Journal of Cardiovascular Disease Research

ISSN:0975 -3583,0976-2833 VOL13, ISSUE 08, 2022

Original research article

N-Terminal Pro-B type natriuretic peptide level in acute decompensated and chronic heart failure patients

[1]Thyakadavil VG, [2]Dr. Girish Konasagara Shanthaveeranna, [3]Rashad PH

[1]MSc, PhD, Professor, Department of Biochemistry, St John's Medical College and Hospital, Bangalore, Karnataka, India

[2]MD Biochemistry, Associate Professor, Department of Biochemistry, Shri Atal Bihari Vajpayee Medical College & Research Institute. Bangalore, Karnataka, India

[3]MSc MLT, Department of Biochemistry, St John's Medical College and Hospital, Bangalore, Karnataka, India

Corresponding Author:

Dr. Girish Konasagara Shanthaveeranna (girishks@outlook.com)

Abstract

Introduction: NT - pro BNP is a natriuretic peptide; elevated levels are seen in patients with heart failure. Apart from the follow up of patients with heart failure it is also currently used for the detection and exclusion of ventricular dysfunction in patients attending the emergency department for acute dyspnea. This study was done to know the NT – pro BNP level in acute decompensated heart failure (ADHF) and chronic heart failure patients (CHF).

Methods: It was a prospective observational study in 200 heart failure patients. The heart failure patients were divided into acute decompensated ADHF and CHF. Patients with kidney diseases were excluded from the study. Descriptive and inferential statistics was done to analyze the data of the study. ANOVA and student t test have been used to study the significance of parameters between the groups.

Results: Of 200 heart failure patients studied, 133 were males and 67 were females. 125 patients had ADHF and 75 were CHF. The mean NT pro – BNP (NTpBNP) levels were higher in ADHF (19754.40 ± 1982ng/L) compared to CHF (3062.30 ± 319ng/L). Along with NT – pro BNP, About 127 patients had hypertension and 113 had diabetes mellitus, and in these patients NT-pro BNP was found to be increased when compared with non-diabetic and non-hypertensive heart failure patients. Troponin I level was also found to be elevated in ADHF.

Conclusion: NT-pBNP levels are significantly increased in ADHF than CHF patients and in patients associated with diabetes, hypertension presenting with heart failure

Keywords: NT-pro BNP, Acute decompensated heart failure, chronic heart failure, troponin I

Introduction

Heart failure is an increasingly common disorder with a prevalence at least 26 million people worldwide [1]. Patients living with heart failure have significantly increased with better access to healthcare and treatment options. Dyspnea, fatigue, edema common to respiratory disorders, misleads early diagnosis and intervention in patients with a history of heart failure [2].

Recently it has been recognized and shown that test for B type natriuretic peptide and NTpBNP are useful as accurate markers for heart failure in an emergency setting [3]. They are released into the circulation in response to increased distention of atria, reflecting increased volume or pressure overload. Brain natriuretic peptide (BNP) is released as prohormone upon secretion is enzymatically cleaved by corin or furin into mature BNP and the NTpBNP [4]. BNP is biologically active and cleared rapidly from circulation, while NTpBNP is biologically inactive component [5].

Several studies have shown that NTpBNP is better marker in diagnosing heart failure compared to BNP. Hence use of NTpBNP in the management of heart failure is recommended in view of increasing prevalence of this serious condition and the need to consider a broadening spectrum of cardiac dysfunction for treatment and improving prognosis [6-8].

In this study NT-pro BNP level in ADHF and CHF patients in Indian population in a tertiary care hospital

Materials and Methods

This study is a prospective observational study on patients with heart failure, and was conducted over a period of one year, in the department of cardiology in a tertiary care hospital after obtaining ethical committee approval. 200 subjects, inclusive of males and females belonging to all age groups with heart failure admitted in coronary care unit and intensive care unit of cardiology department and diagnosed

ISSN:0975 -3583,0976-2833 VOL13, ISSUE 08, 2022

with acute decompensated and chronic heart failure, based on clinical symptoms, echocardiogram findings, serum biochemical changes, were included in the study. Patients with no history of chronic renal failure were excluded from the study. All the selected patient's samples were tested for NTpBNP estimated by immunoassay method using fluorometry on AQT 90 ® FLEX random access analyzer. Descriptive and inferential statistics was done to analyze the data of the study.

Results

This study was undertaken to assess the level of NTpBNP in acute decompensated and CHF patients. Two hundred subjects were included into the study who were admitted in the cardiology department with diagnosis of acute decompensated or CHF. There were 16 subjects less than 50 yrs and 184 subjects were greater than 50 yrs. Highest number of subjects (95) were found between 61-70 yrs including both genders. Average age of the subjects was 66.43yr. All subjects were analyzed for NTpBNP levels.

Subjects were divided based on age into different age groups. It was found that NTpBNP levels increases with increasing age in heart failure patients as shown in table 1. NTpBNP levels after grouping into males and females, it was found that levels were higher in males compared to females as in Table 2. With P value of 0.125.

NTpBNP levels were compared between CHF (75) and ADHF (125) patients. Levels were higher in ADHF patients compared to CHF and NTpBNP levels were significantly different between the two groups with $p< 0.001$ as shown in Table 3.

On further stratification of ADHF, it was found that acute coronary syndrome (96) was the highest number of patients admitted in our group had higher NTpBNP levels compared to other causes of ADHF (uncontrolled hypertension, acute infections and atrial fibrillation) as seen in table 4. Subjects were also classified into 4 groups as per NYHA into class I to Class IV. It was found that NTpBNP levels increases from Class I to Class IV. As seen in Table 5

NTpBNP levels in heart failure patients were also compared with hypertension and diabetes. It was found that patients with diabetes and Hypertension had elevated levels compared to the patients who didn't have the same and there was a significant difference between the patients with and without diabetes and hypertension in heart failure patients. as shown in Table 6.

Table No. 1: Age distribution and their NT – proBNP levels in heart failure patients

Age in yrs	No of patients	%	NT – proBNP (12-132ng/L)	
			Mean	95% CI
<50yrs	16	8.0	6824.5	2936.3 – 12328.3
51-60	27	13.5	15803.6	10638.9 – 21987
61-70	95	47.5	10469.7	8429.5 – 12730 .8
71-80	42	21	10403.5	7070.3 – 14378.4
>80	20	10	15822.3	10344.9 – 22459.1

ISSN:0975 -3583,0976-2833 VOL13, ISSUE 08, 2022

Table No. 2: Gender distribution and their NT – proBNP levels in heart failure patients

Gender	No of patients	%	NT – proBNP (12-132ng/L)	
			Mean	95% CI
Males	133	66.5	12184	10279.2 – 14252.1
Females	67	33.5	9572.1	7004.2 – 12540.2

Table No 3: Distribution of Heart failure patients with their NT – proBNP levels and Troponin I levels

			NT-proBNP (ng/L)		Troponin -I (upto 0.04ng/mL)	
Type of heart failure	No of patients	%	Mean	95% CI	Mean	95% CI
CHF	75	37.5	3062.30	2605.6 – 3555.8	0.03	0.00 – 0.05
ADHF	125	62.5	19757.4	17512.8 – 22137.3	1.20	0.60 – 2.1

Comparision of NT-ProBNP levels comparision between ADHF and CHF - F=230.121; P<0.001

Acute decompensated heart failure (ADHF) , Chronic heart failure (CHF

Table No. 4: Distribution of ADHF patients with their NT – proBNP levels

Type of heart failure (ADHF)	No of patients	%	NT – proBNP (12-132ng/L)	
			Mean	95% CI
ACS	96	77	16532.3	13161 – 20287.6
Uncontrolled hypertension	22	18	9665.2	8013.6 – 11471.3
Acute infections	4	3		
Atrial fibrillation	3	2.0		

ISSN:0975 -3583,0976-2833 VOL13, ISSUE 08, 2022

Acute decompensated heart failure (ADHF) , Chronic heart failure (CHF), Acute coronary syndrome (ACS)

Table No. 5: Distribution of ADHF patients as per NYHA with their NT – proBNP levels

NYHA class	NT – proBNP (12-132ng/L)	
	Mean ± SD	95% CI
Class I	Not studied	Not studied
Class II	2916	2288.7 – 3619.1
Class III	6729.8	5009.5 – 8703.6
Class IV	21056.7	18318.7 – 23985.2

NYHA – New York Heart Association, ADHF – Acute Decompensated heart failure

Table No. 6: Distribution of Hypertension and diabetes in Heart failure patients with their NT – proBNP levels

Heart Failure		NT – proBNP (12-132ng/L)		Significant difference
		Mean	95% CI	
Hypertension in heart failure	Absent (80)	9145.2	7013 – 11559.9	t = 2.046; P – 0.042
	Present (120)	12706.3	10559.3 – 15051.8	
Diabetes in Heart Failure	Absent (95)	9644.5	7446.3 – 12126.6	t = 2.062; P – 0.041
	Present (105)	13203.8	10939.5 – 15680.8	

Discussion

Heart failure is one of the leading causes of morbidity and mortality. The patients with heart failure and acute respiratory disorder have similar symptoms. To differentiate between two disorders, NTpBNP is being extensively used in acute care setting as a point of care testing to differentiate heart failure from respiratory distress. The levels of the marker are also being used in multiple ways for treatment of heart failure [9].

NTpBNP increase with age. Study by Januzzi JL Jr *et al.* [10] showed that age stratified NTpBNP levels aid in the diagnosis of acute heart failure in patients presenting to emergency department with acute

ISSN:0975 -3583,0976-2833 VOL13, ISSUE 08, 2022

dyspnea. NTpBNP of < 300pg/ml strongly excludes the diagnosis of acute heart failure. In our study all the patients NTpBNP levels were greater than 300pg/mL.

We tried to find the levels of NTpBNP in patients diagnosed under ADHF and CHF which showed a significant difference between the groups (p<0.001). Study by Baba M, *et al.* [11] has shown that NTpBNP can be used to differentiate ADHF from CHF.

On further stratification of ADHF, it was found that ACS (96) was the highest number of patients admitted in our group had higher NTpBNP levels compared to other causes of ADHF (uncontrolled hypertension, acute infections and atrial fibrillation). It was found that ACS group NTpBNP levels were elevated compared to the other groups. Khilar S M [12] explained that NTpBNP in acute coronary syndrome is an appropriate marker associated with more coronary artery involvements based on number of vessels affected and severity of stenosis.

Subjects were also classified into 4 groups as per NYHA into class I to Class IV. It was found that NTpBNP levels increases from Class I to Class IV. As the patient with class IV have more cardiac stress with increased wall tension leading to decreased cardiac muscle function and water retention. Level of NTpBNP were significantly different between the groups. Study by Song BG *et al.* [13] have shown that the markers levels are different based on the functional classification of heart failure based on NYHA.

NT-proBNP levels in heart failure patients were also compared with hypertension and diabetes. It was found that patients with diabetes and Hypertension had higher levels compared to the patients who didn't have the same. It was found that there was a significant difference between the patients with and without diabetes and hypertension in heart failure patients. As shown in Table 6. Study by Toshiaki Ohkuma *et al.* [14] concluded that NTpBNP alone can strongly predict the heart failure in patients with type 2 diabetes. Julie K. Bowe *et al.* [15] showed that Patients with elevated NTpBNP, were at increased risk of developing hypertension even with normal blood pressure at baseline.

A study by Yesheng Pan, *et al.* [7] concluded that diagnostic accuracy of NTpBNP levels can be improved by considering additional factors like age, sex and body mass index. It was found that compared with uncorrected NTpBNP, the diagnostic formulation of corrected NTpBNP could improve the diagnostic accuracy of CHF as per New York heart association guidelines. Along with NTpBNP, troponin I also plays an important role in diagnosis of acute decompensated heart failure. This shows the usefulness of using multiple markers with NTpBNP in the diagnosis of heart failure as seen in our study.

Conclusion

NT-proBNP is an important marker to differentiate acute from CHF in an emergency setting where the availability of other diagnostic tools are not available and also NTpBNP levels are significantly increased in ADHF than chronic patients. NTpBNP levels are also significantly increased in patients associated with diabetes and hypertention in patients presenting with heart failure. NTpBNP levels also increased with increased age and the stages of Heart failure.

Limitation of the study

Number of male patients was higher than the female patients. The total sample size, as well as the number of chronic cases was less compared to the acute heart failure cases. Finally, this study could not show the prognostic value of the NTpBNP since, serial values of NTpBNP were not available, and further follow up of the patients with NTpBNP are not been done in our study. Ethical clearance has been obtained from Institutional ethical committee.

No conflict of interest

Nil

References

1. Savarese G, Lund LH. Global Public Health Burden of Heart Failure. Cardiac Failure Review 2017;3(1):7-11.
2. Inamdar AA, Inamdar AC. Heart Failure: Diagnosis, Management and Utilization. J Clin Med. 2016 Jul;5(7):62.
3. Bayes-Genıs A, Santalo-Bel M, Zapico-Muniz E, *et al.* N-terminal pro brain natriuretic peptide (NT-proBNP) in the emergency diagnosis and in-hospital monitoring of patients with dyspnoea and ventricular dysfunction. The European Journal of Heart Failure. 2004:15;6(3):301-86.
4. Zois NE, Bartels ED, HunterI, *et al.* Natriuretic peptides in cardiometabolic regulation and disease. Nat. Rev. Cardiol. 2014;11(7):403-12.
5. Eindhoven JA, van den Bosch AE, Jansen PR, *et al.* The Usefulness of Brain Natriuretic Peptide in Complex Congenital Heart Disease: A Systematic Review. Journal of the American College of Cardiology. 2012;60(21):2140-49.
6. Fonseca C, Sarmento PM, Minez A, *et al.* Comparative value of BNP and NT-proBNP in diagnosis of heart failure. 2004;23(7-8):979-91.
7. Pan Y, Dongjiu Li, Jian Ma, *et al.* NT-proBNP test with improved accuracy for the diagnosis of

ISSN:0975 -3583,0976-2833 VOL13, ISSUE 08, 2022

chronic heart failure. Medicine. 2017;96(51).
8. Gaggin HK, Januzzi JL. Biomarkers and diagnostics in heart failure review. Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease. 2013;1832(12):2442-50.
9. Stienen S, Salah K, Moons AH, Bakx AL, van Pol P, Kortz RAM, *et al.* NT-proBNP (N-Terminal pro-B-Type Natriuretic Peptide)-Guided Therapy in Acute Decompensated Heart Failure: PRIMA II Randomized Controlled Trial (Can NT-ProBNP-Guided Therapy during Hospital Admission for Acute Decompensated Heart Failure Reduce Mortality and Readmissions?). Circulation. 2018 Apr 17;137(16):1671-1683. doi: 10.1161/CIRCULATIONAHA.117.029882. Epub 2017 Dec 14. PMID: 29242350.
10. Januzzi JL, Chen-Tournoux AA, Christenson RH, et N-Terminal Pro-B-Type Natriuretic Peptide in the Emergency Department: The ICON-RELOADED Study. J Am Coll Cardiol. 2018;71:1191-1200.
11. Baba M, Yoshida K, Ieda M. Clinical Applications of Natriuretic Peptides in Heart Failure and Atrial Fibrillation. Int J Mol Sci. 2019 Jun 10;20(11):2824. doi: 10.3390/ijms20112824. PMID: 31185605; PMCID: PMC6600257.
12. Khilar SM. N-Terminal Pro Brain Natriuretic Peptide (NT-ProBNP) For Risk Stratification in Acute Coronary Syndrome (ACS). International Journal of Health and Clinical Research. 2020;3(8):46-50. Retrieved from https://www.ijhcr.com/index.php/ijhcr/article/view/298
13. Song BG, Jeon ES, Kim YH, Kang MK, Doh JH, Kim PH, *et al.* Correlation between levels of N-terminal pro-B-type natriuretic peptide and degrees of heart failure. Korean J Intern Med. 2005 Mar;20(1):26-32. doi: 10.3904/kjim.2005.20.1.26. PMID: 15906950; PMCID: PMC3891409.
14. Ohkuma T, Jun M, Woodward M, Zoungas S, Cooper ME, Grobbee DE, *et al.* Advance Collaborative Group. Cardiac Stress and Inflammatory Markers as Predictors of Heart Failure in Patients With Type 2 Diabetes: The ADVANCE Trial. Diabetes Care. 2017 Sep;40(9):1203-1209. doi: 10.2337/dc17-0509. Epub 2017 Jul 6. PMID: 28684396; PMCID: PMC5892716
15. Bower JK, Lazo M, Matsushita K, Rubin J, Hoogeveen RC, Ballantyne CM, *et al.* N-Terminal Pro-Brain Natriuretic Peptide (NT-proBNP) and Risk of Hypertension in the Atherosclerosis Risk in Communities (ARIC) Study. Am J Hypertens. 2015 Oct;28(10):1262-6. doi: 10.1093/ajh/hpv026. Epub 2015 Mar 16. PMID: 25783741; PMCID: PMC4580540