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LOW SERUM BNP LEVELS IN TYPE II DIABETES MELLITUS

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ABSTRACT

BNP, B type natriuretic peptide , an established marker of heart failure , also has a role to play in obesity and diabetes . The phenomenon of natriuretic handicap (i.e., reduced / impaired natriuretic peptide response is common among type II diabetes mellitus patients.Our aim was to investigate the clinically meaningful associations which implicated low serum BNP levels with obese type II diabetes mellitus patients.The association between low BNP levels and diabetes in the study population supports the phenomenon of natriuretic handicap and so its predisposition to hypertension and other cardiovascular disorders and thereby BNP levels can be assessed as a routine in obese diabetics to assess their status of natriuretic response.

KEY WORDS: Brain natriuretic peptide , Type II diabetes mellitus , Natriuretic peptide clearance receptors , Visceral fat , Body mass index .

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INTRODUCTION

Diabetes mellitus , a disorder of glucose homeostasis caused by absolute or relative insulin deficiency is a common problem in India . Obesity , a much more common problem is increasing in prevalence in developing countries like india , and its increasing prevalence of co morbidities makes it much more significant . BNP , brain natriuretic peptide is a 32 amino acid polypeptide secreted by the ventricles of heart in response to excessive stretching of heart muscle cells . The release of BNP is modulated by calcium ions[1]. It is co secreted along with a 76 amino acid N terminal fragment , NT pro BNP . Both BNP and NT-probnp levels in the blood are used for screening, diagnosis of acute congestive heart failure (CHF) and may be useful to establish prognosis in heart failure, as both markers are typically higher in patients with worse outcome[2]. NPR1 is a membrane-bound guanylate cyclase that serves as the receptor for both atrial and brain natriuretic peptides (ANP and BNP, respectively)[3]. BNP binds to and activates atrial natriuretic factor receptors NPRA and to a lesser extent NPRB in a fashion similar to ANP but with 10 fold lower affinity . Biological half life of BNP is twice as long as that of ANP making these peptides , better targets than ANP for diagnostic blood testing. Physiological actions include a decrease in systemic vascular resistance as well as an increase in natriuresis.

MATERIALS & METHODS

Blood sample (5 ml) , serum separated is obtained from
60 individuals aged 40-60 years
30 obese diabetics ,and controls : 30 non obese non diabetics).Attending medicine / diabetology OPD of our institute Sree Balaji Medical College And Hospital , Chromepet , Chennai , India . All individuals were interviewed at the baseline by the same investigator for a general medical history and complete medical examination including height , weight , waist and hip circumference and blood pressure measured by the same .

EXCLUSION CRITERIA

Those individuals with heart failure , cardiovascular disease , liver dysfunction and renal insufficiency were excluded from the study

INVESTIGATIONS , performed

1. Serum BNP by Immune assay – ELISA
2. FBS , PPBS by GOD – POD method , Diatek Kit , Fully Automated Analyser
3. Serum Creatinine By Jaffes Kinetic Method , Erba Biochem
4. 12 lead ECG

And BMI measured by the quetelet index
Blood pressure measured by Mercury Sphygmomanometer.
The association of BMI with BNP was evaluated by using pearsons correlation co efficient . Statistical analysis was performed manually employing standard methods with the assistance of statistician . The study was approved by the institutional ethical committee of Sree Balaji Medical College Ansd Hospital . An informed consent was obtained from all the study participants both in English and in vernacular languages.

RESULTS OF THE STUDY

1. Non obese non diabetics serum BNP mean value : 26.76
2. Obese diabetics serum BNP mean value : 19.10
3. Correlation co efficient , r = -0.46
4. Student t test , t = 3.40 ($p < 0.001$)

DISCUSSION

The present study observed that obese diabetics have low serum bnp levels than their normal counterparts which signals the lowered natriuretic response in these individuals . BNP , a peptide secreted by the ventricles of the heart in response to excessive stretching of the heart muscle cells . Its physiologic actions include decrease in systemic vascular resistance as well

as an increase in natriuresis . The net effect is a decrease in blood volume which lowers systemic blood pressure and afterload yielding and increase in cardiac output , partly due to a higher ejection fraction .

ASSOCIATION WITH OBESITY AND DIABETES

Obesity , a major risk factor for hypertension ,[4] diabetes and other cardiovascular disorders . it has been speculated that obese individuals have an impaired natriuretic response , the phenomenon called natriuretic handicap , [5] but its existence has not been proven . the demonstration of low serum BNP levels in obese individuals would support the concept. Obesity frequently co exist with diabetes and so it is important to consider the association of diabetes on serum BNP levels . it has been hypothesised by studies that individuals with obesity , metabolic syndrome and insulin resistance seems to have lower serum BNP levesl when compared with normal counter parts supporting the concept of natruiuretic handicap[6]. Natriuretic peptide clearance receptors (NPR–C) are abundant in adipose tissue suggesting that adipocytes participate in the removal of natriuretic peptides from circulation[7,8]. Elevated NPR-C gene expression has been documented in the adipose tissue of humans with obesity and hypertension .the allelic variants of this gene has been associated with lower plasma natiuretic peptide levels[9]. adipocytes also express NPR-A receptors which mediate the biologic effects of natriuretic peptides . the low natriuretic peptide levels may lead to reduced lipolysis[10], additionally perpetuating the obese state .

ROLE OF VISCERAL FAT

Visceral fat or abdominal fat also known as organ fat or intra-abdominal fat, is located inside the abdominal cavity, packed between the organs (stomach, liver, intestines, kidneys, etc.)[11]. An excess of visceral fat is known as central obesity, or "belly fat", in which the abdomen protrudes excessively. Excess visceral fat is also linked to type 2 diabetes, insulin resistance, inflammatory diseases and other obesity-related diseases[12,13,14,15] . Visceral fat expansion can increase the clearance of active natriuretic peptides by means of an increased expression of clearance receptors on adipocytes and so it may contribute to the decreased activity of cardiac endocrine system . moreover , obesity is associated with ectopic lipid deposition even in the heart which may directly exert a lipotoxic effect on the myocardium by secreting in local , several cytokines and adipokines. Diabetes can further accelerate the effect along with its altered lipid metabolism. CReactive protein, a sensitive indicator of inflammation, is an independent risk factor for CAD, and has been shown to be higher in Asian Indians than in Europian whites. Which is accounted for by greater central obesity and insulin resistance in Indians(16) From the above discussion , it is clear that obese diabetics have a lowered natriuretic response and that can play an etiologic role in their predisposition to hypertension and other cardiovascular abnormalities .

LIMITATIONS

A variety of limitations of this study need however also to be addressed . sample size is small which did not allow a multivariate approach for incorporating additional , potentially meaningful factors for modifying the levels of BNP . Nevertheless it seems reasonable that routine screening for serum BNP level among obese diabetics provide additional information and then they can have serial BP measurements and so early detection of cardiovascular abnormalities and so a better quality of life . follow up studies are still needed to find whether this low serum BNP response is associated with cardiovascular abnormalities.

CONFLICT OF INTEREST

Author s declare no conflict of interest .

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