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Original Article

Evaluation and comparison of biomarkers in heart failure

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A R T I C L E   I N F O

A B S T R A C T

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-α, 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-α 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.

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.[1] 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.[1] 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.[2] Studies in which biomarkers are compared are lacking.

The burden of HF in India appears high. However, reliable data are lacking because of inadequate surveillance systems.[3] The epidemiology of HF in India has likely changed from that reported in 1949 by Vakil.[4] 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.[3]

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-α 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 of <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
    Female
	
	34 (56.7)
	26 (43.3)

Diabetes mellitus Number (%)	 14 (23.3)
Hypertension Number (%)	 24 (40)

Table 2 – Univariate analysis between biomarkers and mortality.

	Mortality (n = 60)		
	No	Yes	
BNP			
≤100	26 (96.3%)	1 (3.7%)	χ^2 = 4.913, df = 1, p = 0.033
>100	25 (75.8%)	8 (24.2%)	
Troponin-I			
0–0.03	20 (100.0%)	0 (0%)	χ^2 = 8.240, df = 2, p = 0.008
0.04–0.49	16 (88.9%)	2 (11.1%)	
>0.50	15 (68.2%)	7 (31.8%)	
CRP			
≤0.5	31 (96.9%)	1 (3.1%)	χ^2 = 7.548, df = 1, p = 0.009
>0.5	20 (71.4%)	8 (28.6%)	
Uric acid			
2–7	47 (92.2%)	4 (7.8%)	χ^2 = 13.659, df = 1, p = 0.002
>7	4 (44.4%)	5 (55.6%)	
TNF-α			
<0.075	43 (84.3%)	2 (22.2%)	χ^2 = 15.730, df = 1, p = 0.000
>0.075	7 (15.7%)	8 (77.8%)	
CK-MB			
<20	24 (85.7%)	4 (14.3%)	χ^2 = 0.021, df = 1, p = 1.000
>20	27 (84.4%)	5 (15.6%)	

Table 4 – Univariate analysis between biomarkers and ejection fraction.

	Ejection fraction			
	<40	40–50	>50	
BNP				
<100	0 (0%)	5 (18.5%)	22 (81.5%)	χ^2 = 13.602, df = 2, p = 0.001
>100	10 (30.3%)	9 (27.3%)	14 (42.4%)	
Troponin-I				
0–0.03	0 (0%)	1 (5.0%)	19 (95.0%)	χ^2 = 16.321, df = 2, p = 0.001
0.04–0.49	3 (16.6%)	1 (5.6%)	14 (77.8%)	
>0.50	7 (31.8%)	12 (54.5%)	3 (13.7%)	
CRP				
<0.5	0 (0%)	5 (15.6%)	27 (84.4%)	χ^2 = 19.893, df = 2, p = 0.000
>0.5	10 (35.8%)	9 (32.1%)	9 (32.1%)	
Uric acid				
2–7	9 (17.6%)	10 (19.6%)	32 (62.8%)	χ^2 = 8.489, df = 2, p = 0.012
>7	1 (11.2%)	4 (44.4%)	4 (44.4%)	
TNF-α				
<0.075	2 (5%)	7 (17.5%)	31 (77.5%)	χ^2 = 28.737, df = 2, p = 0.009
>0.075	8 (40%)	7 (35%)	5 (25%)	
CK-MB				
<20	5 (55.6%)	3 (37.5%)	20 (46.5%)	χ^2 = 556, df = 2, p = 0.757
>20	4 (44.4%)	5 (62.5%)	23 (53.5%)	

was statistically significant (p-value = 0.008). The patients with raised troponin values had NYHA III (50%) and NYHA IV (40.9%) whereas all patients who had normal troponin group had NYHA II (100%) which was significant (p = 0.000). Out of 22 patients with raised troponin values, 15 (68.18%) had EF of 40–60% whereas in the normal troponin group 19 out of 20 patients had EF >60% which was highly significant (p = 0.001).

Out of 22 patients with raised troponin group, 17 (77.3%) had a longer duration of stay when compared to 14 out of 20 (70%) patients with normal troponin values had a shorter duration of stay, p = 0.007. The median (IQR) value of CRP in the study group was 0.5 mg/dl (0–1.24 mg/dl) which is above the normal reference range of 0–0.5 mg/dl. 8 out of 9 patients who died had a raised CRP value with mean value being 4.972 which was highly significant (p-value <0.001). The patients with CRP of higher values had 50% NYHA III and 39.3% NYHA IV, whereas patients in the normal CRP group had 96.9% NYHA II, which is

Table 3 – Univariate analysis between biomarkers and NYHA class.

	NYHA class			
	II	III	IV	
BNP				
<100	26 (96.3%)	1 (3.7%)	0 (0%)	χ^2 = 33.766, df = 2, p = 0.000
>100	8 (24.2%)	14 (42.4%)	11 (33.3%)	
Troponin-I				
0–0.03	20 (100.0%)	0 (0%)	0 (0%)	χ^2 = 39.454, df = 2, p = 0.000
0.04–0.49	12 (66.7%)	4 (22.2%)	2 (11.1%)	
>0.50	2 (9.1%)	11 (50.0%)	9 (40.9%)	
CRP				
<0.5	31 (96.9%)	1 (3.1%)	0 (0%)	χ^2 = 50.119, df = 2, p = 0.000
>0.5	3 (10.7%)	14 (50.0%)	11 (39.3%)	
Uric acid				
2–7	34 (66.7%)	10 (19.6%)	7 (13.7%)	χ^2 = 15.126, df = 2, p = 0.000
>7	0 (0%)	5 (55.6%)	4 (44.4%)	
TNF-α				
<0.075	31 (77.5%)	9 (22.5%)	0 (0%)	χ^2 = 32.308, df = 2, p = 0.000
>0.075	3 (15.0%)	6 (30.0%)	11 (55.0%)	
CK-MB				
<20	15 (44.1%)	8 (53.8%)	5 (45.5%)	χ^2 = 363, df = 2, p = 0.834
>20	19 (55.9%)	7 (46.7%)	6 (54.5%)	

Table 5 – Univariate analysis between biomarkers and duration of stay in the hospital.

	Duration of stay		
	<6 days	>6 days	
BNP			
<100	19 (70.4%)	8 (29.6%)	χ^2 = 9.547, df = 1, p = 0.002
>100	10 (30.3%)	23 (69.7%)	
Troponin-I			
0–0.03	14 (70.0%)	6 (30.0%)	χ^2 = 9.914, df = 2, p = 0.007
0.04–0.49	10 (55.6%)	8 (44.4%)	
>0.50	5 (22.7%)	17 (77.3%)	
CRP			
<0.5	20 (62.5%)	12 (37.5%)	χ^2 = 5.511, df = 1, p = 0.019
>0.5	9 (32.1%)	19 (67.9%)	
TNF-α			
<0.075	24 (60.0%)	16 (40.0%)	χ^2 = 0.834, df = 1, p = 0.035
>0.075	3 (15.0%)	17 (85.0%)	
CK-MB			
<20	13 (44.8%)	15 (48.4%)	χ^2 = 0.076, df = 1, p = 0.782
>20	16 (55.2%)	16 (51.6%)	

Table 6 – Multivariate analysis of mortality as biomarkers as predictors.

Variables	β coefficient	S.E.	Wald	p-value	OR (95% CI)
Model 1					
BNP	.154	2.065	.006	.941	1.166 (0.02–66.75)
Gender	−1.718	1.468	1.369	.242	.179 (0.01–3.19)
Age	−.006	.058	.011	.917	.994 (0.89–1.11)
Diabetes	−.945	1.328	.507	.476	.389 (0.03–5.24)
Hypertension	−1.581	1.397	1.280	.258	.206 (0.01–3.18)
Troponin	.784	1.375	.325	.569	2.189 (0.15–32.41)
CRP	−.561	2.276	.061	.805	0.571 (0.007–49.35)
Uric acid	3.527	1.760	4.017	.045	34.015 (1.08–1070.06)
TNF	1.853	1.677	1.222	.269	6.380 (0.24–170.63)
Constant	.289	2.900	.010	.921	1.335
Model 2					
BNP	.011	1.789	.000	.995	1.011 (0.03–33.72)
Troponin	.306	1.244	.060	.806	1.358 (0.119–15.55)
CRP	−1.529	2.175	.494	.482	0.217 (0.003–15.40)
Uric acid	2.542	1.250	4.139	.042	12.710 (1.09–147.18)
TNF	2.887	1.504	3.684	.055	17.935 (0.94–341.84)
Constant	−1.651	1.126	2.152	.142	0.192

Model 1 summary: R^2 (Cox and Snell) = 0.370, p-value = 0.002; Model 2 summary: R^2 (Cox and Snell) = 0.302, p-value = 0.001. Results of multivariate analysis of association between mortality and biomarkers those found significant in the univariate analysis. Multivariate logistic regression analysis showed only uric acid (adjusted OR = 34.01, 95% CI = 1.08–1070.05, p-value = 0.045) as the significant predictor while taking age, gender, diabetes, and hypertension as the confounders. Also uric acid remained significant predictor after leaving confounders and rerun the logistic regression (Table 6). The odds of uric acid biomarker with 2–7 will be 12.7 times those of with >7.

significant (p = 0.000). Out of 28 patients with raised CRP values, 10 (35.8%) had EF <40% whereas in the normal CRP group 27 out of 32 patients (84.4%) had EF >50%. Out of 28 patients with raised CRP values, 19 (67.9%) had a longer duration of stay whereas 20 out of 32 patients with normal CRP values had a shorter duration of stay, p = 0.019. The mean (SD)

value of uric acid was 6.02 mg/dl (1.23 mg/dl) which was in the normal range of 2–7 mg/dl. Out of 9 patients who died, 5 patients had high uric acid which was statistically significant (p = 0.002). Out of 9 patients with raised uric acid levels, 5 (55.6%) had NYHA III and 4 (44.4%) had NYHA IV whereas 34 out of 51 patients in the normal uric acid range had NYHA II which

Table 7 – Biomarkers as predictors for duration of stay in the hospital using multivariate logistic regression.

Variables	B	S.E.	Wald	Sig.	OR (95% CI)
Model 1					
Gender	−.578	.681	.720	.396	0.561 (15–2.13)
Age	−.012	.022	.292	.589	0.988 (0.95–1.03)
Diabetes	1.148	.928	1.530	.216	3.151 (0.51–19.41)
Hypertension	−.181	.804	.050	.822	0.835 (0.17–4.04)
BNP1	−1.757	.901	3.800	.051	0.173 (0.03–1.01)
Troponin	−3.217	1.358	5.614	.018	0.040 (0.003–0.57)
CRP	−.149	1.183	.016	.900	0.862 (0.08–8.76)
Uric acid	2.412	1.128	4.574	.032	11.157 (1.22–101.76)
TNF	1.782	1.300	1.880	.170	5.942 (0.46–75.90)
Constant	.387	1.488	.068	.795	1.473
Model 2					
BNP	−1.695	.846	4.016	.045	0.184 (0.035–0.96)
Troponin	−2.932	1.233	5.655	.017	0.053 (0.005–0.59)
CRP	−.107	1.082	.010	.921	0.898 (0.11–0.83)
Uric acid	2.135	1.052	4.117	.042	8.453 (1.07–7.49)
TNF	1.499	1.128	1.766	.184	4.478 (0.49–66.45)
Constant	−.261	.849	.094	.759	0.770

Model 1 summary: R^2 (Cox and Snell) = 0.323, p-value = 0.009; Model 2 summary: R^2 (Cox and Snell) = 0.294, p-value = 0.002. Results of multivariate analysis of association between duration of stay and biomarkers those found significant in the univariate analysis. Multivariate logistic regression analysis showed that troponin and uric were the significant predictors while taking age, gender, diabetes and hypertension as the confounders. Also uric acid and troponin remained significant predictors including BNP after leaving confounders and rerun the logistic regression (Table 7).

is significant (p = 0.000). Out of 9 patients who had higher uric acid levels, 4 patients had EF >50% and 4 patients had EF 40–50%. Whereas 32 out of 51 patients had EF >50%, who were in the normal uric acid range. The median (IQR) value of TNF-α was 0.034 pg/ml (0.012–0.798 pg/ml) which was significantly above the cut-off value of 3 pg/ml. There were 8 out of 9 patients, who died and had a raised TNF value, and the mean value in the non-survivors was 2091.87 pg/ml, which was significantly higher (p = 0.000). Of 20 patients with raised TNF values, 11 patients had NYHA IV and 6 had NYHA III whereas 31 out of 40 (77.5%), who had normal TNF values had NYHA II, which is significant (p = 0.000). Out of 20 patients with raised TNF group, 7 (35%) had EF of 40–50% and 8 (40%) had EF <40% when compared to the normal TNF group in which 31 out of 40 patients had EF >50%. On comparing BNP with TNF, out of 20 patients with raised TNF values, 17 (85%) had BNP >100 pg/ml which was significant, p = 0.001. The median (IQR) value of CK-MB was 22 U/I (18–27.5 U/I), reference range being >20 U/I. There was no significant association between CK-MB and mortality.

5. Discussion (Tables 3–5)

In this study, out of the 60 patients studied, there were 9 deaths, i.e., 15% mortality rate was prevalent in our hospital amongst the heart failure patients.

In this study, a large percentage of patients with heart failure were due to hypertensive heart disease (37%), second being dilated cardiomyopathy (25%), third being ischemic cardiomyopathy (18%), fourth being CKD (13%), and last being valvular/rheumatic heart disease (7%).

5.1. BNP and mortality and morbidity

The mean BNP value was 444.44 pg/ml in our study, which was in concordance with most of the studies, which showed BNP value in the range of 160–1676 pg/ml.

In our study, out of 27 patients with BNP value of 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%), which shows that there is higher death rate with higher values of BNP (p = 0.027). The mean value of BNP in non-survivors was 1486.2 pg/ml, whereas the mean value of BNP in survivors was 260.6 pg/ml.

In the Italian RED study, out of 247 patients with CHF, 7 deaths occurred with a mean BNP value of 820 pg/ml,[6] when compared to our study, which showed a mean value of 1486.2 pg/ml in the patients whose end-point was death which is significant.

Out of the 33 patients with BNP more than 100 pg/ml, 14 patients (42.4%) had breathlessness of NYHA III and 11 patients (33.3%) had breathlessness of NYHA IV.

Patients with BNP less than 100 pg/ml had predominant breathlessness of NYHA II of 96.3%. p = 0.000, which is again significant.

In the Italian RED study, out of 247 patients, 33% were in NYHA III and 67% were in NYHA IV. No candidates of NYHA II were included in that study and hence the significance reduces, as the comparative figures are not available.[6]

Also, BNP was significantly higher (84.8%) in patients with EF of less than 60%, of which 24.2% had EF <40% and 60.6% had EF 40–60%, which was in concordance with the study done by Dao et al., which showed 51% higher rate of BNP in LVEF of less than 55%.[7]

Another significant finding was that in the group of BNP more than 100 pg/ml, 23 patients had a in-hospital stay of more than 6 days (69.7%) in comparison to the group of BNP value of less than 100 pg/ml, where the in-hospital stay was less than 6 days, p = 0.002.

Thus, in our study there has been a significant relation between the in-hospital stay, mortality, NYHA grading, EF on echocardiography, and BNP.

5.2. Troponin-I and mortality and morbidity

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, with significance of p = 0.013. The mean value of troponin-I in the patients, who dies was 2.03 ng/ml, whereas the mean value of troponin-I in survivors was 0.61 ng/ml. Peacock et al. have stated in a study that troponin-raised patients had a higher rate of in-hospital mortality than troponin-negative patients (8.0% vs. 2.7%, $p < 0.001$).[8]

In our study, out of the 60 patients 20 patients had negative troponin values and all of them were in NYHA class II, and out of the remaining 40 patients, 22 patients had troponin range >0.5 ng/ml, out of which 11 were in NYHA class III and 9 were in NYHA class IV with significance of p = 0.000.

Whereas, a study done by Horwich et al. did not show significance of troponin-I in NYHA grading, with 41% with <0.04 ng/ml of troponin and 59% with >0.04 ng/ml with p = 0.056.[9]

In a study by Biolo et al., the mean EF in acute heart failure patients was 24%.[10]

In our study only 20% of patients with raised troponin values had past history of an acute coronary event. Hence the possibility of a bias due to the acute coronary event is lesser.

In our study, the positivity (90.9%) of troponin was very high in patients with EF <50% of which, 31.8% had EF <40% and in the negative troponin value group, 20 patients (75%) had EF >50%. This clearly shows the importance of troponin-I in heart failure as the p value = 0.000. Hence it is a prognostic marker and not a diagnostic marker.

5.3. CK-MB and mortality

When correlated with death, EF, duration of stay, and NYHA class, there was no significance in the values of CK-MB.

5.4. C-reactive protein

The mean CRP value of the patients, who died was 4.97 mg/dl, which was significantly above the normal range. CRP was also strongly related to the NYHA class. With raised CRP values, the patients were likely to be in NYHA class III and IV when compared to the negative CRP group. In a study by Alonso-Martínez et al., the mean CRP value was 9.35 mg/dl which is

higher than in our study.[11] A study by Suleiman et al., also showed that CRP levels increased with the grading of breathlessness with $p = 0.001$.[12]

5.5. Gamma glutamyl transferase

In our study the mean value of GGT was 34 U/l, which was not significant.

Also, on cross tabulation there was no significance in GGT titers and mortality, NYHA, and EF. Whereas, in a study by Dhingra et al., cumulative incidence curves demonstrated a greater risk of new-onset heart failure among individuals with a serum GGT concentration at or greater than the median compared with those with levels less than the median ($p < 0.001$, log-rank test), which is not corresponding to our study.[13]

5.6. Uric acid

In our study, the mean value of uric acid was 6.023 mg/dl, which is in the normal range of 2–7 mg/dl. In a study by Anker et al., the best cut-off value for predicting mortality was 9.5 mg/dl, which is much higher, when compared to our study.[14] No significant univariate correlation emerged between serum uric acid and left ventricular EF.

5.7. Tumor necrosis factor-α

The mean value of TNF-α in our study was 550 pg/ml. This was a significantly high titer. 55% of the patients with raised TNF titers were in NYHA class IV when compared to 77.5% of patients with negative titers who were in NYHA class II, $p = 0.000$. Also, our study showed higher percentage (85%) of patients with raised titers of TNF with EF <60%, of which 50% of the patients had EF of 40–60% and 35% of them had EF <40%, $p = 0.009$. In a study by Bradham et al., the LVEF mean value was around 22% in patients with raised TNF titers and heart failure.[15]

However, there was no significant correlation between TNF titers and the duration of in-hospital stay in our study, $p = 0.361$. In a study by Dunlay et al., the death rate was 30.2% in comparison to TNF, which was in concordance to our study. No association was found between TNF-α and NYHA functional class in the study by Dunlay et al.[16]

6. Conclusion

The main conclusions from this study are:

- BNP is an established and an excellent predictor of mortality and morbidity in heart failure.
- TNF-α has also been a very good predictor of mortality and morbidity with significant correlation with BNP.
- Troponin-I and CRP have also shown significance in predicting the outcome in heart failure but not as much as BNP and TNF-α.
- GGT, uric acid, and CK-MB play no role in predicting the severity and outcome in heart failure in our study.

Though BNP has already been established as a biomarker for measuring the progress of a patient after regular treatment, the other biomarkers such as troponin-I and CRP, which have been studied here, which are of lower cost can also be used to quantify the response of the treatment given in patients with heart failure.

6.1. Limitations of this study

This was a single center study with a small sample size; but this can be a pilot study for future large-scale multicentric studies.

6.2. Strengths of this study

Many cardiac biomarkers were compared with the outcome in this study. There are no previous studies from this part of the country; multicentric studies might bring out any genetic factors, which might affect the outcome.

Conflicts of interest

The authors have none to declare.

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