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Correlation of N-Terminal Pro B-Type Natriuretic Peptide Level with Severity of Coronary Artery Disease in Patients with Non-ST Elevation Acute Coronary Syndrome with Preserved Ejection Fraction

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Abstract

Background: N-terminal pro-B-type natriuretic peptide (NT-pro BNP) has been established as an important biomarker for diagnosis and prognosis of cardiovascular diseases and serum level of NT-pro BNP also elevates in non-ST elevation acute coronary syndrome (NSTE-ACS) with preserved ejection fraction (LVEF ≥50%). The aim of this study was to correlate NT-pro BNP level with angiographic severity of coronary artery disease in patients with NSTE-ACS having preserved ejection fraction (LVEF ≥50%).

Methods: This cross-sectional study was conducted in the Department of Cardiology, National Heart Foundation Hospital & Research institute, Mirpur, Dhaka, over a period of one year from 01/08/22 to 31/07/23. Total 156 patients of NSTE-ACS who underwent coronary angiography (CAG) selected purposively were included after considering inclusion and exclusion criteria. Baseline characteristics, biochemical variables including NT-pro BNP, left ventricular ejection fraction (LVEF) and coronary artery disease (CAD) severity by Gensini score were assessed and evaluated. After that study populations were categorized into 3 groups according to Gensini score (GS). In Group A (Low GS, ≤24), 30 (19.2%) patients; Group B (Intermediate GS, 25-53), 46 (29.5%) patients and Group C (High GS, ≥54), 80 (51.3%) patients were assessed.

Results: The mean NT-pro BNP levels were 93.07±98.992, 240.04±460.339 & 638.34±645.364 pg/ml in Group A (≤24), Group B (25-53) and Group C (≥54) respectively. The association between NT-pro BNP level with Gensini score was significant ($p < 0.05$). There was positive correlation ($r=0.680$) observed between NT-pro BNP and Gensini score, which was statistically significant ($p < 0.05$). Multiple logistic regression analysis of predictors of intermediate to high Gensini score (≥25) was evaluated and only NT-pro BNP level was found significant (OR=12.629, 95% CI: 3.52-45.303, $p < 0.0001$).

Conclusion: NT-pro BNP is significantly associated with the presence and severity of CAD using Gensini score in patients with NSTE-ACS having left ventricular preserved ejection fraction (LVEF ≥50%).

Keywords: NT-Pro BNP; Gensini score; NSTE-ACS; Coronary angiogram (CAG)

Introduction

Coronary artery disease (CAD) remains the most important cause of death

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in the world. It is the leading cause of death in developed countries and second leading cause of death in developing countries and by the year 2020 ischemic heart disease (IHD) will hold the first place in the WHO's list of leading cause of disability [1]. The World Health Organization (WHO) has estimated that 3.8 million men and 3.4 million women die from cardiovascular disease (CVD) each year, and since 1990, more people have died from CVD than any other cause. Among them 80% occur in low and middle-income countries. This figure is expected to grow to 23.6 million by the year 2030. Coronary artery disease alone caused 7 million deaths worldwide in 2010 and it is an increase of 35% since 1990 [2]. The South Asian countries have among the highest incidence of coronary artery disease globally [3]. In Bangladesh, ACS is the major presenting form of CAD and thus managing the ACS is the real deal on cardiac patient care. Though the exact prevalence of CAD in Bangladesh is not known, recent data indicates that the prevalence of CAD in Bangladesh is between 1.85% [4] and 3.4% in rural area and 19.6% in an urban sample of working professionals [5]. Despite this marked disparity in values, there is a rising prevalence of CAD in Bangladesh both in male and female [6]. It also shows prevalence of CVD ranged from 0.062-77.7% [7]. Acute coronary syndrome (ACS) involves ST elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (NSTEMI), and unstable angina which are important life-threatening diseases, therefore their early diagnosis and management can save thousands of lives annually. Non-ST elevation acute coronary syndrome (NSTE-ACS) is much more common than STEMI; in the United States, 1.4 million patients per year are admitted to hospital with ACS, approximately 70% with NSTE-ACS [8]. By 6 months, NSTE-ACS mortality rates may equal or exceed those of STEMI and by 12 months, rates of death, MI, and recurrent instability in contemporary registries are >10%. Among patients with NSTE-ACS, approximately 15% experienced a reinfarction or death within 30 days of diagnosis [9]. The diagnosis of NSTE-ACS and the urgent revascularization strategy is supported by many biochemical markers and risk scores. However, these markers become elevated when ischemia and infarction has occurred. Therefore, a valuable biomarker for prediction of presence and severity of CAD before occurrence of such events is required [10]. The N-terminal pro B-type natriuretic peptide (NT-pro BNP) is synthesized and secreted from the ventricular myocardium in response to increased left ventricular wall stretch but also myocardial ischemia and infarction may stimulate its excretion. Its diverse actions include natriuresis, vasodilation, inhibition of the renin-angiotensin aldosterone system, and inhibition of sympathetic nerve activity [11]. Serum NT-pro BNP levels increase in several cardiovascular disease, which is the established biomarker for diagnosis, prognosis, and management, in particular in patients with heart failure [12]. Additionally, serum NT-pro BNP levels are closely related to the prognosis as a powerful predictor of both short- and long-term mortality in patients with ACS. NT-pro BNP has emerged as an important biomarker for diagnosis and prognosis for cardiovascular diseases [13]. Some studies have reported the beneficial effects of NT-pro BNP as a prognostic marker for predicting CAD severity based on angiographic findings as well as infarct size and myocardial function after myocardial infarction [14]. Providing the establishment of NT-pro BNP as an approved biomarker for risk stratification and association with CAD severity in patients with ACS, measurement of this peptide as a non-invasive rapid and simple method can alternate costly procedures. Now-a-days, conventional coronary angiography is the gold standard for diagnosis of obstructive CAD [15]. Various scoring systems are used for risk identification in ACS. SYNTAX score (SS), vessel score, and Gensini score (GS) are the most commonly used systems for this purpose, and they can also predict the prognosis and the need for revascularization. The Gensini scoring system was used to determine the severity of CAD [16].

Materials and Methods

Type of study: This study was a cross-sectional analytical study.

Place of study: This study was carried out at the Department of Cardiology of the National Heart Foundation Hospital and Research Institute, Mirpur, Dhaka, Bangladesh.

Study period: This study was carried out from August 2022 to July 2023 in the Department of Cardiology, NHFH and RI. A study protocol was designed, and it was presented and subsequently submitted to the ethical committee. After ethical approval, study population was selected based on the inclusion and exclusion criteria and the study was conducted.

Study population: Patients with NSTE-ACS.

Sample size: Total 156 patients of NSTE-ACS who underwent coronary angiography (CAG) selected purposively were included after considering inclusion and exclusion criteria.

Inclusion criteria:

- All patients with NSTE-ACS with preserved ejection fraction (LVEF ≥50%).
- Exclusion criteria:
- ECG showing new onset LBBB.
- Patients with valvular heart disease, chronic heart failure, cardiomyopathy.
- Patients with end stage renal disease.
- Patients with chronic liver disease.
- Patients with neoplastic, inflammatory & infectious diseases.
- Unwilling to give consent.

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Methods:

- 156 patients who admitted at National Heart Foundation Hospital & Research Institute, Dhaka with NSTE-ACS fulfilling the inclusion and exclusion criteria were included in this study.
- Informed consent was taken from each subject before enrollment.
- All baseline medical histories and clinical criteria were recorded.
- Demographic data was noted.
- Risk factors were recorded for all patients.
- Patient's baseline 12 lead ECG was recorded.
- Echocardiography was performed. Left ventricular ejection fraction was measured by global eyeball estimation method.
- Blood sample was taken for Troponin I, NT-pro BNP, Serum creatinine, fasting lipid profile, FBS/RBS.

Coronary angiography (CAG): All patients underwent coronary angiography via the Judkins technique. All angiograms were evaluated by experienced interventional cardiologists. In cases of discrepancy, the opinion of a third interventional cardiologist was obtained, and the final decision was made by consensus. Angiographic severity of CAD was usually assessed by calculating Gensini score. It is a popular and well-known method. This system was developed in 1975 based on following factors.

1) Severity of coronary artery lesion
2) Segment location multiplying factor

Calculation of the Gensini score was initiated by giving a severity score to each coronary stenosis. Thereafter, each lesion score was multiplied by a factor that takes into account the importance of the lesion's position in the coronary circulation. Finally, the Gensini score was calculated by summation of the individual coronary segment scores including score system for dominant LCX. On the basis of Gensini Score, patients were divided into three groups: Group A (Low GS ≤24), Group B (Intermediate GS 25-53) & Group C (High GS ≥54) [17].

Statistical analysis: All statistical analyses were performed using SPSS version 22.0 software. Obtained data had been expressed in frequency, percentage, mean and standard deviation as applicable. Comparison between groups had been done by ANOVA, Kruskal-Wallis test for continuous variable. Categorical data had been compared by chi-square test. $p<0.05$ was considered to indicate a statistically significant difference. Correlation between NT-pro BNP and severity of coronary artery disease severity by Gensini score had been done.

Results

Total 156 patients were included in this study. They were categorized into 3 groups according to Gensini score (GS). In Group A (Low GS, ≤24), 30 (19.2%) patients; Group B (Intermediate GS, 25-53), 46 (29.5%) patients and Group C (High GS, ≥54), 80 (51.3%) patients were enrolled. Observation and result of the study were as follows:

Table 1: Demographic characteristics of the study patients (N=156).

Age (years)	Frequency (n)	Percent (%)
30-40	7	4.5
41-50	39	25.0
51-60	56	35.9
>60	54	34.6
Total	156	100.0
Mean ± SD (Min-Max)	57.16 ± 10.03 (30-81)	
Gender		
Male	115	73.7
Female	41	26.3
Clinical Diagnosis		
NSTEMI	129	83
UA	27	17
Total	156	100.0
Risk factors		
DM	81	51.9
HTN	101	64.7
Dyslipidemia	90	57.7
Smoking	87	55.8
Obesity	88	56.4
Family history of premature CAD	88	56.4

The maximum patient age group was between 51-60 years. The mean (±SD) age was 57.16 (±10.03) years. Pie chart showing, among the study population, 73.7% (115) were male and 26.3% (41) were female. Among the study population, 83% patients had NSTEMI, and 17% patients had UA. Showing risk factor profile among the study population. About 51.9% patients had diabetes mellitus (DM), 64.7% patients had hypertension (HTN), 57.7% patients had dyslipidemia, 55.8% patients had history of smoking, 56.4% patients were obese, and 56.4% patients had family history of coronary artery disease (Table-1).

Table 2 showing laboratory variables of among the study population. Mean (±SEM) value of Trop I was 2.529 ±0.22 ng/ml. Mean (±SD) serum creatinine was 1.276 ±0.359 mg/dl. Mean (±SEM) value of NT-pro BNP was 416.03 ±46.03. Regarding fasting lipid profile, mean (±SD) of TC, HDL, LDL, TG were 162.21 ±37.654 mg/dl, 38.01 ± 6.199 mg/dl, 100.39 ±27.666 mg/dl, 169.88 ± 47.151 mg/dl respectively. Mean (±SD) LVEF was 53.5 ± 4.5 %.

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Table 2: Distribution of the patients according to laboratory variables and LVEF (N=156).

Variables	Mean ± SD	Min-Max
Creatinine (mg/dl)	1.276± 0.359	0.8-3.0
Trop I (ng/ml) (M±SEM)	2.529± 0.22	0.01-13.06
NT-proBNP (pg/ml) (M±SEM)	416.03± 46.03	28-3080
Fasting lipid profile		
o TC (mg/dl)	162.21± 37.654	92-262
o HDL (mg/dl)	38.01± 6.199	25-58
o LDL (mg/dl)	100.39± 27.666	48-178
o TG (mg/dl)	169.88± 47.151	85-580
LVEF (%)	53.5± 4.5	50-70

Table 3: Distribution of the study population according to Gensini Score (GS) (N=156).

Gensini Score	n (%)
Group A (Low GS) (≤24)	30 (19.2)
Group B (Intermediate GS) (25-53)	46 (29.5)
Group C (High GS) (≥54)	80 (51.3)
Total	**156 (100.0)**

Table 3 showing three groups according to Gensini score. Among the study population, 19.2%, 29.5% and 51.3% of patients were in Group A, Group B and Group C respectively.

Table 4: Distribution of the patients according to age by Gensini score (N=156).

Age (years)	Group A n (%)	Group B n (%)	Group C n (%)	p value*
30-40	3 (10.0)	2 (4.3)	2 (2.4)	0.239
41-50	14 (46.7)	14 (30.4)	11 (13.8)	0.001
51-60	6 (20.0)	18 (39.2)	32 (40.0)	0.129
>60	7 (23.3)	12 (26.1)	35 (43.8)	0.047
Total	**30 (100)**	**46 (100)**	**80 (100)**	
Sex				
Male	21 (70.0)	37 (80.4)	57 (71.2)	0.464
Female	9 (30.0)	9 (19.6)	23 (28.8)	
Total	**30 (100)**	**46 (100)**	**80 (100)**	
Risk factors				
DM	18 (60.0)	17 (37.0)	46 (57.5)	0.05
HTN	17 (56.7)	31 (67.4)	53 (66.2)	0.583
Dyslipidemia	14 (6.7)	29 (19.6)	47 (21.2)	0.049
Family H/O premature CAD	14 (46.7)	24 (52.2)	50 (62.5)	0.259
Obesity	18 (60.0)	26 (56.5)	44 (55.0)	0.895
Smoking	21 (70.0)	29 (63.0)	37 (46.2)	0.041
Clinical Diagnosis				
NSTEMI	20 (66.7)	40 (87.0)	69 (86.2)	**0.036**
UA	10 (33.3)	6 (13.0)	11 (13.8)	**0.035**
Total	30 (100)	46 (100)	80 (100)	

*Chi-square test was done to measure the level of significance. Figure within parenthesis indicates in percentage.

Table 4 showing the distribution of the patients according to age among the groups. Most of the patients (46.7%) in Group A were younger (41-50 years) and most of the patients (43.8%) in Group C were older (>60 years) which were statistically significant (p value <0.05). Showing the distribution of the patients according to gender among the groups. No statistically significant difference was observed among the three groups of patients by Gensini score (p>0.05). Hypertension (HTN), diabetes mellitus (DM), dyslipidemia, family H/O premature CAD and smoking were the most common risk factors in the groups. Statistically significant difference was observed among the three groups of patients (p<0.05) in case of DM, dyslipidemia, and smoking but statistically no significant difference was observed among the three groups of patients (p>0.05) in case of HTN, obesity and family history of premature CAD. Analysis revealed that there was statistically significant difference among the three groups in both NSTEMI and UA patients (p value <0.05).

Table 5: Distribution of the patients according to laboratory variables by Gensini score (N=156).

Biochemical profile	Group A Mean ±SD (mg/dl)	Group B Mean±SD (mg/dl)	Group C Mean ±SD (mg/dl)	p value*
S. creatinine (mg/dl)	1.217±0.394	1.249±0.407	1.313±0.313	0.188
Trop I (ng/ml) (M±SEM)	0.941±0.273	2.386±0.397	3.206±0.327	0.001
TC (mg/dl)	150±34.011	164.09±41.097	165.70±36.389	0.235
Triglycerides (TG)				
(mg/dl)	156.60±28.038	170.11±28.03	174.72±59.457	0.189
LDL-C (mg/dl)	92.27±21.967	101.09±30.789	103.04±27.427	0.221
HDL-C (mg/dl)	38.20±7.131	39.82±6.099	37.12±5.821	0.044

*ANOVA was done to measure the level of significance. Figure within parenthesis indicates in percentage.

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Table 5 showing association of Gensini score with biochemical parameters. Statistically significant (p<0.05) difference was observed in case of Trop I and HDL-C among the Gensini groups.

Table 6 showing distribution of coronary artery involvement in the three groups of patients by number of coronary artery involvement. Statistically significant difference was observed among the three groups of patients regarding the coronary artery involvement (p<0.05).

Table 6: Distribution of coronary artery involvement in the study populations by Gensini score (N=156).

Coronary artery involvement	Group A n (%)	Group B n (%)	Group C n (%)	p value*
LAD	17 (56.7)	45 (97.8)	77 (96.2)	**0.0001**
LCX	9 (30)	38 (82.6)	71 (88.8)	**0.0001**
RCA	16 (53.3)	36 (78.3)	69 (86.2)	**0.001**
LMCA	0 (0)	3 (6.5)	20 (25.0)	**0.001**

*Chi-square test was done to measure the level of significance. Figure within parenthesis indicates in percentage.

Table 7: Severity of coronary artery disease among study population by Gensini score according to vessel score (N=156).

Number of involved vessels	Group A n (%)	Group B n (%)	Group C n (%)	p value*
Normal	11 (36.6)	0 (0)	0 (0)	0.0001
SVD	14 (46.7)	11 (23.9)	8 (10)	0.0001
DVD	5 (16.7)	23 (50)	26 (32.5)	0.01
TVD	0 (0)	12 (26.1)	46 (57.5)	0.0001
Total	30 (100)	46 (100)	80 (100)	

*Chi-square test was done to measure the level of significance. Figure within parenthesis indicates in percentage.

Table 7 showed severity of coronary artery disease in the three groups of patients by number of coronary artery involvement. Statistically significant difference was observed among the three groups of patients (p<0.05) in case of vessel score. SVD and normal coronary artery were predominant in Group A patients, but DVD and TVD were predominant in Group B and Group C patients.

Table 8: Distribution of study population according to Gensini Score (GS) & level of NT- pro BNP (N=156).

Groups by Gensini score	n (%)	Level of NT-pro BNP Mean ± SEM (pg/ml)	p value*
Group A	30 (19.2)	93.07±18.073	0.0001
Group B	46 (29.5)	240.04±67.873	
Group C	80 (51.3)	638.34±72.154	
Total	156 (100.0)	------	

Kruskal-Wallis test was done to measure the level of significance.

Table 8 showing three groups according to Gensini Score (GS) & level of NT-proBNP. Among the study population, the mean NT-proBNP levels were 93.07±18.073, 240.04±67.873, 638.34±72.154 pg/ml in Group A, Group B and Group C respectively. The association between NT-proBNP level with Gensini score was significant (p value <0.05).

Spearman's rank correlation coefficient, r=0.680 & p <0.0001

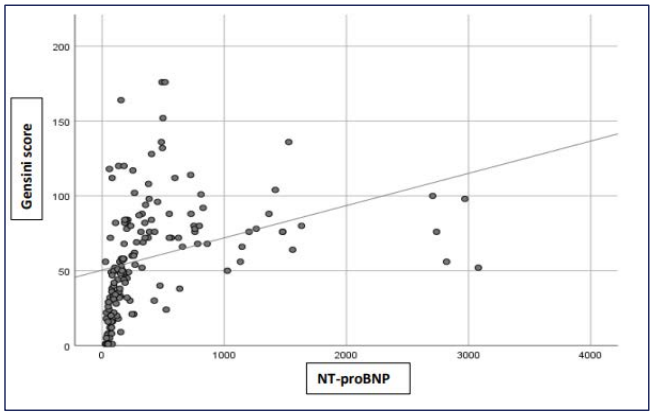

Figure 1: Spearman's rank correlation between NT-pro BNP with Gensini Score.

Correlation between NT-pro BNP and Gensini score were shown in above figure. There was moderate positive correlation (r=0.680) observed between NT-pro BNP and Gensini score, which was statistically significant (p <0.05). Coefficient of determination, $r^2 = 0.462$ means that in 46.2% cases, Gensini score was explained by NT-pro BNP.

Table 9 showing the multiple regression analysis of variables of intermediate to high Gensini score. Final regression model for intermediate to high Gensini score (≥25) was created including variables: Age ≥ 50 years, Diabetes mellitus (DM), Hypertension (HTN), Dyslipidemia, Smoking, Obesity and NT-pro BNP level. In this model only NT-pro BNP level was found significant (p<0.05) independent variable of intermediate to high Gensini score.

Table 9: Multiple Regression Analysis of variables of intermediate to high Gensini score (≥25)

95% C.I. for Odds Ratio						
Variables	**B**	**SE**	**p value**	**Odds Ratio**	**Lower**	**Upper**
Age ≥ 50 years	0.538	0.499	0.281	1.713	0.644	4.553
Sex	-0.031	0.541	0.955	0.97	0.336	2.799
DM	0.324	0.377	0.39	1.383	0.66	2.897
HTN	-0.183	0.407	0.652	0.832	0.375	1.848
Dyslipidemia	0.463	0.488	0.343	1.588	0.611	4.131
Smoking	-0.648	0.464	0.162	0.523	0.211	1.298
Obesity	-0.108	0.376	0.775	0.898	0.429	1.878
NT-proBNP	2.536	0.652	<0.0001	12.629	3.52	45.303

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Discussion

This cross-sectional study was conducted in the department of Cardiology, National Heart Foundation Hospital & Research institute, Dhaka, over a period of one year to evaluate the correlation of NT-pro BNP level with angiographic severity of coronary artery disease in patients with NSTE-ACS having preserved ejection fraction (LVEF ≥50%). Total 156 patients were included in this study. Among the study population, 129 (83%) patients had NSTEMI, and 27 (17%) patients had UA who have preserved ejection fraction (LVEF ≥ 50%). They were categorized into 3 groups according to Gensini score (GS). In Group A (Low GS), 30 (19.2%) patients; Group B (Intermediate GS), 46 (29.5%) patients; Group C (High GS), 80 (51.3%) patients were enrolled. The mean (±SD) NT-pro BNP levels were 93.07±98.992, 240.04±460.339 & 638.34±645.364 pg/ml in Group A (≤24), Group B (25-53) and Group C (≥54) respectively. In this present study, the mean (±SD) age was 57.16 ± 10.03 years. The maximum patient age group was between 51-60 years. South Asians have multiple risk factors that pose potentially atherogenic condition. It may be due to altered metabolic condition, frequent infection, inflammation, constant stress and narrowness of the arteries. CAD most probably occurs in relatively early age groups in our country. Goyal, Sharma and Walia et al [18] showed mean age was 52.7±10.4 almost matched with this study. In another study Palazzuoli et al [19] showed the mean age 68.6 ± 6.9 (BNP <80pg/ml) years and 72.5 ± 8.1(BNP <80pg/ml) years respectively which didn't match with this study. Among study population, 73.7% were male and 26.3% were female. Male were predominant in this study than female which matched the Sinning et al. [20] study in which they included 77.4% male and 22.6% female subjects. In Bangladesh and abroad, the various studies showed, the female patients formed a small percentage. In a study of Goyal, Sharma and Walia et al [18] showed increased male predominance in their study that they included 197 consecutive subjects and out of which male subjects were 154 in number which matched this study. In another study, Palazzuoli et al [19] showed almost similar sex ratio, 154 males and 138 females out of total 282 subjects; the finding which was contrary to our study. In this study, among the study population, 83% (129) patients had NSTEMI, and 17% (27) patients had UA which didn't match the Goyal, Sharma and Walia et al [18] study in which they enrolled 139 of UA patients and 58 of NSTEMI patients respectively. Regarding risk factors, hypertension, diabetes mellitus, obesity, dyslipidemia, family history of premature CAD and smoking were the most common risk factors in patients with NSTE-ACS. In this study, among the study population, about 51.9% patients had diabetes mellitus (DM), 64.7% patients had hypertension (HTN), 57.7% patients had dyslipidemia, 55.8% patients had history of smoking, 56.4% patients were obese, and 56.4% patients had family history of premature coronary artery disease. In this study, no statistically significant difference was observed among the three groups of patients (p>0.05) in case of HTN and family history of premature CAD which matched the Kalkan et al. [17] study. Among the study population, diabetes mellitus was found in 60%, 37% and 57.5% of patients in Group A (Low GS), Group B (Intermediate GS) and Group C (High GS) respectively which showed statistically significant difference (p value < 0.05) and matched the Sinning et al [20] study. About 6.7% of patients had dyslipidemia in Group A, 19.6% and 21.2% of patients had dyslipidemia in the Group B and Group C respectively which was statistically significant (p value < 0.05). About 70% of patients were smoker in Group A, 63% and 46.2% of patients were smoker in the Group B and Group C respectively which was statistically significant (p value < 0.05) which didn't match the Kalkan et al. [17] study and Sinning et al [20] study. About 56.7% of patients had hypertension in Group A, 67.4% and 66.2% of patients had hypertension in the Group B and Group C respectively. Obesity is one of the most important determinants of coronary artery disease. 60% of patients were obese in Group A, 56.5% and 55% of patients were obese in the Group B and Group C respectively. About 46.7%, 52.2% and 62.5% of patients had family history of premature CAD in Group A, Group B and Group C respectively which matched with Sinning et al [20] study. In patients with high GS (Group C), level of total cholesterol, TG, LDL-C & HDL-C were 165.70±36.389, 174.72±59.457, 103.04±27.427 and 37.12±5.821 mg/dl respectively. In patients with intermediate GS (Group B), level of total cholesterol, TG, LDL-C & HDL-C were 164.09±41.097, 170.11±28.03, 101.09±30.789 and 39.82±6.09 mg/dl respectively. In patients with low GS (Group A), level of total cholesterol, TG, LDL-C & HDL-C were 150±34.011, 156.60±28.038, 92.27±21.967 and 38.20±7.131 mg/dl respectively. Statistically significant difference was observed among the three groups of patients (p<0.05) in case of HDL-C which didn't match the Kalkan et al. [17] study. The mean of serum creatinine level was 1.217±0.394, 1.249±0.407, and 1.313±0.313 mg/dl in group A, group B and group C patients respectively. No statistically significant difference was observed among the three groups of patients (p>0.05) which didn't match the Sinning et al. [20] study. Trop I is a biomarker of myocardial injury. The mean of serum troponin-I level was 0.941±1.496, 2.386±2.69, and 3.206±2.924 ng/ml in group A, group B and group C patients respectively. Statistically significant difference was observed among the three groups of patients (p<0.05). In this study, LAD was involved in 56.7% (17), 97.8% (45) and 96.2% (77) of patients in group A, group B and group C respectively which was statistically significant (p<0.05) and matched the Kalkan et al. [17] study. Among the study population, in Group A, single vessel disease (SVD), double vessel disease (DVD) and triple vessel disease (TVD) were 46.7%, 16.7% and 0% respectively. In Group B, single vessel disease (SVD), double vessel disease (DVD) and triple vessel

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disease (TVD) were 23.9%, 50% and 26.1% respectively. In Group C, single vessel disease (SVD), double vessel disease (DVD) and triple vessel disease (TVD) were 10%, 32.5% and 57.5% respectively. Statistically significant difference was observed among the three groups of patients ($p<0.05$). SVD and normal coronary artery were predominant in Group A patients, but DVD and TVD were predominant in Group B and Group C patients. NT-pro BNP was significantly related to the extent of coronary disease. Significant progressive differences were assessed among patients with single vessel disease, double vessel and triple vessel disease. Among the study population, the mean NT-pro BNP levels were 93.07±98.992, 240.04±460.339, 638.34±645.364 pg/ml in group A, group B and group C respectively. The correlation between NT-pro BNP level with Gensini score was significant in each group (p value <0.05) which matched the Sinning et al. [20] study. In this study it was hypothesized that increased N-Terminal pro B-type natriuretic peptide (NT- proBNP) level is associated with severity of coronary artery disease in NSTE-ACS with preserved ejection fraction (LVEF ≥ 50%). After analysis it was found that there was moderate positive correlation (r=0.680), observed between NT-pro BNP and Gensini score which was statistically significant ($p<0.05$). Multiple regression analysis of variables of intermediate to high Gensini score (≥25) was evaluated which included variables like Age ≥ 50 years, Diabetes mellitus (DM), Hypertension (HTN), Dyslipidemia, Smoking, Obesity and NT-pro BNP level. In this model only NT-pro BNP level was found significant (p <0.05) independent association of intermediate to high Gensini score. Palazzuoli et al [19] showed the analysis of the Gensini Score (GS) demonstrated a positive correlation between coronary artery disease extension and BNP levels (r=0.40, $p<0.05$). Goyal, Sharma and Walia et al [18] also showed positive correlation (r=0.675) between BNP and Gensini score which was statistically significant ($p<0.05$). These findings were consistent with this study.

Conclusion

The present study showed that NT-pro BNP has a significant association with the presence and severity of CAD as it had a moderate positive correlation with the severity and complexity of CAD using Gensini score in patients with NSTE-ACS having left ventricular preserved ejection fraction (LVEF ≥ 50%). Thus, measurement of NT-pro BNP level may be considered as an essential parameter during planning treatment strategies like early revascularization, hospital discharge as well as risk stratification.

Study Limitations

Although the result of this study supported the hypothesis, there were some limiting factors which might have an effect on the results:

- The study was conducted in a single center.
- Purposive sampling was done instead of random sampling.
- In this study, assessment of coronary angiographic findings was limited to visual interpretation and angiography is a technique that detect only major coronary arterial lesion.
- The study did not compare NT-pro BNP levels to other biomarkers of myocardial injury such as Troponin, hs-CRP or cytokine levels.

Recommendation

- A simple measurement of NT-pro BNP level might play a crucial role in the assessment of coronary artery disease severity in patients with NSTE-ACS having left ventricular preserved ejection fraction (LVEF ≥ 50%).
- It appears as it can give additional prognostic information to existing traditional biomarkers (i.e., troponin and C-reactive protein).
- Further research should be done to explore the exact situation of the whole country considering all limitations of this study.
- Large scale randomized and multicenter prospective studies are needed to validate the findings of the present study. If the utility of NT-pro BNP level is supported by future studies, this may be added to existing routine cardiovascular risk evaluation for comprehensive assessment and management of patients with NSTE-ACS.

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