Egypt. J. Chem. **Vol. 65,** No. 3 pp. 185 - 189 (2022)

Egyptian Journal of Chemistry

http://ejchem.journals.ekb.eg/

BIOCHEMICAL EFFECT OF THYROID HORMONES ON HEART FAILURE

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Abstract

Thyroid hormones and heart-failure disease (HF) are inextricably linked, as the fact has been established the thyroid causes heart muscle weakness. The goal of the study estimates the link of thyroid hormones and the risk of heart failure disease by measuring T4, T3, fT4, fT3, cholesterol, TG, HDL, LDL, VLDL and BMI in serum of 65 patients of heart failure disease and 40 control group. The results showed a decrease significantly in the concentration of T4, T3, fT4, fT3 and HDL compared to the healthy group at P≤0.001 (53.88±29.5 nmol/ml), P=0.02 (1.77±0.8 nmol/ml), P≤0.001 (8.94±4.1 pmol/ml), P≤0.001(2.85±1.5 pmol/ml) and P≤0.001(31.13±8.2 mg/dL), respectively. Further, there was a significant increase in total cholesterol concentration, TG, LDL, VLDL and BMI compared to the healthy group at P≤0.001 (348.16±87.6 mg/dL), P≤0.001 (172.41±52.9 mg/dL) P≤0.001 (303.22±117.3 mg/dL), P≤0.001 (34.48±10.6 mg/dL) and P≤0.001 (28.68±4.5 Kg/m^2), respectively. The study showed that there is a strong correlation between thyroid hormones and total cholesterol, LDL with high BMI. Therefore, we conclude that thyroid hormones spatially fT3 is a new indicates the increase of heart failure disease.

Keywords: Heart Failure, Thyroid Hormones, Free Thyroid Hormones, TSH, Lipids Profile, Free Thyroid Hormones

1. Introduction

One of the most important organs in the human body is the thyroid gland, the back of the neck under the so-called Adam's apple along the trachea and it takes on a butterfly-like shape and thyroid hormones affect metabolism and growth, as well as body temperature and T4 & T3 most important hormones for brain development during childhood [1, 2]. Hypothyroidism leads to changes in blood pressure, lipid metabolism, cardiac contractility and SVR, all of which are caused by decreased thyroid hormone action on various organs including the heart, liver, and peripheral vasculature and are possibly reversible with thyroid hormone replacement [3, 4]. Hypoxia affects the intracellular cardiomyocyte environment in heart-failure or acute myocardial infarction, which leads to inflammation [5, 6].

Thyroid hormones influence heartbeat strength and pace, blood pressure and blood lipids. As a result, any thyroid gland disorder can lead to complications such as coronary heart disease or worsen existing heart disease [7, 8].

Thyroid disease affects about 6% of persons in the United States, with the majority (80%) suffering from hypothyroidism. When this gland's levels decline, the body's functions slow down, causing weariness, weight gain, cold intolerance, constipation and dry skin, among other symptoms. These symptoms, however, are fairly frequent in people as they get older, even if their thyroid hormone levels are normal [8, 9]. Thus, it's feasible that lowering hormones levels may be used as a treatment alternative for better health. Furthermore, the sickness might cause reversible abnormalities in thyroid action, a condition known as non-thyroidal-sickness (NTI). Thyroid dysfunction in NTI is not linked to main hypothalamic, pituitary, or thyroid disorders [3, 10].

The goal of this research is to see how thyroid hormones affect heart failure.

2. Subjects and Methods:

2.1. Sample Collection:

This research was performed following the criteria stipulated in the Helsinki Declaration and approved by our institution (24880/R.A.D, 20/10/2020). The Hospitals in Ibn-Sena/ Iraq performed a cross-sectional study from 26 October 2020 to 1 June 2021.

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EJCHEM use only: Receive Date: 15 August 2021, Revise Date: 26 August 2021, Accept Date: 14 September 2021
DOI: 10.21608/ejchem.2021.90805.4321

2.1.1. Group of Patients (Inclusion Criteria)

In this study, sixty-five patients of both sexes were included. The Hospital of Ibn-Sena conducted a cross-sectional and hospital-based investigation. Their ages ranged from 25 to 78 years old and their BMI was between 20 and 38.98 kg/m^2.

2.1.2. Control Group (Reference Group)

Forty men and women as control group ranging in age from 26 to 78 years old participated in this study. The BMI ranged from 18.07 to 29.73 kg/m^2.

2.1.3. Blood Collection

Thyroid hormones and lipid profiles were examined in both groups. Within an hour of blood collection, Gels (gel & clot activator) were drawn into the test tube (5ml), centrifuged for serum separation and the serum was stored in a deep freezer at -20°C for subsequent analysis. Samples were examined in batches of 100 to allow for differences in analytical results. Before the investigation, the samples were allowed to reach room temperature.

2.1.3.1. Materials and Procedures

This study was performed using a special kit (Bio Merieux Kits) for each variable from the Minividas–France following hormonal: T4 (total Thyroxin), T3 (total Triiodothyronine), fT4 (free Thyroxin), fT3 (free Triiodothyronine) and lipid profile were also measured using (Biolabo kits/ France) by spectrophotometer, which includes TG (Triacylglycerol), total cholesterol, and HDL (High-Density-Lipoprotein)

LDL (Low-Density-Lipoprotein) and (VLDL) Very-Low-Density-Lipoprotein was determined indirectly using the Friedewald equations:

$$LDL_{(Con.)}(mg/dl) = Cholesterol_{(Con.)} - HDL_{(Con.)} - G/5 \quad \text{(Eq.1)}$$

$$VLDL_{(Con.)}(mg/dl) = Triglyceride/5 \quad \text{(Eq. 2)}$$

2.1.3.2. Statistical Analysis

The data were analyzed using SPSS software. The T-test and Duncan-tests, as well as the Pearson correlation coefficients test, were employed to evaluate parameters between the total control number and patients based on occupancy at $p \leq 0.05$, $p \leq 0.01$ and $p \leq 0.001$, respectively, and the test of Pearson correlation coefficients [11].

2.1.4 Ethical Approval

The research has been carried out and agreed upon by the author's Institutional Review Board following all applicable national legislation, institutional policy and the values of the Helsinki Declaration.

3. Results and Discussion:

3.1. A Comparison between the Level of Hormonal and Biochemical Parameters of Heart Failure Disease and the Control Group:

The results in Table (1) showed an increase significantly in the concentration of total cholesterol, triglyceride, LDL, VLDL and BMI at ($P \leq 0.001$) for each one, A comparison between the level of hormonal and biochemical parameters of heart failure disease and the control group. While there was a significant lower in the concentration of T4, T3, fT4, fT3 and HDL concentration at ($P \leq 0.001$), ($P=0.02$), ($P \leq 0.001$), ($P \leq 0.001$) and ($P=0.001$), respectively.

As a result, adipose cells have easier access to and utilization of fatty acid and lipolysis composition released into the circulatory system. Excess fatty acids in the liver cause VLDL secretion to increase, resulting in dyslipidemia. A high blood concentration of TG causes a drop in HDL and an increase in LDL levels by reversing the cholesterol pathway. Hyperandrogenism may potentially influence lipid metabolism by increasing hepatic lipase activity, which is involved in the degradation of HDL molecules [12]. The pituitary gland regulates the thyroid by releasing TSH to boost thyroid hormone production when thyroid hormone levels are low. Thyroid hormone acts as a feedback mechanism, reducing TSH production thus preserving a unique pituitary-thyroid set point. Lower FT4 and TT3 levels have also been associated. In patients with heart failure, low T3 levels have been associated with myocardial fibrosis, as well as anomalies in myocardial perfusion and metabolism [13].

Table (1): A comparison between the level of hormonal and biochemical parameters of heart failure disease and the control group

Hormonal and biochemical parameters	Heart failure disease (Mean±SD)	Control group (Mean±SD)	P-value
T4 (nmol/ml)	53.88 ±29.5	107.41 ±25.7	≤0.001***
T3 (nmol/ml)	1.77 ±0.8	2.27 ±0.73	0.02*
fT4 (pmol/ml)	8.94 ±4.1	16.39 ±2.69	≤0.001***
fT3 (pmol/ml)	2.85 ±1.5	4.85 ±1	≤0.001***
Total Cholesterol (mg/dL)	348.16 ±87.6	168.84 ±22.56	≤0.001***
Triglyceride (TG) (mg/dL)	172.41 ±52.9	125.8 ±29.54	≤0.001***
HDL (mg/dL)	31.13 ±8.2	46.53 ±8.11	≤0.001***
LDL (mg/dL)	303.22 ±117.3	97.09 ±23.15	≤0.001***
VLDL (mg/dL)	34.48 ±10.6	25.11 ±5.91	≤0.001***
BMI (Kg/m^2)	28.68 ±4.5	21.97 ±2.5	≤0.001***

*Significant differences at P ≤ 0.05, *** Significant differences at P ≤ 0.001

3.2. A Comparison of the Level of Hormonal and Biochemical Parameters in Heart Failure Disease with Different BMI:

When hormone levels and biochemistry of heart failure disease were compared to BMI, the results in Table (2) demonstrated a high increase in the concentration of total cholesterol (P=0.047) at BMI (25–29.9 kg/m^2).

There has been no substantial difference in the levels of T4, T3, fT4, fT3, triglycerides, HDL, LDL, and VLDL

Table 2 Overweight and obesity are common occurrences that have led to serious in advanced nations. Associated with weight gain are caused by abnormal blood lipid styles and in a large percentage of overweight and obese individuals, other cardiovascular disease risk factors such as hypertension, smoking, diabetes, or a family medical history of heart disease coexist [14, 15]. blood lipids profile in obese or overweight patients [16]. A BMI of 25–29.9 kg/m^2 indicates that a person is slightly overweight. A doctor may advise them to lose some weight for health reasons [17, 18, 19].

There is evidence to support the scientific plausibility of a strong incidence of obesity and the CVD risk, particularly heart failure (HF), which is consistent with other studies [20, 21, 22]. According to the process, adipocytes can release a large number of cytokine and active mediators that are important for the diagnosis of many obesity-related disorders [23, 24, 25].

Table (2): A comparison of the level of hormonal and biochemical parameters in heart failure disease with different BMI

BMI(Kg/m^2) Hormonal & biochemical parameters	(18-24.9) N=13 (Mean ± SD)	(25–29.9) No= 29 (Mean ± SD)	(30–34.9) No= 17 (Mean ± SD)	(35–39.9) No= 6 (Mean ± SD)	P-value
T4 (nmol/ml)	68.5±24.7	51.6±29.7	44.3±27.1	60.4±37.8	N
T3 (nmol/ml)	2.0±0.8	1.8±0.9	1.7±0.7	1.5±0.6	N
fT4 (pmol/ml)	9.0±3.8	8.9±4.0	9.4±4.9	8.0±3.3	N
fT3 (pmol/ml)	2.6±1.3	3.0±1.4	2.8±2.0	2.7±1.5	N
Total Cholesterol (mg/dL)	320.3±89.9a	381.9±89.8b	321.4±74.6a	321.1±62.8a	0.047*
Triglyceride (TG) (mg/dL)	165.1±53.8	167.4±48.3	176.6±61.3	200.6±50.3	N
HDL (mg/dL)	27.8±8.9	33.3±8.0	29.7±8.5	32.0±4.9	N
LDL (mg/dL)	281.3±134.1	337.4±106.5	272.2±111.6	273.6±131.5	N
VLDL (mg/dL)	33.0±10.8	33.5±9.7	35.3±12.3	40.1±10.1	N

*Significant differences at P ≤ 0.05, N = No significant differences, a, b denote Duncan-test

3.3. Total Thyroid Hormones Correlation for Heart Failure Patients with Lipid Profile:

Table 3 demonstrating the effect of thyroid hormones on lipids in patients with heart failure, a symptom of elevated heart failure risk factors. Whereas there was a high association between T4 and VLDL, there was also a high association between T3 and total cholesterol and LDL. This explains the association with metabolic disorders and their potential as a sign of increased susceptibility to heart failure through lack of oxygen and influence on metabolic processes [26, 27].

Table (3): The correlation between lipid profile and free thyroid hormones effect on heart failure disease.

Biochemical parameters	**Effect of fT3 on** heart **failure disease**		**Effect of fT4 on** heart **failure disease**	
	R-value	**P-value**	**R-value**	**P-value**
Total Cholesterol (mg/dL)	0.309	0.012*	0.126	N
Triglyceride (TG) (mg/dL)	-0.205	N	-0.299	0.015*
HDL (mg/dL)	0.193	N	-0.100	N
LDL (mg/dL)	0.312	0.011*	0.224	N
VLDL (mg/dL)	-0.205	N	-0.299	0.015*

*Significant differences at P ≤ 0.05, N = No significant differences

3.4. Free Thyroid Hormones Correlation for Heart Failure Patients with Lipid Profile:

Table 4, confirming that free triiodothyronine hormone (fT3) is more effective on fat for patients with heart failure, a sign of increased risk factors for heart failure. It is closely related to total cholesterol and LDL. This demonstrates the association with metabolic disorders like dyslipidemia, obesity. Thyroid hormones affect cardiac health through a variety of mechanisms, including direct genomic effects via nuclear receptor binding, which controls the expression of genes involved in the cardiac myocytes; extranuclear, non-genomic effects on receptors in the myocardial cell membrane; and the impacts both of hormone levels on peripheral blood [28, 29, 30].

Table (4): The correlation between lipid profile and total thyroid hormones effect on heart failure disease.

Biochemical parameters	**Effect of T3 on heart failure disease**		**Effect of T4 on heart failure disease**	
	R-value	**P-value**	**R-value**	**P-value**
Total Cholesterol (mg/dL)	0.443	≤0.001***	-0.018	N
Triglyceride (TG) (mg/dL)	-0.237	N	0.074	N
HDL (mg/dL)	0.042	N	0.007	N
LDL (mg/dL)	0.361	0.003**	-0.018	N
VLDL (mg/dL)	-0.237	N	-0.018	N

**Significant differences at P≤0.01, ***Significant differences at P≤0.001, N = No significant differences

4. Conclusions

This study revealed that there is a significant decrease in the level of the thyroid hormones with heart failure compared to the healthy group. Thyroid and heart failure disease have a close relationship because thyroid dysfunction causes cardiac muscle weakness, which has been shown.

CONFLICT OF INTEREST:

The authors have no conflicts of interest regarding this investigation**.**

ACKNOWLEDGMENTS:

The researchers are grateful the Mosul University, the management.

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