Total | 24.0% | 4.0% | 28.0% |
| more than 60 years | Count | 1 | 2 | 3 |
| % of Total | 4.0% | 8.0% | 12.0% |
| Total | | Count | 22 | 3 | 25 |
| % of Total | 88.0% | 12.0% | 100.0% |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Table 2 : BMI of thyrotoxic patients** | | | | | |
|  | | | gender | | Total |
| female | male |
| BMI | LESS THAN 18.5 | Count | 2 | 0 | 2 |
| % of Total | 8.0% | 0.0% | 8.0% |
| 18.5\_24.99 | Count | 17 | 0 | 17 |
| % of Total | 68.0% | 0.0% | 68.0% |
| 25\_29.99 | Count | 3 | 3 | 6 |
| % of Total | 12.0% | 12.0% | 24.0% |

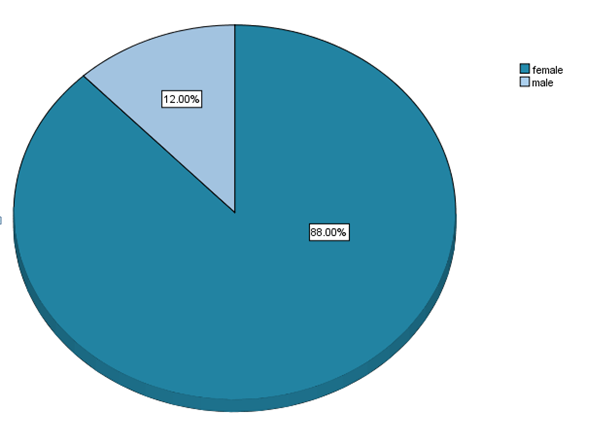
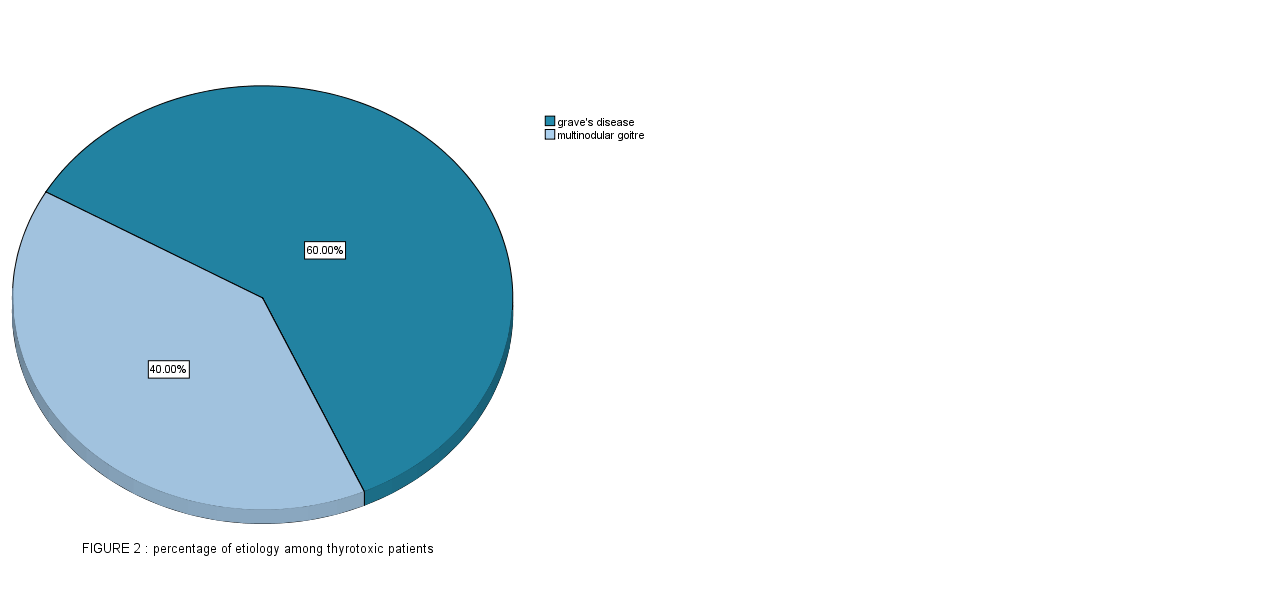


Figure 1: percentage of gender among thyrotoxic patients



|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Table 3: Palpitations among thyrotoxic patients.** | | | | | |
|  | | | gender | | Total |
| female | male |
| Palpitation | Present | Count | 21 | 2 | 23 |
| % of Total | 84.0% | 8.0% | 92.0% |
| Absent | Count | 1 | 1 | 2 |
| % of Total | 4.0% | 4.0% | 8.0% |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Table 4: chest pain among thyrotoxic patients.** | | | | | |
|  | | | gender | | Total |
| female | male |
| Chest pain | present | Count | 3 | 1 | 4 |
| % of Total | 12.0% | 4.0% | 16.0% |
| absent | Count | 19 | 2 | 21 |
| % of Total | 76.0% | 8.0% | 84.0% |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Table 5: Exertional dyspnea among thyrotoxic patients.** | | | | | |
|  | | | gender | | Total |
| female | male |
| exertional dyspnea | present | Count | 6 | 1 | 7 |
| % of Total | 24.0% | 4.0% | 28.0% |
| absent | Count | 16 | 2 | 18 |
| % of Total | 64.0% | 8.0% | 72.0% |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Table 6: Pedal edema among thyrotoxic patients.** | | | | | |
|  | | | gender | | Total |
| female | male |
| Pedal edema | present | Count | 1 | 0 | 1 |
| % of Total | 4.0% | 0.0% | 4.0% |
| absent | Count | 21 | 3 | 24 |
| % of Total | 84.0% | 12.0% | 96.0% |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Table 7 : Pulse range among thyrotoxic patients** | | | | | |
|  | | | gender | | Total |
| female | male |
| Pulse-range | 60\_100 beats/min. | Count | 8 | 0 | 8 |
| % of Total | 32.0% | 0.0% | 32.0% |
| more than 100 beats/min. | Count | 14 | 3 | 17 |
| % of Total | 56.0% | 12.0% | 68.0% |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Table 8:Systolic blood pressure among thyrotoxic patients** | | | | | |
|  | | | gender | | Total |
| female | male |
| Systolic blood pressure | less than 120 | Count | 4 | 0 | 4 |
| % of Total | 16.0% | 0.0% | 16.0% |
| 120\_139 | Count | 12 | 0 | 12 |
| % of Total | 48.0% | 0.0% | 48.0% |
| 140\_159 | Count | 5 | 3 | 8 |
| % of Total | 20.0% | 12.0% | 32.0% |
| more than 159 | Count | 1 | 0 | 1 |
| % of Total | 4.0% | 0.0% | 4.0% |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Table 9 : Diastolic blood pressure among thyrotoxic**  **patients** | | | | | |
|  | | | **gender** | | **Total** |
| **female** | **male** |
| **Diastolic blood pressure** | **less than 80** | **Count** | **13** | **0** | **13** |
| **% of Total** | **52.0%** | **0.0%** | **52.0%** |
| **80\_89** | **Count** | **8** | **3** | **11** |
| **% of Total** | **32.0%** | **12.0%** | **44.0%** |
|  |  |  |  |  |
| **90\_99** | **Count** | **1** | **0** | **1** |
| **% of Total** | **4.0%** | **0.0%** | **4.0%** |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Table 10 : Pulse pressure of thyrotoxic patients** | | | | | |
|  | | | gender | | Total |
| female | male |
| PULSE PRESSURE | 21\_40 | Count | 2 | 0 | 2 |
| % of Total | 8.0% | 0.0% | 8.0% |
| 41\_60 | Count | 18 | 1 | 19 |
| % of Total | 72.0% | 4.0% | 76.0% |
| more than 60 | Count | 2 | 2 | 4 |
| % of Total | 8.0% | 8.0% | 16.0% |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Table 11: ECG changes among thyrotoxic patients.** | | | | | | | |
|  | | gender | | | |
| female | | male | |  |  |
| Count | N % | Count | N % | Total count | Table total N% |
| sinus tachycardia | Present | 11 | 44.0% | 2 | 8.0% | 13 | 52% |
| Absent | 11 | 44.0% | 1 | 4.0% | 12 | 48% |
| Atrial  fibrillation | Present | 2 | 8.0% | 1 | 4.0% | 3 | 12 % |
| Absent | 20 | 80.0% | 2 | 8.0% | 22 | 88% |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Table 12: Echocardiography findings of thyrotoxic patients.** | | | | | |
|  | | gender | | | |
| female | | male | |  |  |
| Count | N % | Count | N % | Total count | Table total N% |
| SYSTOLIC DYSFUNCTION | present | 2 | 8.0% | 1 | 4.0% | 3 | 12.0% |
| absent | 20 | 80.0% | 2 | 8.0% | 22 | 88.0% |
| DIASTOLIC DYSFUNCTION | present | 0 | 0.0% | 1 | 4.0% | 1 | 4.0% |
| absent | 22 | 88.0% | 2 | 8.0% | 23 | 96.0% |
| CHAMBER ENLARGEMENT | present | 2 | 8.0% | 1 | 4.0% | 3 | 12.0% |
| absent | 20 | 80.0% | 2 | 8.0% | 22 | 88.0% |
| PULMONARY HYPERTENSION | present | 0 | 0.0% | 1 | 4.0% | 1 | 4% |
| absent | 22 | 88.0% | 2 | 8.0% | 24 | 96% |

**DISCUSSION**

This is a cross sectional study included 25 patients with newly diagnosed to have thyrotoxicosis.

Concerning with *Age, Sex and BMI*, results in tables 1, 2 and figure 1 showed that the participants were of age ranging from 20 to 70 years, 60% of the participants have age group range up to 40 years, which refers to the occurrence of thyrotoxicosis in young age group rather than the elderly one, other studies showed that the occurrence of thyrotoxicosis in elderly age group more than young one [33, 30]. On the other hand, the presence of 22 females (88%) versus 3 males (12%), suggests that thyrotoxicosis is a disease of women rather than men [32, 36]. Also one can notice that there is no relationship between this disease and change BMI that ranged from 18.33 to 29.03, other studies showed that there is no sufficient data between the BMI and thyrotoxicosis [27, 36].

Concerning with etiology, results in figure 2 showed that 60% of the participants had thyrotoxicosis of grave’s etiology, 40 % had thyrotoxiosis of multinodular etiology, which come with the fact that most common cause of thyrotoxicosis is grave’ disease followed by multinodular, as other studies is had been shown [37, 25, 35].

In the present study the commonest cardio vascular symptoms were palpitation (92%), followed by exertional dyspnoea (28%) and chest pain (16%). This also goes with the fact that palpitation and exertional dyspnoea are the commonest symptoms of hyperthyroidism patients irrespective of the cause. Hence in congruent with earlier studies, this study also had majority of patients presenting with palpitation, dyspnoea and chest pain, {32, 38}.pedal edema was found in 4% of the participants. In this present study the commonest cardio vascular signs were found to be tachycardia (68%), widened pulse pressure (76.0%) ,Tachycardia was particularly common in the elderly age group. Increased pulse pressure is also seen in these patients. In this study 68% of the patients had tachycardia, as comparable with the Zargar et al, 70% of the participants had tachycardia.1In the current study 76% of the patients had widened pulse pressure where as in Klein et al, it is 30%.

Regarding *Hypertension*, results seen in table 8,9 showed that 9 patients (36% ) were having systolic hypertension, while the other 16 one(64%) were clear. And that 4% of them (1 patient) was of diastolic hypertension, One might think that, because a excess of thyroid hormone increase the metabolism , *Hyperthyroidism increases systolic blood pressure by decreasing systemic vascular resistance, increasing heart rate, and raising cardiac output[ 22,39,27].*

*Concerning the ECG findings, sinus tachycardia was found in 52% patients which was 63.5% patients in the study by Zarger et al, however it was mentioned that sinus tachycardia, that is heart rate exceeding 100 beats/min was observed in 40% of patients with hyperthyroidism, occurring more frequently in the younger age group patients, which is comparable with the current study [23, 33]. In hyperthyroid patients the prevalence of atrial fibrillation 12%, in the study by Barsela S et al 21% of patients had atrial fibrillation, while 16% in that of Zarg and 17% of that of Osman et al. In our study 12% patients in this study had atrial fibrillation which is slightly lower than others.*

*In this present study systolic dysfunction was seen in 12% of the patients, where as in Mercé et al, it was present in 3% of the patients.* *. In this study pulmonary hypertension was present in about 4% of patients however in Sui et al, patients with hyperthyroidism and normal LV systolic function, up to 47% of the patients had PHT.14 Inadequate sample size may be the reason for this difference.* *Present study had diastolic dysfunction in about 4% of patients.Over all the cardiovascular manifestations dominated the picture of hyperthyroidism though the frequency is slightly different from the earlier studies. Early identification and management of them is very important since many of them can contribute to serious mortality and morbidity.*

**Conclusion**

**-** Females (88%) were more than males (12%).

**-** The commonest cardio vascular symptom was palpitation (92%).

**-** The commonest cardio vascular signs were found to be tachycardia (68%), widened pulse pressure (76.0%)

**-** The prevalence of systolic dysfunction increases as the age increased.

**-** Systolic dysfunction was seen in 12% of the patients.

**Recommendation:**

Early identification and management of cardiovascular manifestations is very important since many of them can contribute to serious mortality and morbidity.

**REFERENCES**

1. Klein I, Danzi S. Thyroid disease and heart. Circulation. 2007;116:1725-35.

2. Fazio S, Palmieri EA, Lombardi G, Biondi B. Effects of thyroid hormone on the cardiovascular system. Endo Journals Org. 2004;59:31-50.

3. Klein I. Thyroid Hormone and the cardiovascular system. Am J Med. 1990;88(6):631-7.

4. Tribulova N, Knezl V, Shainberg A, Seki S, Soukup T. Thyroid hormones and cardiac arrhythmias. Vascul Pharmacol. 2010;52(3):102-12.

5. Jayaprasad N, Francis J. Atrial Fibrillation and Hyperthyroidism. Indian Pacing Electrophysiol J. 2005;5(4):305-11.

6. Symons C. Thyroid heart disease. Br Heart J. 1979;41:257-62.

7. Von OK. Cardiac arrhythmias and heart rate in hyperthyroidism. Am J Cardiol. 1989;63:930-3.

8. Klein I, Ojamaa K. The cardiovascular system in hyperthyroidism. 8th ed. In: Werner and Ingbar’s The Thyroid: A fundamental and clinical text, Braverman LE, Utiger RD, eds. Philadelphia: Lippincott Williams and Wilkins;2000:777-82.

9. Osman F. Cardiovascular manifestations of hyperthyroidism before and after antithyroid therapy: a matched case-control study. J Am Coll Cardiol. 2007;49(1):71-81.

10. Zarger. Thyrotoxicosis. Annals of Saudi Medicine. 2000;20(5-6):484-7.

11. Parmar MS. Thyrotoxic atrial fibrillation. Med Gen Med. 2005;7(1):74.

12. Bar S, Ehrenfeld M, Eliakim M. Arterial embolism in thyrotoxicosis with atrial fibrillation. Arch Intern Med. 1981;141(9):1191-2.

13. Mercé J, Ferrás S, Oltra C, Sanz E, Vendrell J, Simón I et al. Cardiovascular abnormalities in hyperthyroidism: a prospective doppler echocardiographic study. Am J Medicine. 2005;118:126-31.

14. Siu CW, Zhang XH, Yung C, Kung AW, Lau CP, Tse HF. Hemodynamic changes in hyperthyroidism-related pulmonary hypertension: a prospective echocardiographic study. J Clinic Endocrino Metabo. 2007;92(5):1736-42.

15. Roffi M, Cattano F, Topol JE. Thyrotoxicosis and the cardiovascular system: subtle but serious effects. Cleveland Clinic J Med. 2003;7:57-63.

16. Yue W. Hyperthyroidism-induced left ventricular diastolic dysfunction: implication in hyperthyroidism-related heart failure. Clinical Endocrinology. 2011;74(5):636-43.

17. Fadel BM, Ellahham S, Ringel MD, Lindsay J Jr, Wartofsky L, Burman KD. Hyperthyroid heart disease. Clinical Cardiology. 2000;23:402-8.

18. Poliker R. The thyroid and the heart. Circulation. 1993;87:1435-41.

19. Boindi B. Effects of subclinical thyroid dysfunction on the heart. Annuals Internal Med. 2002;137:904-14.

20. Davis FT, Larsen RP. Thyrotoxicosis. In: William’s Text book of endocrinology, Larsen Melmed, Polonsky, 10th ed. Philadelphia: Saunders. 2003;374-

21. Davis FT, Larsen RP. Hypothyroidism and thyroiditis. In: William’s text book of endocrinology, Larsen Melmed, Polonsky. 10th ed. Philadelphia: Saunders. 2003;423-55.

22. Klein I. Endocrine disorder and cardiovascular diseases. In: Braunwald’s heart disease. 10th ed. Philadelphia: Saunders. 2008;432-49.

23. Parry CH. Enlargement of the thyroid gland in connection with enlargement or palpitation of the heart. Collections from the unpublished papers of the late Caleb Hillier Parry.1825;111-25.

24. Graves RJ. Newly observed affections of the thyroid gland in females. London Med Surg J. 1835;7:516-7.

25. Von BCA. Exophthalmos durch hypertrophie des zellgewebes in der augenho hle. Wschr Ges Heilk. 1840;197-220.

26. Zondek H, Leszynsky HE. Pathogenesis of hyperthyroidism. Dual role of iodine in thyroid function. Lancet. 1968;1(7544):671-2.

27. Anatomy of the Human Body. Available at http://www.bartleby.com/ 107/. Accessed on 12 February 2016.

28. Nussey S, Whitehead S. Endocrinology: An Integrated Approach. Oxford: BIOS Scientific Publishers. 2001.

29. Paul MY. Physiological and molecular basis of thyroid hormone action. Physiological Reviews. 2001;81(3):1097-126.

30. Clare BH, Graham RW. The mechanism of thyroid hormone. Thyroid. 2002;12(6):441-6.

31. Dillmann WH. Cellular Action of Thyroid Hormone on the Heart. Thyroid. 2002;12(6):447-52

32. Denzi S, Klien I. Thyroid hormone and blood pressure regulation. Current Hypertension Reports. 2003;5:513-52.

33. Toft A, Boon N. Thyroid disease and heart. Heart. 2000;84:455-60.

34. Dahl P. Thyrotoxic cardiac disease. Current Heart Failure Reports. 2008;5:170-8.

35. Gammage MD, Parle JV, Holder RL, Roberts LM, Hobbs FD, Wilson S, et al. Association between serum free thyroxine concentration and atrial fibrillation. Arch Intern Med. 2007;167:928-34.

36. Forfar JC, Muir AL, Toft AD. Left ventricular function in hypothyroidism responses to exercise and beta adrenoceptor blockade. Br Heart J. 1982;48:278-84.

37. Moolman JA. Thyroid hormone and the heart. Cardiovascular J South Africa. 2002;13(3):159-63.

38. Kahaly JG, Dillmann HW. Thyroid hormone action in the heart. Endocrine Reviews. 2005;26:704-28.

39. Goland S, Shimoni S, Kracoff O. Dilated cardiomyopathy in thyrotoxicosis. Heart. 1999;81:444-9.

40. Ansari SM, Haider S, Awal MA, Khanam N, Siddique AB. Cardiac complications of hyperthyroidism: echocardiographic evaluation of 69 hyperthyroid patients. Transactional Analysis Journal. 2004;17(1):6-9.