STATE OF THYROID GLAND FUNCTION IN PATIENTS ADMITTED TO CORONARY CARE UNIT

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ABSTRACT

Background

A large number of patients are admitted to coronary care units daily. Thyroid gland abnormalities are one of the reasons which cause people to have cardiac events. Therefore, detecting thyroid gland abnormalities among cardiac care unit patients and early management leads to less morbidity/mortality and a better long-term prognosis for those patients.

Objectives

The study was done to detect the function of thyroid gland abnormalities and their effect on different cardiac conditions among patients admitted to CCU.

Patients Methods

This descriptive cross-sectional study includes a consecutive non-random sampling of 201 patients. All the patients enrolled in this study were admitted to the CCU unit of Sulaimanya Teaching Hospital and Shar Hospital in Sulaimanya city/Iraq between August 2021 and January 2022. Thyroid function test and lipid profile were checked for the participants. The pediatric age group, pregnant women, patients with malignancies/ severe systemic illness /on amiodarone/ congenital heart disease were excluded. Statistical Package analysed the collected data for Social Science (SPSS) (version 22.0).

Results

One hundred fifteen (57.2%) participants were male, and 86(42.8%) were female. The most common age group was between 45-64 years. HTN(%44.3), diabetes (29.9%) and hyperlipidemia (17.9%) were common comorbid conditions. The most common cause of admissions to CCU was due to ACS (63.2%) and then arrhythmia (22.9%), decompensated heart failure (12.9%) and pericardial diseases (1%). In addition, 82.59% (166) of the participants were euthyroid, and 17.41% (35) had thyroid gland function abnormalities.

Conclusion

The effect of thyroid hormone problems on cardiac conditions is one of the important causes of CCU admissions. Patients with ACS and heart failure are presented with hypothyroidism. However, arrhythmia is present more in cases of hyperthyroidism.

Keywords: *Thyroid gland, TFT abnormalities, CCU.*

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INTRODUCTION

Cardiac events are among the most common diseases that occupy many patients in emergency departments[1]. Thyroid hormone has a great impact on every component of the cardiovascular system, including cardiac contractility, cardiac output, myocardial oxygen consumption[1-3].

Thyroid hormones are composed of two types: a large proportion of prohormone thyroxine (T4; 3,5,3`,5`−tetraiodothyronine) and its active form tri-iodothyronine (T3; 3,5,3`-triiodo-L-thyronine) which is formed by removal of iodide from (T4) by deiodinases. Their metabolism is affected by TSH (thyroid stimulating hormone) from the anterior pituitary and TRH (thyrotropin-releasing hormone) from the hypothalamus[3]. Deiodination of T4 to T3 happens in the liver, kidney and thyroid by type 1 deiodinase(D1); in the heart and several other tissues by type 2 deiodinase[4,5]. Type 3 deiodinase (D3) is a physiological inactivator of thyroid hormone and has a great role in controlling thyroid hormone homeostasis[5]. More than 95% of T3 and T4 circulate in blood by binding to thyroxine-binding globin and other binding proteins [6].

The thyroid hormone acts on each part of the cardiovascular system differently in either a genomic or non-genomic way. T3 works on cardiac myocytes positively and negatively through myosin-heavy chains (α-MHC, fast myosin and β-MHC, slow myosin), respectively—also, thyroid hormone affects the heart genomically by thyroid nuclear receptors located in the intracellular compartment [7, 8]. Thyroid hormone regulates vascular tone and endothelial nitric oxide production, decreasing systemic vascular resistance. Another effect of thyroid hormone is the protection of the cardiovascular system through remodelling by cytoprotective mechanisms, increasing coronary blood flow, neo-angiogenesis, metabolic remodelling through improving mitochondrial function by increasing myocardial ATP levels and reduction of lactate levels [7], cell growth stimulation through miRNAs by stress cardiomyocytes after post MI [9]. Thyroid hormone's action on voltage-gated potassium ion channels (Kv 1.5 and Kv 4.2) and sodium/calcium ion exchanger leads to affecting electricity of the heart [7,10]. Lastly, thyroid hormone has effects on risk factors of cardiovascular diseases like lipid profile and thrombogenesis[7,11].

Hypothyroidism (subclinical/overt) and hyperthyroidism (subclinical/overt) have different consequences on the cardiovascular system. Hypothyroidism is defined as high TSH and low T3, T4 [1], but in subclinical hypothyroidism, T3 and T4 are normal despite having slightly increased TSH [12].

Hypothyroidism causes vascular changes (peripheral vasoconstriction, increased peripheral vascular resistance, increased arterial stiffness, increased diastolic arterial pressure, narrow pulse pressure), cardiac problems (reduction of myocardial contractility, decreased preload and cardiac output, decreased stroke volume, LV asynchrony), change in electricity of heart(atrioventricular block, prolonged QT interval, sinus bradycardia due to sinus node dysfunction, heart block, ventricular arrhythmia), pericarditis, pericardial effusion and rarely cardiac tamponade. Also, hypothyroidism leads to an increased risk of atherosclerosis by hypercholesterolemia and hypertension [1, 2, 7].

Hyperthyroidism is low TSH with high T3, T4 [1], and subclinical hyperthyroidism is low TSH with normal T3, T4 [12] .Effects of hyperthyroidism are on vascular level (decreased systemic vascular resistance, decreased diastolic arterial pressure but increased systolic arterial pressure, wide pulse, peripheral vasodilation), cardiac level (increase in preload, afterload, stroke volume, myocardial contractility, LV systolic function; concentric cardiac hypertrophy), pulmonary hypertension [2,8], the electricity of heart (sinus tachycardia, supraventricular arrhythmia (most commonly AF, SVT, ectopic beats) [1, 2, 8, 12] .

The thyroid hormone causes heart failure in both cases of hypothyroidism and hyperthyroidism but in different pathways. Hypothyroidism directly leads to heart failure by bradycardia-induced systolic and diastolic dysfunction. Indirectly, hyperlipidimia may lead to IHD, and it can cause heart failure in hypothyroid patients. In hyperthyroidism, persistent tachycardia leads to diastolic and systolic heart dysfunction. Increasing cardiac preload, decreasing peripheral vascular resistance and increasing total blood volume are other causes of heart failure in hyperthyroid patients[2,8,13]. Lastly, renal perfusion reduction in hyperthyroid patients leads to activation of RAAS, resulting in fluid and sodium retention with increasing blood volume[2,8].

PATIENTS AND METHODS

A descriptive cross-sectional study was done at the Coronary Care Unit of Sulaimanya Teaching Hospital and Shar Hospital in Sulaimanya city/ Iraq during the period of August 2021 and January 2022. A consecutive non-random sampling of 201 participants is included. Inclusion criteria are age older than 13 years, acute coronary syndrome (ST-elevation myocardial infarction, Non-ST-elevation myocardial infarction, unstable angina), decompensated heart failure, pericardial effusion and arrhythmia (atrial fibrillation, supraventricular, ventricular tachycardia and bradycardia). In addition, exclusion criteria are children younger than 13 years, pregnant women, those with congenital heart diseases, severe systemic illness, infection, malignancy and those on amiodarone drug therapy.

Vital signs are checked for all, and cardiologists make their cardiological diagnoses at the centres. Venous blood sampling was taken from the participants within 24 hours of admission for thyroid function tests(free T3, free T4 and TSH), lipid profile (LDL, HDL, Triglyceride and total cholesterol in mg/dL), serum urea (mg/dL), serum creatinine (mg/dL) and haemoglobin A1C(HbA1C in %). The normal range for fT3 is (3.1-7.3 pmol/L), fT4 I (12-22 pmol/L), and for TSH is (0.27-4.2 μIU/mL). The euthyroid state is considered when free T3, T4 and TSH are normal. When TSH is higher than 4.2 μIU/mL is considered hypothyroidism. If free T3 and free T4 are lower than the normal range with high TSH, it is called overt hypothyroidism, and if free T3 and free T4 are normal with high TSH, it is called subclinical hypothyroidism. Hyperthyroidism is considered when TSH is lower than 0.27 μIU/mL. When it is accompanied by normal free T3 and free T4, it is subclinical hyperthyroidism. It is called overt hyperthyroidism if free T3 and free T4 are high with low TSH.

Statistical Analysis

After data collection and prior to data entry and analysis, the questions of the study were coded. Data entry was performed via an excel spreadsheet; then, the statistical analysis was performed using the SPSS program, version 24.0 (IBM SPSS Statistical Package for the Social Sciences). Compliance of quantitative random variables with the Gaussian curve (normal distribution) was analysed using Kolmogorov-Smirnov and Shapiro–Wilk tests. The data presented in tabular forms shows the frequency and relative frequency distribution of different variables among both groups. Chi-square tests were used to compare the categorical data between different groups of patients (CCU admission causes or thyroid status) concerning different variables.

Variables showed to be normally distributed continuous quantitative variables and described by mean and SD (standard deviation). The statistical significance of the difference in mean between the two groups (Male and female) was assessed using an independent sample t-test while comparing the mean of more than two groups (Thyroid status or CCU admissions). ANOVA test has been used. Non-normally distributed quantitative variables such as T3, T4, TSH, HbA1c, Cholesterol levels etc., were described by the median in addition to the mean. The median and interquartile ranges (IQR) were also used for compared groups in such conditions. The difference in the median (IQR) of these (more than two) groups was assessed by the non-parametric test (Kruskal- Wallis test). P values of 0.05 were used as a cut-off point for the significance of statistical tests.

Ethical considerations

The Research Protocol Ethics Committee of the Kurdistan Board of Medical Specialities approved the study protocol. Verbal consent was taken from each patient, and permission was taken from the authorities of the hospitals.

RESULTS

Amoung 201 participants, 115(57.2%) of them were male and 86(42.8%) were female. Ninety-four (46.8%) of them were in between 45-64 years of age, 89 (44.3%) were older than 65 years of age, and only 18 (9%) were between the age groups of 23-44. Regarding smoking;163(81.1%) participants were non-smoker and 38(18.9%) were smoker. Most participants did not consume alcohol, 194 (96.5%), and only 7(3.5%) participants consumed alcohol on special occasions. (Table 1)

The most common chronic condition was hypertension (%44.3), followed by diabetes (29.9%) and hyperlipidemia (17.9%). CKD (7%), lung disease(4.5%) and CLD (0.5%), (Table 2).

The most common causes of CCU admissions were ACS (63.2%) and arrhythmia (22.9%). The third

reason for admission was decompensated heart failure (12.9%), and only (1%) of the admissions were due to pericardial diseases.(Figure 1) Among cases of ACS;(32.34%)of participants were STEMI,(19.4%) were NON-STEMI and (11.44%) were unstable angina. Regarding arrhythmia cases, tachyarrythmias were more common, and it was (17.4%) of cases. (5.5%) of cases has bradyarrhythmia.

Mean TSH was highest among decompensated heart failure group (2.18±2.45, p-value 0.84), followed by ACS (1.91±1.64, p-value 0.84) and arrhythmia group(1.89±1.71, P-value 0.84). The pericardial disease group had the lowest mean TSH (1.26±1.13, p-value 0.84). Free T3 was higher in the arrhythmia group (4.50±1.36, p-value 0.15) and decompensated heart failure group(4.38±1.21, p-value 0.15) and lower in the ACS group (4.08±0.99, p-value 0.15) and pericardial disease group (4.1, p-value 0.15). Free T4 was highest in decompensated heart failure group (18.61±2.96, p-value 0.03) and lowest in ACS (16.72±2.74, p-value 0.003),Table3.

One hundred and sixty-six (166), 82.59% of the participants admitted to coronary care units were euthyroid, and 17.41% (35) had thyroid gland function abnormalities. The most common thyroid gland function abnormality was subclinical hypothyroidism 10.44% (21), second most common was subclinical hyperthyroidism 4.48% (9). Third overt hyperthyroidism 1.99%(4) and overt hypothyroidism 0.5 % (1) were the least common. Only 2 participants had pericardial diseases, and both were euthyroid. The most common thyroid gland abnormality in the ACS group was subclinical hypothyroidism; no patient was found to have overt hyperthyroidism in the ACS group. Regarding decompensated heart failure group, there were no overt hypo- and hyperthyroidism, but the most common abnormality of the group was subclinical hypothyroidism. Hyperthyroidism, including overt and subclinical, was more common in the arrhythmia group. Also, 10.87% of patients had subclinical hypothyroidism, but no cases were recorded as overt hypothyroidism in the arrhythmia group (p-value 0.19), Table 4.

The most common cause of admission to CCU among hypothyroid (overt&subclinical) patients is ACS (63.64%). Only 13.64 % of hypothyroid patients were admitted for decompensated heart failure. However, arrhythmia (53.84%) is the most common cause of admissions in hyperthyroid (overt & subclinical) patients, followed by ACS (38.46%) and decompensated heart failure (7.7%), Figure 2.

More than half of the patients had dyslipidemia (54.23%). Both subclinical hyper- and hypothyroidism had higher dyslipidemic patients than overt hypo and hyperthyroid patients. However, hypothyroid patients (overt and subclinical) presented with dyslipidemia more than hyperthyroidism (overt & subclinical), (p-value 0.61), Table 5.

Table 1. Socio-demographic characteristics of study participants.

		Frequency	%
Age(years)	Mean ± SD	61.8 ± 12.7	
	23 - 44	18	9.0
	45 - 64	94	46.8
	≥ 65 Years	89	44.3
Gender	Male	115	57.2
	Female	86	42.8
Smoking	Yes	38	18.9
	No	163	81.1
Alcohol	Yes	7	3.5
	No	194	96.5
Total		**201**	**100.0**

Table 2. Chronic diseases among study participants.

		Frequency	%
Hypertension	Yes	89	44.3
	No	112	55.7
Diabetes mellitus	Yes	60	29.9
	No	141	70.1
Hyperlipidemia	Yes	36	17.9
	No	165	82.1
CKD	Yes	14	7.0
	No	187	93.0
CBD	Yes	1	0.5
	No	200	99.5
Lung disease	Yes	9	4.5
	No	192	95.5%

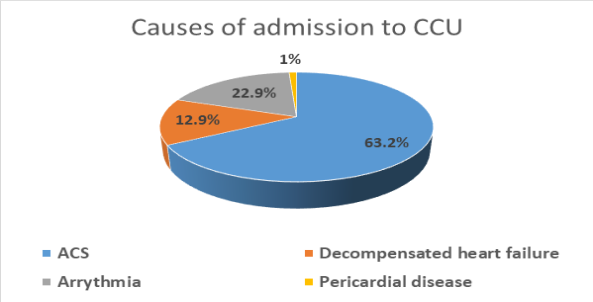

Figure 1. Distribution of study participants with respect to their causes of admission to the Coronary care unit.

Table 3. Comparing the mean of lipid profile and thyroid hormone levels among different causes of CCU admissions.

	Mean ± Standard deviation					
	ACS (n= 127)	**Decompensated Heart failure (n = 26)**	**Arrhythmia (n= 46)**	**Pericardial disease (n = 2)**	**Total (n= 201)**	**P value**
fT3	4.08 ± 0.99	4.38 ± 1.21	4.50 ± 1.36	4.1 ±	4.21 ± 1.12	**0.15**
fT4	16.72 ± 2.74	18.61 ± 2.96	18.09 ± 5.36	17.3 ± 0.14	17.28 ± 2.58	**0.03**
TSH	1.91 ± 1.64	2.18 ± 2.45	1.89 ± 1.71	1.26 ± 1.13	1.94 ± 2.77	**0.84**
LDL	116.94 ± 41.18	102.48 ± 27.67	97.06 ± 28.26	115.55 ± 7.85	110.57 ± 27.72	**0.01**
Cholesterol	169.77 ± 44.86	147.02 ± 33.25	140.68 ± 35.80	166.7 ± 49.07	160.24 ± 33.32	**< 0.001**
HDL	41.98 ± 9.20	42.17 ± 10.03	41.30 ± 9.78	51.05 ± 4.31	41.94 ± 10.40	**0.55**
Triglyceride	152.92 ± 133.80	148.41 ± 69.93	135.24 ± 40.87	86.65 ± 58.95	147.69 ± 69.47	**0.70**
HbA1c	6.93 ± 1.89	7.05 ± 1.64	6.60 ± 1.36	5.75 ± 0.21	6.86 ± 1.74	**0.52**
BUN	38.57 ± 23.05	54.86 ± 24.01	43.11 ± 26.35	22.5 ± 6.36	41.55 ± 24.41	**0.01**
S. Creatinine	1.18 ± 0.66	1.41 ± 0.67	1.27 ± 0.74	1.08 ± 0.46	1.23 ± 0.68	**0.41**

*** Performed by ANOVA test.**

Table 4. Thyroid function status of the participants according to their cause of admission.

	ACS	Decompensated Heart failure	Arrhythmia	Pericardial disease	Total (%)	P value
Thyroid Status						
Euthyroid	108 (85.0%)	22 (84.6%)	34 (73.91%)	2 (100%)	166 (82.59)	
Overt Hypothyroid	1 (0.8%)	0 (0%)	0 (0%)	0 (0%)	1 (0.5%)	**0.19**
Overt Hyperthyroid	0(0%)	0 (0%)	4 (8.7%)	0 (0%)	4 (1.99%)	
Subclinical hyperthyroid	5 (3.9%)	1 (3.8%)	3 (6.52%)	0 (0%)	9 (4.48%)	
Subclinical Hypothyroid	13 (10.2%)	3 (11.5%)	5 (10.87%)	0 (0%)	21 (10.44%)	

Table 5. Frequency of dyslipidemia in different thyroid gland function groups.

	Thyroid Status						
	Euthyroid (%)	Overt Hypothyroid (%)	Overt Hyperthyroid (%)	Subclinical hyperthyroid (%)	Subclinical Hypothyroid (%)	Total (%)	P value (%)
Lipid profile							
Normal	74(44.58)	1(100)	3(75)	4(44)	10(47.62)	92(45.77)	**0.61**
Dyslipidemia	92(55.42)	0(0)	1(25)	5(56)	11(52.38)	109(54.23)	
Total	**166(100)**	**1(100)**	**4(100)**	**9(100%)**	**21(100)**	**201(100)**	

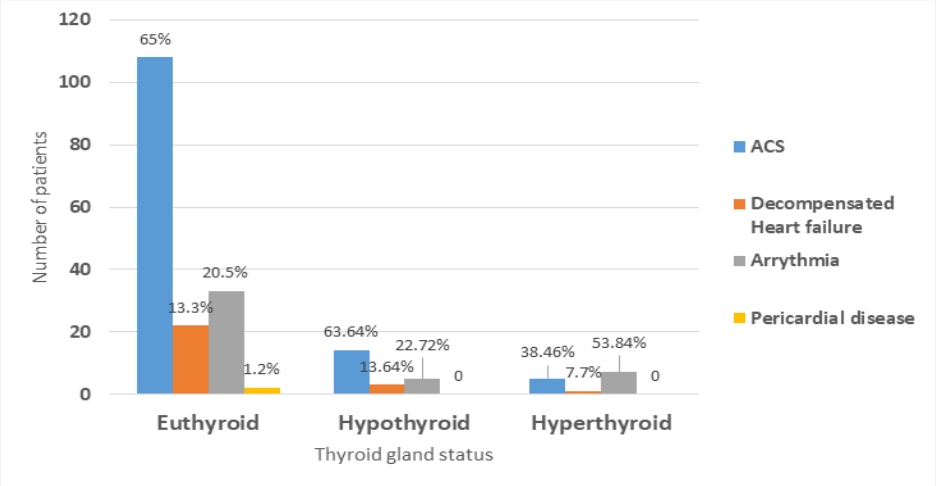

Figure 2. Causes of admission to CCU in different thyroid gland function groups.

DISCUSSION

In our study, we tried to discover thyroid gland function abnormalities in patients admitted to CCU, searching for the prevalence of different thyroid gland functions that could lead to different cardiac conditions. In the study, male participants were more than females gender as recent studies show a higher number of male patients[13,14], and another study shows higher female participants[16]. Furthermore, the frequency of smokers within the study was lower than non-smokers. However, on the contrary, in a study whose smoker participants are higher than non-smokers [3], another study found fewer smoker rates like ours [14] . Regarding the presence of chronic diseases, hypertension, diabetes mellitus, and dyslipidemia were the most common comorbid conditions as in other studies too [15, 17].

The most common causes of admission in our study were acute coronary syndrome and arrhythmia, but in other studies, the most common causes were acute coronary syndrome and decompensated heart failure[14].

In other published studies, the mean free T4 was lower, meaning TSH was higher than ours among ACS patients. At the same time, the mean LDL was lower among patients with coronary artery diseases than the mean LDL of our study [3,14]. Regarding arrhythmia patients, the study was found to lower mean free T4 and lower mean TSH than our findings [17].

In our study, nearly 4 out of 5 patients were euthyroid as in a study which was done recently [3, 18], but in other studies, there were fewer cases of euthyroid when compared to ours [14, 19 ,20]. The most common thyroid gland function abnormality in the ACS of this study is subclinical hypothyroidism and it is followed by subclinical hyperthyroidism and overt hypothyroidism. We did not have overt hyperthyroidism in ACS patients. There are other studies in which the most common causes resemble our study for the ACS group[19, 20] .

Regarding the arrhythmia group of participants, the most common thyroid gland function abnormality was hyperthyroidism (overt & subclinical). However, when we took them individually, we found that the incidence of subclinical hypothyroidism in the arrhythmia group was near the incidence of patients with overt hyperthyroidism and subclinical hyperthyroidism separately. However, a recent study shows no significant correlation between arrhythmia and thyroid gland function abnormality because all of their patients with negative past thyroid history were euthyroid[21]. In contrast, another study shows that hyperthyroidism (overt & subclinical) shows great risk factors for arrhythmia. However, in the same study, there was a lower incidence of arrhythmia in subclinical hypothyroid patients than in subclinical hyperthyroid patients [22].

Regarding the group of decompensated heart failure, thyroid function abnormality did not affect the heart in our patients except for subclinical hypothyroidism. Because the majority of them were euthyroid, and the most common thyroid function abnormality was subclinical hypothyroidism. We did not have overt hypo and hyperthyroidism in this group. Also, in a study, the most common thyroid gland abnormality was subclinical hypothyroidism, but they had other abnormalities, too, including overt hyper- and hypothyroidism [17]. In another study, only subclinical hypothyroid patients were included to study acute decompensated heart failure due to minority cases in other types of thyroid gland function abnormality[23]. We only had 2 cases with the pericardial disease, and they were euthyroid, but pericardial effusion can be found in that study [24].

In our study and other studies, there was no significant difference between the percentages of dyslipidemic patients with euthyroid and those with abnormal thyroid gland function [14]. However, dyslipidemia was more common within subclinical hypo- and hyperthyroidism among thyroid gland function abnormalities in our study.

In conclusion, the thyroid hormone is one of the important factors in cardiovascular health. Patients with ACS and heart failure are presented with hypothyroidism. On the other hand, arrhythmia is present more among cases of hyperthyroidism. Therefore, routinely checking thyroid gland function in the risky age group for cardiovascular disease will prevent cardiac events. Also, detecting thyroid gland dysfunction during the admission of patients to CCU is important to detect abnormality and manage it will play an important role in decreasing mortality and morbidity among patients.

Limitations

Shortage of laboratory resources in teaching hospitals was a factor in collecting a smaller sample within a longer time.

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