Original Research Article

A study of cardiovascular manifestation in patient with hypothyroidism

M. Agila Saravanan[1], S. Geetha[2*]

[1,2]Assistant Professor, Department of General Medicine, Government Royapettah Hospital, Government Kilpauk Medical College, Chennai, Tamil Nadu, India
[*]Corresponding author email: **drgeetharamesh@gmail.com**

International Archives of Integrated Medicine, Vol. 5, Issue 9, September, 2018.

Available online at http://iaimjournal.com/
ISSN: 2394-0026 (P) **ISSN: 2394-0034 (O)**
Received on: 01-09-2018 **Accepted on:** 08-09-2018
Source of support: Nil **Conflict of interest:** None declared.
How to cite this article: M. Agila Saravanan, S. Geetha. A study of cardiovascular manifestation in patient with hypothyroidism. IAIM, 2018; 5(9): 67-73.

Abstract

Background: Reduced production of thyroid hormone is the central feature of the clinical state termed Hypothyroidism. Hypothyroidism is associated with bradycardia, a decreased cardiac output, increased vascular resistance and perhaps a decreased sensitivity of the sympathoadrenal system.
Aim and objective: To assess the cardiovascular functions in diagnosed hypothyroidism patients.
Materials and methods: A total number of 70 hypothyroid patients were enrolled in this study. The clinical features, cardiovascular manifestations were studied by ECG, ECHO, chest X-ray lipid profiles.
Results: Most of the cases fell in the age group of 31-40 years at a percentage of 52.9%. On analysis of 70 cases, 41% of cases were in moderate hypothyroidism group. On analyzing the pulse rate of 34% of the cases had bradycardia (PR <60/min). Mean BP- 131/84 mm Hg (Range: 118-166/66 – 102 mm Hg). Most of the patients fell into the pre-HT group which was around 66%. 24% of hypothyroid patients were hypertensive (BP >140/90 mm Hg). Lipid analysis in hypothyroid patients showed an increase in total cholesterol. 54.3% of patients had hypercholesterolemia (≥ 300 mg/dL). On analyzing the ECG changes in hypothyroid patients the most common finding was sinus bradycardia. It was found in 39% of cases. Next was low voltage complex which is around 34%. Normal ECG was found in 14% of patients. Least common findings were ST-T changes, RBBB and LBBB. Out of 70 cases, 12 (17.14%) patient showed enlarged cardiac silhouette (cardiomegaly). 34% of the patients had pericardial effusion. 30 % of the patients had diastolic dysfunction. Systolic dysfunction occurred in 4.3% of them, while IVST and LVPWT were seen in 14.3% and 12.9% respectively.
Conclusion: Any unexplained diastolic dysfunction or pericardial effusion should be screened for hypothyroidism. Early detection of hypothyroidism and proper replacement therapy found to reverse the cardiovascular complications and thereby can decrease the morbidity and mortality.

Key words

Hypothyroidism, ECG, Echo, Chest X-Ray, Lipid Profiles.

Introduction

Reduced production of thyroid hormone is the central feature of the clinical state termed Hypothyroidism. Permanent loss or destruction of the thyroid, through processes such as autoimmune destruction or irradiation injury, is described as primary hypothyroidism [1]. Primary hypothyroidism is the etiology in 99% of cases of hypothyroidism, with less than 1% being due to TSH deficiency or another causes Hypothyroidism is characterized by a decrease in oxygen and substrate utilization by all the major organ systems of the body. As a result, the demands for cardiac output decrease; in addition, hypothyroidism directly alters cardiac function through changes in myocyte-specific expression [2]. Thyroid hormone has relevant effects on the cardiovascular system. In hypothyroidism the cardiac output at rest is decreased because of reduction in both stroke volume and heart rate, reflecting the loss of the inotropic and chronotropic effects of thyroid hormones. However, in hypothyroidism, cardiac output increases and peripheral vascular resistance decreases normally in response to exercise unless the hypothyroid state is severe and of long standing [3]. Elevated levels of total cholesterol, LDL cholesterol, and apolipoprotein B are well-documented features of overt hypothyroidism. Early studies in humans with hypothyroidism, using isotopically labeled LDL, demonstrated a prolonged half-life of LDL cholesterol because of decreased catabolism, an effect that was reversible with T4 therapy [4]. Additional data in human fibroblasts verified that the T3-induces increase in LDL degradation was mediated through an increase in LDL receptor number, without any change in the affinity of LDL for its receptor. A specific effect of thyroid hormone on the LDL receptor was suggested by a lack of T3 effect on LDL concentration in cultured cells without LDL receptors. These findings were supported by an in vivo study in a hypothyroid woman whose receptor-mediated LDL catabolism was reduced, compared with euthyroid controls, with significant improvement after T4 replacement therapy [5]. Two studies have shown that LDL is more susceptible to oxidation in patients with hypothyroidism, with normalization after the restoration of the euthyroid state. Increased levels of lipoprotein(a) [Lp(a)], a particularly atherogenic LDL variant in which apolipoprotein(a) and apolipoprotein B (apo B)are covalently bound, have also been reported in hypothyroidism, compared with euthyroid controls [6]. Several studies have shown decreases in the Lp(a) concentration after T4 treatment of hypothyroid patients. However, other reports have not confirmed this relationship Clinical trials have not demonstrated an effect of T4 on Lp(a) levels in subclinical hypothyroidism with exception of one trial, which showed a decrease in Lp(a) [7]. The impact of hypothyroidism on vascular and hemostatic risk factors for atherosclerosis has also been investigated in a few studies. Alterations in flow-mediated, endothelium-dependent vasodilatation, which occurs early in atherogenesis, have been noted in patients with hypothyroidism. It is uncertain whether this is attributable to a direct effect of thyroid hormone deficiency or mediated through the hypercholesterolemia induced by hypothyroidism [8].

Materials and methods

This study was conducted in hypothyroid patients who attended the Medicine Department in Government Royapettah Hospital in the year 2017.

Inclusion criteria: They were divided into three categories according to the level of thyroid stimulating hormone (TSH) as follows:

A.Mild: TSH <20 mIU/mL.

B.Moderate: TSH 20-50 mIU/mL.

C.Severe: TSH >50 mIU/mL.

Exclusion criteria:

- Cardiac disease
- COPD

- Severe anemia
- Chronic kidney disease
- Diabetes mellitus and other endocrine disorder
- Hypertension
- On long term medications that alter thyroid function like amiodarone, beta blockers, lithium, steroids, alcohol and oral contraceptives
- Patients already on thyroid replacement therapy.
- Patients with subclinical hypothyroidism.

All new diagnosed hypothyroid patients were meticulously examined for features of hypothyroidism. Their symptoms were analyzed in a detailed manner. A thorough examination of the cardiovascular system another system was done. Patients were evaluated for the following parameters:

-Pulse rate

-Blood pressure was measured thrice and the average was taken (As per recommendations of Joint National Committee – 8)

-Body mass index- BMI was considered abnormal if it was $\geq$ 25 kg/m^2.

-Serum T_3, T_4, TSH – 3 ml of early morning fasting samples of plain clotted blood were collected and sent for Serum T_3, T_4, TSH estimation by chemiluminescence assay. Normal TSH: 0/4 – 4.0 micro IU/mL, Normal T_4: 4-12.3 microg/dL, Normal F T_4: 0.7-1.8 ng/dL, Normal F T_3: 2-50 pg/dL.

-Lipid profile: Values were considered to be abnormal if: Total cholesterol > 200 mg/dL, LDL >100 mg/dL, HDL < 40 mg/dL, TGL > 150 mg/dL.

-A standard 12 lead ECG was taken for all patients and studied for sinus bradycardia, low voltage complex, QT prolongation, ST-T changes, LBBB, RBBB.X-ray chest PA view.

-Echocardiography: Echo was done for all patients using 2D and M-mode echocardiography with color Doppler.

The following parameters were evaluated.

Systolic function: the systolic function was assessed mainly by M-mode measurements. Ejection fraction and fractional shortening were the two parameters used. The ejection fraction is defined as the ratio of stroke volume to end diastolic volume.

Normal: EF – 55 to 75% Grading of systolic dysfunction

Mild: EF 45-55%

Moderate: EF 35 – 45%.

Severe: EF <35%.

Grading of Diastolic function:

1.Normal: 0.75 – 1.5

2.Mild dysfunction: E/A $\leq$ 0.75 with impaired relaxation- grade I

3.Moderate dysfunction: E/A 0.75 -1.5 with pseudo normalization pattern- grade II.

4.Severe dysfunction: EA >1.5 with reversible restrictive pattern- grade III.

5.Severe dysfunction: EA >1.5 with fixed restrictive pattern- grade IV.

Pericardial effusion: The pericardial effusion was quantified by the amount of echo-free space surrounding the heart. The pericardial effusion can be graded as follows:

Mild pericardial effusion: echo-free space <1cm

Moderate pericardial effusion: echo-free space 1-2cm.

Severe pericardial effusion: echo-free space >2cm.

Chamber size and wall thickness: measurement of the interventricular septum, left ventricular posterior wall thickness, left ventricular internal diameter was made in both systole and diastole LVST >11 mm and LVPWT >11 mm in diastole represent concentric hypertrophy. Chi-square analysis was done to analyze the variations of different parameters.

Results

Most of the cases fell in the age group of 31-40 years at a percentage of 52.9%.On analyzing the sex distribution there was an overall female predominance. The female population constituted around 75.7% and male 24.3%.

On analysis of 70 cases, 41% of cases were in moderate hypothyroidism group (**Chart – 1**). On systemic examination, 21.4% of cases had the muffled heart sound (**Chart – 2**).

Mean BP- 131/84 mm Hg (Range: 118-166/66 – 102mm Hg). Most of the patients fell in the pre-HT group which was around 66%. 24% of hypothyroid patients were hypertensive (BP >140/90 mm Hg) as per **Graph – 1**.

Chart – 1: Severity of hypothyroidism according to TSH level.

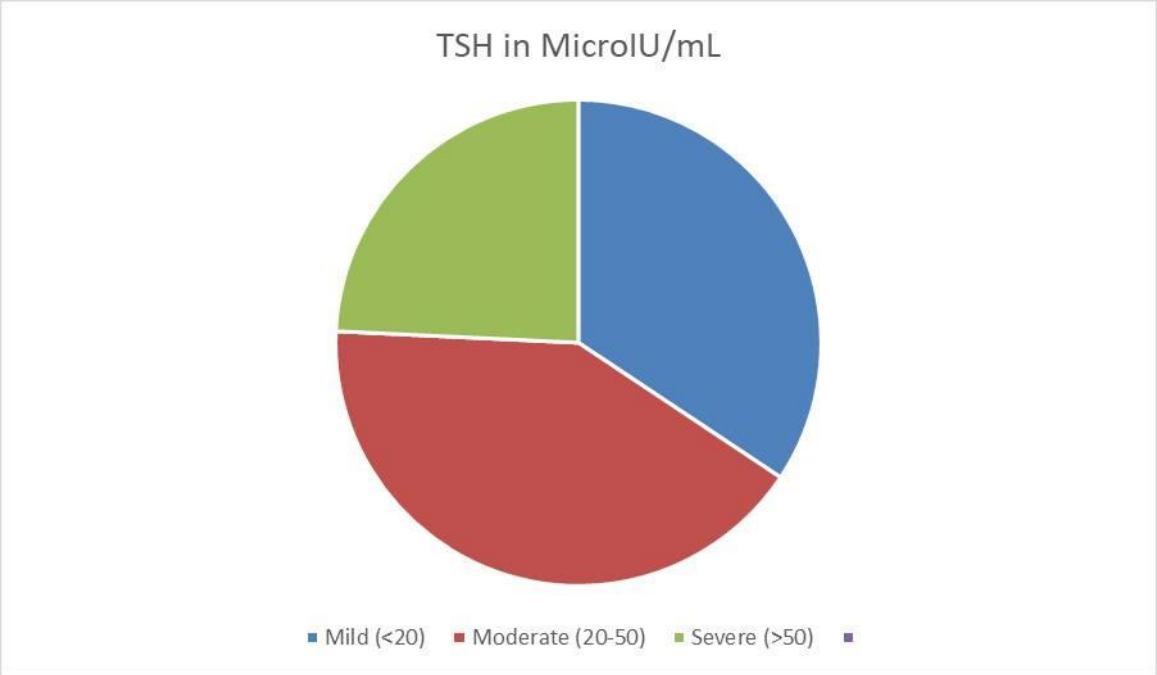


Chart – 2: Systemic examination analysis.

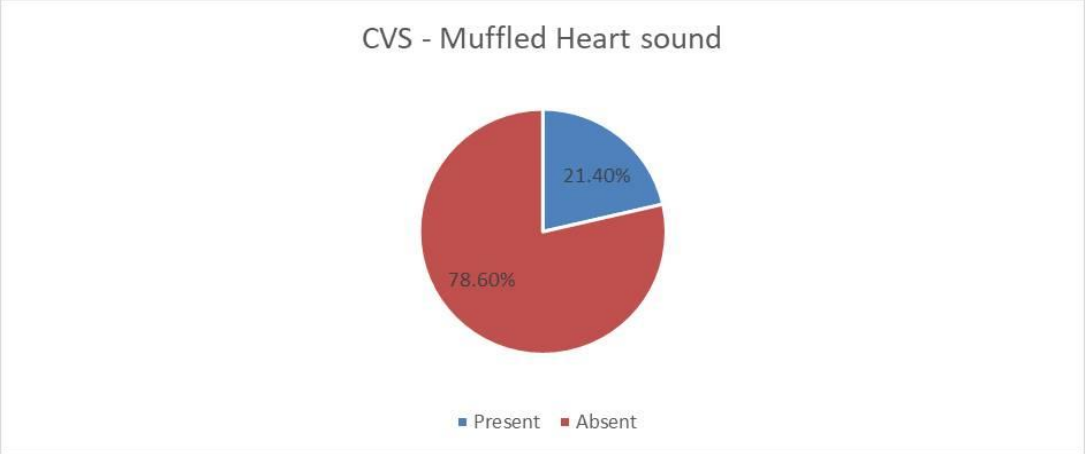
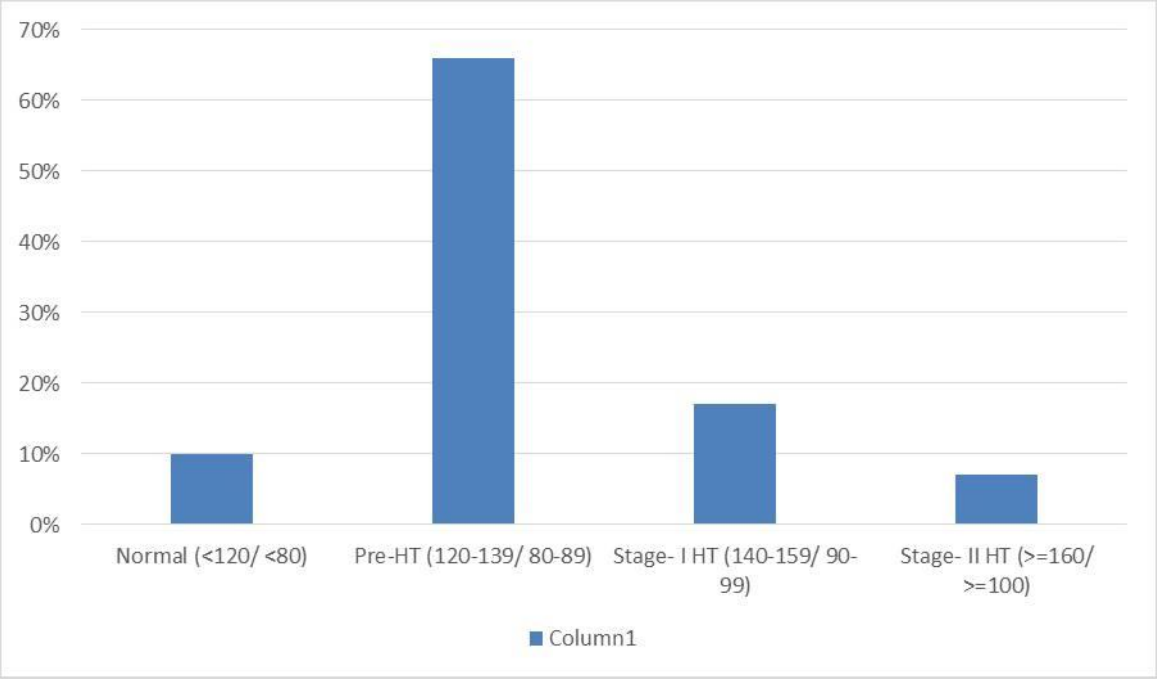


Table – 1: Lipid profile in hypothyroidism patients.

TSH in microIU/mL	TCL in mg/dL			Total number of patients
	<200	200-230	>300	
Mild	9	11	4	24
Moderate	14	6	9	29
Severe	9	3	5	17
Total	32 45.7%	20 28.6%	18 25.7%	70 100%

Graph – 1: Prevalence of hypertension in hypothyroidism.



Lipid analysis in hypothyroid patients showed an increase in total cholesterol. 54.3% of patients had hypercholesterolemia (>= 300 mg/dL) as per **Table – 1**.

Table – 2: ECG findings in hypothyroidism.

ECG Changes	No. of changes	%
Normal	10	14
LBBB	1	1
LVC	24	34
RBBB	2	3
ST-T c	6	9
SB	27	39
Total	70	100

Table – 3: Chest X-ray analysis abnormalities.

Chest X-ray PA view	Present N (%)	Absent N (%)
Cardiomegaly	12 (17.14%)	58 (82.86%)

On analyzing the ECG changes in hypothyroid patients the most common finding was sinus bradycardia. It was found in 39% of cases. Next was low voltage complex which is around 34%. Normal ECG was found in 14% of patients. Least common findings are ST-T changes, RBBB and LBBB as per **Table – 2**.

Out of 70 cases, 12 (17.14%) patient showed enlarged cardiac silhouette (cardiomegaly) as per **Table – 3**.

Table – 4: ECHO findings in hypothyroidism.

Echo findings	No. of patients	%
Normal	27	39%
Pericardial effusion	24	34%
Diastolic dysfunction	21	30%
IVS thickness	10	14.3%
LVPW thickness	8	12.9%
Systolic dysfunction	3	4.3%

34% of the patients had pericardial effusion. 30 % of the patients had diastolic dysfunction. Systolic dysfunction occurred in 4.3% of them, while IVST and LVPWT are seen in 14.3% and 12.9% respectively (**Table – 4**).

Discussion

Of the 70 patients studied, 24 (34%) patients who had TSH values less than 20 mIU/ mL were mild hypothyroidism. around 29 (41%) patients had TSH of 20-50 mIU/mL were classified as moderate hypothyroidism. Severe hypothyroidism with value >50mIU/mL was

seen in17 (24%) of cases. The range of TSH was 9-150 mIU/mL. Mean TSH value was 39.36 mIU/mL. On analyzing the BMI normal weight was noted in 26 (37%) of the patients. 25 (36%) cases were overweight (BMI 25-29.9) and 9 (13%) were obese with BMI > 30. The mean BMI was 24.41. It is well known that hyperthyroidism is associated with atrial fibrillation (AF). Similarly, hypothyroidism is associated with increased cardiovascular risk factors as well as subclinical and diagnosed cardiovascular disease, both of which are thought to predispose one to AF. However, the relationship between hypothyroidism and AF was evaluated in the Framingham Heart Study and was not found to be statistically significant [9]. The QT interval is often prolonged in hypothyroidism due to a prolonged ventricular action potential. This is indicative of increased ventricular irritability and in turn, can lead to acquired Torsades de pointes. Varying degrees of atrioventricular block and low QRS complexes are also seen in patients with hypothyroidism. Generally, the incidence of ventricular fibrillation is decreased in hypothyroidism, and depression of thyroid hormone levels appears to be beneficial in patients with angina and acute myocardial infarction. Bradycardia can be beneficial as it raises the arrhythmogenic threshold, especially in patients with the underlying cardiovascular disease. In patients with subclinical hypothyroidism, cohort studies have not found significant differences in cholesterol levels or diastolic blood pressures [10]. However, small randomized trials have discovered some beneficial effects of treatment with levothyroxine. In a study of women with subclinical hypothyroidism, 18 months of treatment resulted in normalization of systolic and diastolic blood pressure and of total and LDL cholesterol as well as decreased carotid intima thickness [11]. In another study of patients with subclinical hypothyroidism and coronary artery disease, no significant changes occurred in the group randomized to levothyroxine, but those who received placebo had echocardiographic evidence of progression to myocardial diastolic dysfunction [12]. Although there are no randomized clinical trials evaluating long-term cardiovascular outcomes and mortality in patients treated with levothyroxine, a population-based study of levothyroxine-treated patients demonstrated that those with elevated TSH (defined as greater than 4 mIU/L) had a greater risk for cardiovascular events despite receiving the drug [13]. Analysis from a population-based cohort study revealed that patients with treated hypothyroidism noted no increase in all-cause or cancer mortality but did notice an increase in cardiovascular morbidity in terms of ischemic heart disease and dysrhythmias [14]. The observation seen in this study showed normal ECHO findings in 27(39%) of patients and abnormal echo findings in 43(61%) of the patients. The most common abnormality noted was pericardial effusion in 24 (34%) patients; diastolic dysfunction was noted in 21(30%) cases. IVST and LVPWT were seen in 14.3% and 12.9% of cases respectively. Least echo abnormality noted was systolic dysfunction which was around 4.3% [15].

Conclusion

Hypothyroidism can result in decreased cardiac output, increased systemic vascular resistance, decreased arterial compliance, and atherosclerosis. This study suggests that it is very important to evaluate patients of primary hypothyroidism for cardiovascular changes so that prior interventions could be performed to improve the clinical outcomes. Any unexplained pericardial effusion should be screened for Hypothyroidism. Also, all patients found to have the ECG and Echocardiographic changes as reported above should be screened for the presence of hypothyroidism.

Acknowledgments

The author would like to thank the whole General medicine unit cardiology unit, laboratory staffs of Government Royapettah Hospital, Government Kilpauk Medical College, Chennai, Tamil Nadu, for helping with data collection and laboratory analyses.

References

1. Asvold BO, Bjoro T, Nilsen T, Vatten LJ. Association between blood pressure and serum TS concentration within the reference range: a population-based study. J Clin Endocrinol Metab., 2007; 9: 841-845.
2. Batcher EL, Tang XC, Singh BN, Singh SN, Reda DJ, Hershman JM. SAFE-T Investigators. Thyroid function abnormalities during amiodarone therapy for persistent atrial fibrillation. Am J Med., 2007 October; 120(10): 880– 5.
3. Bianco AC, Salvatore D, Gereben B, Berry MJ, Larsen PR. Biochemistry, cellular and molecular biology and physiological roles of the iodothyronine seledeiodinases. Endocrine Rev., 2002; 23: 38-89.
4. Biondi B, Klein I. Hypothyroidism as a risk factor for cardiovascular disease. Endocrine, 2004; 24: 1-13.
5. Boekholdt SM, Titan SM, Wiersinga WM, et al. Initial thyroid status and cardiovascular risk factors: the EPIC-Norfolk prospective population study. Clin Endocrinol (Oxf)., 2010. March; 72(3): 404–10.
6. Bogazzi F, Bartalena L, Gasperi M, Braverman LE, Martino E. The various effects of amiodarone on thyroid function. Thyroid, 2001 May; 11(5): 511– 9.
7. Cohen-Lehman J, Dahl P, Danzi S, Klein I. Effects of amiodarone therapy on thyroid function. Nat Rev Endocrinol., 2010. January; 6(1): 34–41.
8. Diekman MJ, Harms MP, Endert E, Wieling W, Wiersinga WM. Endocrine factors related to changes in total peripheral vascular resistance after treatment of thyrotoxic and hypothyroid patients. Eur J Endocrinol., 2001; 144: 339-346.
9. Fazio S, Palmieri EA, Lombardi G, et al. Effects of thyroid hormone on the cardiovascular system. Recent Prog Horn Res., 2004; 59: 31-50.
10. Forfar JC, Muir AL, Toft AD. Left ventricular function in hypothyroidism Br Heart J., 1982; 48: 278-84.
11. Hiroi Y, Kim H-H, Ying H, Furuya F, Huang Z, Simoncini T, Noma K, Ueki K, Nguyen N-H, Scanlan TS, Moskowitz MA, Cheng S-Y, Liao JK. Rapid nongenomic actions of thyroid hormone. Proc Natl Acad Sci USA, 2006; 103: 14104-14109.
12. Imaizumi M, Akahoshi M, Ichimaru S, et al. Risk for ischemic heart disease and all-cause mortality in subclinical hypothyroidism. J Clin Endocrinol Metab., 2004 July; 89(7): 3365– 70.
13. Kiss E, Jakab G, Kranias EG, Edes I. phospholamban protein expression: regulatory effects on sarcoplasmic reticulum Ca2+ transport and myocardial relaxation. Circ Res., 1994; 7: 245-251
14. Klein I, Ojamaa K. Thyroid hormone and the cardiovascular system. N Engl Med., 2001; 344: 501-509.
15. Markou K, Georgopoulos N, Kyriazopoulou V, Vagenakis AG. Iodine-Induced hypothyroidism. Thyroid, 2001 May; 11(5): 501–10.