Medical Science Journal for Advance Research

Vol. 5, No. 3, September 2024
e-ISSN: 2774-4892

Impact of Age and Gender on Plasma N-Terminal Pro-B-Type Natriuretic Peptide

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ABSTRACT

Background: *Age has a significant impact on the body, which may affect plasma concentrations of NT-proBNP. (e.g., increased fibrosis and heart stiffness, worse renal function, and lower lean body mass). Elevated NT-proBNP levels are commonly reported in advanced age groups, even in seemingly healthy individuals. On the other hand, Some studies suggest that Women have larger plasma concentrations of natriuretic peptides than men.* ***Objective:*** *In a population-based research, we wanted to look at how age and gender affected the plasma N-terminal pro -B-type natriuretic peptide (NT.proBNP) concentration in patients with non-ST elevation acute coronary syndrome (NSTE-ACS) with negative coronary artery disease (CAD) confirmed by percutaneous coronary intervention (PCI).* ***Methods:*** *Electrocardiogram (ECG), serum troponin I, 2D echocardiography, plasma NT.proBNP, and PCI were performed on 48 Iraqi patients from Al-Najaf Center for Cardiac Surgery and Transcatheter Therapy/ Al-Sader Teaching Hospital, department of coronary intervention who have non-ST elevation acute coronary syndrome NSTE-ACS with negative CAD (< 50% arterial blockage) seen by PCI. This group of people had sinus rhythm, no renal or pulmonary illness, normal systolic function, and no valvular abnormality.* ***Results:*** *Within this group, Age differences existed in NT.proBNP distribution. Age-related increases in NT.proBNP were statistically significant. Regarding gender, our results had no statistically significant difference in NT.proBNP between males and females.* ***Conclusions:*** *Our study concluded that Plasma NT.proBNP level increases with age among patients with NSTE-ACS and negative CAD, while there is no significant difference in this hormone between males and females.*

keywords: *N-terminal pro -B-type Natriuretic Peptide, Age, Gender.*

Article Information
Received: June 21, 2024; Revised: August 15, 2024; Online: September, 2024

INTRODUCTION

B-type natriuretic peptide (BNP) or brain natriuretic peptide can be defined as a hormone produced by cardiac ventricles when the wall is exposed to a stressor like volume overload or pressure overload. (1) PreproBNP is A pre-propeptide that consists of 134 amino acids. it is produced by cardiomyocytes and is subsequently divided into a propeptide _which is also known as proBNP and consists of 108 amino acids_ and a signal peptide. (2) ProBNP is divided into the active form BNP (which consists of 32 amino acids), which correlates to the C-terminal part, and the inactive N-terminal segment (NT.proBNP, 76 amino acids), at a ratio of 1:1 during its release from the cardiomyocytes. (3)

https://doi.org/10.46966/msjar.v5i3.202

Released BNP inhibits the renin-angiotensin-aldosterone system and the adrenergic system while simultaneously causing natriuresis and vasodilation. (4) Enhanced myocardial relaxation is the outcome of elevated plasma BNP concentration (2), which also plays a crucial regulatory function in reaction to unexpected rises in ventricular volume by counteracting vasoconstriction, salt retention, and the antidiuretic outcome which is recruited by the renin-angiotensin-aldosterone system. On the other hand, patients with LV dysfunction and acute myocardial infarction have higher plasma NP levels, and these elevated levels continue throughout the late stages of cardiac remodeling. (2) It can be used as a marker in the diagnosis of congestive heart failure (5). Studies have shown that BNP may also be used as a prognostic marker that indicates the prognosis of ischemic heart disease(IHD) (6). The rate of mortality has increased twice when BNP and serum troponin I levels were increased. (1) The potential use of these peptides to diagnose congestive heart failure or detect left ventricular dysfunction has received a lot of attention recently. Factors such as age, gender, and other physiological factors affect the plasma concentration of BNP or NT.proBNP in patients with NSTE-ACS confirmed by PCI. Understanding these variables is crucial for interpreting test findings, especially in non-acute settings when significant increases are unusual. Our study focused on the correlations between plasma NT.proBNP levels and age and gender in a population with negative CAD on PCI.

According to researches, age, and gender have a considerable impact on NT-proBNP levels. According to Hogenhuis, BNP and NT-proBNP levels rise with age, while BNP increases more significantly. (7) Zhang confirmed a positive association between the concentration of NT and age, with greater levels in females below 80. (8) As stated by Alibay , there is no significant link between NT-proBNP, age, gender, or BMI. (9) Leósdóttir found that the relationship between NT-proBNP and glucometabolic disorders may alter depending on age and gender. (10) Younger age, male sex, and increases in obesity-related characteristics were associated with lower levels of N-terminal pro-B-type natriuretic peptide in the general population.(11) Plasma N-terminal-pro-B-type natriuretic peptide levels increase with aging.(12)

METHODS

Study sample:

Participants in a population-based cross-sectional study of ACS without ST elevation but negative CAD on PCI comprise the study population. they were taken from the Al-Najaf Center for Cardiac Surgery and Transcatheter Therapy/ Al-Sader Teaching Hospital, Department of Coronary Intervention. 48 patients aged 38 to 81 years old. They all underwent ECG, serum Troponin I, 2D echocardiography to assess systolic function, plasma NT.proBNP assessment and PCI . Only those with sinus rhythm, left ventricular ejection fraction 55% or above, no significant valvular illness, no signs of pulmonary hypertension on echocardiography, negative CAD on PCI, and no right ventricular dysfunction were included in our recruitment.

Each participant was informed of the study's objectives, protocols, and methods and given the option to choose to participate or not. They gave their explicit, willing consent. Additionally, the study was given approval by the Kufa University Faculty of Medicine's Ethical Committee.

Blood sample collection and analysis:

Each person was given a five-milliliter

venous blood sample, which was then placed in a gel tube using disposable syringes and needles. This sample was thereafter left for roughly fifteen minutes. It was then centrifuged to separate the serum from the entire blood. Then, 75 microliter of serum was added to the detection buffer tube and mixed for 10 minutes. 75 microliter of the sample mixture was added to the cartridge, and had been incubated for 15 minutes. Finally, the results were read.

Statistical analysis:

Version 26 of the Statistical Package of Social Science (SPSS) software was used to analyze the data. Categorical variables were reported as frequency and percentage and evaluated using the Chi-square test to determine the level of significance and the correlations between them. P.value of 0.05 has been used in this study. P value < or =0.05 was regarded as significant.

RESULTS AND DISCUSSION

Table 1 shows the clinical characteristics and risk factors of the patients. This cross-sectional study involved 48 patient, whom ages ranged from 38 to 81 years old , with mean age of 59.52 ± 11.03, with 26 male and 22 female . We categorized the age group in 20-year incremental into 3 categories. 16 (33.3%) were diabetics and 24 (50%) were hypertensive. 17 (35.4%) were smokers. Regarding the BMI, 47.9% had ideal weight, 35.4% were overweight, 14.6% had class I obesity and 2.1% had class II obesity. Regarding the normal value of NT.proBNP, Our lab divided the normal value of NT.proBNP According to the package insert, as the following:

- **< 250 pg/ml in patients aged < 75 years old.**
- **250 – 450 pg/ml in patients aged > 75 years old.**

The results of NT.proBNP are shown in Table 2. The mean NT.proBNP in patients aged <75 year old was 149.06 ± 97.7 and in patients aged >75 years old was 408.2 ± 173.5. The mean NT.proBNP in the age category of 30-49 was 116.45 ± 137.9, in patients aged 50-69 was 151.6 ± 79.8, and in patients aged 70-89, the mean NT.proBNP was 232.6 ± 156.7. Also, our study found that the mean NT.proBNP in males was 158.3 ± 115.2 and in females gender it was 173.5 ± 126.1.

Table (1): Shows the clinical Characteristics and risk factors of the patients.

Variables	Classification	N	%	Mean ± SD
Age	30-49	9	18.8	43.56 ± 3.8
	50-69	27	56.3	58.93 ± 6.3
	70-89	12	25.0	72.83 ± 3.3
	Total	48	100.0	59.52 ± 11.02
Gender	Male	26	54.2	
	Female	22	45.8	
Hypertension	Hypertensive	24	50.0	
	Non-hypertensive	24	50.0	
DM	Diabetics	16	33.3	

	Non-diabetics	**32**	**66.7**	
BMI	**Ideal weight**	**23**	**47.9**	**21.92 ± 1.8**
	Overweight	**17**	**35.4**	**27.2 ± 1.01**
	Obesity class I	**7**	**14.6**	**33.07 ± 1.8**
	Obesity class II	**1**	**2.1**	**37.6**
	Total	**48**	**100.0**	**25.74 ± 4.6**
Smokers	**Smokers**	**17**	**35.4**	
	Non-smokers	**31**	**64.6**	

Table (2) : Shows the results of NT.proBNP level of the patients.

Variable	Category	Mean ± SD	P value
Age	**30-49**	**116.45 ± 137.9**	**0.000**
	50-69	**151.6 ± 79.8**	
	70-89	**232.6 ± 156.7**	
Gender	**Male**	**158.3 ± 115.2**	**0.46**
	Female	**173.5 ± 126.1**	

*The relationship between NT.proBNP and age was found to be statistically significant with a **P value < 0.05**, while the correlation between NT.proBNP and gender was found to be not significant with a P value > 0.05.*

DISCUSSION

Effect of age on NT.proBNP levels:

We found a significant increase in mean NT.proBNP with age, which is consistent with many previous investigations. Experimental and clinical studies provide a physiological explanation for the age-related increase in natriuretic peptide levels. Animal studies have shown an increase in natriuretic peptide gene expression with advanced age. (13) Clinical investigations show that aged patients have lower clearance of natriuretic peptides from their plasma, even without kidney impairment. (14) Reduced non-renal clearance mechanisms, such as platelet-associated clearance receptors, may lead to increased levels in the elderly. (15).

High NT.proBNP levels among older people can be caused by a variety of age-related modifications to the heart, including decreasing heart muscle flexibility, decreased heart pumping efficiency, and an increased risk of heart disease. (16) Redfors and colleagues, who discovered that individuals with increased BNP levels were older, confirm and corroborate our findings. (17) Al Awadi, M. and colleagues studied Prognostic Value of Serum BNP in

NSTEMI patients and Its predictive value on the Extent of CAD. They found a statistically significant relationship between BNP levels and both age and DM. (18)

Effects of gender on NT.proBNP levels:

Although our results showed that mean NT.proBNP was higher in female than male, this finding was not significant, P value > 0.05 . This finding agrees with Amjad S. and colleagues who found the same result (19), while disagree with another study in South Korea that stated that NT.proBNP was higher in females than males.(20) This difference in the result may be related to the huge difference in sample size, age, and BMI. Their study included 39,937 patients of young, Asian obese population.

CONCLUSION

In a small Iraqi population of patients with NSTE-ACS and negative CAD, we concluded that plasma NT.proBNP increases with age, while there was no significant difference in this hormone between males and females.

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