International Journal of Medicine
pISSN 1468-3814 | eISSN 2667-7008
https://theinternationalmedicine.com/

*Original Researcher Article* *DOI: 10.61336/im/26-06-198*

# Effect of SGLT-2 Inhibitors on Left Ventricular Ejection Fraction in Diabetic Cardiomyopathy: A Prospective Observational Study.

**Dr. Devansh Trivedi[1]*, Dr. Dharam P Bansal[2], Dr. Medha Gupta[3].**

[1]*Junior Resident, Department of General Medicine, Mahatma Gandhi Medical College and Hospital, Jaipur (Raj.).*

[2]*Professor, Department of General Medicine, Mahatma Gandhi Medical College and Hospital, Jaipur (Raj.).*

[3]*Assistant Professor, Department of General Medicine, Geetanjali Medical College and Hospital, Jaipur (Raj.).*

**Correspondence:**
***Dr. Devansh Trivedi.***
*Junior Resident, Department of General Medicine, Mahatma Gandhi Medical College and Hospital, Jaipur (Raj.).*

***Email:***
dr.devansh2019@gmail.com

**Received:** 04-05-2026
**Revised:** 25-05-2026
**Accepted:** 06-06-2026
**Published:** 30-06-2026

## Abstract

***Background:*** Heart failure remains one of the leading causes of morbidity and mortality worldwide. Sodium-glucose cotransporter-2 (SGLT-2) inhibitors, originally developed as glucose-lowering agents, have emerged as a cornerstone of modern heart failure management. This hospital-based prospective observational study evaluated the effect of SGLT-2 inhibitor therapy on left ventricular ejection fraction (LVEF) and associated echocardiographic parameters in 44 patients with diabetic cardiomyopathy over a six-month follow-up. Significant improvements were observed in LVEF, left ventricular global longitudinal strain (LVGLS), diastolic function indices, and left atrial mechanics, alongside meaningful gains in glycaemic control, systolic blood pressure, heart rate, and renal function. These findings support the growing evidence for SGLT-2 inhibitors as multidimensional cardioprotective agents.

**Keywords:** Heart Failure (HF), Heart Failure with Reduced Ejection Fraction (HFrEF), Left Ventricular Ejection Fraction (LVEF), SGLT-2 Inhibitors, Diabetic Cardiomyopathy.



## INTRODUCTION

Heart failure (HF) is a major global public health concern, affecting over 64 million people worldwide and imposing a substantial burden on healthcare systems.1 It is clinically classified based on left ventricular ejection fraction (LVEF): heart failure with reduced ejection fraction (HFrEF; LVEF <40%), heart failure with mildly reduced ejection fraction (HFmrEF; LVEF 41–49%), and heart failure with preserved ejection fraction (HFpEF; LVEF ≥50%). Among these subtypes, HFrEF is characterised by impaired systolic function and progressive ventricular remodelling, which carries a particularly poor prognosis.1

LVEF is a central parameter in assessing cardiac function, guiding therapeutic decisions, and predicting clinical outcomes. Improvement in ejection fraction correlates with reduced hospitalisation rates, better quality of life, and improved survival — making pharmacological strategies that enhance LVEF of considerable clinical importance.2

SGLT-2 inhibitors are a relatively recent class of oral antihyperglycaemic agents that selectively inhibit the SGLT-2 transport proteins in the proximal convoluted tubules of the kidneys, responsible for reabsorbing approximately 90% of filtered glucose.3 Beyond glycaemic control, they induce weight loss through glycosuria, and reduce blood pressure through osmotic diuresis and natriuresis.3

Landmark cardiovascular outcome trials — including EMPA-REG OUTCOME, DAPA-HF, EMPEROR-Reduced, DELIVER, and EMPEROR-Preserved — have consistently demonstrated that SGLT-2 inhibitors reduce hospitalisation for heart failure and cardiovascular mortality in both diabetic and non-diabetic patients.4,5 As a result, SGLT-2 inhibitors are now incorporated into contemporary heart failure management guidelines as cornerstone therapy for HFrEF.4

The cardioprotective effects are attributed to multiple mechanisms including haemodynamic unloading, enhanced myocardial energy metabolism via ketone body utilisation, attenuation of myocardial fibrosis and inflammation, and favourable ventricular remodelling.6,7,8

Emerging evidence indicates that SGLT-2 inhibitors may promote left ventricular reverse remodelling — reducing LV volumes and improving systolic function.6,7 The present study aims to evaluate this effect on LVEF using 2D echocardiography in patients with diabetic cardiomyopathy, contributing to better understanding of their role in preventing or reversing myocardial dysfunction.

## MATERIALS AND METHODS

This was a hospital-based prospective observational study conducted in the Department of General Medicine, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, over two years from March 2024 to March 2026. The sample size was calculated using the standard formula ($n = Z^2pq/d^2$) assuming a 12% prevalence of cardiomyopathy in diabetes at 95% confidence, yielding 40 subjects; accounting for 10% attrition, the final sample was 44 patients enrolled by consecutive sampling.

Adult patients (≥18 years) with a confirmed diagnosis of diabetic cardiomyopathy who provided written informed consent were included. Exclusion criteria encompassed ischemic cardiomyopathy, acute coronary syndromes, diabetic ketoacidosis, type 1 diabetes mellitus, secondary diabetes due to pancreatitis, a history of severe hypoglycaemic episodes within six months, pregnancy, and refusal of consent.

All enrolled patients underwent detailed clinical assessment, physical examination, and laboratory investigations including complete blood count, renal and liver function tests, HbA1c, lipid profile, and urinalysis. Cardiac evaluation was performed using 2D echocardiography at baseline and at six months, assessing LVEF, LVGLS, E/A ratio, E/e′ ratio, PASP, LAVI, LAEV, and LAEF. SGLT-2 inhibitor therapy (empagliflozin or dapagliflozin) was prescribed per institutional protocol. Data were analysed using SPSS version 29.0; paired t-test or Wilcoxon signed-rank test was used for pre- and post-treatment comparisons with $p < 0.05$ considered statistically significant. Ethical approval was obtained from the Institutional Ethics Committee.

## RESULTS

### Patient Profile

The study included 44 patients with a mean age of 59.2 ± 6.5 years. The largest age group was 50–59 years (36.36%), followed by 60–69 years (31.82%), 40–49 years (18.18%), and ≥70 years (13.64%), as shown in Table 1. Male patients constituted 70.45% of the cohort (Table 2). The mean BMI was 30.1 ± 2.6 kg/m², indicating most patients were overweight to obese (Table 3).

**Table 1: Age Distribution of Study Population**

| Age (years) | No. of Patients | Percentage (%) |
|---|---|---|
| 40–49 | 8 | 18.18% |
| 50–59 | 16 | 36.36% |
| 60–69 | 14 | 31.82% |
| ≥70 | 6 | 13.64% |
| **Total** | **44** | **100.00%** |
| **Mean ± SD** | **59.2 ± 6.5 years** | |

**Table 2: Gender Distribution of Study Population**

| Gender | No. of Patients | Percentage (%) |
|---|---|---|
| Male | 31 | 70.45% |
| Female | 13 | 29.55% |
| **Total** | **44** | **100.00%** |

**Table 3: Body Mass Index (BMI) of Study Population**

| Parameter | Mean | SD |
|---|---|---|
| BMI (kg/m²) (n=44) | 30.1 | 2.6 |

Over half the patients (52.27%) had a prior history of heart failure admission (Table 4). Acute coronary syndrome was the most common cause of heart failure (65.91%) (Table 5). Among comorbidities, dyslipidaemia was most prevalent (65.90%), followed by prior ischaemic heart disease (59.10%), hypertension (47.70%), and smoking (45.50%) (Table 6).

**Table 4: Previous Heart Failure Admission in Study Population**

| Previous HF Admission | No. of Patients | Percentage (%) |
|---|---|---|
| Yes | 23 | 52.27% |
| No | 21 | 47.73% |
| **Total** | **44** | **100.00%** |

**Table 5: Cause of Heart Failure in Study Population**

| Cause of Heart Failure | No. of Patients | Percentage (%) |
|---|---|---|
| Acute Coronary Syndrome (ACS) | 29 | 65.91% |
| Others | 15 | 34.09% |
| **Total** | **44** | **100.00%** |

**Table 6: Comorbidities in Study Population**

| Comorbidity | No. of Patients | Percentage (%) |
|---|---|---|
| Hypertension | 21 | 47.70% |
| Dyslipidemia | 29 | 65.90% |
| Prior Ischemic Heart Disease | 26 | 59.10% |
| Smoking | 20 | 45.50% |

**Clinical and Laboratory Parameters at Baseline and Six Months**

Following six months of SGLT-2 inhibitor therapy, systolic blood pressure fell significantly from 133.4 ± 15.6 to 125.9 ± 8.2 mmHg (p = 0.003). Heart rate reduced from 71.0 ± 5.8 to 65.5 ± 3.0 bpm (p <0.001). Median HbA1c declined from 8.3% to 7.4% (p <0.001), and eGFR improved modestly from 68.9 to 70.0 ml/min (p = 0.032). DBP reduction was not statistically significant (p = 0.082). Full details are presented in Table 7. (*denotes p <0.05).

**Table 7: Comparison of Clinical and Laboratory Parameters at Baseline and 6 Months**

| Parameter | Baseline (n=44) | 6 Months (n=44) | p-value |
|---|---|---|---|
| SBP (mmHg) | 133.4 ± 15.6 | 125.9 ± 8.2 | **0.003*** |
| DBP (mmHg) | 78.8 ± 10.6 | 75.4 ± 8.1 | 0.082 |
| HR (bpm) | 71.0 ± 5.8 | 65.5 ± 3.0 | **<0.001*** |
| HbA1c (%) | 8.3 [7.7–8.8] | 7.4 [7.2–7.6] | **<0.001*** |
| eGFR (ml/min) | 68.9 ± 11.7 | 70.0 ± 11.3 | **0.032*** |

**Echocardiographic Parameters at Baseline and Six Months**

LVEF increased significantly from 44.3 ± 2.6% to 45.6 ± 3.2% (p = 0.021). LVGLS improved markedly from −13.1 ± 1.6% to −17.3 ± 2.0% (p <0.001). The E/e′ ratio decreased from 13.0 ± 3.1 to 10.9 ± 2.3 (p <0.001), reflecting improved diastolic function. LAVI fell from 49.0 ± 5.6 to 42.8 ± 5.5 ml/m² (p <0.001), and LAEF improved from 31.7 ± 4.1% to 43.0 ± 10.6% (p <0.001). E/A ratio and PASP did not change significantly. Complete data are presented in Table 8. (*denotes p <0.05).

**Table 8: Comparison of Echocardiographic Parameters at Baseline and 6 Months**

| Parameter | Baseline (n=44) | 6 Months (n=44) | p-value |
|---|---|---|---|
| LVEF (%) | 44.3 ± 2.6 | 45.6 ± 3.2 | **0.021*** |
| E/A | 1.02 ± 0.5 | 1.01 ± 0.5 | 0.642 |
| LVGLS | −13.1 ± 1.6 | −17.3 ± 2.0 | **<0.001*** |
| E/e′ | 13.0 ± 3.1 | 10.9 ± 2.3 | **<0.001*** |
| PASP (mmHg) | 25.5 ± 4.4 | 25.2 ± 4.3 | 0.458 |
| LAVI (ml/m²) | 49.0 ± 5.6 | 42.8 ± 5.5 | **<0.001*** |
| LAEV (ml) | 34.2 ± 6.1 | 35.5 ± 7.1 | **0.036*** |
| LAEF (%) | 31.7 ± 4.1 | 43.0 ± 10.6 | **<0.001*** |

## DISCUSSION

The present study demonstrates that six months of SGLT-2 inhibitor therapy in patients with diabetic cardiomyopathy is associated with significant improvements spanning systolic function, diastolic relaxation, and left atrial mechanics.6,7

The significant increase in LVEF, though modest in absolute terms (~1.3 percentage points), is consistent with prior evidence of LV reverse remodelling with SGLT-2 inhibitors.6,16 The more pronounced improvement in LVGLS (from

−13.1% to −17.3%) confirms genuine myocardial functional recovery, as LVGLS is a more sensitive early marker of systolic dysfunction than LVEF alone.10

The reduction in E/e′ ratio from 13.0 to 10.9 indicates meaningful alleviation of LV filling pressures — a central pathophysiological feature of diabetic cardiomyopathy.11 This aligns with the haemodynamic unloading hypothesis whereby SGLT-2 inhibitor-driven natriuresis and osmotic diuresis reduce preload and ventricular filling pressures, an effect also demonstrated by Connelly et al. in an experimental HFpEF model.11,12

The significant reduction in LAVI and improvement in LAEF reflect meaningful left atrial reverse remodelling. Left atrial enlargement is a well-established precursor to atrial fibrillation and adverse cardiovascular events,9 and its reversal here suggests SGLT-2 inhibitors may reduce arrhythmic risk in diabetic cardiomyopathy. These structural improvements are likely underpinned by reduced atrial wall stress secondary to lower LV filling pressures.13

Multiple mechanisms operate synergistically. SGLT-2 inhibitors shift myocardial fuel utilisation toward ketone bodies — a more oxygen-efficient substrate for the failing heart.12,,14, 15 Simultaneously, they attenuate myocardial inflammation and fibrosis through inhibition of TGF-β1 pathways and NLRP3 inflammasome activation,13,14 and reduce sympathetic overactivity, together producing comprehensive structural and functional cardiac recovery.16-18

The significant improvements in SBP, heart rate, HbA1c, and eGFR reinforce the systemic cardio-metabolic-renal benefits of this drug class, consistent with findings from major outcome trials including DAPA-HF, EMPEROR-Reduced, and DELIVER.4,5,7

Limitations include the single-centre observational design, sample size of 44 patients, and absence of a concurrent control group. Larger multicentre randomised controlled trials with extended follow-up are needed to confirm these findings.6,7.

## CONCLUSION

This prospective observational study demonstrates that SGLT-2 inhibitor therapy in patients with diabetic cardiomyopathy is associated with significant improvement in LVEF, LVGLS, E/e′ ratio, LAVI, LAEF, and left atrial strain over six months, alongside meaningful gains in glycaemic control, systolic blood pressure, heart rate, and renal function. These findings support early incorporation of SGLT-2 inhibitors as cardioprotective agents in diabetic cardiomyopathy, guided by serial echocardiographic monitoring. Further large-scale randomised studies are warranted to confirm and extend these observations.

## REFERENCES

1. Shahim B, Kapelios CJ, Savarese G, Lund LH. Global public health burden of heart failure: an updated review. Card Fail Rev. 2023;9:e11.
2. Shams P, Goyal A, Makaryus AN. Left ventricular ejection fraction. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026.
3. Srinivas N, Sarnaik MK, Modi S, et al. Sodium-glucose cotransporter 2 (SGLT-2) inhibitors: delving into the potential benefits of cardiorenal protection beyond the treatment of type 2 diabetes mellitus. Cureus. 2021;13(8):e16868.
4. Talha KM, Anker SD, Butler J. SGLT-2 inhibitors in heart failure: a review of current evidence. Int J Heart Fail. 2023;5(2):82-90.
5. Lopez-Usina A, Mantilla-Cisneros C, Llerena-Velastegui J. Comprehensive benefits of sodium-glucose cotransporter 2 inhibitors in heart failure with reduced ejection fraction: a literature review. J Clin Med Res. 2024;16(10):449-464.
6. Cerar A, Poglajen G, Zemljič G, et al. SGLT2 inhibitors are associated with left ventricular reverse remodeling in patients with non-compaction cardiomyopathy: a prospective observational cohort trial. Biomedicines. 2025;13(11):2773.
7. Makhsham FMA, Nasr KAB, Al-Sewaiee AAS, et al. Impact of SGLT2 inhibitors on cardiovascular outcomes in heart failure with reduced ejection fraction: a systematic review and meta-analysis. Cureus. 2025;17(12):e99014.
8. Balakrishnan B, Somas DM. Diabetic cardiomyopathy: a comprehensive review of diagnosis, management, and future directions. Diabetol Metab Syndr. 2025;17:422.
9. Lorenzo-Almorós A, Tuñón J, Orejas M, Cortés M, Egido J, Lorenzo Ó. Diagnostic approaches for diabetic cardiomyopathy. Cardiovasc Diabetol. 2017;16:28.
10. Negishi K. Echocardiographic features of diabetic cardiomyopathy: where are we now? Cardiovasc Diagn Ther. 2018;8(1):47-56.
11. Lopaschuk GD, Verma S. Mechanisms of cardiovascular benefits of sodium glucose co-transporter 2 (SGLT2) inhibitors: a state-of-the-art review. JACC Basic Transl Sci. 2020;5(6):632-644.
12. Neubauer S. The failing heart—an engine out of fuel. N Engl J Med. 2007;356(11):1140-1151.

13. Dick SA, Epelman S. Chronic heart failure and inflammation: what do we really know? Circ Res. 2016;119(1):159-176.
14. Lee TM, Chang NC, Lin SZ. Dapagliflozin, a selective SGLT2 inhibitor, attenuated cardiac fibrosis by regulating the macrophage polarization via STAT3 signaling in infarcted rat hearts. Free Radic Biol Med. 2017;104:298-310.
15. Verma S, Rawat S, Ho KL, et al. Empagliflozin increases cardiac energy production in diabetes: novel translational insights into the heart failure benefits of SGLT2 inhibitors. JACC Basic Transl Sci. 2018;3(5):575-587.
16. Santos-Gallego CG, Requena-Ibanez JA, San Antonio R, et al. Empagliflozin ameliorates adverse left ventricular remodeling in nondiabetic heart failure by enhancing myocardial energetics. J Am Coll Cardiol. 2019;73(15):1931-1944.
17. Connelly KA, Zhang Y, Visram A, Advani A, Gilbert RE. Empagliflozin improves diastolic function in a nondiabetic rodent model of heart failure with preserved ejection fraction. JACC Basic Transl Sci. 2019;4(1):27-37.
18. Sharifov OF, Schiros CG, Aban I, Denney TS, Gupta H. Diagnostic accuracy of tissue Doppler index E/e′ for evaluating left ventricular filling pressure and diastolic dysfunction/heart failure with preserved ejection fraction: a systematic review and meta-analysis. J Am Heart Assoc. 2016;5(1):e002530.