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## The Importance of Brain Natriuretic Peptide in Assessment Left Ventricle Function Among Patient with Chronic Kidney Disease on Maintenance Hemodialysis: The Impact of the Dialysis Session

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**Abstract:** Background: chronic renal failure (CRF) characterized by increased plasma level of brain natriuretic peptide (BNP) due to increase peptide secretion and decrease BNP clearance due to impaired renal function. This peptide is a biomarker of cardiovascular disorders which are the common causes of morbidity and mortality in patients with CRF. The present study tend to evaluate the role of BNP as a predictor of left ventricular function among patient with chronic renal failure on maintenance hemodialysis(HD) with particular concern to dialysis session frequency. Methods: A total of 90 patients with CRF who visited the dialysis unit at Al-Hussein Teaching Hospital in Thi-Qar city for maintenance hemodialysis were included in this study. They were divided into three groups according to the number of dialysis session per week. BNP level, glomerular filtration rate(GFR) of the patients were measured and left ventricular function (EF%) was detected by echocardiography. Results: There was a significant negative association between BNP level and EF% ( $P < 0.001$ ). BNP level was significantly lower in patients with three dialysis session per week in comparison with those patients who perform single session per week ( $P < 0.001$ ). 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% and GFR in patients with CRF. Patients with frequent dialysis had better left ventricular function manifested by lower BNP level and higher EF% than those patients with less frequent dialysis session.

**Keywords:** brain natriuretic peptide, Chronic renal failure, dialysis frequency, left the ventricular function

### Introduction

B-type natriuretic peptide is a vasopeptide hormone belong to a family of peptide hormones which include in addition to BNP, atrial natriuretic peptide (ANP), C-type (CNP) and Dendroaspis-type natriuretic peptide(DNP) [1]. B-type natriuretic peptide is a counter-regulatory hormone; it induces natriuresis, diuresis, vasodilation, inhibition of the renin-angiotensin system and sympathetic nervous system activity. The main sources of BNP are the ventricular myocyte[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 important goal in the treatment of these patients. In addition to left ventricular hypertrophy which the main stimulus to secrete BNP[5] patients with CRF had extra sodium retention due to impaired renal function, leading to the expansion of the extracellular fluid volume with the compensatory release of BNP due to cardiac wall stretch[6,7]. This study attempt to evaluate the role of BNP as a predictor of left ventricular function among patient with CRF on maintenance HD with special concern to dialysis session frequency.

### Subjects, materials and methods

The present study is a perspective cross-sectional study included 90 patients (46 males and 44 females) with CRF on regular HD with normal cardiac EF% 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. They were divided into three groups according to the number of dialysis session per week :

1. **Group I:** including 4 patients who received a single session of HD per week.
2. **Group II:** included 34 patients who received two sessions of HD per week.
3. **Group III:** include 52 patients who received three sessions of HD 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:

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

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

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

The data obtained by this study was analyzed 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 .

### Results

#### *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. Fourteen (54%) out of 26 patients with EF% value of (40-50) had BNP level higher than 450 pg/ml, and 12 (46%) 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 (1).

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		
<b>40-55</b>	0(0.0%)	12(48%)	14(52%)	26 (100%)	30.441 .0001
<b>56-70</b>	20(31.2%)	44(68.8%)	0(0.0%)	64 (100%)	
<b>Total</b>	20	56	14	90	

***The relationship between the number of dialysis per week sessions and the brain natriuretic peptide level***

Table (2), Shows the statistically significant relationship between a number of dialysis sessions per week and BNP level. The level of BNP was higher among patients who receive only one session of dialysis per week and tend to be lower among patients who receive two sessions of dialysis per week and the most moderate values seen among patients who receive three session of dialysis per week ( $p < 0.0001$ ).

Table (2 ): The relationship between a number of dialysis sessions per week and the brain natriuretic peptide level.

Dialysis/ week	BNP pg/ml LEVEL				X2 P-value
	0-125	126-450	>450	TOTAL	
Single Session	0 (0.0%)	1(25 %)	3 (75%)	4(100%)	16.003 0.0001
Two sessions	13(38%)	15(44. %)	6(18%)	34(100%)	
Three sessions	7 (13.5%)	40(77 %)	5(9.5%)	52( 100%)	
Total	20	56	14	90	

***The relationship between the number of dialysis sessions per week and glomerular filtration rate***

There was a statistically significant relationship between the number of dialysis sessions per week and the GFR level. The GFR level found to be lower among patients who receive only one session of dialysis per week and tend to be higher among patients who receive three sessions of dialysis per week ( $p < 0.001$ ) as shown in table (3).

Table (3): The relationship between the number of dialysis sessions per week and the glomerular filtration rate.

Dialysis/ week	GFR LEVEL			X2 P-value
	>15 ml/min	< 15 ml/min	Total	
Single Session	0( 0.0%)	4(100%)	4 (100%)	14.264 0.0001
Two sessions	13 (38.2%)	21 (61.8%)	34 (100%)	
Three sessions	31 (60 %)	21 (40 %)	52 (100%)	
Total	44	46	90	

***The relationship between the number of dialysis sessions per week and the cardiac ejection fraction***

Table (4) Shows a significant relationship between the number of dialysis sessions per week and EF% level. The value of the EF% found to be low among patients who receive only one session of dialysis per week and tend to be higher among patients who receive three session of dialysis per week ( $p < 0.005$ ).

Table (4): The relationship between the number of dialysis sessions per week and the cardiac ejection fraction.

Dialysis/ week	EF% LEVEL			X2 P-value
	40-55	56-70	Total	
Single Session	4(100%)	0(0.0%)	4(100%)	10.004 0.005
Two sessions	11(32%)	23 (68%)	34(100%)	
Three sessions	10(19%)	41(81%)	52(100%)	
Total	26	64	90	

***The relationship between glomerular filtration rate and the brain natriuretic peptide level***

There was a statistical inverse association between the level 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 (5).

Table (5): The relationship between glomerular filtration rate and the brain natriuretic peptide level.

GFR LEVEL ml/min	BNP LEVEL pg/ml			Total	X2 P-value
	<125	126-450	>450		
>15	13 (65%)	30 (53.6 %)	1(7.7 %)	44	26.414 .001
<15	7 ( 35%)	26 (46.4%)	13 (92 .3 %)	46	
total	20 (100%)	56 (100%)	14(100%)	90	

**Discussion**

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[8,9]. The utility of BNP as a diagnostic tool for left ventricular dysfunction in patients with normal kidney function is well known[10], and this finding explained by the pressure or volume overload which is the main stimulus to synthesis and secretion of BNP[11]. 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 tend to increase as GFR value decline.

Several investigators indicated that elevated BNP concentrations could result from renal failure[12,13]. 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 m<sup>2</sup>. 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.

According to the result of this study, there was a significant decrease in BNP level in patients with CRF who underwent three dialysis sessions per week in comparison with those who had single dialysis sessions per week. The high plasma concentration of BNP in patients with single dialysis is thought to be multifactorial secondary to extracellular volume expansion, concomitant heart disease, and reduced renal clearance[13,14]. BNP is eliminated from plasma mainly through natriuretic peptide receptors and degraded by neutral endopeptidases in addition to being excreted via glomerular filtration. Moreover, frequent dialysis probably plays an important role in the removal of uremic solutes, excess water; it also may improve inflammation that is a prominent risk factor for cardiovascular disorders[14].

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