Original Research Article

To estimate the serum level of N-terminal pro-brain natriuretic peptide levels in acute coronary syndrome

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Abstract

Background: Acute coronary syndromes caused by a sudden blockage of a coronary artery. According to degree and location of the blockage, it ranges from unstable angina to non–ST-segment elevation myocardial infarction (NSTEMI), ST-segment elevation myocardial infarction (STEMI), and sudden cardiac death. The levels of serum cardiac markers get elevated during myocardial necrosis in ACS. B-type natriuretic peptide (BNP), cardiac neurohormone, and its N-terminal fragment (NT-proBNP) are synthesized and secreted from the ventricular myocardium. It is well known that the stimulus for their release is the increase in left ventricular wall stress.
Aim and objectives: To estimate the serum level of N-terminal pro-Brain natriuretic peptide levels in acute coronary syndrome, to assess the levels of NT-pro-BNP and its relationship between STEMI, NSTEMI and Unstable angina patients.
Materials and methods: The study included 40 patients admitted in the medicine ward of RMMCH. The study period was from January 2018- July 2018. Patients with acute coronary syndromes were identified over a period according to the criteria and were included in the study. The patients were completely evaluated and their serum NT-pro BNP levels were noted. Killips Class was recorded if the patient was in acute MI. In NSTEMI, STEMI and unstable angina, TIMI scoring was also calculated.
Results: The common age of the patients was 51 to 60 years (50%). In the age group of 41 to 50 years, 30% was observed. In the age category of 31 to 40 years, 20% was observed. The mean age was 49.10 years. There was 55% of patients with NT pro BNP > 500 in the age category 51-60 years whereas only 16.7% in this range in the age category 41 to 50 years and again only 8%

in the age category 30 to 40 years. The Majority of 30 to 40 years had NT pro-BNP of 100 to 500 (62.5%). In the age category of 41 to 50 years, 50% had NT Pro BNP of 100 to 500 while only 35% was in this range in the age group of 51-60 years. In the age category of 41 to 50 years, 33.3% had NT pro-BNP of < 100 whereas only 10% of 51 to 60 years had NT pro-BNP of < 100 and in the age category of 30 to 40 years, no one had NT pro-BNP of <100. The chi-square test of association was insignificant. Cardiac enzymes (Troponin T and CKMB) was elevated for the majority of the patients (N=27, 67.5%). Cardiac enzymes (Troponin T and CKMB) were normal for only 32.5% of the patients. The correlation of TIMI score with NT pro-BNP was peak positive i.e. if NT pro-BNP is higher, TIMI score was also higher and vice versa but the correlation was insignificant (r=2.54, p = .64).

Conclusion: Even though the study is done in patients without clinical signs of heart failure, the levels of NT-proBNP had an inverse relationship with Ejection Fraction. Low NT-proBNP levels at the time of admission rule out high-risk patients or patients with heart failure.

Key words

NT-PROBNP, Acute Coronary Syndrome, Left Ventricular Hypertrophy, Cardiac Enzymes.

Introduction

According to the World Health Organization (WHO), cardiovascular diseases are the leading cause of deaths globally. Cardiovascular diseases involve the blood vessels, the heart, or both of which coronary artery disease is one of the life-threatening condition [1]. Patients with coronary artery disease consist of two major groups which include *chronic* coronary artery disease (CAD) and *acute* coronary syndromes (ACS). Acute coronary syndromes caused by a sudden blockage of a coronary artery [2]. According to degree and location of the blockage, it ranges from unstable angina to non–ST-segment elevation myocardial infarction (NSTEMI), ST-segment elevation myocardial infarction (STEMI), and sudden cardiac death [3]. Diagnosis of ACS can be done by a strategy which includes a proper detailed history, thorough physical examination, electrocardiogram, cardiac biomarkers and imaging studies of heart [4]. Diagnostic Guidelines for ACS includes ECG changes based on Marriotts Criteria, ST segment is elevated by 1 mm or more in two or more limb leads or precordial leads V_4 to V_6 or by 2 mm or more in two or more precordial leads V_1 to V_3; or ST-segment depressed by 1 mm or more in two or more precordial leads V_1 to V_3. In ECG of STEMI, there may be J-point elevation, hyperacute T waves, ST-segment elevation, and reciprocal-lead ST-segment depression can occur, whereas in NSTEMI and unstable angina ECG changes can be normal or ST-segment depression / T wave inversion [5]. The diagnosis of ACS depends on the levels of Serum cardiac markers which commonly includes Creatine kinase (CK), CKMB, Troponin I and Troponin T, BNP (Brain Natriuretic Peptide), NT Pro-BNP and C-Reactive protein (CRP). The levels of serum cardiac markers get elevated during myocardial necrosis i.e., in ACS. B-type natriuretic peptide (BNP), cardiac neurohormone, and its N-terminal fragment (NT-proBNP) are synthesized and secreted from the ventricular myocardium [6]. It is well known that the stimulus for their release is the increase in left ventricular wall stress. The recent clinical studies have shown that the quantity of raise in BNP or NT- Pro BNP can be used to predict the morbidity and mortality in acute coronary syndrome [7]. Measurement of NT proBNP is indeed an indirect measurement of Brain Natriuretic Peptide itself. The former is measured as it has a longer half-life than hormonally active BNP [8]. The half-life of BNP is around 20 minutes and the half-life of NT- proBNP is around 120 minutes. Here in our study the N- terminal pro-Brain Natriuretic

Peptide (NT-pro BNP) which is an inactive remnant of a hormonally active Brain Natriuretic peptide (BNP) is measured to predict the severity of STEMI, NSTEMI, and unstable angina [9]. This study also intends to see whether the level of NT-Pro BNP taken during an event of an ACS, correlates with Age, Sex, Ejection Fraction between STEMI, NSTEMI and Unstable Angina. Together with these results, we provide evidence that cardiac marker NT-pro BNP is an independent marker for both diagnoses and also for prognosis in patients with the acute coronary syndrome [10].

Materials and methods

The study included 40 patients admitted in the medicine ward of RMMCH. The study period was from January 2018- July 2018. Patients with acute coronary syndromes were identified over a period according to the criteria and were included in the study. The patients were completely evaluated and their serum NT-pro BNP levels were noted. Killips Class was recorded if the patient was in acute MI. In NSTEMI, STEMI and unstable angina, TIMI scoring was also calculated.

Inclusion criteria

- Those attended the OPD/casualty of Rajah Muthiah Medical College having Acute Coronary Syndrome.
- Admitted within 12 hours after the onset of symptoms.
- Patients within the age group 30 -60 years.

Exclusion criteria

- Heart failure.
- Chronic kidney disease.
- Patients who presented 12 hours after the onset of symptoms.
- Patients with age <30 and >60 years.

This study was conducted among 40 patients of age group between 30 to 60 of both sexes who got admitted within 12 hours after onset of symptoms and diagnosed as Acute Coronary Syndrome (STEMI, NSTEMI and Unstable Angina) in Rajah Muthiah Medical College and Hospital, Annamalai University during the period of November 2016 to August 2018 without heart failure (≥ Killip class II were excluded) and chronic kidney disease. 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, TIMI scoring was also calculated. Blood urea and serum creatinine were used to rule out frank renal failure. 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 12 hours of the onset of symptoms, NT-proBNP levels were measured in blood with Rapid NT proBNP Assay Kit.

Description of the NT-proBNP Rapid Assay Kit

The strips were coated with canine antibodies to human NT pro terminal end of Brain Natriuretic Peptide. It is a semi-quantitative assay and it gives the measurement as < 100 pg / ml, 100 – 500 pg/ml and > 500 pg/ml. Values below 100 pg/ml were considered as minimal or insignificant and values above 100 pg/ml were considered significant. Significant values in the range of 100 – 500 pg/ml was taken as moderately elevated and values above 500 pg/ml were taken as markedly elevated.

Statistical analysis

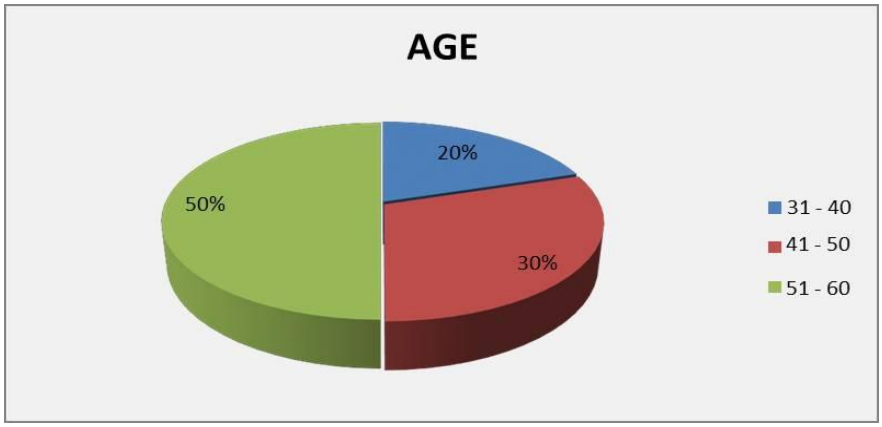
The data collected were analyzed and expressed as Mean ± SD. One way Analysis of variance (one way ANOVA), Pearson's

correlation test was used in the present study. Statistical software namely SPSS 20 was used for the analysis of the data and Microsoft Word and Excel to generate graphs and tables. Level of Significance: P < 0.05 was considered as significant while analyzing the data.

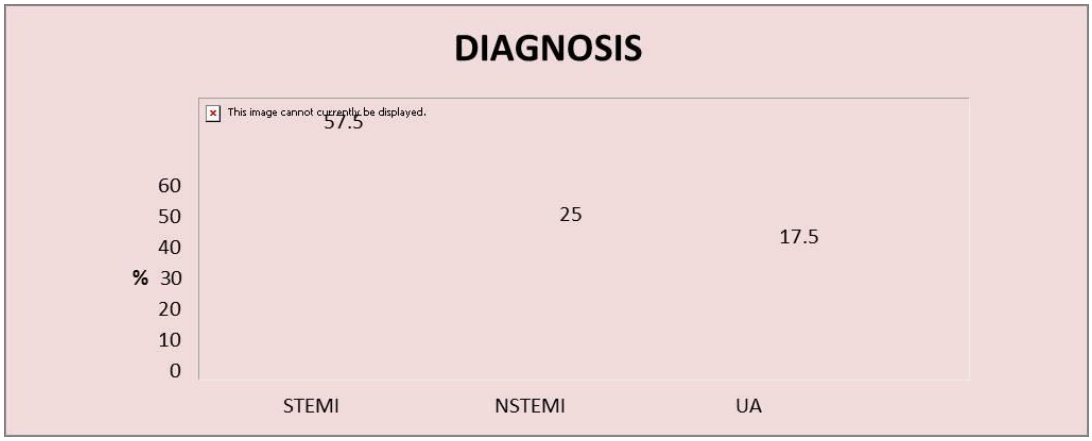
Results

The common age of the patients was 51 to 60 years (50%). In the age group of 41 to 50 years, 30% was observed. In the age category of 31 to 40 years, 20% was observed. The mean age was 49.10 years (**Graph – 1**).

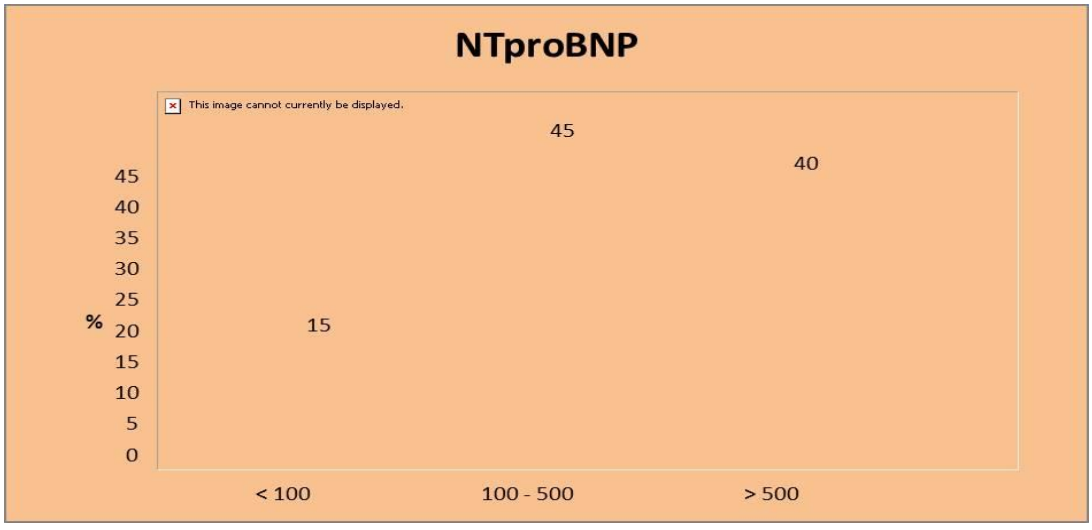
Graph – 1: Age distribution.



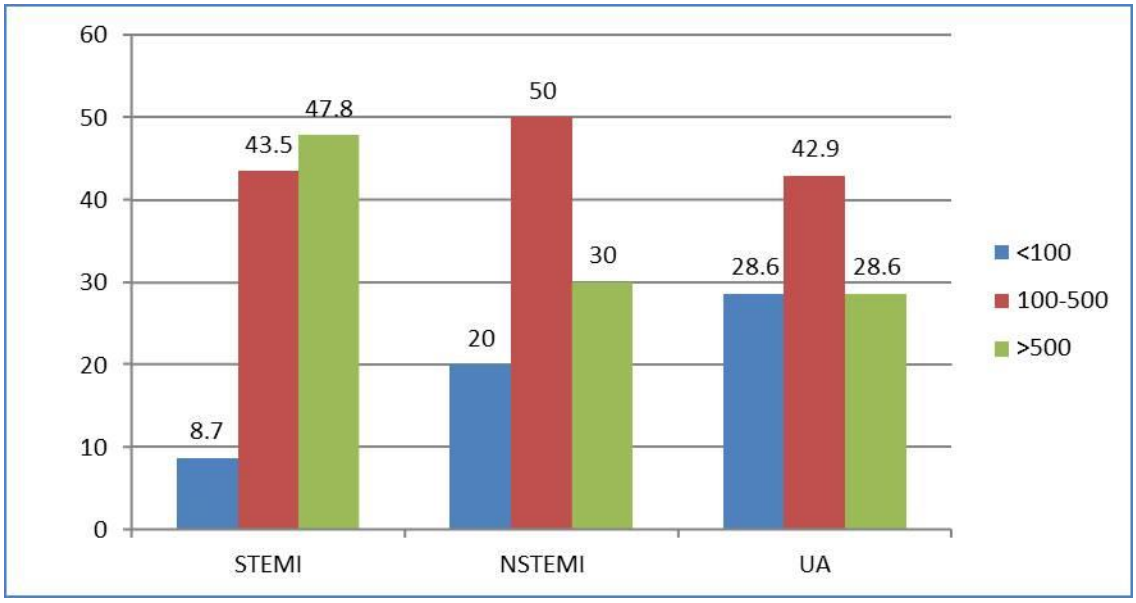
Graph – 2: Diagnosis.



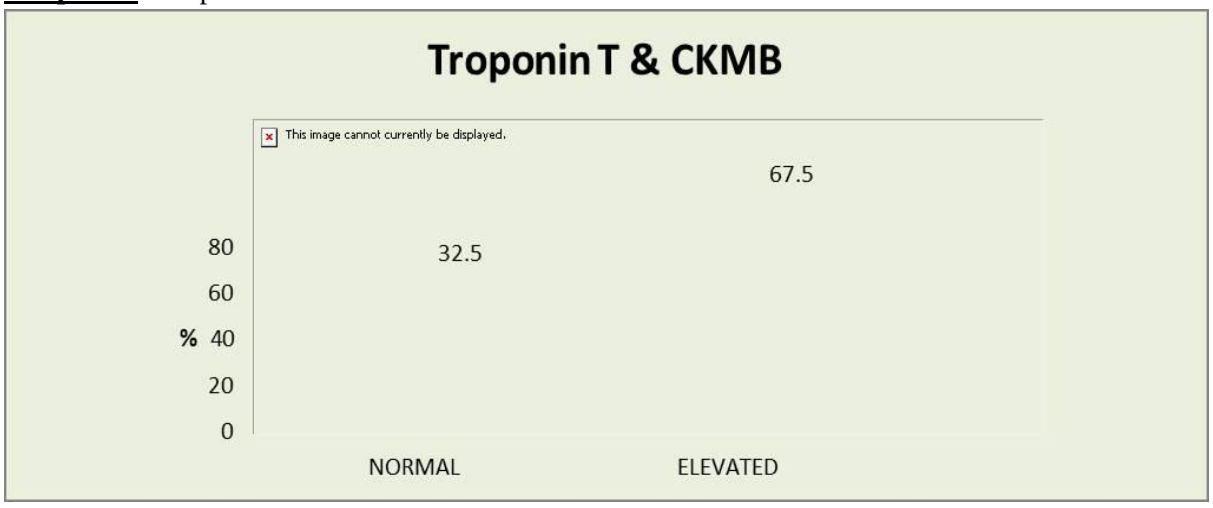
Graph – 3: NT pro BNP.



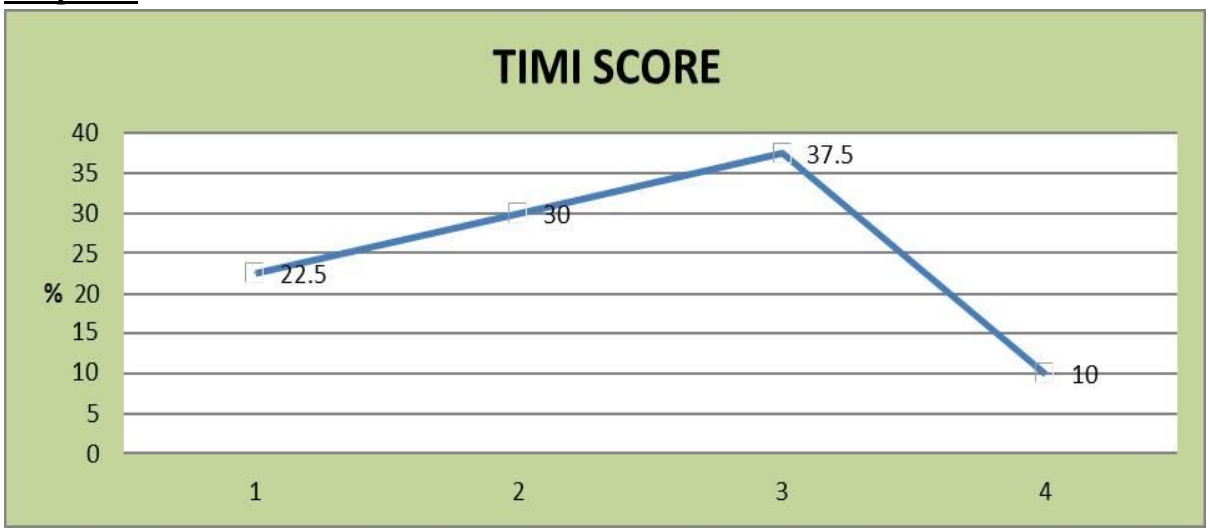
Graph – 4: Association of diagnosis, with the NT pro BNP.



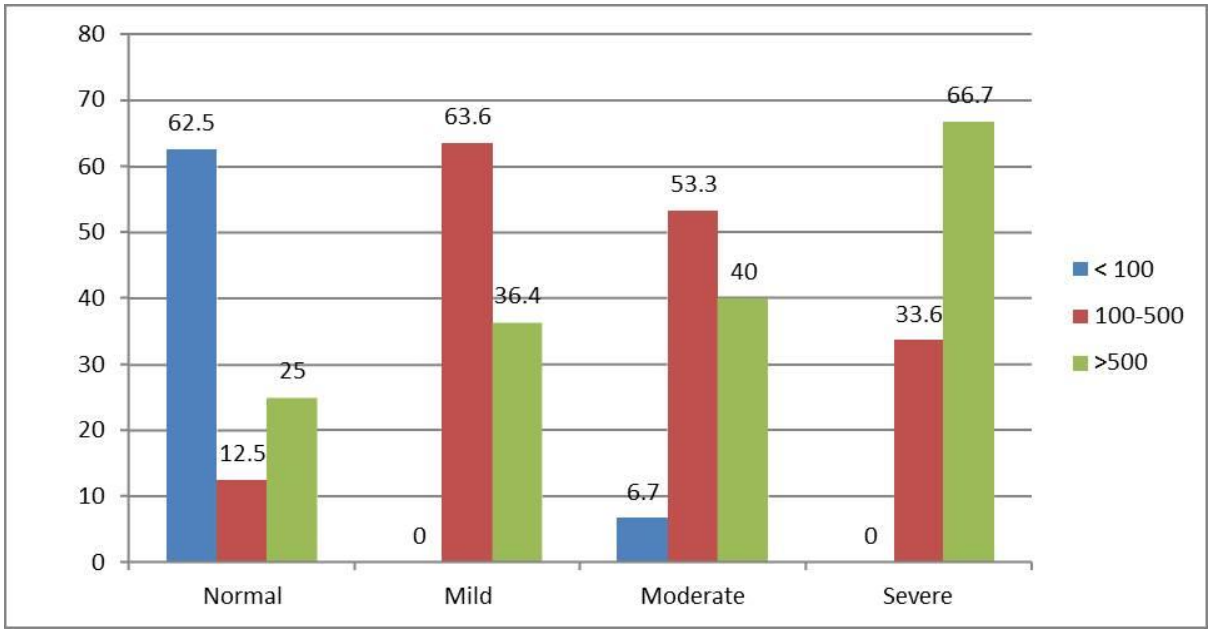
Graph – 5: Troponin T and CKMB.



Graph – 6: TIMI score.



Graph – 7: Association of LV function with NT pro BNP.



The majority of the patients had STEMI (N=23, 57.5%) NSTEMI was the findings for 25% of the patients. UA was the diagnosis for only 17.5% of the patients (**Graph – 2**).

For 85% of the study patients, NTpro BNP was <100. Therefore, for most of the patients, the value was raised. In the NT Pro BNP range 100-500, 45% was observed and in the category of >500, 40% was observed, only 15% had < 100 of NT pro-BNP (**Graph – 3**).

In STEMI >500 values of NTPro BNP was identified for 47.8% whereas in NSTEMI it was only 10% and in UA it was only 7% STEMI patients with 100 to 500 NT pro BNP was 43.5% whereas it was 50% in NSTEMI and 42.9% in UA, In the value of < 100, only 8.7% of STEMI was found whereas in NSTEMI 20% was observed and in UA 28.6% was observed. The association is statistically insignificant (x^2=2.54, p =0 .64) as per **Graph – 4**.

Cardiac enzymes (Troponin T and CKMB) was elevated for the majority of the patients (N=27, 67.5%). Cardiac enzymes (Troponin T and CKMB) were normal for only 32.5% of the patients (**Graph – 5**).

The common TIMI score was 3 and 2 were 37.5% and 30% noted respectively. The Mean TIMI score was 2.35 (**Graph – 6**).

In severe LV dysfunction, 66.7% had NT pro BNP > 500 whereas 40% had NT pro BNP > 500 in moderate LV dysfunction. NT pro BNP was greater than 500 for 11% of mild dysfunction and only 8% for normal LV function. LV function was normal for majority of patients (62.5%) with <100 NT pro BNP. Only 6.7% of moderate LV dysfunction had NT pro BNP < 100 and no one with severe dysfunction had NT pro BNP < 100. The chi-square test of association is significant (x^2= 19.97, p = .003) as per **Graph - 7**.

Discussion

The study population consists of 40 ACS patients which include age group between 30-60 years, the mean age of the patient was 49.10 years and males constitutes the majority of the population around 60%. Majority of patients in the age category of 51-60 years (55%) had NT-pro BNP >500. But the association of both age and sex with NT-pro BNP was statistically insignificant [11]. Among ACS, NT-pro BNP was higher (>100) in most of the patients (85%) patients in the study. Here in this study,

the majority of the patients was STEMI (57.5%) followed by NSTEMI (25%) and Unstable Angina (7%). In several studies of the patients with acute coronary syndrome, the elevation of NT-pro BNP has been observed [12]. In Mueller C, et al. study shows NT-proBNP was significantly higher in the case of STEMI compared with NSTEMI. Like the previous study, our study also had a greater value of NT- proBNP in STEMI patients. Even though STEMI patients (47.8%) had a higher value of NT- proBNP>500 than NSTEMI patients (30%) and UA (28.6%), the association is insignificant (P-value 0.64) [13]. Conversely in McCullough, et al., reported that the highest value of NT- proBNP in NSTEMI group compared to STEMI group. Here the mean TIMI score is 2.35± 95, but the correlation between TIMI scoring and NT-proBNP was insignificant. In Echocardiography, LV dysfunction was observed in 80% of the patients of which 27.5% had mild LV dysfunction, 37.5% had moderate dysfunction and 15% had severe LV dysfunction [14]. In NT-proBNP Investigation of Dyspnoea in the Emergency Department (PRIDE) study the data found to be impressive [15]. In the Landmark BNP study, BNP levels >100pg/ml carried an 89% net present value for excluding heart failure. The majority of patients with severe LV dysfunction (low Ejection Fraction) had greater NT pro-BNP (N=4, 66.7%) and the majority of normal LV function (normal Ejection fraction) (N=5, 62.5%) had lower NT pro-BNP (<100) and the association is statistically significant. Therefore for patients with more severe LV dysfunction, there was significantly higher NT pro BNP (p-value .003) [16, 17].

Conclusion

NT-proBNP is a reliable biomarker for confirming the diagnosis of ACS in not only STEMI and NSTEMI but also in Unstable Angina. NT-pro BNP is elevated more commonly in STEMI than in NSTEMI or Unstable Angina. The association of both age and sex with NT-pro BNP was statistically insignificant. Hence NT-proBNP levels were independent of the gender and age in the below 60 years. Even though the study is done in patients without clinical signs of heart failure, the levels of NT-proBNP had an inverse relationship with Ejection Fraction. Low NT-proBNP levels at the time of admission rule out high-risk patients or patients with heart failure.

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