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STUDY OF CLINICAL PROFILE AND DIFFERENTIATING SYSTOLIC AND DIASTOLIC HEART FAILURE BY ECHOCARDIOGRAPHY

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ABSTRACT

BACKGROUND

Heart failure is a complex clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood. The primary manifestation of heart failure is dyspnoea and fatigue which leads to exercise intolerance and fluid overload which can result in pulmonary congestion and peripheral oedema. Signs and symptoms of heart failure have been classified as being due to left ventricular failure (LVF) or right ventricular failure (RVF). Although most patient initially have LVF, both ventricles eventually fail and contribute to heart failure. The aim of the current study is to evaluate the clinical profile and differentiate systolic and diastolic heart failure. We wanted to study the clinical profile of heart failure patients and identify systolic and diastolic heart failure among those patients using echocardiography.

METHODS

Total 120 patients aged more than 18 years and who gave informed consent, satisfying Framingham criteria for heart failure were included. Relevant history was collected, and thorough clinical examination was done. Non-invasive modalities like 2D echocardiography was used to assess diastolic dysfunction. Appropriate investigations were rendered, and statistical analysis done using SPSS software version 22.0. Chi-square test of Fischer's exact test (for 2 x 2 tables only) was used as a test of significance for qualitative data.

RESULTS

The parameters showed that majority of heart failure patients are males between age group of 51-75 years. Hypertension was the most common comorbidity in these patients. 50.8% of heart failure patients had reduced EF and 40.8% were with preserved EF. 63.26% of the preserved EF patients were females. Presence of anaemia is statistically significant ($p < 0.001$). Statistically significant association was present between coronary artery disease ($P < 0.001$) and reduced EF in our study. Hypertension (67.3%) was most common in patients with preserved EF. No significant association was found with symptoms and signs in heart failure with preserved and heart failure with reduced EF.

CONCLUSIONS

This study of clinical profiles reaffirms the value of clinical assessment in daily practice which includes chronic HF. Clinical profiles are easy to define, predict prognosis, and appear to do so better than traditional markers of disease severity. These profiles may be useful to guide therapy as the treatment modality differs between patients of reduced and preserved EF.

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BACKGROUND

Cardiovascular diseases (CVD) are the leading cause of mortality and morbidity in both developed and developing countries. Increasing life expectancy and better health care have caused heart failure (HF) to be a major public health issue, especially in older adults. India is home to 16% of global population, 25% of the world's coronary artery

disease (CAD) burden, 120 million hypertensives, and a large number of individuals with Rheumatic heart disease (RHD). CVD will be the leading cause of morbidity and mortality in India by 2020.^{1,2}

Heart Failure(HF) is defined, clinically, as a syndrome in which patients have typical symptoms (e.g. breathlessness, ankle swelling, and fatigue) and signs (e.g. elevated jugular venous pressure, pulmonary crackles, and displaced apex beat) resulting from an abnormality of cardiac structure or function.³ HF is not a single entity, but a clinical syndrome that may have different characteristics depending on age, sex, race or ethnicity, left ventricular ejection fraction (LVEF) status, and HF aetiology. Pathophysiological differences are observed among patients diagnosed with HF and reduced LVEF compared with HF and preserved LVEF.⁴ The diagnosis of HF can be difficult. Many of the symptoms of HF are non-discriminating and, therefore, of limited diagnostic value.⁵

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Echocardiography plays a vital role in diagnosis of patients with heart failure, in part because the physical examination, electrocardiogram, and chest radiograph do not provide information that distinguishes diastolic from systolic heart failure.⁶

Aims and Objectives

- To study the clinical profile of heart failure patients.
- To identify systolic and diastolic heart failure among those patients by Echocardiography.

METHODS

Source of Data

A total of 120 patients admitted to Patients admitted to Sri R. L. Jalappa Hospital and RLJH Narayana Heart Centre satisfying Framingham Criteria for diagnosis of heart failure were included in the study. Study was carried out from January 2015 to August 2016.

Framingham Criteria for Diagnosis of Heart Failure

Major Criteria:

- 1) Paroxysmal nocturnal dyspnoea.
- 2) Jugular venous distention (or CVP >16 mmHg).
- 3) Rales or acute pulmonary oedema.
- 4) Cardiomegaly.
- 5) Hepatojugular reflex.
- 6) Response to diuretic (weight loss > 4.5 kg in 5 days).
- 7) S3 Gallop.

Minor Criteria:

- 1) Ankle oedema
- 2) Nocturnal cough
- 3) Exertional dyspnoea
- 4) Pleural effusion
- 5) Vital capacity 120 bpm)⁷

At least two major or one major with two minors should be present to fulfil the diagnosis of heart failure.

Inclusion Criteria

- 1) Patients aged more than 18 years.
- 2) Patients fulfilling Framingham diagnostic criteria for heart failure.

Exclusion Criteria

- 1) Patients aged less than 18 years.
- 2) Patients not fulfilling Framingham diagnostic criteria for heart failure.

Method of Collection of Data

Patient's complete history was taken from the patient or patient's attendees and explained about the study and informed written consent was taken. Patient was examined fully and appropriate investigations like Complete hemogram, Chest X-ray-Postero Anterior view, Renal function tests, Serum electrolytes, Blood sugar level, thyroid profile, 12 Lead Electrocardiogram, Echocardiography (to confirm systolic and diastolic dysfunction) were done.

The World Health Organization defines anaemia as haemoglobin < 13 gm% in males and < 12 gm% in females.⁸

Blood Pressure Grading According to JNC VII Classification

Normal -	<120/80 mm of Hg
Prehypertension	120-139/80-89 mm of Hg
Stage 1 HTN	140-159/90-99 mm of Hg
Stage 2 HTN	≥160/≥ 100 mm of Hg
Isolated systolic HTN	>140/<90 mm of HG

2D Echocardiography

The examination was performed while the patient was in a period of quiet respiration. All recordings performed included complete M-mode, 2-dimensional, and Doppler echocardiographic examinations, with emphasis on evaluation of LV diastolic and systolic function, LV size, and mass. Assessment of PV flow and E/A, E/e' during a Valsalva manoeuvre were done when necessary. A minimum of 10 to 15 beats was recorded for all 2- dimensional, M-mode, and Doppler parameters. Apical 2, 3, and 4 chamber views were obtained in all echocardiographic studies.

Assessment of Left Ventricular Diastolic Function

- 1) Early filling peak velocity (E),
- 2) Atrial filling peak velocity (A),
- 3) E/A ratio
- 4) Deceleration time (DT)
- 5) Isovolumic relaxation time (IVRT)
- 6) E/A ratio during Valsalva manoeuvre and
- 7) e'- Early diastolic myocardial velocities at mitral annulus
- 8) E/e' Left atrial volume index (LAVI) was calculated by the biplane area-length method from apical 2- and 4-chamber views indexed to body surface area.

Assessment of Left Ventricular Systolic Function-

For measurement of LVEF, the modified biplane Simpson's rule is recommended.

LV end diastolic volume (LVEDV) and LV end systolic volume (LVESV) are obtained from apical four- and two-chamber views.

The Simpson method can be used to obtain LV volumes and then the calculated ejection fraction (EF) by the following formula.

Ejection Fraction = End Diastolic Volume (EDV)- End Systolic Volume (ESV)/EDV

Statistical Analysis

Data was entered into Microsoft excel data sheet and was analysed using SPSS 22 version software. Categorical data

was represented in the form of Frequencies and proportions. Chi-square test of Fischer’s exact test (for 2 x 2 tables only) was used as test of significance for qualitative data. Graphical representation of data: MS Excel and MS word was used to obtain various types of graphs such as bar diagram, Pie diagram and Scatter plots. p value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Statistical Software

MS Excel, SPSS version 22 (IBM SPSS Statistics, Somers NY, USA) was used to analyse data. EPI Info (CDC Atlanta), Open Epi, MedCalc and Medley’s desktop were used to estimate sample size, odds ratio and reference management in the study.

RESULTS

GENDER	EF <40%	EF ≥ 50%
Males	43 (70.49%)	18 (36.73%)
females	18 (29.5%)	31(63.26%)

Table 1. Gender Distribution Among Heart Patients with EF <40% and EF ≥ 50%

Age	EF <40%	EF ≥ 50%
<50 years	19 (27.53%)	2 (4.10%)
51-75 years	39 (63.93%)	27 (55.10%)
>75 years	3 (4.98%)	20 (40.82%)

Table 2. Age Distribution Among Heart Patients with EF <40% and EF ≥ 50%

		Ejection Fraction			
		<40%		≥50%	
		Count	%	Count	%
Breathlessness	Grade I	5	8.1%	6	12.2%
	Grade II	17	27.9%	11	22.44%
	Grade III	23	37.8%	18	36.7%
	Grade IV	16	26.2%	11	22.44%
	No breathlessness	0	0%	3	6.1%
	Total	71	100.0%	49	100.0%

$\chi^2 = 10.502, df = 4, p = 0.033^*$

Table 3. Association Between Breathlessness Grade and Ejection Fraction Among Subjects with Heart Failure

		Ejection Fraction				P value
		<40%		≥ 50%		
		Count	%	Count	%	
Hypertension	Present	35	57.4%	33	67.3%	0.285
	Absent	26	42.6%	16	32.7%	
Coronary Artery Disease	Present	46	75.4%	11	22.4%	<0.001*
	Absent	15	24.6%	38	77.6%	
Diabetes Mellitus	Present	39	63.9%	29	59.2%	0.610
	Absent	22	36.1%	20	40.8%	
Atrial Fibrillation	Present	10	16.4%	11	22.44%	0.785
	Absent	51	83.6%	40	81.6%	
COPD	Present	21	34.4%	17	34.7%	0.977
	Absent	40	65.6%	32	65.3%	
Valvular heart diseases	Present	4	6.6%	7	14.3%	0.179
	Absent	57	93.4%	42	85.7%	

Table 4. Association Between Ejection Fraction and Comorbidities Among Subjects with Heart Failure

		Ejection Fraction				P value
		<40%		≥ 50%		
		Count	%	Count	%	
Hb%	Normal	26	42.6%	33	67.3%	0.01*
	Anemia	35	57.4%	16	32.7%	
TSH	Normal	54	88.6%	47	95.9%	0.185
	Hypothyroidism	5	8.2%	1	2.0%	
	Hyperthyroidism	2	3.2%	1	2.0%	

Table 5. Association Between Ejection Fraction and Hb% and TSH Among Subjects with Heart Failure

In subjects with EF <40%, 57.4% had anaemia and with EF ≥ 50%, 32.7% had anaemia. This observation was statistically significant.

		Ejection Fraction				P value
		<40%		≥ 50%		
		Count	%	Count	%	
Rhythm	Normal	2	3.3%	1	2.0%	0.297
	Sinus Tachycardia	49	80.3%	37	75.5%	
	Atrial fibrillation	10	16.4%	11	22.44%	
Chamber Size	LVH	48	78.69%	37	75.51%	<0.001*
	BVH	12	19.67%	5	10.20%	
	LAE	30	49.18%	10	20.41%	
	RAE	14	22.95%	1	2.04%	
	Normal	5	8.20%	11	22.45%	
Ischemia	Present	46	75.4%	11	22.4%	<0.001*
	Absent	15	24.6%	38	77.6%	

Table 6. Association Between Ejection Fraction and ECG Changes Among Subjects with Heart Failure

DISCUSSION

Heart failure is a common and a major health problem and its prevalence increases with age. Epidemiological studies have revealed that 1.5% to 2% population experience heart failure (HF) and it is the main reason for hospital admission of elderly patients.⁹ It has been estimated that the prevalence increases to 6% - 10% in patients over 65 years of age.^{10,11} The increasing mean life expectancy, together with improved survival rates in patients with other cardiovascular diseases and after myocardial infarction, is expected to result in a major increase in the prevalence of heart failure in the future.

Although the diagnosis of HF can be straightforward when the patient presents with a constellation of the classic signs and symptoms in the appropriate clinical setting, no sign or symptom alone can define the presence or severity of HF. Furthermore, the detection of diagnostic physical findings in HF is an imprecise science, often requiring other diagnostic tools. Because treatment strategies for treating HF are based on the differentiation of HFrEF and HFpEF, these distinctions are crucial.¹²

There are only a few Indian population-based studies comprehensively and prospectively assessing the demographic, clinical and prognostic characteristics of patients who are admitted with a clinical diagnosis of HF. Hence this study was undertaken to know the common clinical presentation and comorbidities precipitating HF. Differentiating HFrEF and HFpEF helps in assessing the prognosis and planning the appropriate treatment modality. In our study, a total of one twenty patients satisfying Framingham's criteria for heart failure were studied. 61.2% patients were between 50 and 75 years of age. 57.5% patients were males and 42.5% were females. Heart failure was more common in male patients. A study by Laxman Dubey showed that the incidence of heart failure increases with age.¹³ It is more common in age groups between 45 to

65 years which accounts most number of cases. This is also a similar observation in study by Okechukwu S et al.¹⁴

The results in our study group are consistent with the above-mentioned studies. Karl Swedberg and Joh Cleland et al. stated the clinical profile of HF mainly included breathlessness, ankle swelling and fatigue, peripheral oedema, raised JVP, hepatomegaly and characteristic signs of congestion of systemic veins.¹⁵

In present study, 117 (93.1%) patients presented with breathlessness, majority being grade III (34.2%) followed by grade IV (26.7%). An Indian population-based study by Roby A et al¹⁶ showed similar observation where the commonest presenting symptom was breathlessness (84.51%).

Next commonest symptom was cough with or without expectoration (50.8%) followed by chest pain (41.7%), palpitations (38.3%), lower limb swelling (37.5%) and fever (26.7%) in present study. Study by Roby et al had palpitation (32.54%) as second common symptom followed by chest pain (30.76%), leg swelling (26.6%) and fatigue (22.48%).

General physical signs in present study showed, 47.5% of patients had pallor, 43.3% of patients had oedema and raised JVP. In study by Roby et al, the commonest sign was elevated JVP (85%) followed by peripheral oedema (32.5%). In the present study raised JVP less common compared to study by Roby et al. In the present study, 75% of patients had sinus tachycardia, 20.8% patients had atrial fibrillation. 29.2% had prehypertension, 26.7% had stage 1 HTN, 35.0% had stage 2 HTN and 4.2% had isolated systolic HTN. 97.5% patients had tachypnoea at the time of presentation. 45.67% had S3/S4 on CVS examination. 77.50% had basal crepitations and 18.33% had rhonchi.

Patients with basal crackles were 77.5% in our study which is less compared to study by Roby et al which showed bilateral basal crackles in (89.94%). In study by Laxman

Dubey,¹³ the commonest sign was bilateral basal crepitations (68%) which is similar to the present study.

In this study, smoking was observed in 34.2% and alcohol consumption in 30.0% patients which is less compared to other studies. In a study by Urban Alehagen, smoking was observed in 38% patients, alcohol consumption in 45% patients.¹⁷

In study by Jacob V. Jose smoking was observed in 27% patients, alcohol consumption in 37% patients.¹⁸ 58% had history of smoking in a study by Francesca Bursi et al.¹⁹

Comorbid Conditions not only represent diseases that are risk factors for the development of heart failure but also can complicate diagnosis and management. In our study 65.8% had HTN which is the most common comorbidity, followed by diabetes mellitus in 61.7% and 55.8% had CAD. In study by Okechukwu S et al,¹⁴ hypertension is the most common aetiology of heart failure present in 78.5% of cases. This finding is consistent with our study. Studies done by Adams KF et al¹⁶ and Nieminen MS et al²⁰ showed similar observations.

This study is differing from the results of study by Laxman Dubey et al¹³ where Coronary artery disease (36.5%), was the most common comorbidity leading to HF followed by valvular heart disease (25.5%) and hypertensive heart failure (8.6%). In our study valvular heart disease was present in 10% of HF patients, which was differing from the study by Laxman Dubey et al¹³ where valvular heart diseases constitute 22.5% of HF patients.

In present study AF is present in 20.8% of heart failure patients which is differing from study done by Di Marcco JP et al²¹ in which AF constitute 42%.

In our study COPD was present in 34.2% of HF patients, this observation is consistent with study by Mentz RJ²² in which COPD constitutes 35% of HF patients. In present study, 47.5% of patients are anaemic. A systemic review and meta-analysis study by Hessel F. Groenveld et al showed anaemia in 37.2% of heart failure patients. In our study the prevalence of anaemia in HF patients is more (47.5%) compared to meta-analysis study by Hessel F. Groenveld.²³ Anaemia may lead to increased work load, resulting from an increased heart rate and stroke volume.^{24,25} In response to increased workload, heart undergoes remodelling, marked by LV hypertrophy and dilatation leading to HF.²⁶

In present study 91.7% of HF patients had normal thyroid functions. 5.8% and 2.5% of patients had hypothyroidism and hyperthyroidism respectively. A study by Judith E. Mitchell showed similar results - Out of 2, 225 patients, the majority (87%) had normal TSH levels (0.3 to 5.0 μ U/ml) at baseline, 12% had values suggestive of hypothyroidism, and 1% had values consistent with hyperthyroidism. Majority of HF patients are euthyroid in this study which is consistent with our study.²⁷

On chest X-ray, 40.83% had cardiomegaly and pulmonary oedema, 12.5% had effusion. On ECG: rhythm: sinus tachycardia in 75.0% patients, AF was found in 20.8% patients. Chamber size: LVH was found in 72.5% patients, biventricular hypertrophy in 17.5% patients, LA (Left atrium) hypertrophy/dilatation in 37.5% patients, RA (Right atrium)

hypertrophy/dilatation in 14.2% patients. On 2D Echocardiography: EF in 50.9% of patients was <40% which constitutes heart failure with reduced ejection fraction, 40-49% in 8.3% of patients i.e. HFmrEF and 40.8% of patients had EF \geq 50% which forms heart failure with preserved ejection fraction.

In this study, HFrEF is present in 61 patients (50.9%) and HFpEF in 49 patients (40.8%). This finding is consistent with study done by Stella M et al, 123 where systolic dysfunction was detected in patients (58.5%) and preserved systolic function in 136 (41.5%). This finding is also consistent with other study done by Yancy CW et al.²⁸ This finding in our study is differing from study by Chaturvedi et al²⁹ the largest population based study in India, where HF was present in 20.4%, of which 67% had preserved left ventricular (LV) systolic function and 33% had LV systolic dysfunction.

Preserved (>50%) Versus Reduced (<40%) Ejection Fraction

In our study, out of 120 patients, 61(50.8%) had EF < 40% and 49 (40.8%) had EF \geq 50%. In present study most common age group for patients with preserved and reduced EF is between 51 to 75 years (55.10% versus 63.93% respectively).

Most of the patients of age >75 years were females (20 patients out of 25) and had HFpEF in our study. In the ADHERE registry, 126 women admitted for HF were older than men (74 versus 70 years), and more frequently had preserved systolic function (51% versus 28%).

No significant difference was observed in symptoms and signs on presentation in patients of both preserved and reduced EF. Among patients with EF <40% and EF \geq 50%, majority of them presented with breathlessness of grade III respectively. In the study significant association was observed between Ejection fraction and Breathlessness. This observation is similar to other study done by Stella M et al.³⁰ In present study, patients of HFrEF, 57.7% had anaemia and in those of HFpEF, 32.7% had anaemia. This observation was statistically significant. This observation is differing from a similar study done by Inder S. Anand et al which showed no difference in the distribution of anaemia in both patients with preserved and reduced EF.²⁶

No significant difference was observed between thyroid profile and EF.

In present study, patients with reduced EF, 75.4% of reduced EF patients had CAD followed by diabetes mellitus (63.9%) and hypertension (57.4%). This observation was similar to study done by Bocchi EA et al.³¹ Coronary artery disease is more common in HFrEF patients than in patients with preserved EF. This observation was also consistent with Indian population-based study by Chaturvedi et al.²⁹ This difference was statistically significant in our study.

Hypertension was most common comorbid condition in patients with preserved ejection fraction. In present study 63.7% of HFpEF patients had hypertension followed by diabetes mellitus (59.2%) and coronary artery disease (22.4%) This finding in our study was consistent with other

similar study done by Fonarow G.C et al and Chaturvedi et al.²⁹

No significant difference was observed in other co morbidities.

In present study 16.4% patients with reduced EF had atrial fibrillation and 22.4% of patients with preserved EF atrial fibrillation. In present study atrial fibrillation is more common in patients with preserved EF. This observation is consistent with study done by Rajalakshmi S et al.³²

In present study, 75.4% of reduced EF patients had ischemic changes in ECG and 22.4% of preserved EF patients had ischemic changes. This observation was statistically significant. Myocardial ischemia is more common in patients with EF <40%. This observation is consistent with study by Chaturvedi et al.²⁹

CONCLUSIONS

A total of one twenty patients satisfying Framingham's criteria for heart failure were studied. Heart failure is more predominant in males and elderly females. HFpEF was more predominant in females of elderly age group. Most common age group affected in our study was 51-75 years.

Breathlessness was the commonest presenting symptom followed by cough and chest pain. Most of the patients presented with grade III breathlessness.

Pallor followed by oedema and raised JVP are the common presenting clinical signs. Hypertension is the most common comorbidity present in the HF patients in our study and majority of hypertensives were in stage II of JNC VII classification of hypertension. Other comorbidities are diabetes mellitus, coronary artery disease, COPD and valvular heart diseases.

Anaemia is present in significant number of HF patients in our study which carries poor prognosis. Majority of patients were euthyroid in our study.

Patients with reduced EF were more common than those with preserved EF but there is increasing prevalence of HFpEF compared to past most probably because of advanced diagnostic modalities and increased life expectancy.

No significant difference was observed in symptoms and signs on presentation in patients of both preserved and reduced EF. Anaemia was more common in HFrEF patients than in HFpEF. Most common comorbidity in patients of reduced EF and preserved EF is coronary artery disease and hypertension respectively.

AF is more common in HFpEF patients in our study, but it carries poor prognosis in both HFrEF and HFpEF. Hence this study of clinical profiles reaffirms the value of clinical assessment in the daily practice which increasingly includes heart failure.

Clinical profiles are easy to define, predict prognosis, and appear to do so better than traditional markers of disease severity. These profiles may be useful to guide appropriate therapy.

As the treatment modality and prognosis differs between patients of reduced and preserved EF, it is important to distinguish between HFrEF and HFpEF. Non-

invasive modalities like Echocardiography can be effectively used to identify systolic and diastolic dysfunction in heart failure patients.

There is a variety of comorbidities-interplay in the pathogenesis and precipitation of heart failure; hence thorough knowledge regarding risk factors and comorbidities is essential for appropriate and timely management.

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