DIFFERENT CARDIOVASCULAR MANIFESTATIONS OF PRIMARY HYPOTHYROIDISM IN SULAIMANI TEACHING HOSPITAL

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ABSTRACT

Background

Hypothyroidism is a common clinical condition of variable prevalence in different regions that has significant effect on cardiovascular function. Deficiency of thyroid hormones can cause great changes in cardiovascular hemodynamics and regulation of cardiac function. Hypothyroidism directly influences vascular smooth muscles, provokes diastolic hypertension, changes coagulability, and increases the circulation level of highly atherogenic low-density lipoprotein (LDL) cholesterol particles, which consequently leads to an increase in the risk of atherosclerotic cardiovascular diseases.

Objectives

To identify the different cardiovascular manifestations and complications of primary hypothyroidism.

Patients and methods

A cross-sectional retrospective study was carried out at Sulaimani Teaching Hospital in Sulaimani city, the Kurdistan Region of Iraq from July, first 2018 to Jun, first 2019. A total number of 103 patients were recruited in the study, of whom, 93 were females and 10 were males. The patients' age ranged from (19 to 82) years. The patients were grouped based on their age, sex, residency, heart rate, blood pressure, BMI, and presence of other cardiovascular risk factors. All the participants were sent for thyroid function test (thyroid-stimulating hormone (TSH), and T4), electrocardiogram (ECG), and echocardiogram (Echo), with full history and clinical examination had been done.

Results

The total number of cases were (103) patients with primary overt hypothyroidism who received thyroxin therapy. Their age group was between (19 and 82) years with a mean age of 50.99. Female predominance is obvious with a female-to-male ratio of about 9:1. The results showed that the patients' age, sex, and family history of cardiovascular diseases did not have a significant association with the incidence of hypothyroidism or euthyroid ($p>0.05$).

Conclusions

Cardiovascular risk factors were found to be associated with euthyroid and hypothyroid. Both electrocardiogram (ECG) and echocardiogram (Echo) were significantly effective in detecting cardiovascular complications in patients with thyroid disorders. TSH level assessed through thyroid function test was found as the more reliable means of detecting thyroid diseases.

Keywords: *Primary hypothyroidism, Echocardiogram, Electrocardiogram, Thyroid stimulating hormone.*

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INTRODUCTION

As a typical clinical condition with different rates of prevalence in different regions, hypothyroidism affects 4 to 10 percent of the population all over the world [1]. Its prevalence among adult men and women has been reported to be 0.1-0.2 and 2%, respectively [2]. Research studies have indicated that 0.3 to 3.7% of the American population and 0.2 to 5.3% of the European population develop overt hypothyroidism [3, 4, 5]. It has also been shown that patients with autoimmune diseases, white individuals, older people (>65 years) and women are more frequently diagnosed with hypothyroidism [6].

Hypothyroidism has been classified as primary or secondary [7]. Ninety-nine percent of hypothyroidism cases are primary, and roughly 1% are secondary [6]. It has been indicated that primary hypothyroidism is mostly caused by iodine deficiency and Hashimoto's disease (chronic autoimmune thyroiditis) [8]. It also has a significant effect on cardiovascular function, which is mediated by non-genomic and genomic impacts; therefore, deficiency of thyroid hormones can cause great changes in cardiovascular hemodynamics and regulation of cardiac function [9].

Deficiency of thyroid hormone will lead to a drop in heart rate and causes myocardial contraction and relaxation to become weak with early diastolic and prolonged systolic times. Since no significant deiodinase activity occur in cardiac myocyte, the heart is mainly dependent on serum T3 [9, 10]. According to the evidence provided by research, some traditional risk factors of cardiovascular disease can be changed by overt hypothyroidism [11].

Given the deficiency in relaxation of vascular smooth muscle, leading to an increase in systemic vascular resistance, and a decrease in endothelial nitric oxide availability, it has been reported that there is an association between hypothyroidism and decrease in cardiac output [1]. In acute hypothyroidism, it is probable that pericardial effusion happens.

Although the mechanism is not clear, it is stated that increase in capillary permeability and decrease in lymphatic drainage from the pericardial space play a role [1, 12]. In most cases, achieving a euthyroid state has been referred to as the ultimate treatment. It has also been proposed as the only therapy of pericardial effusions because of hypothyroidism [12].

Managing cardiac arrhythmias has been carried out by amiodarone which is an iodine-rich compound. This compound has also been reported to cause amiodarone-induced hypothyroidism by inhibiting iodine oxidation, known as the Wolff-Chaik off effect [1]. It has also demonstrated that treating patients suffering from overt thyroid dysfunction with levothyroxine postpones atherosclerosis progression and leads to improvement in diastolic dysfunction, heart rate, hypertension, triglycerides, LDL cholesterol, and total cholesterol [1, 2, 9]. According to the results of short-term trials, L-thyroxine has lipid-lowering effects on patients with subclinical hypothyroidism [13, 14].

PATIENTS AND METHODS

The present cross-sectional retrospective study was carried out at Sulaimani Teaching Hospital in Sulaimani city, the Kurdistan Region of Iraq from July, first 2018 to Jun, first 2019. A total number of (103) patients were recruited in the study, of whom, 93 were females and 10 were males. The patients' age ranged from (19 to 82) years. The patients attended medical OPD (28 cases, 26 females and 2 males), were admitted in medical ward (32 cases, 29 females and 3 males) and CCU (43 cases, 38 females and 5 males), had history of hypothyroidism of variable durations, and received levothyroxine treatment (some of the cases stopped taking thyroxine for different periods of time without their doctor's advice).

Well-prepared written informed consent forms were provided and signed by the patients before they enter the study. The patients were grouped based on their age, sex, residency, heart rate, blood pressure, BMI, and presence of other cardiovascular risk factors such as hypertension, diabetes mellitus, dyslipidemia, obesity, smoking, and family history of cardiovascular disease. Moreover, all of the cases included in the study were provided with noninvasive investigations including thyroid function test (thyroid-stimulating hormone (TSH), and T4), electrocardiogram (ECG) (by different ECG machines, Philips and general electric health care machine), and echocardiogram (Echo) (different echocardiogram machines, Philips and Vivd E9 and by different Echo men) in time of collecting the data. It should be noted that 10 cases stopped using thyroxin for variable periods at least 6 months without medical advice before data collection. Biochemical investigations were sent to the laboratories of Sulaimani Teaching Hospital.

The patients were selected based on some inclusion criteria such as having primary hypothyroid, history

of hypothyroidism, symptoms of hypothyroidism, and receiving treatment. Moreover, the study's exclusion criteria were being pregnant, subclinical hypothyroidism patients who had no hypothyroid symptoms and were only diagnosed by biochemical test, having secondary hypothyroidism, having known severe cardiac disease and belonging to child-age group.

Ischemic heart disease patients diagnosed by ECG findings: 18 patients who had been included in the study found to have IHD (17 females and 1 male), 14 cases from CCU ward, 2 cases from OPD and 2 cases had been admitted to hospital. ECG findings include (ST segment depression in 7 cases, ST segment elevation in 3 cases, and T-wave inversion in 8 cases) and these findings had been correlated to history of admission to CCU due to central chest pain, positive other cardiovascular risk factors and coronary angiography result (which had been done for 6 of the patients and proofed the presence of IHD).

Valvular heart disease diagnosed by echocardiogram: it was found in 10 cases as follow (all of them were females): 5 cases of moderate mitral regurgitation (MR), 2 cases of severe mitral regurgitation, 1case of severe Aortic regurgitation (AR) and 2 cases of moderate aortic stenosis (AS). Interestingly, in the ECG finding, low voltage ECG had been found in 8 cases, their TSH range from 23-90 mIU/L. Of different age groups, all of them were females.

According to the American Thyroid Association and WHO and based on the levels of TSH and T4, the patients were grouped into hypothyroid and euthyroid groups:

1. TSH at age of more than 70 years=Euthyroid of 0.25-5.9 mIU/L, hypothyroid >5.9 mIU/L

2. TSH at age of less than 70 years=Euthyroid of 0.25-4.5 mIU/L, hypothyroid >4.5 mIU/L

3. T4=Euthyroid of 64-154 nmol/L, hypothyroid of less than 64 nmol/L

4. Dyslipidemia as total cholesterol of more than 200 mg/dl, triglyceride of more than 160 mg/dl

5. Obesity as BMI of more than 30 kg/m2, waist circumference of more than (88 cm for women and 100 cm for men).

The research protocol was accepted by the Kurdistan Board of Internal Medicine.

The analyzed categorical data are expressed as number and percentages. Data analysis was carried out using Chi-square test through SPSS version 20.

RESULTS

In the present study, the total number of cases were 103 patients with primary overt hypothyroidism who received thyroxin therapy. Of those 103 patients, 93 were females (90.3%) and 10 were males (9.7%). Their age group was between 19 and 82 years with a mean age of 50.99. Female predominance is obvious with a female-to-male ratio of about 9:1. (Table 1).

Analyzing the relationship between cardiovascular risk factors and development of euthyroid and hypothyroid indicated that none of the cardiovascular risk factors were significantly correlated with development of euthyroid and hypothyroid ($p>0.05$) (Table 2).

According to the results of the present study, euthyroid and hypothyroidism had no significant association with the cardiovascular findings of ECG ($p>0.05$ (Table 3).

Low voltage ECG had been found in 8 cases, all of them were females and their TSH range from (23-90) mIU/L, which was expected in such high TSH level.

Ischemic heart disease patients diagnosed by ECG findings: 18 patients who had been included in the study found to have IHD (17 females and 1male). ECG findings include (ST segment depression in 7 cases, ST segment elevation in 3 cases, T-wave inversion in 8 cases). These findings had been correlated to history of admission to CCU due to central chest pain, positive other cardiovascular risk factors and coronary angiography result (which had been done for 6 patients and proved the presence of IHD).

The results also indicated that euthyroid and hypothyroidism could not be reliably diagnosed through Echo cardiovascular findings because there was no significant relationship between euthyroid and hypothyroidism and the cardiovascular

findings of (p>0.05) (Table 4).

Patients with valvular heart diseases: 10 cases have valvular heart diseases all of them were females, mitral valve regurgitation was the commonest finding (5 cases had moderate MR, 2 cases had severe MR), other valvular heart diseases include 2 cases of moderate aortic stenosis (AS) and one case of severe aortic regurgitation(AR). It is obvious that the mitral valve disease was the commonest among valvular heart diseases in the current study.

Comparing the patients with and without cardiovascular risk factors in terms of normal and abnormal ECG demonstrated that these two groups of patients were significantly different regarding normal and abnormal ECG (p=0.000 (Table 5).

The patients with and without cardiovascular risk factors were compared regarding normal and abnormal findings of Echo study, and it was concluded that the two groups of patients were significantly different regarding normal and abnormal Echo findings (p=0.000), such that a highly larger number of patients with cardiovascular risk factors (n=47) had abnormal Echo, while a few patients without cardiovascular risk factors (n=3) had abnormal Echo (Table 6).

The results of the current study showed that the patients' mean age was 50.99 years with a standard deviation of 14.382, a minimum age of 19, and a maximum of 82 years. It was also observed that the mean duration of using thyroxine was 14.88, and the mean TSH and T4 were respectively 9.6484 and 126.5565 (Table 7).

Table 1. Demographic findings and cardiovascular risk factors in relation to thyroid function test.

Demographic characteristics		Euthyroid No. (%)	Hypothyroidism No. (%)	Total	p-value
Age	20 – 69	5 (5.4)	88 (94.6)	93 (100.0)	
	≥ 70	2 (2.0)	8 (80.0)	10 (100.0)	0.08
Total		7(6.8)	96(93.2)	103(100.0)	
Sex	Female	5(5.4)	88(94.6)	93(100.0)	
	Male	2(20.0)	8(80.0)	10(100.0)	1.0
Total		7(6.8)	96(93.2)	103(100.0)	
Family history of CVD	+ve first degree relative	2(6.3)	30(93.8)	32(100.0)	
	+ve Second degree relative	0(0.0)	1(100.0)	1(100.0)	1.000
	Negative	5(7.1)	65(92.9)	70(100.0)	
Total		7(6.8)	96(93.2)	103(100.0)	

Table 2. Association between cardiovascular risk factors and incidence of euthyroid and hypothyroid.

Cardiovascular risk factors		Euthyroid No. (%)	Hypothyroid No. (%)	Total	p-value
DM	Yes	2(13.3)	13(86.7)	15(100.0)	
	No	5(5.7)	83(94.3)	88(100.0)	0.269
Total		7(6.8)	96(93.2)	103(100.0)	
IHD	Yes	2(11.1)	16(88.9)	18(100.0)	
	No	5(5.7)	80 (94.3)	85(100.0)	0.4
Total		7(6.8)	96(93.2)	103(100.0)	
HT	Yes	3(4.8)	59(95.2)	62(100.0)	
	No	4(9.8)	37(90.2)	41(100.0)	0.432
Total		7(6.8)	96(93.2)	103(100.0)	
Dyslipidemia	Yes	1(3.2)	30(96.8)	31(100.0)	
	No	6(8.3)	66(91.7)	72(100.0)	0.672
Total		7(6.8)	96(93.2)	103(100.0)	
Other CVD risk factors	Negative	6(7.8)	71(92.2)	77(100.0)	
	Smoking	0(0.0)	8(100.0)	8(100.0)	
	Smoking & Obesity	0(0.0)	2(100.0)	2(100.0)	
	Obesity	1(6.7)	14(93.3)	15(100.0)	1.000
	Chronic kidney disease	0(0.0)	1(100.0)	1(100.0)	
Total		7(6.8)	96(93.2)	103(100.0)	

TSH in age more than 70 years= Euthyroid (0.25-5.9) mIu/L, hypothyroid (>5.9) mIu/L

TSH in age less than 70 years= Euthyroid (0.25-4.5) mIu/L, hypothyroid (>4.5) mIu/L

Table 3. ECG cardiovascular findings in relation to thyroid function test.

ECG finding	Euthyroid No. (%)	Hypothyroidism No. (%)	Total	p-value
Normal Sinus rhythm	3(5.3)	54(94.7)	57(100.0)	
Ectopic beats	1(20.0)	4(80.0)	5(100.0)	
Ischemic heart disease	2(11.1)	16(88.9)	18(100.0)	
Tachyarrhythmia	0(0.0)	7(100.0)	7(100.0)	0.501
Bradycardia	0(0.0)	6(100.0)	6(100.0)	
Heart block	1(10.0)	9(90.0)	10(100.0)	
Total	7(6.8)	96(93.2)	103(100.0)	

Table 4. Echo cardiovascular findings in relation to thyroid function test.

Echo finding	Euthyroid No. (%)	Hypothyroidism No. (%)	Total	p-value
Normal resting echo	4(7.5)	49(92.5)	53(100.0)	0.699
LVH	1(8.3)	11(91.7)	12(100.0)	
Systolic dysfunction	1(20.0)	4(80.0)	5(100.0)	
Diastolic dysfunction	1(10.0)	9(90.0)	10(100.0)	
Valvular heart disease	0(0.0)	10(100.0)	10(100.0)	
Pericardial effusion	0(0.0)	2(100.0)	2(100.0)	
Segmental wall hypokinesia	0(0.0)	11(100.0)	11(100.0)	
Total	7(6.8)	96(93.2)	103(100.0)	

Table 5. Normal and abnormal ECG in patients with and without cardiovascular risk factors.

Variables	ECG		Total	p-value
	Normal ECG	Abnormal ECG		
Patients with cardiovascular risk factor	33(44.6)	41(55.4)	74(100.0)	0.000
Patients without cardiovascular risk factor	24(82.8)	5(17.2)	29(100.0)	
Total	57(55.3)	46(44.7)	103(100.0)	

Table 6. Normal and abnormal Echo findings in patients with and without cardiovascular risk factors

Variables	Echo		Total	p-value
	Normal Echo	Abnormal Echo		
Patients with cardiovascular risk factor	27(36.5)	47(63.5)	74(100.0)	0.000
Patients without cardiovascular risk factor	26(89.7)	3(10.3)	29(100.0)	
Total	53(51.5)	50(48.5)	103(100.0)	

Table 7. The patients' mean age, thyroxin usage duration, TSH and T4.

	Age	Duration of using thyroxin	TSH	T4
Mean	50.99	14.88	9.6484	126.5565
Median	53.00	13.00	6.8600	135.2000
Std. Deviation	14.382	10.885	11.17418	25.60596
Minimum	19	0	2.25	39.33
Maximum	82	48	100.00	159.70

DISCUSSION

The present study was an investigation into examining different cardiovascular manifestations of hypothyroidism and reassessing the need for early diagnosis and intense management of the disease. For this purpose, 103 patients (93 females and 10 males) with a history of hypothyroidism of variable durations and levothyroxine treatment were recruited. The results of the present study revealed female predominance with a female-to-male ratio of 9:1. This finding is in line with other studies that have demonstrated that thyroid dysfunction is more common in women than men [15, 16].

The results of this study showed that there was no significant association between the patients' age and development of thyroid dysfunction ($p=0.08$) although most cases of hypothyroidism (n=88) were seen in the age group 20-69 years. Similarly, Musa et al. concluded that age has no significant correlation with development of thyroid dysfunction among females [17]. This finding is also in line with another study carried out by Manji et al. [18].

The results also revealed that the patients' sex and development of euthyroid or hypothyroidism were not significantly correlated ($p>0.05$). This finding is not in agreement with those of the study carried out by Andrade et al. who reported a significant correlation between female sex and thyroid disease [19]. This difference is due to the fact that Andrade et al. studied the association between female sex and development of thyroid disease. Research has indicated that thyroid dysfunction can increase the odds of CVD development [20, 21].

According to the results of the study, there was no significant relationship between development of thyroid dysfunction and cardiovascular risk factors. In agreement with this finding, Ravishankar et al. reported that although patients with hyperthyroidism have a poor glycemic control, there is no significant association between diabetes and incidence of thyroid disorders [22-28].

According to research, the relationship between tobacco smoking and development of thyroid disorders has not understood well, yet [29]. Smokers are reported to have lower levels of thyrotropin and a higher level of thyroid hormones [30]. Moreover, it has been concluded that smoking raises the risks of developing Graves hyperthyroidism [31]. These findings are not in line with those of the present study, and this discrepancy can be related to differences in study samples and other underlying factors; therefore, more investigations are needed to clarify the relationship between smoking and incidence of thyroid disorders. However, the results of the present study showed no significant correlation between these two variables. Moreover, no significant relationship was found between chronic kidney disease (CKD) and incidence of thyroid dysfunction. This finding is line with those of the study carried out by Mohamed Ali et al. [32].

According to the results of the present study, no significant correlation was found between the cardiovascular findings of ECG and Echo and those of thyroid function test ($p>0.05$). Therefore, profile changes shown by these two types of tests cannot be reliably used to diagnose thyroid disorders (euthyroid and hypothyroidism). Zhang et al. reported that different changes in ECG are correlated with levels of thyroid hormones in the general population [33]. However, Dorr et al. and van Noord et al. pointed out that little is known about how electrical activities of the heart are influenced by variations in thyroid hormone levels [34, 35]. In her study, Qari concluded that there is a relationship between hypothyroidism and echocardiographic abnormalities such as cardiomyopathy and pericardial effusion [36].

The results obtained from ECG demonstrated that abnormal ECG was more prevalent among the patients with cardiovascular risk factors. In agreement with this result, Cappola et al. pointed out that CVD risks can be diagnosed through ECG in patients with thyroid disorders [37]. Also, Soliman et al. concluded that ECG could reliably be used to diagnose cardiovascular risk factors [38]. The results of the present study also revealed that the studied patients were significantly different regarding their Echo results, such that patients with cardiovascular risk factors had more abnormal Echo results than those without such risks. Similarly, Merce et al. introduced echocardiogram as a reliable method to diagnose cardiovascular abnormalities in patients with thyroid disorders [39]. These two results can be justified by the significant association between thyroid disorders and cardiovascular risk factors which can be diagnosed through Echo and ECG [40].

Echo and ECG are highly recommended as reliable tools to measure cardiovascular morphology, function and cardiac rhythm in patients with thyroid disorders, but not as means to diagnose such disorders [41, 42].

In conclusions; Cardiovascular risk factors were found to be associated with euthyroid and hypothyroid; however, these factors were not significantly correlated with development of these thyroid disorders. Both electrocardiogram (ECG) and echocardiogram (Echo) were found to be significantly effective in detecting cardiovascular complications in patients with thyroid disorders; however, they were not as effective as the thyroid function test in diagnosing thyroid diseases. The results obtained from ECG demonstrated that abnormal ECG was more prevalent among the patients with cardiovascular risk factors. Echo results demonstrated that patients with cardiovascular risk factors had more abnormal Echo results than those without such risks.

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