Prevalence and Phenotypic Clusters of Heart Failure with Preserved Ejection Fraction (HFpEF): A Prospective Observational Cohort Study from a Tertiary Care Centre

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Abstract
Background:
Heart failure with preserved ejection fraction (HFpEF) accounts for nearly half of all heart failure cases worldwide and is characterized by marked clinical, metabolic, and echocardiographic heterogeneity. This diversity has limited the effectiveness of uniform therapeutic strategies. Identification of distinct phenotypic clusters may improve risk stratification and enable individualized management.

Objectives:
To determine the prevalence of HFpEF and to identify distinct phenotypic clusters among patients presenting to a tertiary care center in eastern India.

Methods:
This was a **prospective observational cohort study** conducted over a 12-month period at a tertiary care teaching hospital. Consecutive adult patients diagnosed with HFpEF based on guideline-recommended criteria were enrolled. Detailed demographic, clinical, laboratory, electrocardiographic, and echocardiographic data were collected. Unsupervised cluster analysis using key clinical and echocardiographic variables was performed to identify distinct HFpEF phenotypes.

Results:
HFpEF constituted a substantial proportion of heart failure admissions during the study period. The mean age of patients was 63.4 ± 9.8 years, with a predominance of females. Hypertension (78%), diabetes mellitus (46%), and obesity (41%) were the most common comorbidities. Echocardiography demonstrated preserved systolic function with significant diastolic dysfunction, left atrial enlargement, and increased left ventricular mass. Cluster analysis identified three distinct phenotypes: a metabolic–obese phenotype, a hypertensive–atrial remodeling phenotype, and a cardiorenal–high-risk phenotype. These clusters differed significantly in metabolic burden, renal function, atrial size, diastolic indices, functional status, and hospitalization trends.

Conclusion:
HFpEF is a prevalent and heterogeneous condition in the tertiary care setting. Phenotypic clustering reveals clinically meaningful subgroups with distinct structural remodeling and disease severity, underscoring the limitations of a uniform treatment approach.

Recommendation:
Routine phenotype-based assessment of HFpEF patients should be encouraged to facilitate personalized management strategies and improve clinical outcomes.

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Introduction

As the population ages, the burden of cardiovascular risk factors increases, and the survival rate from acute cardiac events improves, heart failure (HF) continues to be a major global public health concern. Heart failure with preserved ejection fraction (HFpEF), one of the two main subtypes of heart failure, currently makes up 40–60% of all heart failure cases and is more prevalent in patients with numerous comorbidities, women, and the elderly [1]. The diagnosis and treatment of heart failure with decreased ejection fraction (HFpEF) are particularly difficult because, unlike heart failure with reduced ejection fraction (HFrEF), HFpEF is characterized by typical signs and symptoms of heart failure in the presence of a normal or near-normal left ventricular ejection fraction.

Systemic inflammation, endothelial dysfunction, myocardial stiffness, poor ventricular relaxation, and extracardiac comorbidities interact to cause HFpEF, which is a complex and diverse clinical condition rather than a single disease entity [2]. Long-term hypertension, diabetes mellitus, obesity, chronic renal disease, atrial fibrillation, and coronary artery disease are common presentations for patients. These conditions all contribute to structural and functional changes in the heart. Despite maintained systolic function, these pathophysiological pathways result in increased left ventricular filling pressures, pulmonary congestion, exercise intolerance, and repeated hospitalizations [3].

The mortality and rehospitalization rates in HFpEF are similar to those in HFrEF, despite improvements in cardiovascular medicine [4]. However, pharmacological alternatives in HFpEF have historically shown minimal effectiveness, in contrast to HFrEF, where various disease-modifying medications have demonstrated strong survival advantages. The significant variability of HFpEF populations participating in clinical trials, where a "one-size-fits-all" therapy approach fails to address underlying mechanistic differences among patients, is increasingly blamed for this therapeutic failure [5].

Understanding HFpEF as a disease made up of several phenotypes, each motivated by unique clinical traits, comorbidity profiles, and cardiac remodeling patterns, has undergone a paradigm change in recent years [6]. Age, sex, body composition, metabolic status, blood pressure regulation, atrial structure, ventricular geometry, renal function, and degree of diastolic dysfunction are all examples of phenotypic heterogeneity in HFpEF. These variations have a substantial impact on prognosis, responsiveness to treatment, symptom load, and disease progression [7].

A potent data-driven method for deciphering the intricacy of HFpEF is phenotype-based classification utilizing cluster analysis. Several studies have found repeatable HFpEF clusters, including obese–metabolic phenotype, elderly–frail phenotype, hypertensive–left ventricular hypertrophy phenotype, and atrial fibrillation–dominant phenotype, by applying unsupervised statistical techniques to clinical, laboratory, and echocardiographic variables [8,9]. It has been demonstrated that the inflammatory burden, myocardial structure, hemodynamic profiles, and clinical outcomes of these phenotypic clusters vary considerably, indicating that HFpEF treatment should be customized rather than standardized [10].

The majority of current HFpEF phenotyping research comes from Western populations, whose demographics, lifestyle choices, and comorbidity patterns are very different from those found in low- and middle-income nations [11]. Due to rising rates of obesity, diabetes, hypertension, and higher life expectancy, the burden of HFpEF is quickly increasing in India. Nevertheless, there is still a dearth of information from Indian tertiary care settings regarding the frequency, clinical features, and phenotypic grouping of HFpEF. Unique HFpEF phenotypes that are underrepresented in international literature may arise from regional differences in socioeconomic status, healthcare access, dietary habits, and comorbidity profiles [12].

Therefore, enhancing diagnostic precision, directing therapeutic decision-making, and maximizing resource utilization in tertiary care facilities all depend on an understanding of HFpEF phenotypes in the Indian setting. The creation of phenotype-specific therapies, focused follow-up techniques, and early risk stratification may all benefit from the identification of different clinical and echocardiographic clusters. In this regard, the goal of the current study was to assess the prevalence of HFpEF and to find unique phenotypic clusters among patients who visited a tertiary care facility over the course of a year.

Aims & Objectives
Aim of the Study

To evaluate the prevalence of heart failure with preserved ejection fraction (HFpEF) and to identify distinct phenotypic clusters among patients presenting to a tertiary care center.

Primary Objectives

1. To ascertain the frequency of HFpEF among individuals with heart failure diagnoses made during the study period.
2. To outline the clinical, laboratory, echocardiographic, and demographic characteristics of HFpEF patients.
3. To use unsupervised cluster analysis based on important clinical and echocardiographic data to find unique phenotypic clusters of HFpEF.

Secondary Objectives

1. To evaluate the distribution of comorbidities and cardiovascular risk factors among various HFpEF subtypes.
2. To compare the identified phenotypic clusters in terms of hospitalization patterns, disease severity, and functional status.
3. To investigate correlations between structural cardiac remodeling and diastolic dysfunction indicators and phenotypic clusters.

Materials & Methods
Study Design and Setting

This was a **prospective observational cohort study, which** was carried out in the tertiary care teaching hospital Indira Gandhi Institute of Medical Sciences, which serves patients from Bihar and surrounding areas. In addition to managing a sizable number of heart failure patients through both inpatient and outpatient care, the institute acts as a referral center for cardiovascular disorders. The study was conducted at the Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India, from **January 2024 to December 2024**.

Study Population and Sample Size

During the research period, a total of 100 consecutive patients with heart failure with preserved ejection fraction (HFpEF) were included. After meeting certain eligibility requirements, patients were recruited from the cardiology inpatient wards and the outpatient department. Feasibility and the anticipated number of HFpEF patients who would visit the center during the trial were taken into consideration while determining the sample size.

Inclusion Criteria

Patients were included in the study if they met all of the following criteria:

- Age ≥18 years
- Presence of symptoms and/or signs of heart failure such as dyspnea, fatigue, orthopnea, pedal edema, or raised jugular venous pressure
- Left ventricular ejection fraction (LVEF) ≥50% on transthoracic echocardiography
- Objective evidence of structural heart disease (left ventricular hypertrophy or left atrial enlargement) and/or diastolic dysfunction
- Willingness to provide informed written consent

Exclusion Criteria

Patients were excluded if they had:

- Left ventricular ejection fraction <50%
- Significant primary valvular heart disease (moderate to severe)
- Constrictive pericarditis or restrictive cardiomyopathy
- Congenital heart disease
- Acute coronary syndrome within the preceding three months
- Advanced hepatic disease, active malignancy, or systemic inflammatory disease
- Inadequate echocardiographic windows or incomplete clinical data

Diagnostic Criteria for HFpEF

Modern guideline-based criteria, such as the existence of heart failure symptoms and signs, retained left ventricular systolic performance, and objective evidence of diastolic dysfunction or increased filling pressures, were used to diagnose HFpEF. The diagnosis was supported by echocardiographic data such as tricuspid regurgitation velocity, left atrial volume index (LAVI), left ventricular mass index (LVMI), and E/e′ ratio.

Data Collection

A structured case record form was used to collect detailed patient information, including:

- **Demographic variables:** age, sex
- **Clinical variables:** New York Heart Association (NYHA) functional class, blood pressure, heart rate, body mass index
- **Comorbidities:** hypertension, diabetes mellitus, obesity, chronic kidney disease, atrial fibrillation, coronary artery disease

- **Laboratory parameters:** hemoglobin, serum creatinine, estimated glomerular filtration rate, fasting blood glucose, lipid profile, and natriuretic peptide levels, where available
- **Electrocardiographic findings:** rhythm abnormalities, evidence of left ventricular hypertrophy, conduction defects

Echocardiographic Assessment

All patients underwent comprehensive transthoracic echocardiography using standard equipment by experienced cardiologists. Measurements were obtained according to the recommendations of the American Society of Echocardiography. Parameters assessed included:

- Left ventricular ejection fraction (biplane Simpson's method)
- Left ventricular wall thickness and mass index
- Left atrial diameter and volume index
- Mitral inflow velocities (E and A waves)
- Tissue Doppler-derived e′ velocity
- E/e′ ratio as an estimate of left ventricular filling pressure
- Pulmonary artery systolic pressure derived from the tricuspid regurgitation jet

Phenotypic Cluster Analysis

Using specific clinical, laboratory, and echocardiographic characteristics, unsupervised cluster analysis was used to identify unique HFpEF phenotypes. The research included variables that are frequently linked to HFpEF heterogeneity, including age, sex, blood pressure, body mass index, presence of diabetes, renal function, atrial fibrillation, left atrial size, left ventricular mass, and diastolic indices. Clinically significant phenotypes were identified by clustering patients according to commonalities across these characteristics.

Statistical Analysis

Standard statistical software was used to examine the data once it was entered into a secure database. Depending on the distribution, continuous variables were expressed as either the median with interquartile range or the mean ± standard deviation. Frequencies and percentages were used to express categorical variables. Appropriate parametric or non-parametric tests were used to compare the observed phenotypic groups. Statistical significance was defined as a p-value of less than 0.05.

Ethical Considerations

The Institutional Ethics Committee examined and approved the study protocol. Prior to participation, each subject provided written informed consent. All operations were carried out in compliance with the Declaration of Helsinki's principles, and patient anonymity was upheld throughout the study.

Results

The final analysis comprised 100 patients with a diagnosis of heart failure with preserved ejection fraction (HFpEF). All enrolled individuals had access to complete clinical, laboratory, and echocardiographic data.

Baseline Demographic and Clinical Characteristics

The majority of patients were in the older age category, with a mean age of 63.4 ± 9.8 years. There was a minor preponderance of women. The most common comorbidity was hypertension, which was followed by obesity and diabetes mellitus. Advanced functional impairment was seen in a sizable percentage of patients.

Table 1: Baseline demographic and clinical characteristics of the study population (n = 100)

Variable	Value
Age (years), mean ± SD	63.4 ± 9.8
Female sex, n (%)	56 (56%)
Body mass index (kg/m²), mean ± SD	27.8 ± 4.6
NYHA class II, n (%)	32 (32%)
NYHA class III, n (%)	48 (48%)
NYHA class IV, n (%)	20 (20%)

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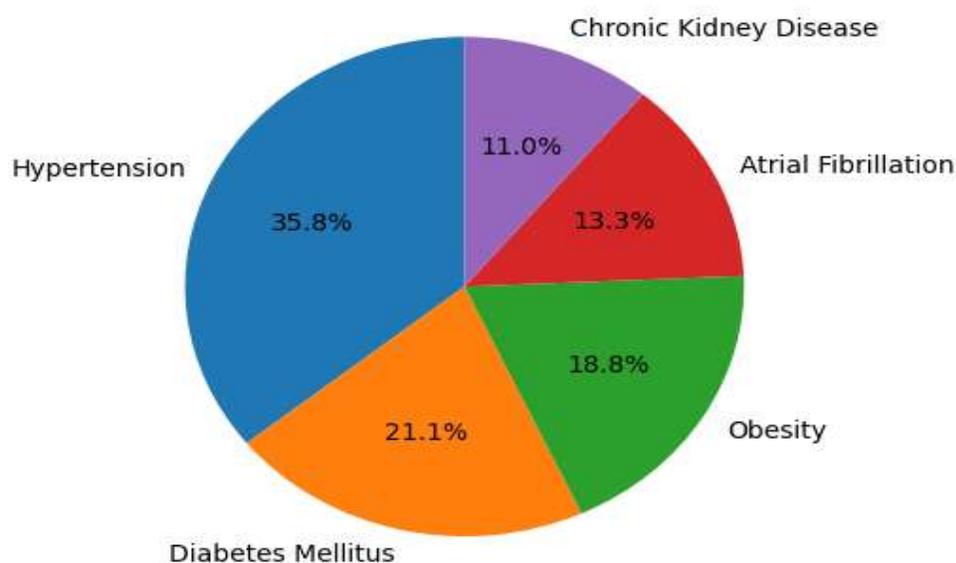|	
Hypertension, n (%)	78 (78%)
Diabetes mellitus, n (%)	46 (46%)
Obesity, n (%)	41 (41%)
Chronic kidney disease, n (%)	24 (24%)
Atrial fibrillation, n (%)	29 (29%)
Coronary artery disease, n (%)	21 (21%)

Fig 1. Prevalence of major comorbidities in HFpEF patients

Laboratory Profile

Renal impairment and anemia were frequent findings. Due to the substantial burden of cardiorenal involvement in HFpEF, approximately 25% of patients had a lower estimated glomerular filtration rate.

Table 2: Laboratory parameters of the study population

Parameter	Mean ± SD
Hemoglobin (g/dL)	11.8 ± 1.6
Serum creatinine (mg/dL)	1.32 ± 0.46
eGFR (mL/min/1.73 m²)	61.5 ± 18.2
Fasting blood glucose (mg/dL)	128 ± 36

| Total cholesterol (mg/dL)	186 ± 42

Echocardiographic Characteristics

The left ventricle's systolic function was maintained in every patient. Nonetheless, diastolic dysfunction and structural remodeling were noticeable. Chronically high filling pressures were often indicated by left atrial enlargement and an increased left ventricular mass index.

Table 3: Echocardiographic parameters

Parameter	Mean ± SD
LVEF (%)	58.6 ± 5.2
Left atrial volume index (mL/m²)	42.8 ± 9.6
LV mass index (g/m²)	121.4 ± 24.8
E/e′ ratio	15.6 ± 4.2
Pulmonary artery systolic pressure (mmHg)	41.2 ± 8.9

Phenotypic Cluster Analysis

Based on demographic, clinical, laboratory, and echocardiographic factors, unsupervised cluster analysis revealed three unique phenotypic groups among HFpEF patients.
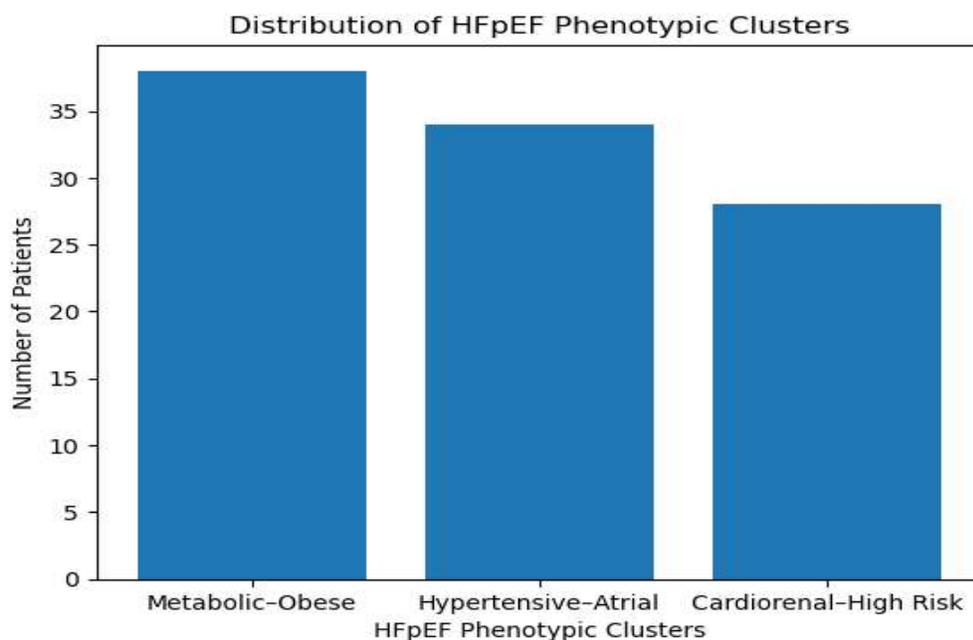
Fig 2. Distribution of HFpEFphenotypic clusters

Cluster 1: Metabolic–Obese Phenotype (n = 38)

Younger age, a higher body mass index, a high prevalence of obesity and diabetes, and somewhat raised diastolic

filling pressures were characteristics of this cluster. Most of the patients in this group had NYHA class II–III symptoms.

### Cluster 2: Hypertensive–Atrial Remodeling Phenotype (n = 34)

Many of the patients in this cluster were older women with a significant incidence of atrial fibrillation and chronic hypertension. Important characteristics included substantial left atrial enlargement and high pulmonary artery pressures.

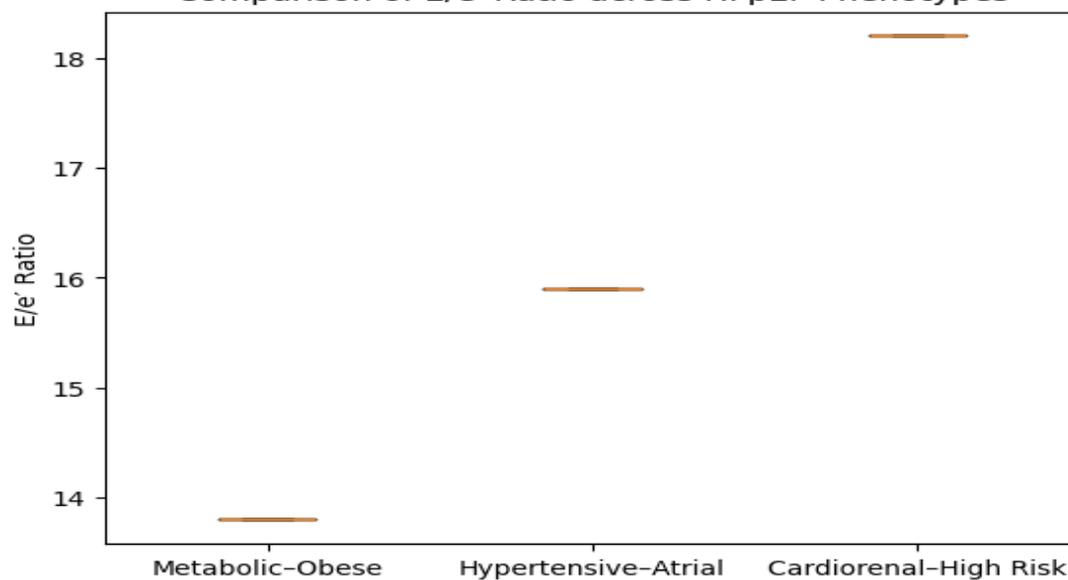### Cluster 3: Cardiorenal–High-Risk Phenotype (n = 28)

Older individuals with severe diastolic dysfunction, anemia, a higher NYHA class, and considerable renal failure made up this cluster. Hospitalization rates and symptom load were higher among these patients.

Table 4: Comparison of clinical and echocardiographic variables across HFpEF phenotypic clusters

Variable	Cluster 1 (n=38)	Cluster 2 (n=34)	Cluster 3 (n=28)
Age (years)	59.2 ± 8.1	64.8 ± 9.4	68.9 ± 7.6
Female sex (%)	45%	68%	57%
BMI (kg/m²)	30.6 ± 3.8	26.4 ± 4.2	24.8 ± 3.9
Hypertension (%)	71%	91%	75%
Diabetes (%)	68%	32%	36%
Atrial fibrillation (%)	18%	47%	25%
eGFR (mL/min)	71.2 ± 15.4	62.6 ± 16.8	49.3 ± 14.1
LAVI (mL/m²)	38.1 ± 7.4	47.6 ± 8.9	44.2 ± 9.1
E/e′ ratio	13.8 ± 3.1	15.9 ± 4.0	18.2 ± 4.6
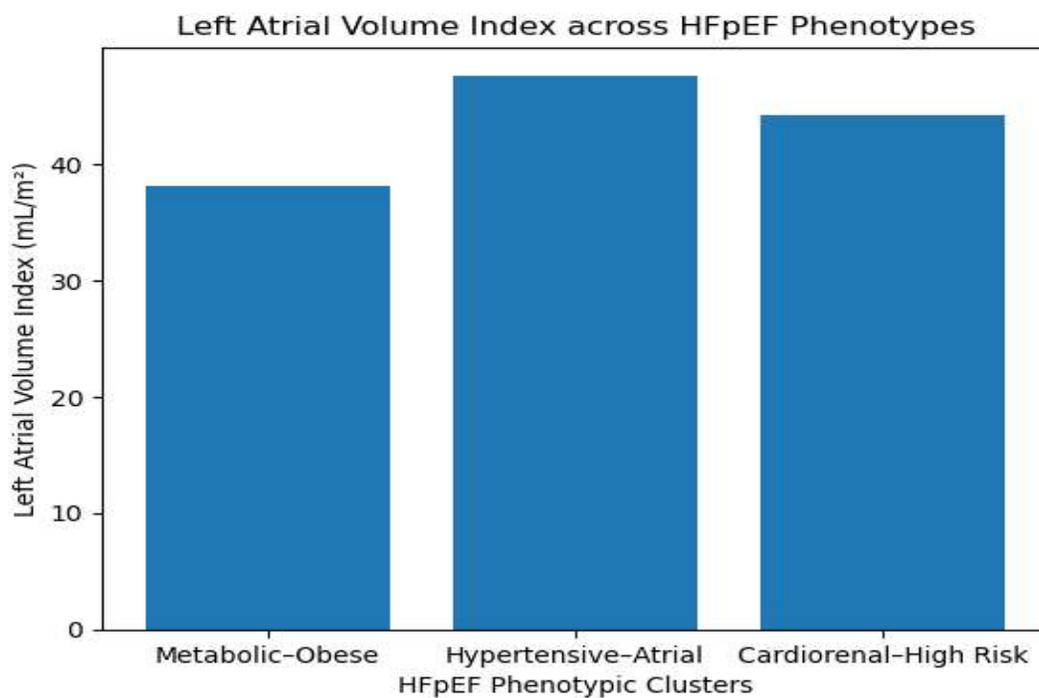
Fig 3. Left atrial volume index across FFpEF phenotypes

Fig 4. Comparison of the E/é ratio across HFpEF phenotypes

Discussion

The current study used cluster analysis to identify unique clinical morphologies and assessed the frequency and phenotypic heterogeneity of heart failure with preserved ejection fraction (HFpEF) in a tertiary care setting. The results support the current understanding of HFpEF as a heterogeneous illness rather than a homogeneous disease entity, with notable differences in diastolic function, heart anatomy, comorbidity burden, and demographics among patient subgroups.

HFpEF was mostly seen in older people in the current sample, with a little female preponderance. This demographic pattern is in line with global epidemiological data showing that women and older persons are disproportionately affected by HFpEF, most likely as a result of sex-specific variations in inflammatory responses, vascular stiffness, and myocardial remodeling [13]. The development of HFpEF in this population is largely influenced by age-related myocardial fibrosis, decreased ventricular relaxation, and increased arterial stiffness.

Over 75% of the study population had hypertension, which was shown to be the most common comorbidity. Long-term hypertension-induced chronic pressure overload causes concentric left ventricular hypertrophy, increased myocardial stiffness, and poor diastolic filling, all of which are essential to the pathogenesis of HFpEF [14]. This cohort's high incidence of hypertension is indicative of both regional cardiovascular risk profiles and its critical function as a cause of HFpEF, especially in low- and middle-income nations.

Obesity and diabetes mellitus were also very common, especially in the metabolic-obese phenotypic cluster. This finding lends credence to the developing theory that HFpEF is not only a cardiac condition but also a systemic metabolic-inflammatory problem [15]. Myocardial fibrosis and reduced relaxation are caused by inflammatory mediators originating from adipose tissue, insulin resistance, and microvascular endothelial dysfunction. Despite having largely intact systolic function, obese HFpEF patients have greater exercise intolerance, higher filling pressures, and increased plasma volume, according to earlier large-scale studies [16].

This study's echocardiographic evaluation consistently showed raised E/e′ ratios, increased left ventricular mass index, and left atrial enlargement, all of which point to persistently high left ventricular filling pressures. In particular, the left atrial volume index was a reliable indicator of chronic illness and persistent diastolic dysfunction. Multicenter HFpEF registries have documented similar echocardiographic remodeling patterns, which are linked to poorer functional class and unfavorable outcomes [17].

This study's use of unsupervised cluster analysis to find clinically significant HFpEF characteristics is one of its main strengths. Each of the three separate phenotypic clusters that were found represented a different pathophysiological route. Higher body mass index, a high frequency of diabetes, and somewhat raised diastolic pressures were characteristics of the metabolic–obese phenotype. This profile is similar to those seen in earlier seminal research in which obese HFpEF patients had increased symptom burden and systemic inflammation but relatively retained renal function [18].

Elderly women with chronic hypertension and a high incidence of atrial fibrillation made up the majority of the hypertensive atrial remodeling phenotype. In HFpEF, atrial fibrillation both contributes to and results from the disease's progression, which raises filling pressures even more and reduces the atrial contribution to ventricular filling. According to earlier research, HFpEF patients with atrial fibrillation have worse quality of life and greater hospitalization rates than those in sinus rhythm [19]. The significant left atrial enlargement shown in this cluster emphasizes how atrial cardiomyopathy is a key component of HFpEF.

The most clinically severe grouping was the cardiorenal–high-risk phenotype, which was marked by advanced age, significant diastolic insufficiency, anemia, and renal dysfunction. The bidirectional nature of the cardiorenal syndrome, in which neurohormonal activation, volume overload, and endothelial dysfunction sustain both cardiac and renal pathology, is reflected in the coexistence of chronic kidney disease with HFpEF [20]. This cluster's prognostic relevance was highlighted by the greatest rates of hospitalization and symptom load.

There are significant clinical ramifications to the discovery of these phenotypic clusters. Due to the diversity of patient populations included in clinical studies, traditional HFpEF therapy approaches have mostly failed. Clinicians may be able to customize treatments using phenotype-guided approaches, such as strict volume and renal function management in cardiorenal phenotypes, rhythm or rate control techniques in atrial fibrillation-dominant phenotypes, and rigorous metabolic control in obese phenotypes [21]. Newer treatment medicines, such as

sodium-glucose cotransporter-2 inhibitors, may improve distinct HFpEF subtypes, according to emerging data [22].

The results are especially pertinent from the standpoint of Indian healthcare. This cohort's high prevalence of diabetes, hypertension, and renal failure is indicative of larger demographic shifts taking place in the area. Patients frequently come at advanced stages of disease due to limited access to early preventive care, underscoring the need for early detection of high-risk phenotypes at the primary and secondary care levels [23].

The study has some shortcomings despite its advantages. The results may not be as broadly applicable as they could be due to the single-center design and small sample size. Furthermore, there was inconsistent availability of biomarker data, such as natriuretic peptides, which could have improved phenotypic classification. However, the study contributes to the scant Indian literature on HFpEF phenotyping and offers useful real-world data from a tertiary care context.

In conclusion, the current investigation shows that HFpEF in a tertiary care population is a very diverse illness made up of unique phenotypic clusters with different comorbidity profiles and clinical severity. Understanding these characteristics is crucial for enhancing risk assessment, directing individualized treatment plans, and creating upcoming clinical studies that are suited to HFpEF subgroups.

Conclusion

In the tertiary care context, heart failure with intact ejection fraction is a prevalent and clinically relevant kind of heart failure that is distinguished by significant variation in patient profiles, comorbidities, and cardiac remodeling patterns. In the current investigation, atrial fibrillation, diabetes mellitus, obesity, hypertension, and renal dysfunction emerged as major related comorbidities with HFpEF, which primarily impacted women and the elderly.

Phenotypic cluster analysis was used to identify discrete HFpEF subgroups with particular echocardiographic and clinical features. Variable symptom load and clinical risk resulted from these phenotypes' differences in metabolic burden, degree of atrial and ventricular remodeling, renal function, and severity of diastolic dysfunction. The discovery of a high-risk cardiorenal phenotype emphasizes how important it is to identify and treat this subgroup as soon as possible.

The results suggest a move toward phenotype-driven assessment and management and draw attention to the drawbacks of a unified treatment approach in HFpEF.

Patients with HFpEF may benefit from improved risk classification, more individualized treatment plans, and better outcomes if clinical phenotyping is integrated into standard practice. To confirm these phenotypic classifications and to direct the development of targeted medicines in a variety of groups, more extensive, multicenter trials including biomarker and longitudinal outcome data are necessary.

Limitations

This study has certain limitations. Being a single-center study with a relatively small sample size, the findings may not be fully generalizable to broader populations. Biomarker data, such as natriuretic peptides, were not consistently available for all patients. Additionally, long-term follow-up outcomes were not assessed.

Generalizability

Despite being a single-center study, the findings are relevant to other tertiary care centers in low- and middle-income countries with similar patient demographics and comorbidity profiles. The identified phenotypic clusters reflect commonly encountered HFpEF presentations in real-world clinical practice.

Recommendations

Routine phenotypic characterization of HFpEF patients should be encouraged in tertiary care settings to guide individualized therapy. Larger multicenter studies incorporating biomarkers and longitudinal outcomes are recommended to validate these phenotypes.

List of abbreviations

- HFpEF – Heart Failure with Preserved Ejection Fraction
- HF – Heart Failure
- LVEF – Left Ventricular Ejection Fraction
- LAVI – Left Atrial Volume Index
- LVMI – Left Ventricular Mass Index
- NYHA – New York Heart Association
- eGFR – Estimated Glomerular Filtration Rate

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Author contributions
PK: Conceptualization, data collection, analysis, manuscript drafting
RVP: Study supervision, critical revision, final approval of manuscript

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References
1. Owan TE, Hodge DO, Herges RM, Jacobsen SJ, Roger VL, Redfield MM. Trends in prevalence and outcome of heart failure with preserved ejection fraction. New England Journal of Medicine. 2006 Jul 20;355(3):251-9.
2. Borlaug BA, Paulus WJ. Heart failure with preserved ejection fraction: pathophysiology, diagnosis, and treatment. European Heart Journal. 2011 Mar 1;32(6):670-9.
3. Zile MR, Baicu CF, Gaasch WH. Diastolic heart failure—abnormalities in active relaxation and passive stiffness of the left ventricle. New England Journal of Medicine. 2004 May 6;350(19):1953-9.
4. Shah KS, Xu H, Matsouaka RA, Bhatt DL, Heidenreich PA, Hernandez AF, Devore AD, Yancy CW, Fonarow GC. Heart failure with preserved, borderline, and reduced ejection fraction: 5-year outcomes. Journal of the American College of Cardiology. 2017 Nov 14;70(20):2476-86.
5. Redfield MM. Heart failure with preserved ejection fraction. New England Journal of Medicine. 2016 Nov 10;375(19):1868-77.
6. Shah SJ. Precision medicine for heart failure with preserved ejection fraction: an overview. Journal of cardiovascular translational research. 2017 Jun;10(3):233-44.
7. Lam CS, Donal E, Kraigher-Krainer E, Vasan RS. Epidemiology and clinical course of heart failure with preserved ejection fraction. European journal of heart failure. 2011 Jan;13(1):18-28.
8. Shah SJ, Katz DH, Selvaraj S, Burke MA, Yancy CW, Gheorghiade M, Bonow RO, Huang CC, Deo RC. Phenomapping for novel classification of heart failure with preserved ejection fraction. Circulation. 2015 Jan 20;131(3):269-79.
9. Kao DP, Lewsey JD, Anand IS, Massie BM, Zile MR, Carson PE, McKelvie RS, Komajda M, McMurray JJ, Lindenfeld J. Characterization of subgroups of heart failure patients with preserved ejection fraction with possible implications for prognosis and treatment response. European journal of heart failure. 2015 Sep;17(9):925-35.
10. Tromp J, Shen L, Jhund PS, Anand IS, Carson PE, Desai AS, Granger CB, Komajda M, McKelvie RS, Pfeffer MA, Solomon SD. Age-related characteristics and outcomes of patients with heart failure with preserved ejection fraction. Journal of the American College of Cardiology. 2019 Aug 6;74(5):601-12.
11. Savarese G, Lund LH. Global public health burden of heart failure. Cardiac failure review. 2017 Apr;3(1):7.
12. Gupta R, Xavier D. Hypertension: The most important non-communicable disease risk factor in India. Indian Heart Journal. 2018 Jul 1;70(4):565-72.
13. Dunlay SM, Roger VL, Redfield MM. Epidemiology of heart failure with preserved ejection fraction. Nature Reviews Cardiology. 2017 Oct;14(10):591-602.
14. Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP. Prognostic implications of echocardiographically determined left ventricular mass in the Framingham Heart Study. New England Journal of Medicine. 1990 May 31;322(22):1561-6.
15. Paulus WJ, Tschöpe C. A novel paradigm for heart failure with preserved ejection fraction: comorbidities drive myocardial dysfunction and remodeling through coronary microvascular

endothelial inflammation. Journal of the American college of cardiology. 2013 Jul 23;62(4):263-71.

16. Obokata M, Reddy YN, Pislaru SV, Melenovsky V, Borlaug BA. Evidence supporting the existence of a distinct obese phenotype of heart failure with preserved ejection fraction. Circulation. 2017 Jul 4;136(1):6-19.

17. Tsang TS, Barnes ME, Gersh BJ, Bailey KR, Seward JB. Left atrial volume as a morphophysiologic expression of left ventricular diastolic dysfunction and relation to cardiovascular risk burden. The American journal of cardiology. 2002 Dec 15;90(12):1284-9.

18. Upadhya B, Kitzman DW. Heart failure with preserved ejection fraction in older adults. Tresch and Aronow's Cardiovascular Disease in the Elderly. 2019 Feb 6:422-41.

19. Santhanakrishnan R, Wang NA, Larson MG, Magnani JW, McManus DD, Lubitz SA, Ellinor PT, Cheng S, Vasan RS, Lee DS, Wang TJ. Atrial fibrillation begets heart failure and vice versa: temporal associations and differences in preserved versus reduced ejection fraction. Circulation. 2016 Feb 2;133(5):484-92.

20. Ronco C, McCullough P, Anker SD, Anand I, Aspromonte N, Bagshaw SM, Bellomo R, Berl T, Bobek I, Cruz DN, Daliento L. Cardio-renal syndromes: report from the consensus conference of the acute dialysis quality initiative. European Heart Journal. 2010 Mar 1;31(6):703-11.

21. Solomon SD, McMurray JJ, Anand IS, Ge J, Lam CS, Maggioni AP, Martinez F, Packer M, Pfeffer MA, Pieske B, Redfield MM. Angiotensin–neprilysin inhibition in heart failure with preserved ejection fraction. New England Journal of Medicine. 2019 Oct 24;381(17):1609-20.

22. Anker SD, Butler J, Filippatos G, Ferreira JP, Bocchi E, Böhm M, Brunner–La Rocca HP, Choi DJ, Chopra V, Chuquiure-Valenzuela E, Giannetti N. Empagliflozin in heart failure with a preserved ejection fraction. New England Journal of Medicine. 2021 Oct 14;385(16):1451-61.

23. D. Huffmann, M.A., Prabhakaran D. Heart failure: epidemiology and prevention in India. The National Medical Journal of India. 2010 Sep;23(5):283.

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