

Frequency and Clinical Characteristics of Heart Failure with Preserved Ejection Fraction Patients in a Tertiary Level Hospital

MOHAMMAD WALIDUR RAHMAN¹, MANZOOR MAHMOOD¹, DIPAL KRISHNAADHIKARY¹, SYED ALIAHSAN¹, CHAUDHURY MESHKAT AHMED¹, HARISUL HOQUE¹, TANJIMA PARVIN¹, FAKHRUL ISLAM KHALED¹, MRM MANDAL¹, MD. ABU SALIM¹, SHAHRINA SHARMIN², ASHADUZZAMAN TALUKDER¹, KHALED MOHAMMAD IQBAL¹, MOHAMED MAUSOOL SIRAJ¹, MSI TIPU CHOWDHURY¹, SAJAL KRISHNA BANERJEE¹

¹Department of Cardiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, ²Department of Anaesthesia, Analgesia, and Intensive Care Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka

Address of Correspondence: Dr. Mohammad Walidur Rahman, Resident, Department of Cardiology, BSMMU, Dhaka
E-mail: walid.dmck61@gmail.com

Abstract:

Background: Heart failure with preserved ejection fraction (HFpEF) has already emerged as the predominant form of heart failure in the western world. We aimed to estimate the frequency and clinical characteristics of HFpEF cohort in Bangladesh as limited data are available about this extremely heterogeneous syndrome.

Methods: This cross sectional study was conducted at the Department of Cardiology, Bangabandhu Sheikh Mujib Medical University, Dhaka from December, 2017 to December, 2018. A total of 124 heart failure patients were enrolled in the study for the estimation of frequency of HFpEF. Comorbidities and presentation of 30 HFpEF patients were assessed. HFpEF diagnosis was made according to the 2016

European Society of Cardiology (ESC) Guidelines.

Results: The frequency of HFpEF was 30 (24.1%) (95% confidence interval 16.6% to 31.7%). The mean (SD) age of was 65.0 (10.1) years. Majority of the patients (73.3 %) were between 60 to 79 years of age. Majority of the patients (60%) were male. Most of the patients had multiple comorbidities and risk factors. Hypertension was the most prevalent risk factor which was present in 80% cases. Dyslipidemia was found in 63.3% cases, DM in 53.3% cases. 36.6% patients had coronary artery disease (CAD). CKD was found in 30% cases. 26.6% patients had atrial fibrillation, which was the most common arrhythmia. 62.0% were overweight to obese. Anemia was found in 55.1% cases. 73.3% patients presented in a decompensated stage of NYHA IV. Breathlessness was the most common (100%) complaint, whereas bilateral lung base crepitations was the most frequent sign (96%).

Conclusions: This study findings has paved the way for characterization of HFPEF in Bangladeshi population but more large scale epidemiological studies are needed.

Key Words: HFpEF, comorbidities, clinical presentation

University Heart Journal 2019; 15(2): 63-67

Introduction:

Heart failure (HF) is a rising epidemic with increasing incidence and prevalence and a major cause of mortality, morbidity, and quality of life impairment.¹ In 2014, approximately 26 million people were affected by heart failure globally.² Though there is no data regarding the incidence and prevalence of HF in Bangladesh but increased life expectancy, wide spread changes in life style and improvement in the management of cardiac disorders, like myocardial infarction, valvular heart diseases, arrhythmia may contribute to the increasing burden of HF in Bangladesh.

In the recent years, Heart failure with preserved ejection fraction (HFpEF) has been increasingly recognized as a complex pathophysiological entity.³ It is more challenging than HFrfEF. The 2016 European Society of Cardiology (ESC) Guidelines for the diagnosis and treatment of acute and chronic heart failure require following criteria for the diagnosis of HFpEF: symptoms and/or signs of HF, Ejection Fraction more than 50%, relevant structural heart disease and/or evidence of diastolic dysfunction.⁴ The prevalence of HFpEF in USA and Europe was 38% to 54% of all heart failure cases in previous studies.^{5,6} The

prevalence of HFpEF relative to HFrEF is increasing at a rate of 1% per year as suggested by recent data.⁷ In Asia, the prevalence of HFpEF was 26% in Japanese Cardiac Registry of Heart Failure in Cardiology.⁸ HFpEF occur in elderly, predominantly female patients, with small atrophied hearts and high prevalence of hypertension, diabetes mellitus, and atrial fibrillation but evidence suggest that HFpEF patients are far more diverse with varying extent of associated comorbidities.⁹ There may be geographical variations in HFpEF prevalence and patients characteristics. So we aimed to estimate the frequency and assess clinical characteristics of HFpEF patients in our setting.

Materials and Methods:

Study population: This cross sectional study was conducted on the admitted heart failure patients at the Department of Cardiology, Bangabandhu Sheikh Mujib Medical University, Dhaka from December, 2017 to December, 2018. A total of 124 heart failure patients were enrolled in the study for the estimation of frequency of HFpEF. The diagnosis of HFpEF was made according to the 2016 European Society of Cardiology (ESC) Heart Failure Guidelines.⁴ Patients hospitalized primarily for acute myocardial infarction or acute coronary syndrome, severe valvular heart disease, congenital heart disease, prosthetic valves & pacemakers, and patients with poor echo window were excluded.

Methodology: All inclusion criteria were established within 72 hour of presentation. The eligible patients were explained about the study, written informed consent was taken, and demographic data were recorded.

On the basis of echocardiogram patients were divided into three categories: HFpEF, HFmrEF, HFrEF. Frequency and percentage of HFpEF was calculated.

Clinical data, including the detailed medical history, cardiovascular risk factors, and associated comorbidities were noted. The symptoms of patients were graded according to NYHA classification. Relevant physical examination was done.

Data about relevant laboratory tests including chest radiography, ECG, and Doppler echocardiography were collected. Blood samples were collected for analysis of BNP on day 1 of admission in relevant cases. Echocardiography was performed by using Vivid E 9 (GE Healthcare, Norway).

Statistical analysis: All analyses were performed using EXCEL data sheet, Microsoft office 2011. Continuous variables were presented as means ± standard deviations

(SDs). Categorical variables were presented as counts and percentages.

Results:

In the study period, 141 HF patients were admitted. Among them 6 patients died, 8 patients had poor echo window, and 3 patients denied to participate. So, a total of 124 patients were enrolled in the study for the estimation of frequency of HFpEF. Detailed analysis of 30 HFpEF patients were done.

The frequency of HFpEF was 30 (24.1%). Table I shows the frequency of HFpEF.

Table-I
Frequency of HFpEF in study population: (N = 124)

HF subtype	Frequency	Percentage	95% CI
HFpEF	30	24.1	16.6–31.7

N = number of study population, CI = confidence interval, HFpEF = heart failure with preserved EF.

The mean (SD) age of 30 HFpEF patients was 65.0 (10.1) years, and the range was 45 – 90 years. Majority of the patients 22 (73.3 %) were between 60 to 79 years of age.

Majority of the patients were male 18 (60%).

Majority of the patients 18 (62.0%) were overweight to obese. Figure 1 shows the distribution of BMI among study population.

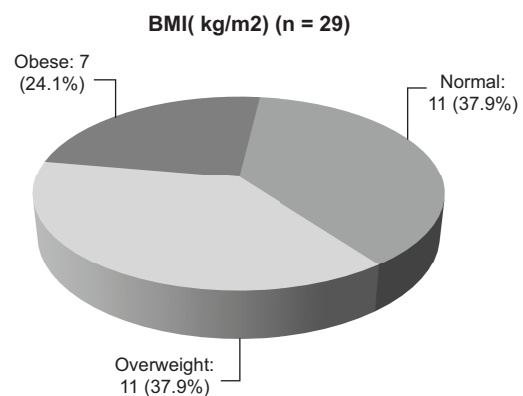


Fig.-1: Pie diagram showing the distribution of BMI n = number of study population

Most of the patients had multiple comorbidities and risk factors. Hypertension was the most prevalent risk factor which was present in 24 (80%) cases. Dyslipidemia was found in 19 (63.3%) cases, DM in 16 (53.3%) cases. 11 (36.6%) patients had coronary artery disease (CAD). CKD was found in 9 (30%) cases. 8 (26.6%) patients had atrial

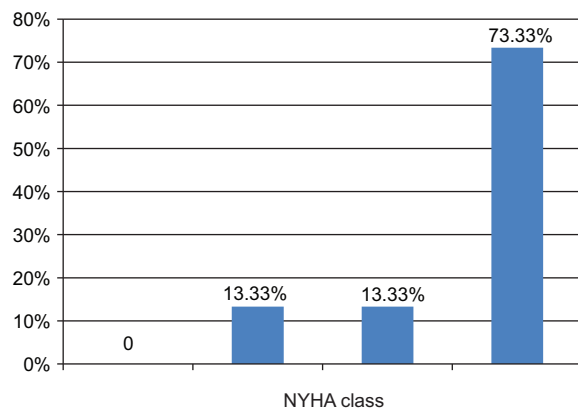
fibrillation, which was the most common arrhythmia. 7 (23.3%) cases were smoker, while, 2 (6.6%) had history of ischemic stroke. Table II shows the major comorbidities.

Table-II
Risk factors and comorbidities among study population (n = 30)

Comorbidities & risk factors	n (%)
Hypertension	24 (80)
Dyslipidemia	19 (63.3)
DM	16 (53.3)
CAD	11 (36.6)
CKD	9 (30)
Atrial fibrillation	8 (26.6)
Smoker	7 (23.3)
Stroke	2 (6.6)

n = number of study population, CAD = Coronary artery disease, CKD = Chronic kidney disease, DM = Diabetes mellitus.

At presentation, all the patients had breathlessness at rest or during exertion (Figure 2). Majority of the patients 25 (83.3%) experienced fatigue, whereas 14 (46.6%) had palpitation.



n = number of study population, NYHA = New York heart association

Fig.-2: Presentation of study population according to NYHA class (n = 30).

Bilateral lung base crepitations was the most common sign, found in 29 (96%) cases. Tachypnea was found in 24 (80%) cases, whereas elevated systolic blood pressure was found in 19 (63.3%) cases. Table III shows the common signs found in the study group.

Bilateral lung base crepitations was the most common sign, found in 29 (96%) cases. Tachypnea was found in 24 (80%) cases, whereas elevated systolic blood pressure was found in 19 (63.3%) cases. Table III shows the common signs found in the study group.

Table-III
Physical examination findings of study population (n = 30)

Examination findings	Result
Pulse b/m, mean (SD), range	98.23 (12.9), 76-120
SBP mmHg, mean (SD), range	143 (18.5), 120-180
DBP mmHg, mean (SD), range	87.83 (11.2), 70-120
Respiratory rate, mean (SD), range	22.53 (4.5), 16-30
Anemia, n (%)	16 (53)
Leg oedema, n (%)	11 (36.6)
Raised JVP, n (%)	3 (10)
Bilateral basal creps, n (%)	29 (96)

n = number of study population, SD = Standard deviation, SBP = systolic blood pressure, DBP = diastolic blood pressure.

Discussion:

The frequency and characteristics of patients with HFpEF have varied widely due to inconsistency in the diagnostic criteria, and also due to inherent heterogeneity of the syndrome itself. To our knowledge, this is the first study in Bangladesh which utilized the diagnostic criteria of HFpEF, according to the 2016 European Society of Cardiology (ESC) Heart Failure.⁴

Frequency of HFpEF: The frequency of HFpEF was found to be 30 (24.1%) in this study, which is almost similar to Japanese Cardiac Registry of Heart Failure in Cardiology (JCARE-CARD) which revealed 26% prevalence of HFpEF.⁸ The prevalence of HFpEF in USA and Europe was 38% to 54% of all heart failure cases in previous studies and also recent large-scale registries.^{5,6} In Acute Decompensated Heart Failure National Registry (ADHERE) database and Organized Program to Initiate Live saving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF) registry, the prevalence of HFpEF was 50.4% and 51.2%; but both of these registries had lower EF ($\geq 40\%$) as inclusion criteria.^{10,11} The discrepancy in frequency of HFpEF with previous trials may be due to stricter inclusion criteria of this study, and lack of awareness about HFpEF among referring physicians might also play a role.

Demographic characteristics: The mean (SD) age of HFpEF patients in this study was 65.0 (10.1) years. These patients were younger than ADHERE database {mean (SD) age: 73.9 (13.2)} and OPTIMIZE-HF registry {mean (SD) age: 75.6 (13.1)}.^{10,11}

In this study, male patients were 60%, and female were 40% with male: female ratio 1.5:1. In JCARE-CARD registry, male patients were 52.7% in HFpEF arm.⁸ However ADHERE and OPTIMIZE-HF registry both

demonstrated female predominance HFpEF patients (62% and 68% respectively).^{10,11} The reason for male predominance in this study can be explained by higher proportion of male patients got admitted in context of Bangladesh. Rahman et al. (2014) demonstrated, 75% of total heart failure patients in a tertiary level hospital in Bangladesh were male.¹²

Majority of the patients (62.0%) were overweight to obese Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist (TOPCAT) trial.¹³

Risk factors and comorbidities: Majority of the HFpEF patients had multiple comorbidities in this study.

Hypertension was the most prevalent risk factor which was present in 80% cases. Previous studies demonstrated hypertension in 55.1% to 100% cases.^{14, 15}

Dyslipidemia was found in 63.3% cases, which was similar to that of TOPCAT trial (60%).¹³ Elderly patients with high incidence of obesity and concomitant presence of CAD, stroke, DM, & renal impairment may explain this high prevalence of dyslipidemia.

DM was present in 53.3% cases, whereas it was found in 22% to 61 % patients in different trials.^{15,16}

High prevalence of all of the components of metabolic syndrome in this study reaffirm the previous findings of association of metabolic syndrome in HFpEF. In metabolic syndrome- chronic heart failure (MetS-CHF) study, metabolic syndrome was associated with HFpEF in 37.7% cases.¹⁷ It may cause coronary microvascular endothelial dysfunction resulting in reduced availability of nitric oxide and protein kinase G which ultimately causes adverse myocardial remodeling and HFpEF.¹⁸ However causal relationship between these two are yet to be established.

36.6% patients of the study had coronary artery disease (CAD) and it was in accordance with the previous result of 32% to 53%.^{10, 19}

CKD was found more commonly in this study than ADHERE registry (30% vs 26%).¹¹

Atrial fibrillation is the commonest arrhythmia found in HFpEF ranging from 21% to 41.3%.^{11, 19} In this study, 26.6% patients had atrial fibrillation. So, in presence of HF symptoms in AF patients with preserved ejection fraction, the diagnosis of HFpEF should be considered.

An important finding of this study is that majority of the patients (55.1%) were anemic, whereas 27.1% cases were anemic in JCARE-CARD registry.⁸ Higher prevalence of renal impairment than JCARE-CARD registry (30% vs

14.9%) and concomitant nutritional deficiency may explain this higher prevalence of anemia in this study.⁸ Anemia was previously found to be more common in HFpEF than HFrEF and considered as a poor prognostic factor.^{8, 20} So every attempts should be taken to identify and treat the cause of anemia in HFpEF.

23.3% cases were smoker, while 6.6% had history of ischemic stroke in this study. Presentation: The clinical presentation of HFpEF and HFrEF are almost identical.⁷ The most common symptom of this study population was breathlessness (100%), followed by fatigue (83.3%), whereas 46.6% patients experienced palpitation. Rahman et al. (2014) also demonstrated breathlessness as most prevalent symptom present in 98% HF patients.¹² Most of the patients (86.6%) were in decompensated stages of NYHA class III-IV during presentation. However, they were in more decompensated stage than Irbesartan in Heart Failure With Preserved Ejection Fraction (I-PRESERVE) cohort (NYHA class IV 73.3% vs 3%).²¹

Bilateral lung base crepitations was the most common sign, found in 96% cases in this study. Rahman et al. (2014) also found basal crepitation in 95% HF patients.¹² Tachypnea was found in 80% cases, whereas elevated systolic blood pressure was found in 19 (63.3%) cases.

Limitations:

First, as number of cases was inadequate, so findings may not absolutely represent Bangladeshi HFpEF cohort. Second, diagnostic criteria of HFpEF varied widely across the different trials making it difficult to compare our result with result of previous studies.

Conclusion:

HFpEF contributed almost one fourth of total HF hospitalization in our setting. They were younger than the western HFpEF cohort. They were predominantly male with multiple comorbidities and presented in a decompensated stage. However, more large scale epidemiological studies are needed to find out the exact prevalence and characteristics of HFpEF patients in Bangladesh.

Reference:

1. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE, and Drazner, MH, et al. American College of Cardiology Foundation; American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2013; 62: e147–239.

2. Ambrosy PA, Fonarow GC, Butler J, Chioncel O, Greene SJ, and Vaduganathan M, et al. The global health and economic burden of hospitalizations for heart failure. Lessons learned from heart failure registries. *J Am Coll Cardiol* 2014; 63: 1123-33.
3. Kitzman DW, Little WC, Brubaker PH, Anderson RT, Hundley WG, and Marburger CT, et al. Pathophysiological characterization of isolated diastolic heart failure in comparison to systolic heart failure. *JAMA* 2002; 288: 2144-50.
4. Ponikowski P, Voors AA, Anker SD, Bueno H & Cleland JGF, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). *Eur Heart J* 2016; 37(27):2129-2200.
5. Abhayaratna WP, Marwick TH, Smith WT, and Becker NG. Characteristics of left ventricular diastolic dysfunction in the community: an echocardiographic survey. *Heart* 2006; 92: 1259-64.
6. Owan TE, Hodge DO, Herges RM, Jacobsen SJ, Roger VL and Redfield MM. Trends in prevalence and outcome of heart failure with preserved ejection fraction. *N Engl J Med* 2006; 355: 251-59.
7. Oktay AA and Shah SJ. Diagnosis and Management of Heart Failure with Preserved Ejection Fraction: 10 Key Lessons. *Current Cardiology Reviews* 2015; 11: 42-52.
8. Tsuchihashi-Makaya M, Sanae H, Shintaro K, Takashi Y, Daisuke G and Hisashi Y, et al., Characteristics and outcome of hospitalized patients with heart failure and reduced vs preserved ejection fraction. *Circulation* 2009; 73: 1893-1900.
9. Sharma K & Kass DA. Heart failure with preserved ejection fraction: Mechanisms, Clinical Features, and therapies. *Circulation* 2014; 115: 79-96.
10. Fonarow GC, Stough WG, Abraham WT, Albert NM, Gheorghiade M and Greenberg BH, et al. OPTIMIZE-HF Investigators and Hospitals. Characteristics, treatments, and outcomes of patients with preserved systolic function hospitalized for heart failure: a report from the OPTIMIZE-HF Registry. *J Am Coll Cardiol* 2007; 50: 768-77.
11. Yancy CW, Lopatin M, Stevenson LW, Marco, T and Fonarow GC. ADHERE Scientific Advisory Committee and Investigators. Clinical presentation, management, and in-hospital outcomes of patients admitted with acute decompensated heart failure with preserved systolic function: a report from the Acute Decompensated Heart Failure National Registry (ADHERE) Database. *J Am Coll Cardiol* 2006; 47: 76-84.
12. Rahman MT, Majumder AAS, Rahman A, & Choudhury AW. Clinical Presentation of Heart Failure Patients Admitted in National Institute of Cardiovascular Diseases, Dhaka. *J Medicine* 2014; 15 : 18-22.
13. Shah AM, Shah SJ, Anand IS, Sweitzer NK, O'Meara E & John F, et al. Cardiac Structure and Function in Heart Failure With Preserved Ejection Fraction: Baseline Findings From the Echocardiographic Study of the Treatment of Preserved Cardiac Function Heart Failure With an Aldosterone Antagonist Trial. *Circ Heart Fail* 2014; 7: 104-115.
14. Bhatia RS, Tu JV, Lee DS, Austin PC, Fang J and Haouzi A, et al. Outcome of heart failure with preserved ejection fraction in a population based study. *N Engl J Med* 2006;355: 260-69.
15. Melenovsky V, Borlaug BA, Rosen B, Hay I, Ferruci L and Morell CH, et al. Cardiovascular features of heart failure with preserved ejection fraction versus nonfailing hypertensive left ventricular hypertrophy in the urban Baltimore community: the role of atrial remodeling/dysfunction. *J Am Coll Cardiol* 2007; 49: 198-207.
16. Lee DS, Gona P, Vasani RS, Larson MG, Benjamin EJ and Wang TJ, et al. Relation of disease pathogenesis and risk factors to heart failure with preserved or reduced ejection fraction: insights from the Framingham Heart Study of the national heart, lung, and blood institute. *Circulation* 2009; 119: 3070-77.
17. Miura Y, Fukumoto Y, Shiba N, Miura T, Shimada K, and Iwama Y, et al. Prevalence and Clinical Implications of Metabolic Syndrome in Chronic Heart Failure. *Circulation Journal* 2010; 4: 2612-21. Paulus WZ, and Tschope C. A Novel Paradigm for Heart Failure With Preserved Ejection Fraction. *JACC* 2013; 62(4): 263-71.
19. Lam CS, Roger VL, Rodeheffer RJ, Bursi F, Borlaug BA, and Ommen SR, et al. Cardiac structure and ventricular-vascular function in persons with heart failure and preserved ejection fraction from Olmsted County, Minnesota. *Circulation* 2007; 115: 1982-90.
20. Latado AL, Passos LCS, Darze' ES, and Lopes AA. Comparison of the effect of anemia on in-hospital mortality in patients with versus without preserved left ventricular ejection fraction. *Am J Cardiol* 2006; 98: 1631-4.
21. Zile MR, Gottdiener JS, Hetzel SJ, McMurray JJ, Komazda M, and McKelvie R, et al. Prevalence and Significance of Alterations in Cardiac Structure and Function in Patients With Heart Failure and a Preserved Ejection Fraction. *Circulation* 2011; 124: 2491-501.