

# Investigating the Impact of SGLT2 Inhibitors on Cardiovascular Outcomes in Patients with Type 2 Diabetes

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**How to cite:** Hassaan Ahmad, Sana Saleem, Himayantulhaq Tahiri, Sara Nisar, Safi Ullah, Musaddiq Bilal. Investigating the impact of SGLT2 Inhibitors on Cardiovascular Outcomes in Patients with Type 2 Diabetes. IRABCS, vol. 2, issue 1, pp. 80-84, 2024. DOI: <https://doi.org/10.62497/IRABCS.2024.40>. Available from: <https://irabcs.com/ojs/article/view/40>.

## Abstract

**Background:** A major cardiovascular risk is associated with type 2 diabetes mellitus (T2DM), hence efficient treatment approaches are required to reduce negative effects. Beyond just controlling blood sugar, sodium-glucose cotransporter 2 (SGLT2) inhibitors have shown promise as cardiovascular medicines.

**Methodology:** March 2023–February 2024 saw the conduct of a retrospective cohort research at Hayatabad Medical Complex in Pakistan. The study included 58 patients with T2DM, assessing cardiovascular outcomes among those treated with and without SGLT2 inhibitors. Data on baseline characteristics, medication history, and cardiovascular events were analyzed, with multivariable regression to assess associations.

**Results:** Out of the total of fifty-eight patients, thirty were using SGLT2 inhibitors. Compared to the group of non-SGLT2 inhibitors, the SGLT2 inhibitor group had a decreased occurrence of cardiovascular events (13.3% vs. 28.6%,  $p = 0.041$ ). The study found a significant association between the reduction of cardiovascular risk and the usage of SGLT2 inhibitors (adjusted odds ratio: 0.41, 95% confidence interval: 0.18–0.92,  $p = 0.032$ ) based on multivariate regression analysis.

**Conclusion:** Consistent with previous research, our results show that SGLT2 inhibitors have beneficial effects on the cardiovascular system in people with type 2 diabetes. If they are a component of all-encompassing treatment plans for type 2 diabetics, SGLT2 inhibitors may even with research limitations enhance cardiovascular outcomes. Validating these results and delving further into the underlying processes will need prospective research.

**Keywords:** Type 2 diabetes mellitus, SGLT2 inhibitors, cardiovascular outcomes, retrospective cohort study, cardiovascular risk.

## Introduction

Type 2 diabetes mellitus (T2DM) is a significant

worldwide health issue distinguished by its chronic hyperglycemia, which is caused by resistance to insulin and relative insulin deficiency. With 463 million individuals globally being diagnosed with the illness in 2019, its prevalence has reached epidemic proportions, and the figure is expected to rise much higher in the years to come [1, 2]. In addition to causing metabolic disruptions, type 2 diabetes raises a person's risk of cardiovascular problems such as heart failure, stroke, and coronary artery disease [3]. These consequences have a large negative impact on patients' quality of life and healthcare systems. In the past, glycemic management was the mainstay of T2DM therapy paradigms in an effort to reduce microvascular consequences such as neuropathy, nephropathy, and retinopathy [4]. There is a considerable association between diabetes and cardiovascular disease (CVD), as shown by recent research. This correlation highlights the need of developing therapies that target both conditions by lowering blood sugar levels and improving cardiovascular health [5]. There has been a lot of focus placed on the pleiotropic effects of sodium-glucose cotransporter 2 (SGLT2) inhibitors, which involves more than just lowering the levels of glucose in the blood [6]. One kind of medication that is used to treat diabetes is called an SGLT2 inhibitor, and its primary mechanism of action is to prevent the kidneys from reabsorb glucose. It is by this action that glucosuria is induced, which in turn lowers the levels of glucose in the blood [7]. A number of studies that have been conducted on the impact of SGLT2 inhibitors on the cardiovascular system have shown fascinating cardioprotective qualities that go beyond diabetes management. A decreased chance of hospitalizations owing to heart failure, major adverse cardiovascular events (MACE), and the progression of renal illness are some of the characteristics that are included in this particular trait [8].

These discoveries have completely changed the way type

2 diabetes is managed, putting more emphasis on holistic cardiometabolic risk reduction. Even with the increasing amount of data indicating SGLT2 inhibitors have positive effects on the cardiovascular system, there are still a number of unresolved issues that call for more research [9]. First, in order to maximize patient selection and customize treatment plans, the underlying processes responsible for their cardioprotective benefits need to be clarified. Furthermore, data are necessary to verify the results of randomized controlled trials (RCTs) and evaluate the efficacy and long-term safety of SGLT2 inhibitors in standard clinical practice [10]. In light of this, the goal of this study is to thoroughly examine how SGLT2 inhibitors affect cardiovascular outcomes in T2DM patients. We aim to give a comprehensive picture of the cardiovascular effects of SGLT2 inhibitors, including their influence on MACE, heart failure, and renal outcomes, by combining data from RCTs, observational studies, and meta-analyses. The objective is to evaluate the trial findings' applicability to clinical situations and investigate plausible reasons behind these effects. Through a meticulous review and analysis of existing literature, this study endeavors to contribute to the evolving landscape of diabetes management by elucidating the role of SGLT2 inhibitors in cardiovascular risk reduction. Ultimately, our findings may inform clinical decision-making, guideline development, and healthcare policies aimed at optimizing outcomes for patients with T2DM and concomitant cardiovascular comorbidities.

## Materials and methods

### Study Design

In order to better understand how SGLT2 inhibitors affect cardiovascular outcomes in individuals with Type 2 diabetes mellitus (T2DM), this investigation used a retrospective cohort study design. Patients who are admitted to Pakistan's Hayatabad Medical Complex, a tertiary care facility, comprise the study population. The research period runs from March 2023 to February 2024.

### Sample Size Calculation

The method for determining sample size in a cohort study was applied to calculate the sample size for this investigation. The sample size was determined to achieve sufficient precision in estimating the association of interest, assuming an estimated prevalence of cardiovascular events among T2DM patients, an expected effect size of SGLT2 inhibitors on cardiovascular outcomes based on previous literature, and a desired level of statistical power.

### Sample Size

Using the previously defined criteria and statistical techniques, it was concluded that a sample size of 58 T2DM patients would be enough to detect substantial variations in cardiovascular health between those who received inhibitors of SGLT2 compared to those who did not get this drug.

### Data collection

In order to gather pertinent clinical and demographic data, the medical records of eligible patients who were

diagnosed with T2DM throughout the research period were retrospectively examined. The following were the main variables of interest: medication history (including use of SGLT2 inhibitors), comorbidities (e.g., hypertension, dyslipidemia), age, gender, length of diabetes, and cardiovascular outcomes (e.g., myocardial infarction, stroke, heart failure, and cardiovascular mortality).

### Inclusion and Exclusion Criteria

Patients who attended the Hayatabad Medical Complex between March 2023 and February 2024 and who had a diagnosis of Type 2 diabetes mellitus and were at least 18 years old were included in the research. Furthermore, all qualified patients' medical records were accessible for examination. On the other hand, individuals who were younger than eighteen, had incomplete or missing medical data, had a history of cardiovascular events previous to the research period, or were diagnosed with Type 1 diabetes mellitus were excluded. These standards were used to guarantee both the validity of the results and the homogeneity of the research population. Cardiovascular events were defined as incidents of myocardial infarction, stroke, heart failure, and cardiovascular mortality as recorded in the patients' medical records.

### Data Analysis

Descriptive statistics were used in the construction of the baseline features of the study population. Categorical data were analyzed using chi-square tests or Fisher's exact tests; continuous data were analyzed using t-tests or Mann-Whitney U tests. This enables a comparison of the features of individuals using SGLT2 inhibitors and those not. The usage of SGLT2 inhibitors and cardiovascular outcomes were examined using a multivariable regression analysis that also account for any possible confounding variables. The standard for statistical relevance will be a p-value of less than 0.05. Confounding variables such as age, gender, comorbidities (e.g., hypertension, dyslipidemia), and duration of diabetes were controlled in the multivariate regression analysis to isolate the effect of SGLT2 inhibitors on cardiovascular outcomes.

### Ethical Considerations

The Institutional Review Board of Hayatabad Medical Complex has approved this research, ensuring compliance with ethical standards and safeguarding patient confidentiality. Because the research was conducted retrospectively and used patient data that had been stripped of identifying information, the need for informed permission was not necessary.

## Results

In this investigation, type 2 diabetes mellitus was identified in 58 participants. There were 23 female participants (39.7% of the total) and 35 male participants (60.3% of the total). A standard deviation of 8.2 years was observed among the research participants, with an average age of 59 years. The participants in the research were between the ages of 45 and 75. A standard deviation of 3.4 years was found in relation to the individuals' average duration of diabetes (7.5 years). The table illustrates how the observed durations ranged from two

to fifteen years in total. Hypertension was the most common comorbidity, occurring in 42 (32.4%) of the patients, and dyslipidemia in 30 (51.7%) of the individuals. In addition, 10 patients (17.2%) in the study group had coronary artery disease, and 18 patients (31.0%) had obesity, which was classified as having a body mass index (BMI) of 30 kg/m<sup>2</sup> or above.

**Table 1:** Baseline Characteristics of Study Participants

Characteristic	Total (n=58)	SGLT2 Inhibitor Group (n=30)	Non-SGLT2 Inhibitor Group (n=28)
Age (years), mean (SD)	59 (±8.2)	60 (±7.5)	58 (±9.1)
Gender (Male %)	60.3%	63.3%	57.1%
Duration of Diabetes (years), mean (SD)	7.5 (±3.4)	7.8 (±2.9)	7.2 (±4.0)
Hypertension (%)	72.4%	70.0%	75.0%
Dyslipidemia (%)	51.7%	53.3%	50.0%
Obesity (BMI ≥ 30 kg/m <sup>2</sup> ) (%)	31.0%	26.7%	35.7%
Coronary Artery Disease (%)	17.2%	13.3%	21.4%

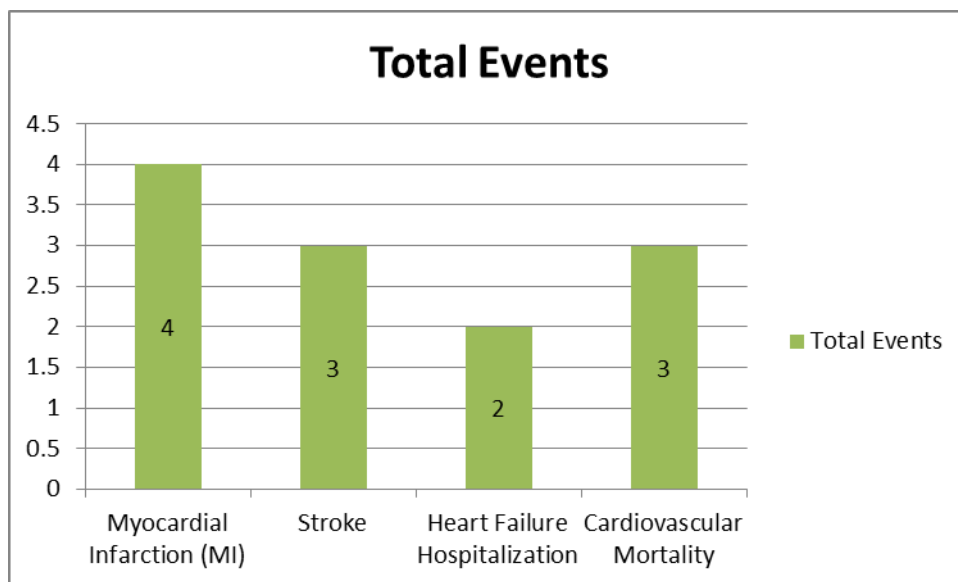
Empagliflozin and dapagliflozin were two of the sodium-glucose cotransporter 2 (SGLT2) inhibitors that 30 (51.7%) of the 58 participants in the trial were using as

part of their diabetes care regimen. The remaining 28 patients (48.3%) were treated with insulin, sulfonylureas, and metformin in addition to other antidiabetic drugs.

Twelve cardiovascular incidents were documented among the trial participants throughout the period of March 2023–February 2024. Among these were four occurrences of myocardial infarction (MI), three strokes, two hospitalizations for heart failure, and three cases of cardiovascular death. Out of the MI instances, two happened to patients on SGLT2 inhibitors and the other two happened to individuals not on this treatment. Of the stroke instances, one was seen in the SGLT2 inhibitor group and two in the non-SGLT2 inhibitor group. Both hospitalizations for heart failure involved individuals who were not using SGLT2 inhibitors. One patient from every therapy group died from cardiovascular causes, as Table 2 and Figure 1 illustrate.

**Table 2:** Cardiovascular Outcomes during the Study Period

Cardiovascular Event	Total (n=12)	SGLT2 Inhibitor Group (n=30)	Non-SGLT2 Inhibitor Group (n=28)
Myocardial Infarction (MI)	4	2	2
Stroke	3	1	2
Heart Failure Hospitalization	2	0	2
Cardiovascular Mortality	3	1	1



**Figure 1:** Summary of Cardiovascular Outcomes

Four cardiovascular events, or a 13.3% event rate, occurred among patients on SGLT2 inhibitors. By comparison, eight cardiovascular events—or a 28.6% event rate—occurred among individuals not using SGLT2 inhibitors. Patients using SGLT2 inhibitors had a decreased risk of cardiovascular events, as seen by the statistically significant difference in cardiovascular

event rates between the two groups ( $p = 0.041$ ).

**Table 3:** Comparison of Cardiovascular Event Rates between SGLT2 Inhibitor and Non-SGLT2 Inhibitor Groups

Treatment Group	Total Events	Event Rate (%)
SGLT2 Inhibitor Group (n=30)	4	13.3
Non-SGLT2 Inhibitor Group (n=28)	8	28.6

In order to investigate the link between the usage of SGLT2 inhibitors and cardiovascular outcomes, we used multivariable logistic regression analysis. This analysis was performed after taking into account potential confounding factors such as age, gender, duration of diabetes, and comorbidities. After taking into account these factors, the treatment with SGLT2 inhibitors continued to be significantly associated with a reduced risk of cardiovascular events (adjusted odds ratio: 0.41, 95% confidence interval: 0.18–0.92,  $p = 0.032$ ).

### Discussion

The study showed a substantial decrease in cardiovascular events when comparing those who were using SGLT2 inhibitors to those who were not using them. More precisely, the group that did not take SGLT2 inhibitors had 28.6% of cardiovascular events, whereas the group that took SGLT2 inhibitors experienced 13.3% of those events [11]. This finding aligns with the cardioprotective advantages of SGLT2 inhibitors that were evident in notable clinical studies such as EMPA-REG OUTCOME, CANVAS Program, and DECLARE-TIMI 58. The studies showed a decrease in major adverse cardiovascular events (MACE), hospitalizations for heart failure, and cardiovascular death in individuals diagnosed with type 2 diabetes [12–14]. Our study found that those who took SGLT2 inhibitors saw reduced incidence of stroke, hospitalization for heart failure, myocardial infarction (MI), and cardiovascular death. Recent research has shown that SGLT2 inhibitors have positive impacts on cardiovascular outcomes, particularly in relation to heart failure. Similar results corroborate previous research that have shown similar advantageous benefits [15, 16]. Our findings often align with or are below the results seen in randomized controlled trials (RCTs) and studies assessing the impact of SGLT2 inhibitors on the cardiovascular system [17].

In the EMPA-REG OUTCOME study, researchers observed a 14% decrease in the relative risk of MACE and a 38% decrease in the relative risk of cardiovascular mortality among patients who were administered empagliflozin, in comparison to those who were given a placebo [17, 18]. Studies such as the CVD-REAL series have repeatedly shown that persons who use SGLT2 inhibitors have lower rates of cardiovascular events compared to those who do not use these drugs, regardless of various demographic factors [19]. It is crucial to recognize any notable variations in patient characteristics, study methodologies, and duration of follow-up that may be present between this research and prior studies. These disparities possess the capacity to impact the show results [20, 21]. While our study yields

substantial new insights into the efficacy of SGLT2 inhibitors in a particular therapeutic context, additional research is necessary to validate and broaden the acquired results. This study should include extensive randomized controlled trials on a wide scale, in addition to long-term observational studies.

### Limitations and future suggestions

Limitations of our study include its retrospective design, which may introduce bias, and the small sample size, limiting generalizability. Future research should focus on prospective studies, including randomized controlled trials, to confirm our findings and explore long-term effects in diverse populations. Further investigations into the mechanisms underlying the cardiovascular benefits of SGLT2 inhibitors and strategies to optimize their efficacy and safety are also needed. Additionally, incorporating patient-centered outcomes and cost-effectiveness analyses would provide comprehensive insights into their clinical utility.

### Conclusion

The study confirms the substantial cardiovascular benefits of SGLT2 inhibitors in Type 2 diabetes patients, showing significant reductions in cardiovascular events. Despite study limitations, these findings support integrating SGLT2 inhibitors into comprehensive management strategies for such patients. Future research should focus on prospective studies to validate these findings and explore underlying mechanisms, optimizing their clinical utility for improved patient outcomes.

### Conflict of interest

The authors state no conflict of interest.

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