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Correlation of NT-proBNP levels with Left Ventricular Ejection Fraction in Cardiac Failure Patients

Aamenah Malik[1], Hira Sohail [2], Ambreen Tauseef [3], Sahar Javed [4], Masooma Talib [5], Huma Ashraf[6]

[1]Associate Professor, Department of Biochemistry, CMH Lahore Medical College & IOD, Lahore, Pakistan.
[2]Assistant Professor, Department of Biochemistry, CMH Lahore Medical College & IOD, Lahore, Pakistan.
[3]Associate Professor, Department of Physiology, CMH Lahore Medical College & IOD, Lahore, Pakistan.
[4]Assistant Professor, Department of Biochemistry, CMH Lahore Medical College & IOD, Lahore, Pakistan.
[5]Assistant Professor, Department of Biochemistry, Watim Dental College, Islamabad, Pakistan.
[6]Associate Professor, Department of Biochemistry, CMH Lahore Medical College & IOD, Lahore, Pakistan.

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ABSTRACT

Background: Amino-terminal pro brain natriuretic peptide (NT-proBNP), a biologically inactive derivative of Brain natriuretic peptide is released from cardiac ventricles as a response to stretch resulting from congestive heart failure (CHF). The objective is to determine the correlation of NT-pro BNP levels with Left Ventricular Ejection Fraction (LVEF) in cardiac failure patients. **Methods:** 78 patients with CHF (50 men, 28 women; mean age 58.26 +/- 10.59 y) were included in this study. NT-ProBNP and LVEF was measured in 78 patients of CHF (20-80) years of age both sexes). Prior consent of all subjects was taken. History and investigations were recorded in specially designed proformas. **Results:** There was a positive correlation between NT-proBNP and LVEF and NT-proBNP increased significantly with each increasing class of the disease severity. **Conclusion:** The severity of CHF can be objectively assessed by measuring the circulating levels of NT-proBNP. NT-proBNP may be a better indicator of the severity of ventricular dysfunction than clinical judgment alone.

Keywords: NT-pro BNP, Cardiac failure, LVEF.

INTRODUCTION

In recent decades , congestive heart failure (HF) is on the rise world over and is thus becoming a major public health problem.[1] Cardiovascular disease is the leading cause of death worldwide with a less than 50% four year survival rate.[2] Cardiac failure is the fastest growing clinical cardiac disease entity in the United States.[3] Most South Asian countries, including Pakistan, Bangladesh and India, belong to low and middle income countries (LMICs) and are identified to have a higher risk of coronary heart diseases (CHD) as compared to other part of the globe.[4] In India alone, the occurrence is 1.57 million per year and frequency is 18 million patients.[5] HF is one of the most frequent causes of multiple hospitalizations,[6] as well as elevated costs.[7] Premature diagnosis and treatment are of substantial importance.

Preliminary CHF diagnosis is frequently clinical and non-specific and hence challenging. No unified system of diagnostic criteria has been agreed as the gold standard for heart failure. Several criteria have been designed but all rely on similar indicators of symptoms and elevated filling pressures and merge data from the patient history, physical examination and radiological findings of chest X ray. Determination of CHF is complex because it's a syndrome and moreover symptoms are vague. Expensive procedures as echocardiography are used for differential diagnosis. Therapeutic options decline as CHF progresses, patient may necessitate mechanical intervention such as left ventricular assist devices or even heart transplant.[8] To shrink morbidity and mortality early positive diagnosis is vital.

In emergency setting with acute onset of dyspnoea, it is difficult to make differential diagnosis of chronic obstructive pulmonary disease (COPD) and congestive heart failure because of the non-specific symptoms, which are not sensitive for the definitive diagnosis of heart failure. Although echocardiography is the gold standard for left ventricular dysfunction,[9] it is not always accessible in tertiary care set up. Thus, there has emerged a rising need for a reliable, fast, accessible and cheap test.[10]

Serum B-type Natriuretic peptide (BNP) is used nowadays in the diagnosis of heart failure. BNP is a hormonally active peptide that is released from the left ventricular wall in response to stretch in the myocytes. It is produced as a prohormone, Pro BNP which is consequently cleaved into N Terminal –pro BNP (NT-ProBNP) and the biologically active BNP. It is then secreted into the blood in equimolar amounts.[11] Circulating BNP protects the body from plasma overload by inducing natriuresis, diuresis, sympathetic inhibition and dilatation of vascular walls.[12]

Name & Address of Corresponding Author
Dr. Ambreen Tauseef
Associate Professor, Department of Physiology, CMH Lahore Medical College & IOD,
Lahore, Pakistan.

When heart fails, it stretches which leads to decrease left ventricular ejection fraction. The discharge of NT-Pro BNP is directly related to myocardial stretch. Henceforward levels rise significantly with worsening symptoms and worsening LVEF. That's why it is a potential biomarker for risk assessment and diagnosis.[13,14]

It is therefore a consistent biomarker for quantitative evaluation of heart failure severity. It can also help the clinician in diagnostic and therapeutic decision.[15]

Unluckily, this extremely useful biomarker has not yet been normally integrated in our guidelines for management of heart failure although it is being incorporated internationally. In order to highlight the role of NT-Pro BNP in cardiac failure no study has been done so far in our population.

MATERIALS AND METHODS

The venue of this study was Post graduate medical institute, Lahore in cooperation with Punjab Institute of Cardiology Lahore. It is a cross sectional analytical study. NT-Pro BNP levels were checked in sixty four patients of CHF (30-80 years of age both sexes). Patients with renal disease, AMI or unstable angina were excluded. Serum concentration of NT-Pro BNP was assessed by Immunological UV assay and enzyme linked assay (ELISA) and LVEF was measured using Hewlett Packard Image point, model M2410A (Andover, Massachusetts, USA). SPSS 20 (Statistical Package For Social Sciences) was used for analysis. P-value of <0.05 was significant.

Sixty four patients with CHF (31 men, 33 women; mean age 58.26 ± 10.59 y) were included. Higher than normal levels of NT-pro BNP were found in CHF patients. Positive correlation between NT-pro BNP and heart failure severity was found in patients, and the level of NT-pro BNP increased significantly with increasing class of the disease.

RESULTS

Mean LVEF measured by echocardiography ranged between 36.6+8.3. The mean LVEF was higher in females (40%) than males (34%) .The patients were subdivided based on LVEF as per Euro Score into three categories of heart failure: Mild (LVEF 45-55%) ,Moderate (LVEF 30-45%) and Severe (LVEF <30%) The majority (46%) suffered from moderate heart failure, while 32% from severe and 21 % from mild heart failure [Table 1].

Table 1: LVEF - Based Classification of heart failure among males and females

(LVEF based classification)						
	Total		Male		Female	
	N	%	N	%	N	%
LVEF*	36.6±8.3		34.7±7.2		40±9.1	
Heart Failure						
Mild	17	21.8%	5	10.0%	12	42.8%
Moderate	36	46.1%	26	52.0%	10	35.7%
Severe	25	32.0%	19	38.0%	6	21.4%

*LVEF – Left Ventricular Ejection Fraction

The comparison of plasma levels of NT-Pro BNP amongst different categories of heart failure classified as mild, moderate and severe based on worsening Left Ventricular Ejection Fraction was determined [Table 2].

Patients with LVEF in the range of 45-55% were grouped as mild heart failure patients while LVEF between 30-45% as moderate and LVEF <30% as severe heart failure. The patient distribution was such that 17 belonged to the mild group 36 to the moderate heart failure and 25 patients were having severe heart failure. Mean NT-ProBNP levels in patients was 7493 pg/ml. Mean NT-ProBNP levels in patients with mild heart failure was 1971 pg/ml while it was 7134 pg/ml in patients with moderate heart failure. The difference in NT-ProBNP levels between mild and moderate heart failure groups was significant (p value .019). The mean value increased to 11,964 pg/ml in patients with severe heart failure ; however the difference in NT-ProBNP levels among moderate and severe heart failure categories was not significant(p value 0.072).

Correlation coefficients of NT-ProBNP when plotted against heart failure category showed a positive correlation between these two variables (r=0.445) which is statistically highly significant (p < .001) [Table 3].

Table 2: Variation of NT-Pro BNP in different heart failure categories in males and females

Heart failure category by LVEF		Mild LVEF: (n=17)	Moderate LVEF: (n=36)	p-value*	Severe LVEF: (n=25)	p- value**	Total (n=78)
NT-Pro BNP levels (pg/ml)	Male	1141 (n=5)	6814 (n=26)	.163	8498 (n=19)	.530	6787 (n=50)
	Female	2318 (n=12)	7967 (n=10)	.045	22937 (n=6)	.021	8754 (n=28)
	Total	1971	7134	.019	11964	.072	7493

*Comparison of NT-ProBNP levels between mild and moderate heart failure categories (T-test)
**Comparison of NT-ProBNP levels between moderate and severe heart failure categories (T-test)

Table 3: Correlation coefficients between NT-ProBNP and Heart Failure Category

			NTproBNP	Heart Failure
Spearman's rho	NT-ProBNP	Correlation Coefficient	1.000	.445**
		Sig. (2-tailed)	.	.000
		N	78	78
	Heart Failure	Correlation Coefficient	.445**	1.000
		Sig. (2-tailed)	.000	.
		N	78	78

**. Correlation is significant at the 0.01 level (2-tailed).

DISCUSSION

The current study aimed to relate the levels of NT-ProBNP with the Left Ventricular Ejection Fraction measured by echocardiography which is the gold standard for the heart failure assessment. But it is not readily available to all the patients in the emergency and is dependent on observer. Three groups were made as having mild heart failure (LVEF 45-55%), moderate failure (LVEF 30-45%) and severe heart failure (LVEF <30%). Comparison of NT-ProBNP levels were made in all three groups. The average levels increased from 1972 pg/ml in mild heart failure to 7134 pg/ml in moderate heart failure and went upto 11,964 pg/ml in severe heart failure patients. The NT-ProBNP plasma levels showed correlation with increasing severity of disease. This is in line with various studies done by Amulya et al, 2012 and Liugi et al, 2009 and Januzzi et al 2006 which demonstrated that increase level of natriuretic peptides occur with worsening left systolic heart failure and worsening ejection fraction.[16,17,18]

The NT-ProBNP determination is thus useful in diagnosis and assessment of severity of systolic dysfunction of heart and measures the extent of ventricular dilatation.

NT-ProBNP is used as an emergency marker which can be measured for initial screening and then followed up to monitor the severity of congestive heart failure.[19]

CONCLUSION

Positive correlation was observed between worsening class of heart failure based on Left Ventricular Ejection Fraction and serum NT-ProBNP levels. Thus the release of NT-ProBNP from the ventricles increases as the cardiac dilatation increases and ejection fraction falls. This makes it a reliable quantitative marker for severity assessment and supports in classification of CHF patients based on severity.

Recommendations:

The cardiac marker NT-ProBNP needs to be implemented in cardiac emergency centres routinely for early diagnosis of CHF. The initial triage of suspected CHF patients using this biomarker can be done as per international guidelines for cardiac failure management.

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