

# Cardiometabolic Risk Factors in Relation to Serum NT-Pro-BNP level: A Cross-Sectional Study Among CKD Patients

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## ABSTRACT

**Introduction:** CKD patients suffer from increased rate of mortality and morbidity due to cardiovascular diseases, compared to general population. Cardiometabolic biomarker N-Terminal Pro-BNP has become a useful tool for quick screening and assessment for cardiovascular diseases. The aim of the present study is to find out the relationship between serum NT-Pro-BNP level and cardiometabolic risk factors among CKD patients without symptoms or history of cardiac diseases.

**Materials & Methods:** This cross-sectional study among 149 CKD patients was conducted from January to December 2020 at National Institute of Kidney Diseases and Urology (NIKDU), Dhaka. Anticoagulant free venous blood samples were assayed for serum NT-Pro-BNP by electrochemiluminescence immunoassay. Serum creatinine, total cholesterol, triglyceride, high-density lipoprotein, calcium, phosphate, uric acid, eGFR, albumin and total protein of the study population were assessed and recorded during data collection.

**Results:** Mean age of study population was  $50.0 \pm 12.4$  years, male predominant (53%). Mean serum NT-Pro-BNP level was lowest ( $335.7 \pm 213.3$  pg/ml) for patients with CKD stage 1 and highest ( $15644.6 \pm 2197.5$  pg/ml) for patients with CKD stage 5. Mean serum creatinine was lowest ( $1.55 \pm 1.54$  mg/dl) for CKD stage 1 patients and highest ( $5.71 \pm 2.75$  mg/dl) for CKD stage 5 patients and this was statistically significant ( $p < 0.05$ ). Mean serum total cholesterol, triglyceride, phosphate and uric acid were increased with disease severity and this increase

was statistically significant ( $p < 0.05$ ). Mean eGFR, serum albumin and total protein were decreasing with disease severity, and this decrease was also statistically significant ( $p < 0.05$ ). Serum NT-Pro-BNP had significant positive correlation ( $r = 0.61$ ,  $p < 0.05$ ) with serum creatinine and significant negative correlation with total cholesterol, triglycerides, serum phosphorus, serum uric acid, eGFR and serum albumin.

**Conclusion:** Serum NT-Pro-BNP could be the potential screening tool for CKD with cardiovascular diseases and can provide prognostic information of major cardiovascular events.

**Keywords:** NT-Pro-BNP, Cardiometabolic Risk Factors, CKD.


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## INTRODUCTION

Plasma concentrations of N-terminal pro-brain natriuretic peptide (NT-Pro-BNP) has been firmly associated with cardiac function.<sup>1</sup> NT-Pro-BNP is the inactive fragment of B-Type Natriuretic Peptide (BNP), and is released from cardiac myocytes into the circulation in response to pressure and volume overload.<sup>2,3</sup> Therefore, measurement of the increased serum levels of NT-Pro-BNP may have the potential to facilitate the accuracy of diagnosis and prognosis for patients with heart failure. The risk of cardiovascular complications is significantly higher among patients with CKD compared to general population.<sup>4</sup> Studies have shown elevated serum NT-Pro-BNP levels to be associated with the advancement of CKD.<sup>5</sup>

Prior studies among CKD patients showed an association between serum NT-Pro-BNP levels and prevalent cardiovascular complications, offering the potential for early detection and risk assessment for cardiac diseases and serve as a prognostic parameter.<sup>6-10</sup> Since serum NT-Pro-BNP clearance depends on renal function, there is a high prevalence of elevated serum NT-Pro-BNP level in asymptomatic patients with chronic kidney disease (CKD), due to reduced renal clearance.<sup>6,11-13</sup> Serum NT-Pro-BNP has been shown to predict cardiovascular events in apparently healthy individuals, where elevated serum NT-Pro-BNP level is often followed by poor cardiac outcome among patients, irrespective of renal function.<sup>8,9,14,15</sup> Thus, NT-Pro-BNP is

recognized as diagnostically and prognostically meaningful biomarker for patients with heart failure.<sup>16</sup> In recent years, NT-Pro-BNP measurement has been widely recognized as an auxiliary diagnostic tool for heart failure.<sup>17</sup> The aim of the present study is to assess the relationship between serum NT-Pro-BNP level and cardiometabolic risk factors among a cohort of CKD patients without symptoms or history of cardiac diseases.

**MATERIALS & METHODS**

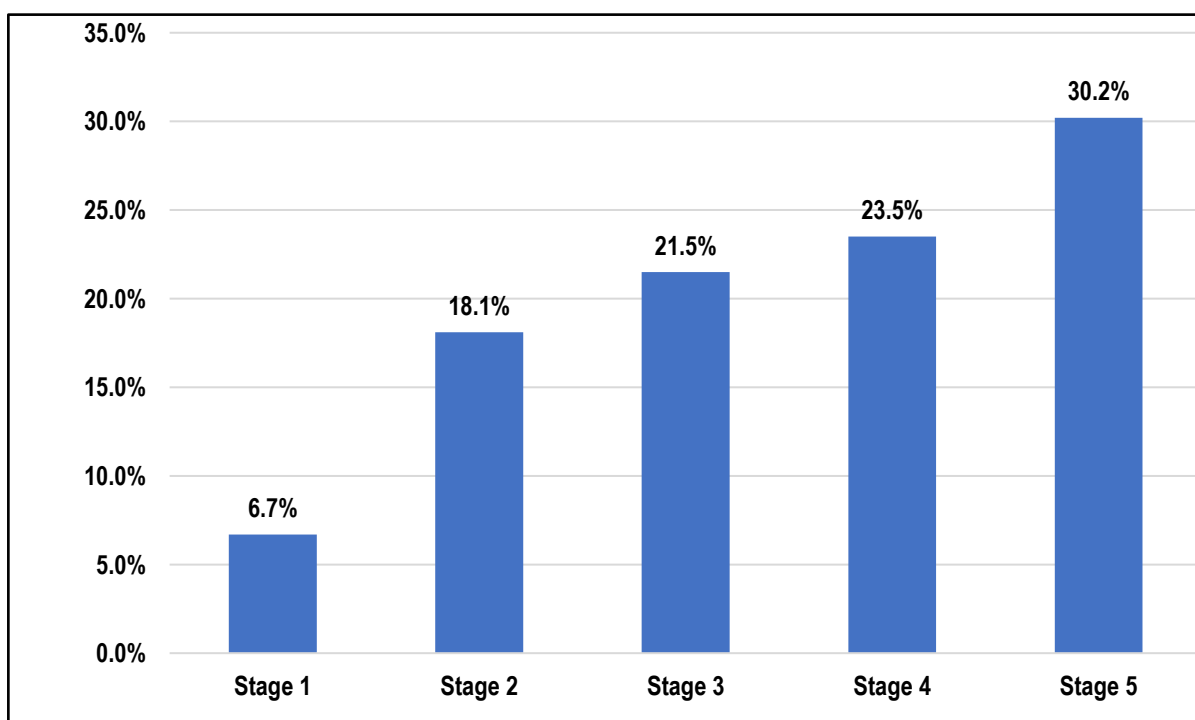
This was a cross-sectional study among 149 CKD patients of stage 1 to 5 was conducted from January to December 2020 at National Institute of Kidney Diseases and Urology (NIKDU), Dhaka. Adult CKD patients age ≥ 18 years were included in the study. CKD patients with symptoms or history of cardiac diseases were excluded from the study, along with patients with malignancy, liver or thyroid dysfunction, nephrotic syndrome, history of organ transplant and on immunosuppressive medications. Purposive sampling technique was used. Ethical clearance was issued from the ethical review committee of NIKDU.

Aims and objectives of the study along with its procedure, risks and benefits of the study were explained to the respondent in easily understandable local language. Data were collected through face-to-face interview using a semi-structured questionnaire and data collection tools, only after Informed written consent was taken from the respondents. Serum NT-Pro-BNP levels were measured for each study subject. Anticoagulant free venous blood samples were assayed for serum NT-Pro-BNP by electrochemiluminescence immunoassay. Serum creatinine, total cholesterol, triglyceride, high-density lipoprotein, calcium, phosphate, uric acid, eGFR, albumin and total protein of the study population was assessed and recorded during data collection. All data were compiled and processed with the help of statistician and were analysed using windows-based computer software with Statistical Packages for Social Sciences (SPSS-25) (SPSS Inc, Chicago, IL, USA). Quantitative data were expressed as mean & standard deviation. Categorical data were expressed as frequency and percentage. Comparison of variables were done by ANOVA and Chi-square test. For all statistical test, p-values less than 0.05 was considered significant.

**Table I: Descriptive statistics of the study population (n = 149)**

| Variables         | Value       |
|-------------------|-------------|
| Age (years)       | 50.0 ± 12.4 |
| Age group (years) |             |
| 18 – 29           | 9 (6.0%)    |
| 30 – 44           | 40 (26.8%)  |
| 45 – 59           | 65 (43.6%)  |
| 60 – 69           | 35 (23.5%)  |
| Sex               |             |
| Male              | 79 (53.0%)  |
| Female            | 70 (47.0%)  |

Data are presented as n (%) or mean ± SD.



**Figure 1: Distribution of study population according to CKD staging (n = 149)**

Table II: Biochemical parameters of study population (n = 149)

| Variables                         | CKD Stage 1 (n = 10) | CKD Stage 2 (n = 27) | CKD Stage 3 (n = 32) | CKD Stage 4 (n = 35) | CKD Stage 5 (n = 45) | Significance (p)    |
|-----------------------------------|----------------------|----------------------|----------------------|----------------------|----------------------|---------------------|
| NT-Pro-BNP level (pg/ml)          | 335.70 ± 213.3       | 790.10 ± 330.5       | 2554 ± 1021.5        | 1144.1 ± 325.2       | 15644.6 ± 2197.5     | < 0.05 <sup>a</sup> |
| Serum Creatinine (mg/dL)          | 1.55 ± 1.54          | 1.72 ± 0.72          | 2.69 ± 2.03          | 3.04 ± 1.65          | 5.71 ± 2.75          | < 0.05 <sup>a</sup> |
| Total Cholesterol (mg/dl)         | 121.27 ± 29.91       | 183.21 ± 41.68       | 185.71 ± 65.08       | 204.57 ± 62.26       | 209.49 ± 74.95       | < 0.05 <sup>a</sup> |
| Triglyceride (mg/dl)              | 132.84 ± 87.63       | 153.66 ± 40.65       | 186.68 ± 78.95       | 214.67 ± 89.41       | 224.25 ± 114.92      | < 0.05 <sup>a</sup> |
| high-density lipoprotein (mg/dl)  | 45.45 ± 25.07        | 44.27 ± 20.72        | 40.18 ± 15.62        | 39.09 ± 18.93        | 38.19 ± 11.47        | 0.53                |
| Calcium (mgm/dl)                  | 10.26 ± 2.76         | 9.39 ± 1.74          | 9.20 ± 1.59          | 9.03 ± 2.06          | 8.94 ± 1.64          | 0.31                |
| Phosphate (mg/dl)                 | 3.70 ± 1.03          | 4.06 ± 0.97          | 4.40 ± 1.46          | 4.88 ± 1.41          | 5.47 ± 2.09          | < 0.05 <sup>a</sup> |
| Uric acid (mg/dL)                 | 4.67 ± 1.45          | 5.03 ± 0.97          | 5.30 ± 1.32          | 5.67 ± 1.51          | 6.01 ± 2.02          | < 0.05 <sup>a</sup> |
| eGFR (ml/min/1.73m <sup>2</sup> ) | 90.80 ± 3.55         | 78.22 ± 11.08        | 45.53 ± 16.46        | 24.20 ± 6.1          | 10.18 ± 2.35         | < 0.05 <sup>a</sup> |
| Albumin (gm/dl)                   | 45.66 ± 4.57         | 45.04 ± 5.72         | 46.00 ± 7.10         | 42.20 ± 7.74         | 38.81 ± 9.61         | < 0.05 <sup>a</sup> |
| Total Protein                     | 8.88 ± 2.25          | 7.49 ± 2.92          | 6.42 ± 2.45          | 7.27 ± 1.8           | 6.95 ± 1.53          | < 0.05 <sup>a</sup> |

Data are presented as mean ± SD.

<sup>a</sup> ANOVA was done and p values < 0.05 was considered statistically significant.

Table III: Association between serum NT-Pro-BNP and biochemical parameters (n = 149)

| Variables                         | Pearson Correlation (r) | Significance (p)    |
|-----------------------------------|-------------------------|---------------------|
| S. Creatinine (mg/dL)             | 0.61                    | < 0.05 <sup>b</sup> |
| Total cholesterol (mg/dl)         | -0.32                   | < 0.05 <sup>b</sup> |
| Triglyceride (mg/dl)              | -0.38                   | < 0.05 <sup>b</sup> |
| HDL (mg/dl)                       | -0.07                   | 0.43                |
| S. Calcium (mg/dL)                | -0.08                   | 0.34                |
| S. Phosphorus (mg/dL)             | -0.19                   | < 0.05 <sup>b</sup> |
| S. Uric Acid (mg/dL)              | -0.33                   | < 0.05 <sup>b</sup> |
| eGFR (mL/min/1.73m <sup>2</sup> ) | -0.41                   | < 0.05 <sup>b</sup> |
| S. Albumin (g/dL)                 | -0.46                   | < 0.05 <sup>b</sup> |
| S. Total protein (g/dL)           | -0.08                   | 0.34                |

<sup>b</sup> Pearson Correlation was done and p values < 0.05 was considered statistically significant.

## RESULTS

Out of 149 CKD patients, 43.6% were from age group 45 – 59 years, followed by 26.8% from age group 30 – 44 years. Mean age of the study population was 50.0 ± 12.4 years (Table I). Study population was predominantly male (53%).

Study included patients from CKD stage 1 to 5 and highest proportion (30.2%) of the study population had CKD stage 5, followed by 23.5% with CKD stage 4 and 21.5% with CKD stage 3 (Figure 1).

Biochemical parameters of the study population were assessed (Table II). Mean NT-Pro-BNP level was lowest (335.7 ± 213.3 pg/ml) for patients with CKD stage 1, which increased with increasing CKD staging, reaching highest (15644.6 ± 2197.5 pg/ml) for patients with CKD stage 5. The difference in serum NT-Pro-BNP among patients with different CKD stages were found to be statistically significant (p < 0.05). Mean serum creatinine was lowest (1.55 ± 1.54 mg/dl) for CKD stage 1 patients and highest (5.71 ± 2.75 mg/dl) for CKD stage 5 patients. The difference in serum creatinine among patients with different CKD stages were found to be statistically significant (p < 0.05). Mean serum total cholesterol, triglyceride, phosphate and uric acid were increased

with disease severity and this increase was statistically significant (p < 0.05). Mean eGFR, serum albumin and total protein were found to be decreasing with disease severity and this decrease was also statistically significant (p < 0.05).

Correlation of serum NT-Pro-BNP with biochemical parameters were observed (Table III). Serum NT-Pro-BNP had significant positive correlation (r = 0.61, p < 0.05) with serum creatinine and had significant negative correlation with total cholesterol, triglycerides, serum phosphorus, serum uric acid, eGFR and serum albumin.

## DISCUSSION

Present study assessed the relationship between serum NT-Pro-BNP level and cardiometabolic risk factors among CKD patients without prior cardiovascular events. Mean age of the CKD patients enrolled in the study was 50.0 ± 12.4 years with 43.6% being from 45 – 59 years of age. This is consistent with a 2019 study where majority of the CKD patients were below 60 years of age with a mean age of 48.6 years.<sup>18</sup> Respondents in present study was predominantly male (53.0%). Similar findings have been shown in

previous studies among CKD patients where 62.9% study population were male.<sup>19</sup>

In present study, mean serum NT-Pro-BNP level was lowest ( $335.7 \pm 213.3$  pg/ml) for patients with CKD stage 1, which significantly increased with CKD staging, reaching highest ( $15644.6 \pm 2197.5$  pg/ml) for patients with CKD stage 5. This change in serum NT-Pro-BNP in relation to CKD staging is consistent with previous study among CKD patients.<sup>20-22</sup> Decreased clearance through kidney and volume overload, along with other comorbidities play crucial parts in this change in serum NT-Pro-BNP level.<sup>23,24</sup> Biochemical parameters of the study population were assessed. Mean NT-Pro-BNP level was lowest ( $335.7 \pm 213.3$  pg/ml) for patients with CKD stage 1, which increased with increasing CKD staging, reaching highest ( $15644.6 \pm 2197.5$  pg/ml) for patients with CKD stage 5. The difference in serum NT-Pro-BNP among patients with different CKD stages were found to be statistically significant ( $p < 0.05$ ). This is consistent with a 2020 study, showing patients with higher NT-Pro-BNP having a significantly higher risk of eGFR decline of more than 40%, compared to patients with lower NT-Pro-BNP.<sup>25</sup> The main way of estimating GFR is a blood test to determine serum creatinine. As kidney function declines, the level of creatinine increases. In the present study, mean serum creatinine was lowest ( $1.55 \pm 1.54$  mg/dl) for CKD stage 1 patients and highest ( $5.71 \pm 2.75$  mg/dl) for CKD stage 5 patients. The difference in serum creatinine among patients with different CKD stages were found to be statistically significant ( $p < 0.05$ ). Serum NT-Pro-BNP also had significant positive correlation ( $r = 0.61$ ,  $p < 0.05$ ) with serum creatinine. Prior studies showed higher NT-Pro-BNP levels were associated with an increased odds of having an increase in serum creatinine by  $\geq 0.3$  mg/dl, which is consistent with present study findings.<sup>25-28</sup>

Mean serum total cholesterol, triglyceride, phosphate and uric acid were increased with disease severity and this increase was statistically significant ( $p < 0.05$ ). CKD patients are at increased risk of developing cardiovascular disease related morbidity and mortality.<sup>29</sup> Dyslipidemia, often present in this patient population, is an important risk factor for CVD development.<sup>30</sup> For cholesterol and triglyceride, specific quantitative and qualitative changes seen at different stages of renal impairment are associated with the degree of glomerular filtration rate decline. Although an elevated uric acid level is commonly observed among CKD patients, whether it is simply a biomarker of impaired kidney function or has a true pathogenic role in kidney function remains inconclusive.<sup>31,32</sup> As uric acid is primarily excreted by the kidneys, it is difficult to evaluate the causal influence of uric acid on the progression of CKD in epidemiological research. Mean eGFR, serum albumin and total protein were found to be decreasing with disease severity and this decrease was also statistically significant ( $p < 0.05$ ). Correlation of serum NT-Pro-BNP with biochemical parameters was observed. Serum NT-Pro-BNP showed significant negative correlation with total cholesterol, triglycerides, serum phosphorus, serum uric acid, eGFR and serum albumin. This is consistent with prior study showing similar relationship between NT-Pro-BNP and total cholesterol and triglycerides.<sup>33</sup>

Prior studies showed that NT-Pro-BNP was negatively correlated with eGFR, which is consistent with present study findings.<sup>34</sup> As for serum albumin, significant negative correlation with NT-Pro-

BNP has been shown in other studies, which is consistent with present study findings.<sup>35-37</sup>

## CONCLUSION

This study was undertaken to evaluate serum NT-Pro-BNP level at different stages of CKD patients and observe its association with cardiometabolic risk factors. Given the significant association of NT-Pro-BNP with cardiometabolic risk factors like serum creatinine, total cholesterol, triglycerides, serum phosphorus, serum uric acid, eGFR and serum albumin found in present study; it was apparent that elevated serum NT-Pro-BNP could function as a screening tool for patients with CKD who should proceed to further evaluation. Serum NT-Pro-BNP has the potential to be used routinely as a screening tool for patients with CKD. Measurements of serum NT-Pro-BNP could provide prognostic information of major cardiovascular events beyond traditional risk factors.

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