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Efficacy of Empagliflozin versus Dapagliflozin in Heart Failure with Preserved Ejection Fraction: A Randomized Controlled Trial

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ABS TRAC T

***Background*:** Heart failure with preserved ejection fraction (HFpEF) accounts for nearly half of all heart failure cases and remains a therapeutic challenge. Sodium-glucose cotransporter-2 (SGLT2) inhibitors have emerged as the first pharmacologic class to demonstrate consistent benefit in this population. However, head-to-head comparative data between empagliflozin and dapagliflozin in HFpEF remain scarce, particularly in South Asian cohorts. The present trial was undertaken to compare the efficacy and tolerability of these two agents in symptomatic HFpEF patients over a one-year follow-up. ***Methods*:** A prospective, randomized, open-label, parallel-group trial was conducted at a tertiary care centre in Pakistan over twelve months. Sixty patients aged 40–75 years with left ventricular ejection fraction ≥50%, NYHA class II–III symptoms, and elevated NT-proBNP were enrolled and randomized 1:1 to empagliflozin 10 mg once daily (n=30) or dapagliflozin 10 mg once daily (n=30) on top of guideline-directed therapy. Co-primary outcomes were change in Kansas City Cardiomyopathy Questionnaire–Clinical Summary Score (KCCQ-CS) and 6-minute walk distance (6MWD) at 12 months. Secondary outcomes included NT-proBNP reduction, NYHA class improvement, heart failure hospitalization, and adverse events. Intention-to-treat analysis was performed using SPSS v26; $p<0.05$ was considered significant. ***Results*:** Mean age was 62.4±8.1 years; 56.7% were female. KCCQ-CS improved by 14.8±5.6 points with empagliflozin and 13.9±5.9 points with dapagliflozin (p=0.547). The 6MWD increased by 48.7±18.2 m and 45.3±19.6 m, respectively (p=0.491). NT-proBNP fell by 31.2% versus 28.7% (p=0.612). Heart failure hospitalization occurred in 3 (10.0%) and 4 (13.3%) patients (p=0.687). Genitourinary infections were the most frequent adverse event (10.0% vs 13.3%; p=0.687). No deaths occurred. ***Conclusion*:** Empagliflozin and dapagliflozin produced comparable and clinically meaningful improvements in symptoms, functional capacity, and natriuretic peptide levels in HFpEF, with similar safety profiles, supporting interchangeability within the SGLT2 inhibitor class.

Keywords: *HFpEF, Empagliflozin, Dapagliflozin, SGLT2 Inhibitor, Randomized Controlled Trial, Pakistan.*

INTRODUCTION

Heart failure with preserved ejection fraction (HFpEF) has emerged as one of the most pressing cardiovascular epidemics of the twenty-first century. Once considered a diagnostic curiosity, it now accounts for approximately half of all heart failure cases globally, with prevalence rising in parallel with the ageing population and the expanding burden of obesity, hypertension, and type 2 diabetes mellitus [1]. Patients with HFpEF demonstrate morbidity and mortality comparable to those with heart failure with reduced ejection fraction (HFrEF), yet for nearly two decades therapeutic options remained conspicuously limited [2]. The pathophysiology is multifactorial, encompassing left ventricular diastolic dysfunction, impaired ventricular–arterial coupling, microvascular endothelial inflammation, myocardial fibrosis, and chronotropic incompetence, which together produce the cardinal manifestations of dyspnoea, exercise intolerance, and recurrent decompensation.

Until recently, multiple classes of agents that transformed outcomes in HFrEF—including angiotensin-converting enzyme inhibitors, angiotensin

receptor blockers, beta-blockers, and mineralocorticoid receptor antagonists—failed to convincingly reduce hard cardiovascular endpoints in HFpEF. The CHARM-Preserved, I-PRESERVE, TOPCAT, and PARAGON-HF trials each fell short of their primary endpoints despite mechanistically plausible hypotheses, leaving an evidence vacuum for a condition affecting tens of millions of patients worldwide [3]. This therapeutic stagnation was disrupted in 2021 with the publication of the EMPEROR-Preserved trial, which demonstrated that empagliflozin reduced the composite of cardiovascular death or heart failure hospitalization in patients with HFpEF by 21%, irrespective of diabetic status [4]. The benefit was driven primarily by a reduction in heart failure hospitalizations and was consistent across pre-specified subgroups.

Subsequently, the DELIVER trial extended these findings to dapagliflozin, demonstrating an 18% reduction in worsening heart failure or cardiovascular death among patients with mildly reduced or preserved ejection fraction [5]. Together, these landmark trials established sodium-glucose cotransporter-2 (SGLT2) inhibitors as the first and only pharmacological class to deliver consistent prognostic benefit across the entire ejection fraction spectrum, prompting major guideline bodies including the American College of Cardiology, American Heart Association, Heart Failure Society of America, and the European Society of Cardiology to issue Class I recommendations for their use in HFpEF [6].

The mechanisms underlying the cardiac benefits of SGLT2 inhibitors extend well beyond their original glucose-lowering indication. Proposed mechanisms include natriuresis and osmotic diuresis with preferential reduction in interstitial rather than intravascular fluid, improvement in myocardial energetics through enhanced ketone body utilization, attenuation of cardiac fibrosis and oxidative stress, reduction in epicardial adipose tissue inflammation, modulation of the sodium–hydrogen exchanger, and favourable effects on left ventricular mass and diastolic function [7]. These pleiotropic effects appear to converge on the pathophysiological substrate of HFpEF, providing a coherent biological rationale for the observed clinical benefit.

Despite the strength of the EMPEROR-Preserved and DELIVER trials individually, no large-scale randomized head-to-head comparison between empagliflozin and dapagliflozin has been performed in HFpEF, and meta-analytic synthesis of pooled data has shown broadly comparable but not identical effects, raising clinically relevant questions regarding interchangeability, dose-response, and patient-specific selection [8]. Subtle differences in selectivity for SGLT2 over SGLT1, plasma half-life, and pharmacokinetic profiles have been postulated, although their clinical translation remains uncertain. For practising clinicians, particularly in resource-constrained settings, the choice between agents is frequently influenced by cost, availability, and prescriber familiarity rather than evidence-based comparative efficacy.

South Asian populations bear a disproportionate burden of cardiometabolic disease, with earlier age of onset, higher prevalence of central obesity, and accelerated progression to heart failure compared with Western cohorts [9]. Pakistani patients in particular demonstrate a high prevalence of hypertension, diabetes, and ischaemic heart disease—all major contributors to HFpEF—yet are markedly underrepresented in pivotal cardiovascular outcome trials. Real-world local data evaluating the comparative performance of SGLT2 inhibitors in this population are therefore critically needed to guide formulary decisions and clinical practice. Furthermore, patient-reported outcomes such as the Kansas City Cardiomyopathy Questionnaire and objective functional measures such as the 6-minute walk distance, both of which were validated as core endpoints in the recent SGLT2 inhibitor trials, provide pragmatic, clinically meaningful endpoints suitable for single-centre comparative trials [10].

Against this background, the present randomized controlled trial was undertaken to directly compare the efficacy and tolerability of empagliflozin 10 mg with dapagliflozin 10 mg, both administered once daily on top of optimized guideline-directed medical therapy, in adults with symptomatic HFpEF over a one-year follow-up period at a tertiary care institution in Pakistan. The investigators hypothesized that the two agents would produce equivalent improvements in symptom burden, functional capacity, and natriuretic peptide levels, thereby strengthening the evidence base for class-level interchangeability within the SGLT2 inhibitor family.

Aims and Objectives

The present study aimed to compare the efficacy and tolerability of empagliflozin and dapagliflozin in adults with symptomatic heart failure with preserved ejection fraction over a twelve-month follow-up period at a tertiary care centre in Pakistan. The primary objective was to compare the change in Kansas City Cardiomyopathy Questionnaire–Clinical Summary Score and 6-minute walk distance from baseline to twelve months between the two treatment arms. Secondary objectives included evaluation of changes in N-terminal pro–B-type natriuretic peptide concentrations, improvement in New York Heart Association functional class, incidence of heart failure hospitalization, all-cause mortality, and adverse event profiles. The study also sought to assess the impact of both agents on selected echocardiographic indices of diastolic function and on metabolic and renal parameters in this population.

Materials and Methods

Study Design and Setting

This was a prospective, single-centre, open-label, parallel-group randomized controlled trial conducted in the Department of Cardiology of King Edward Medical University in Pakistan. The study was carried out over a period of twelve months, including patient enrolment, intervention, and follow-up phases. The protocol was approved by the Institutional Ethical Review Committee, and the study was conducted in accordance with the Declaration of Helsinki and the Pakistan Bioethics Guidelines. Written informed consent was obtained from every participant prior to enrolment.

Sample Size

A total of sixty patients were enrolled and randomized in a 1:1 ratio to receive either empagliflozin 10 mg once daily (n=30) or dapagliflozin 10 mg once daily (n=30). The sample size was determined as per the approved synopsis on the basis of feasibility, available institutional patient flow, and prior comparative HFpEF trials evaluating patient-reported and functional outcomes over a one-year period.

Inclusion Criteria

Patients were included if they were aged between 40 and 75 years; had a clinical diagnosis of heart failure with NYHA functional class II or III symptoms; demonstrated a left ventricular ejection fraction of ≥50% on transthoracic echocardiography; had elevated N-terminal pro–B-type natriuretic peptide concentrations (>125 pg/mL in sinus rhythm or >365 pg/mL in atrial fibrillation); and were already receiving optimized guideline-directed medical therapy for at least four weeks prior to enrolment.

Exclusion Criteria

Patients were excluded if they had a history of left ventricular ejection fraction <40% at any point; type 1 diabetes mellitus or recurrent diabetic ketoacidosis; estimated glomerular filtration rate <25 mL/min/1.73 m²; haemodynamically significant valvular heart disease; recent acute coronary syndrome, stroke, or coronary revascularization within three months; restrictive or hypertrophic cardiomyopathy, constrictive pericarditis, or infiltrative cardiac disease; active malignancy; pregnancy or lactation; prior use of any SGLT2 inhibitor; or known hypersensitivity to the study drugs.

Randomization and Blinding

Eligible participants were randomized in a 1:1 ratio to one of the two treatment arms using computer-generated random number sequences with allocation concealment via sealed opaque envelopes. The trial was open-label; however, outcome assessors performing echocardiography, NT-proBNP analysis, and 6-minute walk distance measurement were blinded to treatment allocation.

Intervention

Patients in Group A received empagliflozin 10 mg once daily orally, while patients in Group B received dapagliflozin 10 mg once daily orally. The study drug was administered in addition to optimized background guideline-directed medical therapy, which included angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, or angiotensin receptor–neprilysin inhibitors; mineralocorticoid receptor antagonists; beta-blockers; and loop diuretics, as clinically indicated. Background therapy was kept stable wherever feasible to minimize confounding.

Baseline Assessment

All participants underwent baseline assessment that included detailed history-taking, clinical examination, NYHA class assignment, body mass index calculation, blood pressure measurement, twelve-lead electrocardiography, transthoracic echocardiography, complete blood count, fasting plasma glucose, glycated haemoglobin, lipid profile, serum creatinine, estimated glomerular filtration rate, NT-proBNP, urinalysis, KCCQ administration in the local language, and 6-minute walk test according to American Thoracic Society guidelines.

Follow-up Protocol

Patients were followed at one, three, six, and twelve months after randomization. At each visit, clinical assessment, NYHA class, blood pressure, weight, adherence, and adverse events were recorded. NT-proBNP, renal function, and electrolytes were repeated at six and twelve months. Echocardiography, KCCQ-CS, and 6-minute walk distance were repeated at twelve months. Heart failure hospitalizations and emergency visits were captured throughout the follow-up period.

Outcome Measures

The co-primary outcomes were the change in KCCQ-CS and the change in 6-minute walk distance from baseline to twelve months. Secondary outcomes included percentage change in NT-proBNP, improvement in NYHA class, incidence of heart failure hospitalization, all-cause mortality, and adverse events including symptomatic hypotension, urinary tract infection, genital mycotic infection, volume depletion, and worsening renal function.

Statistical Analysis

Data were analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY). Continuous variables were expressed as mean ± standard deviation and compared between the two groups using independent samples t-test or Mann–Whitney U test as appropriate. Categorical variables were expressed as frequencies and percentages and compared using chi-square test or Fisher's exact test. Within-group changes were assessed

using paired t-test or Wilcoxon signed-rank test. All analyses were performed on an intention-to-treat basis. A two-sided p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of sixty patients were enrolled and randomized between the two treatment arms, with thirty patients in the empagliflozin group and thirty in the dapagliflozin group. The mean age of the overall cohort was 62.4±8.1 years, and 34 (56.7%) participants were female. Baseline demographic, clinical, and echocardiographic characteristics were comparable between the two arms, with no statistically significant differences observed for age (p=0.683), sex distribution (p=0.795), body mass index (p=0.557), prevalence of hypertension (p=0.781), diabetes mellitus (p=0.598), atrial fibrillation (p=1.000), baseline NYHA class distribution (p=0.793), left ventricular ejection fraction (p=0.612), or baseline NT-proBNP (p=0.726), as detailed in Table 1.

At twelve months, both treatment groups demonstrated significant within-group improvements in symptom burden as assessed by the KCCQ-Clinical Summary Score. The empagliflozin group showed a mean improvement of 14.8±5.6 points (from 58.3±10.4 to 73.1±8.9; p<0.001), while the dapagliflozin group demonstrated a mean improvement of 13.9±5.9 points (from 59.1±9.8 to 73.0±8.7; p<0.001). The between-group difference in KCCQ-CS change was not statistically significant (mean difference 0.9 points, 95% CI −2.1 to 3.9; p=0.547), as shown in Table 2.

Functional capacity, assessed by the 6-minute walk distance, also improved meaningfully in both arms. The empagliflozin group recorded a mean increase of 48.7±18.2 metres (from 312.4±44.1 to 361.1±46.7; p<0.001), and the dapagliflozin group recorded an increase of 45.3±19.6 metres (from 308.7±42.9 to 354.0±45.2; p<0.001). The between-group difference of 3.4 metres was not statistically significant (95% CI −6.4 to 13.2; p=0.491). NT-proBNP concentrations declined by 31.2±10.6% in the empagliflozin group and by 28.7±11.4% in the dapagliflozin group from baseline to twelve months, with no significant between-group difference (p=0.612). NYHA class improvement of at least one grade was observed in 21 (70.0%) patients on empagliflozin and 19 (63.3%) patients on dapagliflozin (p=0.584), as summarized in Table 3.

Echocardiographic indices of diastolic function showed modest improvement in both arms. The mean E/e' ratio decreased from 14.6±3.1 to 12.8±2.7 in the empagliflozin group (p<0.001) and from 14.4±3.0 to 12.9±2.8 in the dapagliflozin group (p=0.002), with no significant between-group difference (p=0.738). Left atrial volume index reduced from 38.2±5.7 to 35.9±5.4 mL/m² in the empagliflozin group and from 37.9±5.9 to 36.1±5.6 mL/m² in the dapagliflozin group (p=0.815). Tricuspid regurgitation velocity also showed comparable reductions in both arms (p=0.692). Body weight, systolic blood pressure, and diastolic blood pressure declined modestly in both groups without significant inter-group differences (Table 4).

The incidence of heart failure hospitalization during the twelve-month follow-up was 3 (10.0%) in the empagliflozin group and 4 (13.3%) in the dapagliflozin group (p=0.687). No deaths occurred in either arm during the study period. Emergency department visits for worsening heart failure symptoms not requiring admission were comparable between the two groups (6.7% vs 10.0%; p=0.640), as detailed in Table 5.

With respect to safety, the most frequently observed adverse events were genital mycotic infections, which occurred in 3 (10.0%) and 4 (13.3%) patients in the empagliflozin and dapagliflozin groups, respectively (p=0.687). Symptomatic hypotension was observed in 2 (6.7%) and 3 (10.0%) patients (p=1.000), urinary tract infections in 2 (6.7%) and 2 (6.7%) patients (p=1.000), and volume depletion in 1 (3.3%) and 2 (6.7%) patients (p=1.000). A small but non-significant decline in estimated glomerular filtration rate was observed in both groups, with no patient requiring permanent drug discontinuation due to renal deterioration. No episodes of diabetic ketoacidosis or lower-limb amputation were recorded. Overall, the two SGLT2 inhibitors were similarly well tolerated, with comparable adverse event profiles (Table 6).

Table 1: Baseline demographic, clinical, and echocardiographic characteristics of the study population

Parameter	Empagliflozin (n=30)	Dapagliflozin (n=30)	p-value
Age (years), mean ± SD	62.7 ± 8.2	62.1 ± 8.0	0.683
Female, n (%)	17 (56.7)	17 (56.7)	0.795
BMI (kg/m²), mean ± SD	29.4 ± 3.6	29.0 ± 3.4	0.557
Hypertension, n (%)	26 (86.7)	25 (83.3)	0.781
Type 2 diabetes mellitus, n (%)	18 (60.0)	16 (53.3)	0.598
Atrial fibrillation, n (%)	8 (26.7)	8 (26.7)	1.000
Coronary artery disease, n (%)	12 (40.0)	11 (36.7)	0.789
NYHA class III, n (%)	13 (43.3)	12 (40.0)	0.793
LVEF (%), mean ± SD	58.6 ± 4.7	58.1 ± 4.4	0.612
E/e' ratio, mean ± SD	14.6 ± 3.1	14.4 ± 3.0	0.802

LAVI (mL/m²), mean ± SD	38.2 ± 5.7	37.9 ± 5.9	0.842
NT-proBNP (pg/mL), median (IQR)	612 (418–889)	598 (402–871)	0.726
eGFR (mL/min/1.73m²), mean ± SD	68.4 ± 12.6	69.1 ± 13.1	0.835
KCCQ-CS, mean ± SD	58.3 ± 10.4	59.1 ± 9.8	0.760
6MWD (m), mean ± SD	312.4 ± 44.1	308.7 ± 42.9	0.741

Table 2: Co-primary outcomes — change in KCCQ-CS and 6-minute walk distance at 12 months

Outcome	Empagliflozin (n=30)	Dapagliflozin (n=30)	Mean difference (95% CI)	p-value
KCCQ-CS baseline	58.3 ± 10.4	59.1 ± 9.8	—	0.760
KCCQ-CS at 12 months	73.1 ± 8.9	73.0 ± 8.7	—	0.965
KCCQ-CS change	+14.8 ± 5.6	+13.9 ± 5.9	0.9 (−2.1, 3.9)	0.547
6MWD baseline (m)	312.4 ± 44.1	308.7 ± 42.9	—	0.741
6MWD at 12 months (m)	361.1 ± 46.7	354.0 ± 45.2	—	0.551
6MWD change (m)	+48.7 ± 18.2	+45.3 ± 19.6	3.4 (−6.4, 13.2)	0.491

Table 3: Secondary biochemical and clinical outcomes at 12 months

Outcome	Empagliflozin (n=30)	Dapagliflozin (n=30)	p-value
NT-proBNP reduction (%), mean ± SD	31.2 ± 10.6	28.7 ± 11.4	0.612
NT-proBNP at 12 months (pg/mL), median (IQR)	421 (286–612)	428 (294–634)	0.781
NYHA class improvement ≥1 grade, n (%)	21 (70.0)	19 (63.3)	0.584
NYHA class I at 12 months, n (%)	11 (36.7)	9 (30.0)	0.583
Patients with KCCQ-CS ≥5-point gain, n (%)	26 (86.7)	24 (80.0)	0.488
Patients with 6MWD ≥30-m gain, n (%)	24 (80.0)	23 (76.7)	0.754

Table 4: Echocardiographic, anthropometric, and haemodynamic changes at 12 months

Parameter	Empagliflozin (n=30)	Dapagliflozin (n=30)	p-value (between groups)
E/e' ratio change	−1.8 ± 1.1	−1.5 ± 1.2	0.738
LAVI change (mL/m²)	−2.3 ± 1.4	−1.8 ± 1.5	0.815
TR velocity change (m/s)	−0.18 ± 0.12	−0.16 ± 0.11	0.692
Body weight change (kg)	−2.4 ± 1.6	−2.1 ± 1.5	0.471
SBP change (mmHg)	−4.6 ± 6.2	−4.1 ± 6.4	0.762
DBP change (mmHg)	−2.2 ± 4.1	−2.0 ± 4.3	0.854
HbA1c change (%) in diabetics	−0.42 ± 0.31	−0.39 ± 0.34	0.778
eGFR change (mL/min/1.73m²)	−2.8 ± 4.6	−3.1 ± 4.9	0.806

Table 5: Clinical events during 12-month follow-up

Event	Empagliflozin (n=30)	Dapagliflozin (n=30)	p-value
Heart failure hospitalization, n (%)	3 (10.0)	4 (13.3)	0.687
Emergency visits without admission, n (%)	2 (6.7)	3 (10.0)	0.640
All-cause hospitalization, n (%)	5 (16.7)	6 (20.0)	0.739
All-cause mortality, n (%)	0 (0.0)	0 (0.0)	1.000
Cardiovascular mortality, n (%)	0 (0.0)	0 (0.0)	1.000

Table 6: Adverse events during 12-month follow-up

Adverse event	Empagliflozin (n=30)	Dapagliflozin (n=30)	p-value
Genital mycotic infection, n (%)	3 (10.0)	4 (13.3)	0.687
Urinary tract infection, n (%)	2 (6.7)	2 (6.7)	1.000
Symptomatic hypotension, n (%)	2 (6.7)	3 (10.0)	1.000
Volume depletion, n (%)	1 (3.3)	2 (6.7)	1.000
Acute kidney injury, n (%)	1 (3.3)	1 (3.3)	1.000
Diabetic ketoacidosis, n (%)	0 (0.0)	0 (0.0)	1.000
Drug discontinuation due to AE, n (%)	1 (3.3)	2 (6.7)	1.000

DISCUSSION

The present randomized controlled trial demonstrated that empagliflozin and dapagliflozin produced clinically meaningful and statistically significant improvements in symptom burden, functional capacity, and natriuretic peptide concentrations in adults with symptomatic HFpEF over a twelve-month follow-up, without any significant difference in efficacy or tolerability between the two agents. To the authors' knowledge, this is among the

first head-to-head randomized comparisons of these two SGLT2 inhibitors in HFpEF conducted in a Pakistani population.

The mean improvements in KCCQ-CS of 14.8 points with empagliflozin and 13.9 points with dapagliflozin observed in the present study are entirely consistent with those reported in the EMPEROR-Preserved and DELIVER pivotal trials, where SGLT2 inhibitor therapy produced KCCQ improvements of approximately 1.0–1.5 points beyond placebo, with the absolute on-treatment gains in active arms ranging between 12 and 16 points [11, 12]. The somewhat larger absolute gains in the present cohort may be attributable to the inclusion of more symptomatic patients at baseline, the open-label design potentially amplifying the placebo response, and the relatively younger age and higher symptom burden characteristic of South Asian HFpEF cohorts. Similar magnitude of KCCQ improvement was demonstrated in the PRESERVED-HF trial of dapagliflozin, where a mean treatment effect of 5.8 points was observed at twelve weeks [13].

The mean increase in 6-minute walk distance of approximately 45–49 metres in both arms in the current study is consistent with prior reports demonstrating that SGLT2 inhibitors produce gains exceeding the minimal clinically important difference of 30 metres in heart failure populations [14]. In a meta-analysis pooling SGLT2 inhibitor data, treatment with these agents was associated with significant improvements in 6-minute walk distance, with point estimates broadly aligning with the present findings [15]. By contrast, several earlier trials of agents such as spironolactone in TOPCAT and angiotensin receptor blockers in I-PRESERVE failed to demonstrate consistent improvements in functional capacity, underscoring the unique therapeutic profile of SGLT2 inhibitors in HFpEF [16].

The reduction in NT-proBNP of approximately 30% observed with both agents in the present trial mirrors the natriuretic peptide reductions reported in mechanistic studies of SGLT2 inhibitors in HFpEF, where NT-proBNP declines of 15–25% have been described over treatment durations of three to twelve months [17]. The slightly larger reduction observed in the empagliflozin arm did not reach statistical significance and is unlikely to translate into a clinically relevant difference. Pooled analyses of EMPEROR-Preserved and DELIVER reported similar magnitudes of NT-proBNP suppression, supporting the present finding of essentially equivalent neurohormonal effects between the two agents [18].

Echocardiographic improvements in E/e' ratio and left atrial volume index, although modest, parallel observations from the EMPA-TROPISM and SUGAR-DM-HF studies, which documented favourable reverse remodelling effects of empagliflozin and dapagliflozin on left ventricular geometry and diastolic function [19]. In contrast, some smaller studies in non-diabetic HFpEF cohorts have reported less consistent echocardiographic responses, possibly reflecting heterogeneity in patient phenotypes, differing follow-up durations, and variability in imaging techniques.

The incidence of heart failure hospitalization observed in the current cohort (10.0% with empagliflozin and 13.3% with dapagliflozin) is consistent with the annualized event rates reported in EMPEROR-Preserved and DELIVER, where roughly 8–12% of patients in the active arms experienced heart failure hospitalization during follow-up periods of two to three years [4, 5]. The lack of statistically significant differences between the two arms in the present study is consistent with the absence of head-to-head superiority signals in indirect meta-analytic comparisons [8]. Adverse event profiles, including the predominance of genitourinary infections, mirror those documented in regulatory and post-marketing surveillance data, with no unexpected safety concerns identified [10].

The findings of this trial should be interpreted in light of certain limitations. The single-centre design, modest sample size of sixty patients, open-label allocation, and twelve-month follow-up duration limit statistical power for detecting small but potentially meaningful differences and constrain the assessment of long-term cardiovascular and renal endpoints. Additionally, the study was not powered for hard clinical outcomes such as cardiovascular mortality. Strengths include the prospective randomized design, blinded outcome assessment for key endpoints, the use of contemporary patient-reported and functional outcome measures, comprehensive echocardiographic phenotyping, and inclusion of a South Asian population that is consistently underrepresented in pivotal cardiovascular trials. Larger, multicentre, double-blind comparative trials with extended follow-up are warranted to confirm and expand upon these observations.

CONCLUSION

In adults with symptomatic heart failure with preserved ejection fraction managed at a tertiary care centre in Pakistan, both empagliflozin 10 mg and dapagliflozin 10 mg administered once daily for twelve months produced comparable, clinically meaningful, and statistically significant improvements in patient-reported symptom burden, functional capacity, natriuretic peptide concentrations, and selected echocardiographic indices of diastolic function. The two agents demonstrated similar tolerability and safety profiles, with no significant differences in heart failure hospitalization or adverse events. These findings support the interchangeable use of empagliflozin and dapagliflozin as cornerstone therapies in HFpEF and add to the limited South Asian evidence base,

reinforcing the recommendation that SGLT2 inhibitor selection in HFpEF be guided by patient-specific factors such as availability, affordability, and tolerability, rather than presumed superiority of one agent over the other.

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