

# Association of Serum NT-Pro-BNP Level with Echocardiography Results Among CKD Patients: A Cross Section Study at NIKDU in Dhaka Bangladesh

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## ABSTRACT

**Background:** Mortality of CKD patients remains high because of high prevalence of cardiovascular diseases among them. Identifying serum biomarkers that are useful in profiling cardiovascular risk is an important goal in the treatment of CKD patients. The aim of the present study is to assess the relationship between serum NT-Pro-BNP level as a biomarker and Echocardiography findings among CKD patients without symptoms or history of cardiac diseases.

**Method:** 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. Serum NT-Pro-BNP levels were measured for each study subject. All patients had a comprehensive M-mode, two-dimensional, and doppler echocardiogram. Association between serum NT-Pro-BNP levels and echocardiogram findings were assessed.

**Result:** 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, which significantly increased with the progression of CKD stages, reaching highest ( $15644.6 \pm 2197.5$  pg/ml) for patients with CKD stage 5. There was statistically significant ( $P < 0.05$ ) reduction in LVEF with increasing severity of CKD and significant negative correlation ( $r = -0.316$ ,  $p < 0.001$ ) between

serum NT-Pro-BNP level and LVEF. Mean IVSTd and PWTd, both significantly ( $p < 0.05$ ) increased with the progression of CKD stages. Significant positive correlation was seen between serum NT-Pro-BNP and IVSTd ( $r = 0.361$ ,  $p < 0.001$ ) and between serum NT-Pro-BNP and PWTd ( $r = 0.448$ ,  $p < 0.001$ ).

**Conclusion:** NT-Pro-BNP has the potential to be used routinely as a screening tool for patients with CKD for cardiac structural and functional abnormalities.

**Keywords:** NT-Pro-BNP, Echocardiography, Chronic Kidney Disease.


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## INTRODUCTION

N-Terminal Pro-BNP (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>1,2</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>3-6</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>7-10</sup>

The risk of cardiovascular complications is significantly higher among patients with CKD compared to general population.<sup>11</sup> Studies have shown elevated serum NT-Pro-BNP levels to be associated with the advancement of CKD.<sup>12</sup> Prior studies among CKD patients also 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>5-7,13</sup>

However, controversy remains regarding the precise influence of CKD on serum NT-Pro-BNP levels.<sup>14</sup> Serum NT-Pro-BNP can be used as a biomarker to identify and predict cardiac diseases, but the effect of CKD on this marker is not fully understood.

The aim of the present study is to assess the relationship between serum NT-Pro-BNP level and Echocardiography findings among a cohort of CKD patients without symptoms or history of cardiac diseases.

## MATERIALS & METHODS

This 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 under the strict supervision of the institute authority and only after receiving the ethical clearance from the ethical review committee of NIKDU.

Only adult CKD patients on the basis of selection criteria were enrolled 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. 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. All patients had a comprehensive M-mode, two-dimensional, and Doppler echocardiogram. For each individual radiological parameters were evaluated through Left Ventricular Ejection Fraction (LVEF), Left Ventricular Internal Diameter End Diastole (LVIDd), Interventricular Septum Thickness in Diastole (IVSTd), Posterior Wall Thickness End Diastole (PWTd) and Regional Wall Motion Abnormalities (RWMA).

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%)
CKD Stage	
Stage 1	10 (6.7%)
Stage 2	27 (18.1%)
Stage 3	32 (21.5%)
Stage 4	35 (23.5%)
Stage 5	45 (30.2%)

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

**Table II: Distribution of study population according to NT-Pro-BNP level (n = 149).**

CKD Stage	NT-Pro-BNP level (pg/ml)	Significance (p)
Stage 1	335.7 ± 213.3	0.001 <sup>a</sup>
Stage 2	790.1 ± 330.5	
Stage 3	2554 ± 1021.5	
Stage 4	1144.1 ± 325.2	
Stage 5	15644.6 ± 2197.5	

Data are presented as mean ± SD.

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

**Table III: Distribution of study population according to Echocardiography findings (n = 149).**

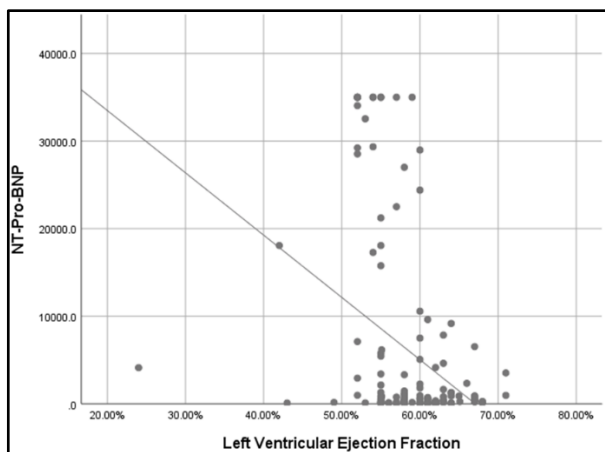
Variables	CKD Stage 1 (n = 10)	CKD Stage 2 (n = 27)	CKD Stage 3 (n = 32)	CKD Stage 4 (n = 35)	CKD Stage 5 (n = 45)	Significance (p)
LVEF (%)	61.1 ± 4.86	60.44 ± 3.66	60.28 ± 6.21	59.26 ± 7.3	56.82 ± 4.21	0.019 <sup>a</sup>
LVIDd (mm)	43.2 ± 8.07	42.04 ± 7.29	40.16 ± 5.52	39.94 ± 6.57	38.71 ± 5.42	0.132 <sup>a</sup>
IVSTd (mm)	8.5 ± 1.43	9.02 ± 1.48	9.41 ± 1.49	9.55 ± 1.91	10.51 ± 1.4	0.001 <sup>a</sup>
PWTd (mm)	8.1 ± 1.52	8.5 ± 0.78	8.79 ± 1.5	9.07 ± 1.61	10.11 ± 1.66	0.001 <sup>a</sup>
RWMA						
Yes	0	1 (3.7%)	1 (3.7%)	2 (5.7%)	1 (2.2%)	0.887 <sup>b</sup>
No	10 (100.0%)	26 (96.3%)	31 (96.9%)	33 (94.3%)	44 (97.8%)	

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

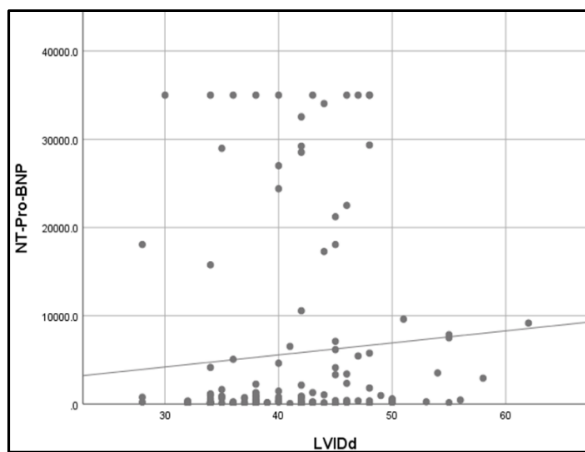
LVEF – Left Ventricular Ejection Fraction, LVIDd – Left Ventricular Internal Diameter End Diastole, IVSTd – Interventricular Septum Thickness in Diastole, PWTd – Posterior Wall Thickness End Diastole, RWMA – Regional Wall Motion Abnormalities.

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

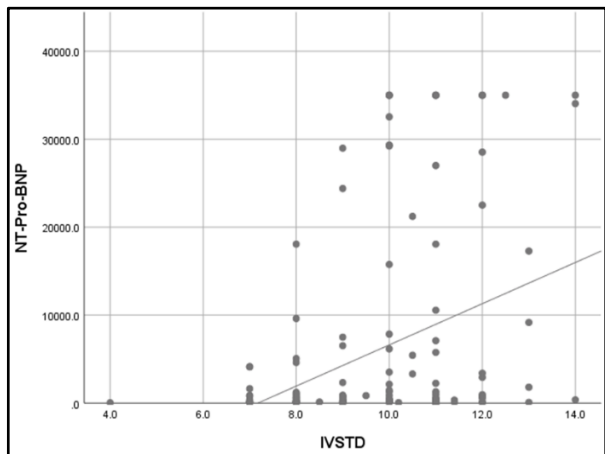
<sup>b</sup> Chi-square test was done and p values < 0.05 was considered statistically significant.



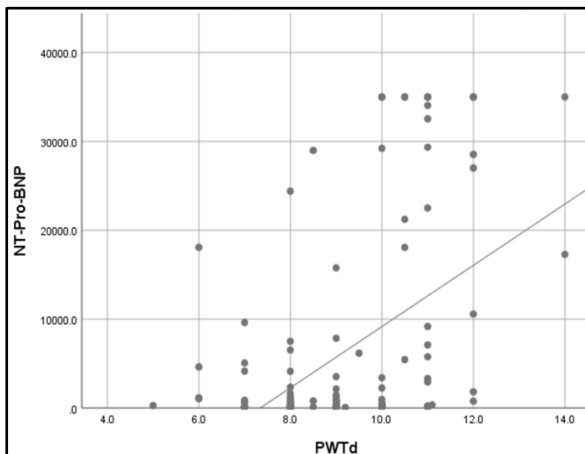
**Fig 1 (a): Correlation between Left Ventricular Ejection Fraction and NT-Pro-BNP (r = - 0.316, p < 0.001).**



**Fig 1 (b): Correlation between LVIDd and NT-Pro-BNP (r = 0.119, p = 0.150).**



**Fig 1 (c): Correlation between IVSTd and NT-Pro-BNP (r = 0.361, p < 0.001).**



**Fig 1 (d): Correlation between PWTd and NT-Pro-BNP (r = 0.448, p < 0.001).**

**Figure 1: Scatter diagram showing Pearson’s correlations between NT-Pro-BNP and echocardiography results.**

**RESULTS**

This study included 149 CKD patients of CKD stage 1 to 5. Mean age was 50.0 ± 12.4 years, while age group 45 – 59 years had highest proportion (43.6%) of CKD patients (Table I). Study population was male predominant with 53% male and 47%

female. As for CKD staging, 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. NT-Pro-BNP level was measured for the study population. Mean NT-Pro-BNP level was lowest (335.7 ± 213.3

pg/ml) for patients with CKD stage 1 (Table II), 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 ( $P = 0.001$ ).

Echocardiogram was done for each of the study subjects (Table III). Mean left ventricular ejection fraction (LVEF) was found to be highest ( $61.1 \pm 4.86\%$ ) for patients with CKD stage 1 which subsequently decreased with the severity of the CKD. Difference in LVEF among different CKD stages were found to be statistically significant ( $p < 0.05$ ). Mean left ventricular internal diameter end diastole (LVIDd) was also highest ( $43.2 \pm 8.07$  mm) among patients with CKD stage 1 and lowest ( $38.71 \pm 5.42$  mm) among patients with CKD stage 5. The difference in LVIDd among different CKD stages were found to be statistically not significant ( $p = 0.132$ ). Mean interventricular septum thickness in diastole (IVSTd) was lowest ( $8.5 \pm 1.43$  mm) for patients with CKD stage 1 and subsequently increased with CKD progression, reaching peak ( $10.51 \pm 1.4$  mm) at patients with CKD stage 5. The difference among different CKD stages were statistically significant ( $p < 0.05$ ). Similarly mean posterior wall thickness end diastole (PWTd) also increased with CKD stages, starting from  $8.1 \pm 1.52$  mm for patients with CKD stage 1 and peaking at  $10.11 \pm 1.66$  mm for patients with CKD stage 5 and these differences were statistically significant ( $p < 0.05$ ). Presence of regional wall motion abnormalities (RWMA) were also observed and no statistically significant differences among different CKD stages were found ( $p = 0.887$ ).

Correlation of serum NT-Pro-BNP with various Echocardiography findings were observed (Figure 1). Serum NT-Pro-BNP was found to have significant negative correlation ( $r = -0.316$ ,  $p < 0.001$ ) with left ventricular ejection fraction (LVEF). Serum NT-Pro-BNP was found to have weak positive correlation ( $r = 0.119$ ,  $p = 0.150$ ) with left ventricular internal diameter end diastole (LVIDd). Significant positive correlation was seen between serum NT-Pro-BNP and interventricular septum thickness in diastole (IVSTd) ( $r = 0.361$ ,  $p < 0.001$ ) and between NT-Pro-BNP and posterior wall thickness end diastole (PWTd) ( $r = 0.448$ ,  $p < 0.001$ ).

## DISCUSSION

This cross-sectional study was carried out with the aim to measure serum NT-Pro-BNP level in patients at different stages of CKD and its association with cardiac morphology measured by echocardiogram. Mean age of the CKD patients enrolled in the study was  $50.0 \pm 12.4$  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>15</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>16</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 the progression of CKD stages, 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>14,17,18</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>19,20</sup>

Present study showed a statistically significant reduction in LVEF with increasing severity of CKD and significant negative correlation ( $r = -0.316$ ,  $p < 0.001$ ) between serum NT-Pro-BNP level and LVEF. This is consistent with other studies among similar patients, indicating that LVEF declined with increase in serum NT-Pro-BNP level and serum NT-Pro-BNP can be used in the diagnosis and prognosis of heart failure. Moreover, analyses of factors related to the occurrence of heart failure in patients with different cardiac functions suggested that increased NT-Pro-BNP level and decreased LVEF level were the relevant and independent risk factors for heart failure.<sup>21–25</sup>

Mean LVIDd showed non-significant reduction with CKD severity and weak positive correlation ( $r = 0.119$ ,  $p = 0.150$ ) with serum NT-Pro-BNP level. This is consistent with a 2005 study showing serum NT-Pro-BNP increasing with left ventricular internal dimensions.<sup>26</sup> Mean IVSTd was lowest ( $8.5 \pm 1.43$  mm) for patients with CKD stage 1 and subsequently significantly ( $p < 0.05$ ) increased with CKD progression, reaching peak ( $10.51 \pm 1.4$  mm) at patients with CKD stage 5. Similarly mean PWTd also significantly ( $p < 0.05$ ) increased with the progression of CKD stages, starting from  $8.1 \pm 1.52$  mm for patients with CKD stage 1 and peaking at  $10.11 \pm 1.66$  mm for patients with CKD stage 5. Significant positive correlation was seen between serum NT-Pro-BNP and IVSTd ( $r = 0.361$ ,  $p < 0.001$ ) and between NT-Pro-BNP and PWTd ( $r = 0.448$ ,  $p < 0.001$ ). RWMA had no statistically significant differences among different CKD stages. These findings are consistent with prior studies on similar patients.<sup>27–31</sup>

## CONCLUSION

This study was undertaken to evaluate serum NT-Pro-BNP level at different stages of CKD patients and observe its association with different cardiac parameters. Given the significant association of NT-Pro-BNP with LVEF, IVSTd and PWTd found in present study, it was evaluated whether serum NT-Pro-BNP could function as a screening tool for patients with CKD who should proceed to further evaluation with echocardiography and the study findings suggest that NT-Pro-BNP has the potential to be used routinely as a screening tool for patients with CKD for cardiac structural and functional abnormalities. Measurements of serum NT-Pro-BNP could provide prognostic information of major cardiovascular events beyond traditional risk factors.

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## ETHICAL CLEARANCE

The confidentiality and responsibility of patients have followed the method of the World Medical Association Declaration of Helsinki 2000.

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