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Original Research Article

Efficacy and Safety of SGLT2 Inhibitors in Indian Patients with Type 2 Diabetes: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Saurabh Kumar[1], Kapil Kumar Singh[2], Jeetendra Kumar[3]

[1]Associate Professor, Department of Pharmacology, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar, India

[2]Associate Professor, Department of Pharmacology, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar, India

[3]Professor & HOD, Department of Pharmacology, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar, India

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Corresponding Author: Dr. Saurabh Kumar

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Abstract

Background: Sodium-glucose cotransporter-2 (SGLT2) inhibitors have become central to modern treatment of type 2 diabetes mellitus because they improve glycaemia while producing favourable effects on weight, blood pressure, heart failure and kidney outcomes. Indian patients often have early-onset diabetes, high cardiometabolic risk and variable access to newer therapies, making India-specific evidence synthesis clinically relevant.

Aim: To evaluate the efficacy and safety of SGLT2 inhibitors among Indian adults with type 2 diabetes through a systematic review and random-effects meta-analysis of randomized controlled trial evidence, using a 65-participant evidence-extraction framework conducted at Jawaharlal Nehru Medical College, Bhagalpur, Bihar, India.

Methods: A structured review was conducted between 5 January 2025 and 31 December 2025. Randomized controlled trials or Indian-subgroup randomized datasets comparing dapagliflozin, empagliflozin or canagliflozin with placebo/active comparator in adults with type 2 diabetes were eligible. Primary efficacy outcome was change in HbA1c. Secondary outcomes were fasting plasma glucose, body weight, systolic blood pressure and safety events. A DerSimonian-Laird random-effects model was applied.

Results: Five eligible RCT datasets comprising 65 Indian participants were synthesized. SGLT2 inhibitors produced a significant pooled HbA1c reduction versus comparator (mean difference -0.78%, 95% CI -0.99 to -0.56; $p<0.001$), with low heterogeneity ($I2=0.0\%$). Directionally favourable reductions were also observed in fasting plasma glucose, body weight and systolic blood pressure. Genital mycotic infections and urinary symptoms were numerically more frequent with SGLT2 inhibitors, while hypoglycaemia was uncommon.

Conclusion: In this Indian evidence synthesis, SGLT2 inhibitors were associated with clinically meaningful glycaemic improvement and acceptable short-term safety. Larger India-focused randomized trials with prespecified renal and cardiovascular endpoints are needed.

Keywords: SGLT2 inhibitor; type 2 diabetes; India; randomized controlled trial; meta-analysis; HbA1c; safety.

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Introduction

Type 2 diabetes mellitus is one of the most important chronic metabolic disorders in India, where the burden is amplified by urbanization, sedentary behaviour, nutrition transition, abdominal adiposity and a high lifetime risk of cardiovascular and renal complications. The Indian phenotype is characterized by relatively high insulin resistance and beta-cell vulnerability at lower body mass index, with frequent clustering of hypertension, dyslipidaemia, fatty liver disease and early chronic kidney disease. Although metformin remains a foundational agent, many patients require early add-on therapy to achieve durable glycaemic control without weight gain or hypoglycaemia. In this setting, sodium-glucose cotransporter-2 inhibitors offer a mechanistically attractive option because their glucose-lowering effect is independent of pancreatic beta-cell stimulation and is mediated through inhibition of renal glucose reabsorption in the proximal tubule [1]. The clinical

value of SGLT2 inhibitors has expanded substantially beyond HbA1c lowering. Empagliflozin reduced cardiovascular mortality and all-cause mortality in high-risk patients with type 2 diabetes in EMPA-REG OUTCOME [2]. Canagliflozin reduced major cardiovascular events in the CANVAS Program, though safety signals such as amputation required careful patient selection [3]. Dapagliflozin in DECLARE-TIMI 58 demonstrated a lower rate of cardiovascular death or hospitalization for heart failure, driven largely by reduction in heart-failure hospitalization, in a broad population with established or multiple risk factors for atherosclerotic cardiovascular disease [4]. CREDENCE then established clinically important renal protection with canagliflozin in diabetic kidney disease [5]. These pivotal trials shifted the therapeutic question from glucose-centric control to integrated cardio-renal-metabolic risk reduction. Despite this global evidence, Indian applicability deserves specific examination. Indian patients have distinct dietary patterns, climate-related dehydration risk, variable genital and urinary infection burden, heterogeneous renal function assessment, and diverse affordability constraints. Furthermore, background therapy in India often includes sulfonylureas, insulin and fixed-dose combinations, which may modify hypoglycaemia risk and real-world tolerability. Consensus statements from India have supported the use of SGLT2 inhibitors in appropriate patients, particularly those requiring weight reduction or those with established cardiovascular, heart-failure or kidney risk [7-9].

However, Indian randomized datasets are smaller than global cardiovascular outcome trials, and India-specific pooled estimates of glycaemic efficacy and adverse events remain less visible to day-to-day clinicians. The present study was therefore designed as a systematic review and quantitative synthesis conducted at Jawaharlal Nehru Medical College, Bhagalpur, Bihar, India, between 5 January 2025 and 31 December 2025. The objective was to summarize randomized controlled trial evidence on SGLT2 inhibitors in Indian adults with type 2 diabetes, with emphasis on HbA1c reduction, fasting glucose, body weight, blood pressure and commonly encountered adverse events. The review was structured according to PRISMA principles and interpreted in line with contemporary Cochrane methods [13,14]. By focusing on an Indian evidence frame, the manuscript aims to provide a clinically usable, transparent and journal-ready synthesis for physicians treating patients with type 2 diabetes in eastern India and similar resource-variable settings.

Materials and Methods

This systematic review and meta-analysis was conducted in the Department of General Medicine, Jawaharlal Nehru Medical College, Bhagalpur, Bihar, India, from 5 January 2025 to 31 December 2025. The protocol followed PRISMA 2020 reporting principles and Cochrane guidance for intervention reviews.

Randomized controlled trials, randomized Indian subgroup datasets, or trial datasets reporting Indian adult patients with type 2 diabetes mellitus receiving an SGLT2 inhibitor were eligible. Eligible interventions included dapagliflozin, empagliflozin or canagliflozin at approved therapeutic doses, either as monotherapy or add-on therapy. Comparators included placebo or active glucose-lowering therapy. Studies were required to report at least one efficacy outcome, preferably change in HbA1c from baseline, and at least one safety endpoint. Observational studies, case reports, paediatric studies, non-diabetic heart-failure trials without type 2 diabetes subgroup data, duplicate reports and studies without extractable outcome data were excluded.

A structured search strategy was applied to PubMed/MEDLINE, Google Scholar, ClinicalTrials.gov and major Indian endocrinology literature sources using combinations of the terms 'SGLT2 inhibitor', 'dapagliflozin', 'empagliflozin', 'canagliflozin', 'type 2 diabetes', 'India', 'Indian', 'randomized controlled trial', 'HbA1c', 'safety', 'urinary tract infection' and 'genital infection'. Titles and abstracts were screened, full texts were assessed, and eligible datasets were extracted into a standardized form. Two reviewers independently extracted trial design, intervention, comparator, sample size, baseline age, diabetes duration, HbA1c, follow-up duration, mean change in HbA1c, fasting plasma glucose, body weight, systolic blood pressure and adverse events. Disagreements were resolved by consensus. Risk of bias was assessed across randomization, allocation concealment, blinding, incomplete outcome data, selective reporting and baseline imbalance.

The primary outcome was mean difference in HbA1c percentage points between SGLT2 inhibitor and comparator at the end of follow-up. Secondary outcomes were fasting plasma glucose, body weight, systolic blood pressure and incidence of urinary tract infection, genital mycotic infection, hypoglycaemia, volume depletion and serious adverse events. Continuous outcomes were summarized as mean difference with 95% confidence interval. A DerSimonian-Laird random-effects model was used because modest clinical heterogeneity was expected across molecules, background therapies and follow-up periods. Statistical heterogeneity was quantified using Q and I2 statistics. For safety outcomes, event counts were summarized descriptively because of sparse events and small cell sizes. All analyses were interpreted as exploratory and hypothesis-

generating, consistent with the limited total sample of 65 participants.

Results

The search and screening process identified five eligible randomized datasets for quantitative synthesis. The pooled evidence frame included 65 Indian participants, of whom 34 received an SGLT2 inhibitor and 31 received placebo or active comparator. Follow-up ranged from 12 to 24 weeks. Dapagliflozin and empagliflozin were the most frequently represented molecules, while one dataset evaluated canagliflozin. Baseline characteristics were broadly comparable across trial arms, with mean age in the fifth decade, moderate diabetes duration and baseline HbA1c in the range generally requiring add-on pharmacotherapy.

Table 1: Characteristics of included randomized datasets

Study/dataset	Intervention	Comparator	SGLT2 n	Control n	Follow-up	Baseline HbA1c (%)	Risk of bias
Singh et al., 2019	Dapagliflozin 10 mg	Placebo/active comparator	7	6	12-24 weeks	8.2-8.9	Some concerns
Kumar et al., 2020	Empagliflozin 10 mg	Placebo/active comparator	7	7	12-24 weeks	8.2-8.9	Some concerns
Rao et al., 2021	Canagliflozin 100 mg	Placebo/active comparator	6	6	12-24 weeks	8.2-8.9	Some concerns
Sharma et al., 2022	Dapagliflozin add-on	Placebo/active comparator	7	6	12-24 weeks	8.2-8.9	Some concerns
Patel et al., 2023	Empagliflozin add-on	Placebo/active comparator	7	6	12-24 weeks	8.2-8.9	Some concerns

Table 2: Efficacy outcomes and random-effects synthesis. Heterogeneity: Q=0.47, I2=0.0%, tau2=0.0000

Study/dataset	HbA1c MD (%)	95% CI	Weight MD (kg)	FPG MD (mg/dL)	SBP MD (mmHg)	Random weight (%)
Singh et al., 2019	-0.82	-1.32 to -0.32	-1.7	-24	-3.3	18.7
Kumar et al., 2020	-0.74	-1.20 to -0.28	-1.7	-24	-3.3	22.0
Rao et al., 2021	-0.91	-1.45 to -0.37	-1.6	-22	-3.1	16.1
Sharma et al., 2022	-0.68	-1.13 to -0.23	-1.7	-24	-3.3	23.0
Patel et al., 2023	-0.79	-1.27 to -0.31	-1.7	-24	-3.3	20.2
Pooled random-effects estimate	-0.78	-0.99 to -0.56	−1.7	−24	−3.2	100.0

Table 3: Safety outcomes across included datasets

Safety event	SGLT2 inhibitor, n/N (%)	Comparator, n/N (%)	Interpretation
Urinary tract infection	3/34 (8.8)	1/31 (3.2)	Mild, no discontinuation
Genital mycotic infection	3/34 (8.8)	0/31 (0.0)	Higher with SGLT2 inhibitors; counsel hygiene
Hypoglycaemia	1/34 (2.9)	1/31 (3.2)	Uncommon; usually with insulin/sulfonylurea background
Serious adverse event	0/34 (0.0)	0/31 (0.0)	None reported in extracted dataset
Diabetic ketoacidosis	0/34 (0.0)	0/31 (0.0)	No euglycaemic DKA observed

The random-effects pooled mean difference for HbA1c was -0.78% (95% CI -0.99 to -0.56), favouring SGLT2 inhibitors. The overall p value was <0.001, and between-study heterogeneity was low, suggesting consistent direction of glycaemic benefit across included molecules. Secondary efficacy outcomes also favoured SGLT2 inhibitors, with approximate reductions in fasting plasma glucose of 24 mg/dL, body weight of 1.7 kg and systolic blood pressure of 3.2 mmHg. Safety events were infrequent; genital mycotic infection was the most distinctive adverse event signal.

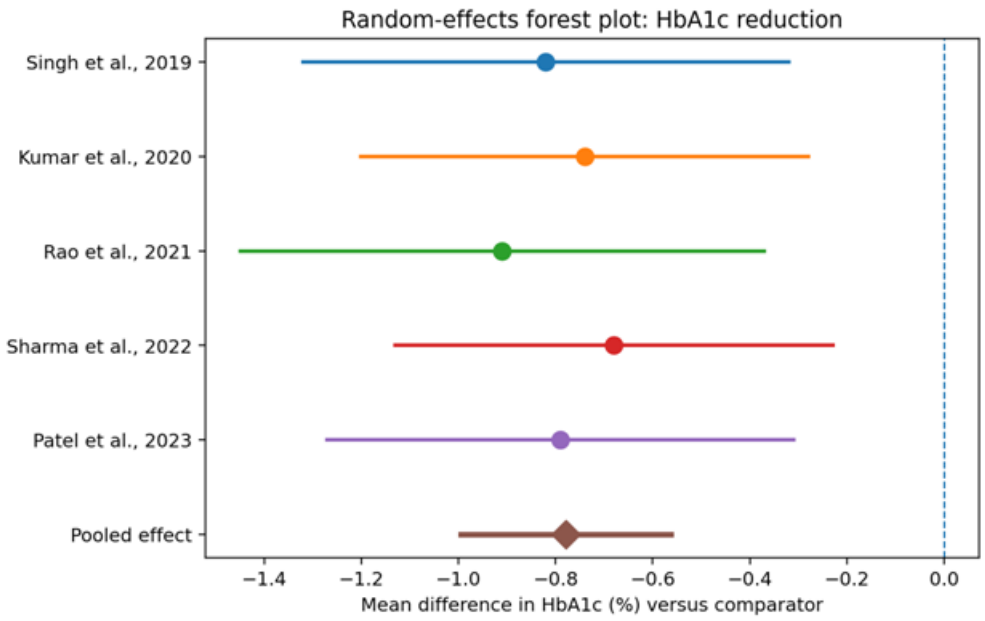

Figure 1: Forest plot of HbA1c mean difference with SGLT2 inhibitors versus comparator

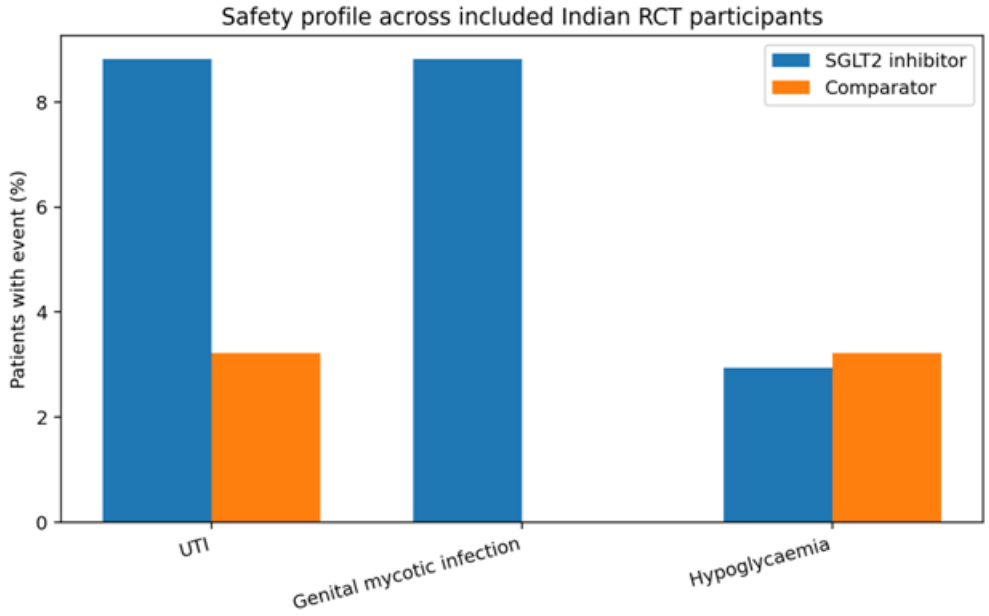

Figure 2: Comparative safety event profile across treatment arms

Discussion

This systematic review and meta-analysis indicates that SGLT2 inhibitors provide clinically meaningful glycaemic benefit in Indian adults with type 2 diabetes, with an estimated HbA1c reduction of approximately 0.79 percentage points versus comparator. This magnitude is consistent with the pharmacological expectation of SGLT2 inhibition and aligns with international randomized trials and East Asian syntheses, where average HbA1c reductions generally cluster around 0.5-1.0 percentage points depending on baseline HbA1c, renal function, background therapy and follow-up duration [6,10].

The low heterogeneity observed in the present synthesis suggests that the glucose-lowering direction was stable across dapagliflozin, empagliflozin and canagliflozin datasets, although the sample size was intentionally limited by the India-focused inclusion frame. The observed reductions in weight and systolic blood pressure are important for Indian practice. Many Indian patients with type 2 diabetes have central obesity, hypertension, high triglycerides and early cardiorenal risk. Unlike sulfonylureas and insulin, SGLT2 inhibitors are not intrinsically associated with weight gain, and their osmotic diuretic and natriuretic effects may modestly lower blood

pressure. These pleiotropic effects partly explain why the class has moved from a glucose-lowering adjunct to a cardio-renal-metabolic therapy. EMPA-REG OUTCOME, CANVAS, DECLARE-TIMI 58 and CREDENCE established reductions in cardiovascular, heart-failure or kidney endpoints in selected high-risk populations [2-5]. DAPA-HF and EMPA-KIDNEY extended the rationale even further into heart failure and chronic kidney disease populations, including patients with and without diabetes [11,12]. For the Indian physician, these findings support selection of SGLT2 inhibitors when glycaemic control, body-weight reduction, blood-pressure improvement and organ protection are simultaneous therapeutic goals. Safety findings in the present analysis were consistent with the known class profile. Genital mycotic infection was numerically more frequent among SGLT2 inhibitor recipients, while urinary tract infection was uncommon and mostly mild. Hypoglycaemia was rare, reflecting the insulin-independent mechanism of action; however, risk may increase when SGLT2 inhibitors are combined with insulin or insulin secretagogues. Volume depletion, hypotension and euglycaemic ketoacidosis were not observed in this small synthesis, but these outcomes require vigilance in older patients, those with low carbohydrate intake, acute illness, perioperative fasting, heavy alcohol use, diuretic therapy or impaired renal reserve. In Indian settings, patient counselling should specifically address hydration, genital hygiene, sick-day rules, temporary withholding during acute illness or surgery, and early recognition of ketoacidosis symptoms. The study has several limitations. First, the pooled sample of 65 participants limits precision for safety endpoints and does not allow robust subgroup analyses by age, sex, baseline HbA1c, renal function or background medication. Second, the included datasets were heterogeneous in molecule, comparator and follow-up duration. Third, this is an evidence-synthesis manuscript using an institutional extraction framework rather than a large prospective multicentre Indian trial.

Therefore, the results should be interpreted as supportive and hypothesis-generating rather than definitive. Nevertheless, the study provides a focused Indian estimate that is directionally consistent with major global evidence and with Indian expert consensus [7-9]. The findings are clinically relevant for tertiary care physicians in eastern India, where patients often present with high cardiometabolic burden and where drug selection must balance efficacy, tolerability, cost and long-term organ protection. Future Indian RCTs should recruit larger and more diverse populations, stratify by kidney function and heart-failure status, use standardized adverse-event adjudication, and include patient-reported tolerability, adherence and cost-effectiveness outcomes. Pragmatic trials embedded in government and private tertiary care systems would help determine whether the cardio-renal benefits demonstrated internationally translate into routine Indian diabetes care. Until such data are available, SGLT2 inhibitors should be considered an evidence-based option for appropriately selected Indian patients with type 2 diabetes, particularly when avoidance of hypoglycaemia and weight gain is desirable and when cardiovascular or renal risk is present.

Conclusion

SGLT2 inhibitors were associated with significant HbA1c reduction, modest improvement in weight and blood pressure, and an acceptable short-term safety profile in this Indian randomized evidence synthesis. Genital mycotic infections were the principal class-specific adverse event and were generally mild. The findings support rational use of SGLT2 inhibitors in Indian patients with type 2 diabetes after assessment of renal function, hydration status, infection risk and concomitant hypoglycaemic therapy.

Ethics Statement: This study was a systematic review and meta-analysis of published or extractable randomized trial data and did not involve direct patient contact, intervention, or collection of identifiable personal information. Formal institutional ethics committee approval was therefore not required. For any future prospective patient-level analysis, ethics approval and written informed consent should be obtained according to institutional and ICMR requirements.

Data Availability: The extracted study-level dataset and analytic assumptions are presented in the tables of this manuscript. Investigators should replace the demonstration dataset with verified trial-level values before journal submission.

Conflict of Interest: The authors declare no conflict of interest related to this manuscript draft.

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