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Nt Pro Brain Natriuretic Peptide Levels in Cardiac Asymptomatic Type 2 Diabetes Mellitus Patients

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Keywords:

Type 2 Diabetes mellitus, Heart Failure, Nt Pro BNP, Echocardiography, Ventricular Dysfunction.

Abstract

Background of the story
Heart failure is twice more common in diabetics than in non-diabetics. Nt pro-BNP level increases in symptomatic and asymptomatic left ventricular dysfunction with hemodynamic overload. Recent advances in treating heart failure have improved survival for diabetics and non-diabetics. However, the case fatality rate is double in people with diabetes compared with non-diabetics. Thus, Nt Pro-BNP is beneficial for screening heart failure risk in diabetic patients.
AIM: To estimate Nt Pro Brain Natriuretic Peptide (Nt Pro-BNP) levels in asymptomatic cardiac type 2 diabetes mellitus patients.
METHODS: Patients attending BLDE (Deemed to be University) Shri BM Patil Medical College Hospital with diagnosed Diabetes Mellitus as per WHO criteria were selected for the study. The study's nature and purpose were explained to patients, and informed consent was taken from those willing to participate.
RESULTS: The study evaluated the correlation between Nt pro-BNP levels, left ventricular diastolic dysfunction, and left ventricular ejection fraction. There was a positive correlation between Nt pro-BNP levels and diastolic dysfunction. (P value is < 0.0001) .There was a negative correlation between Nt pro-BNP and ejection fraction. ('r'- 0.882; 'p' < 0.001).
CONCLUSION: Grades of diastolic dysfunction and pro-BNP had a positive correlation, and LVEF pro-BNP BNP had a negative correlation. This study can therefore infer that measuring the levels of Nt pro-BNP in patients with diabetes will therefore be helpful in the early detection of heart failure and predicting its prognosis and adverse outcomes.

1. Introduction

Diabetes Mellitus is considered one of the primary causes of morbidity and mortality worldwide. Therefore, early diagnosis and assessment of the disease's severity are crucial for predicting prognosis, treating the condition, and avoiding/decreasing morbidity and mortality [1].

Type 2 diabetes mellitus patients are twice as likely to experience heart failure. Patients with diabetes mellitus experience worse cardiovascular outcomes than those without the condition. The high prevalence of heart failure among people with diabetes remains despite the availability of numerous efficient treatments that lower blood sugar levels in patients with type 2 diabetes mellitus. Several cellular mechanisms are dysregulated

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in diabetic cardiomyopathy, including inflammation, oxidative stress, aberrant insulin signalling, endoplasmic reticulum stress, variations in the metabolism of cardiac substrates and the lipo-toxicity, mitochondrial bioenergetics, altered signal transduction, RAAS (renin-angiotensin-aldosterone system). [2]

BNP is primarily produced as a 108 AA protein called pre-pro BNP in the heart's left ventricle. Pre-pro BNP is produced in response to the myocardial wall stretching. And it is then converted into pro-BNP, which is then converted into the biologically active BNP fragment and the physiologically inactive NT-pro BNP fragment [3].

To aid in the diagnosis of heart failure, the 2016 European Society of Cardiology guidelines for the diagnosis and management of HF (acute and chronic) advise that all patients suspected of having the condition have their serum natriuretic peptide levels (pro-BNP) checked. In a non-acute context, the upper limit of normal for BNP is 35 pg/mL, while the upper limit normal for pro-BNP is considered to be 125 pg. /ml. In the acute context, the cut-off result for pro-BNP is around 100 pg/mL, while for pro-BNP, it is 300 pg. /ml. Pro BNP levels can be used to distinguish between heart failure and other causes of dyspnoea. In this context, the current study aims to examine Nt pro-Brain Natriuretic Peptide (Nt pro-BNP) levels in non-cardiac Type 2 Diabetes Mellitus patients who are asymptomatic [3].

2. Materials and Methods

STUDY DESIGN:
This is an observational prospective study.

METHODS:

Patients attending BLDE (Deemed to be University) Sri B.M. Patil Medical College, Hospital and Research Centre, Vijayapura, diagnosed with Diabetes Mellitus as per WHO criteria were selected for the study.

The study's nature and purpose were explained to patients, and informed consent was taken from those willing to participate. Patients' present and past medical histories were recorded, and a detailed physical examination was done.

SAMPLE SIZE: With the anticipated Proportion of Nt-pro BNP value (above 350 pmol/l) among Type 2

Diabetes patients at 61.3%, the study required sample size of 64 patients with a 95% level of confidence and 12% precision.

Formula used $n = \dfrac{z^2 \, p * q}{d^2}$

Where Z = Z statistic at α level of significance, d^2= Absolute error, P =Proportion rate,

Q = 100 – p

Statistical Analysis

The data thus obtained was entered into an MS Excel sheet, and THE statistical analysis was performed using an (SPSS) statistical package for the social sciences (Version 20).The results are presented as Mean (Median) ± Standard deviation, count and percentage, and diagram. Categorical variables between variables were compared using the Chi-square test. A correlation coefficient was used to find the correlation between the quantitative variables. The receiver Operative curve (ROC) was performed to find Sensitivity and specificity.

INCLUSION CRITERIA: Patients with Diabetes Mellitus diagnosed according to WHO criteria, i.e. Fasting blood sugar levels more than or equal to 126 mg/dl (OR) Post-prandial blood sugar more than or equal to 200 mg/dl (OR) HbA1c ≥ 6.5 %.

EXCLUSION CRITERIA: Diabetic Patients with any cardiovascular disease like IHD, MI, Cardiomyopathies, Congestive Cardiac Failure, or congenital heart disease. Patients aged >75 years. Patients with chronic liver and kidney diseases.

3. Results

Distribution of mean plasma Nt pro-BNP levels in study subjects and its correlation with diastolic function

64 patients admitted to the hospital with Diabetes Mellitus were taken up for the study. We observed that the subjects with normal diastolic function had mean pro-BNP levels of 374.32 ± 220.793 pg/ml, while with grade I diastolic dysfunction had 1201.35 ± 258,552 pg/ml, with grade II diastolic dysfunction, had 1698.21 ± 578.522 pg/ml and with Grade III diastolic

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dysfunction had 7963.50 ± 5844.544 pg/ml. The P
value of the correlation is 0.0001.

Table 1: Distribution of plasma Nt pro-BNP levels in the study subjects and its correlation with diastolic function

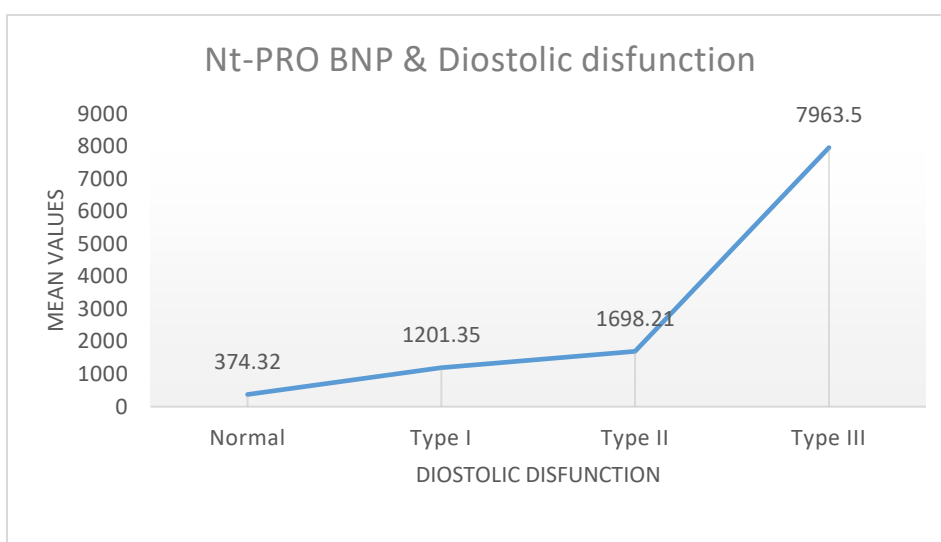| Diastolic function	Mean ± SD (pg/mL)
Normal (n=25)	374.32 ± 220.793
Grade I Diastolic Dysfunction (n=17)	1201.35 ± 258,552
Grade II Diastolic Dysfunction (n=14)	1698.21 ± 578.522
Grade III Diastolic Dysfunction (n=8)	7963.50 ± 5844.544

Figure 1: Distribution of plasma Nt pro-BNP levels in the study subjects and its correlation with diastolic function

Association between LVEF and Nt pro-BNP

The association between LVEF and serum Nt pro-BNP level was evaluated with Pearson's correlation coefficient. A negative correlation was found between LVEF and Nt pro-BNP level ('r'- 0.882; 'p' < 0.001).

Table 2: Association between LVEF and pro-BNP

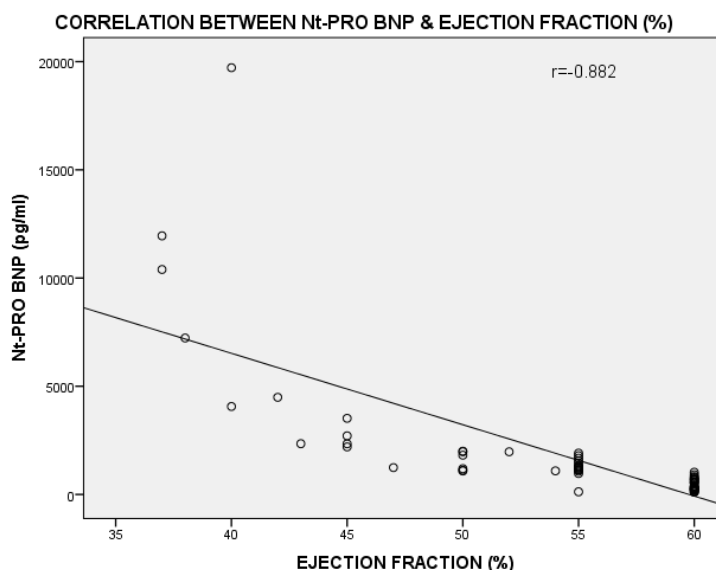| Pearson's correlation coefficient		LVEF
Nt PRO-BNP (pg/mL)	'r' value	-0.882
	'p-value	<0.001

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Figure 2: Correlation between Nt Pro-BNP and LVEF

Association between age and pro level BNP

The association of pro BNP level in subjects according their age was evaluated. The mean pro BNP level in subjects who had age less than 50 years had mean pro BNP of 747.3747.3±1005.987 pg/mL while in subjects with age more than 50 years had mean pro BNP of 6067.37±7506.701pg/mL. The association was between them was statistically significant ('t'-2.52, 'p'=0.007).

Table 3: Frequency distribution of pro BNP levels according to age of the study population
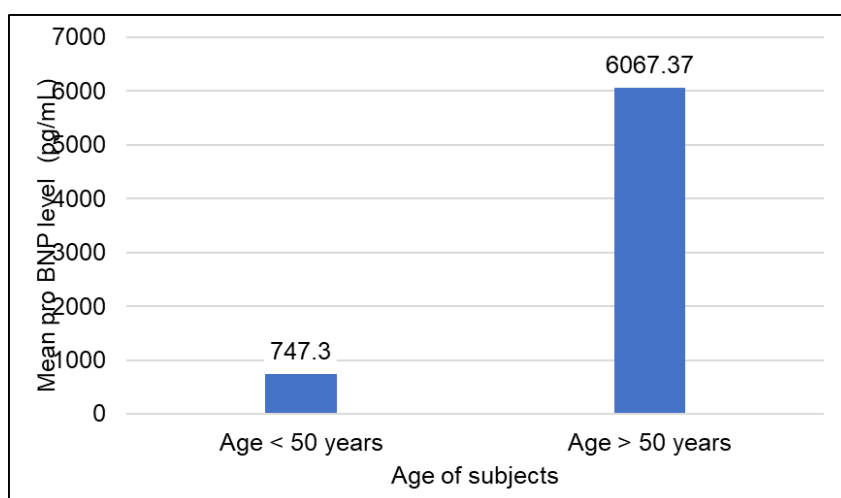
Age	Mean ± SD	't' value	'p' value
< 50 years	747.3 ± 1005.987	-2.52	0.007
> 50 years	6067.37 ± 7506.701		

Figure 3: Frequency distribution of pro-BNP levels according to the age of the study population

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4. Discussion

Diabetes mellitus is becoming more common every day in emerging nations like India. The primary reason for illness & mortality among people with diabetes mellitus is heart failure. In the present study, pro-BNP was studied and compared to results from different other studies.

Distribution of mean serum pro-BNP levels in the study subjects and its correlation with diastolic function

64 patients with type 2 diabetes mellitus were taken up for the study. We observed that the subjects with normal diastolic function had mean pro-BNP levels of 374.32 ± 220.793 pg/ml, while with grade I diastolic dysfunction had $1201.35 \pm 258,552$ pg/ml, with grade II diastolic dysfunction, had 1698.21 ± 578.522 pg/ml and with Grade III diastolic dysfunction had 7963.50 ± 5844.544 pg/ml. The P value of the correlation is 0.0001. There is a strong correlation between pro-BNP and diastolic dysfunction. In a study conducted by Bong Geun Song et al., there was a statistically significant higher level of serum Nt pro-BNP in patients with heart failure [4]. Similar results were obtained in a study by Sahadeb Prasad Dhungana et al [5].

Age distribution in the study group & the association with Nt pro-BNP

64 patients were selected for this prospective observational study. A total of 4 subjects were of less than 30 years ago, 4 subjects were of the 31 to 40 years age group, and 10 subjects were of 41 to 50 years age group, while 12 subjects were of 51 to 60 years age group, 22 subjects were between 61 & 70 years and all the remaining patients, above 70 years of age. Most of the patients were of age group above 50 years of age. It was found that the age of the study participants and pro-BNP levels had a slightly positive correlation. (P value is 0.031).

According to research conducted by Huei Gang et al., the mean age of the study population was 63 ± 9 years, and a positive correlation was found between pro-BNP levels & individuals' ages ('p' 0.05) [6]. Similarly, Kumiko Hamano et al. stated that the study population's mean age was 64.312 years, and that was a strong positive correlation between age and the pro-BNP level ('p'= 0.001) [7]. Rosiak M et al. observed a positive correlation (p' 0.01) between age and Nt pro-BNP levels [8]. The study population's mean age was 59.5 ± 6.8 years, according to Alain Bertoni et al. (p=0.05), and there was a significant positive correlation between age and the pro-BNP level [9]. Thus, the results of the studies mentioned above can be compared to those of the current study.

5. Conclusion

Heart failure has a high-risk factor associated with type 2 diabetes mellitus. Indeed, the prevalence of heart failure in the Indian population would eventually reflect the overall situation due to the rise in type 2 diabetes mellitus patients in India. In light of this, the current study assessed the relationship between the plasma Nt pro-BNP levels & several variables in individuals with diabetes. Grades of diastolic dysfunction and pro-BNP had a positive correlation, and LVEF and pro-BNP had a negative correlation. This study can therefore infer that measuring the levels of Nt pro-BNP in patients with diabetes will therefore be helpful in the early detection of heart failure and predicting its prognosis and adverse outcomes.

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