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# Estimation and Comparison of Pro-BNP level in patient with Heart Failure due to COPD and LV dysfunction

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**Introduction:** Diagnosis of heart failure and chronic obstructive pulmonary disease remains predominantly clinical decision. Many times both the condition may mimic each other and differentiation may be difficult specially in elderly and obese individuals. Pro-BNP is an important marker to distinguish the above conditions. We did a study to estimate and compare the levels of Pro-BNP in patients with heart failure due to COPD and LV dysfunction. **Material and methods:** The study subjects were 60 patients of comparable age group admitted in department of medicine and cardiology. Level of pro BNP was assessed using Immune electro chemiluminescence assay (IECMA). **Results:** The mean level of pro BNP was significantly raised in patients with heart failure due to LV dysfunction. Left Ventricular Ejection Fraction and levels of Pro BNP were not related. **Conclusion:** Pro BNP can serve as a good clinical tool in differentiation of dyspnea arising out of congestive heart failure and chronic obstructive pulmonary airway diseases specially in elderly and obese patients. It is easy to perform and bedside test.

**Keywords:** Congestive heart failure (CHF), Left ventricular dysfunction (LVD), Pro BNP, Chronic obstructive pulmonary airway disease (COPD), Ischemic heart disease (IHD)

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# Introduction

Heart failure (HF) is a principle complication of virtually all forms of heart disease. Heart failure is relatively common disorder and a major public health problem in industrialized nation. The information about the prevalence and incidence of heart failure in the Southeast Asia is scare. However as the incidence of coronary artery disease (CAD) is increasing, the prevalence and incidence of heart failure is also increasing and approximate prevalence is 0.8 to 2% in general population [1]. It is estimated that 4-6 million persons in the United States are being treated for heart failure, with 570,000 new cases diagnosed each year [2, 3]. The worldwide prevalence of heart failure was estimated to be 23 millions [4]. Same trends are anticipated in India as the healthcare improves and average life expectancy improves.

The prevalence of heart failure increases dramatically with age [5]. The Framingham heart study reported the prevalence in men of 8/1000 at age of 50-59 years which increased to 66/1000 at ages 80-89 years [3]. In women it was also 8/1000 at ages 50-59 years and 79/1000 at ages 80-89 years. In patient younger than 40 years, the prevalence is only 1%; in patient older than 80 years or older, it is 20%. The 2011 American Heart Association (AHA) update reported that in the American men and women the prevalence was 3% and 2% respectively [2]. The lifetime risk of developing heart failure has been estimated, and it is about 20% for both men and women. In absence of CAD at age 40 years, it is 11.4% in men and 15.4% in women [6].

As the population is aging, improvement in longevity is due to salvage of a greater proportion of patient with acute coronary syndrome with the modern therapy and the increase in diabetes and obesity in the population both the incidence and prevalence of heart failure continue to rise. In the United States, approximately 45,000 death each year are primarily caused by heart failure is listed as a contributing cause in 260,000 death [2].

HF is frequently but not always caused by a defect in the myocardial contraction and then the term myocardial failure is appropriate. Although HF may occur as consequences of most form of heart disease, in the United States and Western Europe, ischemic heart disease is responsible for about three quarter (3/4) of all cases. Hypertension (HTN) alone is responsible for approximate 7% of Heart failure cases, other risk factor for heart failure are obesity, diabetes, increasing age, insulin resistance. Idiopathic Cardiomyopathies are approximately 12% cause for heart failure [7].

The clinical recognition of heart failure when based on a careful history, distinctive sign, and radiographic evidence of pulmonary venous congestion, is usually not difficult. However in some circumstances particularly in the elderly, the obese and/or in presence of primary lung disorder such as COPD recognition of the early manifestation of cardiac failure may be difficult yet critical to effective management. There is no gold standard methodology for such diagnosis, and variation in criteria has been noted in previous studies. The American heart association / American college of cardiology and European society of cardiology have recognized the importance of simple and reproducible criteria and have developed guidelines for the diagnosis of HF. According to these recommendations, the diagnosis is based on clinical parameters and auxiliary laboratory test in order to determine the etiology and degree of functional impairment.

Several natriuretic peptides have been isolated from the heart and vessels, namely, the Brain Natriuretic Peptide (BNP) and the Atrial Natriuretic Peptide (ANP). B-type natriuretic peptide (BNP), a neuro-hormone synthesized in the cardiac ventricles, is released as pre-pro BNP and then enzymatically cleaved to the N-terminal pro-BNP (NT-pro BNP) and BNP upon ventricular myocyte stretch. Blood measurements of BNP and NT-pro BNP have been used to identify patients with congestive heart failure (CHF) [8, 9]. These peptides have systemic and local action inducing natriuresis and vasodilatation [10]. The recognition of B-type natriuretic peptide (BNP) and N-terminal-pro BNP (NT-proBNP) as markers for the diagnosis, severity, and prognosis of CHF is truly a breakthrough for clinicians and patients diagnosed with CHF [11]. Previous studies have evaluated the diagnostic accuracy of BNP as marker of left ventricular systolic as well as diastolic dysfunction and HF in different population. Patient with dyspnea due to heart failure haves higher BNP level than dyspnea due to respiratory diseases [12].

The present study was designed to estimate value of Pro BNP in patients with heart failure either with systolic or diastolic dysfunction and COPD and comparison of level of Pro BNP in patient of heart failure and COPD.

# Material and Method

The present study conducted in 60 cases of comparable age group was admitted in department of Cardiology and Department of Medicine of a tertiary care teaching hospital of central India.

**Selection of cases**

**Group I:** comprises all the patients with primary left ventricular dysfunction/ Heart failure.

**Inclusion criteria:** All cases of dyspnea (CCF, myocardial infarction, post MI, valvular heart disease, hypertension, cardiomyopathy which admitted in department of Cardiology and diagnosed on the basis of history, physical examination and investigation like ECG, Chest X-ray, Echocardiography, CAG study.

**Exclusion Criteria:** Exclude the cases which are suffering from systemic illness which can alter the results of Pro BNP, and its clinical correlation like-

- Renal failure
- Severe anaemia,
- Nephrotic syndrome
- Chronic obstructive pulmonary disease
- Bronchial asthma.

**Group II:** included Patients with Primary pulmonary disease.

**Inclusion criteria:** Cases of dyspnea (COPD, Bronchial Asthma, COPD with cor pulmonale diagnosed on the basis of history, physical examination, chest x-ray, echocardiography and routine investigation.

**Exclusion criteria:** Exclude the cases which are suffering from systemic or local illness which can alter result of pro. BNP and its clinical correlation like

**Infectious lung disease like**

- Pneumonitis
- Pulmonary tuberculosis
- Pleural Effusion
- Lung Abscess
- Hydropneumothorax
- Renal failure
- Primary cardiac disease as, MI, valvular lesion, cardiomyopathy

**Methods:** A detailed history, clinical examination and appropriate investigations were done in all cases.

**Following investigation were done in all cases**

Complete blood profile including - Hb%, TLC, DLC, ESR, Blood sugar, Blood urea, Serum creatinine Urine - Routine and Microscopy Chest X-ray ECG, CD-Echo, Pro- BNP Pro BNP, N- terminal level was assessed by Immune electro chemiluminescence assay (IECMA)

**Reference Range for Pro BNP NT (Yasue H et al) [13]**

| | Pro BNP, N terminal pg/mL |
|---|---|
| Healthy Males | <=60 |
| Healthy Females | 12-150 |

# Results

In present study 60 patients were enrolled who fulfilled the inclusion criteria. Out of 60 patients 40 patients (66.67%) were having LVD, and 20 patients (33.33) were having pulmonary disease.

**Table No 1: Distribution of cases included in study**

| S. No. | Case | No. of Case | Percentage % |
|---|---|---|---|
| 1 | Patient with left ventricular Dysfunction | 40 | 66.67% |
| 2 | Patients with Pulmonary disease | 20 | 33.33% |
| | Total | 60 | 100% |

Out of this 60 patients 39 were males and 21 were females, in LVD group 25 were males and 15 were females, while in pulmonary group 14 patients were males and 6 patients were females.

Out of 40 patients who were having LVD, 21 cases (52.5%) having LVD due to myocardial infarction, 7 cases(17.50%) were having LVD due to unstable angina/ischemia, 3 cases (7.50%) were having LVD due to rheumatic heart diseases, 5 cases (12.50%) were having cardiomyopathy, and 4 cases (10%) were due to hypertension.

**Table No 2: Correlation between left ventricular ejection fraction (LVEF) (%) and Pro-BNP in cases with LV dysfunctions**

| S. No. | LVEF % | No. of Pt. | Mean Value [Pg/ ml] |
|---|---|---|---|
| 1 | 30% | 3 | 28,431 |
| 2 | 31-35% | 5 | 18078.40 |
| 3 | 36-40% | 3 | 10758.68 |
| 4 | 41-45% | 2 | 20181.50 |
| 5 | 46-50% | 7 | 11238.29 |
| 6 | 51-55% | 6 | 7000.00 |
| 7 | 56-60% | 13 | 1092.54 |
| 8 | 61-65% | 1 | 148 |

In pulmonary disease group (20), 13 cases (65%) were having COAD, and 7 cases (35%) were having bronchial asthma.

In our study we observed that LVEF alone has no direct correlation with pro BNP and level of pro BNP markedly varies with a constant LVEF. Pro- BNP was elevated in patient of heart failure, both with preserved and impaired LVEF.

**Table No 3: Correlation between Pro BNP and** LVEF% **in patient with Pulmonary Disease.**

| % LVEF | No of Pt. | Pro BNP |
|---|---|---|
| 50-55% | 3 | 2612-7549(5689) |
| 56-60% | 8 | 108-32324(5191) |
| 61-65% | 9 | 104-225(155) |
| Total | 20 | |

Level of pro BNP was also increased in patient with pulmonary disease, and it again showed that there is no direct correlation between LVEF and Pro BNP level.

**Table No 4: Correlation between Pro BNP and Right ventricular end diastolic diameter (RVEDD)**

| RVEDD | No. Of. Pt. | Pro. BNP |
|---|---|---|
| 12 | 3 | 104, 106, 108, [106] |
| 13 | 3 | 108, 112, 118 [112.67] |
| 15.20 | 5 | 142, 148, 145, 150 [146.50] |
| 18.50 | 3 | 148,196, 196 [196] |
| 23 | 1 | 225 |
| 34 | 1 | 2612 |
| 38 | 1 | 6908 |
| 42 | 1 | 7549 |
| 45 | 1 | 8418 |
| 58 | 1 | 32324 |

**Table No 5: Comparison of pro. BNP in cases of LVD, Pulmonary disease & heart failure due to pulmonary disease.**

| | LVD | | Pulmonary disease | | Pulmonary disease with Heart Failure | |
|---|---|---|---|---|---|---|
| No. of Pt. | 40 | | 15 | | 5 | |
| | Mini | Maxi | Mini | Maxi | Mini | Maxi |
| Pro. BNP | 150 | 35000 | 108 | 225 | 2612 | 32324 |
| Mean | 9360+7416 | | 146+17.91 | | 11562+8707 | |

In present study pro BNP level was markedly high in patients who were having pulmonary disease with Dilated right ventricle (cor pulmonale). And as the right ventricular end diastolic diameter increases Pro BNP level is also increases in linear relationship.

Finally on comparison in different group Pro- BNP was markedly raised in LVD group, it was normal or mildly raised in patient with pulmonary disease with normal RV, and was markedly raised in patients with pulmonary disease with dilated RV

In the Present study a comparison of level of Pro-BNP was done in total L.V. dysfunction cases and pulmonary disease cases.

Mean value of Pro-BNP in L.V. dysfunction cases was 9360 + 7416 (pg/ml) S.D. and mean Pro-BNP Pulmonary disease cases was 3008 + 6391 (pg/ml) S.D. Here the $Z = 3.38$ that is $>2$ than $P < 0.05$ which is significant than present study shows that level of Pro-BNP significantly raised with L.V. dysfunction than with lung disease.

# Discussion

The prevalence of heart failure is rapidly increasing, because more number of patients surviving acute coronary syndrome and they are left at risk for development for heart failure. On an average the 5 year mortality rate for Heart failure is 50% and 10 year mortality rate is 90% [14, 15]. Although patients admitted to the hospital with heart failure frequently improve with treatment, traditionally there has been no practical way to evaluate the long-term effects of such treatment. Indeed, inhospital mortality and readmission rates for HF patients are extremely high [14].

Conventional cardiac functions tests are time consuming and often do not correlate well with symptomatic changes in a patient's condition. Therefore, most patients are discharged when they "feel better" Which may preclude further titration of medical therapy. The recognition of Btype natriuretic peptide (BNP) and N-terminal-pro BNP (NT-proBNP) as markers for the diagnosis, severity, and prognosis of CHF is truly a breakthrough for clinicians and patients diagnosed with CHF [11].

In present study we correlated the level of Pro-BNP with the Left ventricular ejection fraction (LVEF), Right ventricular end diastolic size in pulmonary disease group of patients. In cases with left ventricular dysfunction, level of Pro-BNP does not directly correlate with LVEF, it markedly varies with a constant LVEF. As in our study one case with LVEF

30% had Pro-BNP level 15293 Pg/ml and another case with LVEF 30% had Pro-BNP >35000 Pg/ml, similarly with LVEF 60% Pro-BNP level varies from 212 to 2369 Pg/ml. Similarly in case with pulmonary disease level of Pro-BNP does not directly correlate with LVEF, as with LVEF 60% the level of ProBNP varies from 109-32324 Pg/ml. Although Pro-BNP level do not accurately predict the Ejection fraction, its measurement has been suggested as way to screen candidates for serial echocardiography.

Daoq et al. found that Pro-BNP has very high negative Predictive value 99.2% [16]. Therefore although the specificity is not so extremely high (87%), the high negative predictive value makes this an appropriate method for selectivity of patients who need Echocardiography.

A. Mark Richards et al done a study and found that ProBNP and LVEF is Complementary independent predictor of major adverse events on follow up after myocardial infarction. Combined measurement provides risk stratification substantially better than that provided by either alone [17].

In patients with pulmonary disease we correlated the level of Pro-BNP with right ventricular end diastolic diameter (RVEDD). With mean RVED diameter 12mm mean ProBNP was 106 Pg/ml, with RVEDD 18.50 mm Pro-BNP 196Pg/ml, RVEDD 23mm Pro-BNP 402 Pg/ml and with mean RVED diameter 58mm the mean Pro-BNP was 32324 Pg/ml so that present study show a direct correlation between level of Pro-BNP and RVED diameter (Correlation Coefficient = 0.54)

Matusuo K. et al. In their study found that BNP appears to be elevated in right ventricular dysfunction regardless of the cause of the dysfunction although not to the same extent in right ventricular dysfunction as in left ventricular dysfunction [18].

Comparison of Pro-BNP level was done in between cases with L.V. dysfunction and cases with only pulmonary disease. Study showed that level of Pro-BNP was markedly raised in cases of L.V. dysfunction where mean Pro- NP level was 9360+ 7416 (pg/ml) S.D. but not raised in case of dyspnea due to only lung disease where mean Pro-BNP level was 146 + 17.91 (pg/ml) S.D. ($P < 0.05$). Thus study showed that level of Pro-BNP rises significantly ($P < 0.05$) with L.V. dysfunction

And not with pulmonary disease. Davis M et al also showed that level of Pro-BNP markedly rises with L.V. dysfunction and not with. Pulmonary disease, this study also concluded that level of Pro-BNP markedly rises with development of Cor-Pulmonale or right heart involvement [19, 20].

In present study Comparison of Pro-BNP was done in between cases with only lung disease had mean Pro-BNP 146 + 17.91 (pg/ml) S.D. and cases with Cor Pulmonale or Right heart involvement, mean Pro-BNP 11562 + 6391 (pg/ml) S.D. than $P < 0.05$, than it is significant so level of Pro-BNP does not raised with dyspnea due to only pulmonary involvement though it raised markedly in right ventricular involvement and this difference is significant $P<0.05$. Jansen KT et al, done a study in 60 patients with primary Pulmonary hypertension and showed that BNP level independently predicted 24 month mortality. During follow up mortality was also markedly lower in patients whose BNP level decreased than in those whose level increased [21].

In present study the level of Pro-BNP in patient with L.V. dysfunction varies from 150 Pg/ml to >35000 Pg/ml, this value is much higher than other previous studies. This is because of late presentation and unawareness of patients towards the disease in rural areas of Indian scenario. The Pro-BNP assay now a rapid, 15-minutes bed side blood test is highly sensitive and fairly specific for diagnosing heart failure and is useful in evaluating suspected heart failure in outpatients and in emergency cases. It has a negative Predictive value of greater than 95% [16], a normal BNP level can exclude heart failure and other cause of neurohormone activation from differential diagnosis.

# Conclusion

Pro BNP level significantly ($P< 0.05$) rise in patient with left ventricular dysfunction than patients with pulmonary diseases. Pro-BNP can be an important diagnostic marker to differentiate origin of dyspnea in cardiac and pulmonary disease. Level of Pro BNP does not directly correlate with LVEF in both groups and it is independent indicator for severity of symptoms. Level of Pro BNP rises with increase in RVED diameter. (Correlation coefficient = 0.56). In patient presenting in the emergency care unit, the accuracy of measurement of BNP is superior to that of clinical judgement. Hence it can be used as a sensitive and fairly specific tool for diagnosis

Of heart failure in cases where clinical judgement is alone not sufficient especially in elderly and obese population. It is a simple, quick, cost effective and bedside test.

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