International Journal of Advances in Medicine
*Varma S et al. Int J Adv Med. 2021 Apr;8(4):563-568*
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: https://dx.doi.org/10.18203/2349-3933.ijam20211056

**Original Research Article**

# NT-pro brain natriuretic peptide in patients with type 2 diabetes mellitus without overt heart failure: a hospital based cross sectional study

**Sanjay Varma*, Archana Toppo, Khagdev Ram, Rajeev Lochan Khare, Yogendra Malhotra, Devpriya Lakra**

Department of Medicine, Pt. JNM Medical College, Raipur, Chhattisgarh, India

**Received:** 11 February 2021
**Accepted:** 09 March 2021

***Correspondence:**
Dr. Sanjay Varma,
E-mail: roopalisanjay@hotmail.com



## ABSTRACT

**Background:** Increased secretion of brain natriuretic peptide (BNP) and N-terminal proBNP (NT-proBNP) occurs mainly with increased tension in the ventricular walls, decreased oxygen supply, acute myocardial infarction, chronic cardiac heart failure, and in hypertrophy of the heart. Objective was to find out the prevalence and profile of NT-pro BNP levels in patients with type 2 diabetes mellitus (DM) without overt heart failure.
**Methods:** Hospital based cross sectional observational study was conducted in the Department of Medicine, Pt. JNM Medical College and associated Dr. BRAM Hospital Raipur, Chhattisgarh involving 106 patients of type 2 DM during the period of April 2019 to April 2020, after ethical approval from institutional ethical committee.
**Results:** The levels of NT pro BNP was found to be elevated in 87.7% patients of DM type 2. Majority of them were from 51-60 years age group (35.5%). Elevated NT proBNP levels was seen in 23.58% of patients having grade I diastolic dysfunction, 3.7% patients with grade II diastolic dysfunction and 1.88% patients having grade III diastolic dysfunction on echocardiography out of the 106 patients. Regardless of presence of diastolic dysfunction on echo, 93 (87.73%) patients out of the total study group of 106 patients had elevated BNP suggesting cardiac dysfunction. In the present study, 30.19% patients with diabetes were found to have varying degrees of diastolic dysfunction on echocardiography.
**Conclusions:** The prevalence of elevated NT pro BNP was 87.7%. Commonly observed age group with elevated NT pro BNP was 51-60 years. NT pro BNP was elevated in 88.7% of males and in 88.36% of females. Prevalence of elevated NT pro BNP was higher in grade 1 diastolic dysfunction with DM duration of more than 5 years (33.3%). Higher prevalence of elevated NT pro BNP was seen in grade I diastolic dysfunction (23.58%).

**Keywords:** NT-pro BNP, Type 2 diabetes mellitus, Echocardiography, Diastolic dysfunction

## INTRODUCTION

The term diabetes mellitus describes a metabolic disorder with heterogeneous etiologies which is characterized by chronic hyperglycaemia and disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both. The long–term relatively specific effects of diabetes include development of retinopathy, nephropathy and neuropathy.[1] People with diabetes are also at increased risk of cardiac, peripheral arterial and cerebrovascular disease.[2]

Diabetes and lesser forms of glucose intolerance, impaired glucose tolerance (IGT) and impaired fasting glucose

(IFG), can now be found in almost every population in the world.[3,4]

Type 2 diabetes mellitus (DM) is associated with the development of microvascular and macrovascular complications. Macrovascular complications lead to a spectrum of cardiovascular disease, to which accelerated atherosclerosis is usually a contributor.

Although microangiopathy represents a severe threat to the population with diabetes, macroangiopathy and subsequent cardiovascular disease are the major causes of morbidity and mortality in these patients.[5] Screening for kidney and retinal complications is already an established part of routine diabetes care today, but there is no comparable screening for cardiac complications of diabetes.[6] This may simply be due to the lack of cost-effective methods; an echocardiographic examination is both expensive and time consuming and, therefore, not suited for screening purposes.

Diabetes is also more prevalent among patients with heart failure. In the Framingham study, male patients with diabetes had twice the risk and female patients with diabetes had five times the risk of developing heart failure as compared to control population.[7] At least partially, this could be explained by the increase in severity and incidence of ischemic heart disease among patients with diabetes. However, data from autopsy studies have suggested that hearts from patients with diabetes also have an increased collagen content.[8]

Moreover, patients with diabetes have a disproportionate increase in left ventricular mass independent of blood pressure.[9-11]

All of these factors may contribute to increased myocardial stiffness. This is especially important because left ventricular hypertrophy in a meta-analysis has been associated with a 1.5 to 3.5 fold increased risk of future cardiovascular morbidity and a 1.5 to 6.8 fold increase of all-cause mortality. Increased secretion of brain natriuretic peptide (BNP) and N-terminal (NT)-proBNP occurs mainly with increased tension in the ventricular walls, decreased oxygen supply, acute myocardial infarction, chronic cardiac heart failure and hypertrophy of the heart.[12]

So, the present study was carried out to find out the prevalence of elevated NT-proBNP and its association with left ventricular dysfunction which is common in type 2 diabetes patients.

### *Objective*

Objective of the study was to find out the prevalence and profile of abnormal level of NT-pro BNP in patient with type 2 DM without overt heart failure.

## METHODS

The present hospital based cross sectional observational study was conducted in the Department of Medicine, Pt. JNM Medical College and associated Dr. B.R.A.M. Hospital, Raipur involving 106 patients of type 2 diabetes coming to outpatient department (OPD) and inpatient department (IPD) of Department of Medicine Dr. BRAM Hospital, Raipur, Chhattisgarh. Patients of type 2 DM without sign and symptoms of overt heart failure attending medicine OPD and admitted in medicine ward of Dr. BRAM Hospital, Raipur, Chhattisgarh. The study was conducted during the period of April 2019 to April 2020.

### *Sampling technique*

Systemic random sampling method was used as a sampling technique.

### *Inclusion criteria*

Diagnosed cases of type 2 DM and patients willing to participate in study after written consent were included in the study.

### *Exclusion criteria*

Patients with known cardiovascular disease; patients with end stage renal disease, chronic kidney disease; cirrhosis of liver; subject under drug treatment with digitalis or nitrates; pulmonary disease like chronic obstructive pulmonary disease (COPD); sepsis; atrial fibrillation; and patient with sign and symptoms of heart failure were excluded from the study.

NT-proBNP analysis using Roche diagnostics cobas e 411 analyzer in the department of biochemistry. It is a fully automated, random-access, software controlled system for immunoassay analysis. NT-proBNP values range from 5-35.000 pg/ml. Cut off value in <50 years, 50-75 years and >75 years patients are 450 pg/ml, 900 pg/ml and 1800 pg/ml respectively. Values greater than 3000 pg/ml were considered as extreme elevation.[13]

Echocardiography was done using Philips EPIQ 7C cardiology ultrasound system. Detailed echocardiography examination was done with analysis of parameters determining LV diastolic dysfunction like mitral inflow, Deceleration time and E/A ratio. Valsalva manoeuvre was applied to detect pseudnormal pattern of mitral inflow.

### *Statistical analysis*

Data thus was entered in MS excel sheet and analysed by using SPSS 24.0 version IBM USA. Association between two qualitative variables was seen by using Chi square/Fischer's exact test. Comparison of mean and standard deviation (SD) between two groups was done by using unpaired t test. Descriptive statistics of each variable was presented in terms of mean, standard deviation, and

standard error of mean. Correlation between two quantitative variables was assessed by using Pearson's correlation coefficient test (r).

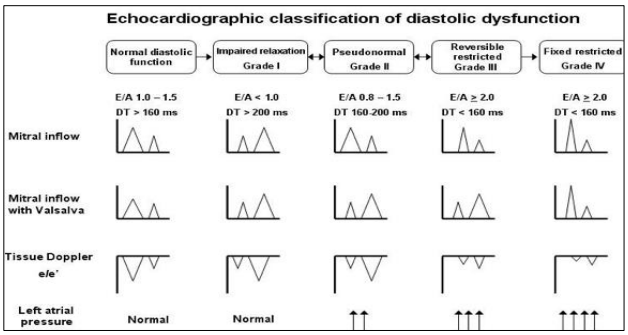


**Figure 1: Echocardiographic classification of diastolic dysfunction as per E/A ratio and deceleration time.**

## RESULTS

We included a total 106 patients in our study. Majority of them were from 51-60 years age group i.e. 39(36.8%) followed by 26 (24.5%) from 41-50 years, 23 (21.7%) from 61-70 years and 10 (9.4%) from above 70 years age group. Least were from above 30-40 years age group (7.5%). Mean age of the study population was 48.71±13.13 years.

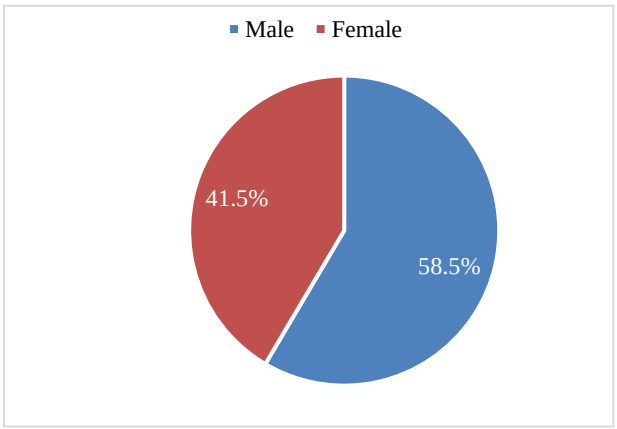


**Figure 2: Distribution according to gender.**

Majority of the participants were males i.e. 62 (58.5%) and remaining were females 44 i.e. 41.5%. Males were predominant with male to female ratio as 1.44:1 (Figure 2).

NT pro BNP was raised in 93 patients out of 106. So, the prevalence of elevated NT pro BNP was 87.7%. In 13 patient (12.3%) the NT pro BNP was normal (Figure 3).

Out of 93 patients with elevated NT pro BNP, majority of them were from 51-60 years age group i.e. 33 (35.5%) followed by 23 (24.7%) were in the age group of 61-70 years and 22 (23.7%) were in the age group of 41-50 years. The least were from 30-40 years age i.e. 6 (6.5%) NT pro BNP was elevated in all 23 patients between the age group of 61-70 years and in 9 out of 10 patients >70 years of age. In each age group, the proportion or percentage of patients and the difference in the proportion of patients was not significant (p>0.05) (Table 1).

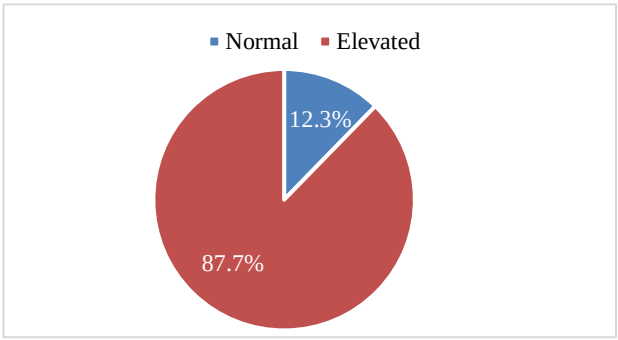


**Figure 3: Distribution according to NT pro BNP value.**

In our study 93 (87.7%) patients out of total 106 patient had elevated NT pro BNP. Out of 93 (87.7%) patient 55 (51.88%) were male and 38 (35.84%) were female. Proportion of males with elevated NT pro BNP were 88.7% as against 11.29% of normal and Proportion of females with elevated NT pro BNP were 86.4% as against 13.6% of normal. This difference in the proportion of gender with respect to NT pro BNP was found to be statistically not significant (p>0.05) (Table 2).

**Table 1: Distribution of NT pro BNP value according to age group.**

| Age group in years | NT pro BNP | | | | Total |
|---|---|---|---|---|---|
| | Normal | | Elevated | | |
| | Number | Percent | Number | Percent | |
| **30-40** | 2 | 15.4 | 6 | 6.5 | 8 |
| **41-50** | 4 | 30.8 | 22 | 23.7 | 26 |
| **51-60** | 6 | 46.2 | 33 | 35.5 | 39 |
| **61-70** | 0 | 0.0 | 23 | 24.7 | 23 |
| **>70** | 1 | 7.6 | 9 | 9.6 | 10 |
| **Total** | 13 | 100.0 | 93 | 100.0 | 106 |

Chi square test=5.05, p=0.28 (>0.05), not significant.

In the present study 26 (24.5%) patients had grade I diastolic dysfunction, in this subgroup majority 25 (23.58%) patients out of 26 had elevated BNP. A total of 4 (3.7%) patients had grade II diastolic dysfunction, and all 4 patients in this group had elevated BNP. 2 (1.88%) patients were found to have grade III diastolic dysfunction and all 2 patients in this group had elevated BNP. In our study 74 (69.8%) patients had normal diastolic function, and 62 (58.5%) patients out of 74 patients were found to have elevated BNP. Proportion of patients having grade I diastolic dysfunction and elevated NT pro BNP were 26.9% as against 7.6% of normal NT pro BNP. Proportion of patients having grade 3 diastolic dysfunction and elevated NT pro BNP were 2.2% and with grade 2 dysfunction as 4.3%. So regardless of presence of diastolic dysfunction on echo, 93 (87.73%) patients out of the total study group of 106 patients had elevated BNP suggesting cardiac dysfunction (Table 3).

Out of 39 patients with DM duration of more than 5 years, majority were having grade 1 diastolic dysfunction i.e. 33.3%. Out of 38 patients with DM duration of 1 to 5 years, majority were having grade 1 diastolic dysfunction i.e. 13.2%. Out of 29 patients with DM duration of less than one year, majority were having grade 1 diastolic dysfunction i.e. 27.6%. This difference in the proportion of patients with grade 1 dysfunction with respect to duration of diabetes was found to be statistically not significant (p>0.05) (Table 4).

**Table 2: Distribution of NT pro BNP value according to gender.**

| Gender | NT pro BNP | | | | Total |
|---|---|---|---|---|---|
| | Normal | | Elevated | | |
| | Number | Percent | Number | Percent | |
| **Male** | 7 | 53.8 | 55 | 59.1 | 62 |
| **Female** | 6 | 46.2 | 38 | 40.9 | 44 |
| **Total** | 13 | 100.0 | 93 | 100.0 | 106 |

Chi square test=0.13, p=0.71 (>0.05), not significant

**Table 3: Distribution of NT pro BNP value according to grades of diastolic dysfunction.**

| Diastolic dysfunction | NT pro BNP | | | | Total |
|---|---|---|---|---|---|
| | Normal | | Elevated | | |
| | Number | Percent | Number | Percent | |
| **Grade 1** | 1 | 7.7 | 25 | 26.9 | 26 |
| **Grade 2** | 0 | 0.0 | 4 | 4.3 | 4 |
| **Grade 3** | 0 | 0.0 | 2 | 2.2 | 2 |
| **Normal** | 12 | 92.3 | 62 | 66.6 | 74 |
| **Total** | 13 | 100.0 | 93 | 100.0 | 106 |

Chi square test=3.62, p=0.3 (>0.05), not significant

**Table 4: Distribution of grades of diastolic dysfunction according to duration of diabetes.**

| Diastolic dysfunction grade | Duration of DM | | | | | | Total |
|---|---|---|---|---|---|---|---|
| | <1 year | | 1 to 5 years | | >5 years | | |
| | Number | Percent | Number | Percent | Number | Percent | |
| **Grade 1** | 8 | 27.6 | 5 | 13.2 | 13 | 33.3 | 26 |
| **Grade 2** | 0 | 0.0 | 0 | 0.0 | 4 | 10.3 | 4 |
| **Grade 3** | 1 | 3.4 | 0 | 0.0 | 1 | 2.6 | 2 |
| **Normal** | 20 | 69.0 | 33 | 86.8 | 21 | 53.8 | 74 |
| **Total** | 29 | 100.0 | 38 | 100.0 | 39 | 100.0 | 106 |

Chi square test=14.41, p=0.025 (<0.05), significant

## DISCUSSION

Over time, our understanding of the development of LV dysfunction and heart failure has evolved, and it is now viewed as a complex syndrome characterized by both hemodynamic and neurohormonal derangements.[14] It then follows that measurements of hemodynamic and neurohormonal levels may be of benefit in establishing both the absolute and relative state of cardiac performance in patients at risk for the development of LV dysfunction. The role of BNP and NT-BNP in the diagnosis of heart failure has been shown in both the outpatient and emergency care settings, and it has been shown that

elevated BNP levels correlate with the presence of both systolic and diastolic dysfunction on echocardiography.[15,16]

We included a total 106 patients in our study. Majority of them were from 51-60 years age group i.e. 39 (36.8%) followed by 26 (24.5%) from 41-50 years, 23 (21.7%) from 61-70 years and 10 (9.4%) from above 70 years age group. Least were from above 30-40 years age group (7.5%). Mean age of the study population was 48.71±13.13 years.

Rodriguez et al reported the mean age in their study as 65.1±8.3 years with male preponderance as 59%.[17] Magnusson et al reported mean age of 59.6 (range of 54.3–63.9) years with 51.4% women and 48.6% males in their study.[18] Mean age of the study population was 48.71±13.13 years which is less as compared to the findings of above-mentioned authors.

In our study, NT pro BNP was raised in 93 patients out of 106. So, the prevalence of elevated NT pro BNP was 87.7%. In 13 patient (12.3%) the NT pro BNP was normal. Out of 93 patients with elevated NT pro BNP, majority of them were from 51-60 years age group i.e. 33 (35.5%) followed by 23 (24.7%) were in the age group of 61-70 years and 22 (23.7%) were in the age group of 41-50 years.

In our study, NT proBNP was elevated in 55 (88.7%) and normal in 7 (11.29%) of total 62 male patient. NT proBNP was elevated in 38 (88.36%) and normal in 6 (13.6%) of total 44 female patient.

## CONCLUSION

The prevalence of elevated NT pro BNP was 87.7%. Commonly observed age group with elevated NT pro BNP was 51-60 years i.e. 35.5%. NT pro BNP was elevated in 88.7% of males and in 88.36% of females. Prevalence of elevated NT pro BNP was higher in grade 1 diastolic dysfunction with DM duration of more than 5 years (33.3%). Higher prevalence of elevated NT pro BNP was seen in grade I diastolic dysfunction.

*Funding: No funding sources*
*Conflict of interest: None declared*
*Ethical approval: The study was approved by the Institutional Ethics Committee*

## REFERENCES

1. Hanseen KF, Bangstad HJ, BB rinchmann-Hansen O. Blood glucose control and diabetic microvascular complications: Long term effects of near normoglycemia. Diabet Med. 1992;9:697-705.
2. Fox CS, Coady S, Sorlie PD, D'Agostino RB Sr, Pencina MJ, Vasan RS, et al. Increasing cardiovascular disease burden due to diabetes mellitus: The Framingham Heart study. Circulation. 2007;115:1544-50.
3. Zimmet P, Alberti KG, Shaw J. Global and societal implications of diabetes epidemic. Nature. 2001;414:782-7.
4. Alberti KG, Zimmet P, Shaw J. International diabetes federation: A consensus on Type 2 diabetes prevention. Diabet Med. 2007;24:451-63.
5. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections. Diabetes Care. 1998;21:1414-31.
6. Steiner G. Diabetes and atherosclerosis: an overview. Diabetes. 1981;30:1-7.
7. Butler R, MacDonald TM, Struthers AD, Morris AD: The clinical implications of diabetic heart disease. Eur Heart J. 1998;19:1617-27.
8. Vanninen E, Mustonen J, Vainio P, Lansimies E, Uusitupa M. Left ventricular function and dimensions in newly diagnosed non-insulin-dependent diabetes mellitus. Am J Cardiol. 1992;70:3718.
9. Palmieri V, Bella JN, Arnett DK, Liu JE, Oberman A, Schuck MY, et al. Effect of type 2 diabetes mellitus on left ventricular geometry and systolic function in hypertensive subjects: Hypertension Genetic Epidemiology Net- work (HyperGEN) study. Circulation. 2001;103:102-7.
10. Grossman E, Shemesh J, Shamiss A, Thaler M, Caroll J, Rosenthal T. Left Ventricular mass in diabetes-hypertension. Arch Intern Med. 1992;152:1001-4.
11. Vakili BA, Okin PM, Devereux RB. Prognostic implications of left ventricular hypertrophy. Am Heart J. 2001;141:334-41.
12. Tateyama H, Hino J, Minamino N, Kangawa K, Ogihara T, Matsuo H. Characterization of immunoreactive brain natriuretic peptide in human cardiac atrium. Biochem Biophys Res Commun. 1990;166:1080-7.
13. Downie PF, Talwar S, Squire IB, Davies JE, Barnett DB, Ng LL, et al. Assessment of the stability of N-terminal pro-brain natriuretic peptide in vitro : implications for assessment of left ventricular dysfunction. Clin Sci (Lond). 1999;258:255-8.
14. Packer M. How should physicians view heart failure? The philosophical and physiological evolution of three conceptual models of the disease. Am J Cardiol. 1993;71:3-11.
15. Cheng V, Kazanegra R, Garcia A, Lenert L, Krishnaswamy P, Gardetto N, Clopton P, Maisel A. A rapid bedside test for peptide (BNP) predicts treatment outcomes in patients admitted for decompensated heart failure. J Am Coll Cardiol. 2001;37:386-91.
16. Maisel AS, Koon J, Krishnaswamy P, Kazenegra R, Clopton P, Gardetto N, et al. Utility of B-natriuretic peptide as a rapid, point-of-care test for screening patients undergoing echocardiography to determine left ventricular dysfunction. Am Heart J. 2001;141:367-74.

17. Castano Rodriguez S, Coma-Canella I, Lopez Salazar B, Barba Cosials J. Echocardiographic findings and NT-proBNP level in type-2 diabetic patients with and without ischemic heart disease. Revista Española de Cardiología (English Edition). 2009;62(10):1184-8.
18. Magnusson M, Melander O, Israelsson B, Grubb A, Groop L, Jovinge S. Elevated plasma levels of Nt-proBNP in patients with type 2 diabetes without overt cardiovascular disease. Diabetes Care. 2004;27(8):1929-35.

**Cite this article as:** Varma S, Toppo A, Ram K, Khare RL, Malhotra Y, Lakra D. NT-pro brain natriuretic peptide in patients with type 2 diabetes mellitus without overt heart failure: a hospital based cross sectional study. Int J Adv Med 2021;8:563-8.