العراقية
المجلات الاكاديمية العلمية

IRAQI
Academic Scientific Journals

Entedhar R. Sarhat [*] [(1)]

Moayad MY Al-Anzy [(2)]

Mutaz S. Ahmeid [(3)]

Thuraia R. Sarhat [(4)]

(1) Department of Basic Science, Dentistry College
Tikrit University
Salahuddin
Iraq
(2) Department of pharmaceutical chemistry
College of pharmacy
Tikrit University
Salahuddin
Iraq.
(3) Department of Biochemistry
College of Medicine
Tikrit University
Salahuddin
Iraq.
(4) B.Sc. of College of Education, Iraq

Characteristic Abnormalities in Serum Biochemistry during Congestive heart failure

ABSTRACT:

Background: Congestive heart failure (CHF) is a complex clinical syndrome characterized by dyspnea, fatigue, and signs of volume overload, which may include peripheral edema and pulmonary rules.

Aim: The goal of the current study was to evaluate the alterations in different biochemical parameters including leptin, Adiponectin, ghrelin, Ceruloplasmin , concentration in patients with congestive heart failure.

Patients and Methods: The total of 60   patients (19 Males and 11 Females) were enrolled in this study, 30   of them with congestive heart failure (study group) and 30 with apparently healthy subjects (13Males and 17 Females) (control group).

Results: The levels of leptin, ceruloplasmin, copper, and sialic acid , TNF-α, and CRP were significantly elevated in patients group, while adiponectin , ghrelin, Vitamin C and E were significantly lower in patients group compared to control group, there was positive correlation between leptin with adiponectin and ghrelin , adiponectin with ghrelin, Vitamin C with E ,ceruloplasmin with copper in congestive heart failure patients.

Conclusions: Serum leptin, ghrelin and adiponectin are biomarkers for and correlated to CHF not only in the role they might play in the pathogenesis of the disease but also in their severity. Serum ceruloplasmin, copper, and sialic acid, levels, may serve as prognostic indicators in patients with CHF.

*Corresponding Author E mail: entedharr@tu.edu.iq

INTRODUCTION

Congestive heart failure (CHF) is a complex clinical syndrome characterized by dyspnea, fatigue, and signs of volume overload, which may include peripheral edema and pulmonary rules [1] .CHF is a consequence the complex interplay of genetic, neurohormonal, inflammatory, and biochemical changes in cardiac myocytes, interstitium, or both, associated with release of various biochemical markers like cytokines, neurohormones, enzymes, etc., which could be estimated in blood [2].

The aim of the present study is to investigate the changes in serum levels of leptin, adiponectin, ghrelin, ceruloplasmin, copper, sialic acid , vitamin C and E concentration in patients with CHF.

Patients and Methods

This prospective study had been conducted between March 2014 and January 2016. The present study included 60 individuals, categorized into two groups. The first group includes 30 patients consecutively admitted Kirkuk Teaching Hospital / Kirkuk / Iraq, were taken as a study group. Their ages ranged between 33-64 years (51.23±63), 19 were males and 11were females. Patients were admitted diagnosed as recent CHF. A 30 normal healthy volunteers (13Males and 17 Females) considered as apparently by clinical examination and with no history of any disease were enrolled.

We collected 5 mL fasting blood samples from participants at baseline between 8:30 a.m. and 10:30 a.m. The sera were obtained by centrifugation within 30 min at 4000 rpm for 10 min. Sera was separated, for the measurement of leptin, adiponectin, ghrelin determined using standard ELISA technique using a kit from ALPCO. The ceruloplasmin assay was done by p-phenylene diamine method [3].Serum copper was measured by atomic absorption spectrometry. Serum sialic acid was estimated by thiobarbituric acid assay of Warren [4].Measurement of Vitamin E and C were performed according to the method described by Tietz [5].

Echocardiographic measurements were performed according to guidelines and recommendations by the European Association of Echocardiography [6].

All results are presented as mean ± SD. Student's *t*-test , and correlation coefficient were used for the analysis of data.

Results

The demographic profiles of all the subjects under study are shown in Table 1.

Table 1: Demographic characteristics of CHF, & Control patients:

	CHF	Control
No. of subjects	30	30
Male/Female	19/11	13/17
Age (years)	51.23±6.3	61.4±11.4

In this study, the mean level of leptin ,ceruloplasmin, copper, TNF-α, and CRP were significantly increased in CHF group(29.7870± 1.69282ng/ml), (46± 7.15165 mg/dl), and (141.7±3.17µg/dl), (34.1853±4.95828 pg/ml), (1.1302±.22157 pg/ml)compared to the control Group (10.0133±.1.69282ng/ml), (21.2523± 2.63237mg/dl), and (125.8 ± 2.8 µg/dl), (9.3277±1.03671 pg/ml), and (0.7600±0.15229 pg/ml) respectively.

On the other hand, a significant decrease in the activity of adiponectin, and ghrelin were observed in CHF group(3.5227±1.17002µg/ml) (12.3777±2.24527 ng/ml) respectively, comparing to the control(8.0878±1.04333 µg/ml) (38.1±4.66783 ng/ml) respectively. Also, the mean values of vitamin C and E were significantly increased (0.66±0.15957 mg/dl),(0.7600±0.14057 mg/dl) in the CHF group comparing to the control (1.3±0.17025mg/dl), (1.42±0.15079 mg/dl) respectively as illustration in Table (2).

Table (2): Baseline biochemical parameters of CHF patients and healthy controls

Parameter	Control group	CHF group
Leptin (ng/ml)	10.0133±.1.69282	29.7870± 1.69282[**]
Adiponectin (µg/ml)	8.0878±1.04333	3.5227±1.17002[**]
Ghrelin (ng/ml)	38.1±4.66783	12.3777±2.24527[**]
Ceruloplasmin (mg/dl)	21.2523±2.63237	46± 7.15165[**]
Copper (µg/dl)	125.8 ± 2.8	141.7 ± 3.17[*]
Vitamin C (mg/dl)	1.3±0.17025	0.66±0.15957[**]
Vitamin E(mg/dl)	1.42±0.15079	0.7600±0.14057[**]
Sialic acid (mg/dl)	47±6.31949	65±7.47871[**]
TNF-α (pg/ml)	9.3277±1.03671	34.1853±4.95828[**]
CRP (mg/l)	0.7600±0.15229	1.1302±.22157[**]

[*]$P < 0.05$, [**]$P < 0.01$.

Correlation of Paraoxonase to other Parameters

The positive correlation was found between leptin with adiponectin (r=0.228), and with ghrelin (r=0.061) , in CHF group, also between adiponectin with ghrelin (r=0.540), Vitamin C with E (0.692), ceruloplasmin with copper (r=0.445), TNF-α CRP(r=0.686) as in table table(3).

Table 3. Correlations within CHF groups

parameters	CHF group (r)
leptin with adiponectin	0.228
leptin with ghrelin	0.061
Adiponectin with ghrelin	0.540
Vitamin C with E	0.692
Ceruloplasmin with copper	0.445
TNF-α with CRP	0.686

DISCUSSION

Leptin was found to have many roles in the cardiovascular system as a vasoactive substance, in rule of myocardial blood flow, and it may have a prothrombotic effect [7]. Leptin may be modulate cardiac function immediately, it can also exert other proinflammatory effects like the maturation of lymphocytes more proinflammatory phenomena, is characterized by producing proinflammatory cytokines[8]. Leptin may be involved in a catabolic state, leading to the development of cardiac cachexia in the context of CHF[9,10].Our study shows that serum leptin levels was increased in CHF individuals, Such finding is in line with previous studies [11-12]whom reported that leptin levels increased, which is consistent with an increased metabolic rate associated with high concentrations of catecholamines and proinflammatory cytokines present in CHF. Whereas dis agreement with the work of Toth et al. [13],who found no difference in plasma leptin concentrations between patients with CHF and healthy controls.

Adiponectin acts as an anti-inflammatory and antiatherogenic

cytokine that is involved in vascular remodeling [14].The present study indicated that the significant decrease in levels of adiponectin in CHF group versus the control group, which is in the line with previous reports[14,15]whereas disagreement with other studies [16,17].

In present study, serum ghrelin levels decreased significantly in CHF as compared with control, which is in accordance with previous reports [18] whom revealed that ghrelin can decrease peripheral vascular resistance, resulting in an increase in cardiac index and stroke volume in healthy volunteers and patients with CHF. The possible mechanisms postulated include inhibition of ghrelin secretion owing to impaired lipid metabolism and dysfunction of insulin-secreting pancreatic cells, also enhanced binding of ghrelin with its receptor in reperfusion /ischemia reperfusion [19].

Our findings show that the levels of leptin are correlated positively with the values of ghrelin in CHF group which is dis agree with the results obtained by [20,21] who demonstrate that the the ability of high FFA levels to block ghrelin secretion, also correlated positively with the adiponectin, which is

disagreement with the results obtained by Samir et al. [22].

The results of figure (1) demonstration a significant increase sialic acid level in patients in comparing with control groups. This increase may be due to releasing of sialic acid from the cell into the bloodstream due to cell damage[23]. Similar observation was supported by [24,25].

We observed significant increase in ceruloplasmin and copper levels in CHF patients , which is in agreement with earlier report, Shukla et al, [62]. Ceruloplasmin acts as an antioxidant can catalyze the oxidation of Fe^{2+} ,and it also scavenges superoxide anion radical [27].Reactive oxygen species deactivate binding of copper to ceruloplasmin, and thus weaken the antioxidant proprietary, and to continue to encourage the oxidation of Pathology.

The study revealed a positive correlation between ceruloplasmin and copper inpatients with CHF , these results are expected due to the fact that the to rise in the copper binding capacity of ceruloplasmin [28]. This result is consistent with the findings of the previous study [29] indicates that the increasing levels of copper in the serum are part of concrete a defense mechanism to provide

extra copper in the infarction site to reduce its size and the extent of the damage.

Our analysis revealed statistically significant decrease in the level of Vitamin E and C in patients compared to the control group, due to their free radical scavenging action and to preserve the body antioxidant reserve and in normalization of vascular superoxide formation [30].

The current results are in line with the work of other investigators [31,32]. Who found that TNF level is lower in patient group than the controls, a possible explanation for the decrease in serum TNF activity may be mediated by increase chemokine and scavenger receptor expression. The level of CRP is higher in patients with CHF ,These findings are in harmony with preceding reports which stated that the increased CRP concentrations in patients with AMI may stimulate production by the monocytes of the tissue factor which initiates the coagulation process.

Conclusion:

1. Serum leptin, ghrelin and adiponectin are biomarkers for and correlated to CHF not only in the role they might play in the pathogenesis of the disease but also in their severity.

2. Serum ceruloplasmin, copper, and sialic acid, levels, may serve as prognostic indicators in patients with CHF.

3. Further studies should be applied to confirm our data in a larger number of patients and to clarify the mechanism.

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