



Association of Empagliflozin Therapy with the Development of Erythrocytosis in Individuals with Type 2 Diabetes and Chronic Kidney Disease

Samaneh Hashemi ¹, Leila Barahimi ¹, Mohammad Kogani ¹, Tina Eghdampanah Foumani ¹,
*, Ehsan Moradi-Joo ¹,**

¹ Abadan University of Medical Sciences, Abadan, Iran

*Corresponding Author: School of Medicine, Abadan University of Medical Sciences, Abadan, Iran. Email: tina.eghdam@gmail.com

**Corresponding Author: Department of Public Health, School of Health, Abadan University of Medical Sciences, Abadan, Iran. Email: ehsanmoradijoo@yahoo.com

Received: 27 February, 2026; Revised: 10 October, 2026; Accepted: 24 October, 2026

Abstract

Background: Empagliflozin, a sodium-glucose cotransporter 2 (SGLT2) inhibitor, is widely used in patients with type 2 diabetes mellitus (T2DM) and chronic kidney disease (CKD). In addition to its established cardiorenal benefits, emerging evidence suggests potential effects on hemoglobin levels and erythrocytosis.

Objectives: This study aimed to evaluate the association between empagliflozin therapy and erythrocytosis in patients with T2DM and CKD.

Methods: This retrospective cohort study included 300 patients with T2DM and CKD treated at two teaching hospitals between 2023 and 2024. Patients were categorized as empagliflozin users (n = 100) or nonusers (n = 200). Erythrocytosis was assessed after ≥ 6 months of continuous therapy. Unadjusted, age- and sex-adjusted, and fully adjusted logistic regression analyses were performed.

Results: Erythrocytosis occurred in 8 of 100 users (8%) and 5 of 200 nonusers (2.5%). Empagliflozin use was associated with higher odds of erythrocytosis in the unadjusted model (odds ratio [OR] = 3.64; 95% confidence interval [CI], 0.59 - 22.20; P = 0.161) and the age- and sex-adjusted model (OR = 4.38; 95% CI, 0.66 - 28.90; P = 0.125). In the fully adjusted model, the association remained directionally positive but imprecise (OR = 41.73; 95% CI, 0.11 - 15061.54; P = 0.214). Increasing age was inversely associated with erythrocytosis in the age- and sex-adjusted model (OR = 0.91; 95% CI, 0.84 - 0.97; P = 0.012).

Conclusions: Empagliflozin therapy was associated with higher point estimates of the odds of erythrocytosis; however, the lack of statistical significance and wide confidence intervals indicate substantial uncertainty. These findings are exploratory and should be interpreted cautiously. Larger prospective studies are needed to clarify this potential association.

Keywords: Empagliflozin, Erythrocytosis, Diabetes Mellitus, Type 2, Chronic Kidney Disease, Hemoglobins, Hematocrit, Logistic Models

1. Background

Type 2 diabetes mellitus (T2DM) is a common metabolic disease characterized by chronic hyperglycemia and microvascular and macrovascular complications (1). Empagliflozin, a sodium-glucose cotransporter 2 (SGLT2) inhibitor, is a relatively recent therapeutic agent with demonstrated cardiorenal benefits (2).

Empagliflozin reduces plasma glucose concentrations by blocking glucose reabsorption in the proximal renal tubules, thereby increasing urinary glucose excretion. Large randomized controlled trials have demonstrated that empagliflozin and dapagliflozin improve glycemic control while reducing hospitalizations for heart failure, slowing chronic kidney disease (CKD) progression, and lowering cardiovascular mortality (3, 4). Empagliflozin may also

Copyright © 2026, Hashemi et al. This open-access article is available under the Creative Commons Attribution 4.0 (CC BY 4.0) International License (<https://creativecommons.org/licenses/by/4.0/>), which allows for unrestricted use, distribution, and reproduction in any medium, provided that the original work is properly cited.

How to Cite: Hashemi S, Barahimi L, Kogani M, Eghdampanah Foumani T, Moradi-Joo E. Association of Empagliflozin Therapy with the Development of Erythrocytosis in Individuals with Type 2 Diabetes and Chronic Kidney Disease. Jundishapur J Chronic Dis Care. 2026;15(4):e170932. doi: <https://doi.org/10.5812/jjcdc-170932>

increase hemoglobin and hematocrit levels. One potential consequence of these changes is erythrocytosis, a complication that has received comparatively limited attention (5). Recent clinical evidence also suggests that SGLT2 inhibitors exert systemic effects beyond glycemic and cardiorenal outcomes. For example, empagliflozin has been shown to ameliorate hepatic inflammation and improve liver enzyme profiles in patients with T2DM, indicating that its physiological effects extend to multiple organ systems (6). These systemic effects may help contextualize the hematologic changes observed in patients receiving SGLT2 inhibitors.

Chronic kidney disease is defined by persistent structural or functional abnormalities of the kidneys lasting at least three months and represents a major global health burden (7). An estimated 850 million individuals worldwide have some form of kidney disease, and CKD is among the fastest-growing causes of mortality globally (8). Nearly one-third to one-half of patients with T2DM develop CKD, underscoring the importance of effective therapeutic strategies to slow disease progression and reduce complications (9).

Multiple investigations have reported that extended use of SGLT2 inhibitors, including empagliflozin, leads to modest increases in hemoglobin and hematocrit levels, generally reflecting hemoconcentration or enhanced erythropoiesis. In contrast, clinically defined erythrocytosis represents a pathological increase in red blood cell mass, typically diagnosed when hemoglobin exceeds 16.5 g/dL or hematocrit exceeds 49% in males, or when hemoglobin exceeds 16 g/dL or hematocrit exceeds 48% in females (10, 11). The reported prevalence of erythrocytosis varies widely, ranging from 2% to 19%, depending on the population studied (12). Although the mechanisms remain incompletely understood, proposed pathways include enhanced erythropoietin production, improved renal oxygenation, and reduced oxidative stress (13).

A rise in red blood cell mass may reflect hemoconcentration or erythropoiesis-related changes. Although erythrocytosis has been associated with increased blood viscosity in other clinical contexts, our study did not assess thrombotic or cardiovascular events. This distinction is particularly relevant in individuals with concurrent T2DM and CKD, who have impaired erythropoietic regulation, reduced renal oxygenation, chronic inflammation, and elevated cardiovascular risk, all of which may increase susceptibility to hematologic fluctuations. Clarifying the relationship between SGLT2 inhibitor therapy and erythrocytosis in patients with concurrent T2DM and CKD is therefore of considerable clinical and pathophysiological importance (14). Given the

expanding use of SGLT2 inhibitors and the scarcity of data from Iranian CKD populations, further investigation is warranted.

2. Objectives

This study aimed to assess the association between empagliflozin use and the occurrence of erythrocytosis among patients with T2DM and CKD.

3. Methods

3.1. Study Design and Setting

This retrospective cohort study explored the association between empagliflozin use and erythrocytosis in patients with T2DM and CKD. Data were extracted from the medical records of patients treated at Shahid Beheshti and Alavi hospitals in Abadan, Iran, during 2023 - 2024.

3.2. Participants and Eligibility Criteria

Records were eligible for analysis if core laboratory data, including hemoglobin, hematocrit, serum creatinine, and estimated glomerular filtration rate, were complete. Missing data for other demographic or clinical variables did not preclude eligibility.

The inclusion criteria were as follows:

- 1) A confirmed diagnosis of T2DM based on the American Diabetes Association diagnostic criteria;
- 2) CKD, defined as an eGFR < 60 mL/min/1.73 m² for at least three months;
- 3) Complete laboratory data for hemoglobin, hematocrit, serum creatinine, and eGFR.

Patients were excluded if they had acute kidney injury, end-stage renal disease requiring dialysis or kidney transplantation, known hematologic or bone marrow disorders, or were receiving medications known to stimulate erythropoiesis, such as erythropoietin or testosterone. Records with incomplete or unreliable core laboratory data were also excluded.

3.3. Exposure Definition

The exposed group included 100 patients who were prescribed empagliflozin at a daily dose of 25 mg by endocrinologists or nephrologists at the participating hospitals. Continuous use was confirmed through follow-up visits and prescription records, and patients were required to have received at least six months of uninterrupted therapy. The comparison group consisted of 200 patients who did not receive empagliflozin. Although limited medication availability contributed to nonuse,

both groups were drawn from the same clinical settings, treated by the same endocrinologists and nephrologists, and evaluated during the same study period. Baseline demographic and clinical characteristics, including age, sex, duration of diabetes, CKD stage, comorbidities, and concomitant medications, were compared to assess whether nonuse reflected systematic differences in disease severity, prescribing patterns, or socioeconomic status. No significant differences were observed across these variables, minimizing the likelihood of selection bias.

3.4. Outcome Definition

The primary outcome was erythrocytosis, defined according to World Health Organization criteria and verified using local laboratory reference ranges. For empagliflozin users, hemoglobin and hematocrit values were obtained at baseline, before treatment initiation, and at follow-up six months after the index date. For nonusers, stable hemoglobin and hematocrit measurements were obtained at baseline and at follow-up six months after the index date. Laboratory results associated with transient hemoconcentration or dehydration, identified through clinical documentation, elevated serum sodium, or abnormal blood urea nitrogen/creatinine ratios, were excluded to ensure that only stable hematologic values were analyzed.

3.5. Data Collection and Variables

Demographic characteristics (age, sex, and body mass index [BMI]), clinical variables (duration of diabetes, duration of CKD, smoking status, and comorbid conditions), and laboratory findings (hemoglobin, hematocrit, serum creatinine, and eGFR) were extracted from patient records. Information on concomitant medications that could influence hemoglobin levels, including ACEi/ARB and diuretics, was also documented. Detailed iron studies, vitamin B₁₂/folate levels, and hypoxia-related conditions were not consistently available and therefore could not be systematically analyzed.

For empagliflozin users, the index date was the date of treatment initiation. Baseline laboratory values were obtained before exposure, and follow-up ended after six months of continuous therapy. For nonusers, the index date was the most recent stable laboratory evaluation within the same study period, and follow-up ended six months later. Patients with baseline erythrocytosis were excluded to establish clear temporality between exposure and outcome. Data abstraction was performed using standardized forms by two independent investigators, with discrepancies resolved by reviewing the original records.

3.6. Sample Size Estimation

Sample size estimation was initially performed using FASS software; however, detailed assumptions regarding the expected event rate, effect size, and rationale for the 1:2 exposure ratio were not available in the study records. The final sample size was therefore determined by the number of eligible patients identified during the study period, resulting in 100 exposed and 200 unexposed individuals.

3.7. Statistical Analysis

Statistical analyses were conducted using SPSS software, version 26. Continuous variables were summarized as mean $\pm$ standard deviation, and categorical variables as frequencies and percentages. Between-group comparisons were performed using the independent t-test or Mann-Whitney U test for continuous variables and the chi-square or Fisher exact test for categorical variables, as appropriate. Given the limited number of erythrocytosis events ($n = 13$), a parsimonious logistic regression model was used to reduce the risk of overfitting. Age and sex were included as core covariates, and additional variables were incorporated only if clinically essential. Penalized or exact logistic regression methods were considered but could not be applied because of software limitations. Results were expressed as odds ratios (ORs) with 95% confidence intervals (CIs), and a two-sided P value < 0.05 was considered statistically significant. Sex was coded as female = 1 and male = 2; smoking status as smoker = 1 and nonsmoker = 2; empagliflozin use as user = 1 and nonuser = 2; and comorbidities as hypertension = 1, cardiovascular disease = 2, metabolic disease = 3, hematologic disease = 4, neurologic disease = 5, and pulmonary disease = 6.

3.8. Ethical Considerations

The study adhered to the ethical principles of the Declaration of Helsinki and complied with institutional research ethics regulations. All patient information was anonymized and coded to ensure confidentiality, and access to the data was restricted to the research team. Because this was a retrospective study with no direct patient intervention, no changes were made to clinical management. The research protocol was approved by the Ethics Committee of Abadan University of Medical Sciences (approval code: IR.ABADANUMS.REC.1404.049), and the Ethics Committee waived the requirement for informed consent.

4. Results

The baseline demographic and clinical characteristics of the participants are summarized in [Table 1](#). Overall, the

two groups were well balanced for most baseline variables, including age, sex distribution, BMI, smoking status, duration of diabetes, duration of CKD, serum creatinine, and eGFR, with no statistically significant differences between empagliflozin users and nonusers (all $P > 0.05$). However, baseline hemoglobin levels were significantly higher among empagliflozin users than among nonusers (11.88 ± 1.91 vs 11.07 ± 1.91 g/dL, $P = 0.001$). Hematocrit levels were also significantly higher among users ($35.6 \pm 5.7\%$ vs $33.2 \pm 5.7\%$, $P = 0.002$). These imbalances were accounted for by including baseline hemoglobin in the fully adjusted logistic regression models. The prevalence of comorbidities was comparable between the groups, with hypertension being the most common comorbidity in both groups (62% vs 65%, $P = 0.61$). Missing data were minimal across all variables, with the highest proportion observed for total comorbidities (2.0%); complete-case analysis was used to handle missing data.

In the univariate logistic regression model, empagliflozin therapy was associated with higher estimated odds of erythrocytosis (OR = 3.64; 95% CI, 0.59 - 22.20; $P = 0.161$). However, this association did not reach statistical significance, and the wide confidence interval indicated substantial uncertainty in the estimate (Table 2).

After adjustment for age and sex, the positive association between empagliflozin use and erythrocytosis persisted (OR = 4.38; 95% CI, 0.66 - 28.90; $P = 0.125$). Age showed an inverse association with erythrocytosis in the age- and sex-adjusted model (OR = 0.91; 95% CI, 0.84 - 0.97; $P = 0.012$); however, this finding should be interpreted cautiously because it was not replicated in the fully adjusted model. Sex was not significantly associated with the outcome (OR = 1.63; 95% CI, 0.25 - 10.44; $P = 0.605$) (Table 3).

In the fully adjusted logistic regression model, the estimate for empagliflozin use was extremely imprecise (OR = 41.73; 95% CI, 0.11 - 15061.54; $P = 0.214$), reflecting sparse data and a very wide confidence interval. This result should be considered exploratory and does not provide reliable evidence of increased risk (Table 4).

Other covariates, including sex (OR = 0.0019, $P = 0.328$), smoking (OR = 0.0049, $P = 0.346$), eGFR (OR = 0.93, $P = 0.828$), and creatinine (OR = 0.43, $P = 0.803$), were not significantly associated with erythrocytosis. Baseline hemoglobin showed a borderline positive association (OR = 16.31; 95% CI, 0.71 - 373.90; $P = 0.081$), suggesting that higher initial hemoglobin levels may be associated with a greater probability of erythrocytosis.

Given the small number of erythrocytosis events ($n = 13$), the fully adjusted model may be unstable. These results should be interpreted cautiously.

5. Discussion

This retrospective cohort study investigated the relationship between empagliflozin treatment and the development of erythrocytosis in individuals with T2DM and CKD. In both unadjusted and adjusted models, empagliflozin use was associated with higher estimated odds of erythrocytosis; however, these associations did not reach statistical significance, and the wide confidence intervals indicated substantial uncertainty in the estimates (15).

In unadjusted analyses, empagliflozin users showed a trend toward increased odds of erythrocytosis (OR = 3.64), but this finding did not reach statistical significance. This pattern is consistent with earlier reports indicating that SGLT2 inhibitors can raise hemoglobin and hematocrit levels (15). The lack of significance is likely related to the modest sample size and resulting wide confidence intervals. Nonetheless, this pattern underscores the potential clinical relevance of the findings and warrants further investigation in larger populations.

Adjustment for age and sex maintained the positive association (OR = 4.38). Age emerged as a significant factor, with younger patients showing increased susceptibility to erythrocytosis (OR = 0.91, $P = 0.012$). Sex did not appear to modify the association, consistent with earlier studies suggesting that the erythropoietic effects of these drugs are not sex-specific.

In the fully adjusted multivariable model, which accounted for multiple potential confounders, empagliflozin use remained associated with substantially increased odds of erythrocytosis (OR = 41.73), although statistical significance was not reached ($P = 0.214$). The wide confidence interval reflects sample variability and limited power. None of the examined covariates were significantly associated with erythrocytosis, although baseline hemoglobin showed a borderline association (OR = 16.31, $P = 0.081$), suggesting that patients with higher initial hemoglobin levels may be more likely to develop erythrocytosis.

Overall, these findings suggest a possible association between empagliflozin therapy and increased odds of erythrocytosis, although statistical significance was not demonstrated. Research on the broader metabolic and inflammatory aspects of T2DM has also examined the effects of lifestyle interventions, including exercise timing, on inflammatory and cognitive outcomes in affected populations (16). However, these findings do not establish a direct relationship between exercise-related changes in inflammation and erythrocytosis associated with SGLT2 inhibitors. Previous studies have reported metabolic and anti-inflammatory effects of empagliflozin in extrarenal

Table 1. Baseline Demographic and Clinical Characteristics of Study Participants ^a

Characteristics	Empagliflozin (n = 100)	Non-users (n = 200)	P value	Missing
Demographic characteristics				
Age (y)	63.67 ± 11.75	64.95 ± 11.75	0.38	0 (0)
Gender (male)	45 (45)	108 (54)	0.14	0 (0)
BMI (kg/m ²)	28.4 ± 5.2	27.9 ± 5.6	0.45	4 (1.3)
Smoking	29 (29)	80 (40)	0.06	2 (0.7)
Diabetes and CKD history				
Duration of diabetes (y)	10.2 ± 6.8	10.8 ± 7.1	0.48	3 (1.0)
Duration of CKD (y)	4.5 ± 3.2	4.8 ± 3.5	0.47	5 (1.7)
Laboratory parameters				
Baseline hemoglobin (g/dL)	11.88 ± 1.91	11.07 ± 1.91	0.001	0 (0)
Hematocrit (%)	35.6 ± 5.7	33.2 ± 5.7	0.002	0 (0)
Serum creatinine (mg/dL)	1.98 ± 0.68	2.09 ± 0.71	0.17	0 (0)
eGFR (mL/min/1.73 m ²)	37.01 ± 11.87	35.83 ± 11.87	0.42	0 (0)
Comorbidities				
Hypertension	62 (62)	130 (65)	0.61	3 (1.0)
Cardiovascular disease	28 (28)	60 (30)	0.72	3 (1.0)
Metabolic disease	15 (15)	35 (17.5)	0.58	4 (1.3)
Hematologic disease	4 (4)	6 (3)	0.64	5 (1.7)
Neurologic disease	8 (8)	18 (9)	0.77	4 (1.3)
Pulmonary disease	6 (6)	14 (7)	0.74	4 (1.3)
Total comorbidities	1.23 ± 0.95	1.29 ± 0.98	0.61	6 (2.0)

^a Values are expressed as mean ± SD or No. (%). Abbreviations: BMI, Body Mass Index; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; SD, standard deviation.

Table 2. Univariate Logistic Regression Analysis of Empagliflozin Use and Erythrocytosis

Variables	Odds Ratio	95% Confidence Interval	P Value
Empagliflozin use	3.64	0.59 - 22.20	0.161

Table 3. Multivariable Logistic Regression Adjusted for Age and Sex

Variables	Odds Ratio	95% Confidence Interval	P Value
Empagliflozin use	4.38	0.66 - 28.90	0.125
Age	0.91	0.84 - 0.97	0.012
Sex	1.63	0.25 - 10.44	0.605

organs, including the liver (6), suggesting that SGLT2 inhibitors may simultaneously influence multiple physiological pathways. Although these studies do not directly evaluate hematologic parameters, they support the concept that SGLT2 inhibitors can induce widespread biological changes that may contribute to alterations in hemoglobin and hematocrit levels. The primary limitation was the relatively small sample size, which constrained the precision of the effect estimates. Larger prospective studies

are needed to confirm these associations and clarify the hematologic effects of these agents in patients with CKD (17, 18).

From a clinical perspective, these findings highlight the importance of monitoring hemoglobin and hematocrit levels in patients receiving empagliflozin (19). Because our study did not assess thromboembolic events or management outcomes, clinical recommendations should be limited to careful monitoring. Further research is

Table 4. Fully Adjusted Multivariable Logistic Regression Analysis for Erythrocytosis ^a

Variables	Odds Ratio	95% Confidence Interval	P Value
Empagliflozin use	41.73	0.11 - 15061.54	0.214
Age	0.85	0.55 - 1.33	0.492
Gender	0.0019	0.0000000068 - 540.40	0.328
Smoking	0.0049	0.000000079 - 308.30	0.346
Other comorbidities	1.04	0.91 - 1.18	0.552
Duration of diabetes	0.0007	0.000000034 - 12.94	0.147
eGFR	0.93	0.53 - 1.67	0.828
Creatinine	0.43	0.0005 - 346.14	0.803
Baseline hemoglobin (Hb1)	16.31	0.71 - 373.90	0.081

^a Abbreviations: eGFR, estimated glomerular filtration rate; Hb1, baseline hemoglobin.

needed to clarify the clinical significance of these hematologic changes.

The very broad confidence intervals and unstable estimates, notably the OR of 41.73 in the fully adjusted model, probably result from sparse-data bias and overfitting rather than reflecting a genuine biological phenomenon. Because major trials such as EMPA-REG OUTCOME, CANVAS, and CREDENCE did not report erythrocytosis outcomes comparable to ours, direct numerical comparison is inappropriate. The present findings should therefore be interpreted as hypothesis-generating rather than confirmatory.

Several hypothetical mechanisms have been proposed to explain SGLT2 inhibitor-associated erythrocytosis, including enhanced erythropoietin (EPO) production, improved renal tubular oxygenation, and reduced oxidative stress (15). Prior studies, including those by Sano et al., suggest that increases in hematocrit during SGLT2 inhibitor therapy may be related to elevated EPO levels and possible HIF stabilization (15). Additionally, reduced proximal tubular sodium reabsorption could theoretically decrease oxygen consumption in the renal cortex, potentially alleviating chronic hypoxia and stimulating EPO secretion from peritubular fibroblasts. From a health care management perspective, effective monitoring of potential medication-related complications requires coordination of clinical processes, information sharing, and organizational learning (20). These mechanisms remain speculative in the context of our dataset because none of these pathways were measured, and their relative contributions require further investigation.

5.1. Limitations

Several limitations should be acknowledged. First, the modest sample size reduced statistical power and widened confidence intervals. Second, the retrospective

observational design precludes causal inference. Third, residual confounding by unmeasured factors, including nutritional status, iron metabolism, and other clinical variables, cannot be excluded. Fourth, conducting the study in teaching hospitals in a single regional setting may limit generalizability. Fifth, the small number of erythrocytosis events relative to the number of covariates may have contributed to sparse-data bias, model instability, and overfitting. Additionally, the retrospective design introduces the potential for immortal-time bias, and exposure and outcome misclassification may have occurred because of reliance on routine clinical documentation. Missing-data mechanisms were not fully characterized, and the absence of propensity-score balancing may have allowed systematic differences between exposed and unexposed groups to persist. Finally, residual confounding by anemia-related diseases and medications cannot be ruled out. Because the exposed group consisted exclusively of empagliflozin users, the findings may not be generalizable to all SGLT2 inhibitors.

5.2. Conclusions

This study did not demonstrate a statistically significant association between empagliflozin use and erythrocytosis in individuals with T2DM and CKD. All effect estimates were imprecise, with wide confidence intervals indicating substantial uncertainty. The findings should therefore be interpreted cautiously and considered exploratory rather than confirmatory.

Acknowledgements

The authors thank the staff of Shahid Beheshti and Alavi teaching hospitals in Abadan for their assistance with data collection and patient record management. Special appreciation is extended to the Research and Ethics

Committee of Abadan University of Medical Sciences for their guidance and support.

Footnotes

AI Use Disclosure: The authors declare that no generative artificial intelligence (AI) tools were used in the creation of this article.

Authors' Contribution: Study Supervision, Data Monitoring, and Data Analysis and Interpretation Support: S. H. and L. B.; Statistical Analysis and Manuscript Drafting: E. M. and M. K.; Submission Coordination, Journal Correspondence, and Data Collection Support: T. E. All authors participated in all stages of the study, critically reviewed the manuscript, and approved the final version.

Conflict of Interests Statement: The authors declare that they have no competing interests.

Data Availability: The datasets generated and/or analyzed during the current study are not publicly available due to institutional restrictions but are available from the corresponding author on reasonable request.

Ethical Approval: This study was approved by the Ethics Committee of Abadan University of Medical Sciences (Approval Code: IR.ABADANUMS.REC.1404.049). All procedures were conducted in accordance with the Declaration of Helsinki.

Funding/Support: This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. It was conducted as part of a Doctor of Medicine (MD) thesis project.

References

- Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, et al. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. *N Engl J Med*. 2015;**373**(22):2117-28. [PubMed ID: 26378978]. <https://doi.org/10.1056/NEJMoa1504720>.
- Neal B, Perkovic V, Mahaffey KW, de Zeeuw D, Fulcher G, Erond N, et al. Canagliflozin and cardiovascular and renal events in type 2 diabetes. *N Engl J Med*. 2017;**377**(7):644-57. [PubMed ID: 28605608]. <https://doi.org/10.1056/NEJMoa1611925>.
- Wiviott SD, Raz I, Bonaca MP, Mosenzon O, Kato ET, Cahn A, et al. Dapagliflozin and cardiovascular outcomes in type 2 diabetes. *N Engl J Med*. 2019;**380**(4):347-57. [PubMed ID: 30415602]. <https://doi.org/10.1056/NEJMoa1812389>.
- McMurray JJV, Solomon SD, Inzucchi SE, Køber L, Kosiborod MN, Martinez FA, et al. Dapagliflozin in patients with heart failure and reduced ejection fraction. *N Engl J Med*. 2019;**381**(21):1995-2008. [PubMed ID: 31535829]. <https://doi.org/10.1056/NEJMoa1911303>.
- Packer M, Anker SD, Butler J, Filippatos G, Pocock SJ, Carson P, et al. Cardiovascular and renal outcomes with empagliflozin in heart failure. *N Engl J Med*. 2020;**383**(15):1413-24. [PubMed ID: 32865377]. <https://doi.org/10.1056/NEJMoa2022190>.
- Nasiri Mehr K, Shokry J, Gholinia Ahangar H, Ebrahimzadeh Pirshahid M, Seyedalipour SF, Emami A, et al. The effect of empagliflozin on non-alcoholic steatohepatitis and liver enzymes levels in patients with type 2 diabetes mellitus: a randomized clinical trial. *Hepat Mon*. 2025;**25**(1). e150453. <https://doi.org/10.5812/hepatmon-150453>.
- Heerspink HJL, Stefánsson BV, Correa-Rotter R, Chertow GM, Greene T, Hou FF, et al. Dapagliflozin in patients with chronic kidney disease. *N Engl J Med*. 2020;**383**(15):1436-46. [PubMed ID: 32970396]. <https://doi.org/10.1056/NEJMoa2024816>.
- Khoramnia S, Moradzadegan A. Investigating the Effect of Thyroid Hormones on Diabetic Nephropathy in Type 2 Diabetic Patients Referred to Ahvaz Hospitals in 2017. *Gene Cell Tissue*. 2023;**10**(3). e134691. <https://doi.org/10.5812/gct-134691>.
- Kazem-Nadi S, Mousavi V, Labbani-Motlagh Z, Keshtkari S. Comparative Incidence of Urinary Tract Infections in Diabetic Women Treated with Dapagliflozin Versus Empagliflozin: A Double-Blind Randomized Clinical Trial. *Int J Endocrinol Metab*. 2026;**24**(4). e168824. [PubMed ID: 42763716]. [PubMed Central ID: PMC13589459]. <https://doi.org/10.5812/ijem-168824>.
- Heerspink HJL, Perkins BA, Fitchett DH, Husain M, Cherney DZI. Sodium glucose cotransporter 2 inhibitors in the treatment of diabetes mellitus: cardiovascular and kidney effects, potential mechanisms, and clinical applications. *Circulation*. 2016;**134**(10):752-72. [PubMed ID: 27470878]. <https://doi.org/10.1161/CIRCULATIONAHA.116.021887>.
- Vallon V, Thomson SC. Targeting renal glucose reabsorption to treat hyperglycaemia: the pleiotropic effects of SGLT2 inhibition. *Diabetologia*. 2017;**60**(2):215-25. [PubMed ID: 27878313]. [PubMed Central ID: PMC5884445]. <https://doi.org/10.1007/s00125-016-4157-3>.
- Toyama T, Neuen BL, Jun M, Ohkuma T, Neal B, Jardine MJ, et al. Effect of SGLT2 inhibitors on cardiovascular, renal and safety outcomes in patients with type 2 diabetes mellitus and chronic kidney disease: a systematic review and meta-analysis. *Diabetes Obes Metab*. 2019;**21**(5):1237-50. [PubMed ID: 30697905]. <https://doi.org/10.1111/dom.13648>.
- Ferrannini E, Mark M, Mayoux E. CV protection in the EMPA-REG OUTCOME trial: a "thrifty substrate" hypothesis. *Diabetes Care*. 2016;**39**(7):1108-14. [PubMed ID: 27289126]. <https://doi.org/10.2337/dc16-0330>.
- Cherney DZI, Perkins BA, Soleymanlou N, Maione M, Lai V, Lee A, et al. Renal hemodynamic effect of sodium-glucose cotransporter 2 inhibition in patients with type 1 diabetes mellitus. *Circulation*. 2014;**129**(5):587-97. [PubMed ID: 24334175]. <https://doi.org/10.1161/CIRCULATIONAHA.113.005081>.
- Sano M, Takei M, Shiraishi Y, Suzuki Y. Increased hematocrit during sodium-glucose cotransporter 2 inhibitor therapy indicates recovery of tubulointerstitial function in diabetic kidneys. *J Clin Med Res*. 2016;**8**(12):844-7. [PubMed ID: 27829948]. [PubMed Central ID: PMC5087622]. <https://doi.org/10.14740/jocmr2760w>.
- Mohammadpanah Ardakan A, Hemati Farsani Z, Heydari Z, Habibi Ghahfarrokhi S, Raisi Z. Effect of Exercise Timing on Inflammation and Cognition in Aged Women with Type 2 Diabetes Mellitus: A Randomized Controlled Trial. *Iran J Psychiatry Behav Sci*. 2025;**19**(2). e158682. <https://doi.org/10.5812/ijpbs-158682>.
- de Boer IH, Caramori ML, Chan JCN, Heerspink HJL, Hurst C, Khunti K, et al. KDIGO 2020 clinical practice guideline for diabetes management in chronic kidney disease. *Kidney Int*. 2020;**98**(4S):S1-S15. [PubMed ID: 32998798]. <https://doi.org/10.1016/j.kint.2020.06.019>.
- Anker SD, Butler J, Filippatos G, Ferreira JP, Bocchi E, Böhm M, et al. Empagliflozin in heart failure with a preserved ejection fraction. N

- Engl J Med.* 2021;**385**(16):1451-61. [PubMed ID: [34449189](#)].
<https://doi.org/10.1056/NEJMoa2107038>.
19. Solomon SD, McMurray JJV, Claggett B, de Boer RA, DeMets D, Hernandez AF, et al. Dapagliflozin in heart failure with mildly reduced or preserved ejection fraction. *N Engl J Med.* 2022;**387**(12):1089-98. [PubMed ID: [36027570](#)].
<https://doi.org/10.1056/NEJMoa2206286>.
20. Baboli M, Moradi-Joo E, Delshad I, Hamedpour R, Hamedpour H, Karamianpoor J, et al. The relationship between social capital and organizational learning from the perspective of hospital managers. *J Adv Pharm Educ Res.* 2020;**10**(S1):102-6.