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RESEARCH ARTICLE

An Assessment of Brain Natriuretic Peptide (BNP), Urokinase Plasminogen Activator (uPA) and Wingless Type 5A (WINT5A) in Iraqi Patients with Heart Failure

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ABSTRACT

Biochemical markers like brain natriuretic peptide (BNP) are being identified in patients with heart failure (HF) to indicate the severity of the condition. Little is known about Urokinase plasminogen activator (uPa) and wingless type 5A(Wint5a) markers. The study investigates the role of serum BNP concentration in diagnosing HF and its impact on survival and prognosis in patients with impaired renal function. 150 individuals participated in this study (100 as patients and 50 as control), patients were classified according to renal dysfunction into two groups 50 patients with HF and renal dysfunction (RD), 50 patients with HF without RD. According to the area under curve 81 %, indicated BNP is a good indicator to determine HF with RD p-value <0.05, cutoff value 0.35 at which HF is diagnosed, sensitivity 0.78 and specificity 0.73, CI 95% (0.74–0.88). While uPa and Wint5a revealed fair indicator. BNP and Wint5a showed significant correlations with urea, creatinine, and uric acid but not with uPa. BNP levels of patients with RD showed a positive significant correlation with creatinine levels, and the critical point of BNP level for diagnosis of heart failure was 0.855 ng/mL while in Wint5a was 0.877 ng/ml and fair result with uPa. As the survival rate in patients with BNP level above the critical point was significantly low, this level was a useful indicator for predicting their prognosis. Care should be taken in interpreting BNP and Wint5a level because patients with RD may show a high concentration of BNP with and without heart failure.

Keywords: Brain natriuretic peptide, Heart disease, Heart failure, Urokinase, Wingless

Introduction

Role of b-type natriuretic peptide (BNP) in heart failure

Natriuretic peptides (NP), particularly B-type (BNP), have been regarded as biomarkers of volume overload and instruments to exclude heart failure (HF) in the general population for a considerable amount of time. HF is the leading cause of mortality among patients with renal dysfunction (RD). [1] Nevertheless, a limited number of studies have examined the relationship between increased production of B-type natriuretic peptide (BNP) in cardiac cells and lower BNP clearance in the kidney, which may be attributed to the elevated water content in the bodies of patients with impaired renal function. The objective of this research was to investigate the diagnostic use of serum B-type natriuretic peptide (BNP) concentration in the identification of heart failure as well as assessing its impact on the survival and prognosis of individuals with compromised renal function. [2]

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Wnt5a is elevated in heart failure and affects cardiac fibroblast function

Dysregulated signalling pathways characterize failing myocardium. The quiescent wingless (Wnt) signalling pathway is triggered during cardiac disease.[3] Wnt proteins initiate signalling by binding to a Frizzled receptor and a low-density lipoprotein receptor-related protein receptor complex,[4] resulting in distinct intracellular responses that involve -catenin (canonical pathway),[5] Ca^{2+} and other second messengers Wnt signalling is dysregulated in heart failure (HF) and may promote cardiac hypertrophy, fibrosis, and inflammation.[6] Inhibiting Wnt ligand Wnt5a protects animal models from HF. However, the role of Wnt5a in human HF and its functions in cardiac cells is not well understood blocking the Wnt ligand Wnt5a prevents HF in animal models. However, the role of Wnt5a in human HF and its functions in cardiac cells remain unclear.[7] Serum Wnt5a was higher in HF patients and related to hemodynamic, neurohormonal, and clinical disease severity. Wnt5a protein seems to be linked to IL-6 and TIMP-1 in failing human hearts.[8]

Urokinase-type plasminogen activator improves risk prediction in patients with heart failure

A 53-kDa serine protease, uPA activates plasminogen. Like most mammalian proteases, uPA starts as a catalytically inactive single-chain polypeptide.[9] The uPA/uPAR system is crucial for the pathogenesis of vascular diseases.[10] The pathophysiology of atherosclerotic lesion formation involves complex interactions between arterial wall cells, such as endothelial cells, smooth muscle cells, macrophages, plasma lipoproteins, and molecular systems involved in thrombosis, fibrinolysis, oxidation, and inflammation.[11] During the beginning stages of atherogenesis, circulating monocytes adhere to endothelial cells in the arterial wall, infiltrate the subendothelial space, and then differentiate into macrophages.[12] Due to the absorption of changed lipoproteins such as oxidized LDL, macrophages collect cholesterol and oxidized lipids, resulting in foam cells.[13] Atherosclerotic lesions are also characterized by accelerated oxidative stress and the production of reactive oxygen species (ROS), which attack lipids in lipoproteins and arterial macrophages.[14]

Materials and methods

Selection of patients

One hundred and fifty individuals were enrolled in this study (75 women and 75 men), age ranged between (40-70) years and the samples collection started from November 2022 to March 2023. Each participant was recruited at Shaikh Zayed Hospital and all patients were diagnosed by consults physicians as HF patients and it was caused by left ventricle dysfunction. The study protocol and ethical approval were permitted by Shaikh Zayed Hospital. Informed consent was obtained from all subjects involved in the study. Samples classified according to RD (by measuring urea, creatinine, and uric acid) into three groups G1: 50 patients (25female and 25 male) HF without RD, G2: 50 patients (25 female and 25 male) HF with RD, and G3: 50 apparently healthy control (25 females and 25 males). The kits used in the study were manufactured by Sunlog-China and Roche–Germany. ELISA and Copas were used for measurements of parameters.

Statistical analysis

Categorical variables are expressed as Mean ± SD. The student t-test was used for comparison of means, and analysis of variance (ANOVA) for comparisons of multiple groups with the Scheffe test (post hoc). A Pearson correlation was made for continuous quantitative variables. Analysis of ROC curves were also used. The optimal sensitivity and specificity were estimated by the position on the resulting curve of the minimum distance to the perfect sensitivity and specificity point (100%, 100%). The area under the curve indicated the degree of discrimination of the variable analyzed, ranging from 0.5, or non-discriminative, to 1.0, fully discriminative.

Results and discussion

Table 1 shows a highly significant difference p-value (<0.001) of BNP and Wint5a between patients compared with control while there was non-significant difference (p-value = 0.543) in uPa between studied groups.

Numerous studies by Tsutsui H et al. indicated that BNP is a significant marker for the diagnosis and prognosis of heart failure (HF).[15] It is the most dependable biomarker for HF, and its association with left ventricular (LV) diameter and ejection fraction is well-established.[16] Christopher P. et al. reported that RD is associated with elevated levels of natriuretic peptides and that patients with RD often have increased BNP(15). Even after accounting for renal dysfunction, Thanh et al. indicated that BNP likely reflects early HF pathogenesis in patients with RD, which is consistent with our findings.[17]

The first factor that could explain the stimulation and release of BNP from the myocardium is cardiac

Table 1. Comparison of biochemical parameters in studied groups (HF patients with control).

	HF patients	Control	P -value
Parameters			
BNP (ng/ml) (mean ± SD)	0.45 ± 0.14	0.26 ± 0.06	<0.001
uPa (ng/ml) (mean ± SD)	0.19 ± 0.07	0.21 ± 0.07	0.543
Wint5a (ng/ml) (mean ± SD)	0.75 ± 0.22	0.44 ± 0.09	<0.001
Enzymes			
CK (U/L)	46.25 ± 9.54	10.72 ± 3.72	<0.001
LDH (U/L)	315.23 ± 34.47	148.24 ± 25.43	<0.001
AST (U/L)	39.75 ± 9.91	28.9 ± 9.58	0.093
Parameters			
RBG (mg/dl)	290.6 ± 45.63	94.74 ± 5.9	<0.001
K (mmole/l)	4.47 ± 1.05	4.07 ± 0.55	0.002
Ca (mg/dl)	9.15 ± 1.35	9.26 ± 0.72	0.028
CRP (mg/dl)	44.96 ± 8.21	0.92 ± 0.22	<0.001
Troponin (ng/l)	20.31 ± 3.75	1.25 ± 0.5	<0.001
Lipid Profile			
Cholesterol (mg/dl)	259.67 ± 23.93	172.96 ± 17.96	<0.001
TG (mg/dl)	334.29 ± 28.25	120.3 ± 11.68	<0.001
HDL (mg/dl)	45.66 ± 10.13	48.56 ± 6.17	0.002
LDL (mg/dl)	208.17 ± 31.86	106.26 ± 17.98	<0.001
VLDL (mg/dl)	40.13 ± 22.42	18.14 ± 8.91	<0.001
Renal Function Test:			
Urea (mg/dl)	101.37 ± 32.88	25.68 ± 5.95	<0.001
Creatinine (mg/dl)	1.52 ± 0.89	0.67 ± 0.14	<0.001
Uric Acid (mg/dl)	5.62 ± 1.25	3.99 ± 0.62	<0.001

stress,[18] another factor contributing to this phenomenon is the heightened levels of sodium and fluid retention, which afterwards result in elevated vascular tension. Consequently, this leads to an augmented preload of the heart. The elevation in ventricular wall pressure will result in the secretion of B-type natriuretic peptide (BNP).[19] Finally, the findings of our investigation elucidated a robust correlation between B-type natriuretic peptide (BNP) indicators and heart failure (HF); specifically suggesting that heightened cardiac stress leads to an elevation in BNP release.[20]

Elevated uPa concentrations in patients are significantly linked to heart failure. Endothelial cells, vascular smooth muscle cells, and blood monocytes and macrophages can generate urokinase plasminogen activator (uPA) and its receptor (suPAR), potentially contributing to their presence in plasma and extracellular fluids.[21]

Urokinase plasminogen activator receptor (uPAR) has been shown to form complexes and interact with vitronectin and integrin family components, modulating adhesion, migration, and proliferation of various cell types.[22] Chemotaxis can be triggered in cells that don't have the glycosyl-phosphatidylinositol-anchored receptor by fragments of the suPaR protein. In addition to fibrinolysis, the uPA/uPAR system may be able to change a number of stages in the inflammatory cascade, which could affect how inflammation and immune responses develop. These functions of the uPA/suPAR system probably show up at sites of vascular disease, like the atherosclerotic plaque, where these parts may be turned up.[9]

This study examined Wint5a levels in patients with HF and found that they were significantly elevated. Embryonic development and tissue homeostasis are dependent on the WINT5 signalling pathway. The abnormal activation of this pathway has been linked to numerous diseases, including cardiovascular and renal disorders.[23] WNT5A has been associated with cardiac remodelling processes such as fibrosis, hypertrophy, and inflammation. Its dysregulation may contribute to the detrimental cardiac remodelling seen in heart disease.[24] Wint5a has a role in the regulation of vascular smooth muscle cell function and the development of endothelial dysfunction. The association between its expression and the development of atherosclerosis and vascular calcification the involvement of Wint5a signalling in the stimulation of fibroblasts and the deposition of extracellular matrix has been suggested in the context of renal fibrosis. This mechanism has a role in the development of chronic renal disease.[25] Wint5a's inflammation has an impact on renal health. It may contribute to renal disease inflammation. The complex relationship between cardiac and renal health may entail Wint5a signalling. Dysregulated Wint5a may worsen cardiorenal syndrome by affecting cardiac remodelling and RD. Wint5a may be a cardiorenal impairment biomarker. Greater levels in renally impaired HF patients may indicate a greater risk of unfavourable

Table 2. ANOVA test of studied group.

Parameters	M ± SD			P value (sig ≤ 0.05)		
	G1	G2	G3	G1 Vs G2	G1 Vs G3	G2 Vs G3
Marker of Heart Failure						
BNP, (ng/ml)	0.36 ± 0.11	0.27 ± 0.04	0.28 ± 0.05	<0.001	<0.001	0.93
uPA, (ng/ml)	0.17 ± 0.06	0.2 ± 0.07	0.19 ± 0.06	0.01	0.03	0.61
Wint5a, (ng/ml)	0.39 ± 0.09	0.43 ± 0.08	0.39 ± 0.10	0.01	0.8	0.02
Enzymes						
CK (U/L)	20.92 ± 2.93	28.29 ± 14.44	11.58 ± 4.19	<0.001	<0.001	<0.001
LDH (U/L)	458.31 ± 188.98	228.67 ± 111.04	148.24 ± 25.43	<0.001	<0.001	0.002
AST (U/L)	43.55 ± 16.06	28.71 ± 9.07	28.88 ± 9.56	<0.001	<0.001	0.94
Parameters						
RBG (mg/dl)	87.21 ± 12.21	214 ± 85.76	94.62 ± 11.54	0.42	<0.001	<0.001
K (mmole/l)	4.81 ± 0.93	4.19 ± 0.94	4.07 ± 0.55	<0.001	<0.001	0.49
Ca (mg/dl)	9.23 ± 1.44	8.97 ± 1.28	9.26 ± 2.70	0.27	0.89	0.22
CRP (mg/dl)	33.65 ± 12.91	10.59 ± 4.60	1.33 ± 0.39	<0.001	<0.001	<0.001
Troponin (ng/l)	8.33 ± 3.16	7.29 ± 3.38	0.82 ± 0.32	0.05	<0.001	<0.001
Lipid Profile						
Cholesterol (mg/dl)	180.61 ± 75.72	177.35 ± 60.86	172.96 ± 17.96	0.77	0.5	0.7
TG (mg/dl)	235 ± 102.19	194.41 ± 84.82	112.14 ± 35.14	0.7	<0.001	<0.001
HDL (mg/dl)	45.96 ± 10.93	45.78 ± 10.02	48.56 ± 6.17	0.92	0.16	0.14
LDL (mg/dl)	96.34 ± 35.45	92.16 ± 40.46	106.26 ± 17.98	0.52	0.13	0.03
VLDL (mg/dl)	40.66 ± 17.14	38.88 ± 15.22	18.14 ± 7.7	0.52	<0.001	<0.001
Renal Function Test:						
Urea (mg/dl)	110.47 ± 43.69	33.1 ± 7.28	28.56 ± 5.94	<0.001	<0.001	0.38
Creatinine (mg/dl)	2.22 ± 0.76	0.85 ± 0.23	0.67 ± 0.14	<0.001	<0.001	0.05

G1: HF Patients without RD G2: HF Patients with RD G3: Control group

outcomes. Targeting Wint5a signalling may help RD heart patients. This pathway modulation may reduce cardiac remodelling, vascular problems, and renal fibrosis. Complex interactions and feedback mechanisms characterize the non-canonical Wint5a pathway. Understanding this complexity is essential to developing targeted medicines without unwanted side effects.[26]

Table 2 shows a comparison between all parameters in studied group by using ANOVA test, Fig. 1 shows the comparison of BNP, uPa, and Wint5a in patients and control.

Regarding to ROC curves in Table 3 and Figs. 2 and 3 BNP and Wint5a are considering a good diagnostic marker for HF patients according to AUC 0.901 and 0.918 respectively. Our findings are in agreement with Hanan et al.[27] who revealed in their study that levels of cardiac biomarkers NT-proBNP raise in patients with cardiovascular disease (CVD).

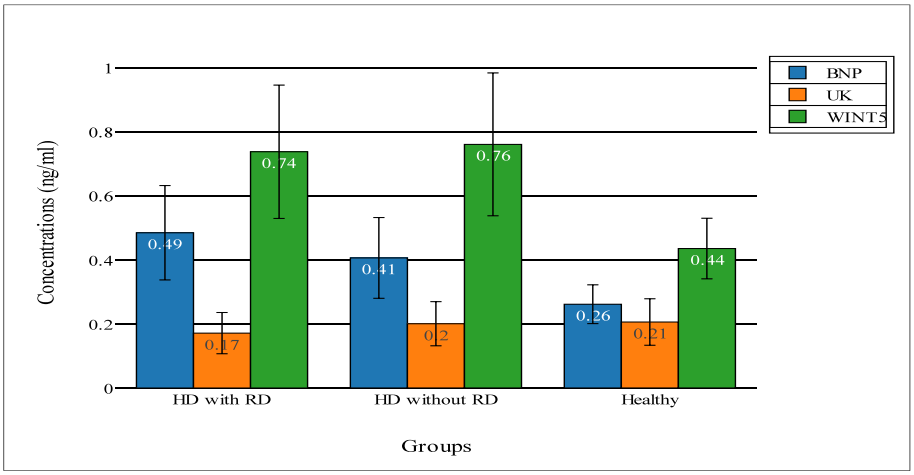

Fig. 1. BNP, uPa, and Wint5a comparison by ANOVA.

Table 3. Receiver operating characteristics (ROC) of biochemical parameters in studied group.

Parameters	AUC	Sensitivity (%)	Specificity (%)	Cut-off Value	Asymptotic 95% Confidence Interval		P value
					Lower Bound	Upper Bound	
Marker of Heart Failure							
BNP, pg/ml	90.1	85	98	0.36	0.85	0.94	<0.0001
uPA, pg/ml	38.3	20.2	88.9	0.44	0.290	0.476	0.02
WINT5A, pg/ml	91.8	80	90.1	0.54	0.877	0.959	<0.0001
Enzymes							
CK (U/L)	95.6	98	96.7	26	0.945	0.996	<0.0001
LDH (U/L)	88.5	98	95	280	0.819	0.935	<0.0001
AST (U/L)	79.6	80	60	43	0.521	0.709	0.022
Parameters							
RBG (mg/dl)	99	95.6	97	187	0.997	1	<0.0001
K (mmole/l)	60.7	45.5	87.2	4.5	0.517	0.697	0.034
Ca (mg/dl)	41.7	87.5	48.5	8.2	0.325	0.509	0.099
CRP (mg/dl)	96.7	82	92.3	41.9	0.943	0.992	<0.0001
Troponin (ng/l)	85.9	98.4	91.7	14	0.801	0.916	<0.0001
Lipid Profile							
Cholesterol (mg/dl)	90.1	92.4	96	253	0.852	0.949	<0.0001
TG (mg/dl)	94.8	86	91	231	0.907	0.99	<0.0001
HDL (mg/dl)	42.1	82.4	86	47	0.331	0.511	0.115
LDL (mg/dl)	98.8	99	92	124	0.320	0.499	0.07
VLDL (mg/dl)	85.6	68	88	28.2	0.794	0.918	<0.0001
Renal Function Test:							
Urea (mg/dl)	82.3	87.9	91.2	62	0.758	0.887	<0.0001
Creatinine (mg/dl)	85.5	95.1	84	1.4	0.797	0.913	<0.0001
Uric Acid (mg/dl)	89.7	76	67.3	6.7	0.83	0.935	<0.0001

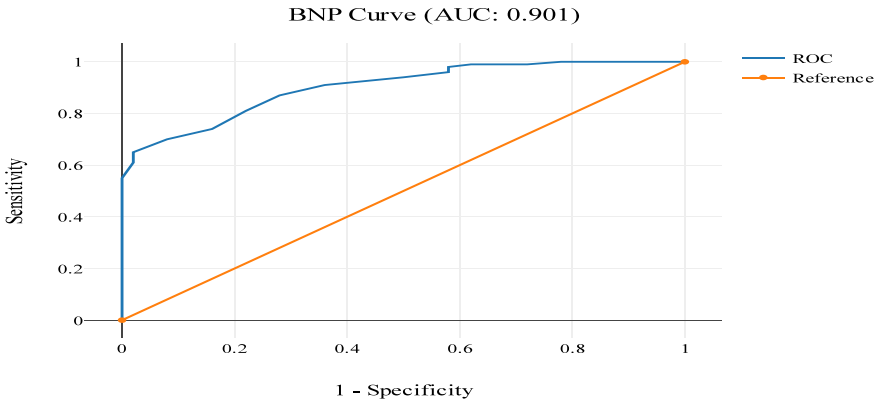

Fig. 2. ROC curve for evaluation of BNP in patients with HF.

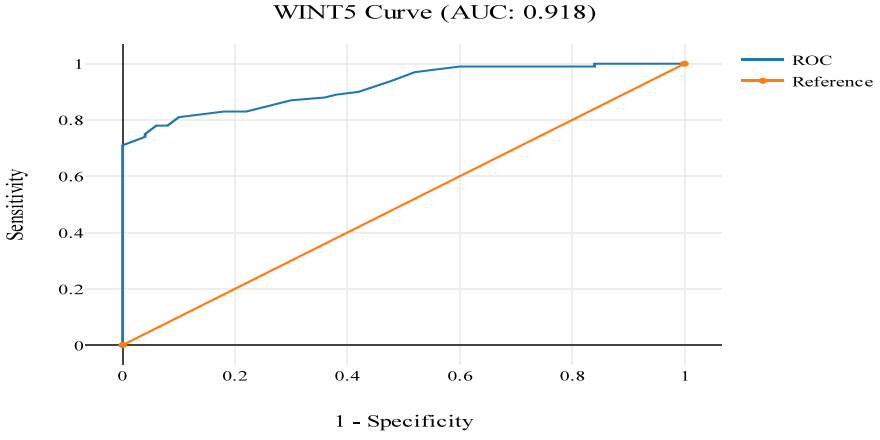

Fig. 3. ROC curve for evaluation of Wint5a in patients with HF.

Table 4. Pearson's correlation of BNP, uPa, Wint5a with other parameters.

Parameters		Marker of Heart Failure		
		BNP	uPa	Wint5a
Cardiac Enzymes				
BNP	R	1	–0.04	0.35
	P	-	0.602	< 0.001
uPa	R	–0.04	1	–0.06
	P	0.602	-	0.453
Wint5a	R	0.35	–0.06	1
	P	< 0.001	0.453	-
CK	R	0.56	–0.13	0.61
	p	< 0.001	0.119	< 0.001
LDH	R	0.56	–0.1	0.62
	p	< 0.001	0.238	< 0.001
AST	R	0.33	–0.12	0.27
	p	< 0.001	0.139	0.001
Variable Parameters				
RBG	R	0.48	–0.14	0.59
	P	< 0.001	0.098	< 0.001
K	R	0.18	0.02	0.11
	P	0.026	0.831	0.186
Ca	R	–0.04	–0.02	–0.07
	P	0.668	0.842	–0.382
CRP	R	0.56	–0.12	0.64
	P	< 0.001	0.154	< 0.001
Troponin	R	0.57	–0.11	0.59
	P	< 0.001	0.163	< 0.001
Lipid Profile				
Cholesterol	R	0.52	–0.08	0.61
	P	< 0.001	0.359	< 0.001
TG	R	0.55	–0.12	0.61
	P	< 0.001	0.129	< 0.001
HDL	R	–0.19	–0.04	0.03
	P	0.018	0.609	0.693
LDL	R	0.56	–0.14	0.53
	P	< 0.001	0.098	< 0.001
VLDL	R	0.32	–0.01	0.26
	P	< 0.001	0.925	0.001
Renal Function				
Urea	R	0.47	–0.03	0.46
	P	< 0.001	0.697	< 0.001
Creatinine	R	0.45	–0.11	0.28
	p	< 0.001	0.175	< 0.001
Uric Acid	r	0.41	–0.2	0.37
	p	< 0.001	0.013	< 0.001

Table 4 shows Pearson's correlations between BNP, uPA and Wint5a and other parameters, we found significant positive correlation between BNP and Wint5a, our patients have diabetes and RD that's mean increment of Wint5a explained by the important role in the presence of T2DM and chronic kidney complications. [25]

Creatine kinase, lactate dehydrogenase, and aspartate dehydrogenase in HF patients

This research demonstrated a substantial increase in creatine kinase (CK), which is similar to Lizzy M et al. [28] The increase in CK may imply more muscle injury in elderly persons. [28] Creatine kinase (CK) plays a pivotal role in the diagnosis and treatment of heart failure (HF), and its raised levels have been linked to the progression of the disease and heightened death rates. Nevertheless, it is crucial to acknowledge that the levels of CK may also be increased in alternative medical disorders, including renal failure, rhabdomyolysis, and hypothyroidism, [29] in the current study we noted that patients with both HF and RD have higher levels of CK than patients have only HF as shown in Table 2.

Lactate dehydrogenase (LDH) serves as a cytoplasmic enzyme diagnostic for myocardial damage. [30] The presence of elevated amounts of LDH has been

documented in several cardiac illnesses, as seen in Table 2 Specifically, the G1 group exhibits greater LDH levels, and these patients are diagnosed with both heart failure (HF) and respiratory distress (RD). The observed increase in blood LDH levels resulting from organ damage may be attributed to substantial cellular demise, leading to the loss of cytoplasmic content. Diseases such as sudden myocardial infarction, anemia, pulmonary embolism, hepatitis, and acute renal failure are among the potential causes of tissue damage.[31] Our findings are consistent with other research that has shown a positive association between increased LDH levels and worse outcomes in individuals diagnosed with acute decompensated heart failure, acute aortic syndromes, and acute aortic dissection.[32]

In this study there was increase of AST levels in HF patients as shown in Table 2 but it is non-significant, in previous studies by Eman S. Mahmood and Luay A. Al-Helaly evaluated AST in animal model. Decrease in the level of AST may be the patients treated with drug that effect on AST levels also there was association between AST and the risk for CVD or mortality are mostly hypothetical.[33]

Diabetes in HF patients

Individuals diagnosed with heart failure (HF) are more susceptible to the development of diabetes mellitus;[34] the coexistence of diabetes in individuals diagnosed with heart failure has been shown to be linked with elevated rates of hospitalization, cardiovascular morbidity, and death. Moreover, patients with heart failure are more likely to acquire diabetes, thereby increasing their susceptibility to this condition.[35] In our investigation, all participants exhibit diabetes, a condition in which both heart failure (HF) and renal dysfunction (RD) often co-occur.[36]

Potassium, calcium, troponin, c-reactive protein in studied groups

Patients with heart failure (HF) should be worried about hyperkalemia, and there may be a link between the use of angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) and an increased risk of hyperkalemia.[37] The K levels of our patients exhibit a notable disparity when compared to the control group, as seen in Table 1 Elevated levels of potassium have the potential to cause arrhythmias that pose a significant risk to an individual's life, particularly in individuals with reduced heart function.[38] Previous studies have shown a significant association between hyperkalemia and adverse outcomes in individuals with heart failure (HF), such as heightened rates of hospitalization and death.[39] The monitoring and regulation of potassium levels play a critical role in the treatment of heart failure (HF) in order to maximize the advantages of medicine while minimizing the dangers associated with hyperkalemia (elevated potassium levels).[40]

Calcium is of utmost importance in facilitating the contraction of heart muscle and the transmission of electrical signals.[41] Disruptions in calcium management may manifest in heart failure patients, hence impacting the myocardium's contractile function.[42] Several investigations have shown that the presence of aberrant calcium handling in heart failure might potentially contribute to the deterioration of cardiac function and the occurrence of arrhythmias.[43] Nevertheless, the precise processes and the significance of calcium in the context of heart failure remain subjects of ongoing investigation. Calcium channel blockers and other pharmaceutical agents that specifically target calcium channels are sometimes used in the treatment of heart failure.[44]

C-reactive protein (CRP) is a biomarker of inflammation that has been linked to the development and progression of heart failure (HF).[45] Elevated levels of C-reactive protein (CRP) in individuals with heart failure (HF) often signify heightened inflammation within the cardiovascular system.[46] Elevated levels of C-reactive protein (CRP) have been associated with unfavorable outcomes in heart failure (HF), such as heightened rates of hospitalization and an increased risk of death.[47] Monitoring CRP levels can provide valuable insight into the inflammatory status of patients with heart failure and may aid in treatment decision-making.[48]

Troponin serves as a cardiac biomarker that is used for the purposes of diagnosing and evaluating cardiac injury.[49] Elevated levels of troponin in individuals with heart failure (HF) often signify cardiac stress or damage, since the myocardium is impaired in the context of HF.[50] The elevation of troponin is often seen in acute diseases such as heart attacks. However, studies have shown that even slight elevations in troponin levels among patients with heart failure are correlated with worse outcomes.[51]

Lipid profile in HF patients

Lipids are an essential component for individuals with heart failure (HF) due to the crucial involvement of fatty acids (FA) in maintaining cellular membranes, regulating gene expression, and exhibiting anti-inflammatory characteristics.[52] The maintenance of the heart's structural and functional integrity heavily relies on lipid metabolism. Cardiac

myocyte plays a vital role in this process by coordinating the management of fatty acid absorption, beta-oxidation, and mitochondrial oxidative phosphorylation, which are all critical for the synthesis of ATP in the heart. Prior research has shown that the heart mostly generates adenosine triphosphate (ATP) via metabolizing fatty acids, which accounts for around 40–60% of ATP generation.[53] Triglyceride (TG) serves as a fundamental provider of necessary fatty acids for the production of myocardial ATP, and the regulation of TG metabolism plays a crucial role in governing myocardial lipid metabolism. Furthermore, an excessive buildup of lipids in the cardiac tissue might interfere with the regular communication between cells, resulting in programmed cell death, enlargement of the heart muscle, and impaired cardiac function.[54] The malfunction of mitochondrial substrate oxidation and respiration, excessive lipid buildup, and heart failure are consequences of cardiac pressure overload.[55]

The complex interplay between renal function and cardiac disease has attracted considerable interest within the medical field. The kidneys and the heart exhibit a strong interconnection, wherein impairment in one organ often impacts the functioning of the other. This article examines the complex role of renal function in the context of cardiac disease, emphasizing the reciprocal influence and clinical significance of this association. Renal failure has the potential to cause compromised control of salt and water, leading to the accumulation of fluid in the body.[56] The presence of excessive fluid in the body is a contributing factor to the elevation of blood pressure, which is recognized as a significant risk factor for the development of heart disease.[57] Hypertension exerts pressure on the heart by augmenting its workload and facilitating the remodelling of cardiac tissues, which may result in the development of diseases such as left ventricular hypertrophy and heart failure.[58]

As renal function deteriorates, there is a progressive buildup of uremic toxins in the circulation. The presence of these toxins is associated with endothelial dysfunction, oxidative stress, and inflammation, all of which have a role in the pathogenesis and advancement of atherosclerosis and coronary artery disease. Uremic toxins have the potential to cause direct harm to cardiac myocytes, resulting in compromised contractility and heightened vulnerability to arrhythmias.[59] The coexistence of acute kidney injury (AKI) and chronic kidney disease (CKD) is often seen in conjunction with cardiovascular illness. Acute kidney injury (AKI) has the potential to initiate cardiac events, but chronic kidney disease (CKD) is a robust and autonomous indicator of unfavorable cardiovascular outcomes. Both illnesses exhibit overlapping risk factors and pathophysiological pathways, highlighting the interconnectedness of renal and heart health.[60]

Conclusion

In HF patients, BNP serves as a valuable biomarker with diagnostic and prognostic significance. Combining BNP measurements with clinical assessment and additional biomarkers can enhance the evaluation of heart and renal health, ultimately guiding treatment strategies and improving patient outcomes. For the uPA, the utilization of urokinase in HF patients with RD requires a cautious and individualized approach.

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Authors' declaration

- Conflicts of Interest: None.
- We hereby confirm that all the figures and tables in the manuscript are ours. Furthermore, any figures and images, that are not ours, have been included with the necessary permission for republication, which is attached to the manuscript.
- No animal studies are presented in manuscript.
- Authors sign an ethical consideration's approval.
- Ethical Clearance: The project was approved by the local ethical committee at University of Technology- Iraq.

Authors' contribution statement

Conception and Study Design: M. A. H. A. Acquisition of data: M. A. H. A. and W. R. A. Data analysis and interpretation: W. R. A. and R F S. Drafting of the article: R F S. Revision and proofreading: W. R. A. Final approval: M. A. H. A., W R A., and R F S.

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تقييم الببتيد الدماغي الناتريوتريك و منشط البلازمينوجين يوروكيناز والونكلس من النوع الخامس في المرضى العراقيين الذين يعانون من قصور القلب

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المستخلص

في مرضى قصور القلب الذين يعانون من ضعف وظائف الكلى ، يكون الببتيد الدماغي الناتريورتك بمثابة علامة حيوية ذات أهمية تشخيصية وإنذارية. بينما ضعف وضائف الكلى تؤثر على مستويات ال الببتيد الدماغي الناتريورتك، وان فهم العلاقه بين الضغط على القلب وضعف وظائف الكلى والحاله السريريه امر بالغ الاهميه في دقه التفسير .إن الجمع بين قياسات الببتيد الدماغي الناتريورتك والتقييم السريري والمؤشرات الحيوية الإخرى يمكن أن تعزز تقييم صحة القلب والكلى، مما يؤدي في النهاية إلى توجيه استراتيجيات العلاج وتحسين نتائج المرضى. بالنسبة لليوروكاينيز، فإن استخدام اليوروكيناز في مرضى قصور القلب المصابين بأمراض الكلى يتطلب اتباع نهج حذر وفردي.في حين أن خاصيه التخثر تعمل على معالجة مضاعفات القلب والأوعية الدموية، فإن التعقيد المشترك بين وظائف الكلى، ومخاطر النزيف، وتوازن السوائل يتطلب تقييمًا دقيقًا وإدارة بحذر. يعد النهج المتكامل والمراقبه باستمرار والتواصل المنتظم بين المتخصصين أمرًا ضروريًا للتغلب على تعقيدات علاج اليوروكيناز في هذه الفئة من المرضى. ودورالونكلس في مرضى القلب الذين يعانون من خلل في وظائف الكلى يدل على إمكاناته كرابط قوي يربط بين صحة القلب والأوعية الدموية والكلى. وفي حين لا تزال هناك تحديات، ان فهمنا ومعرفه مسار الإشارات قد يمهد الطريق لأدوات تشخيصية مبتكرة وتداخلات علاجية تعالج التداخل المعقد بين مضاعفات القلب والكلى.

الكلمات المفتاحية: الببتيد الدماغي الناتريوتريك، فشل القلب، اليوروكاينيز، الونكلس النوع الخامس، امراض القلب.