IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS)
e-ISSN:2278-3008, p-ISSN:2319-7676. Volume 12, Issue 5 Ver. VI (Sep. – Oct. 2017), PP 46-52
www.iosrjournals.org

Determination of the level of some metabolic hormones in congestive heart failure patients in Baghdad city

Bushra H. Rasheed, Dr. Suha A. Al-Jowari
Department of Biology, College of Science, University of Baghdad, Baghdad, Iraq
Corresponding Author: Bushra H. Rasheed

Abstract: *The present study was designed to study the changes in metabolic hormones in congestive heart failure in Baghdad city. The target population of this study was 65 male individual from Teaching Baghdad Hospital and 25 healthy male as a control with age ranged between 27 – 73 years. The diagnosis was made by the consultant medical staff, which based on a history, symptoms, clinical examination and other investigation. The patients groups were divided according to their age into three groups (less than 40, 40-50 and more than 50 years). Blood samples were collected from each patient and control and used for analysis of renal function parameters, potassium, calcium, liver function as well as metabolic hormones: thyroid (T3 and T4), TSH, parathyroid and cortisol. These results demonstrate non-significant difference in the TSH and T4 of congestive heart failure (CHF) patients compared with the control group. A significant (P< 0.05) decrease in the T3 of CHF patients compared with control group. There is also significant (P< 0.05) increase in level parathyroid and cortisol hormones of CHF patients compared with the control group.*

Keywords: *Thyroid stimulating hormone, Triiodothyronine, Thyroxine, Parathyroid hormone, Cortisol, Congestive heart failure.*

Date of Submission: 04-10-2017 Date of acceptance: 18-10-2017

تحديد مستوى بعض الهرمونات الأيضية في مرضى قصور القلب الاحتقاني في مدينة بغداد

بشرى حميد رشيد , سهى عبد الخالق الجواري
قسم علوم الحياة، كلية العلوم، جامعة بغداد، بغداد، العراق

الخلاصة:

شملت هذه الدراسة تسعين ذكر تتراوح اعمارهم بين 27-73 سنة. قسم المشاركين الى مجموعتين, تضمنت المجموعة الاولى 65 ذكر مصاب بالفشل القلبي الاحتقاني اما المجموعة الثانية فتضمنت 25 ذكر غير مصاب الفشل القلبي الاحتقاني من مستشفى بغداد التعليمي. تم إجراء التشخيص من قبل الموظفين الطبيين الاستشاريين، والتي تقوم على تاريخ والأعراض والفحص السريري وغيرها من التحقيقات.

تم تقسيم مجموعات المرضى وفقا لعمرهم إلى ثلاث مجموعات (أقل من 40، 40-50 وأكثر من 50 عاما). جمعت عينات الدم من كل مريض والاصحاء واستخدمت لتحليل مقاييس وظائف الكلى والبوتاسيوم والكالسيوم ووظائف الكبد وكذلك الهرمونات الأيضية: الغدة الدرقية (T3 و T4)، ، الغدة الجار الدرقية والكورتيزول.

أظهرت هذه النتائج فرق غير هام في TSH و T4 من المرضى الفشل القلبي الاحتقاني مقارنة مع مجموعة السيطرة. انخفاضا معنويا (P<0.05) في T3 للمرضى الفشل القلبي الاحتقاني مقارنة مع مجموعة السيطرة. هناك أيضا زيادة معنوية(P<0.05) في مستوى هرمون الغدة جار الدرقية لمرضى الفشل القلبي الاحتقاني مقارنة مع مجموعة السيطرة. في حين أن هناك زيادة معنوية (P<0.05) في هرمون الكورتيزول لمرضى الفشل القلبي الاحتقاني مقارنة مع مجموعة السيطرة.

I. Introduction

Heart failure can be described as an abnormality of cardiac structure or function leading to failure of the heart to deliver oxygen at a rate commensurate with the needs of the metabolizing tissues, despite normal filling pressures (McMurray *et al.*, 2012). Congestive heart failure (CHF) is a complex clinical syndrome that can result from any functional or structural cardiac disorder that impairs the ventricle's ability to fill with or eject blood (Figueroa and Peters, 2006).

Thyroid hormones (THs) play critical roles in differentiation, growth, and metabolism. Indeed, TH is required for the normal function of nearly all tissues, with real effects on oxygen consumption and metabolic rate (Yen, 2001). Thyroid hormone is produced by the thyroid gland, which consists of follicles in which thyroid hormone is formed through iodination of tyrosine residues in the glycoprotein thyroglobulin (Zimmermann, 2009; Rubio and Medeiros-Neto, 2009).

The parathyroid glands play a pivotal role in regulating extracellular calcium homeostasis, which is important to many physiological processes such as muscle contraction, blood coagulation, and synaptic activity (Chen *et al.*, 2013). The parathyroid glands respond to low serum calcium levels by releasing PTH, which is an 84-amino acid peptide. The parathyroid hormone increases serum calcium levels through direct action on bone and the kidneys. It stimulates osteoclasts to resorb bone and mobilize calcium into the blood (Michels and Kelly, 2013).

Cortisol is a hormone that affects a variety of biological processes and health-related outcomes. Moreover, although research has found much variability in the age-related trajectories of cortisol secretion there is accumulating evidence that advancing age can be associated with a higher level of diurnal cortisol secretion and an increased cortisol response to challenge (Wrosch *et al.*, 2009).

The present study aimed to investigate the changes of some metabolic hormones in congestive heart failure as compared with control.

II. Materials and Methods

Subjects

The target population of this study was 65 male individual from Teaching Baghdad Hospital, Baghdad, Iraq during the period between December 2016 & March 2017 with age ranged between 27 to 73 years. The patients were diagnosed with congestive heart failure disease by the consultant medical staff, according to clinical examination and symptoms. Patients were divided into three age groups which included less than 40, 40-50 and more than 50 years. A control group was composed of 25 healthy male individual with the same age range.

Collection of Blood Samples

Blood samples were obtained by venipuncture, using 10ml disposable syringe from patients and control group. The blood dispensed in a plain tube, and left for 15 minutes at room temperature to clot. Then, it was centrifuged at 3000 rpm for 10 minutes to collect serum and kept in the freezer (-20ºC) until it was used in the biochemical analysis.

Hormonal Assay

Determination of hormones was carried out according to procedures recommended by: ichroma™ T3 kit, ichroma™ T4 kit, ichroma™ TSH kit and ichroma™ Cortisol kit from Boditech Inc. Korea by using Enzyme -Linked Immunosorbent Assay (ELISA). And Determination of PTH hormones was carried out according to procedures recommended by MAGLUMI Intact PTH (CLIA) from Shenzhen New Industries Biomedical Engineering Co., Ltd. China by Fully-auto chemiluminescence immunoassay (CLIA) analyzer MAGLUMI.

Statistical Analysis:

The result was analyzed statistically using System (SAS) program, (2012). Then, the significance among means was tested depending on least significant difference (LSD) test (SAS, 2012).

III. Results

The results of the present study show non-significant difference in the thyroid-stimulating hormone (TSH) and thyroxine (T4) of CHF patients compared with the control group. Levels of TSH are (1.897 ± 0.14 and 1.981 ± 0.06 micIU/L) of control and patients groups, respectively. While the levels of T4 is (114.76 ± 4.47 and 125.52 ± 3.03 nmol/L) of control group and patients, respectively in Table 1 and Figure 1and 2. There is also illustrates a significant decrease ($P< 0.05$) in the triiodothyronine (T3) of CHF patients compared with control group. The levels of T3 hormone are (2.002 ± 0.10 and 1.083± 0.05 nmol/L) of control group and patients, respectively Table 1 and Figure 3. There is also significant ($P< 0.05$) increase in level Parathyroid hormone of CHF patients compared with the control group. The levels of Parathyroid hormone are (31.68 ± 2.16 and 59.92 ± 2.05) IU/L of control group and patients groups respectively. While there is significant ($P< 0.05$) increase in the cortisol hormone of CHF patients compared with control group. The levels of the cortisol hormone are (180.44 ± 11.74 and 266.57 ± 9.03 05) nmol/L of control group and patients, respectively.

Table 1 Effect of HF patients on levels of metabolic hormones.

groups	Mean ± SE				
	TSH(micIU/L)	T3(nmol/L)	T4(nmol/L)	PTH(IU/L)	Cortisol(nmol/L)
Patients (No.= 65)	1.981 ± 0.06	1.083 ± 0.05	125.52±3.03	59.92± 2.05	266.57 ± 9.03
Control (No. = 25)	1.897 ± 0.14	2.002 ± 0.10	114.76± 4.47	31.68± 2.16	180.44 ± 11.74
T-test	0.461 NS	0.539 *	12.77 NS	7.021 *	31.884 *
P-value	0.294	0.0362	0.071	0.0269	0.0355
* (P<0.05), NS: Non-significant.					

Concerning the results in table 2 showed non-significant difference in the level of TSH, T3, and T4 between CHF patients group compared with control group. The concentrations of TSH are (1.987 ± 0.11, 1.963 ± 0.11, 1.996 ± 0.13) micIU/L in More than 50, Less than 40 and 40-50 age groups of CHF patients, respectively. And the levels of T3 are (2.557 ± 0.21, 2.11 ± 0.16, 2.13 ± 0.20) nmol/L in More than 50, Less than 40 and 40-50 age groups of CHF patients, respectively. while the level of T4 are (131.53 ± 8.19, 128.38 ± 5.28, 124.58 ± 6.85) nmol/L in More than 50, Less than 40 and 40-50 age groups of CHF patients, respectively.

While there is a significant increase ($p < 0.05$) in the level of parathyroid hormone between (more than 50) age groups compared with (less than 40) and (40-50) age groups of CHF patients, the level of PTH (30.68 ± 1.96, 28.69 ± 2.52, 23.01 ± 2.24) IU/L in More than 50, Less than 40 and 40-50 age groups of CHF patients, respectively. And there is non-significant difference in the cortisol hormone in CHF patients, the concentration of cortisol (155.09 ± 11.72, 150.76 ± 13.28, 155.08 ± 14.51) nmol/L in More than 50, Less than 40 and 40-50 age groups of CHF patients, respectively in table 2.

2 Effect of age group on metabolic hormone of HF patients

Age groups (year)	SE ±Mean				
	TSH(micIU/L)	T3(nmol/L)	T4 (nmol/L)	PTH(IU/L)	Cortisol(nmol/L)
Less than 40	1.996± 0.13	2.13 ± 0.20	124.58±6.85	23.01± 2.24	155.08±14.51
40-50	1.963 ± 0.11	2.11 ± 0.16	128.38±5.28	28.69± 2.52	150.76±13.28
More than 50	1.987 ± 0.11	2.557± 0.21	131.53±8.19	30.68± 1.96	155.09±11.72
LSD	0.366 NS	0.648 NS	24.266 NS	6.077 *	40.743 NS
P-value	0.983	0.213	0.850	0.047	0.965
.* (P<0.05), NS: Non-significant					

Figure 1 Compare between patients and control in TSH

Figure 2 Compare between patients and control in T4

Figure 3 Compare between patients and control in T3

Figure 3.12 Compare between patients and control in PTH

Figure 3.13 Compare between patients and control in Cortisol

IV. Discussion

In this study we have shown that thyroid hormone metabolic is frequently altered in patients with heart failure. These results are in accordance with other studies (Hamilton et al., 1990; Danzi and Klein, 2004, Rodondi et al., 2005; Berry and Clark, 2000; Kozdag et al., 2005; Pingitore and Iervasi, 2005). Which indicate to changes of metabolic hormone in congestive heart failure, Progression of chronic heart failure is mediated largely via persistent activation of various neuroendocrine systems (Güder et al., 2007).

The most important finding of our study is that abnormal thyroid function, Patients with cardiovascular disease, like patients with other non-thyroidal illnesses, have changes in thyroid hormone metabolism that may effect on cardiac function (Klein and Ojamaa, 2001). The results of several studies are suggestive of relationship between the endocrine hormone system and heart function (Galli et al., 2010; Biondi, 2012).

Over the last decades, several studies have attempted to demonstrate the mechanisms underlying the changes on circulating thyroid hormones in non–thyroidal illness syndrome. Increased inflammatory cytokines, which occurs in response to virtually any illness, has long been speculated to play important role in derangements of deiodinase expression (Wajner and Maia, 2012).

More than 80% of the biologically active hormone triiodothyronine originates from peripheral conversion of prohormone thyroxin secreted by the thyroid gland. Clinical and experimental evidence have shown that T3 plays an important role in modulating heart rate and cardiac contractility as well as arterial peripheral resistance (Klein and Ojamaa, 2001).

In HF, the main and earlier change of the thyroid function is referred to as “low T3” syndrome characterized by the decreased in serum total T3 and free T3 with normal levels of thyroxine (T4) and thyrotropin (TSH). This syndrome may influence till one-third of advanced HF patients (Iervasi and Nicolini, 2013).

Review of multiple cross-sectional studies demonstrates that 30 % of patients with congestive heart failure have low T3 levels (Schmidt-Ott and Ascheim, 2006; Klein and Danzi, 2007). The decrease in serum T3 is proportional to the severity degree of the heart disease as assessed by the New York Heart Association functional classification (Schmidt-Ott and Ascheim, 2006). The low T3 syndrome is defined as a low in level of serum T3 accompanied by normal serum T4 and TSH levels, and the syndrome results from impaired hepatic conversion of T4 to the biologically active hormone, T3, by 5-monodeiodination. The cardiac myocyte has no appreciable deiodinase activity and therefore relies on the plasma as the source of T3. In experimental animals the low T3 syndrome cause same changes in cardiac function and gene expression as does primary

hypothyroidism (Klein and Danzi, 2007). Low thyroid hormone level, in particular low serum T3 concentrations, are a common finding in patients with non-thyroidal illnesses, including cardiac disease (Iervasi et al., 2003).

Amiodarone is an iodine-rich benzofuran derivative utilized to treat and prevent cardiac arrhythmias. It may precipitate a number of thyroid conditions including thyroiditis, which appears to be related to a cytotoxic effect (Bogazzi et al., 2001; Daniels, 2001; Klein and Danzi, 2007). Amiodarone is a lipid soluble benzofuranic antiarrhythmic drug that has complex effects on the thyroid and may interfere significantly with thyroid hormone metabolism. Owing to its high iodine content amiodarone may cause thyroid impairment in patients with preexisting thyroid disease; it can also lead to a destructive thyroiditis in patients with an inherently normal thyroid gland (Toft and Boon, 2000). Because of its high iodine content, amiodarone can cause changes in thyroid function tests that result in either hypothyroidism (5% to 25% of treated patients) or hyperthyroidism (2% to 10% of treated patients) (Klein and Danzi, 2007).Thyroid hormone has relevant effects on the cardiovascular system (Klein and Ojamaa, 2001). Increased or reduced action of thyroid hormone on certain molecular pathways in the heart and vasculature causes relevant cardiovascular derangements (Fazio et al., 2004).

Cortisol, the major human glucocorticoid, is essential for maintenance of normal blood pressure and in excess, either general or local, produces hypertension (Whitworth et al., 2005). Evidence exists for associations of incident coronary heart disease with three specific negative emotions related to psychological stress: anxiety, anger, and depression (Suls and Bunde, 2005; Kubzansky et al., 2007). While some work has considered how acute negative affective states may activate acute cardiac events, much of this research has been concerned with long-term etiology, and with demonstrating that exposure to chronic psychological stress promotes higher rates of CVD incidence (Steptoe and Brydon, 2009).

One of the note of acute and chronic stress is activation of the HPA axis, and the corticotropin-releasing hormone (CRH)–adrenocorticotropic hormone (ACTH)–cortisol cascade represents the prototypic stress hormone system, often synonymous with the meaning of stress for many investigators (Johnson and Grippo, 2006).

Numerous studies have demonstrated how cortisol may influence hypertension via increases in the production of angiotensinogen by the liver (Vinson, 2007) and by effects on vascular smooth muscle, endothelial cells, kidney and the heart (Hadoke et al., 2006; Walker, 2007).

Cortisol has also been linked with many measures of chronic stress and side effect (including trait anxiety, depressive symptoms, caregiver stress, unemployment), and appears to have the greatest response to stressors that are uncontrollable and socially threatening (Dickerson and Kemeny, 2004). A great deal of work linking psychosocial stress and disease outcomes has concentrate on alterations in cortisol as one mechanism by which psychological stress might influence physical health outcomes. However, little number of epidemiologic or psychological studies has successfully demonstrated direct links between psychological stress, cortisol and CVD outcomes (Girod and Brotman, 2004).

In CHF, inflammatory and neurohormonal system activation is a response to the dysfunction of the failing human heart (Tzanis et al., 2014). Progression of CHF is associated with activation of neuroendocrine stress response systems including the hypothalamic-pituitary-adrenal axis (HPA) that modulates the production and secretion of glucocorticoids including cortisol from the adrenal cortex (Brotman et al., 2007).Hormonal alterations can lead to abnormal behavior and vice versa, in response to stressful situations, endocrine glands, hormone production often increase (Rugulies, 2002).

Few common factors, namely, pro-inflammatory cytokines and the adrenal hormones, glucocorticoids and mineralocorticoids, and their primary hormonal controllers, CRF-ACTH and renin-angiotensin, respectively, are activated in both heart failure and in depression. In general, these factors can be considered as major stress hormones. St (Johnson and Grippo, 2006).

Psychological stress and negative affective states stimulate the HPA axis, leading to release of ACTH. Release of ACTH leads to release of both cortisol and aldosterone. It has been recently shown that exercise capacity and ventilatory efficiency are related to anabolic impairment of either the adrenal (Pastor- Pérez et al., 2011). This study investigates the role of hormonal anabolic impairment and showing its relationship with exercise intolerance in heart failure or the peripheral axis (Jankowska et al., 2009) in CHF male patients. However, the association of CHF functional impairment with catabolic hormonal status has not been thoroughly investigated yet (Agapitou et al., 2013).

Parathyroid hormone (PTH), a peptide hormone of 84 amino acids, is secreted by the parathyroid glands to promote Vitamin D activation and acts to control calcium homeostasis (Fraser, 2009). The release of PTH is mediated by serum calcium, phosphorus, and vitamin D metabolites (Altay and Colkesen, 2013).Increased PTH levels have been associated with increased blood pressure, cardiac contractility, cardiomyocyte hypertrophy, and apoptosis, as well as structural and functional alterations in the vascular system (Perkovic et al., 2003, Kosch et al., 2000).A recent study demonstrated that high serum PTH levels were

strongly associated with advanced HF (Altay et al., 2012). This relationship has been explained by the fact that secondary hyperparathyroidism may contribute to the systemic illness that accompanies advanced HF (Alsafwah et al., 2007).

This systemic illness and chronic nature of HF may contribute to depression. The association of depressive disorders and primary hyperparathyroidism has been shown before (Watson and Marx, 2002), Where the resultant hypercalcemia was thought to be the mechanism responsible for the production of depressive symptoms. High serum PTH levels are thought to be related to the systemic induction of oxidative stress that leads to tissue impairment and contributes to the pathophysiology of HF (Sun et al., 2006). Elevated oxidative stress may also play important role in the pathophysiology of depression in chronic HF (Michalakeas et al., 2011).

It is well known that PTH control blood calcium and phosphorus concentrations. Higher level of calcium is a risk factor for vascular disease, and it is associated with increased vascular stiffness and high pulse pressure (Hagström et al., 2015). Previous studies showed that elevated levels of PTH are associated with high risks for cardiovascular mortality and morbidity and is suggest that CAD was associated with higher level of PTH, rather than normal or lower, PTH levels (Kamycheva et al., 2004).

PTH is elevated in patients with HF (Ogino et al., 2002). Many studies investigated the relationship between CAD and PTH, but conflicting results were obtained (Rashid et al., 2007; Reis et al., 2009; Öztürk et al., 2012). Two studies have shown elevated PTH to be associated with HF independent of known risk factors, including hypertension and renal dysfunction (Hagström et al., 2010; Kestenbaum et al., 2011) whereas one study suggested the association to be present in obese subjects only (Di Giuseppe et al., 2013).

Chronic PTH elevation with low serum calcium (secondary hyperparathyroidism) is usually secondary to renal injury or vitamin D deficiency. Renal dysfunction is a common cause of secondary hyperparathyroidism. However, the relationship between PTH and HF was stronger in those with no evidence of chronic kidney disease (Wannamethee et al., 2014). However, excess PTH may have possible effects beyond the regulation of calcium homeostasis (Altay and Colkesen, 2013). In epidemiological studies PTH is increased in patients with HF (Ogino et al., 2002) and has shown to be independently associated with hospitalization for HF in these patients (Sugimoto et al., 2009).

Heart failure is common, especially in older patients, and its incidence is predicted to increase (Johansen et al., 2003). Concerning Few prospective studies have specifically examined the association between PTH and incident HF in the general population. Two prospective studies in older adults have shown PTH levels to be related to incident HF (Hagström et al., 2010; Kestenbaum et al., 2011).

V. Conclusion:

There is non-significant increase difference in the TSH and T4 and significant decrease in the T3 of HF patients compared with control group, while there was significant increase in the cortisol hormone and parathyroid hormone of HF patients compared with control group. There was a positive relationship between ages of patients with heart failure.

References

[1]. Agapitou, V.; Dimopoulos, S.; Kapelios, C.; Karatzanos, E.; Manetos, C.; Georgantas, A.; Ntalianis, A.; Terrovitis, J.; Karga, H.; and Nanas, S. (2013). Hormonal imbalance in relation to exercise intolerance and ventilatory inefficiency in chronic heart failure. J. Heart and Lung Transplantation, 32(4), 431-436.
[2]. Alsafwah, S.; LaGuardia, S. P.; Arroyo, M.; Dockery, B. K.; Bhattacharya, S. K.; Ahokas, R. A.; and Newman, K. P. (2007). Congestive heart failure is a systemic illness: a role for minerals and micronutrients. Clin. Med. Res., 5 (4): 238-243.
[3]. Altay, H.; and Colkesen, Y. (2013). Parathyroid hormone and heart failure: novel biomarker strategy. Endocrine, Metabol. Immune Disorders, 13 (1): 100-104.
[4]. Altay, H.; Zorlu, A.; Binici, S.; Bilgi, M.; Yilmaz, M. B.; Colkesen, Y.; Erol T.; and Muderrisoglu, H. (2012). Relation of serum parathyroid hormone level to severity of heart failure. Am. J. Cardiol., 109 (2): 252-256.
[5]. Berry, C.; and Clark, A. L. (2000). Catabolism in chronic heart failure. Eur. heart J., 21(7): 521-532.
[6]. Biondi, B. (2012). Mechanisms in endocrinology: Heart failure and thyroid dysfunction. Eur. J. Endocrinol., 167(5): 609-618.
[7]. Bogazzi, F., Bartalena, L., Gasperi, M., Braverman, L. E., and Martino, E. (2001). The various effects of amiodarone on thyroid function. Thyroid, 11(5): 511-519.
[8]. Brotman, D. J.; Golden, S. H.; and Wittstein, I. S. (2007). The cardiovascular toll of stress. The Lancet, 370(9592): 1089-1100.
[9]. Chen, H.; Senda, T.; Emura, S.; and Kubo, K. Y. (2013). An update on the structure of the parathyroid gland. Open Anatom. J. 5(1).
[10]. Daniels, G. H. (2001). Amiodarone-induced thyrotoxicosis. J. Clin. Endocrinol. Metabol., 86 (1): 3-8.
[11]. Danzi, S.; and Klein, I. (2004). Thyroid hormone and the cardiovascular system. Minerva endocrinol., 29(3): 139-150.
[12]. Di Giuseppe, R.; Buijsse, B.; Hirche, F.; Wirth, J.; Arregui, M.; Westphal, S.; Isermann, B.; Hense, W.H.; Dierkes, J.; Boeing, H.; Stangl, G. I.; and Weikert C. (2013). Plasma fibroblast growth factor 23, parathyroid hormone, 25-hydroxyvitamin D3, and risk of heart failure: a prospective, case-cohort study. J. of Clin. Endocrinol. and Metabolism, 99(3): 947-955.
[13]. Dickerson, S. S.; and Kemeny, M. E. (2004). Acute stressors and cortisol responses: a theoretical integration and synthesis of laboratory research. Psychol. bulletin, 130(3): 355.
[14]. Fazio, S.; Palmieri, E. A.; Lombardi, G.; and Biondi, B. (2004). Effects of thyroid hormone on the cardiovascular system. Recent progress in hormone res., 59(1): 31-50.

[15]. Figueroa, M. S.; and Peters, J. I. (2006). Congestive heart failure: diagnosis, pathophysiology, therapy, and implications for respiratory care. Respiratory care, 51(4): 403-412.
[16]. Fraser, W. D. (2009). Hyperparathyroidism. The Lancet, 374(9684): 145-158.
[17]. Galli, E.; Pingitore, A.; and Iervasi, G. (2010). The role of thyroid hormone in the pathophysiology of heart failure: Clin. evidence. Heart failure reviews, 15(2): 155-169.
[18]. Girod, J. P.; and Brotman, D. J. (2004). Does altered glucocorticoid homeostasis increase cardiovascular risk?. Cardiovasc. Res., 64(2): 217-226.
[19]. Güder, G.; Bauersachs, J.; Frantz, S.; Weismann, D.; Allolio, B.; Ertl, G.; Angermann, C.E.; Störk, S. (2007). Complementary and incremental mortality risk prediction by cortisol and aldosterone in chronic heart failure. Circulation, 115(13): 1754-1761.
[20]. Hadoke, P. W. F.; Lindsay, R. S.; Seckl, J. R.; Walker, B. R.; and Kenyon, C. J. (2006). Altered vascular contractility in adult female rats with hypertension programmed by prenatal glucocorticoid exposure. J. Endocrinol., 188(3): 435-442.
[21]. Hagström, E.; Ahlström, T.; Ärnlöv, J.; Larsson, A.; Melhus, H., Hellman, P.; and Lind, L. (2015). Parathyroid hormone and calcium are independently associated with subclinical vascular disease in a community-based cohort. Atherosclerosis, 238(2): 420-426.
[22]. Hagström, E.; Ingelsson, E.; Sundström, J.; Hellman, P.; Larsson, T. E.; Berglund, L.; Håkan M.; Claes, H.; Karl, M.; Lars L.; and Ärnlöv, J. (2010). Plasma parathyroid hormone and risk of congestive heart failure in the community. Eur. J. heart failure, 12(11): 1186-1192.
[23]. Hamilton, M. A.; Stevenson, L. W.; Luu, M.; and Walden, J. A. (1990). Altered thyroid hormone metabolism in advanced heart failure. J. Am. College Cardiol., 16(1): 91-95.
[24]. Iervasi, G.; and Nicolini, G. (2013). Thyroid hormone and cardiovascular system: from basic concepts to clinical application. Inter. emergency Med., 8(1): 71-74.
[25]. Iervasi, G.; Pingitore, A.; Landi, P.; Raciti, M.; Ripoli, A.; Scarlattini, M.; L'Abbate, A.; and Donato, L. (2003). Low-T3 syndrome. Circulation, 107(5): 708-713.
[26]. Jankowska, E. A.; Filippatos, G.; Ponikowska, B.; Borodulin-Nadzieja, L.; Anker, S. D.; Banasiak, W.; Poole-Wilson P. A.; and Ponikowski, P. (2009). Reduction in circulating testosterone relates to exercise capacity in men with chronic heart failure. J. cardiac failure, 15(5): 442-450.
[27]. Johansen, H.; Strauss, B.; Arnold, J. M. O.; Moe, G.; and Liu, P. (2003). On the rise: The current and projected future burden of congestive heart failure hospitalization in Canada. Canad. J. Cardiol. 19(4): 430-435.
[28]. Johnson, A. K.; and Grippo, A. J. (2006). Saddens and broken heart: neurohumoral mechanisms. J. Physiol. Pharmacol., 57(11): 5-29.
[29]. Johnson, A. K.; and Grippo, A. J. (2006). Saddens and broken heart: neurohumoral mechanisms. J. Physiol. Pharmacol., 57(11): 5-29.
[30]. Kamycheva, E.; Sundsfjord, J.; and Jorde, R. (2004). Serum parathyroid hormone levels predict coronary heart disease: the Tromsø Study. Eur. J. of Cardiovascular Prevention and Rehabilitation, 11(1): 69-74.
[31]. Kestenbaum, B.; Katz, R.; De Boer, I.; Hoofnagle, A.; Sarnak, M. J.; Shlipak, M. G.; Jenny. N. S.; and Siscovick, D. (2011). Vitamin D, parathyroid hormone, and cardiovascular events among older adults. J. Am. Coll. Cardiol., 58(14): 1433-1441.
[32]. Klein, I. and Danzi, S. (2007). Thyroid disease and the heart. Circulation, 116(15): 1725-1735.
[33]. Klein, I. and Ojamaa, K. (2001). Thyroid hormone and the cardiovascular system. N. Eng. J. Med., 344(7): 509-501.
[34]. Kosch, M.; Hausberg, M.; Vormbrock, K.; Kisters, K.; Rahn, K. H.; and Barenbrock, M. (2000). Studies on flow-mediated vasodilation and intima-media thickness of the brachial artery in patients with primary hyperparathyroidism. Am. J. hypertension, 13(7): 759-764.
[35]. Kozdag, G.; Ural, D.; Vural, A.; Agacdiken, A.; Kahraman, G.; Sahin, T.; Ural, E.; and Komsuoglu, B. (2005). Relation between free triiodothyronine/free thyroxine ratio, echocardiographic parameters and mortality in dilated cardiomyopathy. Eur. J. heart failure, 7(1): 113-118.
[36]. Kubzansky, L. D.; Koenen, K. C.; Spiro, A.; Vokonas, P. S.; and Sparrow, D. (2007). Prospective study of posttraumatic stress disorder symptoms and coronary heart disease in the Normative Aging Study. Archives of general psychiatry, 64(1): 109-116.
[37]. McMurray, J. J.; Adamopoulos, S.; Anker, S. D.; Auricchio, A.; Böhm, M.; Dickstein, K.; Volkmar, F.; Gerasimos F.; Cândida, F.; Angel, G. M.; Tiny, J.; Lars, K.; Lip Gregory, Y.H.; Pietro, M. A.; Alexander P.; Pieske, B.M.; Popescu, B. A.; Rønnevik, P. K.; Rutten, F. H.; Petar S.; Janina, S.; Trindade, P.; Voors, A. A.; Faiez, Z.; and Andreas, Z. (2012). ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012. Eur. J. Heart failure, 14(8): 803-869.
[38]. Michalakeas, C. A.; Parissis, J. T.; Douzenis, A.; Nikolaou, M.; Varounis, C.; Andreadou, I.; Antonellos, N.; Markantonis-Kiroudis, S. C.; Paraskevaidis, I.; Ikonomidis, I.; Lykouras, E.; and Kremastinos, D. (2011). Effects of sertraline on circulating markers of oxidative stress in depressed patients with chronic heart failure: a pilot study. J. of cardiac failure, 17(9): 748-754.
[39]. Michels, T. C.; and Kelly, K. M. (2013). Parathyroid disorders. Am. Fam. Physician, 88(4): 249-57.
[40]. Ogino, K.; Ogura, K.; Kinugasa, Y.; Furuse, Y.; Uchida, K.; Shimoyama, M.; Kinugawa, T.; Osaki, S.; Kato, M.; Tomikura, Y.; Igawa. O.; Hisatome, I.; Bilezikian, J. P.; and Shigemasa, C. (2002). Parathyroid hormone-related protein is produced in the myocardium and increased in patients with congestive heart failure. The J. Clin. Endocrinol. Metabolism, 87(10): 4722-4727.
[41]. Ogino, K.; Ogura, K.; Kinugasa, Y.; Furuse, Y.; Uchida, K.; Shimoyama, M.; Kinugawa, T.; Osaki, S.; Kato, M.; Tomikura, Y.; Igawa. O.; Hisatome, I.; Bilezikian, J. P.; and Shigemasa, C. (2002). Parathyroid hormone-related protein is produced in the myocardium and increased in patients with congestive heart failure. The J. Clin. Endocrinol. Metabolism, 87(10): 4722-4727.
[42]. Oztürk, D.; Ozcan, Ç. O.; Ulusoy, F. V.; and Aydoğdu, S. (2012). The relationship between serum parathormone levels and the severity of coronary artery disease. Turk Kardiyoloji Dernegi arsivi: Turk Kardiyoloji Derneginin yayin organidir, 40(7): 589-594.
[43]. Pastor-Pérez, F. J.; Manzano-Fernández, S.; Bravo, I. P. G.; Nicolás, F.; Tornel, P. L.; Lax, A.; Morena, G. L.; Valdés, M.; Domingo and Pascual-Figal, D. A. (2011). Anabolic status and functional impairment in men with mild chronic heart failure. J. Am. Coll. Cardiol., 108(6): 862-866.
[44]. Perkovic, V.; Hewitson, T. D.; Kelynack, K. J.; Martic, M.; Tait, M. G.; and Becker, G. J. (2003). Parathyroid hormone has a prosclerotic effect on vascular smooth muscle cells. Kidney and Blood Pressure Research, 26(1): 27-33.
[45]. Pingitore, A.; and Iervasi, G. (2005). Thyroid (dys) function in heart failure: is it a potential target for medical treatment?. Vascular health and risk management, 1(2): 97.
[46]. Rashid, G.; Bernheim, J.; Green, J.; and Benchetrit, S. (2007). Parathyroid hormone stimulates endothelial expression of atherosclerotic parameters through protein kinase pathways. Am. J. of Physiol.-Renal Physiol., 292(4): 1215-1218.
[47]. Reis, J. P.; von Mühlen, D.; Michos, E. D.; Miller, E. R.; Appel, L. J.; Araneta, M. R.; and Barrett-Connor, E. (2009). Serum vitamin D, parathyroid hormone levels, and carotid atherosclerosis. Atherosclerosis, 207(2): 585-590.

[48]. Rodondi, N.; Newman, A. B.; Vittinghoff, E.; de Rekeneire, N.; Satterfield, S.; Harris, T. B.; and Bauer, D. C. (2005). Subclinical hypothyroidism and the risk of heart failure, other cardiovascular events, and death. Archives of internal Med., 165(21): 2460-2466.
[49]. Rubio, I. G.; and Medeiros-Neto, G. (2009). Mutations of the thyroglobulin gene and its relevance to thyroid disorders. Current Opinion in Endocrinol. Diabetes and Obesity, 16(5), 373-378.
[50]. Rugulies, R. (2002). Depression as a predictor for coronary heart disease: a review and meta-analysis. Am. J. of preventive Med., 23(1): 51-61.
[51]. SAS. 2012. Statistical Analysis System, User's Guide. Statistical. Version 9.1th ed. SAS. Inst. Inc. Cary. N.C. USA.
[52]. Schmidt-Ott, U. M.; and Ascheim, D. D. (2006). Thyroid hormone and heart failure. Current Heart Failure Reports, 3(3): 114-119.
[53]. Steptoe, A.; and Brydon, L. (2009). Emotional triggering of cardiac events. Neuroscience and Biobehavioral Rev., 33(2): 63-70.
[54]. Sugimoto, T.; Tanigawa, T.; Onishi, K.; Fujimoto, N.; Matsuda, A.; Nakamori, S.; Koji, T.; Ito, M. (2009). Serum intact parathyroid hormone levels predict hospitalisation for heart failure. Heart, 95(5): 395-398.
[55]. Suls, J.; and Bunde, J. (2005). Anger, anxiety, and depression as risk factors for cardiovascular disease: the problems and implications of overlapping affective dispositions. Psychological bulletin, 131(2): 260.
[56]. Sun, Y.; Ahokas, R. A.; Bhattacharya, S. K.; Gerling, I. C.; Carbone, L. D.; and Weber, K. T. (2006). Oxidative stress in aldosteronism. Cardiovascular research, 71(2): 300-309.
[57]. Toft, A. D.; and Boon, N. A. (2000). Thyroid disease and the heart. Heart, 84(4): 455-460.
[58]. Tzanis, G.; Dimopoulos, S.; Agapitou, V.; and Nanas, S. (2014). Exercise intolerance in chronic heart failure: the role of cortisol and the catabolic state. Current heart failure reports, 11(1): 70-79.
[59]. Vinson, G. P. (2007). Angiotensin II, corticosteroids, type II diabetes and the metabolic syndrome. Med. hypotheses, 68(6): 1200-1207.
[60]. Wajner, S. M.; and Maia, A. L. (2012). New insights toward the acute non-thyroidal illness syndrome. Frontiers in Endocrinol., 3(8): 7.
[61]. Walker, B. R. (2007). Glucocorticoids and cardiovascular disease. Eur. J. Endocrinol., 157(5): 545-559.
[62]. Wannamethee, S. G.; Welsh, P.; Papacosta, O.; Lennon, L.; Whincup, P. H.; and Sattar, N. (2014). Elevated parathyroid hormone, but not vitamin D deficiency, is associated with increased risk of heart failure in older men with and without cardiovascular disease. Circulation: Heart Failure, 7(5): 732-739.
[63]. Watson, L. C.; and Marx, C. E. (2002). New onset of neuropsychiatric symptoms in the elderly: possible primary hyperparathyroidism. Psychosomatics, 43(5): 413-417.
[64]. Whitworth, J. A.; Williamson, P. M.; Mangos, G.; and Kelly, J. J. (2005). Cardiovascular consequences of cortisol excess. Vascular health and risk management, 1(4): 291.
[65]. Wrosch, C.; Miller, G. E.; and Schulz, R. (2009). Cortisol secretion and functional disabilities in old age: importance of using adaptive control strategies. Psychosomatic Med., 71(9): 996.
[66]. Yen, P. M. (2001). Physiological and molecular basis of thyroid hormone action. Physiol. Rev., 81(3): 1097-1142.
[67]. Zimmermann; M. B. (2009). Iodine deficiency. Endoc. Rev., 30(4): 376-408.

Bushra H. Rasheed. “Determination of the level of some metabolic hormones in congestive heart failure patients in Baghdad city.” IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS) , vol. 12, no. 5, 2017, pp. 46–52.