

A study of association between heart failure with preserved ejection fraction with hypertension and diabetes mellitus



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ABSTRACT

Background: Heart failure is a common clinical entity which we come across in our daily practice and accounts for significant mortality and morbidity. The basic pathophysiology lies in the inability of the heart to pump adequate blood (output) to meet the demands of circulation/tissue or can do so only at the expense of elevated left ventricular filling pressure. Among various types of heart failure, heart failure with preserved ejection fraction (HFpEF) is still a poorly understood entity and several comorbidities such as hypertension, diabetes, coronary artery disease, obesity, and CKD are common association of HFpEF. Diabetes causes heart failure by increasing the risk of CAD and by direct injury to myocardium (cardiomyopathy). Hence, in this cross-sectional observational study, we assess the cardiovascular risk factors such as hypertension and diabetes mellitus in association with HFpEF. **Aims and Objectives:** This study aims to establish the hypothesis that hypertension and diabetes mellitus are associated with a predictor of HFpEF. **Materials and Methods:** Ninety patients were selected. NTproBNP, HbA1C, FBS, PPBS level, and blood pressure was measured and echocardiogram was performed to assess ratio of transmitral flow velocity and annular velocity (E/E'); left ventricular end-diastolic pressure; and left ventricular ejection fraction (LVEF). **Results:** The mean age was 64 ± 7 . Forty-two (46.67%) were men and 48 (53.33%) were female. Hypertension was present in 73 (81.11%) and diabetes in 44 (48.89%). E/E', a parameter of LV diastolic function, showed positive correlation to both risk factors in study ($r=0.653$, $p<0.001$). Linear regression indicated that E/E' (β -coefficient=0.845, $p<0.001$) was significantly associated with the presence of risk factors. **Conclusion:** The data show that the prevalence of HTN and DM is significantly higher in patients with HFpEF and establishes a strong association between duration of HTN and DM with symptomatic HFpEF.

Key words: Heart failure with preserved ejection fraction; Diastolic heart failure; NTproBNP; Ventricular ejection fraction; Diabetes complications; Hypertension.

INTRODUCTION

Heart failure is a clinical syndrome that results from structural or functional impairment of ventricular filling or ejection of blood, which, in turn, leads to the cardinal clinical symptoms of dyspnea and fatigue and signs of heart failure, that is, edema and rales.¹ Based on underlying mechanism, it could be divided into heart failure with preserved ejection fraction (left ventricular ejection fraction

[LVEF] >50%, that is, heart failure with preserved ejection fraction [HFpEF]) or heart failure with mid-range ejection fraction (LVEF 40–49%, i.e., HFmrEF) or heart failure with reduced ejection fraction (LVEF <40%, i.e., HFrEF).² The number of cases of HFpEF has been increasing in the Western countries and consists more than 50% of total heart failure hospitalizations. The prevalence of HFpEF sharply increases with advancement of age, with a female predominance.³ There are limited data on heart failure in

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Indian population. Comparative data from Asian Heart Failure Registry showed that Indian patients with HFpEF were younger with mean age of 63.4 years in males and 46.4 years in females. Risk factors included hypertension (40.3%) and DM (28.8%). It has also been proved that HFpEF is prognostically as bad as HFrEF.⁴

Aims and objectives

To study the prevalence of HTN and DM in HFpEF.

MATERIALS AND METHODS

It was a prospective observational study among patients visiting outpatient department and IPD of Jagannath Gupta Institute of Medical Sciences and Hospital, a Medical College near Kolkata from 2020 to 2021 seeking advice in the Gen Medicine Dept. The study was pre-approved by Institutional Ethics Committee and the study was conducted after obtaining permission accordingly. Sample size was 90 patients between 30 and 90 years both male and female.

The risk factors in study, that is, hypertension and diabetes were based on the following criteria

1. Hypertension, that is, systolic blood pressure >140 mmHg and/or diastolic blood pressure >90 mmHg at least on two occasions or receiving antihypertensive drug
2. Diabetes, that is, history of type 2 diabetes diagnosed with American Diabetic Association criteria, that is, symptoms of diabetes plus random blood glucose concentration more than or equal to 200 mg/dl or, fasting plasma glucose more than or equal to 126 mg/dl or, glycosylated hemoglobin more than or equal to 6.5% or, 2 h plasma glucose more than or equal to 200 mg/dl during an oral glucose tolerance test or were on medications for diabetes.⁵

Inclusion criteria

1. The diagnosis of HFpEF has been made based on the following criteria^{6,7}
 - Signs and symptoms of heart failure by clinical examination
 - LVEF >50% by echocardiography
 - Echocardiographical evidence consistent with structural or functional anomaly including left diastolic dysfunction/increased left ventricular filling pressure or raised serum NTproBNP.
2. Age more than 30 years and <90 years.

Exclusion criteria

1. Presence of structural heart diseases, for example, hemodynamically significant valvular heart disease, prosthetic valve replacement, H/O HOCM, arrhythmias, implanted pacemaker, post-CABG, or peripheral vascular diseases

2. Pre-existing renal disease/CKD (eGFR < 60 ml/min)
3. History of cocaine or heroin use in the past 6 months
4. History of significant alcohol intake
5. Body mass index (BMI) <18.5 or >40
6. Severe anemia (Hb < 8 g %).

The patients who satisfied inclusion and exclusion criteria have been identified and included in this study. Proper history including demographic details, specific comorbidities, duration of HTN and DM, and medication details was taken and detailed clinically examination was done. For further clinical evaluation, a 12-lead ECG with long rhythm strip, straight X-ray skiagram of chest, and routine blood investigations such as complete blood count, renal function test, glycosylated hemoglobin, fasting plasma glucose, and ser. NTproBNP was performed.

Finally, transthoracic echocardiogram was performed with M-mode, 2D (two-dimensional), Doppler, and tissue Doppler imaging using standard techniques. At first, the following parameters were measured by M-mode: Interventricular septal thickness, left ventricular posterior wall thickness, end-systolic dimension of left atrium (LAD), and left ventricular internal diameter (LVID) at end diastole (LVIDd) and end systole (LVIDs). The LVEF was estimated by 2D approximation and wall motion abnormalities were noted, if any. Next, the following LV diastolic function parameters were measured by recording transmitral flow velocity using Doppler echocardiography, that is, peak early-diastolic transmitral flow velocity (E), peak late-diastolic transmitral flow velocity (A), deceleration time, and E/A ratio. Then, tissue Doppler echocardiography was performed at medial mitral annulus. Peak early (E') and late (A') diastolic mitral annular velocities and their ratio (E'/A') were measured. The ratio of transmitral flow velocity and annular velocity (E/E') was calculated to assess LV end-diastolic pressure (LVEDP) which was used as a parameter of LV diastolic dysfunction. Elevated filling pressure was based on E/E' ratio >10. Diastolic dysfunction was classified into four grades as per ASE guidelines⁸ as tabulated (Table 1).

Statistical analysis

Quantitative data thus obtained have been analyzed and exported to statistical software SPSS V.27-2020 for proper interpretation. The continuous variables will be presented as mean ± standard deviation, performed by Student's t-test or variance analysis. Percentage analysis was used to describe distribution of demographic variables. The association between HFpEF with diabetes and hypertension was obtained by Chi-square test separately and binary logistic regression analysis was done between predictor variable and dichotomous variable (hypertensive/diabetic or not). P < 0.05 was considered as statistically significant.

Table 1: LV diastolic dysfunction as per LV relaxation, filling pressures, and 2D and Doppler findings⁹

Echo parameter	Normal	Grade I	Grade II	Grade III
LV relaxation	Normal	Impaired	Impaired	Impaired
LAP	Normal	Low or normal	Elevated	Elevated
Mitral E/A ratio	≥0.8	≤0.8	>0.8 to <2	>2
Average E/e' ratio	<10	<10	10–14	>14
Peak TR velocity (m/s)	<2.8	<2.8	>2.8	>2.8
LA volume index	Normal	Normal or increased	Increased	Increased

RESULTS

A total of 90 patients between 30 and 90 years both male and female who met the inclusion criteria were selected by simple random sampling. Majority belonged to the age group of 60–70 years with mean age 64 ± 7 years. Forty-two (46.67%) were men and 48 (53.33%) were female. Hypertension was present in 73 (81.11%) and diabetes in 44 (48.89%) patients. Majority had ejection fraction between 55 and 60% and mean was $58.3 \pm 5.3\%$; mostly with normal or near normal systolic function. The elevated mean LVMI indicated LV hypertrophy and decreased mean E/A indicated LV diastolic dysfunction, often produced by hypertension or diabetes. Mean E/E' was 9.78 ± 4.4 . All variables were normally distributed by Kolmogorov–Smirnov goodness-of-fit test other than LVEF, E/A, E'/A', and E/E'.

Grade-2 (DD2) diastolic dysfunction patients were maximum in number (44, i.e., 48.89%) followed by Grade-1 (DD1) diastolic dysfunction (38, i.e., 42.22%), and only eight persons (i.e., 8.89%) had Grade-3 (DD3) diastolic dysfunction (Figure 1). The prevalence of comorbidities in study (i.e., hypertension or diabetes) is progressively increasing along with the severity of diastolic dysfunction (from Grade-1 to Grade-2) to a fact that all patients having DD-3 were having at least one comorbidity and most of them have both (Figure 2). Apart from this, age of the patient and duration of hypertension/diabetes seemed to be an important determining factor.

DISCUSSION

In our study, high prevalence of hypertension (and also diabetes) in HFpEF was the most significant finding and signifies a strong etiological association (Figure 3). Patients having longer duration of HTN/DM or having both together were shown to have advanced DD with elevated LVEDP along with advancement of age. These findings are consistent with other large scale trials where hypertension has been identified as the commonest risk factor¹⁰ presenting in 50–90% of patients of HFpEF, and prevalence is even more than that of HFrEF.^{11,12} To study individual etiological association of HTN/DM with HFpEF, we also excluded certain other confounding risk factors such as chronic kidney disease, atrial fibrillation,

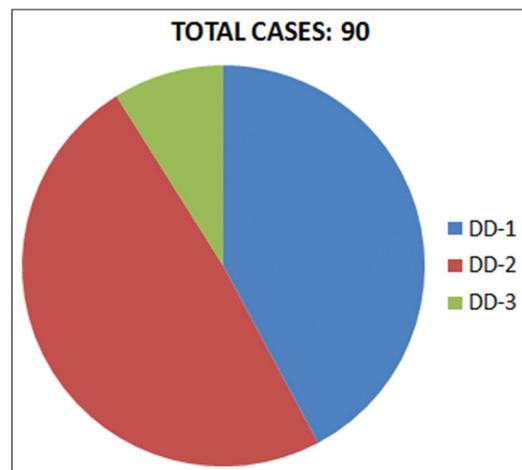


Figure 1: Severity of diastolic dysfunction

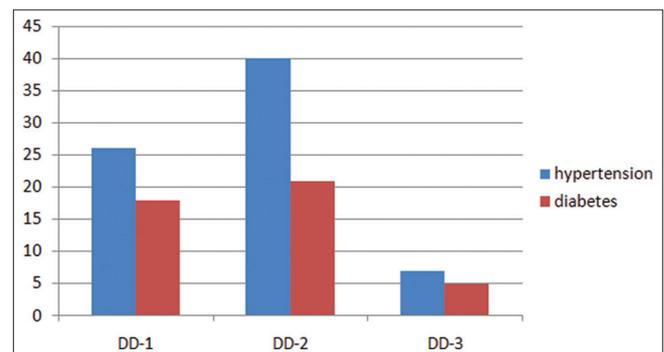


Figure 2: Comparison of number of cases

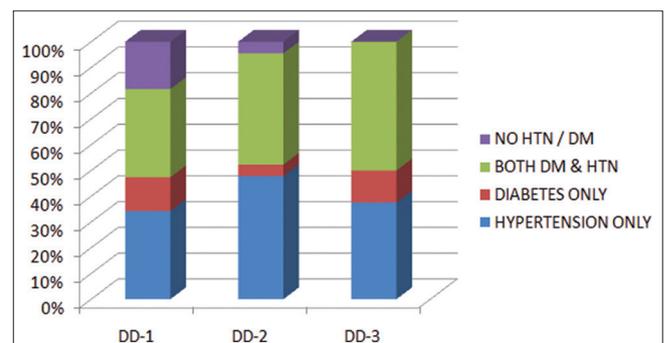


Figure 3: Relative prevalence of comorbidity with severity of diastolic dysfunction

and coronary artery disease which are a complication of HTN/DM itself and also being an important risk factor for HFpEF.^{13,14}

Limitations of the study

E/E' was measured at septal mitral annulus. However, some studies recommended measuring velocities of lateral mitral annulus or averaged velocities of lateral and septal mitral annulus.

The inherent variability of risk factors such as alcohol intake, smoking, exercise, medications, and other unknown variables was not included in the study.

Finally, a multicenter trial with larger population is needed to further investigate etiological factors of HFpEF and its association with comorbidities.

CONCLUSION

Etiology and treatment approach of HFpEF differs from that of HFrEF. Moreover, HTN and DM are the modern day epidemics. Hence, if further studied by multicenter, prospective, longitudinal studies, this association may be used to identify the population at risk for HFpEF and to establish new targets for the management of diastolic dysfunction at the herald of its onset and prevention of symptomatic HFpEF resulting in longer survival and better prognosis.

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To find out the association between risk factors (i.e. HTN and DM) with the severity of diastolic dysfunction as a predictor of HFpEF.

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SS- Concept and design of study; and guidance for preparation of manuscript; **JB-** Review of literature, preparation of draft, and interpretation of result; **SG-** Collection of data and interpretation of results, preparation of 1st draft.

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