Role of Nt- Pro Bnp Levels in Predicting the Prognosis in Acute Coronary Syndromes

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Keywords	Abstract:
NT- pro bnp levels, prognosis, acute coronary syndromes	Background: Cardiovascular diseases contribute 29.3% of global deaths as per WHO, with half due to ischemic heart diseases1. In India, it's the top cause of death at 15%, followed by respiratory infections (11%) and cerebrovascular diseases (7%)2. Despite new pharmacological strategies, hypertension therapy, and lifestyle changes, cardiovascular diseases remain the leading cause of death 3. Acute coronary syndromes like MI with ST elevation, NSTEMI, and UA are significant health issues, accounting for 20% of emergency department admissions with high risks. Materials & Methods: This is hospital based cross sectional observational study which was conducted in the Department of general medicine of Private medical college with study period of 1 year. The total sample size of the study was 50 patients. The collected data was entered in Microsoft Excel. Coding of the variables was done. Analysis was done using SPSS software (Version 27, IBM). Results: Among the study patients, 38 (76%) were males and 12 (24%) were females. STEMI (ST-Elevation Myocardial Infarction) 62% of cases, Unstable angina 28%, and NSTEMI (Non-ST-Elevation Myocardial Infarction) 10% of cases. Association Levels of NT proBNP in various Acute Coronary Syndromes was significant. Association of Cardiac Enzymes and NT ProBNP Levels was significant. Association of Follow up sympstoms and NT ProBNP Levels was significant. Conclusion: NT proBNP is a reliable biomarker for predicting recurrent symptoms, hospital admissions, and left ventricular dysfunction in patients with STEMI, as it is more commonly elevated in this group compared to NSTEMI or unstable angina. Its predictive value is also high for recurrent unstable angina, NSTEMI, STEMI, and cardiovascular mortality. A cutoff level of NT proBNP above 100 pg/mL can be used to determine prognostic endpoints. Additionally, NT proBNP levels are not influenced by gender in patients under 60 years of age.

INTRODUCTION

Cardiovascular diseases contribute 29.3% of global deaths as per WHO, with half due to ischemic heart diseases[1]. In India, it's the top cause of death at 15%, followed by respiratory infections (11%) and cerebrovascular diseases (7%)[2]. Despite new pharmacological strategies, hypertension therapy, and lifestyle changes, cardiovascular diseases remain the leading cause of death [3]. Acute coronary syndromes like MI with ST elevation, NSTEMI, and UA are significant health issues, accounting for 20% of emergency department admissions with high risks[4]. Recent advances in biomarkers for diagnosing MI include Ischemia-Modified Albumin, Myeloperoxidase, and IL-6, while prognostic biomarkers like high sensitivity CRP and Troponin I are limited. Ideally, MI patients treated

promptly at specialized centers with PCI or thrombolysis achieve good outcomes, but still face a higher risk of subsequent coronary events[5]. Patients often wonder about symptom recurrence, chest pain, heart function, and complications post MI. This study explores using NT-proBNP to predict prognosis after an acute coronary syndrome, assessing its correlation with recurrent symptoms and adverse outcomes within six months post-event[6].

Measurement of NT proBNP indirectly measures Brain Natriuretic Peptide. NT proBNP is measured due to its longer half-life compared to hormonally active BNP. BNP is released from left ventricular cardiac myocytes in response to myocardial wall stretch. Pro hormone proBNP splits into BNP and N-terminal proBNP, both secreted equimolarly[7]. It helps regulate plasma overload by inducing diuresis, natriuresis, vascular dilatation, and inhibiting the sympathetic nervous system[8]. BNP has a half-life of around 20 minutes, while NT proBNP's half-life is around 120 minutes. Scoring systems like TIMI score and Troponin I levels are currently used to predict prognosis in acute coronary syndrome[9]. Some studies suggest BNP can predict cardiac failure in ACS patients in the Western population. As a sensitive biomarker for cardiac muscle strain, this study aims to assess Brain Natriuretic Peptide's use as a prognostic biomarker in Acute Coronary Syndromes patients in South Indian Population[10].

MATERIALS & METHODS

• This is hospital based cross sectional observational study which was conducted on patients admitted in general medicine department of Meenakshi medical college hospital and research institute with study period of 1 year. The total sample size of the study was 50 patients. **Inclusion criteria** – 1) Patients with Acute Coronary Syndromes with no prior history of cardiac disease. 2) Unstable Angina , NSTEMI , STEMI. 3)Age less than 60 years. **Exclusion criteria** – 1) Age more than 60 yrs. 2) Patients with Valvular Heart Disease 3) Patients with Anemia 4) Patients with Renal Failure. The study was approved by Institutional Ethics Committee of the private medical college. A written informed consent was obtained from all the patients.

Data collection method: A questionnaire was prepared. Noted the age, sex, address, phone number of the patient ,phone number of the relatives and in case the family had no phone , number of neighbours were recorded. Primary complaints like angina, dyspnoea, symptoms of cardiac failure were recorded. Risk factors for coronary artery disease like diabetes mellitus, systemic hypertension, smoking, hyperlipidemia, renal failure and other complaints if any were noted. Clinical examination included a detailed general examination including vital signs and systemic examination of cardiac, respiratory, gastrointestinal, and nervous systems. Killips Class was recorded if the patient was in acute MI. In NSTEMI,STEMI and unstable angina. Laboratory Investigations: Blood urea and serum creatinine were used to rule out frank renal failure. 37 Electrocardiogram was taken to look for ST elevation or new onset left bundle branch block identified by comparison with previous ECG if available. In all cases an initial Echocardiography was obtained to assess the left ventricular function and ejection fraction. Within 2 to 24 hours of the onset of symptoms, NT-proBNP levels were measured in blood with Rapid NT proBNP Assay Kit.

The collected data was entered in Microsoft Excel. Coding of the variables was done. Analysis was done using SPSS software (Version 27, IBM). Descriptive statistics was used. Association between categorical tests. The outcomes of the treatment groups were compared using a test to reach the hypothesis, a P value less than 0.5 was considered significant.

RESULT

This is hospital based cross sectional observational study which was conducted on patients admitted in general medicine department of Meenakshi medical college hospital and research institute with a study period of 1 year. The total sample size of the study was 50 patients.

**Chart 1: Gender distribution among the study participants**
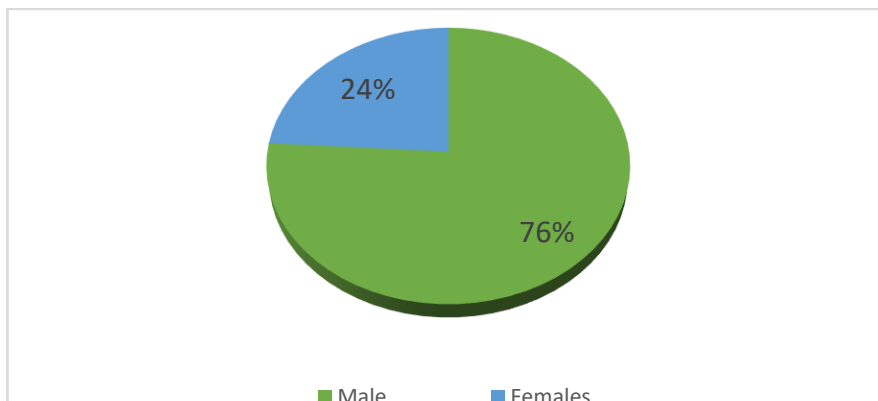
Among the study patients, 38 (76%) were males and 12 (24%) were females. (**Chart 1**)

Table 1: Age distribution among the study participants

Age	Frequency (n)	Percentage (%)
< 30 years	2	4%
31 – 40 years	9	18%
41 – 50 years	22	44%
51. – 60 years	17	34%

The age distribution data shows that the majority of the individuals fall within the 41-50 years age bracket, accounting for 44% of the total sample. The next largest group is those aged 51-60 years, representing 34%. Individuals aged 31-40 years make up 18%, while those under 30 years constitute the smallest group at 4%. This indicates a predominantly middle-aged population, with a significant portion in the 41-50 and 51-60 age ranges. (**Table 1).**

Chart 2: Details of Diagnosis
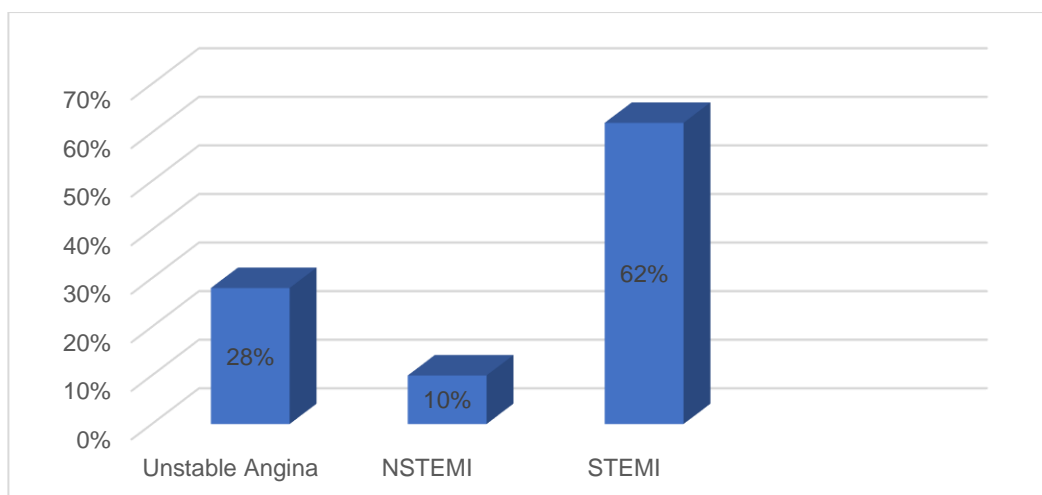
The data on types of acute coronary syndrome shows that the most common condition is STEMI (ST-Elevation Myocardial Infarction), accounting for 62% of cases. Unstable angina follows with 28%, and NSTEMI (Non-ST-Elevation Myocardial Infarction) is the least common, representing 10% of cases. This indicates that the majority of patients are experiencing the most severe form of heart attack, STEMI, while a smaller proportion are dealing with less severe conditions such as unstable angina and NSTEMI.(**Chart 2**)

Tables 2: Association Levels of NT proBNP in various Acute Coronary Syndromes

NT ProBNP Levels	Unstable Angina	NSTEMI	STEMI	P-value
Normal (<100pg/ml)	**5 (10%)**	**2(4%)**	**9(18%)**	**0.002***
Significant Elevation (>100pg/ml)	**9(18%)**	**1(2%)**	**24(48%)**	
Total No: Patient	**14(28%)**	**3(6%)**	**33(66%)**	

The data on NT ProBNP levels among patients with different types of acute coronary syndrome reveals notable patterns. Among patients with unstable angina, 10% have normal NT ProBNP levels and 18% show significant elevation. For NSTEMI patients, 4% have normal levels and 2% show significant elevation. Among STEMI patients, 18% have normal NT ProBNP levels while a substantial 48% exhibit significant elevation. This indicates that a majority of STEMI patients have elevated NT ProBNP levels, suggesting a higher severity of cardiac stress in these patients. Overall, out of the total patients, 28% have unstable angina, 6% have NSTEMI, and 66% have STEMI, which statistically significant.

Table 3: Association Levels of NT proBNP with gender

Gender	NT pro BNP		P value
	Not elevated	elevated	0.000*
Male	11	20	
Female	9	10	

The data on NT ProBNP levels by gender shows a significant difference in the distribution of elevated levels between males and females, with a P value of 0.000, indicating statistical significance. Among males, 20 have elevated NT ProBNP levels while 11 do not. For females, 10 have elevated levels while 9 do not. This suggests that elevated NT ProBNP levels are more common in males compared to females, and the difference is highly significant statistically. (**Table 3**)

Table 4: Association of Cardiac Enzymes and NT ProBNP Levels

| Cardiac Enzymes	NT pro BNP		P value
	Not elevated	elevated	0.003*
elevated	12	21	

Not elevated	8	9	

The data on the relationship between cardiac enzymes and NT ProBNP levels shows a significant correlation, with a P value of 0.003, indicating statistical significance. Among patients with elevated cardiac enzymes, 21 also have elevated NT ProBNP levels, while 12 do not. Conversely, among patients without elevated cardiac enzymes, 9 have elevated NT ProBNP levels and 8 do not. This suggests that there is a significant association between elevated cardiac enzymes and elevated NT ProBNP levels, indicating that patients with higher cardiac enzyme levels are more likely to also have elevated NT ProBNP levels. **(Table 4)**

Chart 3: Recurrence symptoms on follow up
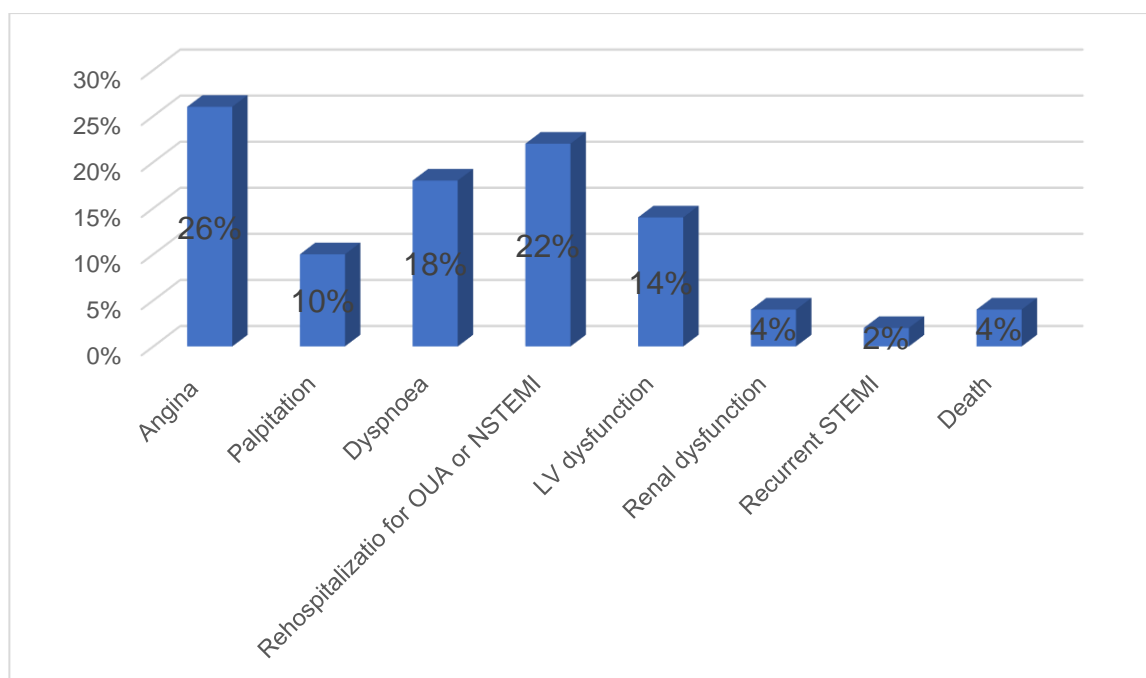
The data outlines the prevalence of various complications and outcomes among a patient group. Angina is the most common, affecting 26% of the patients. Rehospitalization for OUA (unstable angina) or NSTEMI (Non-ST-Elevation Myocardial Infarction) follows, with 22%. Dyspnoea (shortness of breath) affects 18%, while left ventricular (LV) dysfunction is seen in 14%. Palpitations are experienced by 10% of patients. Renal dysfunction and death each account for 4%, and recurrent STEMI (ST-Elevation Myocardial Infarction) is the least common at 2%. This distribution highlights that angina, rehospitalization, and dyspnoea are the most prevalent complications, whereas severe outcomes like recurrent STEMI and death are relatively rare. (**Chart 3**)

NT proBNP elevation was associated with Recurrent Angina (P value – 0.004), Palpitations (P value 0.001), Dyspnoea (P Value – 0.002) and more frequent cardiac related hospital admissions including unstable angina and NSTEMI (P Value - 0.001). Patients with elevated NT proBNP levels also had more chances for deterioration of left ventricular function (P Value - 0.000) as quantified by the left ventricular ejection fraction, in the follow up echocardiography.

DISCUSSION:

The study involved individuals diagnosed with Acute Coronary Syndromes, including Unstable Angina, NSTEMI, and STEMI. Only patients under the age of 60 were included, and those with a prior history of cardiac problems or renal failure were excluded due to the possibility of elevated NT proBNP levels. Blood samples

for NT ProBNP levels were obtained within the 2-hour to 24-hour window after symptom onset[11].

The research revealed no connection between gender and NT proBNP levels (P Value 1.00), despite other studies indicating a slight increase in NT proBNP levels among females, but these studies were limited to the geriatric population[12]. Furthermore, there was no correlation between NT proBNP levels and Cardiac Enzymes in ACS (P value - 1.00), as Cardiac Enzymes were only elevated in STEMI and NSTEMI and not in Unstable Angina, while NT proBNP levels were increased in Unstable Angina. Additionally, both NT proBNP and Cardiac Enzymes were found to be independent variables[13].

When assessing NT proBNP as a prognostic biomarker, this study uncovered that patients with increased levels experienced more recurrent symptoms and lower quality of life than those with normal levels during a 6-month follow-up period[14].

Patients with NT ProBNP levels above 100 pg/ml demonstrated a higher incidence of STEMI during the 6-month follow-up period (P Value: 0.001) compared to those with lower levels. This finding is consistent with previous studies on this topic. A positive correlation was observed between NT ProBNP levels and renal function impairment. Among the 52 patients, six had consistently deteriorating renal function, as indicated by elevated serum creatinine levels, and showed higher NT ProBNP levels[15].

The results of this study, however, were not statistically significant (P Value - 0.231), unlike other studies that found NT proBNP to be a good predictor of deteriorating renal function (1)(32). Nevertheless, this study population had other risk factors such as diabetes mellitus, hypertension, and atherosclerosis, which could have contributed to the development of renal failure. According to the Hosmer Lemeshow statistical analysis test, initial proBNP levels correctly predicted mortality in 85.7% of cases. Therefore, NT proBNP has a good positive predictive value for mortality. In this study, patients with NT proBNP levels above 500 pg/ml had a higher mortality rate (P Value 0.003). Additionally, when the NT proBNP level cutoff was set at 100 pg/ml, it was still significantly associated with mortality (P Value – 0.021). Hence, a NT proBNP value of more than 100 pg/ml is a strong predictor of mortality[15].

CONCLUSION:

NT proBNP is a reliable prognostic biomarker. NT proBNP is elevated more commonly in STEMI than in NSTEMI or Unstable Angina. During follow up NT proBNP can be used to predict recurrent symptoms like angina, palpitations, dyspnoea, recurrent hospital admissions and progression to left ventricular dysfunction. NT proBNP also had a good predictive value for recurrent Unstable Angina , NSTEMI, STEMI and cardio vascular mortality. The cut off level of NT proBNP for prognostic end points can be taken as values above 100 pg/ml. NT proBNP levels were independent of the gender in the below 60 age group.

REFERENCES

1. Grabowski M, Filipiak KJ, Malek LA, et al. Admission B-type natriuretic peptide assessment improves early risk stratification by Killip classes and TIMI risk score in patients with acute ST elevation myocardial infarction treated with primary angioplasty. Int J Cardiology 2006;115(3):386-390

2. Bibbins-Domingo K, Gupta R, Na B, et al - N-terminal fragment of the prohormone brain-type natriuretic peptide cardiovascular events, and mortality in patients with stable coronary heart disease. Jama2007;297(2):169-176.

3. A clinician's experience of using the Cardiac Reader NT-proBNP point-of-care assay in a clinical setting European J Heart Fail (2008) 10(3): 260-266 66

4. Mueller C, Scholer A, Laule-Kilian K, et al. Use of B-type natriuretic peptide in the evaluation and management of acute dyspnoea. NEJM ed2004;350(7):647-654.

5. McCullough PA, Nowak RM, McCord J, et al. B-type natriuretic peptide and clinical judgement in emergency diagnosis of heart failure: analysis from

breathing not properly multinational study. Circulation 2002; 106:416"422.

6. Januzzi JL, van Kimmenade R, Lainchbury J, et al. NT-proBNP testing for diagnosis and short-term prognosis in acute destabilized heart failure: an international pooled analysis of 1256 patients: the international collaborative of NT-proBNP study. European Heart Journal 2006; 27(3):330-337

7. Rothenburger M, Wichter T, Schmid C, et al. Aminoterminal pro type B natriuretic peptide as a predictive and prognostic marker in patients with chronic heart failure. Journal of Heart Lung Transplant 2004;23(10):1189-1197.

8. James SK, Lindahl B, Timmer JR, et al. Usefulness of biomarkers for predicting long-term mortality in patients with diabetes mellitus and non-ST-elevation acute coronary syndromes . American Journal of Cardiology 2006;97(2):167-172

9. James S K, Lindahl B, Siegbahn A, et al., "N-terminal pro-brain natriuretic peptide and other risk markers for the separate prediction of mortality and subsequent myocardial infarction in patients with unstable coronary artery disease: GUSTO IV substudy", Circulation, (2003),108: p. 9.

10. Brain natriuretic peptide as a potential marker of acute coronary syndromes Emerg. Med. J. (2006) 23(5): 403-407

11. Serial analyses of N-terminal pro-B-type natriuretic peptide in patients with non-ST-segment elevation acute coronary syndromes: A Fragmin and fast Revascularisation during InStability in coronary artery disease (FRISC)-II substudy J Am College Cardiology (2005) 45(4): 533-541

12. Cheng V, Kazanagra R, Garcia A. et al. A rapid bedside test for BNP predicts treatment outcomes in patients admitted for decompensated heart failure: a pilot study. J Am College of Cardiology. 2001 Feb;37(2): 386–91.

13. Maisel AS, Krishnaswamy P, Nowak RM, McCord J, Hollander JE, Duc P, Omland T, Storrow AB, Abraham WT, Wu AH, Clopton P, Steg PG, Westheim A, Knudsen CW, Perez A, Kazanegra R, Herrmann HC, Breathing Not Properly Multinational Study Investigators. Rapid measurement of BNP in the emergency diagnosis of heart failure. N England J Med 2002; 347:161-7. 68

14. Jernberg T, Stridsberg M,Venge P and Lindahl B,"N-terminal pro brain natriuretic peptide on admission for early risk stratification of patients with chest pain and no ST-segment elevation", J.Am. Coll. Cardiol. (2002), 40:p

15. Thejus ET al N-terminal Pro-Brain Natriuretic Peptide and Atrial Fibrillation Indian Pacing Electrophysiology J. 2009 Jan–Feb; 9(1): 1–4.

16. The N-terminal Pro-BNP Investigation of Dyspnoea in the Emergency department (PRIDE) study American Journal of Cardiology Volume 95, Issue 8 , Pages 948-954, 15 April 200520