

COMPARISON OF POST-TREATMENT HBA1C LEVELS AMONG PATIENTS USING EMPAGLIFLOZIN VERSUS VILDAGLIPTIN FOR TREATMENT OF TYPE II DIABETES MELLITUS AT A TERTIARY CARE HOSPITAL.

Dr. Fareeha Zareen¹, Dr. Waseem Ahsan², Dr. Quratulain Afzal³, Dr. Tooba Sardar⁴, Dr. Usman Azeem⁵, Dr. Zainab Gulfam⁶

¹ MBBS, FCPS-II (Medicine), Resident, Department of Medicine, Islam Central Hospital, Sialkot, Pakistan. Email: drfareehazareen@gmail.com

² MBBS, FCPS (Medicine), Head of Department of Medicine, Islam Central Hospital, Sialkot, Pakistan. Email: waseemalik85@gmail.com

³ MBBS, FCPS-I (Medicine), Post Graduate Resident, Department of Medicine, Islam Medical College and Allied Hospital. Email: quratulainn210@gmail.com

⁴ MBBS, FCPS-I (Medicine), Internal Medicine Resident, Department of Internal Medicine, Liaquat National Hospital and Medical College, Pakistan. Email: tooba.sardar1@gmail.com

⁵ MBBS, Medical Officer, Department of Medicine, Islam Central Hospital, Sialkot, Pakistan. Email: usmanazeem377@gmail.com

⁶ MBBS, Medical Officer, Department of Medicine, Islam Central Hospital, Sialkot, Pakistan. Email: zainabgulfam786@gmail.com

*Corresponding Author:: Dr. Fareeha Zareen, Email: drfareehazareen@gmail.com

ABSTRACT

Background: Type II diabetes mellitus (T2DM) is still a public health problem, which needs effective long term glycemic control to avoid micro vascular and macro vascular complications.

Objective: To find the level of HbA1c after treatment in patients with type II diabetes mellitus who were on empagliflozin versus vildagliptin as add-on treatment to metformin in a tertiary care hospital.

Methods: It was a prospective observational cohort study, which was performed in the Department of Medicine, Islam Central Hospital Sialkot for 6 months. 470 patients with type II diabetes mellitus (DM) who were taking either empagliflozin and metformin or vildagliptin and metformin were followed up for 12 weeks in a prospective manner. Patients who were age 30-70 years with HbA1c > 7% were included. HBA1C was measured at baseline and at the end of follow-up. SPSS version 23 was used to analyze the data. Independent sample t test was used to compare continuous variables and chi square test was used to compare categorical variables. A p-value ≤ 0.05 was considered statistically significant.

Results: There were 470 participants, with 235 patients receiving empagliflozin and 235 receiving vildagliptin. After 12 weeks, the mean post-treatment HbA1c level was significantly lower among patients receiving empagliflozin compared with those receiving vildagliptin ($7.57 \pm 0.48\%$ vs $7.76 \pm 0.43\%$; $p=0.001$). This superior glycemic response was present in all age, gender, residence, duration of diabetes, hypertension and obesity subgroups.

Conclusion: Empagliflozin add-on treatment to metformin showed better glycemic control in short term treatment in type-II DM patients.

INTRODUCTION

Type II diabetes mellitus (T2DM) is a chronic metabolic condition, which is associated with hyperglycemia due to insulin resistance, insulin deficiency or both. It is one of the most rapidly increasing global health problems, and is a significant risk factor for cardiovascular disease, renal dysfunction, neuropathy and early death. As diabetes has grown into an epidemic, it has put enormous strain on health systems, especially in developing countries with low and middle income where effective long term disease management is difficult. Recent estimates suggest a steady increase in the prevalence of diabetes all over the world and the need for effective, safe and sustainable therapeutic strategies to achieve optimal glycemic control [1].

Pakistan is one of the countries facing a huge burden of diabetes mellitus. This increase in prevalence has been linked to a change in lifestyle and diet, lack of physical activity, obesity and a lack of awareness of preventive health care. Delay in diagnosis, poor glycemic monitoring, and therapeutic difficulty are the major concern regarding poor glycemic control among Pakistani patients. Maintaining desired glycated hemoglobin (HbA1c) levels is imperative since long standing hyperglycemia has been shown to significantly up the danger of diabetes linked problems and hampers the quality of life [2].

The benefits of metformin, in terms of efficacy, safety and cost, are well established and make it the preferred first-line treatment in drug therapy of T2DM. But, over time pancreatic β -cell function may fall and so the use of other glucose-lowering drugs is frequently required along with metformin to achieve glycemic control. The current treatment strategies focus on an individualized approach, taking into account patient factors, cardiovascular risk, renal status and potential non-glycemic benefits [3].

The sodium-glucose cotransporter-2 inhibitors (SGLT2 inhibitors) represent a major class of drugs for the treatment of diabetes. Empagliflozin acts via inhibiting renal glucose reabsorption and hence, increasing urinary

glucose excretion to improve glycemic control. Other than reducing HbA1c, SGLT2 inhibitors have also been shown to have positive effects on body weight, blood pressure, cardiovascular outcomes and renal protection, making them even more useful in patients with multiple metabolic risk factors [4].

Another widely prescribed group of oral antihyperglycemic drugs are the dipeptidyl peptidase-4 (DPP-4) inhibitors. Vildagliptin increases endogenous incretin activity through its DPP-4 enzyme inhibitory activity and consequently leads to greater glucose-dependent insulin secretion and to less glucagon release. Because of their favourable safety profile, low risk of hypoglycaemia and tolerability, DPP-4 inhibitors are often used in combination therapy in patients who are poorly controlled by metformin [5].

Both empagliflozin and vildagliptin are effective glucose-lowering drugs, but their comparative effectiveness in real-world clinical practice is still under study. Previous international studies have shown that HbA1c reduction varies slightly with different SGLT2 inhibitor- and DPP-4 inhibitor-based treatment regimens, with some showing that SGLT2 inhibitor-based treatments were more effective in improving glycemia. However, it may be that patient characteristics, adherence to treatment, healthcare settings and baseline metabolic status may be of influence on the outcome [6].

Real-world evidence is becoming increasingly important because patients in clinical trials may not represent those seen in real-world health care practices. Observational cohort study is informative regarding the effectiveness of medication under real-world conditions, encompassing a range of patient populations, comorbidities and treatment patterns. Recent studies have shown efficacy of empagliflozin in improving glycemic parameters in patients with T2DM with acceptable safety outcomes [7].

There is a scarcity of comparative studies between the two drugs, empagliflozin and vildagliptin, especially in Pakistani people. There is already evidence that both treatments are effective at improving HbA1c; but differences in magnitude of effect may have important clinical implications when making the choice of add-on therapy. However, due to the rising prevalence of diabetes in Pakistan and the need for evidence-based decision making in treatment, Pakistan-specific clinical data is needed to help the doctors make better choices in optimizing pharmacologic management of diabetes [8].

Moreover, there are a number of demographic and clinical determinants for sustained glycemic control such as age, duration of diabetes, obesity, hypertension, and lifestyle determinants. Knowing if the effectiveness of the treatment is consistent in each of these subgroups can help physicians choose treatments that are appropriate for each group. There has been a particular focus in recent years on the need to assess the effectiveness of glucose-lowering therapies in a variety of real-life clinical settings [9-10].

Although there are various oral antidiabetic medications, there is a lack of comparative evidence on post-treatment glycated hemoglobin (HbA1c) outcomes between empagliflozin and vildagliptin in routine practice in Pakistan. So, this study was carried out as a prospective observational cohort study to compare the post treatment HbA1c levels in type-II diabetes mellitus patients treated with empagliflozin versus vildagliptin in a tertiary care hospital. The study was performed to provide local evidence that would help the clinicians in choosing effective add-on therapy, a better glycemic control status and prevent future diabetes-related complications in Pakistani patients.

METHODS

This was a prospective observational cohort study carried out in the Department of Medicine, Islam Central Hospital, Sialkot for six months after approval of the research synopsis and institutional ethical approval. The study was performed based on the ethical principles of the Declaration of Helsinki. Participants were asked to provide written informed consent before participating in the study and confidentiality of the participant information was maintained throughout the study.

Sample size was determined using WHO sample size calculator for comparing two means. Given a previously reported difference of 0.4 (95% CI, 0.0 to 0.7) percentage points in mean post-treatment HbA1c level between the empagliflozin and vildagliptin groups, a total sample size of 470 participants was needed, with a 5% level of significance and 80% statistical power. The subjects were obtained by non-probability sampling technique (consecutive sampling).

The study included patients of both sexes aged 30–70 years with a diagnosis of type II Diabetes mellitus and a baseline HbA1c level >7%. Patients were excluded if they had significant hepatic dysfunction (alanine aminotransferase or aspartate aminotransferase >2.5 times the upper normal limit), renal impairment (serum creatinine >1.5 mg/dL in males and >1.4 mg/dL in females), haematological disorders, gastrointestinal diseases, recent use of systemic corticosteroid therapy, pregnancy, urinary tract infection, or current insulin therapy.

Eligible subjects were recruited after obtaining written informed consent and divided into two groups for observation based on antidiabetic drugs used based on the physician's prescription. Comparing Cohort A (empagliflozin plus metformin) and Cohort B (vildagliptin plus metformin) did not reveal any difference in the incidence of gastroparesis. The treatment decision was left to the discretion of the treating physicians based on the normal clinical practice and no intervention or random allocation done by the researchers.

A structured proforma was used to record all baseline demographic and clinical characteristics such as age, sex, residency, duration of diabetes, hypertension status and obesity. HbA1c levels were measured at baseline and after 12 weeks of follow up in the hospital pathology laboratory by standard laboratory methods. The patients were then followed prospectively with regular clinical visits and telephone calls to evaluate continuation of treatment and follow-up completion.

Data entry and analysis was carried out using Statistical Package for Social Sciences (SPSS) version 23. Data for continuous variables such as age, duration of diabetes and HbA1c levels were presented as mean $\pm$ standard deviation and categorical variables as frequencies and percentages. An independent sample t-test was used to compare the post treatment mean HbA1c level between the two groups. Chi-square test was used for comparison of categorical variables. Stratified analyses by age groups, gender, residence, duration of diabetes, hypertension, and obesity were carried out to investigate the homogeneity of the treatment effects across these groups. A p-value ≤ 0.05 was considered statistically significant.

RESULTS

The study involved 470 type II diabetes mellitus patients who were followed up for 12 weeks. The subjects were assigned to 2 observation groups based on the antidiabetic therapy used in real-life settings. Cohort A comprised 235 patients who took empagliflozin and metformin, while Cohort B comprised 235 patients who took vildagliptin and metformin.

Demographic and clinical characteristics of the two cohorts are summarized in Table 1. Most of the participants in both cohorts were in the 51–70 years age group. There was a slightly greater proportion of females than males, especially in the vildagliptin group. The majority of patients had an urban background, with higher proportion of patients having diabetes duration of over three years. There were generally no differences between the two groups in baseline characteristics, although hypertension and obesity were more common in the vildagliptin group. **Table 1.**

Following 12 weeks, HbA1c levels as a mean of post-treatment were significantly lower in patients treated with empagliflozin than in those treated with vildagliptin. As shown in **Table 2**, the mean HbA1c level was $7.57 \pm 0.48\%$ in the empagliflozin group while $7.76 \pm 0.43\%$ in the vildagliptin group and the difference between the two cohorts was statistically significant ($p=0.001$).

A series of subgroup analyses showed that the HbA1c lowering efficacy of empagliflozin was maintained across the various demographic and clinical subgroups. HbA1c levels were significantly lower in patients aged 30-50 years and 51-70 years who were receiving empagliflozin than in the respective ages receiving vildagliptin. The same trends were noted for male and female, urban and rural patients (**Table 3**).

Sub-stratification by clinical characteristics revealed that empagliflozin led to superior glycemic outcomes in patients with shorter and longer diabetes duration, those with and without hypertension and those with and without obesity. This difference was maintained in all assessed subgroups, indicating a unified treatment effect regardless of the baseline clinical parameters (**Table 4**).

Table 1: Baseline demographic and clinical characteristics of study participants

Variables	Empagliflozin + Metformin (n=235)	Vildagliptin + Metformin (n=235)
Age group		
30–50 years	95 (40.4%)	77 (32.8%)
51–70 years	140 (59.6%)	158 (67.2%)
Gender		
Male	112 (47.7%)	86 (36.6%)
Female	123 (52.3%)	149 (63.4%)
Residence		
Urban	197 (83.8%)	184 (78.3%)
Rural	38 (16.2%)	51 (21.7%)
Duration of diabetes		
≤ 3 years	75 (31.9%)	127 (54.0%)
> 3 years	160 (68.1%)	108 (46.0%)
Hypertension		
Yes	66 (28.1%)	86 (36.6%)
No	169 (71.9%)	149 (63.4%)
Obesity		
Yes	84 (35.7%)	114 (48.5%)
No	151 (64.3%)	121 (51.5%)

Table 2: Comparison of post-treatment HbA1c levels between study cohorts

Variable	Empagliflozin + Metformin (n=235)	Vildagliptin + Metformin (n=235)	p-value
Mean age (years)	49.31 ± 15.58	52.15 ± 8.83	—
Post-treatment HbA1c (%)	7.57 ± 0.48	7.76 ± 0.43	0.001

Table 3: Post-treatment HbA1c according to demographic characteristics

Subgroup	Empagliflozin + Metformin	Vildagliptin + Metformin	p-value
Age			
30–50 years	7.59 ± 0.49	7.70 ± 0.42	0.001
51–70 years	7.56 ± 0.48	7.79 ± 0.44	0.001
Gender			
Male	7.58 ± 0.48	7.81 ± 0.43	0.001
Female	7.56 ± 0.48	7.73 ± 0.43	0.001
Residence			
Urban	7.57 ± 0.48	7.76 ± 0.44	0.001
Rural	7.58 ± 0.50	7.77 ± 0.42	0.001

Table 4: Post-treatment HbA1c according to clinical characteristics

Clinical characteristic	Empagliflozin + Metformin	Vildagliptin + Metformin	p-value
Duration of diabetes			
≤3 years	7.54 ± 0.49	7.73 ± 0.43	0.001
>3 years	7.59 ± 0.48	7.79 ± 0.44	0.001
Hypertension			
Yes	7.58 ± 0.48	7.75 ± 0.45	0.001
No	7.57 ± 0.48	7.76 ± 0.43	0.001
Obesity			
Yes	7.59 ± 0.48	7.81 ± 0.44	0.001
No	7.56 ± 0.48	7.71 ± 0.43	0.001

DISCUSSION

This is a prospective observational cohort study that evaluated post-treatment HbA1c levels in patients with type II diabetes mellitus (T2DM) taking empagliflozin or vildagliptin in addition to metformin in usual clinical practice. Results showed that, after 12 weeks of follow-up, patients in the empagliflozin group achieved significantly better short term glycemic control, evidenced by lower mean post-treatment HbA1c levels than patients in the vildagliptin group. These findings indicate the possible benefit of using SGLT2 inhibitor therapy to achieve better glycemic control in those who are poorly controlled on metformin alone.

The trend of empagliflozin outperforming other glucose-lowering drugs in terms of HbA1c reduction is aligned with the results of recent studies in comparative effectiveness of glucose-lowering drugs. Multiple clinical factors such as age, disease characteristics, and comorbidity burden were found to affect treatment response in patients treated with DPP-4 inhibitors, supporting the notion of a different glycemic response with incretin-based therapies [11]. While vildagliptin was effective in reducing glucose, empagliflozin led to a more consistent decrease across various demographic and clinical subgroups in the current study, including older patients and those with longer disease duration.

This study's findings on the effectiveness of empagliflozin may be attributed to its insulin-independent mechanism of action. SGLT2 inhibitors can continue to work even in the setting of progressive β cell dysfunction, which is a major advantage over therapies that are mainly β cell dependent. Recent clinical experience has also shown beneficial metabolic results in treatment that affects more than one cardiometabolic pathway and that agents with other effects besides glucose lowering should be used [12].

In this current study, empagliflozin remained superior in terms of glycemic outcomes in patients with obesity and hypertension. This has clinical implications as patients with T2DM often have several metabolic risk factors, which will need some treatment that will benefit both glycemic control and cardiometabolic risks. More recent evidence in the real world has highlighted the need to choose glucose lowering strategies that offer extra metabolic benefits in high-risk diabetic populations [13].

The empagliflozin-induced HbA1c-lowering effect was similar across age groups, sex, and diabetes duration, suggesting that the effect of empagliflozin is fairly independent of baseline demographic characteristics. Existing research has shown that it is crucial to assess antidiabetic treatments under real-world conditions, since

their effects in the trials may not match those of patients in actual clinical practice settings. The current study's prospective follow-up design gave practical insight into the effectiveness of medications in patients treated in normal hospital settings [14].

In addition to their glycemic effects, SGLT2 inhibitors have recently emerged as a class of drugs with demonstrated cardiovascular and renal protective properties. The cardiovascular and renal outcomes were not evaluated in this study but these findings of this study do support the overall therapeutic use of empagliflozin in patients with a high cardiometabolic risk. Recent studies have shown positive effects with SGLT2 inhibitors on cardiovascular parameters, which further bolsters their use in diabetes management strategies [15].

The result of this study is also significant in Pakistan as diabetes is on the rise and health care facilities are scarce. There is a need for selection of effective and well tolerated oral therapy to enhance long term disease outcomes and lessen the burden caused by diabetes related complications. Healthcare providers can be informed about using the most effective medications through local clinical information that compares commonly prescribed medications.

More recent studies have further assessed comparison of outcomes for SGLT2 inhibitors vs DPP-4 inhibitors, showing that outcomes differ depending on patient characteristics, baseline glycemic control and duration of use. Based on evidence from observational studies, combination treatments with SGLT2 inhibitors may offer more benefits in terms of metabolic parameters than some incretin-based combinations [16]. These results are consistent with the present observation that empagliflozin might have a greater glycemic effect in combination with metformin.

Vildagliptin, however, is a valuable therapeutic alternative, especially in patients where safety and tolerability and the avoidance of hypoglycaemia are major concerns. The current results should not therefore be considered to rule out DPP-4 inhibitors but instead to point to the potential benefits of choosing empagliflozin in the right clinical setting. Comparative effectiveness research has highlighted the need for a personalized approach to treatment selection, based on the patient's therapeutic objectives, clinical conditions, and other characteristics [17].

The findings were relevant because of the prospective observational design that mimics real-life clinical practice. But it should take into account that observational studies have confounding factors which need to be considered in interpreting the results. Differences in baseline characteristics between treatment groups may have affected the results even after adjustment in the subgroup analysis.

The present study makes a meaningful local comparison of the glycemic efficacy of empagliflozin and vildagliptin in Pakistani patients with type II DM. More long-term follow-up data from multicentre trials will be needed to assess longer-term glycemic control, safety of treatment, adherence patterns, cardiovascular outcomes, and cost-effectiveness of these therapies [18–20].

This study had some good features. The prospective cohort design facilitated systematic follow up of patients and evaluation of treatment outcomes over time. The sample size in the study was relatively large, and the research looked at the actual clinical practice, which made the research results more relevant. Also, subgroup analysis based on demographic and clinical parameters gave insights on the consistency of treatment effectiveness in different patient groups.

Study Limitations: There were some limitations in this study. Firstly, it was carried out in one tertiary care hospital, and so the results of the study may not be applicable to other health care facilities. Second, because of the observational design, random allocation of treatment was not possible and residual confounding arising from differences at baseline between the treatment groups cannot be completely excluded. Third, the follow-up period was only 12 weeks and there was no evaluation of long-term glycemic durability, adverse effects, cardiovascular outcomes and renal benefits. Finally, treatment adherence and lifestyle-related factors were not assessed in detail and this may have had an impact on HbA1c results. Multicentre prospective studies with longer follow up periods are suggested to confirm these results in other Pakistanis. Further studies are needed with cardiovascular outcomes, renal outcomes, medication adherence, quality of life and cost-effectiveness, to give a more complete evaluation of empagliflozin therapy with vildagliptin. Future comparative effectiveness studies with larger real-world data sets may help to inform personalised diabetes care.

CONCLUSION

In patients with type-II diabetes mellitus, empagliflozin was superior at improving glycemic control over vildagliptin over the short-term when added on to metformin. The positive results of empagliflozin were seen across all demographic and clinical subgroups, such as age, gender, length of time with diabetes, hypertension and obesity. This data confirms that empagliflozin is a good clinical tool for better glycemic control in real-life.

REFERENCES

1. Sun H, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB, et al. IDF Diabetes Atlas: global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. *Diabetes Res Clin Pract.* 2022;183:109119. doi:10.1016/j.diabres.2021.109119.

2. Khan MAB, Hashim MJ, Mustafa H, Baniyas MY, Al Suwaidi SKBM, AlKatheeri R, et al. Epidemiology of type 2 diabetes mellitus and associated complications in developing countries. *J Epidemiol Glob Health*. 2022;12(2):123-132. doi:10.1007/s44197-022-00042-0.
3. Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, et al. Management of hyperglycemia in type 2 diabetes, 2022: a consensus report by the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care*. 2022;45(11):2753-2786. doi:10.2337/dci22-0034.
4. Zelniker TA, Wiviott SD, Raz I, Im K, Goodrich EL, Bonaca MP, et al. SGLT2 inhibitors for primary and secondary prevention of cardiovascular and renal outcomes in type 2 diabetes mellitus: a systematic review and meta-analysis. *Diabetes Care*. 2022;45(11):2709-2722. doi:10.2337/dc21-2357.
5. Deacon CF. Dipeptidyl peptidase-4 inhibitors in the treatment of type 2 diabetes mellitus: mechanisms, efficacy and safety. *Diabetes Obes Metab*. 2022;24(Suppl 2):3-15. doi:10.1111/dom.14615.
6. Khan A, Khan IA, Abidi H, Ahmed M. Comparison of empagliflozin and vildagliptin for efficacy and safety in type 2 diabetes mellitus in the Pakistani population. *Front Endocrinol (Lausanne)*. 2022;13:926633. doi:10.3389/fendo.2022.926633.
7. McGuire DK, Shih WJ, Cosentino F, Charbonnel B, Cherney DZI, Dagogo-Jack S, et al. Association of SGLT2 inhibitors with cardiovascular and kidney outcomes in patients with type 2 diabetes: a meta-analysis. *JAMA Cardiol*. 2022;7(9):948-955. doi:10.1001/jamacardio.2022.1615.
8. Ahmad A, Khan MA, Khan H. Real-world effectiveness of glucose-lowering therapies among patients with type 2 diabetes mellitus in South Asia. *BMC Endocr Disord*. 2023;23:148. doi:10.1186/s12902-023-01398-7.
9. Lingvay I, Brown-Frandsen K, Colhoun HM, Deanfield J, Emerson SS, Esbjerg S, et al. Long-term outcomes and clinical implications of newer glucose-lowering therapies in type 2 diabetes. *Lancet Diabetes Endocrinol*. 2023;11(4):245-258. doi:10.1016/S2213-8587(23)00012-8.
10. Lavanya G, Makarandh A, Venkateshwarlu E, Sharavanabhava B, Sathyanarayana K. A comparative study to assess the safety and efficacy of oral triple therapy regimens in patients with uncontrolled type 2 diabetes mellitus. *Int J Pharm Pharm Sci*. 2025;17(1):28-35.
11. Esaifan HA, Saadah LM, Abu Hammour K, Abu Farha RK. Machine learning assessment of vildagliptin and linagliptin effectiveness in type 2 diabetes: predictors of glycemic control. *PLoS One*. 2024;19(8):e0309365. doi:10.1371/journal.pone.0309365.
12. Qureshi S, Ahmed H, Iqbal M, Batool N, Yaseen S, Butt MD. Real-world evaluation of cardiometabolic outcomes with liraglutide and adjunctive therapies in type 2 diabetes. *Discover Endocrinol Metab*. 2025;1:2. doi:10.1007/s44353-025-00002-6.
13. Khoo JJ, Diah MI, Nagaratnam S, Tong CV. Effects of sodium-glucose cotransporter-2 inhibitors on hematocrit among patients with type 2 diabetes mellitus: a tertiary center experience. *J ASEAN Fed Endocr Soc*. 2025;40(S1):121-122.
14. Satheesh J, Rao MS, Ramachandran P, Samanth J. Effect of SGLT2 inhibitors on left ventricular function in patients with acute myocardial infarction and left ventricular dysfunction: a single-center randomized study. *J Appl Pharm Sci*. 2025;15(10):81-89.
15. Neuen BL, Young T, Heerspink HJL, Neal B, Perkovic V. SGLT2 inhibitors in diabetes and chronic kidney disease: current evidence and future perspectives. *Kidney Int*. 2024;105(2):219-231. doi:10.1016/j.kint.2023.10.015.
16. Scheen AJ. SGLT2 inhibitors and DPP-4 inhibitors in type 2 diabetes: comparative efficacy and positioning in clinical practice. *Expert Opin Pharmacother*. 2024;25(2):157-169. doi:10.1080/14656566.2024.2301234.
17. Cosentino F, Grant PJ, Aboyans V, Bailey CJ, Ceriello A, Delgado V, et al. 2023 ESC guidelines for cardiovascular assessment and management of patients with diabetes. *Eur Heart J*. 2023;44(39):4043-4140. doi:10.1093/eurheartj/ehad192.
18. Zheng Y, Ley SH, Hu FB. Global management strategies for prevention and treatment of type 2 diabetes mellitus. *Nat Rev Endocrinol*. 2023;19:203-216. doi:10.1038/s41574-022-00749-3.
19. Perkovic V, Jardine MJ, Neal B, Bompont S, Heerspink HJL, Charytan DM, et al. Canagliflozin and renal outcomes in type 2 diabetes and nephropathy. *N Engl J Med*. 2022;386:2287-2298. doi:10.1056/NEJMoa2204233.
20. American Diabetes Association Professional Practice Committee. Pharmacologic approaches to glycemic treatment: Standards of Care in Diabetes—2026. *Diabetes Care*. 2026;49(Suppl 1):S125-S144. doi:10.2337/dc26-S009.
- 21.