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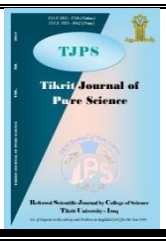

Evaluation N-terminal pro-B-type natriuretic peptide and other biochemical parameters in heart failure with or without chronic kidney disease in Kirkuk city

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ABSTRACT

Backgrounds: Individuals who are diagnosed with chronic kidney disease (CKD) are at a significantly increased risk of developing cardiovascular (CV) disease. **Aim of the study:** This study evaluated N-terminal pro-B-type natriuretic peptide, urea, creatinin, and albumin in heart failure with or without chronic kidney disease. **Materials and methods:** The study was done at Amal Dialysis Centre, General Kirkuk Hospital Lab and Azadi Teaching Hospital Lab. The age range of the participants was between 18-68 years old. The study was conducted from January to Augest 2023. The current study examined 90 participants that divided in to four groups as: G1=Kidney failure patients (n:23), G2=Heart failure patients (n:22), G3=Heart and kidney failure (n:23), and G4=apparently healthy normal individuals. **Results:** This study show highly significant increase NT Pro- BNP in G1, G2 and G3(123.88±22.73, 107.86± 20.15, 134.85± 26.05), as compared with G4 (67.19±18.44) at p-value<0.0008. While highly decrease albumin in G1,G2 and G3(4.318±0.486, 4.028±0.991, 5.500± 0.652), as compared with G4 (7.028± 0.991) at p-value <0.01**Conclusion:** This study concluded increase in NTpro Pro- BNP, urea and creatinin in all three groups as compared with control group and decrease in albumin level.

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تقييم ببتيد الناتريوريتيك من النوع B الطرفي الأميني والمعايير الكيميائية الحيوية الأخرى في قصور القلب مع أو بدون مرض الكلى المزمن في مدينة كركوك

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الملخص

الخلفية: الاشخاص الذين تم تشخيصهم بمرض الكلى المزمن معرضون لخطر متزايد بشكل كبير للإصابة بمخاطر امراض القلب والأوعية الدموية.

أهداف الدراسة: هدفت هذه الدراسة تقييم ببتيد الناتريوريتيك من النوع B الطرفي الأميني، واليوريا، والكرياتينين، والألبومين في قصور القلب مع أو بدون مرض الكلى المزمن.

المواد والطرق: أجريت الدراسة في مركز أمل لغسيل الكلى ومختبر مستشفى كركوك العام ومختبر مستشفى آزادي التعليمي. تراوحت أعمار المشاركين بين 18 و68 عامًا. أجريت الدراسة من يناير إلى أغسطس 2023. فحصت الدراسة الحالية 90 مشاركًا تم تقسيمهم إلى أربع مجموعات على النحو التالي: G1 = مرضى الفشل الكلوي (عدد: 23)، G2 = مرضى فشل القلب (عدد: 22)، G3 = فشل القلب والكلى (عدد: 23)، وG4 = أفراد طبيعيون يتمتعون بصحة جيدة. النتائج: أظهرت هذه الدراسة زيادة كبيرة في NT Pro-BNP في G1 وG2 وG3 (22.73 ± 123.88, 20.15 ±107.86, 26.05 ±134.85) مقارنة بـG4 (18.44 ± 67.19) عند قيمة p <0.0008. بينما انخفض الألبومين بشكل كبير في G1 وG2 وG3 (0.486 ± 4.318, 0.991±4.028 , 0.652± 5.500) مقارنة بـ (0.991 ± 7.028) G4 عند قيمة p <0.01.

الاستنتاج: خلصت هذه الدراسة إلى زيادة في NTpro Pro- BNP واليوريا والكرياتينين في جميع المجموعات الثلاث مقارنة بمجموعة التحكم وانخفاض في مستوى الألبومين.

Introduction

Chronic kidney disease (CKD) often leads to heart failure (HF), which is a common cardiovascular complication. Heart failure (HF) in CKD patients is linked to increased mortality rates, frequent hospitalization, and a decline in health-related quality of life [1]. Given that over 80% of individuals suffering from heart failure are aged 65 years old or over, a majority of these patients experience one or more comorbidities. Furthermore, heart failure is categorized as a syndrome rather than a distinct disease, indicating that it is frequently triggered by one

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or more underlying factors [2]. Hypertension, coronary artery disease, diabetes, and chronic kidney disease (CKD) are commonly observed as comorbidities in heart failure patients, and are considered to be among the main factors contributing to the development of heart failure [3]. Cardiac biomarkers have considerable potential in identifying individuals at higher risk for heart failure and could indicate potential mechanistic routes. NT-proBNP is cardiac biomarkers which demonstrated their ability to predict HF in the general population [4,5]. NT-proBNP is released by cardiac myocytes due to myocardial strain caused by either pressure or volume overload which its levels increase in correlation with the increase in left ventricular mass [6]. Renal failure, commonly known as end-stage renal disease, is a medical condition in which kidney function declines, preventing waste removal from the bloodstream [7]. This disorder occurs when kidneys operate below 15% of normal. Acute renal failure is sudden and treatable, while chronic kidney failure develops slowly and is usually permanent [8]. NT-proBNP, also known as BNPT, is an inactive precursor molecule consisting of a 76 amino acid N-terminal protein. The protein is cleaved to produce brain natriuretic peptide 32 (BNP), which is also referred to as B-type natriuretic peptide [9]. Both BNP and N- NT-proBNP levels in the bloodstream are employed for the purpose of screening and diagnosing acute congestive heart failure. Moreover, these markers can be valuable in evaluating the prognosis of heart failure, as they tend to be elevated in individuals with a more unfavorable result [6].

Individuals with left ventricular dysfunction typically exhibit elevated levels of both BNP and NT-proBNP in their blood, regardless of whether they experience symptoms or not. The increase is associated with coronary artery disease, myocardial ischemia, and the severity of aortic valve stenosis [10]. This study evaluated N-terminal pro-B-type natriuretic peptide, urea, creatinin, and albumin in heart failure with or without chronic kidney disease

Material and methods

Study Design

The study was conducted at three locations: Amal Centre of Dialysis, General Kirkuk Hospital Lab and Azadi Teaching Hospital Lab. The study was conducted from January 2023 to August 2023, with a study population ranging in age from 18 to 68 years old. The study included a total of 90 subjects, divided in to 22 individuals in the control group and 78 individuals in the patients group who had kidney and heart failure. Sample categorized based on the assays conducted, which included BNP (brain natriuretic peptide), NT-proBNP (N-terminal. The sample that used in present study divided in to four groups include: G1, consisting of 23 kidney failure patients; G2, consisting of 22 heart failure patients; G3, consisting of 23 patients with both heart and kidney failure; and G4, consisting of 22 seemingly healthy normal individuals.

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Exclusion criteria for Heart failure and chronic kidney diseases

Subjects diagnosed with the specified disorders were not included in the present investigation due to the potential for inducing alterations. Diabetes mellitus, primary hyperparathyroidism, and thyroid disorders. Patients with rheumatoid arthritis, hepatic or renal impairment, or any tumor or cancer instances.

Samples collection

A 5 ml blood sample was collected in a tube without any additives and left undisturbed for around 20-30 minutes to facilitate the formation of a blood clot. Subsequently, the substance was subjected to centrifugation using a high-capacity centrifuge operating at a velocity of 3000 revolutions per minute for a duration of 5 to 15 minutes. The serum that was not hemolyzed was collected and stored in a deep freeze at a temperature of -20 degrees Celsius. The acquired serum was divided into two tubes to identify disparities in the amounts of specific immunological, biochemical and physiological factors.

Human N-terminal pro-brain natriuretic ELISA kit

The method employed by this ELISA kit is Sandwich-ELISA. The Micro Elisa strip plate included in this kit has been pre-coated with an antibody that specifically targets NT-pro BNP. A Horseradish Peroxidase (HRP)-conjugated antibody that specifically targets NT-pro BNP is introduced into each well of the Micro Elisa strip plate. The optical density (OD) is determined using spectrophotometry at a specific wavelength of 450 nm.

Statistical analysis

SPSS was used for statistical analysis. One-way analysis of variance (ANOVA) was used to compare groups, and the Duncan multiple ranges test was used to test parameter arithmetic means for significant differences. Regression plots were used to determine the Pearson correlation coefficient (r) between the parameters and other factors. The statistical significance level was set at $P<0.05$

Results and Discussion

As shown in table (1), the mean of the serum level **NT Pro- BNP (**N-terminal pro-BNP brain natriuretic peptide**)**, in patients groups compared with the control group. This study show highly significant increase **NT Pro- BNP** in G1, G2 and G3 (123.88±22.73, 107.86± 20.15, 134.85± 26.05) respectively, as compared with G4 (67.19±18.44) at p-value<0.0008.

Table 1: Measurement of NT-Pro- BNP in the study groups and Control Group regarding the mean and S.D of NT Pro- BNP

parameter	**G1**	**G2**	**G3**	**G4**
NT Pro-BNP	123.88± 22.73 ab	107.86± 20.15 b	134.85± 26.05 a	67.19± 18.44 c
P-value	<0.0008			

- Different letter mean statistical differences between groups

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The present study show highly significant decrease in albumin level in G1,G2 and G3(4.318±0.486, 4.028±0.991, 5.500± 0.652) respectively, as compared with G4 (7.028± 0.991) at **p-value <0.01.** As shown in table (2).

Table 2: The mean ± SD of Albumin level in study groups compared to the control group

parameter	G1	G2	G3	G4	P-value
Albumin g/dL	4.318± 0.486 b	4.028± 0.991 b	5.500± 0.652 ab	7.028± 0.991 a	0.01

The present study show highly significant increase in urea level in G1 and G2 and G3 (112.78 ±12.13, 70.45 ± 5.390, 101.39 ±20.19) respectively, as compared with G4 (32.45± 5.390) at **p-value <0.01.** In addition significant increase Creatinin level in G1 and G2 and G3 (6.6780±1.2830, 7.3220± 0.9610, 6.7545 ± 0.9017) respectively, as compared with G4 (0.8636 ± 0.1866) at **p-value <0.01.** As shown in table (3).

Table 3: Estimate urea and creatinin levels in study groups compared to the control group

Parameters	G1	G2	G3	G4	P-value
Urea mg/dl	112.78 ± 12.13 a	70.45 ± 5.390 ab	101.39 ± 20.19 a	32.45± 5.390 b	0.01
Creatinin mg/dl	6.6780 ± 1.2830 a	7.3220± 0.9610 a	6.7545 ± 0.9017 a	0.8636 ± 0.1866 b	0.01

The current study demonstrates an elevation in NT Pro-BNP levels in individuals with HF and CKD as compared to the control group. The controversy lies in determining the extent to which the rise in NT-proBNP levels can be attributed to reduced renal clearance versus heightened cardiac production. This conclusion is consistent with the findings of [11], which demonstrate an increase in the prevalence of HF among patients with CKD compared to those without CKD. Prior evaluations have moderated the excitement to determine that heart disease is the main cause of an elevation in NT-proBNP level. The study done by (12) suggested that elevated NT-proBNP levels are mostly associated with the existence and severity of heart disease, rather than being caused by decreased kidney function. NT-proBNP has been identified as a substantial prognostic indicator for mortality in cardiovascular conditions such as HF and coronary artery disease CAD [13,14]. The prognoses of patients with CKD based on the NTproBNP level have not been extensively investigated. In fact, only limited studies have demonstrated the capacity of NT-proBNP to predict bad outcomes on its own.8 Prior research has demonstrated that NT-proBNP offers separate and comparable predictive data for prognosis in the total CHF population, as well as in subgroups with and without CKD [15,16].

This study agree with the findings of [17], which demonstrate the presence of hypoalbuminemia. For individuals with CKD and HF, the amount of albumin is highly significant in predicting the likelihood of mortality and cardiovascular events. Also agree with [18], which demonstrate

the presence of hypoalbuminemia in individuals with CKD. This study done by [19] showed a reduction in albumin levels in individuals with renal failure compared to those who are healthy. Hypoalbuminemia, a condition characterized by low levels of albumin in the blood, has been identified as a separate factor that can predict heart failure [20]. Hypoalbuminemia contributes to the development of pulmonary edema by causing a decrease in the concentration of proteins in the plasma [21]. Furthermore, CKD is the main physiological process that leads to the development of hypoalbuminemia in individuals with HF [22]. Concurrently, hypoalbuminemia is present in approximately one-third of patients with HF [23] and is believed to predominantly stem from starvation, inflammation, and cachexia [24]. Hypoalbuminemia is a frequent occurrence in chronic diseases including end-stage renal failure or dialysis and advanced cancer. This condition is often linked to an increase in inflammatory mediators [22]. This study demonstrated a substantial elevation ($p \leq 0.01$) in the levels of urea and serum creatinine in CKD patients compared to the healthy group. These results were corroborated by other studies [25]. Another study done by [26] demonstrated that an elevation in creatinine levels occurs as a result of kidney injury, leading to a decrease in glomerular filtration rate (GFR) caused by kidney inflammation.

Conclusion

This study concluded increase NT Pro- BNP, urea and creatinine in all three groups as compared with control group and decrease albumin level in all study groups

Conflict of interests

The authors declared no conflicting interests.

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This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contribution

Authors contributed equally in the study.

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