Original Research Article

Association between N-terminal pro-brain natriuretic peptide and acute ischemic stroke in male patients

Abstract

Aims: Stroke is among the major cause of mortality and disability globally. Many types of research are ongoing in search of a reliable biomarker for acute ischemic stroke. This study was aimed to see the association of the serum N-terminal proBNP (pro-brain natriuretic peptide) or NT-proBNP with acute ischemic stroke.

Study design: Case-control study.

Methodology: This case-control study was conducted from January 2023 to June 2023. A total of 30 acute ischemic stroke male patients were enrolled as cases with 30 healthy male controls. Serum NT-proBNP level was measured in all the participants. Clinical features including the National Institute of Health Stroke (NIHSS) scale score were recorded in cases.

Results: The mean ages of the cases and controls were 61 ± 9.22 and 62.40 ± 8.23 years respectively. Among the acute ischemic stroke patients, more than half of the patients (53%) had lacunar stroke. According to the NIHSS score, more than 90% of the patients had minor or moderate stroke (93.3%). The mean NT-proBNP of cases was significantly higher than the controls (266.99 ± 357.88 vs 46.32 ± 18.59) (*P = .04*). The mean logNT-proBNP level (1.96 ± 0.72) was also significantly higher among the cases than the controls (1.61 ± 0.22) (*P = .04*). We did not find any association of serum logNTpro-BNP with the duration of stroke (*P = .40*). There was also no statistically significant association between the NIHSS score and NT-proBNP or logNTpro-BNP levels (*P = .36*).

Conclusion: Serum NT-proBNP level was significantly higher in acute ischemic stroke patients. There was no association of NT-proBNP level with the stroke severity and duration.

Keywords: *Acute Ischemic Stroke; NT-proBNP; National Institute of Health Stroke Scale (NIHSS); Stroke Biomarker; Stroke Severity*

1. Introduction:

Stroke is the second leading cause of death globally [1]. Stroke is also one of the major causes of disability. Many prognostic factors are available and under investigation to assess the outcome after a stroke. One of the widely used parameters is the National Institute of Health Stroke (NIHSS) scale and mNIHSS (modified NIHSS) scale. However, these tools have some limitations, as it requires skill to assess the patient according to these scales. Other than anterior circulation stroke, NIHSS and mNIHSS scores may not represent the scenario [2]. So, there is always a crying need for a reliable biomarker, which is easy to interpret and does not require special skill to assess the stroke severity and prognosis.

Brain natriuretic peptide (BNP) is secreted mostly from the ventricular myocardium as a polypeptide and acts as a natriuretic hormone. A prohormone name proBNP (pro-brain natriuretic peptide)is synthesized and after release into blood, it is divided into biologically active BNP and inactive N-terminal fragment named NT-pro BNP. Both BNP and NT-proBNP are important biomarkers for heart failure and other cardiac conditions [3]. Though both biomarkers are equally effective in assessing heart failure patients,

NT-pro BNP is superior for predicting mortality and morbidity [4,5]. There are other additional factors which impact the level of BNP and NT-proBNP levels. These factors are increasing age, female gender, renal impairment and sepsis [5,6].

NT-pro BNP levels were also found to be raised in ischemic stroke patients and in some studies, it was used as a novel prognostic biomarker of acute ischemic stroke [7-10]. There was a previous study done in Bangladesh showing the association between plasma BNP and ischemic stroke [11]. As far as our best knowledge, the association between serum NT-proBNP and acute ischemic stroke is yet to be seen in the Bangladeshi population. We have tried to find any association of this biomarker in acute ischemic stroke male patients. We did not include the female patients due to the role of the female gender in raised NT-proBNP levels. Also, our hospital is a military hospital, where most of the patients are male.

2. Materials and Methods:

This was designed as a case-control study. This study was carried out from January 2023 to June 2023 in the Department of Neurology, Combined Military Hospital, Dhaka. The NT-proBNP assay was done in the Department of Biochemistry, Armed Forces Institute of Pathology, Dhaka. After ethical clearance from the Ethical Committee of Combined Military Hospital, Dhaka, informed written consent was taken from each patient or their attendant. Thirty male patients with acute ischemic stroke (less than seven days of symptoms onset) fulfilling the inclusion and exclusion criteria were enrolled as cases. All the patients were aged more than 18 years, without previous history of cardiovascular events, heart failure, stroke, or any evidence of sepsis, and renal impairment. CT scan/MRI of the brain was done in all cases and lesions were classified as total anterior circulation infarct (TACI), partial anterior circulation infarct (PACI), posterior circulation infarct (POCI), and lacunar infarct (LACI) according to Oxfordshire Community Stroke Project (OCSP) classification [12]. Age-matched 30 control were taken from outpatient and inpatient departments who presented with other problems which are not related to NT-proBNP levels, like essential tremor, dementia, headache etc.

To measure NT-proBNP level, blood samples were taken from all the cases within 24 hours of hospitalization. Relevant demographic data and clinical examination findings were recorded accordingly. NIHSS score was recorded by neurologists and neurology residents who are trained in NIHSS score assessment.

We analyzed data using Statistical Package for the Social Sciences (SPSS) version 25 (IBM Corp., Armonk, NY, USA). Continuous parameters were expressed as mean ± SD (standard deviation), median and categorical parameters as percentages. The Shapiro-Wilk test of normality was done and most of our continuous variables were not distributed normally. So, the majority of our statistical tests were nonparametric tests. To determine the difference between continuous variables, the independent sample t-test, the independent sample Mann–Whitney U test, and the independent sample Kruskal-Wallis test were done. To determine the association between qualitative variables, a Fisher's exact test was done. To assess the correlation between two continuous variables the Spearman's rank correlation test was done. A P value of ≤ 0.05 was considered significant. The result was presented by using tables, figures, charts, and textual summaries.

3. Result:

Most of our patients were within the 51-60 years range followed by 61-70 years. The mean ages of the cases and controls were 61 ± 9.22 and 62.40 ± 8.23 years respectively. The distribution of age was similar in both groups (*P= .88*) (Table 1).

Table 1. The distribution of age between cases and controls.

		Group		P value
		Cases	Controls	
Distribution of age	41-50 years	2	1	
	51-60 years	15	15	.88
	61-70 years	9	9	
	71-80 years	3	5	
	>80 years	1	0	
Total		30	30	
Mean ± SD		61 ± 9.22	62.40 ± 8.23	.65

The P value was determined by Fisher's exact test and independent sample t-test

Among the acute ischemic stroke patients, more than half of the patients (53%) had a lacunar stroke. Partial anterior circulation stroke was found in 36.67 % of patients. None of the patients had total anterior circulation stroke (Figure 1).

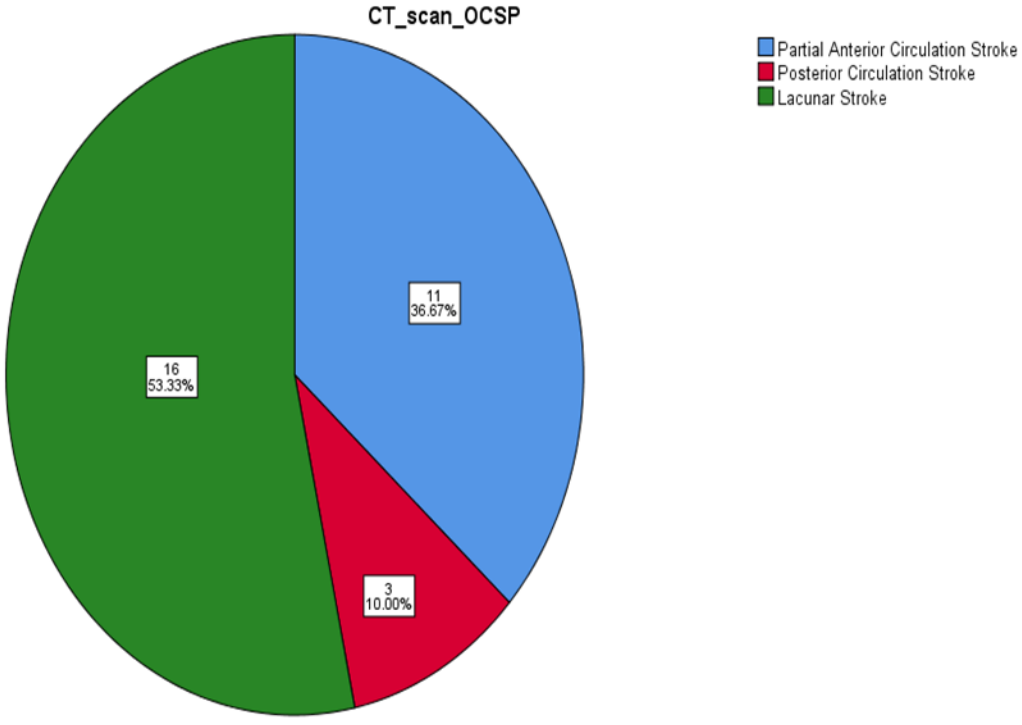

Figure 1. Types of acute ischemic stroke according to OCSP classification [12].

According to the NIHSS score, more than 90% of the patients had a minor or moderate stroke (93.3%). During our study period, no patient was admitted with an NIHSS score of more than 20 (Table 2).

Table 2. The stroke subtypes according to severity (NIHSS score)

NIHSS score with stroke subtypes	Frequency	Percent
(1-4) Minor stroke	10	33.3
(5-15) Moderate stroke	18	60.0
(16-20) Moderate to severe stroke	2	6.7
Total	30	100.0

We have compared the means of the NT-proBNP levels of both groups (Table 3). SD (standard deviation) was wide, indicating high variance. The Shapiro-Wilk test of normality was done and as the data were not distributed normally, Mann–Whitney U test was done to compare the means. The mean NT-proBNP of cases was significantly higher than the controls (266.99 ± 357.88 vs 46.32 ± 18.59) (*P = .04*). Due to the high variance of the NT-proBNP levels, we have also compared the mean logNT-proBNP between two groups. The mean logNT-proBNP level (1.96 ± 0.72) was significantly higher among the cases than the controls (1.61 ± 0.22) (*P = .04*).

Table 3. The comparison of mean NT-proBNP and logNT-proBNP among two groups.

Mean ± SD	**Case**	**Control**	**P value**
NT-proBNP (pg/ml)	266.99 ± 357.88	46.32 ± 18.59	.04
logNT-proBNP	1.96 ± 0.72	1.61 ± 0.22	.04

The P value was determined by the Mann–Whitney U test

The cases were divided according to three groups according to serum NT-proBNP levels. Most of the patients had NT-proBNP levels of less than 100 pg/ml (50%), whereas 23.3% of the cases had between 100-400 pg/ml range. 26.7% of the cases had NT-proBNP levels of more than 400 pg/ml. Among these three groups of patients, mean NIHSS scores were compared. We did not find any association between the higher NT-proBNP levels with the mean NIHSS score (*P = .55*) (Table 4).

Table 4. Comparison between mean NIHSS score levels among the groups according to serum NT-proBNP levels.

NT-proBNP	Mean ± SD (NIHSS)	N (%)	P value
less than 100	7.26 ± 3.80	15 (50)	
101 to 400	5.57 ± 3.20	7 (23.3)	.55
more than 400	8.00 ± 4.62	8 (26.7)	
Total	7.06 ± 3.88	30 (100)	

The P value was determined by the Kruskal-Wallis test

The relation of logNT-proBNP and the duration of stroke was sought by the scattered diagram. There were very weak negative relations or no relation between these two variables (Figure 2, Table 5).

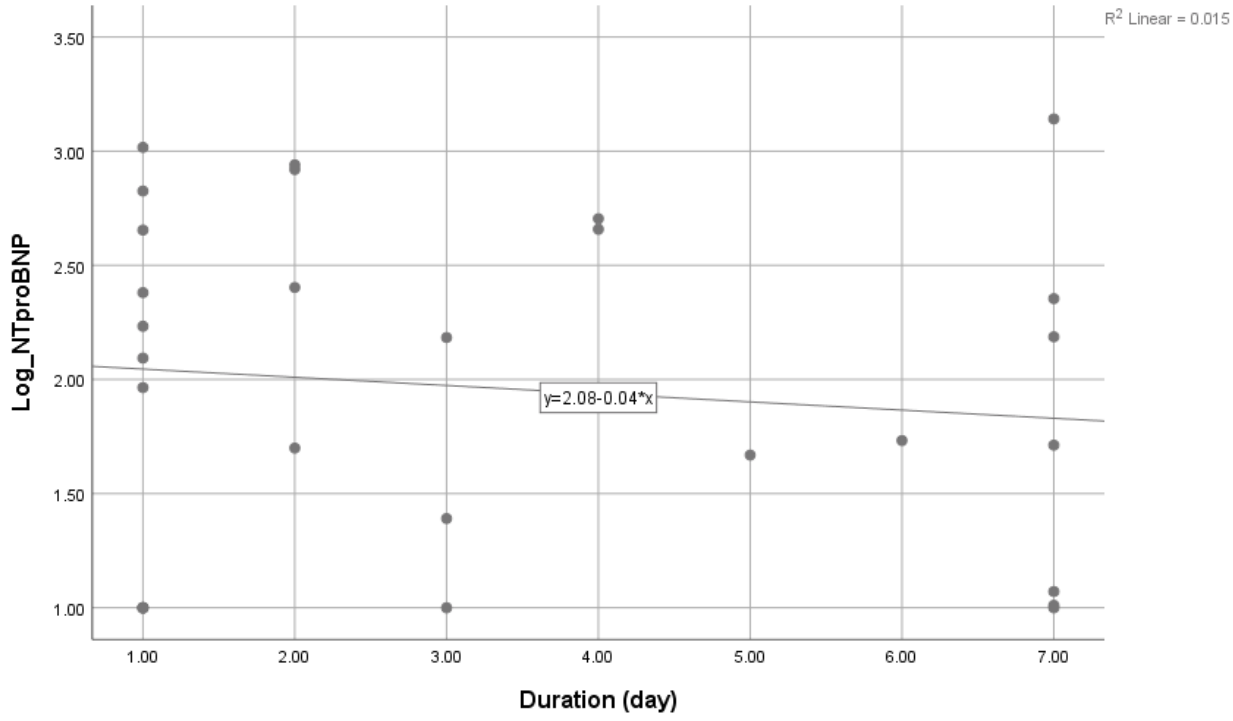

Figure 2. Scatter diagram showing the relationship of serum NT-proBNP levels with the duration of acute ischemic stroke (no significant correlation, r^2 linear = coefficient of determination).

We have searched for any relation between serum NT-proBNP and logNT-proBNP with the stroke severity (NIHSS score). There were very weak positive relations or no relation between these two variables (Figure 3-4, Table 5).

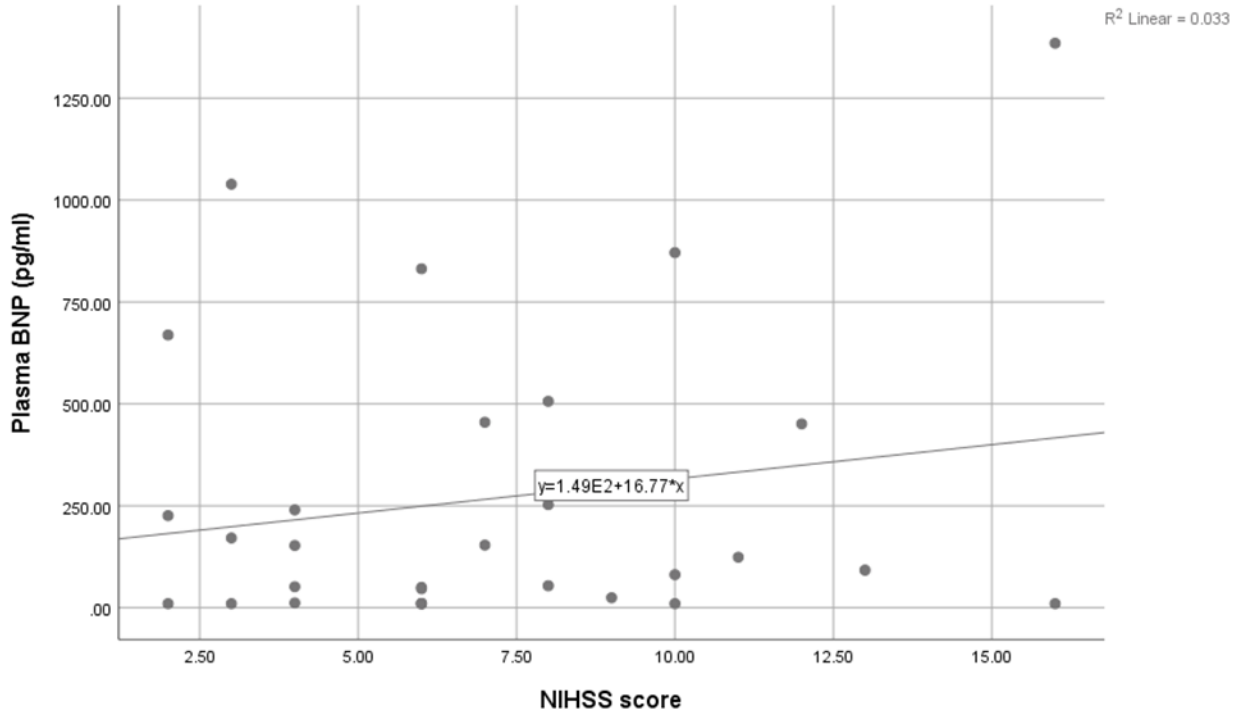

Figure 3. Scatter diagram showing the relationship of serum NT-proBNP levels with severity of acute ischemic stroke according to NIHSS score (no significant correlation, r^2 linear = coefficient of determination).

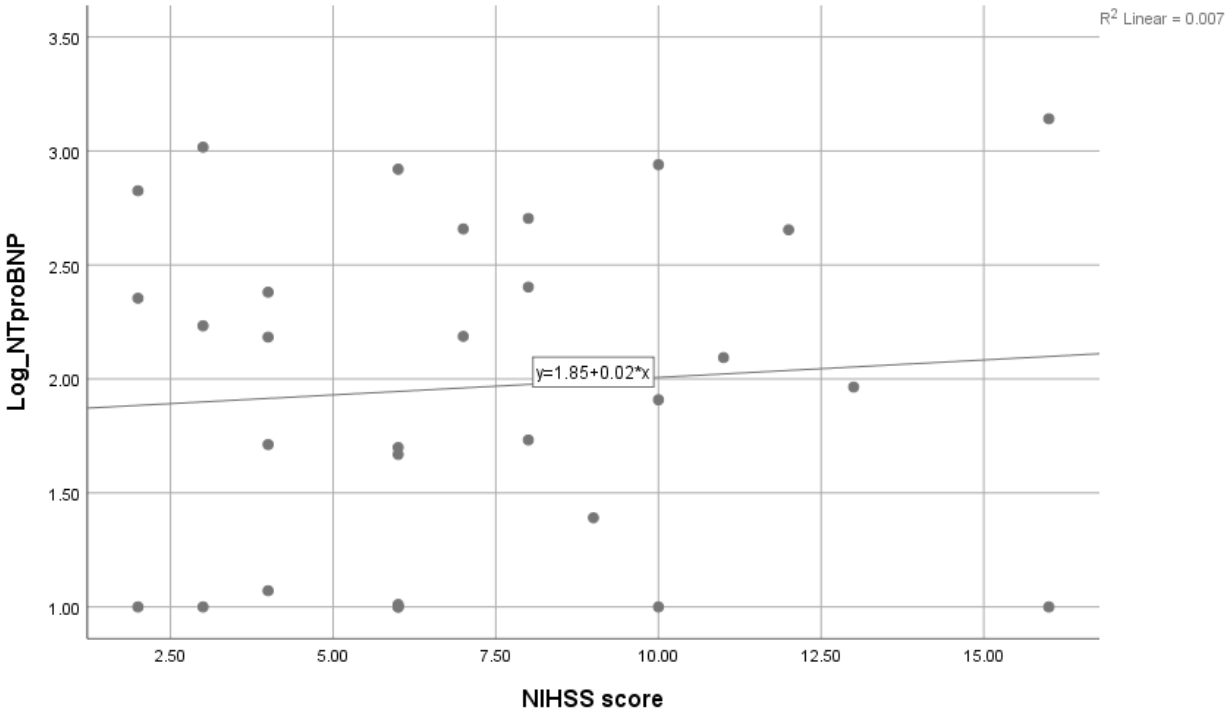

Figure 4. Scatter diagram showing the relationship of serum logNT-proBNP levels with severity of acute ischemic stroke according to NIHSS score (no significant correlation, r^2 linear = coefficient of determination).

We have done Spearman's rank correlation test to see the relations between these continuous variables. We did not find any significant correlation (Table 5).

Table 5. The correlation between different continuous variables.

Correlation	**Spearman's r (correlation coefficient)**	**P value (Significance 1-tailed)**
NT-proBNP with NIHSS score	.067	.36
LogNT-proBNP with NIHSS score	.067	.36
NT-proBNP with stroke duration	-.047	.40

The P value was determined by the Spearman's rank correlation test

4. Discussion:

This study was aimed to see an association between serum NT-proBNP level and acute ischemic stroke. We have found significantly higher serum NT-proBNP levels in acute ischemic stroke patients compared to the control group (*P = .04*) . As the variance was high, we compared the means of logNT-proBNP between the cases and control groups, and it was also significantly high in the cases group. In other previous studies also, it was found that the NT-proBNP levels were significantly high in acute ischemic stroke patients [10,13].

However, the mean NTpro-BNP levels were less in our study compared to other studies [10,13]. Most of our stroke patients were between 51-60 years (48 %) and also the majority of patients had either minor or moderate (93.3%) stroke. We did not include women in our study, who have higher NT-proBNP levels due to secretion from female reproductive organs [8]. All these factors may be responsible for relatively lower NT-proBNP levels in our cases.

We did not find any association of logNTpro-BNP level with the duration of the stroke. We assessed the NTpro-BNP level within seven days of ischemic stroke. In some previous studies, it was found that NT-proBNP level was more in the initial days of acute ischemic stroke [14]. Our relatively smaller sample size may have an effect on our result. Further studies with a larger sample and serial NT-proBNP assay are recommended in this regard.

We did not find any association between serum NT-proBNP levels with stroke severity. There was no statistically significant association between the NIHSS score and NT-proBNP or logNTpro-BNP levels. Also, mean NIHSS scores were compared between different groups according to serum NTproBNP levels. However, we did not find any statistically significant association. Some previous studies found an association between the NIHSS score and the NT-proBNP level [7,8]. Larger normally distributed data are needed to see this association in our population.

Our study has some limitations. The purposive sampling method was used which was prone to bias. The sample size was small and we included only male patients. Most of our cases were relatively younger and had less severe stroke. So, a larger multicenter study is recommended in the Bangladeshi population on this topic.

5. Conclusion:

We have found significantly higher NTpro-BNP levels in acute ischemic stroke male patients. However, a further large-scale study is needed to find any association between the serum NT-proBNP level and stroke severity.

CONSENT

Informed written consent was taken from each patient or from his/her attendant.

ETHICAL APPROVAL

Ethical approval was obtained from the Ethical Committee of Combined Military Hospital, Dhaka.

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