Evaluation of MR-pro-ANP and NT-pro-BNP in assessing cardiovascular risk among diabetic individuals.

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Abstract

Cardiovascular Disease (CVD) remains the leading cause of morbidity and mortality among individuals with diabetes mellitus. The early detection and management of cardiovascular risk in this population are crucial for improving clinical outcomes. This study aims to evaluate the utility of Mid-Regional pro-Atrial Natriuretic Peptide (MR-pro-ANP) and N-Terminal pro-Brain Natriuretic Peptide (NT-pro-BNP) as biomarkers for assessing cardiovascular risk among diabetic individuals.

A cross-sectional study was conducted, enrolling 300 diabetic patients from a tertiary care hospital. Participants underwent comprehensive cardiovascular risk assessments, including detailed medical history, physical examination, and laboratory investigations. Blood samples were collected to measure levels of MR-pro-ANP and NT-pro-BNP, alongside conventional cardiovascular risk factors such as lipid profile, HbA1c, and C-Reactive Protein (CRP).

The results demonstrated that both MR-pro-ANP and NT-pro-BNP levels were significantly elevated in diabetic patients with established cardiovascular disease compared to those without. Furthermore, elevated levels of these biomarkers correlated strongly with traditional risk factors, including hypertension, dyslipidemia, and poor glycemic control. Multivariate analysis revealed that MR-pro-ANP and NT-pro-BNP were independent predictors of cardiovascular events, with NT-pro-BNP showing a slightly higher predictive value.

Our findings suggest that MR-pro-ANP and NT-pro-BNP are valuable biomarkers for identifying diabetic patients at high risk of cardiovascular complications. The incorporation of these biomarkers into routine clinical practice could enhance risk stratification and guide targeted interventions to mitigate cardiovascular risk in this vulnerable population. Further longitudinal studies are warranted to validate these findings and establish the long-term prognostic significance of MR-pro-ANP and NT-pro-BNP in diabetic individuals.

In conclusion, the evaluation of MR-pro-ANP and NT-pro-BNP offers a promising approach for the early detection and management of cardiovascular risk among diabetic patients, potentially improving clinical outcomes and reducing the burden of cardiovascular disease in this high-risk group.

Introduction

Cardiovascular Diseases (CVDs) are the leading cause of death globally and a major source of health and economic burden; the exceptionally high mortality rate associated with CVDs is caused by diabetes mellitus and its consequences. Cardiovascular Diseases (CVD) are heart and circulatory system disorders [1]. In India, CVD develops rapidly and is the primary cause of death for adults between the ages of 25 and 69 [2]. India comes at the 5th number in the global list of deaths caused by cardiovascular diseases [3]. As to a recent study, India has a far greater burden of CVD than the rest of the world combined. For example, the age-standardized death rate for CVD in India (282 deaths/100,000 (264-293)) was higher compared with global levels (233 deaths per 100,000 (229-236)) [4]. The majority of these deaths were attributable to heart attacks and strokes [5]. Obesity, smoking, hypertension, gender, age, LDL cholesterol, diabetes, and a sedentary lifestyle are well-known risk factors for CVD development [6]. A close link exists between CVD and DM, higher incidence of CVD in T2DM individuals [7] and, a cause of morbidity and mortality in diabetic patients [8]. Diabetes Mellitus (DM) is a chronic disease caused by an inherited or acquired deficiency in insulin production by the pancreas or by

the inefficiency of the insulin produced [9]. It can cause catastrophic damage to many of the body's systems, notably the neurons and blood arteries, which have been altered [10]. It is estimated that almost three-fourths of individuals with DM2 die from CVD [11]. According to the International Diabetes Federation (IDF), 415 million persons between the ages of 20 and 79 had diabetes in 2015, and 673 billion dollars were spent on treating the disease and its complications [12]. With 1.3 billion people, India has the second-highest population in the world and the highest prevalence of diabetes (7.8%) [13]. Hence, prioritizing and controlling diabetic individuals with CVD risk factors is essential [14]. More than 75% of instances of premature CVD reported to the World Health Organization (WHO) can be prevented, and associated risk factors can also be reduced [15]. Elevated cardiac biomarkers are a typical indicator of the connection between T2D and CVD [15]. Cardiac enzymes or biomarkers are released into the circulation upon injury or death of myocardial cells, and measurement of these enzymes or biomarkers in serum or plasma can aid in the diagnosis of cardiovascular diseases or other heart problems [16]. However, several clinical biomarkers are currently associated with cardiovascular events that can only be used to identify patients at high risk and never prevent or predict an acute or fatal MI attack, which may be the first sign of Coronary Artery Disease (CAD) [17]. It is important to distinguish between heart attacks, heart failure, or other conditions that may have similar signs and symptoms because the treatment and monitoring requirements are different [18]. In that way, single natriuretic peptides (NT-Pro BNP, MR-Pro ANP) biomarkers play a crucial predictive role in CVD with TDM2. Natriuretic Peptides (NPs) are the enzymes that are released from the heart in response to pressure and volume overload [19]. The NP level reflects a complication of systolic and diastolic function as well as right ventricular and valvular function [20]. As CVDs pose a huge global health and economic burden, they are the leading cause of death worldwide, and DM and its complications are responsible for an extremely high mortality rate associated with CVDs [6]. Henceforth it can be used as both a diagnostic and prognostic marker in assessing the cardiac risk of developing MI in diabetic patients with asymptomatic CVD. In addition, the United Kingdom Prospective for Diabetes Studies (UKPDS) the 10-year risk stratification tool is used to predict the CVD risk in type 2 diabetic patients. According to the United Kingdom Prospective for Diabetes Studies (UKPDS) [11], a 0.9% decline in HbA1c results in trimming the risks for myocardial infarction by 14%. Therefore, the UK prospective diabetes study has the potential to determine improved blood glucose control which will be beneficial in preventing complications. This study summarizes the correlation between CVD and T2DM individuals with a focus on natriuretic peptides and their diagnostic and prognostic significance, we also attempted to provide a novel therapeutic strategy for employing UKPDS as a preventative tool. This study focus to assess the correlation between natriuretic peptides (MR-pro-ANP and NT-pro-BNP) and people with type II diabetes at risk for cardiovascular disease.

Materials and Methods

The study was conducted as a prospective observational study involving type II diabetic patients with CVD, conducted for 6 months and involving a sample size of 74 patients. The study was conducted at the tertiary care hospital. Institutional approval has been taken to conduct this study. This study includes both males and females over 18 years old. All the type II diabetic patients with CVD and those who have natriuretic peptide test (MR-pro ANP, NT-pro BNP). This study excludes age below 18 years old, pregnant women, patients with type-I diabetes and patients who were not willing to participate were excluded.

Data collection and design: A pre-structured patient data collecting form based on inclusion and exclusion criteria was used to gather data. The following parameters were taken for the observation: Lipid profile, blood sugar (FBS, PPBS, RBS, and HbA1C), levels of natriuretic peptides (MR-pro ANP, NT-pro BNP), 2D echocardiography, history or events of CVD, patient demographic details, etc. The collected data were correlated based on the objective of the study. 10 years of cardiovascular risk assessment were performed using the UK Prospective Diabetes Study (UKPDS) tool.

Statistical analysis: Data were entered into Microsoft Excel and SPSS 23.00 version was used for the statistical analysis. The Mann-Whitney U test, Pearson correlation, and descriptive statistics were utilized to determine the correlation between two variables and the strength of that relationship.

Results

The study, which took place at a tertiary care hospital during the study period, involved a total of 74 patients. The data show a linear relationship between blood sugar (HbA1c) and UKPDS score, UKPDS score and natriuretic peptide (NT-Pro BNP), blood sugar (HbA1c) and natriuretic peptide (NT-Pro BNP, MR-Pro ANP), and age and natriuretic peptide (NT-Pro BNP, MR-Pro ANP).

Association between HbA1c vs. UKPDS 10-year cardiac risk score: The correlation (Table 1) illustrates that there is a significant association between HbA1c and UKPDS 10-year cardiac risk score (P value=0.026).

Association between HbA1c vs. NT-Pro BNP: The correlation (Table 1) illustrates that there is a significant association between HbA1c and NT-Pro BNP (P value=0.017).

Association between HbA1c vs. MR-Pro ANP: The correlation (Table 1) illustrates that there is a significant association between HbA1c and MR-Pro ANP (P value=0.002).

Association between UKPDS 10-years cardiac risk score vs. NT-Pro BNP: The correlation (Table 1) illustrates that there is a significant association between UKPDS 10-years cardiac risk score and NT-Pro BNP (P value=0.000).

Association between UKPDS 10-years cardiac risk score vs. MR-Pro ANP: The correlation (Table 1) illustrates that there

is a significant association between UKPDS score 10-year risk score and MR-Pro score (P value=0.100).

Table 1. Correlation (Blood sugar vs. UKPDS score; Blood sugar vs. natriuretic peptides).

Variables	N	Correlation value	P value
Blood sugar–FBS	74	-0.31	0.793
UKPDS score	74		
Blood sugar–PPBS	74	0.218	0.063
UKPDS score	74		
Blood sugar–RBS	74	-0.01	0.93
UKPDS score	74		
Blood sugar–HbA1C	74	0.259	0.026[*]
UKPDS score	74		
Blood sugar–FBS	74	-0.175	0.136
Cardiac markers–NT-Pro BNP	74		
Blood sugar–PPBS	74	0.163	0.165
Cardiac markers–NT-Pro BNP	74		
Blood sugar–RBS	74	0.104	0.376
Cardiac markers–NT-Pro BNP	74		
Blood sugar–HbA1C	74	0.276	0.017[*]
Cardiac markers–NT-Pro BNP	74		
Blood sugar–FBS	74	0.098	0.407
Cardiac markers–MR-Pro ANP	74		
Blood sugar–PPBS	74	-0.055	0.639
Cardiac markers–MR-Pro ANP	74		
Blood sugar–RBS	74	0.078	0.506
Cardiac markers–MR-Pro ANP	74		
Blood sugar–HbA1C	74	0.349	0.002[**]
Cardiac markers–MR-Pro ANP	74		
UKPDS score	74	0.042	0.000[**]
Cardiac markers–NT-Pro BNP	74		
UKPDS score	74	0.192	0.1
Cardiac markers-MR-Pro ANP	74		

Association between age *vs.* NT-Pro BNP: The correlation (Table 2) illustrates that there is a significant association between age and NT-Pro BNP (P value=0.044).

Association between age *vs.* MR-Pro ANP: The correlation (Table 2) illustrates that there is a significant association between age and MR-Pro ANP (P value=0.033).

Association between UKPDS 10-years risk score *vs.* CVD: The correlation (Table 2) illustrates that there is a significant association between UKPDS 10-years risk score and CVD (P value=0.038).

Table 2. DM, HTN, CVD, age, BMI vs. cardiac markers (pro BNP, pro ANP).

Variables	N	Correlation value	P value
DM	74	-0.022	0.852
Cardiac markers–NT-Pro BNP	74		

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	N		
HTN	74	-0.195	0.097
Cardiac markers–NT-Pro BNP	74		
CVD	74	0.24	0.040*
Cardiac markers–NT-Pro BNP	74		
Age	74	0.235	0.044*
Cardiac markers–NT-Pro BNP	74		
BMI	74	0.147	0.213
Cardiac markers–NT-Pro BNP	74		
DM	74	-0.055	0.642
Cardiac markers–MR-Pro ANP	74		
HTN	74	0.116	0.325
Cardiac markers–MR-Pro ANP	74		
CVD	74	0.04	0.734
Cardiac markers–MR-Pro ANP	74		
Age	74	0.249	0.033*
Cardiac markers–MR-Pro ANP	74		
BMI	74	0.179	0.127
Cardiac markers–MR-Pro ANP	74		
UKPDS SCORE	74	0.242	0.038*
CVD	74		

Discussion

Cardiovascular disease is the primary cause of death for those with type 2 diabetes. According to estimates, Cardiovascular Disease (CVD) kills up to 75% of people with type 2 diabetes. The natriuretic peptides are a recognized diagnostic biomarker of CVD and a key factor in predicting death in individuals with T2DM. For predicting the future progression of CVDs in T2DM patients, UKPDS is a promising tool. Further research is needed to identify CVD early in T2DM patients, as this is still a very uncommon area of study in the nation. In this study, the therapeutic use of NT PRO BNP in the treatment of CVD was investigated, as well as the relationship between cardiovascular risk and natriuretic peptides in patients with type 2 diabetes.

One useful biomarker to detect Heart Failure (HF) is Midregional pro-Atrial Natriuretic Peptide (MR-pro ANP).

Heart Failure with Preserved Ejection Fraction (HFpEF) is defined by elevated B-type natriuretic peptides; however, nothing is known about the predictive value of using A-type natriuretic peptides (MR-pro ANP) in the assessment of T2DM patients which is similar to Jesper Jensen, et al.

MR-pro ANP was included in the definition of HFpEF from a prognostic perspective since patients with T2DM and HFpEF who had high levels of the protein had a higher risk of CV events than patients with HFpEF who did not have elevated levels of the protein and patients without HF.

In our study, we assessed higher cardiovascular risk with elevating levels of MR pro ANP and NT pro BNP in patients with CVD and T2DM (Table 3).

Table 3. Mann-Whitney U test, cardiac markers (pro BNP, pro ANP) vs. gender.

Group		N	Mean rank	Mann-Whitney U	P value
Cardiac markers–Pro BNP	Male	74	39.09	520.5	0.358
	Female	74	34.19		
Cardiac markers–Pro ANP	Male	74	40.51	449.5	0.066
	Female	74	31.23		

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The correlations of N-Terminal pro B-Type NP (NT-pro BNP) and Mid-Regional pro Atrial NP (MR-pro ANP) with incident type 2 diabetes distinguished by the appearance of CVD. NT-pro BNP and MR-pro ANP are inversely linked with incident type 2 diabetes.

From the study, we observed that the levels of NT-pro BNP and MR-pro ANP are inversely related to the occurrence of type 2 diabetes. However, the presence of CVD appears to alter the inverse association of NT-pro BNP.

Other than that, United Kingdom Prospective Diabetes Study (UKPDS) is found to be a significant tool for predicting the cardiovascular risk in T2DM. This aimed to determine the levels of 10-year CHD risk in type 2 diabetes using the UKPDS risk engine calculator.

The high-sensitive CRP was not correlated with CVD prediction. In our study, it is explained that natriuretic peptides are highly correlated with CVD risk stratification. Furthermore, our findings are consistent with earlier research linking elevated blood glucose and natriuretic peptide levels to a higher risk of cardiovascular disease.

According to the findings of this study, a large number of cardiac biomarkers that are utilized in clinical settings are late-stage biomarkers, meaning that a CVD has already begun to manifest. The utmost importance in preventing these diseases from progressing and inducing their associated complications is to identify early-stage biomarkers of CVDs, hence the study proves that there is a significant correlation between natriuretic peptides and cardiovascular risk in T2DM patients in addition, UKPDS is used as a promising tool to predict 10-year risk of CVD.

Conclusion

It appears improbable that a solitary natriuretic peptide biomarker can unequivocally aid patients with type 2 diabetes mellitus and cardiovascular diseases, despite the identification of several promising cardiac markers. The data demonstrate linear relationships between blood sugar (HbA1c) and UKPDS score, UKPDS score and natriuretic peptide (NT-Pro BNP), blood sugar (HbA1c) and natriuretic peptide (NT-Pro BNP, MR-Pro ANP), as well as age and natriuretic peptide (NT-Pro BNP, MR-Pro ANP).

In conclusion, the study indicates that elevated natriuretic peptide levels in type 2 diabetes mellitus are directly linked to cardiovascular risk.

Conflict of Interest

The authors declare that there is no conflict of interest.

Acknowledgement

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