https://nephropathol.com DOI: 10.34172/jnp.2023.21477 J Nephropathol. 2023;12(4):e21477

Journal of Nephropathology

Administration of sodium-glucose cotransporter-2 inhibitors in kidney transplant patients with diabetes: a systematic review and meta-analysis

Hamidreza Khodabandeh[1], Zahra Bakhshizade[2], Mohammad Hossein Taklif[2], Halime Zaeri Fakhrabadi[3], Soleyman Alivand[4], Noorbakhsh Alivand[5], Ghazaleh Rashidizadeh[6], Leila Jampour[6], Mahsa Shirani[7*]

[1]Department of Radiology, Imam Hossein Hospital, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[2]Department of Nursing, Student Research Committee, Faculty of Nursing and Midwifery, Hormozgan University of Medical Sciences, Bandar Abbas, Iran
[3]Department of Health Management and Economics, School of Health, Tehran University of Medical Sciences, Tehran, Iran
[4]Department of Biostatistical and Epidemiology, School of Health, Isfahan University of Medical Sciences, Isfahan, Iran
[5]Department of Nutrition, School of Health, Shiraz University of Medical Sciences, Shiraz, Iran
[6]Department of Nutrition, School of Nutrition and Food Sciences, Shiraz University of Medical Sciences, Shiraz, Iran
[7]Student Research Committee, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran

ARTICLE INFO

Article type:
Meta-analysis

Article history:
Received: 13 June 2023
Accepted: 19 August 2023
Published online: 31 August 2023

Keywords:
Diabetes mellitus,
Sodium-glucose cotransporter two protein,
Human,
SGLT2 protein,
Dapagliflozin,
Canagliflozin,
Empagliflozin,
Kidney transplantation,
Renal transplantation

ABSTRACT

Introduction: Sodium-glucose cotransporter-2 (SGLT2) inhibitors are a new diabetes treatment. Considering the prescription of these medicines for kidney transplant patients, this systematic review and meta-analysis aimed to investigate the impact of SGLT2 inhibitors on kidney transplant patients.

Material and Methods: This meta-analysis study was performed based on the PRISMA guideline. The necessary data were collected by searching the databases of Scopus, PubMed, Cochrane, Google Scholar search engine, and Web of Science without a time limit until March 1, 2023. The data were analyzed in STATA 14. A *P* value less than 0.05 was considered significant.

Results: The authors assessed eight articles with a sample size of 960 patients. The SGLT2 inhibitors showed no significant impact on levels of estimated glomerular filtration rate [SMD: -0.21 (95% CI: -0.65, 0.25)], serum creatinine [SMD: -0.02 (95% CI: -0.19, 0.15)], plasma hemoglobin A1c (HbA1c) [SMD: -0.62 (95% CI: -1.43, 0.18)], systolic blood pressure [SMD: -0.64 (95% CI: -1.80, 0.52)], and diastolic blood pressure [SMD: -0.64 (95% CI: -1.41, 0.14)], and on the patient's weight [SMD:-0.31 (95% CI: -0.80, 0.18)]. Patient age did not influence the impact of SGLT2 inhibitors on estimated glomerular filtration rate (50–59 years-old age group: [SMD: 0.13 (95% CI: -0.04, 0.30)], 60–69 years-old age group: [SMD: -0.56 (95 % CI: -1.38, 0.26]). Duration of medicine use did not affect the impact of SGLT2 inhibitors on estimated glomerular filtration rate [6 months after medicine use: SMD: -0.56 (95% CI: -1.38, 0.26)], 12 months after medicine use: [SMD: 0.10 (95% CI: -0.05, 0.26)].

Conclusion: SGLT2 inhibitors were not effective in lowering blood pressure, estimated glomerular filtration rate, serum creatinine, and hemoglobin A1c levels, or weight in kidney transplant patients. Although SGLT2 inhibitors were ineffective in improving kidney transplant patients' renal function, there were no side effects, and the administration of this drug in kidney transplant patients can continue. Further research is required to ensure safety and determine the appropriate dosage and duration of drug use.

Registration: The study was compiled according to the PRISMA checklist and its protocol was registered on the PROSPERO (ID: CRD42023407501) and Research Registry (UIN: reviewregistry1666) websites.

Meta-analysis

*Corresponding author: Mahsa Shirani, Email: Shiranimahsa95@gmail.com

Implication for health policy/practice/research/medical education:
The administration of SGLT2 inhibitors did not significantly affect blood pressure and weight in kidney transplant patients. In addition, no significant change was observed in the levels of estimated glomerular filtration rate, serum creatinine, and HbA1c in patients at the end of the study compared with the baseline values. Considering the special conditions of kidney transplant patients and the risks associated with kidney transplantation, more clinical trials should be conducted before SGLT2 inhibitors are widely prescribed. These studies would give us a more complete view of the effects of SGLT2 inhibitors on these patients.

Please cite this paper as: Khodabandeh H, Bakhshizade Z, Taklif MH, Zaeri Fakhrabadi H, Alivand S, Alivand N, Rashidizadeh G, Jampour L, Shirani M. Administration of sodium-glucose cotransporter-2 inhibitors in kidney transplant patients with diabetes: a systematic review and meta-analysis. J Nephropathol. 2023;12(4):e21477. DOI: 10.34172/jnp.2023.21477.

Introduction

Diabetes mellitus and post-transplant diabetes mellitus (PTDM) are common in kidney transplant patients (1). According to the 2021 annual report of the United States Scientific Registry of Transplant Recipients (SRTR), about 47% of the candidate kidney transplant patients who are on the waiting list had diabetes mellitus, and this number is increasing year by year (2). Various types of diabetes (e.g., PTDM) substantially increase the risk of graft failure, cardiovascular disease, infection, and death in kidney transplant recipients (3,4).

Sodium-glucose cotransporter 2 (SGLT2) inhibitors are novel therapeutics for treating patients with type 2 diabetes that lower plasma glucose levels by decreasing glucose reabsorption and increasing urinary glucose excretion (5). SGLT2 inhibitors has been shown to improve the health of renal and cardiovascular systems by reducing plasma levels, blood pressure, body weight, inflammation, and oxidative stress (6,7).

Recent meta-analyses have confirmed the cardio-renal protective effects of SGLT2i such as slowed progression of diabetic nephropathy, reduced cardiovascular mortality, reduced heart failure hospitalization rates, and increased weight loss in patients with diabetes (8-10). In recent years, SGLT2i have been found to effectively slow the progression of diabetic kidney disease and reduce albuminuria in non-transplant patients (11,12). Clinical trials have clearly demonstrated the benefits of SGLT2 inhibitors; however, there have been concerns regarding urinary tract infections, acute kidney injury, and genital tract infections (13). One study found the effect of SGLT2 inhibitors on the estimated glomerular filtration rate of kidney transplant patients to be effective(14). On the other hand, another study found this relationship to be ineffective(15). Moreover, in one study, the administration of SGLT2 inhibitors significantly changes the plasma hemoglobin A1c (HbA1c) level of kidney transplant patients(16), however, another study stated that the administration of SGLT2 inhibitors has no effect on the plasma HbA1c of kidney transplant patients(17). Given the conflicting findings of previous studies, this systematic review and meta-analysis investigated the effect of SGLT2 inhibitors on kidney transplant patients with diabetes.

Material and Methods

Study design

The present systematic review and meta-analysis was performed based on the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guideline, and the study protocol was registered on the PROSPERO (ID: CRD42023407501, https://www.crd.york.ac.uk/prospero/#recordDetails) and Research Registry (UIN: reviewregistry1666) website (https://www.researchregistry.com/browse-the-registry#registryofsystematicreviewsmeta-analyses/).

Search strategy

The international databases of Cochrane, Web of Science, Scopus, and PubMed, and the Google Scholar search engine were searched without time limit using the standard MeSH (Medical Subject Headings) search terms of "Diabetes; Sodium-glucose cotransporter 2 protein, human; SGLT2 protein, human; Dapagliflozin; Canagliflozin; Empagliflozin; Kidney Transplantation; and Renal Transplantation".

Different combinations of keywords were searched using the operators "AND" and "OR". A manual search was also performed, and the search was updated until March 1, 2023. The following search strategy was conducted in PubMed: (((((((Sodium-glucose cotransporter 2 protein, human) OR (SGLT2 protein, human)) OR (Dapagliflozin)) OR (Canagliflozin)) OR (Empagliflozin)) AND (Diabetes))) AND (Kidney Transplantation OR Renal Transplantation)

Components of PICO

- Population: Kidney transplant patients
- Intervention: Administration of SGLT2 inhibitors
- Comparison: Comparison of participants' scores before and after the intervention (no comparison group)
- Outcomes: Assessment of estimated glomerular filtration rate, serum creatinine, HbA1c, systolic and

diastolic blood pressure levels, and patients' weight.

Inclusion criteria

All studies that had investigated the effect of SGLT2 inhibitors on kidney transplant patients were included.

Exclusion criteria

Case reports, letters to the editors, articles that had used median instead of mean and standard deviation (SD), repeated articles, low quality articles, articles without full text, articles that had reported only qualitative results, and those that did not contain sufficient data for data analysis were removed.

Quality evaluation

After the initial article list was compiled, two researchers independently evaluated the quality of the articles using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist (18). STROBE is a 22-item checklist that evaluates different parts of a study. Cases of discrepancy in each article were resolved using the inter-reviewer agreement method, and the cut-off point was set at 16.

Data extraction

To avoid data collection errors and possible biases, two members of the research team extracted the following data: first author's name, sample size, number of female and male participants, year of publication, country, mean age of patients, type of SGLT2, dosage, duration of use, and the mean scores before and after the intervention.

Statistical analysis

Given the quantitative nature of the initial outcome, the effect size of the intervention was calculated using the standardized mean difference (SMD). This classic effect size statistic reveals the strength of the relationship between an intervention and the respective outcome. The authors combined the selected articles based on the frequency, mean, and SD of different variables. The I^2 index and a random effects model were conducted to examine the heterogeneity of the selected articles. The data were analyzed in STATA 14, and *P* values<0.05 were considered significant.

Results

A total of 302 articles were assessed, of which "122", "35", and "5" articles were removed due to "similar titles", "irrelevant abstracts", and "incomplete texts," respectively. In addition, 132 articles that did not meet other exclusion criteria were removed. Finally, 8 high-quality articles were selected for systematic review and meta-analysis (Figure 1).

The meta-analysis included eight articles published between 2018 and 2023, with a total sample size of 960. Table 1 provides additional relevant information.

No significant difference was found in the mean estimated glomerular filtration rate of patients after taking SGLT2 inhibitors [SMD: -0.21 (95% CI: -0.65, 0.25)] (Figure 2).

Patients were allocated based on the duration of medicine use in two groups. No significant change in estimated glomerular filtration rate was observed in patients who used SGLT2 inhibitors for 6 months [SMD: -0.56 (95% CI: -1.38, 0.26)]. In addition, no significant change was found in the estimated glomerular filtration rate level of patients who took the medicine for 12 months [SMD: 0.10 (95% CI: -0.05, 0.26)]. In other words, the duration of medicine use did not significantly affect the impact of SGLT2 inhibitors on estimated glomerular filtration rate (Figure 3).

Patient age did not significantly influence the impact of SGLT2 inhibitors on estimated glomerular filtration rate (50–59 years-old age group: [SMD: 0.13 (95% CI: -0.04, 0.30)], 60–69 years-old age group: [SMD: -0.56 (95 % CI: -1.38, 0.26]) (Figure 4).

The use of SGLT2 inhibitors showed no significant impact on patients' plasma creatinine levels [SMD: -0.02 (95% CI: -0.19, 0.15)] (Figure 5).

The administration of SGLT2 inhibitors showed no significant effect on participants' HbA1c levels [SMD: -0.62 (95% CI: -1.43, 0.18)] (Figure 6).

The administration of SGLT2 inhibitors did not significantly affect patients' systolic blood pressure levels [SMD: -0.64 (95% CI: -1.80, 0.52)] (Figure 7).

The administration of SGLT2 inhibitors did not significantly affect the kidney transplant patients' diastolic blood pressure levels [SMD: -0.64 (95% CI: -1.41, 0.14)] (Figure 8).

The SGLT2 inhibitors administration did not have a significant impact on the kidney transplant patients' weight [SMD: -0.31 (95% CI: -0.80, 0.18)] (Figure 9).

Discussion

The administration of SGLT2 inhibitors did not significantly reduce levels of blood pressure, estimated glomerular filtration rate, serum creatinine, HbA1c, and weight in kidney transplant patients. The diversity of SGLT-2 inhibitors used in different studies led to heterogeneity in the results. However, the authors were not able to classify and compare the results based on the type of medicines, because some articles used only one type of medicine, whereas others used two different SGLT-2 inhibitors or even more.

The limited number of articles and the varying dose and duration of drug administration may also have influenced the final results. Due to the limited number of studies,

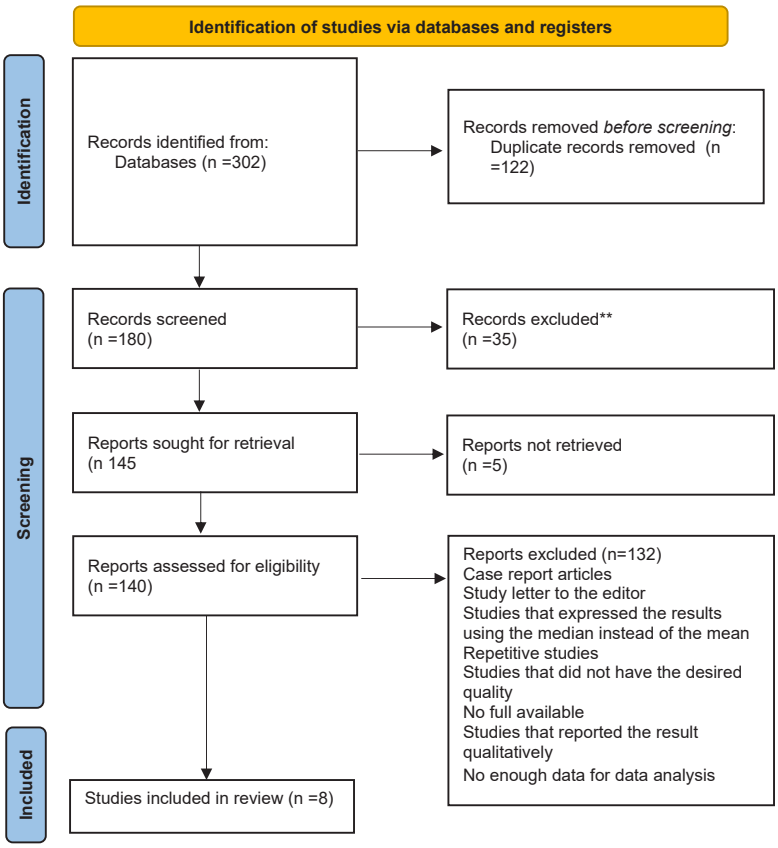

Figure 1. PRISMA flow diagram for included studies.

there was no statistical analysis based on the type of SGLT2 inhibitors and the dose of SGLT2 inhibitors. Therefore, this issue caused heterogeneity among the studied studies. In this way, they might have found the most effective SGLT-2 inhibitor or the best dose of a particular drug. It should be noted that variables such as age, weight, and gender also influenced the final results.

In the study of AlKindi et al, kidney transplant patients with diabetes, with the administration of SGLT2 inhibitors, along with the stable function of the kidneys, their blood sugar was also in a better condition (15). Moreover, Hisadome et al, showed that the administration of SGLT-2 inhibitors had no effect on the HbA1c and estimated glomerular filtration rate levels of kidney transplant patients, however it was able to significantly reduce the body weight of the patients (21).

In the study by García-Carro et al, the administration of SGLT-2 inhibitors in kidney transplant patients was associated with better control of blood sugar and blood pressure, as well as reduction of albuminuria and improvement of cardiovascular risk factors, since the administration of this drug in kidney transplant patients

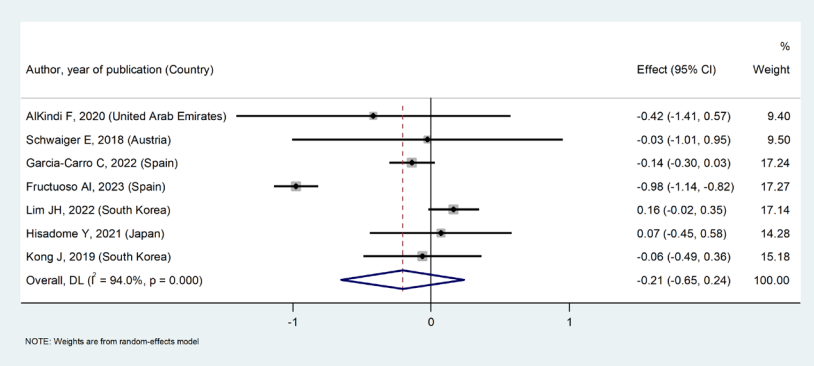

Figure 2. Forest plot showing estimated glomerular filtration rate changes after the administration of SGLT2 inhibitors.

Table 1. Characteristics of reviewed articles

Author, year of publication	Country	Type of study	Sample size	No. of females	No. of males	Mean age (y)	Study period	Type of SGLT2 inhibitors	Dose of SGLT2 inhibitors	Duration of treatment (month)
AlKindi, 2020 (15)	United Arab Emirates	Cohort study	8	6	2	56.8	June 2016-Jan 2019	Empagliflozin (6 patients), dapagliflozin (2 patients)	Empagliflozin 10 mg (5 patients), empagliflozin 25 mg (1 patient), and dapagliflozin 5 mg (2 patients)	12
Schwaiger, 2018 (17)	Austria	Pilot study	8	NR	NR	56.5	Dec 2016-June 2017	Empagliflozin	10 mg	12
Garcia-Carro, 2022 (16)	Spain	Observational study	284	73	211	61.2	NR	Empagliflozin was started in 55.8%, dapagliflozin in 23.2% and canagliflozin in 20.6%	NR	6
Shah, 2019 (19)	India	Pilot study	24	1	23	53.8	NR	Canagliflozin	100 mg	6
Fructuoso, 2023 (14)	Spain	Observational study	339	89	250	61.6	Jan 2021-March 2022	Empagliflozin (N=193, 56.9%), followed by dapagliflozin (N=81, 23.9%), and canagliflozin (N=64, 18.9%)	NR	6
Lim, 2022 (20)	South Korea	Cohort study	226	69	157	51.2	Before Dec 31, 2019	Empagliflozin N=150 (66.4%) and dapagliflozin N=76 (33.6%)	NR	12
Hisadome, 2021 (21)	Japan	Observational study	29	17	12	52.9	October 2003-October 2019	Canagliflozin N = 9 patients, ipragliflozin N = 7, luseogliflozin N = 5 , empagliflozin N = 4, dapagliflozin N = 3, and tofogliflozin N =1	NR	12
Kong, 2019 (22)	South Korea	Cohort study	42	NR	NR	NR	NR	Dapagliflozin	NR	12

NR, not reported.

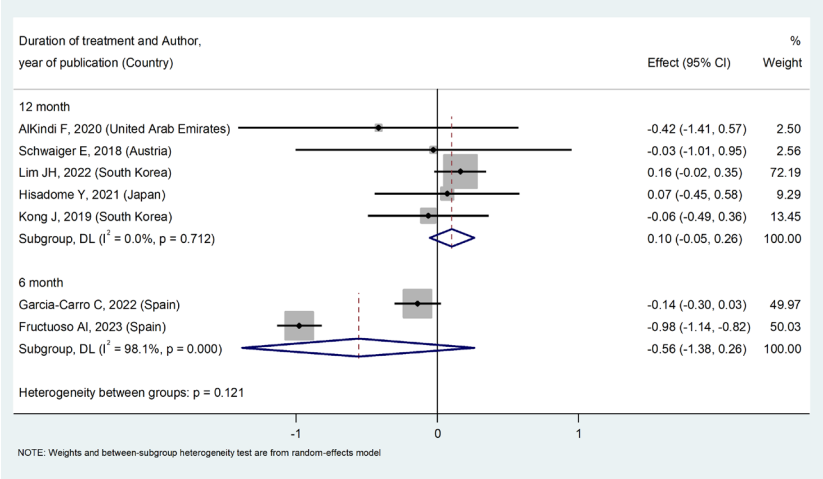

Figure 3. Forest plot showing estimated glomerular filtration rate level changes after the administration of SGLT2 inhibitors by duration of treatment.

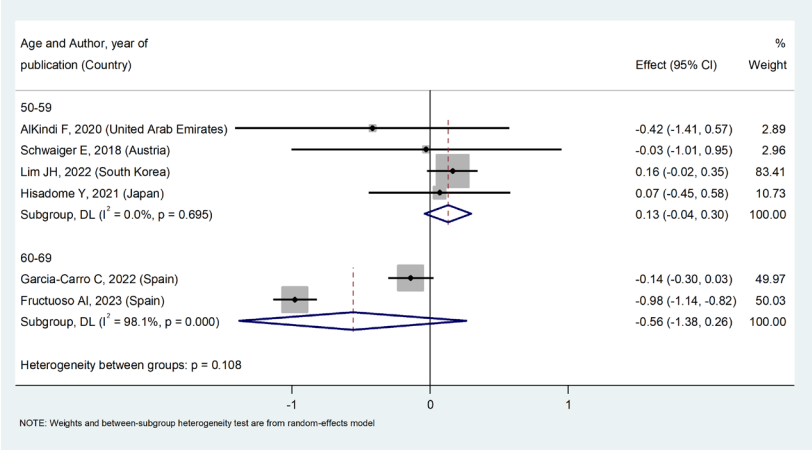

Figure 4. Forest plot showing estimated glomerular filtration rate changes after SGLT2 inhibitors administration by age group.

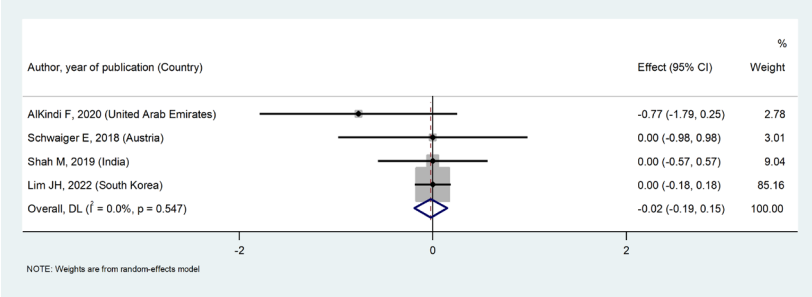

Figure 5. Forest plot showing plasma creatinine level changes following SGLT2 inhibitors administration

was found to be useful and effective (16). In the study of Shah et al, 24 patients were examined. The researchers in this study concluded that the use of SGLT-2 inhibitors had no effect on the serum creatinine of kidney transplant patients, but it reduced the body weight and blood pressure of the patients (19).

The results of the above studies were different. Some studies reported that the use of SGLT-2 inhibitors was effective in improving kidney function, as well as reducing the weight and blood pressure of patients, and on the other hand, some studies reported that the use of SGLT-2 inhibitors had no effect on kidney function. The

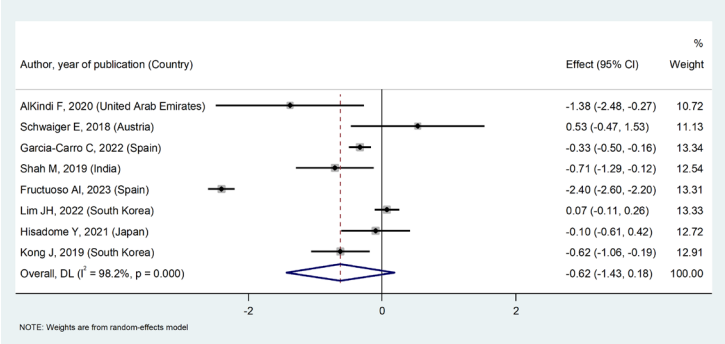

Figure 6. The forest plot of HbA1c level changes after SGLT2 inhibitors administration.

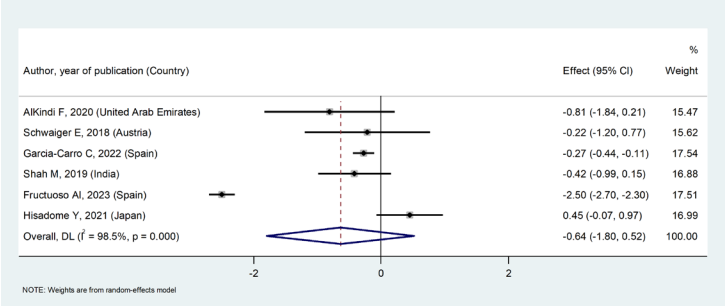

Figure 7. The forest plot shows systolic blood pressure level changes after the SGLT2 inhibitors administration.

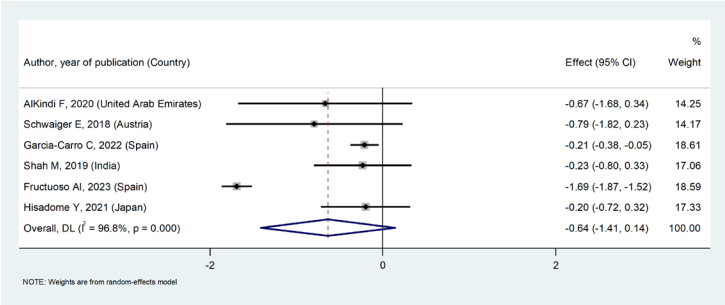

Figure 8. The forest plot shows diastolic blood pressure level changes after the SGLT2 inhibitors administration.

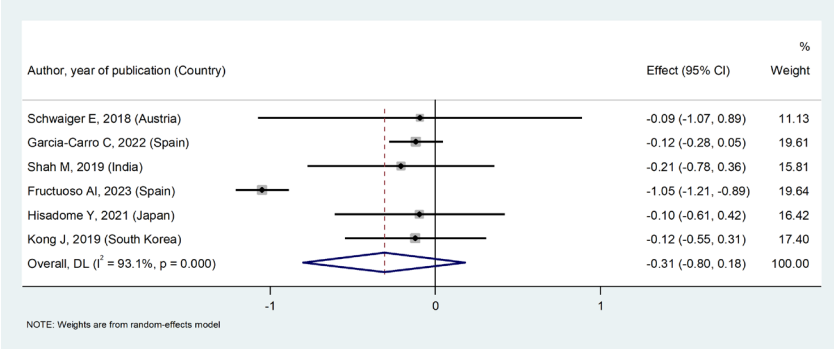

Figure 9. The forest plot shows weight changes after the SGLT2 inhibitors administration.

contradictory results of the studies are due to the different number of samples in each study, the age of the patients, the underlying diseases of the patients, other drugs taken by the patient, as well as the time interval between the kidney transplant and the administration of SGLT-2 inhibitors. For this reason, we presented a single report in the current meta-analysis by combining the results of previous studies.

The authors assessed meta-analyses that are somewhat related to the research topic. In a meta-analysis on 132 diabetic kidney transplant patients, Chewcharat et al found that SGLT-2 inhibitors significantly reduced hemoglobin A1c (HbA1c) (Weighted mean deference = -0.56% [95% CI: -0.97, -0.16]; P = 0.007) and body weight (Weighted mean deference = -2.16 kg [95% CI: -3.08, -1.24]; P < 0.001) of patients at the end of the study compared with the baseline value (23). In line with the present results, Chewcharat et al found no significant change in the estimated glomerular filtration rate of the patients, serum creatinine, and blood pressure. However, regarding changes in weight and HbA1c, these two studies did not agree with each other.

Baigent et concluded that the administration of SGLT-2 inhibitors can reduce the risk of progression of kidney disease by 37% in patients with and without diabetes compared with placebo (Risk ratio: 0.63, 95% CI: 058–0.69). They also observed that SGLT-2 inhibitors reduce the risk of acute kidney injury by 23% and the risk of cardiovascular death or hospitalization for heart failure by 23% (24). In contrast to the present meta-analysis, the study of Baigent et al found the use of SGLT-2 inhibitors to be beneficial and effective. This discrepancy may be due to the fact that the number of articles, the number of samples, and the evaluation criteria used in the present meta-analysis differed from those used by Baigent et al (24).

In a meta-analysis conducted on a large number of chronic kidney disease patients, Li et al (2021) found that SGLT-2 inhibitors reduce the risk of primary renal outcome by 30% in patients with estimated glomerular filtration rate<60 mL/min/1.73 m^2 (HR 0.70, [95 % CI: 0.58–0.83]. However, SGLT-2 inhibitors did not significantly reduce the risk of major renal outcome in chronic kidney disease patients with heart failure (25). Comparison of the above results with the findings of the present study indicates that underlying diseases can also affect the effectiveness of SGLT-2 inhibitors.

In their meta-analysis, Seidu et al observed that in individuals without renal failure, the administration of SGLT-2 inhibitors does not significantly alter estimated glomerular filtration rate compared with placebo (MD: 0.51 mL/min/1.73 m2; 95 % CI: -0.69, 1.72; p = 403) (26). In populations with or without renal failure, SGLT-2 inhibitors were associated with reduced urinary albumin excretion, improved albuminuria, reduced progression of macroalbuminuria, reduced risk of worsening renal failure, initiation of kidney transplantation, and death compared with placebo (26). In patients without kidney failure (e.g., kidney transplant patients), the administration of SGLT-2 inhibitors did not significantly affect estimated glomerular filtration rate levels.

Limitations of the study

Given the limited number of articles reviewed, subgroups were not analyzed based on variables such as type and dose of SGLT-2 inhibitors, and gender and weight of participants. To overcome this limitation, it is recommended that researchers conduct more studies in the future.

Conclusion

The administration of SGLT-2 inhibitors did not significantly affect blood pressure and weight in kidney transplant patients. In addition, no significant change was observed in levels of estimated glomerular filtration rate, creatinine, and HbA1c in patients at the end of the study compared with the baseline values. Considering the special conditions of kidney transplant patients and the risks associated with kidney transplantation, more clinical trials need to be conducted before SGLT-2 inhibitors are widely prescribed for these patients. These studies would give us a more complete view of the effects of SGLT-2 inhibitors on these patients.

Acknowledgments

The authors would like to thanks Hamid Nasri and Diana Sarokhani for guidance and editing of manuscript registration on the PROSPERO website.

Authors' contribution

Conceptualization: Hamidreza Khodabandeh and Mahsa Shirani.
Data curation: Mahsa Shirani and Ghazaleh Rashidizadeh.
Formal analysis: Soleyman Alivand and Leila Jampour.
Investigation: Noorbakhsh Alivand and Mohammad Hossein Taklif.
Methodology: Mohammad Hossein Taklif.
Project Management: Mahsa Shirani.
Resources: Zahra Bakhshizade and Soleyman Alivand.
Supervision: Hamidreza Khodabandeh.
Validation: Zahra Bakhshizade.
Visualization: Halime Zaeri Fakhrabadi and Ghazaleh Rashidizadeh.
Writing–original draft: Soleyman Alivand, Noorbakhsh Alivand, Ghazaleh Rashidizadeh, Leila Jampour, and Hamidreza Khodabandeh.
Writing–reviewing and editing: Mahsa Shirani, Halime Zaeri Fakhrabadi, Mohammad Hossein Taklif, and Zahra Bakhshizade.

Conflicts of interest

There are no competing interests.

Ethical issues

Ethical issues (including plagiarism, data fabrication,

double publication) have been completely observed by the author. This study has been compiled based on the PRISMA checklist, and its protocol was registered on the PROSPERO (International Prospective Register of Systematic Reviews) (ID: CRD42023407501) and Research Registry (UIN: reviewregistry1666) website.

Funding/Support

None.

References

1. Kaposztas Z, Gyurus E, Kahan B. New-onset diabetes after renal transplantation: diagnosis, incidence, risk factors, impact on outcomes, and novel implications. Transplant Proc. 2011;43:1375-94. doi: 10.1016/j.transproceed.2011.04.008
2. Hart A, Lentine K, Smith J, Miller J, Skeans M, Prentice M, et al. OPTN/SRTR 2019 annual data report: kidney. Am J Transplant. 2021;21:21-137. doi: 10.1111/ajt.16502
3. Eide I, Halden T, Hartmann A, Dahle D, Åsberg A, Jenssen T. Associations between posttransplantation diabetes mellitus and renal graft survival. Transplantation. 2017;101:1282-9. doi: 10.1097/TP.0000000000001259
4. Cooper L, Oz N, Fishman G, Shohat T, Rahamimov R, Mor E, et al. New onset diabetes after kidney transplantation is associated with increased mortality—A retrospective cohort study. Diabetes Metab Res Rev. 2017;33:e2920. doi: 10.1002/dmrr.2920
5. Bays H. From victim to ally: the kidney as an emerging target for the treatment of diabetes mellitus. Curr Med Res Opin. 2009;25:671-81. doi: 10.1185/03007990802710422.
6. DeFronzo R, Norton L, Abdul-Ghani M. Renal, metabolic and cardiovascular considerations of SGLT2 inhibition. Nat Rev Nephrol. 2017;13:11-26. doi: 10.1038/nrneph.2016.170.
7. Oh T, Moon J, Hur K, Ko S, Kim H, Kim T, et al. Sodium-glucose cotransporter-2 inhibitor for renal function preservation in patients with type 2 diabetes mellitus: a Korean Diabetes Association and Korean Society of Nephrology consensus statement. Diabetes Metab J 2020;44:489-97. doi: 10.4093/dmj.2020.0172.
8. Zelniker T, Wiviott S, Raz I, Im K, Goodrich E, Bonaca M, et al. SGLT2 inhibitors for primary and secondary prevention of cardiovascular and renal outcomes in type 2 diabetes: a systematic review and meta-analysis of cardiovascular outcome trials. Lancet. 2019;393:31-9. doi: 10.1016/S0140-6736(18)32590-X.
9. Liu X, Zhang N, Chen R, Zhao J, Yu P. Efficacy and safety of sodium–glucose cotransporter 2 inhibitors in type 2 diabetes: a meta-analysis of randomized controlled trials for 1 to 2 years. J Diabetes Its Complications. 2015;29:1295-303. doi: 10.1016/j.jdiacomp.2015.07.011.
10. Vergara A, Jacobs-Cacha C, Soler M. Sodium-glucose cotransporter inhibitors: beyond glycaemic control. Clin Kidney J. 2019;12:322-5. doi: 10.1093/ckj/sfz019.
11. Perkovic V, Jardine M, Neal B, Bompoint S, Heerspink H, Charytan D, et al. Canagliflozin and renal outcomes in type 2 diabetes and nephropathy. N Engl J Med. 2019;380:2295-306. doi: 10.1056/NEJMoa1811744
12. Heerspink H, Stefánsson B, Correa-Rotter R, Chertow G, Greene T, Hou F, et al. Dapagliflozin in patients with chronic kidney disease. N Engl J Med. 2020;383:1436-46. doi: 10.1056/NEJMoa2024816.
13. Zaccardi F, Webb D, Htike Z, Youssef D, Khunti K, Davies M. Efficacy and safety of sodium-glucose co-transporter-2 inhibitors in type 2 diabetes mellitus: systematic review and network meta-analysis. Diabetes, Obes Metab. 2016;18:783-94. doi: 10.1111/dom.12670.
14. Fructuoso A, Raba A, Deras E, Sánchez L, Cecilio R, Esteve A, et al. Sodium-glucose cotransporter-2 inhibitor therapy in kidney transplant patients with type 2 or post-transplant diabetes: an observational multicenter study. Clin Kidney J. 2023. doi: 10.1093/ckj/sfad007.
15. AlKindi F, Al-Omary H, Hussain Q, Al Hakim M, Chaaban A, Boobes Y. Outcomes of SGLT2 inhibitors use in diabetic renal transplant patients. Transplant Proc. 2020;52:175-8. doi: 10.1016/j.transproceed.2019.11.007.
16. García-Carro C, Bedia Raba A, Banegas Deras E, Alberto Vigara L, Valero San Cecilio R, Cruzado Vega L, et al. SGLT2 inhibitors in kidney transplantation: a multicenter study. Nephrol Dial Transplant. 2022;37:I884-I. doi:10.1093/ndt/gfac124.001
17. Schwaiger E, Burghart L, Signorini L, Ristl R, Kopecky C, Tura A, et al. Empagliflozin in posttransplantation diabetes mellitus: A prospective, interventional pilot study on glucose metabolism, fluid volume, and patient safety. Am J Transplant. 2019;19:907-19. doi: 10.1111/ajt.15223
18. Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol. 2008;61:344-9. doi: 10.1016/j.jclinepi.2007.11.008.
19. Shah M, Virani Z, Rajput P, Shah B. Efficacy and safety of canagliflozin in kidney transplant patients. Indian J Nephrol. 2019;29:278-81. doi: 10.4103/ijn.IJN_2_18
20. Lim J, Kwon S, Jeon Y, Kim Y, Kwon H, Kim Y, et al. The efficacy and safety of SGLT2 inhibitor in diabetic kidney transplant recipients. Transplantation. 2022;106:e404-12. doi: 10.1097/TP.0000000000004228
21. Hisadome Y, Mei T, Noguchi H, Ohkuma T, Sato Y, Kaku K, et al. Safety and Efficacy of Sodium-glucose Cotransporter 2 Inhibitors in Kidney Transplant Recipients With Pretransplant Type 2 Diabetes Mellitus: A Retrospective, Single-center, Inverse Probability of Treatment Weighting Analysis of 85 Transplant Patients. Transplant Direct. 2021;7:e772. doi: 10.1097/TXD.0000000000001228.
22. kong J, Joon J, Chul Y, Eun W, Hyuk K, Sung Hyun S. Sodium/glucose cotransporter 2 inhibotor for the treatment of diabetes in kidney transplant patients. Nephrol Dial Transplant. 2019;34:gfz103-SP770.
23. Chewcharat A, Prasitlumkum N, Thongprayoon C, Bathini T, Medaura J, Vallabhajosyula S, et al. Efficacy and safety of SGLT-2 inhibitors for treatment of diabetes mellitus

among kidney transplant patients: a systematic review and meta-analysis. Med Sci (Basel). 2020;8:47. doi: 10.3390/medsci8040047
24. Baigent C, Emberson J, Haynes R, Herrington W, Judge P, Landray M, et al. Impact of diabetes on the effects of sodium glucose co-transporter-2 inhibitors on kidney outcomes: collaborative meta-analysis of large placebo-controlled trials. Lancet. 2022;400:1788-801. doi: 10.1016/S0140-6736(22)02074-8
25. Li N, Lv D, Zhu X, Wei P, Gui Y, Liu S, et al. Effects of SGLT2 inhibitors on renal outcomes in patients with chronic kidney disease: a meta-analysis. Front Med. 2021;8:728089. doi: 10.3389/fmed.2021.728089
26. Seidu S, Kunutsor S, Cos X, Gillani S, Khunti K. SGLT2 inhibitors and renal outcomes in type 2 diabetes with or without renal impairment: a systematic review and meta-analysis. Prim Care Diabetes. 2018:265-83. doi: 10.1016/j.pcd.2018.02.001