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Serum NT-pro BNP and Other Biochemical Markers in Patients with Cardiorenal Syndrome (CRS) in Thi-Qar Province- Iraq

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Abstract

"Any chronic or acute problem in the kidneys or heart which can lead to a chronic or acute problem of the other" is known as "cardiorenal syndrome" (CRS). To examine the serum levels of creatinine, urea, IL-1β, NT-pro BNP, albumin, lipid profile, and Troponin levels in the CRS group and compare them to the values in the healthy group. Cardio Renal Syndrome as well as 35 controls were both included in the presented study. All subjects had measured serum levels of creatinine, urea, IL-1β, NT-pro BNP, lipid profile, albumin, and Troponin. This clinical study was completed at private clinics, labs, and the Heart Center in Thi-Qar. Patients diagnosed with CRS had significantly higher mean levels regarding serum triglyceride, LDL, cholesterol, and VLDL, as well as serum creatinine, urea, IL-1β, NT-pro BNP, and Troponin ($p \leq 0.05$) in comparison with the control group. The patients had lower serum albumin and HDL than the controls ($p \leq 0.05$). ROC curve showed that NT-BNP, Troponin, TCH, IL-1β, LDL, and HDL levels have shown a good approach for differentiating between patients with cardiorenal syndrome and healthy persons. Test results for LDL, TG, urea, VLDL, and creatinine showed a significant ability to distinguish between patients with cardiorenal syndrome and healthy persons. Lastly, the ability of albumin to predict cardiorenal syndrome was found to be low validity. To better comprehend the overall disease burden related to such particular CRS subtypes, an explanation of epidemiology regarding heart-kidney interaction is essential.

Keywords: Cardio-renal syndrome, Troponin, NT-pro BNP, IL-1β, and lipid profile.

Introduction

Any chronic or acute problem in the kidneys or heart that can lead to a chronic or acute problem of the other [1] is the definition of cardio-renal syndrome. Both renal and cardiac problems are related to vascular risk factors, like hypertension and diabetes. Overlapping risk factors include various hemodynamic connections between kidney and heart failure, chronic kidney disease (CKD), neurohormonal interactions, and atherosclerotic diseases [2,3].

There are 5 cardio-renal syndrome sub-types:

Type1: acute renal function drop brought on by a severe decline in cardiac function

Type2: prolonged renal function decline due to chronic cardiac failure

Type 3: an acute loss in cardiac function caused by a rapid fall in renal function.

Type 4: chronic cardiac dysfunction brought on by a chronic loss in kidney function

Type 5: renal and cardiac disease caused by systemic diseases.

Each variety has a different etiology, different treatment options, and various prognoses [4,5].

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Cardiac troponin is released into the bloodstream due to cardiac damage and includes troponin T, troponin I, and troponin C which control actin-myosin interaction as well as calcium-mediated contraction of the muscles [6]. The levels of N-terminal-pro Brain Natriuretic Peptide (NT-pro BNP) are typically higher in the elderly, as well as in individuals with myocardial ischemia, tachycardia, renal insufficiency sepsis, hypoxemia, cirrhosis, and infections. Furthermore useful in heart failure diagnoses is NT-proBNP [7,8]. In myocardial and kidney damage, IL-1β has a role in the activation of the NLRP3-inflammasome [9]. This discovery indicates that there may be a causative relationship between systemic diseases like cardiovascular diseases and periodontitis due to IL-1β [10]. Since cholesterol is a lipid that is insoluble in water, it is taken in. Micelles are formed by vesicle aggregates. Phospholipids with associated cholesterol, spherical bilayers of bile salts, and phospholipids are enclosed in vesicles [11, 12]. Dyslipidemia, which lowers the amount of high-density lipoprotein (HDL) and raises the plasma concentration regarding low-density lipoproteins (LDL), represents a major risk factor for atherosclerosis [13–15]. Furthermore, new atherosclerotic lesions develop as a result of a modest increase in triglycerides [15]. The onset of dyslipidemia may occur at different times based on medication and dialysis treatments, and the kidneys' overall health. Additionally, lipid profile changes quicken renal disease progression [16]. Those processes collectively support the construction of a pro-atherogenic profile, given triglyceride-rich lipoprotein function such as the very low-density lipoproteins (VLDL), chylomicrons (CM), and their remnants, and smaller LDL in the development of atherosclerotic damage [17–22]. Patients who have chronic renal disease might experience increased oxidative stress as a result of high serum urea levels; research in animals and individuals with elevated urea levels has already demonstrated an increase in lipid and protein peroxidation [23–25]. Serum creatinine is a useful indicator of kidney health because it is a readily measured muscle metabolism by-product, which is excreted unaltered by kidneys [26,27]. Approximately 40% of albumin is found in plasma, with the remaining 60% found in extra-cellular space [28]. Yet, the albumin concentration in a smaller intra-vascular compartment is substantially larger due to the blood artery wall's relative impermeability. The concentration gradient of the capillary membrane is necessary to maintain plasma volume [29, 30]. Evaluating the biochemical markers of patients with cardio-renal syndrome was the aim of the current investigation. Examining the disease's metabolic alterations that enable diagnosis and treatment was made possible by the research.

Methods and Materials

Design of Study

All samples used in this investigation, which was intended to be a case-control study, were from patients who visited specialty clinics and the Heart Center in Thi-Qar. It contained seventy subjects, thirty-five blood samples from patients suffering from cardio-renal syndrome—fifteen of whom were female and twenty of whom were male—and thirty-five blood samples taken from healthy people as renal group controls.

Blood Sample Collection

Five ml of blood have been extracted from patients with cardio-renal syndrome and controls, allowed to clot at room temperature in empty, sterile tubes, and centrifuged at 3000xg for ten minutes. Serum samples have then been separated and kept at a temperature of -20ºC until needed unless they were used right away for analyzing biochemical parameters.

Biochemical Parameters:

With the use of an ELISA reader and a kit provided by De Meditec, Germany, serum troponin was calculated. Using an ELISA Reader from Getein Biotech in China, the enzyme-linked immunoassay approach was used to assess serum NT-pro BNP. With the use of a kit from Elabscience, USA, the

enzyme-linked immunoassay approach was used to measure serum IL-1β using an ELISA reader. With the use of kits provided by Biolabo, France, the serum (Urea, TG, Albumin, and Creatinine) was subjected to an enzymatic colorimetric technique analysis with the use of a UV/VIS spectrophotometer, Japan. With the use of kits from Spinreact, Spain, an enzymatic colorimetric approach was used to evaluate serum cholesterol (TCH) utilizing a UV/VIS spectrophotometer located in Japan. With the use of kits from Biomerieux, France, the serum HDL was measured with the use of an enzymatic colorimetric technique with a UV/VIS spectrophotometer in Japan. To determine serum LDL, use the next equation: -

LDL=Total Cholesterol–(HDL+VLDL)

The equation used for calculating serum VLDL is as follows:

VLDL = Triglyceride/5

Statistical Analyses

Statistical analyses have been carried out with the use of the SPSS v20.0 software. Findings have been presented in the form of mean ± SD or mean ± standard deviations. A one-way ANOVA test has been run to compare parameters across research groups. The statistical significance has been assessed with the use of p-values ($p \leq 0.05$).

Results and Discussion

A total of 70 participants divided into two groups participated in the presented research: Thirty-five patients in the Cardio-Renal Syndrome group were compared to thirty-five people in the Healthy group, who were all of the same age. Table 1 displays the characteristic data for every group under study. Table 1 illustrates the specifics of the two groups' numbers and ages.

Table (1): Details of age and numbers of studied groups

Groups	N	Age (years) mean±SD	Body mass index(kg/m2) mean±SD
Patients	**35**	**61.3±13.2**	**27.6±6.1**
Controls	**35**	**60.8±11.9**	**23.2±5.4**

Table 2: Serum levels of NT-proBNP and Troponin measurement in both Cardio-renal patients and control groups

Groups	N	Troponin (pg/ml) mean±SD	NT-proBNP (ng/L) mean±SD
Patients	**35**	**1207.54±150.4[a]**	**894.23±113.0 [a]**
Controls	**35**	**199.29±30.5 [b]**	**210.31±51.1 [b]**

Note: every one of the values represents values of mean ± SD with the non-identical superscript (a, b, or c…. etc), which have been considered significant differences ($p \leq 0.05$).

N: denotes the number of subjects.

SD: denotes the standard deviation

Table 3: Serum level of IL-1β measurement in both Cardio-renal patients and controls groups

Groups	N	IL-1β (pg/mL) mean ±SD
Patients	**35**	**575. 42±100.1[a]**
Controls	**35**	**221.03±63.13 [b]**

- Legend as in Table 2.

Table 4: Lipid profile measurement Serum levels in Cardio-renal patients as well as the control groups

Groups	N	TCH (mg/dl) mean±SD	TG (mg/dl) mean±SD	HDL (mg/dl) mean±SD	LDL (mg/dl) mean±SD	VLDL (mg/dl) mean±SD
Patients	**35**	**200.91±50.5[a]**	**195.34±31.4 [a]**	**43.73±7.2 [b]**	**98.03±19.4 [a]**	**42.62±10.0[a]**
Controls	**35**	**150.15±32.3[b]**	**110.08±21.5 [b]**	**65.21±6.3 [a]**	**81.63±11.8 [b]**	**20.33±4.2[b]**

- Legend as in Table 2.

Table 5: Serum levels of Urea, Creatinine, and Albumin measurement in both Cardio-renal patients and control groups

Groups	N	Urea (mg/dl) mean±SD	Creatinine (mg/dl) mean±SD	Albumin (g/dl) mean±SD
Patients	**35**	**76.53±12.1[a]**	**3.41± 0.3[a]**	**3.06±0.64 [b]**
Controls	**35**	**25.74±4.6[b]**	**0.71± 0.09 [b]**	**5.41±0.1 [a]**

- Legend as in Table 2.

Table 6: Area Under the ROC Curve for all of the analyzed Biomarker

Area Under the Curve					
Variable(s) of Test Results	Area	Standard Error	Asymptotic Sig.	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
NT-BNP(ng/l)	**0.967**	**0.025**	**0.000**	**0.919**	**1.000**
Troponin(pg/ml)	**0.935**	**0.045**	**0.009**	**0.848**	**0.994**
IL-1β (pg/ml)	**0.965**	**0.027**	**0.000**	**0.912**	**0.979**
TCH (mg/dl)	**0.937**	**0.044**	**0.004**	**0.850**	**0.957**
TG (mg/dl)	**0.895**	**0.057**	**0.000**	**0.783**	**1.000**
HDL (mg/dl)	**0.986**	**0.015**	**0.000**	**0.957**	**1.000**
LDL (mg/dl)	**0.894**	**0.046**	**0.007**	**0.804**	**0.984**
VLDL (mg/dl)	**0.895**	**0.057**	**0.010**	**0.783**	**1.000**
Urea (mg/dl)	**0.753**	**0.089**	**0.020**	**0.579**	**0.827**
Creatinine (mg/dl)	**0.755**	**0.070**	**0.009**	**0.618**	**0.892**
Albumin (g/dl)	**0.425**	**0.087**	**0.377**	**0.254**	**0.596**

Discussion:

Kidney and heart conditions often coexist in the same patient and are related to increased complications, costs, and mortality in the healthcare system [31, 32]. Strong links between cardiac troponins as well as renal function have been observed by researchers [33]. The levels of Troponin could be a useful surrogate for the indication of persistent inflammation or myocyte injury and declining renal function in acute settings, where almost all of the patients who have acute HF arrive. Furthermore, the concentration of serum troponin stays high in the blood for a longer period compared to creatine kinase, creatine kinase-MB, and myoglobin because of its much longer half-life, which lengthens the diagnostic period. In patients who have acute heart failure, in-hospital mortality is often higher when there is insufficient renal function. Thanks to serial troponin readings, patients hospitalized with HF could benefit from enhanced monitoring. Since ischemic heart disease represents the primary cause of acute heart failure (HF), monitoring troponin levels to track ongoing myocardial damage could aid in the successful management of patients who have HF and renal impairment [34]. Since the kidney just metabolizes BNP in trace amounts, NT-proBNP is more favorable for assessing renal function because it is mostly metabolized through renal clearance. Regarding the prognosis and diagnosis of heart failure, NT-proBNP is useful [35,36]. Although it raised the risk of fatal infections, canakinumab, which is a humanized monoclonal antibody that targets IL-1β, reduced cardiovascular events by 15% in a total of 10,061 patients who had previously experienced a myocardial infarction [37]. The CKD subgroup reported similar outcomes [38]. The concentration of serum albumin is significantly influenced by a number of factors, which include nutrition, inflammations, and dialysis efficacy. Consequently, serum albumin's predictive value is primarily explained by inflammations [39–41].

Serum albumin is mostly associated with inflammation and hypoalbuminemia in cardiovascular diseases, which is why it has prognostic relevance. Wiedermann claimed that acute albumin loss in systemic inflammatory reactions and underlying hypoalbuminemia, which raises the likelihood of acute infectious infections, make all medical, trauma, and surgical issues have a more challenging clinical course [40]. The signs of dyslipidemia are often lower levels of HDL-C and greater levels of LDL-C and plasma triglycerides [42]. According to human epidemiologic studies, individuals with chronic kidney disease who have dyslipidemia are substantially more likely to experience renal dysfunction [43–45]. Low HDL-C levels have been linked in certain studies to a quicker rate of kidney disease progression [46]. Even though the kidneys excrete 90% of their waste nitrogen as urea, several possible mechanisms can lead to increased urea reabsorption in patients with heart failure [47]. Elevated BUN can be a sign of severe heart failure, which is characterized by an active neurohormonal system and decreased cardiac output. Since BUN is dependent on protein intake, catabolism, and tubular reabsorption, it is not a good measure of renal function [48]. The only discernible indication of a decrease in glomerular filtration was the rise in serum creatinine. The drawbacks of creatinine include its association with total body muscle mass and creatine, which causes it to fluctuate based on body size and the rate of renal elimination [49,50]. Furthermore, in patients with essential hypertension, a raised serum creatinine level is a late indicator of renal damage and is associated with a bad prognosis [51, 52]. In clinical epidemiology, ROC curve analysis is utilized to assess how well medical diagnostic tools distinguish patients with and without disease. The idea behind it is a "separator" scale, in which the distributions that result from the two conditions alternate. A useful indicator for assessing the sensitivity as well as precision of a diagnostic test is the Area Under Curve (AUC). ROC curves have been used in this study to examine the outcomes of tests and experiments that were carried out. ROC curves were used to examine the results of the experiments and tests conducted as part of this study. The information is provided in Table (6).

It is feasible to state that the hypothesis AUC result is significant if the test value is larger than the Table value (0.5) and all tested parameters have some validity for predicting cardiorenal syndrome. In this instance, the table (6) included the AUC values in addition to the other factors. The ROC curve showed that NT-BNP, Troponin, TCH, IL-1β, LDL, and HDL levels have shown a good approach for differentiating between patients with cardiorenal syndrome and healthy persons. Test results for LDL, TG, urea, VLDL, and creatinine showed a significant ability to distinguish between patients with cardiorenal syndrome and healthy persons. Lastly, the ability of albumin to predict cardiorenal syndrome was found to be low validity.

Conclusion

An epidemiological description regarding the heart-kidney link will help us understand the overall disease burden related to such specific CRS subtypes and will guide future research into their diagnosis, pathophysiology, prognosis, and therapy. It is anticipated that such markers will help differentiate between various forms of CRS and facilitate an early diagnosis of the condition. It is anticipated that some of such biomarkers might either provide adequate risk prediction or early diagnosis of all patients, hence improving the course of CRS and the long-term outcome.

Conflict of interest: None

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