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FREQUENCY AND CLINICAL PROFILE OF HEART FAILURE WITH PRESERVED EJECTION FRACTION USING CLINICAL CRITERIA AND ECHOCARDIOGRAPHY

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ABSTRACT

Background: Heart failure with preserved ejection fraction (HFpEF) presents a significant global burden. The frequency and clinical as well as echocardiographic characteristics of HFpEF are still under characterised.

Objective: To determine the frequency, clinical and echocardiographic profile of HFpEF among patients presenting with heart failure.

Methods: This was a cross-sectional study which included 149 adult patients with clinical heart failure at a tertiary care cardiology center from date to date. All patients included in the study were equally divided into HFpEF (LVEF ≥50%) and non-HFpEF (LVEF <50%) groups. Demographic, clinical, echocardiographic and biochemical parameters were compared with stratified analysis by age.

Results: HFpEF was present in 45.6% (n=68/149) of patients. HFpEF patients were significantly older (70.28±5.68 vs. 64.04±8.92 years; p<0.001). These patients had higher BMI (31.92±6.40 vs. 27.72±4.36 kg/m²; p<0.001) and higher blood pressure readings (138.09±16.94 vs. 124.63±18.16 mmHg; p<0.001). Hypertension (83.6% vs. 66.7%; p=0.019), dyslipidemia (60.9% vs. 40.8%; p=0.018) and obesity (59.7% vs. 28.4%; p<0.001) were more common in HFpEF group. Coronary artery disease was found to be more prevalent in non-HFpEF (50.6%). HFpEF patients had significantly higher left atrial volume index (42.05±9.86 vs. 35.87±9.43 mL/m²; p<0.001) but their NT-proBNP levels were lower than non HFpEF group(median: 1556.5 vs. 3910.0 pg/mL; p<0.001). In older patients the association between obesity and HFpEF was significant (p<0.001).

Conclusion: HFpEF constituted nearly half of heart failure cases with older age, more metabolic comorbidities, and significant left atrial issues. There is a need for phenotype specific diagnostic and therapeutic approaches in South Asian populations.

KEYWORDS: Preserved Ejection Fraction, Echocardiography, Heart Failure

INTRODUCTION

Heart failure with preserved ejection fraction (HFpEF) is a complex clinical syndrome. Patients present with typical heart failure symptoms. Their left ventricular ejection fraction remains normal or near-normal (LVEF ≥50%). The global burden of HFpEF continues to rise. HFpEF now accounts for approximately 50% of all heart failure hospitalizations[1]. Heart failure prevalence is high in Pakistan. A recent large-scale registry shows that heart failure affects a substantial proportion of adults. Regional studies report an increasing prevalence of HFpEF . This rise reflects the high burden of metabolic risk factors [2, 3]. South Asian cohorts demonstrate a distinct HFpEF phenotype. Patients are often younger than those in Western populations. They also show higher rates of diabetes [3].

HFpEF arises from multiple pathophysiologic mechanisms. Myocardial stiffness contributes to disease progression. Impaired diastolic relaxation further limits cardiac filling. Systemic microvascular inflammation also drives the syndrome [4]. HFrEF and HFpEF differ in their therapeutic options. Clinicians historically managed HFpEF with diuretics alone. This approach provided only symptomatic relief. Recent clinical trials have changed this paradigm. SGLT2 inhibitors are now established as first-line therapy and help in reducing cardiovascular mortality rate and also lower hospitalization rates in HFpEF patients [5, 6]. Current international guidelines recommend a multi-modal diagnostic strategy. Clinicians perform a detailed clinical assessment. They measure natriuretic peptide levels. Echocardiography provides key markers. The E/e′ ratio reflects diastolic function. The left atrial volume index indicates chronic elevation of filling pressures [7].

Recent investigations have clarified key clinical features in HFpEF. Hypertension affects approximately 70–80% of patients . Obesity and metabolic syndrome drive the inflammatory phenotype [8]. Echocardiographic studies identify strong prognostic markers. A high Left Atrial Volume Index (LAVI) predicts hospitalization independently [9]. A pivotal local study informed our sample size calculation. Irfan et al. (2021) evaluated patients presenting with heart failure symptoms. They found HFpEF in 45.5% of this cohort [10].

HFpEF remains under-diagnosed in Pakistan. Its clinical presentation shows marked heterogeneity. Many tertiary care settings lack standardized echocardiographic profiling. Characterizing clinico-echocardiographic features will improve diagnostic accuracy. It will also guide therapeutic interventions for the local population. The objective of this study was to determine the frequency of HFpEF among patients presenting with heart failure.

METHODOLOGY

This was a cross-sectional study conducted at the Department of Cardiology, [Hospital Name], from [Date] to [Date]. The study was conducted to determine the frequency and echocardiographic profile of Heart Failure with Preserved Ejection Fraction (HFpEF). Institutional Ethical Review Committee approval (Ref No: [Placeholder]) was obtained prior to the commencement of data collection. An informed consent was secured from all participants. The WHO sample size calculator was used to calculate the sample size of this study keeping the expected frequency of HFpEF in HF patients as 45.5% based on a previously published study by Irfan et al.[10] A 95% confidence interval and 8% margin of error was used and that yielded a minimum requirement of 149 patients. Adult patients of both genders aged >18 years with clinical symptoms of HF were included in the study using the Framingham criteria. A non probability purposive sampling technique was used for enrollment. Patients with a known history of severe valvular heart disease, pericardial disease and inadequate echocardiographic windows were excluded.

The study participants were categorized into two groups based on echocardiographic findings, HFpEF group with LVEF ≥50% and non-HFpEF group (HFrEF/HFmrEF, LVEF <50%. Baseline demographic data including age, gender, BMI and smoking status was recorded. A systematic assessment of clinical characteristics including but not limited to NYHA class, heart rate, BP readings and comorbidities was conducted. An experienced cardiologist performed echocardiography using (machine name here) and measured parameters including LVEF, LAVI, E/A ratio, E/é ratio, LVMI and pulmonary artery systolic pressure. A complete biochemical assessment was also undertaken for all patients.

All data was analysed using IBM SPSS version 24.0. Qualitative variables were tested for normality using shapiro wilk test including BMI, age and echocardiographic parameters. Mean ± Standard Deviation (SD) was used to express normally distributed variables. Non normally distributed data was reported as median (IQR). The independent samples t-test and Mann-Whitney U tests were used to perform comparative analysis between HFpEF and Non-HFpEF groups. Frequencies and percentages were used to present qualitative variables including age and comorbidities. The Chi-square test was used for cells with small expected counts. A stratified analysis was conducted by dividing the cohort into age strata to evaluate the impact of age as an effect modifier. A chi-square test was again used to examine association between groups after stratification. A p-value of ≤0.05 was considered statistically significant.

RESULTS

Out of all patients most affected with HFpEF were significantly older with high BMI values and higher blood pressure readings compared to the non-HFpEF group (all, p<0.001). Hypertension, dyslipidemia and obesity were significantly more prevalent in the HFpEF group. In the non-HFpEF group coronary artery disease was more common. There was no significant difference found between gender distribution, diabetes, AF, NYHA class and smoking status. Heart rate was modest but it was significantly lower in the HFpEF group. Complete baseline demographic and clinical characteristics of study participants are given in Table 1.

Table 1: Baseline Demographic and Clinical Characteristics of Study Participants (N = 149)

Variable	Non-HFpEF(n = 81)	HFpEF(n = 68)	p-value
Age (years), Mean ± SD	64.04 ± 8.92	70.28 ± 5.68	<0.001*
BMI (kg/m²), Mean ± SD	27.72 ± 4.36	31.92 ± 6.40	<0.001*
Systolic BP (mmHg), Mean ± SD	124.63 ± 18.16	138.09 ± 16.94	<0.001*
Diastolic BP (mmHg), Mean ± SD	71.45 ± 14.01	79.59 ± 14.63	0.001*
Heart Rate (beats/min), Mean ± SD	81.76 ± 14.45	76.12 ± 12.53	0.014*
Gender, n (%)			
Male	47 (58.8)	33 (41.3)	**0.247**
Female	34 (49.3)	35 (50.7)	
NYHA Class, n (%)			
I	2 (50.0)	2 (50.0)	**0.731**
II	25 (49.0)	26 (51.0)	

Variable	Non-HFpEF(n = 81)	HFpEF(n = 68)	p-value
III	38 (58.5)	27 (41.5)	
IV	12 (60.0)	8 (40.0)	
Hypertension, n (%)	54 (48.6)	57 (51.4)	0.017*
Diabetes Mellitus, n (%)	23 (46.0)	27 (54.0)	0.145
Atrial Fibrillation, n (%)	16 (43.2)	21 (56.8)	0.117
Coronary Artery Disease, n (%)	41 (64.1)	23 (35.9)	0.039*
Dyslipidemia, n (%)	31 (43.7)	40 (56.3)	0.014*
Obesity, n (%)	23 (35.9)	41 (64.1)	<0.001*
Smoking, n (%)	31 (51.7)	29 (48.3)	0.515

LVEF was significantly higher in the HFpEF group while LAVI and E/A ratio were significantly different in both groups. The LV mass index was low in the HFpEF group and NT-proBNP was significantly higher in the non-HFpEF group. There was no significant difference in both groups in terms of E/e′ and PASP values. A detailed comparison of echocardiographic and biochemical parameters between both groups is given in Table 2.

Table 2: Comparison of Echocardiographic and Biochemical Parameters between HFpEF and Non-HFpEF Groups

Parameter	Non-HFpEF(n = 81) Mean ± SD	HFpEF(n = 68) Mean ± SD	p-value
LVEF (%)	n=81, 31.64 ± 7.59	n=68, 59.32 ± 5.44	<0.001*
LAVI (mL/m²)	n=80, 35.87 ± 9.43	n=63, 42.05 ± 9.86	<0.001*
E/A ratio	n=76, 1.65 ± 0.59	n=66, 1.10 ± 0.38	<0.001*
E/e′ ratio	n=77, 13.85 ± 4.13	n=63, 14.65 ± 4.03	0.255
LV Mass Index (g/m²)	n=78, 131.83 ± 26.93	n=63, 123.40 ± 22.30	0.048*
PASP (mmHg), Median (IQR)	n=79, 35.00 (17.50)	n=63, 40.00 (14.50)	0.113
NT-proBNP (pg/mL), Median (IQR)	n=74, 3910.0 (3848.0)	n=66, 1556.5 (2254.3)	<0.001*

LVEF ranged between 17.80% to 72.80% (mean 44.27%) in the pooled cohort. The most variability could be seen in NT-proBNP (SD ≈ 3984; range 253–35,000 pg/mL). These pooled values define the overall reference range before group stratification.

The Overall Descriptive Statistics are given in detail in Table 3.

Table 3: Overall Descriptive Statistics of Echocardiographic and Biochemical Parameters in the Study Population (N = 149)

Parameter	N	Minimum	Maximum	Mean	Std. Deviation
LVEF (%)	149	17.80	72.80	44.2711	15.35986
LAVI (mL/m²)	143	18.70	69.60	38.5930	10.07199
E/A ratio	143	0.52	3.38	1.3941	0.56888
E/e′ ratio	141	5.20	23.70	14.2234	4.07644
LV Mass Index (g/m²)	142	66.80	208.10	128.1549	25.16880
PASP (mmHg)	143	16.00	73.00	38.3706	11.79978
NT-proBNP (pg/mL)	141	253.00	35000.00	3652.1844	3984.63890

The association between HFpEF and comorbidities was strongly dependent on age. There was a significant association of obesity with HFpEF in the older population ($p<0.001$). Coronary artery disease, dyslipidemia and hypertension showed no significant association within either age groups. It became significant when pooled (overall $p<0.05$), which suggests that age is an effect modifier. The Stratified Analysis of Comorbidities Associated with HFpEF, by Age Group are given in detail in Table 4.

Table 4: Stratified Analysis of Comorbidities Associated with HFpEF, by Age Group

Comorbidity	AgeStratum	Non-HFpEFn (%)	HFpEFn (%)	p-value	N
Coronary ArteryDisease	Group 1	14/25 (56.0)	2/3 (66.7)	0.724	28
	Group 2	27/56 (48.2)	21/64 (32.8)	0.086	120
	Overall*	41/81 (50.6)	23/67 (34.3)	0.046*	148
Dyslipidemia	Group 1	8/22 (36.4)	2/3 (66.7)	0.315	25
	Group 2	23/54 (42.6)	37/61 (60.7)	0.053	115
	Overall*	31/76 (40.8)	39/64 (60.9)	0.018*	140
Obesity	Group 1	8/25 (32.0)	1/3 (33.3)	0.963	28
	Group 2	15/56 (26.8)	39/64 (60.9)	<0.001*	120
	Overall*	23/81 (28.4)	40/67 (59.7)	<0.001*	148
Hypertension	Group 1	14/25 (56.0)	2/3 (66.7)	0.724	28
	Group 2	40/56 (71.4)	54/64 (84.4)	0.086	120
	Overall*	54/81 (66.7)	56/67 (83.6)	0.019*	148

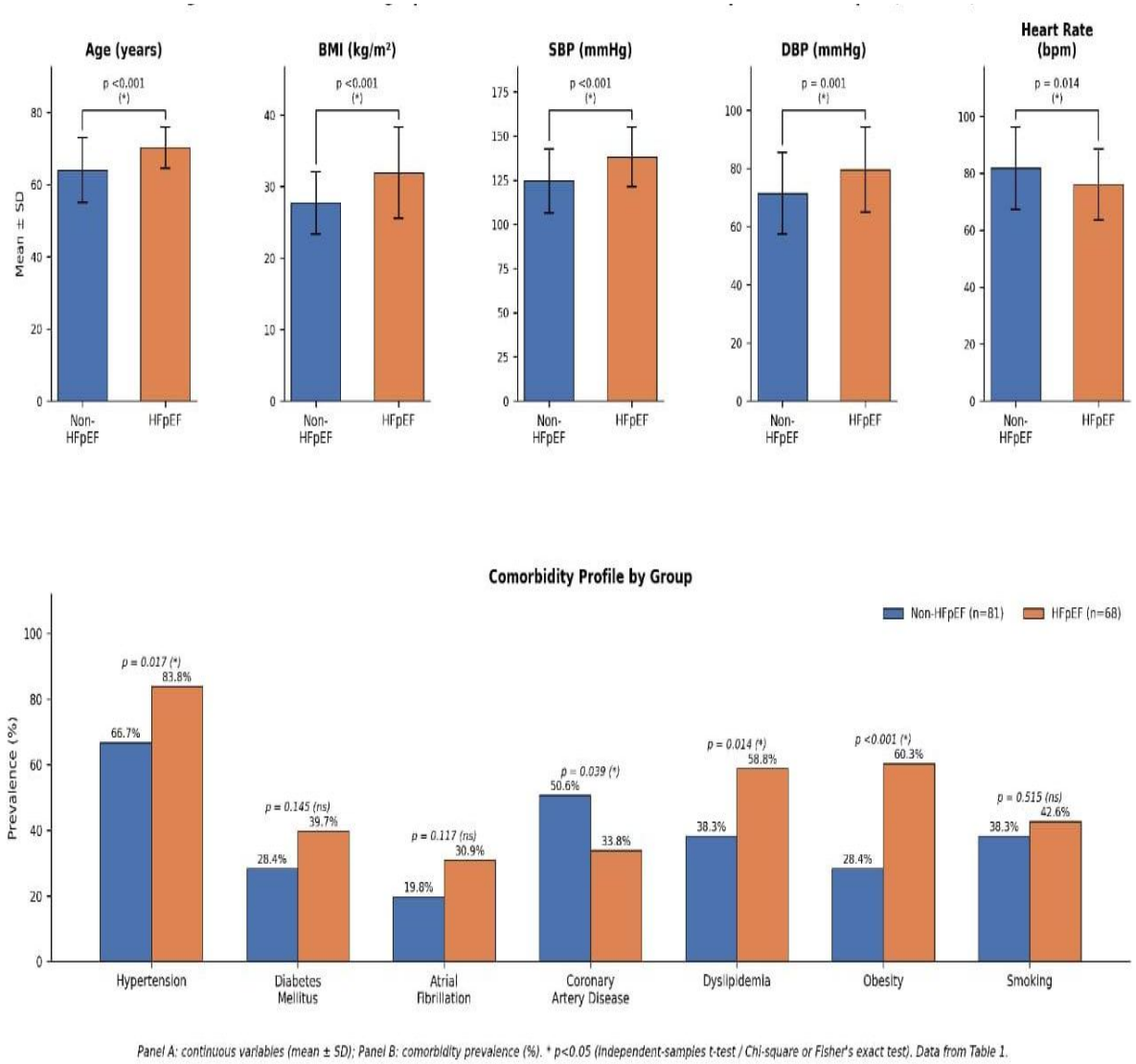

Figure 1: Comparison of baseline demographic and clinical characteristics between HFpEF and Non-HFpEF groups.

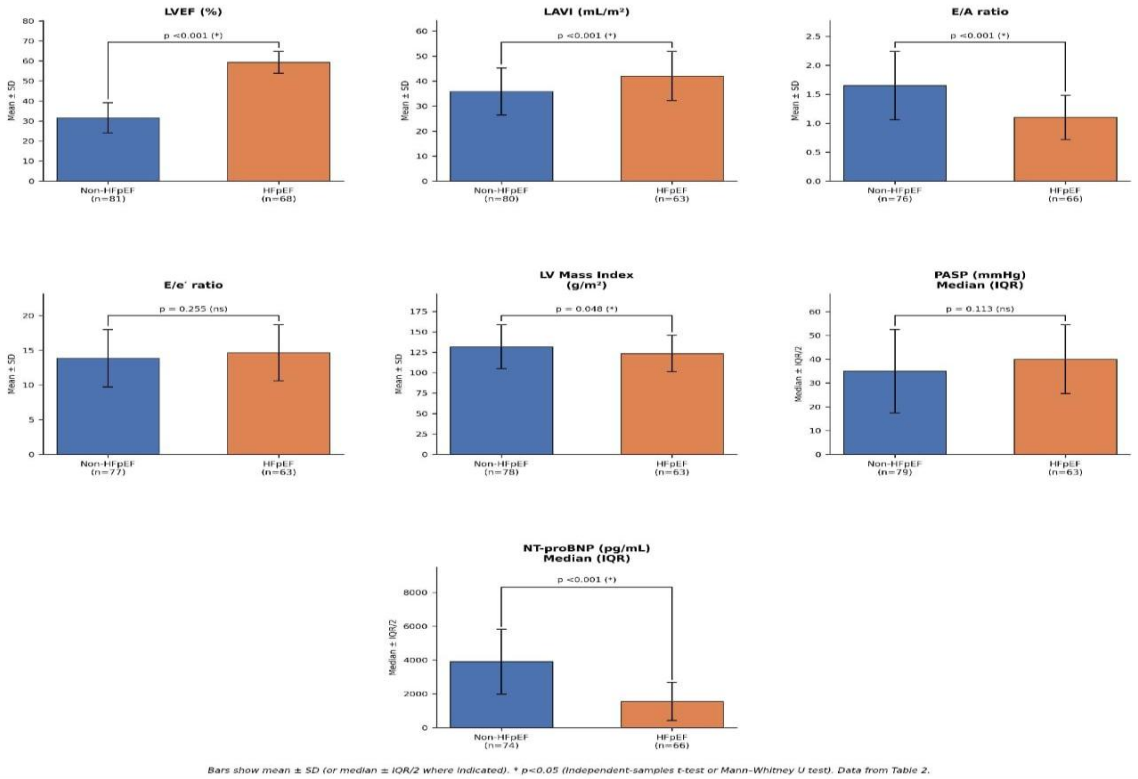

Figure 2: Comparison of echocardiographic and biochemical parameters between HFpEF and Non-HFpEF groups.

DISCUSSION

The cross sectional study from the local clinical landscape highlighted a high frequency of heart failure with preserved ejection fraction (HFpEF), which accounted for 45.6% (n=68/149) of patients presenting with heart failure consistent with the shifting global epidemiological trend. Savarese et al. reported in a comprehensive 2023 update that HFpEF now constitutes nearly 50% of heart failure cases in several international registries [1]. Boombhi et al reported 45.5% frequency in the parent study used for our sample size calculation [10]. This rising prevalence is associated with the demographic transition and the high burden of metabolic risk factors in the South Asian population.

A key finding of our study was that the HFpEF patients were significantly older than those without HFpEF Mean age of 70.28 ± 5.68 years compared with 64.04 ± 8.92 years respectively ($p<0.001$). This age difference is a characteristic feature of the HFpEF phenotype. In an analysis of the ESC heart failure Long-Term Registry (n=9,134) Uijl et al., reported that the median age for HFpEF was 73 years compared to 66 years for those with reduced ejection fraction [11]. In our local population, HFpEF mainly affects the older patients, although the mean age is slightly lower than that observed in Western cohorts, possibly because of earlier vascular aging in South Asians.

Our cohort also demonstrated that, Body Mass Index (BMI) is higher in the HFpEF group (31.92 ± 6.40 kg/m ²) compared to the non-HFpEF group (27.72 ± 4.36 kg/m ²; $p<0.001$). The "obese-HFpEF" phenotype is a well-recognized clinical entity.In the Get With The Guidelines-Heart Failure registry, Butala et al. noted that the median BMI for HFpEF patients was 30.6 kg/m ², which closely resembles our mean BMI[12]. In the stratified analysis the association between obesity and HFpEF was only significant in the older age stratum ($p<0.001$). According to D'Amario et al., our findings raise the possibility that adiposity and aging may increase myocardial stiffness, with epicardial fat contributing to diastolic impairment through pro-inflammatory cytokine release [13].

Hypertension was significantly more common among patients with the HFpEF group (83.6%) than in the non-HFpEF group (66.7%; $p=0.019$). Sardu et al. found a similar prevalence of hypertension (81%) in their cohort, highlighting chronic pressure overload as the major contributor to the structural changes associated with HFpEF [14]. Coronary artery disease (CAD) was significantly more common in our non-HFpEF group (50.6% vs 34.3%; $p=0.046$). Raza et al., reported that CAD remains the dominant etiology for reduced ejection fraction (HFrEF) in Pakistan, while HFpEF is more frequently associated with non-ischemic metabolic factors [15].

Echocardiography in our patients demonstrated significant left atrial (LA) remodeling. The Left Atrial Volume Index (LAVI) was significantly higher in the patients with HFpEF (42.05 ± 9.86 mL/m²) compared to those without HFpEF (35.87 ± 9.43 mL/m²; $p<0.001$). Omote et al., showed that a mean LAVI of 41 mL/m² was strongly predictive of HFpEF and could serve as a surrogate for chronic elevation of left ventricular filling pressures [16]. The E/e′ ratio was higher in the HFpEF group (14.65 vs 13.85) than those without HFpEF , the difference was not

of statistical significance (p=0.255). According to Peikert et al. a mean E/e′ of 15.2 in HFpEF patients suggested that the degree of diastolic filling pressure in our cohort was consistent with that observed in international cohorts[17].

Paradoxical finding reported that the Left Ventricular Mass Index (LVMI) was lower in the HFpEF group (123.40 ± 22.30 g/m²) compared to the non-HFpEF group (131.83 ± 26.93 g/m²; p=0.048). HFpEF is associated with hypertrophy, modern phenotyping by Cohen et al. demonstrated that up to 30% of HFpEF patients have a "non-hypertrophic" phenotype despite experiencing significant symptoms [18]. Our Biochemical analysis showed that the HFpEF group had significantly lower NT-proBNP levels (Median: 1556.5 pg/mL) compared with the non-HFpEF group (3910.0 pg/mL; p<0.001). Januzzi et al. confirmed this "NT-proBNP gap," and also observed that patients with preserved ejection fraction were often associated with lower levels due to less ventricular wall stress compared with HFrEF [19].

Although this difference was not statistically significant (p=0.247), gender distribution showed a slightly higher proportion of females in the HFpEF group (50.7%) compared to the non-HFpEF group (41.3%). Pagnesi et al. reported a high female prevalence of 62% in European cohorts, whereas our findings suggested more balanced gender distribution in South Asia. Our study found that dyslipidemia was present in 60.9% of patients with HFpEF, with an overall significance association (p=0.018), highlighting the metabolic nature of the disease described by Greene et al. in their 2023 review on multi-organ involvement [21].

This study is limited by factors including its cross-sectional design and the use of purposive sampling at a single tertiary center. Our structured echocardiographic evaluation provides a detailed snapshot of the HFpEF burden in Pakistan. Tromp et al., highlighted that the Asian HFpEF phenotype is essential, with patients often having a lower BMI but greater metabolic derangements [22]. Our study concluded that local HFpEF patients are older, more hypertensive, and exhibit significant LA remodeling, despite having lower NT-proBNP levels compared with those with HFrEF. Bank et al., argued for the need of specialized diagnostic strategies in South Asian patients to minimize the risk of underdiagnosing this phenotype [23].

CONCLUSION

The study found that almost half of HFpEF patients had HF presentations. Most of these patients were significantly older, with higher body mass index and had higher prevalence of hypertension than those with reduced ejection fraction. Echocardiographic profiling showed significant left atrial remodeling and lower NT-proBNP levels in HFpEF. The results highlight the need for age stratified diagnostic strategies and targeted management of metabolic comorbidities to improve HFpEF detection and outcomes.

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