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## Original Article

# Evaluation and comparison of biomarkers in heart failure



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## ABSTRACT

**Objectives:** To establish biomarkers available as predictors of prognosis and mortality in heart failure (HF) patients and to correlate the biomarkers with the severity and outcome of HF.

**Methods:** This was a prospective study. 60 patients of HF were taken into the study based on the inclusion and exclusion criteria and were studied for the markers – BNP, TNF- $\alpha$ , troponin-I, CK-MB, CRP, uric acid, GGT and were compared with the severity and outcome in these patients.

**Results:** Of 27 patients with BNP value less than 100 pg/ml, only 1 death occurred (3.7%) and out of 33 patients with BNP value of more than 100 pg/ml, 8 deaths occurred (24.2%). Out of the 9 deaths that had occurred, 7 deaths were in the troponin range of >0.5 ng/ml, 2 deaths in the troponin range of 0.04–0.49 ng/ml, and no deaths in the range of 0–0.03 ng/ml. 8 deaths had an elevated titer of TNF (40%) and 39 patients out of 40 were survivors who had TNF titers in the normal range (97.5%).

**Conclusion:** BNP and TNF- $\alpha$  are excellent predictors of mortality and morbidity in HF. Troponin-I and CRP have shown significance in predicting the outcome in HF. GGT, uric acid, and CK-MB play no role in predicting the severity and outcome in HF.

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## 1. Introduction

Heart failure (HF) is a syndrome, rather than a primary diagnosis, which results from any structural or functional cardiac disorder that impairs the ability of the heart to support the physiological circulation.<sup>1</sup> Unfortunately, there is no single diagnostic test for HF, and the accuracy of diagnosis by clinical

means only is often inadequate. Although natriuretic peptides have been shown to be reliable diagnostic and prognostic tools, the extent to which these markers could be used as aids in the titration of medical therapy for chronic heart failure remains uncertain.<sup>1</sup> There is an increasing interest in the development of new biomarkers in evaluation of heart failure, and a great number of laboratory tests have recently been proposed.<sup>2</sup> Studies in which biomarkers are compared are lacking.

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The burden of HF in India appears high. However, reliable data are lacking because of inadequate surveillance systems.<sup>3</sup> The epidemiology of HF in India has likely changed from that reported in 1949 by Vakil.<sup>4</sup> The prevalence of HF in India is possibly on the rise, as India remains doubly burdened by the rise in the risk factors of traditional cardiovascular disease (CVD) and by the persistence of pretransitional diseases.<sup>3</sup>

## 2. Objectives

To correlate and compare the biomarkers and its values with the severity outcome of heart failure.

## 3. Methods

### 3.1. Source of data

Patients admitted in JSS Hospital, from November 2009 to November 2011 fulfilling the inclusion criteria and exclusion criteria. Informed consent was taken from all the subjects enrolled in the study.

### 3.2. Methodology

Data were collected in a pretested pro forma for 60 in-patients. Investigations tests such as BNP, CRP, GGT, uric acid, troponin-I, and CK-MB were done. At the same time, serum samples of the patients were collected and stored at  $-20^{\circ}\text{C}$ . Patients' duration of stay, echocardiography findings, and outcome in the hospital were followed up.

Later, the serum samples were thawed and brought to room temperature and ELISA testing of TNF- $\alpha$  was done using ELISA kits.

### 3.3. Inclusion criteria

In-patients above 18 years of age and of both sexes admitted to JSS Hospital fulfilling the Framingham criteria for heart failure.

### 3.4. Exclusion criteria

1. Age less than 18 years.
2. Patients with septic shock, rheumatoid arthritis, ankylosing spondylosis, Crohn's disease, psoriasis, osteoporosis, colonic cancer, leukemia, tuberculosis, alcoholics, chronic kidney disease, end stage renal disease patients, and all other conditions, which can falsely elevate BNP levels were excluded. Acute coronary syndrome patients were also excluded from the study.

### 3.5. Statistical methods

Data were entered in MS-Excel and the statistical methods were carried out using SPSS for Windows (version 22.0). Descriptive statistics such as mean, standard deviation (SD), and percentages were used to describe the variables. In case of non-normality median and interquartile range (IQR) were

used. Fisher's exact test was used to find the association of biomarkers with mortality, NYHA classification, ejection fraction (EF), and duration of hospital stay. Biomarkers found significant on univariate analysis were identified as potential predictors for mortality and duration of hospital stay and were further evaluated using multivariate logistic regression analyses adjusting for confounding variables. A value of  $p < 0.05$  was considered statistically significant.

## 4. Results

A total of 60 patients with age ranging from 21 years to 95 years (mean (SD): 58.2 (15.73) years) were included in the study. Baseline characteristics of the patients were given in Table 1. There were 34 (56.7%) males and 26 (43.3%) females. There were 14 (23.3%) diabetic patients and 24 (40%) hypertensive patients. 11 (18.33%) patients with both diabetic and hypertension. Total number of deaths were 9, maximum being in 41–60 years age group (44%), whereas least was in the 20–40 years and 81–95 years age group of 11% each.

The results of univariate analyses for association between biomarkers and mortality, NYHA classification, EF, and duration of stay showed that all the biomarkers except CKMB found statistically significant association (Table 2). The median (IQR) value of BNP was 120 pg/ml (54.25–662 pg/ml), reference range being 0–100 pg/ml. 33 (55%) patients had BNP >100 pg/ml. 8 (24.2%) deaths occurred in this range which was statistically significant ( $p$ -value = 0.033). In association of BNP with NYHA grading, it was observed that 14 out of 33 patients and 11 out of 33 patients who had BNP values of >100 pg/ml, had NYHA grade of III and IV respectively which was significant when compared with 26 out of 27 patients having BNP <100 pg/ml had breathlessness of NYHA II which was found to have highly significant association ( $p$ -value < 0.001). Out of 33 patients who had BNP >100 pg/ml, 10 (30.3%) had EF <40% whereas 22 out of 27 patients (81.5%) who had BNP <100 pg/ml had EF >50% which was statistically significant ( $p$ -value = 0.001). Out of 33 patients, 23 (69.7%) had a longer duration of stay when compared to the lower BNP range in which 19 out of 27 (70.4%) patients had a shorter duration of stay which was significant ( $p$ -value = 0.002). The median (IQR) value of troponin-I was 0.15 ng/ml (0.02–0.86 ng/ml), reference range being >0.50 ng/ml. 22 (36%) patients fall into this reference range with 7 out of 9 deaths in this range which

**Table 1 – Baseline characteristics of patients.**

Variables	Characteristics of patients
Age (years) (mean (SD))	58.2 (15.73)
Gender	
Number (%)	
Male	34 (56.7)
Female	26 (43.3)
Diabetes mellitus	
Number (%)	14 (23.3)
Hypertension	
Number (%)	24 (40)

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