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Investigation of factors related to N-terminal pro-B type natriuretic peptide levels in hemodialysis patients; a single center study

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ABSTRACT

Introduction: Introduction: N-terminal pro-B type natriuretic peptide (NT-proBNP) can be used to diagnose cardiac and renal disease. The association of NT-pro BNP with demographic, clinical and biochemical factors in hemodialysis is unclear.
Objectives: This study aimed to examine association of NT-pro BNP and mentioned factors in hemodialysis patients.
Patients and Methods: This study was conducted on 78 end-stage renal disease (ESRD) patients under hemodialysis. Demographic data, lipid profile and electrolytes were recorded. NT-proBNP was checked simultaneously and its association with mentioned factors were assessed.
Results: The average NT-pro BNP level was 890.52 ± 700.87 pg/mL (range: 0.1-3343 pg/mL). Serum level of NT-pro BNP was statistically in association with total cholesterol ($P = 0.002$; r=-0.348), low density lipoprotein (LDL) ($P = 0.09$; r= -0.292), high density lipoprotein (HDL) ($P = 0.06$; r=-0.310) and serum triglyceride ($P = 0.018$; r=-0.269) while having a direct relationship with serum ferritin ($P = 0.022$; r=0.274), alkaline phosphatase (ALP) ($P = 0.048$; r=0.224) and duration of hemodialysis ($P = 0.005$; r=0.321).
Conclusion: Lipid profile and ferritin are associated with NT-pro BNP levels. This can reflect possible prognostic role of NT-proBNP among ESRD patients on hemodialysis.

Original

Implication for health policy/practice/research/medical education:
In a study on 78 end-stage renal disease patients under hemodialysis, we found serum level of NT-pro BNP was statistically in association with total cholesterol, LDL, HDL and serum triglyceride while having a direct relationship with ferritin, ALP and duration of hemodialysis.
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Introduction

End-stage renal disease (ESRD) is known as impairment in kidneys function, which is associated with reduced glomerular filtration rate (GFR). In this term, patients with ESRD may need renal replacement therapy (RRT) that hemodialysis is one of the most common methods of RRT (1,2).

Patients under hemodialysis are seriously prone to cardiovascular complications. N-terminal pro-B type natriuretic peptide (NT-proBNP) is a compound secreted from ventricle in response to increased blood volume causing natriuresis, antagonizing sympathetic nervous system and renin-aldosterone system (3).

Previous studies have presented that heart diseases, such as ischemia and heart failure are directly correlated with increased levels of NT-proBNP, since this level plays a prognostic role in cardiac diseases. Furthermore higher levels of this factor are in correlation with the prognosis of diabetic patients and stroke (5,6). It is possible that NT-proBNP had an association with the prognosis of chronic kidney diseases, although information about this association is inadequate and limited (7).

Objectives

Considering the importance of kidney failure, its subsequent problems and potential effects of NT-pro BNP

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on this disease, we aimed to assess the association of NT-pro BNP level with various demographic and biochemical factors of ESRD patients under dialysis.

Patients and Methods

Patient selection

This is a cross-sectional study on 78 ESRD patients referred to Amin hospital (affiliated to Isfahan University of Medical Sciences). All hemodialysis patients willing to participate in this study were included and patients with acute infection and history of acute coronary artery disease were excluded. Then patients' demographic data were collected through interviewing and their records.

Demographic information were age, gender, duration of hemodialysis in a session, total duration of hemodialysis, history of diabetes, history of hypertension and amount of fluid used for dialysis.

Additionally, height, weight, abdominal circumference and body mass index (BMI) of patients were measured before hemodialysis. Then a blood sample of 5 cc was taken from each patient before initiation of hemodialysis and the serum was separated. The level of NT-pro BNP was measured using ELISA method.

In addition complete blood count (CBC), uric acid level, lipid profile including triglyceride (TG), total cholesterol (TC), high density lipoprotein (HDL-C) and low density lipoprotein (LDL-C), electrolytes including sodium (Na), potassium (K), magnesium (Mg), calcium (Ca) and phosphorus (P), liver tests including aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP), renal associated tests including creatinine (Cr) and blood urea nitrogen(BUN), serum iron, ferritin, transferrin iron binding capacity (TIBC), albumin and vitamin D levels were assessed.

Ethical issues

The research followed the Tenets of the Declaration of Helsinki. The Ethics Committee of Isfahan University of Medical Sciences approved the study (No. IR.MUI.REC.1396.3.198). Written informed consent was obtained from the study patients. This study was extracted from M.D thesis of Farbod Bonakdar at this university (#396198).

Statistical analysis

Data were analyzed using SPSS software version 20. Descriptive statistics were reported in percentage and mean± standard deviation. For analytics, independent *t* test, and covariance, Pearson's correlation test and Spearman's test were used. *P* value less than 0.05 was considered significant.

Results

This study was conducted on 78 ESRD patients under hemodialysis with a mean age of (59.09 ± 15.091) years. Fifty (64.1%) patients were male. The average NT-pro BNP level was 890.52±700.87 pg/mL (range; 0.1-3343 pg/mL). Demographic, clinical and laboratory characteristics of the samples are summarized in Table 1.

Table 2 shows that gender, diabetes and hypertension had no significant relationship with NT-proBNP levels ($P > 0.05$).

We also found, significant inverse associations of cholesterol ($P = 0.002$; r = -0.348), triglyceride ($P = 0.018$; r = -0.269), LDL-C ($P = 0.009$; r = -0.292) and HDL-C ($P = 0.006$; r = -0.310) with levels of NT-pro BNP. However, ferritin ($P = 0.022$; r = 0.274), alkaline phosphatase ($P = 0.048$; r=0.224) and total number of months that patients have been hemodialysis ($P = 0.005$; r = 0.321) had a significant positive association with NT-proBNP level.

Multiple linear regression test shows, variables such as

Table 1. Demographics and laboratory data

	N	Mean	SD
Age (y)	78	59.44	15.10
Height (cm)	77	163.21	10.44
Weight (kg)	78	68.33	14.10
Abdominal circumference (cm)	70	86.67	21.55
Dialysis per week (n)	78	2.87	0.41
Duration of each dialysis (h)	78	3.8367	0.44381
Duration of dialysis treatment (mon)	74	35.34	23.72
URR (%)	78	0.95	2.43
BMI (kg/m^2)	77	25.81	6.33
NT-proBNP (pg/mL)	78	890.53	700.87
Vitamin D (ng/mL)	78	28.35	35.74
Hemoglobin (g/dL)	78	11.02	1.90
Hematocrit (%)	78	35.93	5.61
BUN (mg/dL)	78	104.44	33.30
Cr (mg/dL)	78	7.24	2.27
Cholesterol (mg/dL)	77	164.09	41.91
Triglyceride (mg/dL)	77	140.48	72.84
Calcium (mg/dL)	78	8.40	0.63
Phosphorus (mg/dL)	78	4.94	1.33
AST (IU/L)	78	22.23	13.07
ALT (IU/L)	78	21.06	16.27
ALP (IU/L)	78	543.68	397.09
Albumin (g/dL)	78	3.77	0.46
Iron	76	91.61	58.01
Transferrin iron binding capacity	73	264.64	85.04
HDL (mg/dL)	78	57.58	29.26
LDL (mg/dL)	78	89.87	35.74
Ferritin (ng/mL)	70	536.64	337.16
Parathyroid hormone (pg/mL)	74	182.28	125.50
Uric acid (mg/mL)	72	5.67	1.18
Magnesium (mg/dL)	78	2.08	0.24

Abbreviations: URR, Urea reduction rate; BMI, body mass index; BUN, blood urea nitrogen; Cr, Creatinine; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, and alkaline phosphatase; HDL, High density lipoprotein; LDL, Low density lipoprotein.

Table 2. Association of NT-proBNP level with gender, diabetes mellitus and hypertension

	(SD) Mean	Median (min-max)	*P* value
Gender			
Male	913.4 (704.2)	772.5 (0.1-2966)	0.702
Female	849.6 (705.8)	768 (93-3343)	
Diabetes mellitus			
Yes	875.8 (623.1)	823 (93-2966)	0.779
No	833.2 (688.5)	621 (0.1-2570)	
Hypertension			
Yes	875.83 (623.16)	823 (93-2966)	0.507
No	833.2 (688.6)	621 (0.1-2570)	

MCH, ferritin, cholesterol and uric acid, can predict 37% of variations of NT-pro BNP level (R2 = 0.37, $P < 0.005$). The association of serum NT-pro BNP with ferritin is significant and positive, however, this association for other variables such as MCH, cholesterol and uric acid, were negatively significant because the influence of cholesterol was higher than the MCH and uric acid (significant negative effect) (Table 3 and Figures 1 to 4).

Discussion

In the current study, we examined the association of demographic, clinical and laboratory factors of CKD patients under hemodialysis with serum level of NT-pro BNP. We found the level of NT-pro BNP had an inverse association with total cholesterol, LDL-C, HDL-C and triglycerides while serum NT-pro BNP was positively correlated with serum ferritin and ALP and also duration of hemodialysis.

Our results on lipid profile were similar to the study by Bao et al, which presented inverse relationship of NT-pro BNP level with lipid profile among cases with metabolic syndrome (8). Our results were similar to the study of Zhu et al, who assessed association of NT-pro BNP with metabolic factors among a large number of normal population. They also detected an inverse association of NT-pro BNP level with mentioned lipid factors (3). Previous studies have presented similar results (9). It is possible that dyslipidemia can damage endothelial cells, as a result, the release of endopeptidase leads to a reduction in NT-pro BNP (3).

Table 3. Multiple regression analysis to test whether PBNP is dependent on ferritin, cholesterol, MCH and uric acid

Model	Unstandardized Coefficients B	Standardized Coefficients Beta
Constant	4154.49**	
Ferritin	0.66**	0.385**
Cholesterol	-5.39**	-0.391**
MCH	-72.92**	-0.317**
Uric acid	-120.06*	-0.237*

B, Unstandardized regression coefficients; Beta, standardized regression coefficients. *P<0.05 , **P<0.001.

While no association was found between NT-pro BNP, weight, BMI, and abdominal circumference, Wang et al found decreased levels of NT-pro BNP among obese people compared with normal BMI ones(10). It was concluded that presence of higher levels of fat cells is accompanied with higher rate of NT-pro BNP removal from circulation as there are many receptors for this compound in adipose tissue (11).

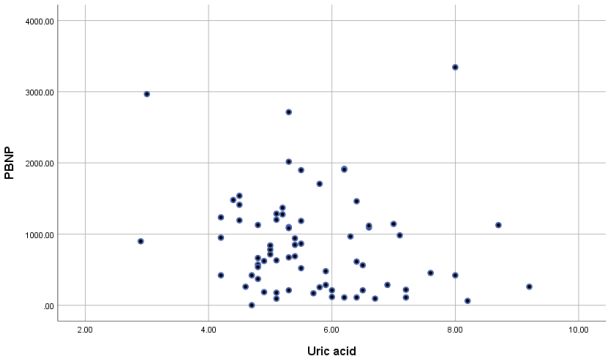

Figure 1. Association of serum NT-proBNP with serum uric acid.

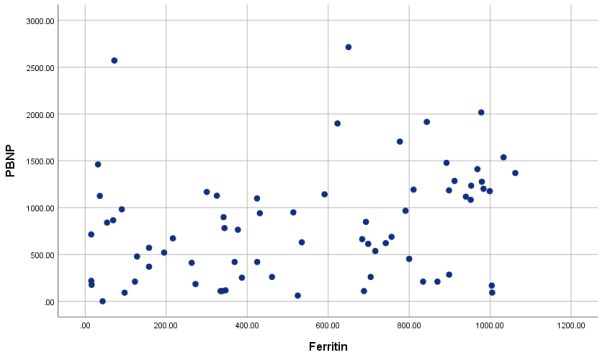

Figure 2. Association of serum NT-proBNP with serum ferritin.

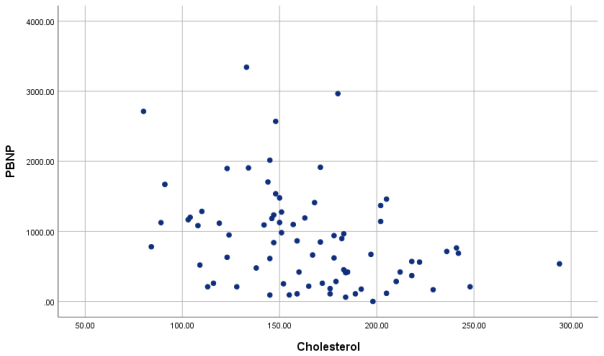

Figure 3. Association of serum NT-proBNP with serum cholesterol.

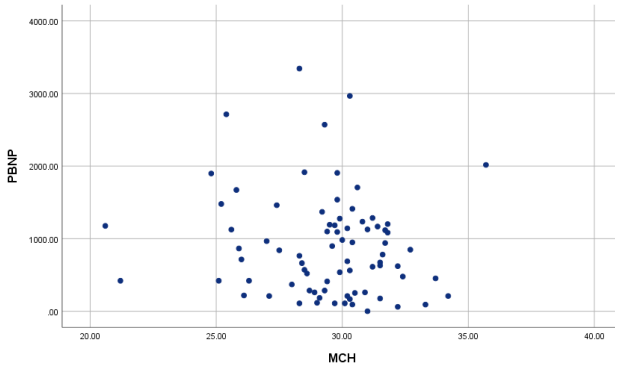

Figure 4. Association of serum NT-proBNP with MCH.

The other finding of our study was direct association of ALP with NT-pro BNP. Increased levels of ALP among ESRD patients under dialysis is associated with their mortality (12, 13). Another study conducted on 68 patients with 4th and 5th stages of chronic kidney disease (CKD) mentioned an increase end-diastolic volume in heart failure, which leads to an increase in end-diastolic pressure leading to an increase in left atrial and pulmonary capillary wedge pressure, causing pulmonary hypertension. Finally, pulmonary hypertension can induce right-side heart failure and liver congestion. In addition, volume overload leads to higher secretion of NT-pro BNP, thus control of volume overload and blood pressure may lead to lower levels of ALP and also BNP (14). Accordingly, NT-pro BNP can be considered as a prognostic factor of mortality among CKD cases. We also found the association of dialysis duration with NT-pro BNP levels. Santosh et al presented that ESRD gradually causes increased pulmonary arterial pressure and consequently right ventricular heart failure. These both can lead to higher levels of NT-pro BNP in these patients (15,16).

Conclusion

This study showed a possible association of NT-pro BNP with various metabolic and clinical factors of CKD patients under hemodialysis. It seems that NT-pro BNP can be considered as a prognostic factor in these critical patients, however, further studies with larger populations are recommended.

Limitations of the study

This is a pilot study requires larger samples to better find the possible association of NT-pro BNP with other metabolic and clinical factors of hemodialysis patients.

Authors' contribution

HN; the concept and design. FB gathered the data and manuscript preparation. PH supervised data collection and guidance. PN analyzed the data and interpretation. HN finalized the manuscript. All authors read and signed the final paper.

Conflicts of interest

The authors declared no competing interests.

Ethical considerations

Ethical issues (including plagiarism, misconduct, data fabrication, falsification, double publication or submission, redundancy) have been completely observed by the authors.

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