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# The Efficacy of Nt- Pro Bnp with Reference To LVEF As A Marker of Ventricular Dysfunction in Cardiac Failure.

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***Abstract:****Heart failure comprises the constellation of clinical symptoms and signs leading to frequent hospitalisation, poor quality of life due to failing heart muscle that cannot pump blood around the body effectively. The early and reliable diagnosis of left ventricular systolic function is done by ECHO to measure Left Ventricular Ejection fraction (LVEF). Due to the cost and limited availability, cost effective tools needs to be found out.*

*The aim of the study is to determine the efficacy of neuro-hormonal markers like NT pro BNP in predicting ventricular systolic dysfunction and its interrelationship with LVEF in heart failure cases.*

*The current case-control study includes 50 numbers of cardiac failure patients and an equal number of age and sex matched controls.*

*The biochemical parameters like fasting plasma glucose, cholesterol, creatine kinase (CK) and CK-MB were increased significantly ($p < 0.001$) while HDL was decreased significantly ($p < 0.05$) in cases in comparison to control. There was a significant increase of NT-pro BNP in cases compared to controls ($p < 0.001$).There was an inverse correlation betweenLVEF and NT- pro BNP ($r = -0.64752$). A cut off value of 97.9pg/ml gives a specificity of75%, sensitivity of 76%, positive predictive value of 28% and negative predictive value of 97%*

*NT- pro BNP could be helpful in diagnosis of ventricular systolic dysfunction and immediate intervention.*

***Keywords:-****Heart failure, Brain Natriuretic peptides, LVEF.*

## I. Introduction

Heart failure (HF) is a clinical syndrome in which there is an abnormality of cardiac structure or function responsible for the inability of the heart to eject or fill with blood at a rate commensurate with the requirement of the metabolised tissue. HF results in constellation of clinical manifestations including in various combinations circulating congestion, dyspnoea, fatigue and weakness affecting up to 6-10% of people above 65 years .In HF cardiac output and stroke volume may be depressed. A more sensitive index is a decrease in ejection fraction (Stroke volume/ End diastolic volume)the normal value of which is 67 ± 8 %, although in approximately half of patients EF tends to remain normal.[(2)]

HF begins with the initial decline in the pumping capacity followed by varieties of compensatory mechanism. As time elapses the activity of compensatory mechanism leads to end organ damage within the ventricle, worsening left ventricular remodelling and subsequent decompensation.An early and reliable diagnosis of left ventricular systolic dysfunction is important for the patients. Because of costs and limited availability, ECHO (echocardiography) and radionucleotide ventriculography are not suitable as primary diagnosing screening tools, so new diagnostic tools are needed. LVEF has also certain limitations as a true measure of contractility as it is influenced by alteration in preload and or after load. In this respect, neurohormonal markers could be helpful in the diagnosis of left ventricular dysfunction.[(4,5,6)]

Natriuretic peptides are of three types known as ANP (atrial natriuetic peptide), BNP (B- type natriuetic peptide / brain natriuetic peptide) and CNP (C- type natriuetic peptide). ANP is secreted primarily from atrium, BNP from cardiac ventricles and CNP is localisedin endothelium. In case of acute loading BNP is shown to be produced quickly. Thus in this regard BNP is superior than ANP.BNP was first isolated from porcine brain (32 amino acids protein) and also found in the human brain. It is predominantly secreted from the heart ventricle.[(8)] Pro BNP (108 amino acid) is stored in secretary granules in myocyte, is then broken down by protease to 32 amino acid BNP and N-terminal pro BNP (NT- pro BNP) as a result of increased wall tension in ventricles. [(9)] NT- pro BNP has longer half life than BNP and is not affected by the administration of exogenous BNP.[(10)] NT- pro BNP is more dependent on renal clearance and the half life is 2 hrs as compared to BNP (t½ = 22 min.).Both serum pro BNP and NT- pro BNP levels are consistently increased with the severity of the disease according to the heart failure classification of NewYork heart Association(NYHA).[(12)]

## II. Materials And Methods

This case control study was undertaken in the department of Biochemistry in collaboration with the department of Cardiology, SCB Medical College, Cuttack. 50 numbers of patientswith diagnosed cardiac failure were included as cases. The inclusion criteria were sign, symptoms of cardiac failure (respiratory rate ≥ 40/ min, pulmonary oedema, generalised oedema, evidence of ischemia and LVEF ≤ 50% of normal). The patients having h/o major surgery or trauma within 6 months, malignancy, pregnancy, acute coronary syndrome, and serum creatinine > 2.5 mg% were excluded from the study. 50 numbers of healthy control (age & sex matched) taken for the study.

The routine biochemical parameters (FPG, urea, creatinine, lipid profile) were estimated using standard kits with TOSHIBA 120 FR auto analyzer. Serum electrolytes were estimated by using ion selective electrode. CK and CK-MB were estimated by dry chemistry analyser. NT pro BNP was estimated by ELISA kit with LISASCAN EM. All values were expressed in mean ± SD.

## III. Observation

**Table – 1** –Incidence of different causes leading to cardiac failure.

| Disease present | No. of cases | Incidence in % |
|---|---|---|
| Coronary arterial disease | 19 | 38 |
| Chronic volume overload | 06 | 12 |
| Rheumatic heart disease | 05 | 10 |
| Valvular disease | 05 | 10 |
| Cardiomyopathy | 03 | 06 |
| Conduction defect | 02 | 04 |
| Others(includingcorpulmonale) | 10 | 20 |

**Table -2** – Biochemical parameters among case & control groups

| Parameters | Control (50 no) Mean ± SD | Cases (50 no) Mean ± SD | 'P' value |
|---|---|---|---|
| FPG (mg%) | 90.94 ± 14.25 | 125 ± 63.18 | < 0.001 * |
| S. Urea (mg%) | 23.61 ± 6.09 | 34.36 ± 11.19 | > 0.05 |
| S. Creatinine( mg%) | 0.89 ± 0.17 | 1.02 ± 0.52 | < 0.001 * |
| Cholesterol (mg%) | 153.71 ± 35.41 | 184.12 ± 48.77 | < 0.001 * |
| TG (mg%) | 123.13 ± 33.11 | 199.6 ± 73.29 | > 0.05 |
| LDL (mg%) | 86.19 ± 23.28 | 106.64 ± 39.96 | < 0.05 * |
| HDL (mg%) | 38.40 ± 6.05 | 35.28 ± 8.34 | < 0.05 * |
| VLDL (mg%) | 25.53 ± 8.51 | 40.14 ± 14.73 | > 0.05 |
| $Na^+$ (mmol/lt) | 137.61 ± 2.2 | 131.0 ± 14.45 | < 0.05 * |
| $K^+$ (mmol/lt) | 3.67 ± 0.29 | 4.52 ± 1.29 | < 0.001 * |
| CK (IU/Lt) | 35.8 ± 11.2 | 77.3 ± 28.9 | < 0.001 * |
| CK-MB (IU/Lt) | 3.3 ± 1.23 | 21.4 ± 9.5 | < 0.001 * |

The biochemical parameters assigned with '*' shows p- value significantly raised in cases in comparison to control group.

**Table-3** – Comparison of NT-pro BNP level between cases and controls

| | NT-pro BNP (pg / ml) | 'p' value |
|---|---|---|
| Controls (50 nos) | 41.06 ± 17.67 | |
| Cases (50 nos) | 194.7 ± 68.9 | < 0.001 |

**Table-4** – Co-relation between NT-pro BNP value and left ventricular Ejection fraction (LVEF) in heart failure cases.

| NT-pro BNP pg /ml) | Average LVEF in % | 'r' value |
|---|---|---|
| 100-200 | 46.99 | |
| 200-300 | 44.19 | -0.647552 |
| 300-400 | 39.74 | |
| > 400 | 35.25 | |

**Table -5** – Diagnostic value of NT-pro BNP for detection of a LVEF of ≤ 40 % (cut off value of 97.9 pg/ml)

| Sensitivity | Specificity | Positive predictive value | Negative predictive value |
|---|---|---|---|
| 75 % | 76 % | 48 % | 97 % |

## IV. Discussion

There is no agreed upon first line test for the diagnosis of heart failure and no simple method for measuring the adequacy of cardiac output in relation to normal levels of activity. To confirm clinically suspected heart failure usually LVEF is estimated which is seldom affected in diastolic heart failure with preserved systolic function. Natriuretic peptides like BNP secreted by heart have following functions (1) down regulation of the sympathetic nervous system and rennin-angiotensin system (2) facilitates natriuresis (3) decreases peripheral vascular resistance (4) increases smooth muscle relaxation. Natriuretic peptides also inhibit cardiac growth and hypertrophy, counteracting the mitogenesis that causes ventricular remodelling.[13,14,15]BNP Is secreted in response to left ventricular stretching , wall tension or overload and thus can also diagnose diastolic heart failure with preserved LVEF which is common in women and at old age which is evaluated in the present study.[16]

Table-1 shows the incidence of various aetiologies leading to cardiac failure. The most common cause is coronary vascular disease (38 %) followed by hypertension.The biochemical parameters in table-2 shows significant increase in FPG among cases ($P<0.001$) due increased incidence of heart failure in of diabetic patients. Serum creatinine shows significantly increased vales in cases without a concomitant rise in urea values. This could be due to associated hypertrophy or degeneration of cardiac myocytes. There is also significant increase in cholesterol ($P<0.001$) and decrease in HDL values ($p<0.05$) respectively. The decrease in $Na^+$ & increase in $K^+$ provide additional evidence of cardiac failure and may also be due to use of diuretics and antihypertensive agents.

The CK and CK-MB isozymes are increased significantly in cases ($p<0.001$) as a marker of acute coronary syndrome which is the major cause of heart failure in our study.The specific biomarker estimated is NT-pro BNP (Table 3) increased significantly in cases in comparison to control group ($p<0.001$). Here we tried to eliminate the effect of age by taking age matched controls.The results of this study are in accordance with other studies. Table 4 shows the correlation between NT Pro BNP and LVEF in cardiac failure cases. We found a concomitant increase in NT Pro BNP values with a fall in LVEF values. Thus a significant negative correlation exists between these two values ($r = - 0.64752$) which is in accordance other studies. [17, 18, 19]

When the value of NT Pro BNP was evaluated as a diagnostic biomarker for cardiac failure, we found a good sensitivity of 75%, specificity of 76%, positive predictive value of 48% and a strong negative predictive value of 97% using a cut off value of 97. 9 pg/ml.

## V. Conclusion

The main finding of this study is significant rise in NT- pro BNP with decrease in LVEF. The strong negative predictive value makes it a valuable biomarker which can be used to exclude heart failure in patients presenting with similar signs and symptoms of heart failure. It can also be used as a biomarker in institutions lacking echocardiography or in heart failure cases with preserved LVEF

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