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ORIGINAL ARTICLE

ASSOCIATION OF NT-PROBNP LEVEL WITH SEVERITY IN ACUTE ISCHEMIC STROKE PATIENTS

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Abstract:

Background: *This study was aimed to assess association of NT-proBNP levels with severity in acute ischemic stroke patients which may help in severity assessment of these patients.* ***Methods:*** *This case-control study was conducted in the Department of Neurology, Sir Salimullah Medical College Mitford Hospital, Dhaka, Bangladesh from November, 2023 to October, 2024.Total 100 subjects were enrolled in this study. Among this, 50 acute ischemic stroke patients with history within 3 days and confirmed by CT scan of head or MRI of brain were selected purposively from the Neurology Department of Sir Salimullah Medical College Mitford Hospital, Dhaka, Bangladesh. Another 50 age and gender matched subjects were selected from this place for comparison. Venous blood samples were collected from these patients and analyzed for estimation of plasma NT-proBNP.* ***Results:*** *This study found mean plasma NT-proBNP level was significantly higher (333.0±221.9pg/ml) in acute ischemic stroke patients (Case group) than control group (109.4±131.1pg/ml). A moderately strong positive correlation was observed between plasma NT-pro BNP level and NIHSS score at admission (r = 0.566; p <0.001).* ***Conclusion:*** *Plasma NT- Pro BNP level was significantly associated with acute ischemic stroke and correlated with severity. It reveals plasma NT- proBNP as an important marker for severity assessment of acute ischemic stroke.*

Key words: *Acute Ischemic Stroke, N-terminal pro-brain natriuretic peptide (NT-proBNP),National Institute of Health Stroke Scale (NIHSS).*

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Introduction :

Stroke is the second most common cause of death worldwide and one of the leading cause of disability.[1] Stroke prevalence is 11.39 per thousand individuals in Bangladesh. [2] Stroke is the leading cause of death in Bangladesh, followed by ischemic heart disease and infectious disease.[3]

Early and exact assessment of the severity and prognosis of acute ischemic stroke may help physicians in selecting the best therapeutic strategy and minimizing the consequences of ischemic stroke. Several blood-based biomarkers have been developed to their potential applications in ischemic stroke prognosis.[4]

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B-type natriuretic peptide (BNP) is a cardiac hormone formed by the cleavage of its precursor pro-BNP, which results in the release of equimolar amounts of the inactive N-terminal peptide (NT-proBNP).[5]Previous research has shown that NT-proBNP can be used to predict the prognosis of patients with heart failure, atrial fibrillation (AF), and acute coronary syndromes.[6] There is currently substantial evidence that an acute stroke can cause cardiac abnormalities and NT-proBNP was found to be elevated in acute stroke patients.[7]

Several studies have shown that elevated NT-proBNP levels in ischemic stroke patients were independently associated with unfavorable outcomes including cardiovascular and other mortality.[8] Several studies, however, found no significant link between higher levels of NT-proBNP and unfavorable outcomes.[9] Thus, it is suggestive from above discussion that a potential biomarker may add valuable and time sensitive prognostic information in the early evaluation of ischemic stroke. The study was designed to assess the association of NT-proBNP level with severity in Acute Ischemic Stroke Patients which may help in severity assessment of these patients.

Methods:

The study was designed as a Case - Control study . The study was carried out in the in patient department of Neurology , Sir Salimullah Medical College Mitford Hospital, Dhaka from November, 2023 to October, 2024 . Ethical clearance for the study was obtained from the Institutional Ethics Committee of Sir Salimullah Medical College. Data were collected through preformed semi-structured questionnaire. Subjects were selected based on inclusion and exclusion criteria. Subjects were excluded from the study if inclusion and exclusion criteria were not fulfilled. Informed written consent was obtained from the respondents or their guardians.CT scan or MRI were used to diagnose Acute Ischemic Stroke .

Blood samples were taken from all selected patients within 48 hours of admission to measure plasma NT-proBNP. Venous blood samples were centrifuged at 3000 rpm for 10mins and serum samples were obtained. NT-proBNP measurement was performed using an electro-chemiluminescence sandwich immunoassay (ECLIA, Roche Diagnostics) on a Modular analytics Hitachi Cobas 6000 using original Roche kits. Values were expressed in pg/ml.

Demographic data, examination findings , laboratory findings, radiological data recorded and copies of investigation reports were preserved. Stroke severity on admission was categorized according to the NIHSS.With the end of each interview participant were asked for any queries or clarifications and responded accordingly. At the end of each data collection, questionnaires were checked for completeness and organized carefully to ensure quality of the data.

The control group included age and gender matched subjects who have no history of stroke, cardiac diseases or other risk factors.

Data input was done through Microsoft Office Excel version 2016 and Statistical analysis was done by using SPSS 25.

Results:

Table-I shows age range of 20 to 75 years in acute ischemic stroke patients (Case group) and non-stroke patients (Control group) . Majority of the patients of case group belongs to 61-75 years age group (62%) while about half of control group subjects were in 41 – 60 years age group (42%). Mean age of case group subject was statistically higher than that of control group .The proportional difference were measured and it was statistically significant (p value <0.001).

Table-I

Distribution of the study subjects by age group (n=100)

Age group (years)	Case (n=50)	Control (n=50)	*p*-value
20-40	6(12.0%)	20(40.0%)	<0.001*
41-60	13(26.0%)	21(42.0%)	
61-75	31(62.0%)	9(18.0%)	
Total	50(100.0%)	50(100.0%)	
Mean±SD	60.6±13.93	46.3±17.16	

p-value obtained by Unpaired t-test, p ≤0.05 considered as a level of *significant

Table-II shows 23% were male in case group and 25% were in control group and 27 % were female in case group and 25% in control group. No statistically significant difference was observed in terms of gender of the study subjects in case & control group (p= 0.689).

Table-II

Gender distribution of the study subjects (n=100)

Sex	Case (n=50)	Control (n=50)	*p*-value
Male	23(46.0%)	25(50.0%)	0.689
Female	27(54.0%)	25(50.0%)	
Total	50(100.0%)	50(100.0%)	

p-value obtained by Chi-square test, p ≤0.05 considered as a level of significant .

Table-III

Distribution of study subjects in case group based on the presence of ischemic risk factors among them (n=50)

Baseline characteristics		Frequency	Percentage (%)
Smoking	Non-smoker	29	58.0
	Ex-smoker	13	26.0
	Smoker	8	16.0
DM		37	74.0
Hypertension		38	76.0
Hypercholesterolemia		39	78.0
Presence of Family history of stroke		14	28.0
Alcohol		3	6.0
Previous vascular events		8	16.0
Atrial fibrillation	Absent	45	90.0
	Present	5	10.0

Table-III shows majority of the subjects of case group were diabetic, hypertensive and had hypercholesterolemia.

Fig 1 shows the highest percentage of study subjects of case group was Cardioembolic stroke.

Table IV shows the Serum NT-proBNP levels were raised in all subtypes and the differences among them were statistically significant.

Table-IV shows raised plasma NT-prBNP above 125 pg/ml in 46% of acute ischemic stroke patients (Case group) but only 8% subjects of non-stroke group(Control group) . The mean plasma NT-proBNP in acute ischemic stroke patients (Case group) and control group was 333.0 pg/ml and 109.4 pg/ml respectively. The proportional difference of raised NT-proBNP among the two groups were measured and it was statistically significant (p value <0.001).

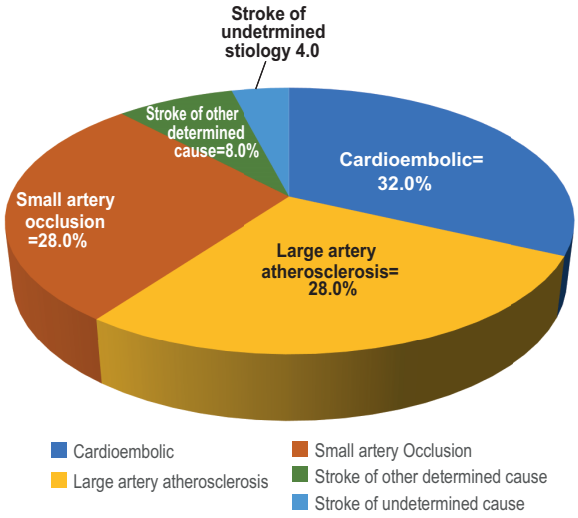

Fig.-1: *Pie diagram shows the stroke subtype according to TOAST classification in case group (n=50)*

Table-IV

Serum NT-proBNP levels among subjects with different sub-types of ischemic stroke according to TOAST classification (n=50)

SerumNT-Pro BNP level	TOAST classification					*p*-value
	Cardioembolic (n=16)	Large artery atherosclerosis (n=14)	Small artery Occlusion (n=14)	Stroke of other determined cause(n=4)	Stroke of Undetermined Cause (n=2)	
Mean±SD	435.7±217.2	380.6±226..5	230.5±188.3	181.0±158.8	202.5±166.2	0.039*
Median	534	386.0	127.5	180.9	202.5	
Range (min-max)	45-640	25-680	40-600	28-335	85-320	

p-value obtained by Kruskal Walis test, p ≤0.05 considered as a level of *significant
Normal serum NT-proBNP level is < 125pg/ml

Table-IV

Comparison of Serum NT-proBNP levels in subjects of case and control group (n=100)

Serum NT -Pro BNP level (pg/ml)	Case (n=50)	Control (n=50)	*p*-value
< 125	27(54%)	46(92%)	<0.001*
>125	23(46%)	4(8%)	
Total	50(100.0%)	50(100.0%)	
Mean±SD	333.0±221.9	109.4±101.1	
Median	108.5	39.0	
Range (min-max)	25-680	19.7-540.0	

Table-V shows distribution of stroke severity according to NIHSS score among acute ischemic stroke patients at admission (n=50). Here shows most stroke severity was moderate type (46%).

Table-V

Distribution of stroke subjects according to severity by NIHSS score at admission (n=50)

Ischemic stroke severity by NIHSS score	Frequency	Percentage
Minor stroke 1-4	4	8.0
Moderate stroke 5-15	23	46.0
Moderate/Severe stroke 15-20	14	28.0
Severe stroke >20	9	18.0
Total	50	100.0

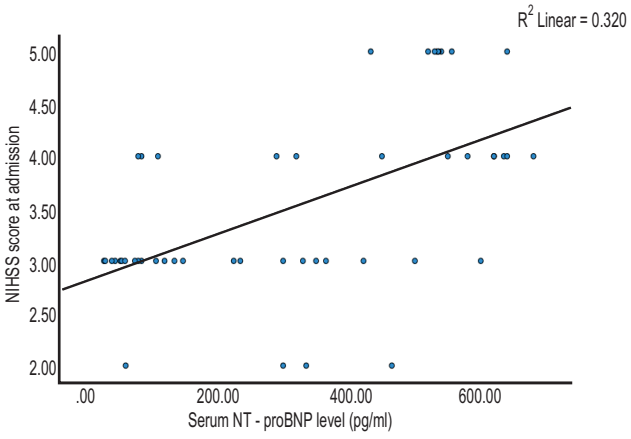

Fig-2: *Scatter plot shows the correlation of plasma NT-proBNP levels with severity of acute ischemic stroke patients at admission by NIHSS score*

Spearman's correlation test of these two variables revealed a statistically significant (p < 0.001) moderately strong (r=0.566)positive correlation.

Discussion:

This case-control study was done with 50 acute ischemic stroke patients with 50 age and gender matched non stroke subjects .The study subjects were taken from Sir Salimullah Medical College Mitford Hospital, Dhaka, Bangladesh. Any relation of plasma NT-proBNP level with severity of acute ischemic stroke by NIHSS score was evaluated through this study . Study was conducted from November, 2023 to October, 2024.

Analysis of age distribution of the study population showed thatmean age is found 60.6 years in acute ischemic stroke patients (Case group) and 46.3 years in control group. Maximum patients of case group is 62% in 61-75 years group and control group is 42 % in 41 – 60 years age group.

Analysis of gender distribution revealed 23% were male in case group and 25% were in control group and 27 % were female in case group and 25% in control group.

Increased plasma NT-proBNP level above 125pg/ml was found in 46% of acute ischemic patients but only in 8% of the non-stroke patients. This finding is consistent with Arslan et al.[10] with elevated plasma NT-proBNP in 34% subjects of acute ischemic stroke but only 2% of non-stroke control group.

Significantly increased mean NT-proBNP value of (333.0±221.9pg/ml) was observed in the acute ischemic stroke patients than the non-stroke patients (109.4±101.1pg/ml). In another study, Yang and Zhong et al.[11]reported similar result, with higher mean NT-proBNP of 273.7 pg/ml in acute ischemic stroke patients and 85.29 pg/ml in non-stroke healthy control. The higher mean plasma NT-proBNP in the above-mentioned studies may be due to early access of patient to health care services in those studies where sampling of blood was possible without any delay from onset of stroke symptoms. Yang and Zhong et al. in their study followed strict time frame of 72 hours from symptom appearance for plasma NT-proBNP estimation. Another possibility of high mean plasma

NT-proBNP in the above-mentioned studies may be due to inclusion of all subjects irrespective of their cardiac and renal function status. However, Yang and Zhong et al.[11] found mean NT-proBNP of 85.29 pg/ml in their controls, which is consistent with finding of control group (109.4 pg/ml) in current study. The similarity for plasma NT-proBNP level in control groups of Yang and Zhong with current study may be due to the exclusion criteria set in this study where effort was made to exclude factors already established for rising plasma NT-proBNP.

A statistically significant difference observed (p= 0.039) in plasma NT-proBNP level and by TOAST classification. Plasma NT-proBNP concentration was found highest (435.7pg/ml) in Cardioembolic Stroke and then (380.6pg/ml) in Large artery atherosclerosis and (230.5pg/ml) in Small artery occlusion. This finding accords with (Zecca et al., 2014)[13] with highest mean NT-proBNP value among the patients of Cardioembolic Stroke.

This study found statistically significant positive correlation between plasma NT-proBNP and severity of stroke measured by National institute of health stroke scale, at admission($r=0.566$;$p<0.001$)through Spearman's correlation test. This correlation was also observed by et Zhao et al.[12] in a study.

Conclusion:

This study reveals that high plasma NT-proBNP level is significantly associated with acute ischemic stroke and correlated with severity.

Limitations:

The study was done in single center , so that the results may not reflect the exact picture of the country.

The method of sampling was purposive. Small sample size was also a limitation of the study. Further multi-center studies with longer follow-up periods would provide more comprehensive insights.

Data Availability:

The datasets analysed during the current study are not publicly available due to the continuation of analyses but are available from the corresponding author on reasonable request.

Conflict of Interest:

There is no conflict of interest in this study.

Funding:

The research received no external funding.

Ethical consideration:

The study was approved by the Institutional Ethics Committee of Sir Salimullah Medical College. Informed consent was obtained from each participant or relatives of the patients.

Author Contributions:

All authors made a significant contribution to the work reported, whether that is in the conception,study design , execution , acquisition of data, analysis and interpretation , or in all these areas; took part in drafting , revising or critically reviewing the article ; gave final approval of the version to be published ; have agreed on the journal to which the article has been submitted ; and agree to be accountable for all aspects of the work.

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