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Study of aetiology, clinical profile and B-type natriuretic peptide levels in heart failure with preserved and reduced ejection fraction

Dr. Sunil Kumar
Associate Professor, Department of General medicine, SBKS MIRC, Sumandeep Vidyapeeth, Vadodara

Dr. Jeevana Sudha Ande
Resident, Department of General medicine, SBKS MIRC, Sumandeep Vidyapeeth, Vadodara

Dr. Vidhi Shah
Resident, Department of General medicine, SBKS MIRC, Sumandeep Vidyapeeth, Vadodara
Corresponding author email: vidhi282615@gmail.com

Dr. Shaival Trivedi
Associate Professor, Department of general medicine, SBKS MIRC, Vadodara

***Abstract*---**Since from the last one decade, new cardiac biomarkers specifically BNP levels are being used widely as a marker of diagnosis, severity and prognosis of HF. A Cross Sectional Study was conducted at Department Of General Medicine, Dhiraj Hospital, Sbks MIRC, Pipariya, Vadodara with a sample size of 70. A total of 70 patients with heart failure were studied and found that 41 (58.57%) patients had reduced ejection fraction and 29 (41.43%) patients had preserved ejection fraction. In our study majority of the patients were found in NYHA Grade IV (37.14). The mean BNP levels of the whole study group is 1148.73±876.61. The mean level of BNP in HFpEF is 905.28± 823.73 and in HFrEF is 1320.93 ± 881.60. There was statistically significant difference was observed in between the two groups (p value P = 0.0499). In our present study the BNP levels are increasing with increasing NYHA severity of breathlessness (p= 0.0113). The study showed as the severity of NYHA grading increases the BNP levels increase. BNP levels tend to increase more in hypertensive patients as compared to non hypertensive patients. Although BNP levels increase in both the groups, HFrEF showed more increase in BNP levels as compared to HFpEF and a statistically significant difference was found in between the two groups. The study can reveal that higher the

BNP levels there will be higher risk of morbidity and mortality in heart failure patients.

***Keywords*---**aetiology, clinical profile, B-type natriuretic peptide levels, heart failure.

Introduction

Heart failure is a growing epidemic and one of the leading causes of hospitalisation and death throughout the world. The current American College of Cardiology Foundation (ACCF) /American Heart Association (AHA) guidelines define Heart Failure as a complex clinical syndrome that results from structural or functional impairment of ventricular filling or ejection of blood, which in turn leads to the cardinal clinical symptoms of dyspnea and fatigue and signs of HF, namely oedema and rales[1]. To date, HF is classified as systolic and diastolic but non-invasive methods including Doppler echocardiography cannot provide unequivocal evidence of LV diastolic dysfunction. [2,3,4]

Currently, the diagnosis of HF is made primarily on the basis of symptoms, normal or minimally impaired systolic function and exclusion criteria.Recently ESC guidelines have provided classification based on EF. According to it, now HF is classified as HFpEF (EF>50%), HFmrEF(40-49%), HFrEF(<40%). HFpEF & HFrEF tend to occur in different patient populations. Furthermore, they respond differently to therapies like ARB and ACEIs.[5,6] Because the signs and symptoms of HF are nonspecific and many times could not be able to differentiate between HFrEF & HFpEF. Even echocardiography may fail to give objective parameters for severity and prognosis of HF. So from the last one decade, new cardiac biomarkers specifically BNP levels are being used widely as a marker of diagnosis, severity and prognosis of HF. [7,8,9,10]

Materials and Methods

A cross-sectional study of 70 patients was done in the department of general medicine at Dhiraj hospital, Vadodara. All participants included in this study underwent complete history taking including symptoms of present illness, co-morbidities, details of causes, risk factors, past history, personal history, and drug history and were subjected to complete examination and all the positive findings of examination will be noted and patients were graded based on severity grading of heart failure according to NYHA classification. Routine investigations like CBC, RFT, LFT, serum electrolytes, urine routine and microscopy, ECG, chest X-ray, 2D Echo, and BNP levels were done. The findings in 2D Echo like EF, RWMA, diastolic dysfunction, PAH, and IVC were noted. BNP levels were measured. The patient was followed up daily till the outcome of up to a maximum of 7 days for clinical status of CCF, primary aetiology, biochemical profile, and ECG. The details of treatment modalities were also noted. The outcome of the patient was noted on the day of discharge or death.

Results

In the present study, 70 patients who were diagnosed with heart failure reduced and preserved ejection fraction were studied based on their aetiology, clinical features and BNP levels.The mean age of the whole study group was 55.5±12.93 years. The mean age of heart failure with preserved ejection fraction and reduced ejection fraction was 56.3+13.88 and 55.12+12.38 respectively. The mean age of male and female patients was 57.54 + 9.87 years and 53.21 + 15.52 years, respectively. The majority of the patients were above the age of 50 years.

Table 1: Distribution according to ejection fraction

Ejection Fraction	No Of Cases (n)	Percentage(%)
Preserved (>=50)	29	41.43
Reduced (<=40)	41	58.57
Grand Total	70	100.00

Out of 70 patients, Males were 37 (52.86%) and Females were 33 (47.14%). Male patients outnumbered female patients. Male: Female ratio was found to be 1.12:1. In the present study 41(58.57%) patients had reduced ejection fraction and 29 (41.43%) patients had preserved ejection fraction. All the patients in this study presented with breathlessness (100%) , followed by Pedal oedema (65.71%), PND (55.71%) ,Easy fatiguability (50.00%), Orthopnoea (45.71%), palpitations (38.57%) , chest pain(37.14%) , cough(32.86%) , abdominal pain(12.86%), syncope (8.57%) and other symptoms(4.28%). Amongst patients with preserved ejection fraction, the majority of the patients were among Grade III NYHA (44.82%) followed by NYHA II (34.48), and NYHA IV (20.68). Among patients with reduced ejection fraction majority of the patients were observed in NYHA IV(48.78%), followed by NYHA III(25.53%), and II(21.95%).

The most frequent finding in ECG was LAFB (20.00%) followed by LVH (18.57%). other findings were atrial fibrillation (14.29%), anterior wall MI (12.86%), sinus tachycardia (7.14%), bi-fascicular block (5.71%), P mitrale (5.71%), LV strain was seen in (5.71%). Other less common findings were tri-fascicular block, ventricular tachycardia, ventricular bigeminy, RBBB, and Atrial fibrillation with VPC each contributed (1.43%) and IWMI, new onset LBBB (2.86%). The ECG was normal at 4.29 %.

Basal crepitations were seen in almost 88.57% of the subjects. Raised JVP was seen in 81.43%. Pallor and Pedal edema was present in 68.57%, and hepatomegaly in 18.57%, MR murmur was present in 22.86%, third heart sound (S3) heard in 12.86%. Basal crepitations were seen in 82.75% of the patients with HFpEF and 92.68% of patients in HFrEF. Raised JVP was seen in 95.12% in HFrEF and 62.06% of patients with HFpEF. Pallor was of 58.62% in HFpEF and 75.60% in HFrEF. Pedal edema was present in 65.51% of patients with HFpEF and 70.73% in HFrEF. Hepatomegaly in 6.89 % in HFpEF and 26.82% in HFrEF. S3 was present in 0 % patients in HFpEF and 21.95% in HFrEF. MR Murmur was seen in 6.89% and 34.14% of patients of HFpEF and HFeEF respectively.

HFpEF pulmonary oedema was most commonly seen (44.82%), followed by pulmonary plethora (27.58%), pleural effusion (13.79%), No abnormality was detected (13.79%), and no patient had cardiomegaly. In HFrEF cardiomegaly was seen in (43.90%), pulmonary oedema was seen in (26.82%), pleural effusion and no abnormality were detected in (12.19%), and pulmonary plethora was seen in (4.87%).

In HFpEF 12 patients had BNP levels >700, 7 patients had BNP levels between 301-700, 10 patients had BNP levels 101-300, 0 patients had BNP levels <100. In HFrEF 33 patients had BNP levels >700, 8 patients had BNP levels between 301-700, 0 patients had BNP levels 101-300, 0 patients had BNP levels <100. The difference between BNP levels in the two groups is statistically significant (p-value-0.0001).

Table 2: BNP levels in HFpEF and HFrEF

BNP LEVEL (Pg/Ml)	Preserved (>=50)	PERCENTAGE (%)	Reduced (<=40)	PERCENTAGE (%)
<=100	0	0.00	0	0.00
101-300	10	34.48	0	0.00
301-700	7	24.14	8	19.51
>700	12	41.38	33	80.49
TOTAL	29	100.00	41	100.00

P = 0.0001

Table 2 shows the distribution of BNP levels in both study groups. In HFpEF 12 patients had BNP levels >700, 7 patients had BNP levels between 301-700, 10 patients had BNP levels 101-300, 0 patients had BNP levels <100. In HFrEF 33 patients had BNP levels >700, 8 patients had BNP levels between 301-700, 0 patients had BNP levels 101-300, 0 patients had BNP levels <100. The difference between BNP levels in the two groups is statistically significant (p value-0.0001) The patients with NYHA grade IV had >700 BNP levels in 31.42% of patients, 301-700 in 5.71% of patients, 101-300 in 0% of patients, no patient had BNP levels below 100. In patients with NYHA III , 22.85% of patients had > 700 BNP levels, 5.71% had BNP levels of 301-700, 7.14% of patients had BNP levels of 101-300, 0% of patients had BNP levels below 100. In patients with NYHA II 10% of patients had BNP levels >700, 10% of patients had BNP levels between 301-700, 7.14% of patients had BNP levels of 101-300, 0% of patients had BNP of <100. No patients were found in NYHA grade I. This demonstrates that with increasing grade of NYHA grading of breathlessness the BNP levels also increase with a significant p value of 0.0113.

Table 3: Comparison of characteristics of HFPEF and HFREF

Characteristics	n=41	n=29	p value
	HFrEF	HFpEF	
Age	55.12 ±12.38	56.03 ±13.88	0.7742

Male	23	14	0.9024
Female	18	15	0.9220
SBP	107.7 ±21.55	158.48 ±37.47	0.0001
DBP	68.35 ±13.78	93.1 ±16.71	0.0001
BMI	22.24 ±1.87	25.13 ±2.74	0.0001
Orthopnoea	22	10	0.5319
PND	29	10	0.0981
Edema	28	18	0.9079
Cough	17	6	0.6771
Fatigability	19	16	0.8562
Palpitations	17	10	0.9605
Chest pain	18	8	0.7252
Pallor	31	17	0.3704
Pedal edema	29	19	0.9502
JVP/HJR	39	18	0.0047
S3	9	0	N.A.
Hepatomegaly	11	2	0.7688
MR Murmur	14	2	0.9698
Crepts	38	24	0.4270
Smoking	12	4	0.9623
Alcohol	6	2	0.3463
SPO2			
Normal	25	20	0.8079
VENT	4	1	0.0715
BIPAP	3	4	0.3426
NP	9	4	0.6773
DMII	10	8	0.6982
HTN (known comorbidity)	9	23	0.0089
IHD (cause)	28	4	0.1221
RHD	4	4	0.0715
DCMP	5	0	N.A.
COPD	2	0	N.A.

Characteristics	n=41	n=29	p value
Tachyarrhthmias	4	4	0.3575
Thyroid Dysfunction	5	4	0.352
Hyperlipidemia	2	9	0.8981
CVA	4	1	0.0715
NYHA III	12	13	0.6967
NYHA IV	20	6	0.4530
Potassium	3.99 ±0.43	4.05 ±0.37	0.5449

SGOT	44.15 ±24.2	43.34 ±20.52	0.8838
SGPT	48.76 ±28.55	46.38 ±26.53	0.7247
LFT	1.23 ±0.64	1.05 ±0.41	0.1873
Sodium	135.02 ±4.44	135.41 ±4.36	0.7165
HB	10.87 ±2	10.39 ±1.17	0.2508
BNP	905.28 ±823.73	1320.93 ±881.6	0.0499
Pulmonary edema	11	13	0.9112
Cardiomegaly	18	0	N.A.
Ejection fraction	41	29	N.A.
Sinus tachycardia	2	3	0.1473
LVH	0	13	N.A.
RBBB	1	0	N.A.
LAFB	13	1	0.5895
Ventricular trigemini	0	0	N.A.
Ventricular tachycardia	0	1	N.A.
Ventricular bigemini	1	0	N.A.
Bifasccular block	4	0	N.A.
Trifascicular block	1	0	N.A.
Atrial fibrillation	6	4	0.3762
Deaths	6	3	0.3869
Recovery	35	26	0.9136

Discussion

A total of 70 patients with heart failure were studied and found that 41(58.57%) patients had reduced ejection fraction and 29 (41.43%) patients had preserved ejection fraction. Among 70 patients diagnosed with heart failure Males were 37 (52.86%) and Females were 33 (47.14%). The mean age of the whole study group was 55.5+12.93 years. All the patients in this study presented with breathlessness (100%) , followed by Pedal edema (65.71%), PND (55.71%) ,Easy fatigability (50.00%), Orthopnoea (45.71%), palpitations (38.57%) , chest pain(37.14%) , cough(32.86%) , abdominal pain(12.86%), syncope (8.57%) and other symptoms(4.28%). However the differences in signs and symptoms were not statistically significant except for JVP ($p< 0.0047$). In our study majority of the patients were found in NYHA Grade IV (37.14%), followed by Grade III(35.71%), Grade II (27.14%).

The most common ECG finding of the study was LAFB (20.00%). The most common arrhythmia was atrial fibrillation (14.29%). In most of the patients The most common x ray finding in our study was Pulmonary edema (34.29%). In HFrEF most common abnormality detected was Cardiomegaly (43.90%). Pulmonary edema was seen more commonly in HFpEF group (44.82%) than HFrEF(26.82%). The most common cause of heart failure in the present study was Coronary artery disease (ischemic DCMP and IHD) (45.71%), Hypertensive heart disease (28.57%), Tachyarrhythmias (11.43%), Rheumatic heart disease

(7.14%), DCMP (7.14%). In our present study, in HFrEF CAD (ischemic DCMP and IHD) was the most common cause (68.29%), in HFpEF hypertension was the most common cause (68.96%).

In our present study majority of the patients were hypertensives (79.31%) in HFpEF as compared to HFrEF hypertension was seen in (21.95%). In the present study group, 47(67.14%) patients were admitted in ICU and 23 (32.86%) were admitted in ward. In our present study 45 patients (64.29%) were on room air, 13(18.57%) patients needed nasal prongs, 12 patients (17.14%) needed ventillatory support. In the present study 9 deaths were seen due to heart failure and 61 recoveries were seen.

The mean BNP levels of the whole study group is 1148.73±876.61. The mean level of BNP in HFpEF is 905.28± 823.73 and in HFrEF is 1320.93 ± 881.60. There was statistically significant difference was observed in between the two groups (p value P = 0.0499). In our present study the BNP levels are increasing with increasing NYHA severity of breathlessness (p= 0.0113). When BNP levels were compared with hypertensives and non hypertensives, significance was observed in between the two groups with a p value of P = 0.0009. In our present study all the nine deaths were seen in BNP levels>700, correlating with higher risk of mortality with higher BNP levels.

Although BNP levels could not differentiate between heart failure reduced and preserved ejection fraction, a low BNP level in the setting of normal systolic function by echocardiography can rule out clinically significant diastolic dysfunction seen on echo. In a study by Maisel AS et al [7] described BNP levels are higher in patients with reduced ejection fraction when compared with preserved ejection fraction , more possibly reflecting an association with greater pathology (remodeling, fibrosis) in patients presenting with reduced ejection fraction , as reflected by their higher NYHA classifications which is correlating with our study, reduced ejection fraction group had higher BNP levels compared to preserved group. So from this study we can draw an attention that BNP levels may not able to able to differentiate in between heart failure reduced and preserved ejection fraction but BNP levels can differentiate patients with heart failure and without heart failure. BNP levels correlate with severity of heart failure.

Conclusion

The BNP levels can diagnose heart failure and they correlate with severity of NYHA grading. BNP levels tend to increase more in hypertensive patients as compared to non hypertensive patients. Although BNP levels increase in both the groups and could not differentiate between the both groups, HFrEF showed more increase in BNP levels as compared to HFpEF and a statistically significant difference was found in between the two groups. The study shows that higher the BNP levels there will be higher risk of morbidity and mortality in patients.

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