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The role of Brain Natriuretic Peptide in evaluating Left Ventricle function among patient with chronic renal failure on maintenance hemodialysis: the impact of body mass index

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Abstract: Both chronic renal failure (CRF) and heart failure (HF) can predispose to pressure load or volume overload with subsequent elevation of serum brain natriuretic peptide (BNP) levels. This study tends to evaluate the role of BNP as a predictor of left ventricular function among patient with chronic renal failure on maintenance hemodialysis. Methods: This is a perspective cross-sectional study, including 89 (45 males and 44 females) patients on maintenance hemodialysis followed up for six months. BNP level, glomerular filtration and body mass index of the patients were measured and left ventricular function (EF%) was detected by echocardiography at the start of the study and after three and six months between October 2016 and April 2017. Results: Of 89 patients, 13 were underweight, 56 had a healthy weight, and 20 were overweight. There was a significant negative association between BNP level and both EF% and BMI ($P < 0.001$, $P < 0.001$) respectively. During the follow up of these patients there was a clear trend for BNP to be higher among patients with impaired left the ventricular function. There was also a strong inverse association between BNP level and GFR ($P < 0.001$). Conclusion: BNP levels show a strong inverse association with EF%, BMI and GFR in patients with CRF. Currently, BNP widely used by most health institutions to predict left ventricular function. However, both BMI and GFR considered a significant confounder of BNP measurement in patients with compromised renal status.

1 Introduction

The natriuretic peptide family include a group of peptides, like atrial and B-type which are myocardial cell origin, C-type of endothelial cell origin and Dendroaspis-type natriuretic peptide. These agents attract considerable attention in the last few decades due to their essential role in the physiology of heart, blood vessels, kidneys and body fluid [1]. B-type natriuretic peptide has been proposed as an efficient biomarker for prediction of left ventricular function and in diagnosis and treatment of heart failure [2,3]. Chronic renal failure kills millions of population each year, and cardiovascular disease is the leading cause of death among these patients, accounting for more than 50% of all deaths[4]. Early identification of patients with CRF who are at a heightened cardiovascular risk is an essential goal in the treatment of these patients. Excess weight gain



considered as a significant risk factor for several diseases including diabetes, essential hypertension and chronic kidney diseases [5]. Overweight also associated with low B-type natriuretic peptide in patients with preserved left ventricular function and those with impaired left ventricular function [6]. Thus two significant factors can confound the interpretation of elevated BNP in patients with CRF are renal dysfunction and BMI. This study is an attempt to evaluate the role of B-type natriuretic peptide in the assessment of left ventricular function in patients with CRF with particular emphasis on the impact of body mass index.

2 SUBJECTS, MATERIALS and METHODS

The present study is a perspective cross-sectional study included 89 patients (45 males and 44 females) with CRF on regular hemodialysis (HD) with normal cardiac ejection fraction who is attending dialysis unit at Al-Hussien Teaching Hospital in Thiqr city during the period from March 2016 to January 2017. Their ages ranged from 15-75 years old. All patients enrolled in this study underwent two sessions of dialysis per week. The hemodialysis was done with patients on supine position and each dialysis session last 3 hours.

For every patient participated in this study, the following investigations were performed

2.1 About ten ml of blood was collected from every participant into two separate tubes containing lithium heparin for measurement of plasma creatinine and plasma BNP.

2.2 BMI was calculated as the body weight in (kilograms) divide by the square of height in (meters):

BMI kg/ m²= weight in (kilograms) / square of height in (meters)

According to the values of BMI patients with CRF were classified into three groups

- group I, include 13 patients with underweight (BMI below 18.9 kg/m²).
- Group II, include 56 patients with normal body weight (BMI of 18.9-24.9 kg/m²)
- Group III, including 20 patients with overweight (BMI of 25-30 kg/m²) (WHO, 2006).

2.3 The glomerular filtration rate measured depending on plasma creatinine (PCr) level to estimate the creatinine clearance(Ccr) by Cockcroft-Gault equation :

$$\text{Ccr (mL /min)} = \frac{(140 - \text{age in years}) \times \text{lean body weight (kg)}}{\text{PCr (mg/dL)} \times 72}$$

2.4 The measurement of EF% done by M-mode echocardiogram.

The data obtained by this study was analysed By using SPSS (statistical package of social science version 23). Chi-square and Fissure test had been used for studying the association. P value of < 0.05 where consider as significant.

3 Results

3.1 Relationship between EF% and the brain natriuretic peptide

The result of this study shows a highly significant inverse relationship ($P < 0.0001$) between levels of EF % and BNP pg/min. Thirteen(52%) out of 25 patients with EF% value of (40-50) had BNP level higher than 450 pg/ml, and 12(48%) of them had BNP level more than 125 pg/ml. While almost all patients with EF% value of (56-70) had a BNP level less than 450 pg/ml. In general, the level of the BNP tends to increase as the level of the EF % decrease as shown in Table (.15).

Table 1: The relationship between EF% and the brain natriuretic peptide level among patients with CRF.

EF%	BNP pg/ml			Total	X2 p value
	<125	126-450	>450		
40-55	0 (0.0%)	12 (48%)	13 (52%)	25 (100%)	30.441
56-70	20 (31.2%)	44 (68.8%)	0 (0.0%)	64 (100%)	.0001

Total	20	56	13
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3.2 Relationship between glomerular filtration rate and the EF% level. The result of this study also exhibits a significant relationship ($p < 0.0001$) between values of EF% and the GFR ml/min. Thirty-eight (86.4%) of patients with GFR more than 15 ml/min have EF% value of (56-70), and only 6 (13.6 %) patients had EF% value of (40-55). While 26 (57.8%) patients out of 45 patients with GFR < 15 ml/min had EF% value of (56-70) and 19 (42.2 %) patients had EF% value of (40-55). as shown in figure (1).

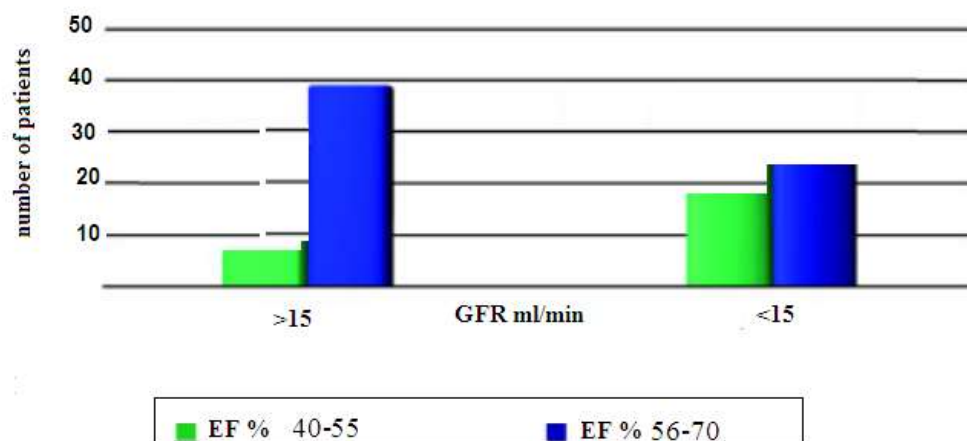


Figure1: The relationship between glomerular filtration rate and the EF% level.

3.3 The relationship between glomerular filtration rate and the brain natriuretic peptide level: There was a statistical inverse association between the concentration of GFR ml/min and BNP pg/ml (P -value = 0.001). As the level of GFR decline, the plasma level of the BNP tends to increase as shown in table (2) and figure(2).

Table 2: The relationship between glomerular filtration rate and the brain natriuretic peptide level.

GFR LEVEL	BNP LEVEL pg/ml			Total	X2
ml/min	<125	126-450	>450		p value
>15	13 (65%)	30 (53.6 %)	1 (7.7 %)	44	26.414
<15	7 (35%)	26 (.46.4%)	12 (92 .3 %)	45	.001
total	20 (100%)	56 (100%)	13(100%)	89	

3.4 Relationship between BMI and BNP

The result of this study showed a statistically significant inverse relationship between BMI (kg/m²) and the level of BNP (pg/ml) when measured by fischer exact test ($p < 0.0001$) as shown in table (2). The serum level of BNP in patients with underweight (BMI of less than 18.9) was more than 450 pg/ml while in patients with healthy body weight (BMI 18.9-24.9) the BNP level was (126-450 pg/ml), and in overweight patients (BMI 25-30) the level of BNP was (0-125 pg/ml) as shown in table (3).

Table 3: Relationship between BMI and BNP.

BNP level pg/ml	BMI kg/m ²			Total	Fischer exact and p-value
	Below 18.9	18.9-24.9	25-30		
0-125	0 (0.0%)	0 (0.0%)	20 (100%)	20	178.000
126-450	0 (0.0%)	56 (100%)	0 (0.0%)	56	0.0001
>450	13 (100%)	0 (0.0%)	0 (0.0%)	13	
Total	13	56	20	89	

3.5 Relationship between BMI and EF%

Concerning the relationship between BMI and EF % , the result of this study showed that 11 (55%) patients with overweight have EF% values of (40-55) while 13 (23%) patients with healthy body weight and only 1(8%) patient with underweight have an EF% values of (40-55). On the other hand, about 43 (77 %) patients with healthy body weight and 12 (92 %) of patients with underweight have an EF% value of (56-70). According to these results, there was great statistically significant relationship between BMI and the level of EF% when measured by Fischer exact test ($p < 0.0001$) as shown in table (4).

Table 4: Relationship between BMI and EF%.

EF% LEVEL	BMI(kg/m ²)			Total	Fischer exact and p-value
	<18.9	18.9-24.9	25-30		
40-55	1 (7.7 %)	13 (23.2%)	11 (55 %)	25	41.106
56-70	12 (92.3 %)	43 (76.8 %)	9 (45%)	64	0.0001
Total	13 (100%)	56 (100%)	20 (100%)	89	

4 Discussion

The Left ventricular hypertrophy and left ventricular dysfunction are among the most common complication in patients with CKD. Furthermore, cardiovascular diseases represent the major underlying causes of morbidity and mortality in patients with CRF [7,8]. The utility of BNP as a diagnostic tool for left ventricular dysfunction in patients with normal kidney function is well known [9], and this finding explained by the pressure or volume overload which is the primary stimulus to synthesis and secretion of BNP [10]. However, most studies showed that the volume of water content was elevated and renal clearance of BNP was decreased in patients with CKD compared to patients with normal kidney function both factors may contribute to further increase of BNP level in patients with CRF who had compromised ventricular function. The result of this study shows a highly significant inverse relationship ($P < 0.0001$) between levels of EF % and BNP pg/min among patients with CRF. The increase in serum BNP level also inversely correlated with GFR ($P < 0.0001$), where the level of BNP tends to increase as GFR value decline.

Several investigators indicated that elevated BNP concentrations could result from renal failure [11,12]. The results of this study confirmed previous studies that BNP concentrations were progressively higher in patients with progressively more advanced CRF, especially in patients with a GFR of less than 15 mL/min/1.73 m², as shown in Figure 2. Decreased renal clearance is the major underlying causes of raises BNP concentrations.

According to the result of this study and other studies, the presence of renal dysfunction complicates the interpretation of the concentration of BNP as a diagnostic biomarker for cardiovascular disorder. The upper limit of normal also has to be considered. Using manufacturer's recommended cutoffs for BNP (100 pg/mL for male and 150 pg/mL for women) as a "diagnostic test" for impaired left ventricular dysfunction will over-diagnose heart failure in patients with CRF.

The result of this study also showed a statistically significant inverse relationship between BMI (kg/m²) and the level of BNP (pg/ml) when measured by fischer exact test ($p < 0.0001$) as shown in table (2). Despite the inverse relationship between BMI and BNP, the BNP levels were higher in patients with low EF% and lower GFR levels among patients with overweight. The inverse relationship between obesity and circulating BNP levels can be explained in obese subjects with normal renal function by high GFR among such individual which result in the effective clearing of these molecules from circulation [12]. In patients with impaired renal function, the possible explanation is an increased synthesis of clearance receptor(c-receptor) by adipose tissues [12].

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