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Comparative assessment of kidney function biomarkers related to anti-diabetic medication consumption; a cross-sectional analysis

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ABSTRACT

Introduction: Diabetic nephropathy is a main cause of chronic kidney disease (CKD) throughout the world, which requiring early detection and management. Anti-diabetic medications, like sodium-glucose cotransporter-2 (SGLT2) inhibitors, metformin, dipeptidyl peptidase-4 (DPP-4) inhibitors, and sulfonylurea compounds have determined various kidney protective efficacies; nevertheless, their effects on renal biomarkers remained disputing.

Objectives: This study intended to assess renal function biomarkers, regarding anti-diabetic consumption, providing insights into their usefulness for risk categorization and management decision-making in diabetic nephropathy.

Patients and Methods: This cross-sectional investigation, conducted in Basra Governorate, Iraq (October 2024–January 2025) with ethical approval from Basra University's College of Pharmacy, enrolled participants to evaluate renal function biomarkers across antidiabetic medication regimens. Demographic and clinical data, including age, body mass index, gender, diabetes duration, hypertension status, and treatment regimen like metformin, sulfonylurea, DPP-4 inhibitors and SGLT-2 inhibitors, or combination therapies were gathered by interviews and clinical document reviews. In this study, fasting blood samples were analyzed for kidney function biomarkers, comprising serum creatinine, urea, blood urea nitrogen (BUN), and estimated glomerular filtration rate (eGFR). The study outcomes comprised comparing renal function biomarkers among antidiabetic medication regimens.

Results: The study population comprised of 250 diabetes mellitus individuals (50.8% female) with a mean age of 55.67 ± 8.58 years. The findings showed considerable alterations of BUN, creatinine, urea and eGFR among the five groups. The individuals who received DPP-4 inhibitors had significantly higher BUN and urea levels than individuals treated with metformin or sulfonylurea monotherapy and higher serum creatinine concentration compared to metformin monotherapy, sulfonylurea monotherapy and combination therapy. Regarding eGFR, the DPP-4 inhibitor users had considerably lower value compared to all the other groups, both in metformin monotherapy, sulfonylurea monotherapy, and SGLT-2 inhibitor groups and also in patients under combination therapy.

Conclusion: We found that the consequences of the antidiabetic drug therapy on kidney function are not the same. This study showed that DPP-4 cases had early indications of diminished kidney function than the individuals receiving metformin, sulfonylurea, SGLT-2, or a combination of them. This finding focuses on the importance of considering the potential impact on renal health in cases of selecting diabetes treatments.

Original Article

Implication for health policy/practice/research/medical education:
Our study on 250 participants with diabetes mellitus detected significant differences in renal function biomarkers across five antidiabetic treatment groups. Individuals treated with dipeptidyl peptidase-4 inhibitors showed meaningfully higher blood urea nitrogen, urea, and serum creatinine concentration compared to cases receiving metformin monotherapy, sulfonylurea monotherapy, and sodium-glucose cotransporter-2 inhibitors. Meanwhile, estimated glomerular filtration rate was significantly lower in the dipeptidyl peptidase-4 inhibitor group compared to all other treatment groups, representing an initial kidney function disturbance. These findings propose a potential association among DPP-4 inhibitor use and adverse effects on kidney function biomarkers in individuals with diabetes mellitus.

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Introduction

Diabetic kidney disease (DKD) is one of the most common microvascular complications of diabetes mellitus and is the main contributing factor to end-stage kidney failure around the world (1,2). It is manifested by progressive kidney dysfunction such as glomerular enlargement, podocytopenia, proteinuria and reduced renal function which can lead to end-stage renal failure (3,4). In the case of diabetic nephropathy, various etiological factors containing, hyperglycemia, development of oxidative stress, inflammation, and genetic susceptibility are responsible for irreversible kidney function and structure (3,5). Still, the cardiorenal risks persist in many patients undergoing the previously developed therapies including renin–angiotensin system blockade or sodium-glucose co-transporter-2 inhibitors (SGLT2i) (6,7). Recent findings focus on the strategies such as delivery of the drugs to renal proximal tubular cells and altering the pathways involved in autophagy and oxidative stress (1,2). Recently, much attention has been directed toward, the development of more effective therapies to treat/delay the progression of diabetic nephropathy and enhance patient's prognosis. Diabetic kidney disease is one of the most common microvascular complications of diabetes mellitus and is the major contributing factor to progressive kidney failure around the world (1,2). This condition demonstrated by continuing renal dysfunction such as glomerular enlargement, podocytopenia, proteinuria and reduced kidney function which can lead to irreversible renal function (3,4). In the case of diabetic nephropathy, various etiological factors include hyperglycemia, development of oxidative stress, inflammation, and genetic susceptibility (3,5). Meanwhile, the cardiorenal hazards persist in many individuals undergoing the previously developed therapies including renin-angiotensin system blockade or SGLT2i (6,7). Current findings focus on the strategies like delivery of the drugs to renal proximal tubular cells and changing the pathways interacted in autophagy and oxidative stress (1,2). These findings emphasize on the development of more effective modalities to treat/delay the progression of diabetic nephropathy and improving patient's prognosis.

It has been detected that serum creatinine, blood urea nitrogen (BUN), serum urea and estimated glomerular filtration rate (eGFR) are renal function parameters that are instrumental in the diagnosis of kidney diseases. Remarkably, BUN and serum creatinine are two biochemical biomarkers that represent the renal ability to excrete various waste products (8,9). Accordingly, serum urea concentration is a waste product related to protein metabolism and its plasma level depends on the patient's renal excretory abilities (10). In addition, creatinine is derived from proteins that breakdown in muscle tissue and is the most popular substance used to assess eGFR to detect the standard measurement of renal filtration rate that is required for recognizing stages of chronic renal failure (11,18). Therefore, changes in these biomarkers can be affected by factors like age, sex, muscular bulk, and stage of hydration (11,12). Other studies have assessed the use of these biomarkers by developing better models to predict other outcomes such as heart disease too (8).

Available antidiabetic treatments incorporate metformin monotherapy, sulfonylurea monotherapy, dipeptidyl peptidase-4 (DPP-4) inhibitors, SGLT-2 inhibitors and their combination therapy to treat type 2 diabetes mellitus. Metformin is the first-line therapy since it is among the most effective and safe medications despite the limitations concerning its use in patients with advanced chronic kidney disease due to the strengthened risk of lactic acidosis (13,14). Sulfonylureas are still administered in lowering blood glucose levels even though their use has been considerably limited by side effects such as hypoglycemia and weight gain (14). Sitagliptin and linagliptin are more preferred DPP-4 inhibitors, since they enhance glycemic efficacy without compromising safety and are mostly administered in conjunction with other medicinal products (13,15). Accordingly, SGLT-2 inhibitors are useful for reforming glycaemia and cardiovascular risk factors, particularly in individuals with strengthened or heart failure (15, 16). The intensity of the new algorithm is in combination therapies like sitagliptin-metformin or SGLT-2 inhibitors and DPP-4 inhibitors involving target of different aspects of the pathophysiology of diabetes while exposing patients to fewer side effects (15). These regimens show that the treatment plan differs according to different characteristics of the patients and the presence of other diseases.

On the one hand, the influence of anti-diabetic medications on kidney function biomarkers varies in their pharmacological mechanisms, while some agents, like SGLT2i or GLP-1RAs (glucagon-like peptide-1 receptor agonists) are found to have renoprotective impacts apart from diabetic retinopathy in CKD individuals with diabetes (16,17). These medications act by both glucose dependent and independent mechanisms and they work through using pathways that include inflammation, fibrosis and lipid balance to protect renal function (16). However, we know that with the reduced kidney function, most of the anti-diabetic drugs will be affected in their pharmacokinetics. Thereby the dosage adjustment requires to reduce the risks like hypoglycemia or lactic acidosis predominantly at later CKD stages (18).

Objectives

This study aimed to comparatively evaluate the impact of different antidiabetic medication regimens (metformin monotherapy, sulfonylurea monotherapy, DPP-4 inhibitors,

SGLT-2 inhibitors, and combination therapies) on kidney function biomarkers (BUN, urea, creatinine and eGFR) in patients with diabetes mellitus.

Patients and Methods

Study design and participants

The cross-sectional study was carried out in Basra governorate, Iraq from October 2024 to January 2025. The study was approved by the institutional ethical review committee of Basra university, college of pharmacy. In line with the Declaration of Helsinki, participants were informed about the study's objectives, procedures and possible risks and all of them voluntarily signed a consent form. In this present study, potential impacts of different types of anti-diabetic drugs on the renal health indicators were to be assessed. Therefore, 250 diabetic patients were included for the present study through consecutive sampling from three private endocrinology and internal medicine clinics in Basra.

Inclusion and exclusion criteria

The inclusion criteria included patients aged more than 30 years with type 2 diabetes mellitus (T2DM) of at least three years' duration, who had been on stable treatment with one or a combination of anti-diabetic drugs for at least six months. Nevertheless, it was essential for the participants not to have acute disorders or had not been admitted to the hospital within the last three months. Patients with a history of chronic liver disease (cirrhosis, hepatitis B or C, hepatocellular carcinoma), CKD stage 4 and 5 (eGFR <30 mL/min/1.73 m^2), pregnancy or lactation as well as use of hepatotoxic and nephrotoxic drugs except for anti-diabetic ones were excluded.

Data collection

Some of the demographic and clinical variables recorded included; participant's age, gender, mean BMI, duration of diabetes, co-morbidity of hypertension and anti-diabetic drugs. This information on anti-diabetic medication included details on metformin monotherapy, sulfonylurea monotherapy, DPP-4 inhibitors, SGLT-2 inhibitors, and combination therapies, obtained through participant interviews or review of clinical documents. Blood samples of 5 mL were obtained from each participant via venous puncture during a 10-hour fasting period, between 8:00 and 10:00 AM. The samples were processed within one hour of collection, involving centrifugation at 3500 rpm for 10 minutes to isolate serum for biochemical analysis. This study assessed biomarkers of kidney health. Renal function tests (RFTs) included measurements of serum creatinine, serum urea, BUN, and eGFR. All biochemical analyses were conducted by an automated clinical chemistry analyzer (Abbott Architect c4000 USA) at AL-Eman private central laboratory in Basrah, Iraq, with intra- and inter-assay coefficients of variation (CVs) lower than 5%.

Anti-diabetic drugs classification

Individuals in this investigation were categorized into five distinct treatment groups according to their antidiabetic regimen. Group one contained of cases getting metformin monotherapy (n = 60), while group two comprised those on sulfonylurea monotherapy, either glibenclamide or gliclazide (n = 50). Group three contained individuals treated with DPP-4 inhibitor monotherapy, mainly sitagliptin or vildagliptin (n = 40), and group four comprised individuals received SGLT-2 inhibitor monotherapy, like empagliflozin or dapagliflozin (n = 45). Finally, group five consisted of individuals undergoing combination therapy comprising of metformin paired with any other oral antidiabetic drugs (n = 55).

Outcomes

The outcomes in this investigation focused on comparing renal function biomarkers like serum creatinine, urea, BUN, and eGFR, throughout their antidiabetic medication regimens, across evaluating the differences amid metformin monotherapy, sulfonylurea monotherapy, DPP-4 inhibitors, SGLT-2 inhibitors, and their combination therapies. Key comparisons incorporated recognizing which regimens showed statistically significant associations with improved eGFR values, diminished serum creatinine concentration, and favorable BUN and urea profiles.

Statistical analysis

The dataset was subjected to rigorous analysis utilizing IBM SPSS (Statistical Package for the Social Sciences) statistical software, version 27 (IBM Corp., USA). The calculation of the normality of the data distribution was conducted by Kolmogorov-Smirnov test, revealing that all quantitative parameters conformed to a normal distribution. Accordingly, mean differences of kidney function tests like serum creatinine, urea BUN, and eGFR in the groups, counting sulfonylurea monotherapy, DPP-4 inhibitors, metformin monotherapy, SGLT-2 inhibitors and combination therapies were analyzed by analysis of variance (ANOVA), followed by a post hoc Scheffe test to discriminate specific intergroup differences. The criterion for statistical significance was established at a threshold of $P < 0.05$ for all conducted analysis.

Results

The study included 250 participants with diabetes mellitus, with a nearly equal gender distribution (50.8% female, 49.2% male) and a mean age of 55.67 ± 8.58

years. Participants had a mean BMI of 29.17 kg/m² and an average duration of diabetes of 9.98 years. Hypertension was prevalent in the majority of the patients. Anti-diabetic medication distribution showed metformin monotherapy as the most commonly prescribed regimen, followed by sulfonylurea monotherapy, SGLT-2 inhibitors, DPP-4 inhibitors, and combination therapies (Table 1).

The demographic and clinical characteristics analysis among five treatment groups of different anti-diabetic drugs use, including metformin monotherapy, sulfonylurea monotherapy, SGLT-2 inhibitors, DPP-4 inhibitors, and combination therapies, showed that the distribution of gender was similar among the groups, with no noteworthy difference. We found, hypertension prevalence varied, nevertheless this variation was not statistically meaningful. The age, BMI, and diabetes duration showed no significant differences among the groups. Nonetheless, significant differences were found in kidney function biomarkers. We detected, the levels of BUN, urea, creatinine, and eGFR differed significantly across the treatment groups (Table 2).

The results established that the comparison of BUN and urea levels across the five treatment groups revealed meaningful differences in certain pairwise comparisons. For BUN, significant differences were observed between metformin monotherapy and DPP-4 inhibitors, as well as between DPP-4 inhibitors and SGLT-2 inhibitors. The BUN level in patients who consumed DPP-4 inhibitors was significantly greater than patients who underwent metformin monotherapy and SGLT-2 inhibitors use. However, no significant differences were found in other comparisons, such as between metformin and sulfonylurea monotherapies, or between sulfonylurea monotherapy and

Table 1. The baseline characteristics of the included patients in the study

Variable	Sub-variable	Frequency	Percent
Gender	Female	127	50.8
	Male	123	49.2
HTN	No	108	43.2
	Yes	142	56.8
Anti-diabetic drugs	Metformin monotherapy	60	24
	Sulfonylurea monotherapy	50	20
	DPP-4 inhibitors therapy	39	15.6
	SGLT-2 inhibitors therapy	45	18
	Combination therapy	56	22.4

Variable	Mean	SD	Min	Max
Age (year)	55.67	8.58	32	90
BMI (kg/m²)	29.17	4.31	18.2	42.2
Diabetes duration (year)	9.98	3.41	3	19

DPP-4, Dipeptidyl peptidase-4; SGLT-2, Sodium-glucose cotransporter-2; HTN, Hypertension; SD, standard deviation; BMI, Body mass index.

Table 2. The frequency distribution of demographic characteristics and clinical data between the five treatment groups of included patients

Variables		Treatment group					*P* value
		Metformin monotherapy (n = 60)	Sulfonylurea monotherapy (n = 50)	DPP-4 inhibitors (n = 39)	SGLT-2 inhibitors (n = 45)	Combination therapy (n = 56)	
		No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	
Gender	Female	29 (48.3)	27 (54)	21 (53.8)	23 (51.1)	27 (48.2)	0.958*
	Male	31 (51.7)	23 (46)	18 (46.2)	22 (48.9)	29 (51.8)	
HTN	No	24 (40)	27 (54)	16 (41)	22 (48.9)	19 (33.9)	0.262*
	Yes	36 (60)	23 (46)	23 (59)	23 (51.1)	37 (66.1)	
Variable		**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	***P* value**
Age (year)		24.27 ± 8.05	54.46 ± 7.46	56.87 ± 8.10	56.33 ± 9.72	56.88 ± 9.32	0.317**
BMI (kg/m²)		29.41 ± 4.17	28.83 ± 3.91	29.50 ± 4.78	29.82 ± 4.41	28.48 ± 4.39	0.533**
Diabetes duration (year)		9.33 ± 3.27	10.22 ± 3.71	9.54 ± 3.64	10.38 ± 3.72	10.45 ± 3.18	0.344**
BUN (mg/dL)		14.21 ± 3.30	15.57 ± 4.09	16.76 ± 3.65	13.81 ± 3.81	15.10 ± 3.90	0.003**
Urea (mg/dL)		30.49 ± 6.15	30.01 ± 5.21	34.56 ±7.19	31.85 ± 5.59	30.99 ± 5.09	0.003**
Cr (mg/dL)		0.85 ± 0.18	0.93 ± 0.26	1.06 ± 0.17	0.95 ± 0.20	0.91 ± 0.16	<0.001**
eGFR (mL/min/1.73 m²)		85.17 ± 10.54	79.35 ± 8.92	72.01 ± 9.36	89.71 ± 11.88	79.47 ± 10.89	<0.001**

DPP-4, Dipeptidyl Peptidase-4; SGLT-2, Sodium-glucose cotransporter-2; HTN, Hypertension; SD, standard deviation; BMI, Body mass index; BUN, Blood urea nitrogen; Cr, Creatinine; eGFR, Estimated glomerular filtration rate. *Chi-square, **One way ANOVA

combination therapy. For urea levels, significant differences were noted between metformin monotherapy and DPP-4 inhibitors, and between sulfonylurea monotherapy and DPP-4 inhibitors. The DPP-4 inhibitor users also showed significantly greater levels of urea compared to metformin and sulfonylurea monotherapy users; however, no significant difference was found between other groups (Table 3).

For serum creatinine levels, significant differences were observed between metformin monotherapy and DPP-4 inhibitors, as well as between sulfonylurea monotherapy and DPP-4 inhibitors, and between DPP-4 inhibitors and combination therapy. Patients on DPP-4 inhibitors had significantly higher creatinine levels compared to those on metformin monotherapy, sulfonylurea monotherapy, and combination therapy. For eGFR, significant differences were noted between metformin monotherapy and DPP-4 inhibitors, sulfonylurea monotherapy and DPP-4 inhibitors, sulfonylurea monotherapy and SGLT-2 inhibitors, DPP-4 inhibitors and SGLT-2 inhibitors, DPP-4 inhibitors and combination therapy, and SGLT-2 inhibitors and combination therapy. The eGFR was significantly lower in patients treated with DPP-4 inhibitors compared to those on all four treatment groups, including metformin monotherapy, sulfonylurea monotherapy, SGLT-2 inhibitors, and combination therapy (Table 4).

Discussion

In our study, the results indicated that, among patients with diabetes mellitus, those receiving DPP-4 inhibitors had significantly higher BUN levels compared to those treated with metformin monotherapy or SGLT-2 inhibitors. Similarly, urea levels were significantly elevated in patients using DPP-4 inhibitors compared to those on metformin or sulfonylurea monotherapy. In contrast, no significant differences in BUN or urea levels were observed between the patients who were under treatment of metformin and sulfonylurea monotherapies, nor between sulfonylurea monotherapy and combination therapy. The observed increase in serum urea and BUN with DPP-4 inhibitor use aligns with prior studies investigating their kidney effects by mechanisms remained unclear. A previous Thai study by Chanawong et al detected that SGLT-2 inhibitors slowed the decline in eGFR more efficiently than DPP-4 inhibitors in individuals with diminished baseline kidney function (19). A study by Choe et al in Korean patients found that switching from SGLT-2 inhibitors to DPP-4 inhibitors resulted in a more pronounced reduction in HbA1c, especially in those with lower eGFR (20). The renoprotective effects of SGLT-2 inhibitors are further supported by their ability to reduce the progression of CKD; Khan et al found that DPP-4 inhibitors are known for their glucose-lowering effects but

Table 3. Comparison of BUN and urea biomarkers among the five treatment groups

Treatment group		Mean difference	*P* value*
First	**Second**		
BUN (mg/dL)			
Metformin monotherapy	Sulfonylurea monotherapy	1.36	0.468
	DPP-4 inhibitors	2.50	0.031
	SGLT-2 inhibitors	0.39	0.990
	Combination therapy	0.88	0.806
Sulfonylurea monotherapy	DPP-4 inhibitors	1.1	0.703
	SGLT-2 inhibitors	1.75	0.272
	Combination therapy	0.47	0.981
DPP-4 inhibitors	SGLT-2 inhibitors	2.94	0.014
	Combination therapy	1.65	0.347
SGLT-2 inhibitors	Combination therapy	1.28	0.572
Urea (mg/dL)			
Metformin monotherapy	Sulfonylurea monotherapy	0.49	0.996
	DPP-4 inhibitors	4.07	0.023
	SGLT-2 inhibitors	1.36	0.844
	Combination therapy	0.50	0.995
Sulfonylurea monotherapy	DPP-4 inhibitors	4.56	0.011
	SGLT-2 inhibitors	1.85	0.665
	Combination therapy	0.99	0.943
DPP-4 inhibitors	SGLT-2 inhibitors	2.71	0.344
	Combination therapy	3.57	0.075
SGLT-2 inhibitors	Combination therapy	0.86	0.969

BUN, Blood urea nitrogen; DPP-4, Dipeptidyl peptidase-4; SGLT-2, Sodium-glucose cotransporter-2. *One-way ANOVA followed by post hoc Scheffe test.

Table 4. Comparison of creatinine and eGFR biomarkers among the five treatment groups

Treatment group		Mean difference	*P* value*
First	**Second**		
Cr (mg/dL)			
Metformin monotherapy	Sulfonylurea monotherapy	0.07	0.426
	DPP-4 inhibitors	0.21	<0.001
	SGLT-2 inhibitors	0.10	0.161
	Combination therapy	0.06	0.585
Sulfonylurea monotherapy	DPP-4 inhibitors	0.13	0.034
	SGLT-2 inhibitors	0.02	0.981
	Combination therapy	0.01	0.999
DPP-4 inhibitors	SGLT-2 inhibitors	0.11	0.160
	Combination therapy	0.15	0.012
SGLT-2 inhibitors	Combination therapy	0.03	0.918
eGFR (mL/min/1.73 m²)			
Metformin monotherapy	Sulfonylurea monotherapy	5.82	0.077
	DPP-4 inhibitors	13.16	<0.001
	SGLT-2 inhibitors	4.54	0.301
	Combination therapy	5.70	0.072
Sulfonylurea monotherapy	DPP-4 inhibitors	7.33	0.030
	SGLT-2 inhibitors	10.36	<0.001
	Combination therapy	0.12	0.999
DPP-4 inhibitors	SGLT-2 inhibitors	17.70	<0.001
	Combination therapy	7.45	0.021
SGLT-2 inhibitors	Combination therapy	5.70	<0.001

Cr, Creatinine; eGFR, Estimated glomerular filtration rate; DPP-4, Dipeptidyl peptidase-4; SGLT-2, Sodium-glucose cotransporter-2. *One-way ANOVA followed by post hoc Scheffe test.

may exhibit diminished efficacy over time compared to SGLT-2 inhibitors (21). Furthermore, it has been noted that compared to DPP-4 inhibitors, SGLT-2 inhibitors may have some cancer-protective effect, specifically, leukemia, colorectal, as well as liver cancer (22). Such outcomes remind of the necessity of controlling BUN and urea before setting on glucose-lowering agents, especially in cases with early renal dysfunction or other complications. The changes in the levels of BUN and creatinine due to the DPP-4 inhibitors have revealed differential effects on urea metabolism – a finding that should raise further questions regarding their chronic applicability on renal and metabolic complications of diabetes are now worth further enquiry given the reported relationship between BUN levels and disease progression in diabetes type 1 and 2 (23,24). These data support the approach to select the therapy targeted, especially in patients suffering from diabetes mellitus and impaired renal function, as certain kinetics of urea observed in them may predict the clinical result. Further independent investigations should be conducted on whether it is possible to regulate urea synthesis or its elimination in order to enhance the treatment outcomes in selected patient categories.

The result of the present study also showed statistical differences in the patients under DPP-4 inhibitors with regard to their creatinine level compared to those only on metformin, sulfonylurea or both. Additionally, patients treated with DPP-4 inhibitors had significantly lower eGFR values compared to all other treatment groups, including those on metformin monotherapy, sulfonylurea monotherapy, SGLT-2 inhibitors, and combination therapy. The findings of elevated serum creatinine and diminished eGFR in diabetic individuals using DPP-4 inhibitors align with some previous investigation but are contrast with others, highlighting nuanced kidney effects. A 2021 meta-analysis of 47,955 patients demonstrated that DPP-4 inhibitors were associated with a greater annual eGFR decline (-1.12 mL/min/1.73m²) compared to controls, consistent with the observed eGFR reduction in this study (25). Nevertheless, contradictory evidence exists; since, a recent meta-analysis of 16,378 participants found no meaningful differences in eGFR changes among DPP-4 inhibitors and controls, though it confirmed albuminuria decrease (26). Importantly, the elevated creatinine levels reported here contrasted with a 2016 observational study founding that DPP-4 inhibitors mitigated eGFR decline in macroalbuminuric individuals over four years, proposing potential variability based on baseline renal function (27). These inconsistencies may reflect differences in study populations, comparator therapies, or treatment

durations. Though DPP-4 inhibitors consistently display albuminuria benefits, their effect on serum creatinine and eGFR remains inconsistent, accentuating on the need for individualized kidney monitoring in individuals received these medications.

Conclusion

Our cross-sectional investigation established that separate patterns of antidiabetic medications are related to different effects on renal function biomarkers in diabetic individuals. Importantly, the administration of DPP-4 inhibitors was noticed by a meaningful escalation of BUN, serum urea, and creatinine across with a diminution in eGFR in comparison with metformin monotherapy, monotherapy with sulfonylureas, SGLT-2, and their combination therapy. Corresponding to these finding, the type of antidiabetic medication seems to affect kidney flow in a different manner and these effects should be taken into account when choosing better treatment plan for diabetic individuals.

Limitations of the study

Sample size disparities across treatment groups, predominantly the smaller cohorts receiving DPP-4 inhibitors (n=40) and SGLT-2 inhibitors (n=45), may diminish statistical power to detect clinically meaningful differences, outstandingly when comparing monotherapies against combination regimens. The exclusion of cases with advanced chronic renal failure cases limits generalizability to populations with severe kidney impairment. Although the study adjusted for key covariates like high blood pressure and diabetes duration, unmeasured confounders, comprising dietary patterns, physical activity levels, and concomitant use of non-nephrotoxic medications, could influence observed associations. Medication adherence verification relied on self-report rather than objective measures like prescription refill data or drug level monitoring, potentially introducing misclassification bias. Additionally, generalizability of the study may be slightly restricted due to the investigation being conducted in one region only, that is, Basra Governorate, and this may be due to variations in the diabetes management protocols across regions and genetic/environments factors affecting kidney outcomes. The analysis did not also capture any differences in agents with the drugs in the major class, this might possess different renoprotective medications like empagliflozin as compared to dapagliflozin respectively.

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Authors' contribution

Conceptualization: Qutaiba A. Qasim.
Data curation: Qutaiba A. Qasim.
Formal analysis: Hiba Dawood.
Investigation: Hiba Dawood.
Methodology: Hiba Dawood.
Project Management: Qutaiba A. Qasim
Resources: All authors.
Supervision: Hiba Dawood.
Validation: Qutaiba A. Qasim.
Writing–original draft: All authors.
Writing–review and editing: All authors.

Ethical issues

The research was conducted in accordance with the Declaration of Helsinki. Informed written consent was obtained from all participants. This study resulted from a research project that received ethical approval from the institutional ethical review committee of Basra University, College of Pharmacy, Basra Governorate, Iraq. Furthermore, the authors have addressed ethical issues, including plagiarism, data fabrication, and double publication.

Conflicts of interest

The authors declare no conflict of interest.

Declaration of generative artificial intelligence (AI) and AI-assisted technologies in the writing process

During the preparation of this work, the authors utilized AI (Perplexity.ai, typeset.io, and grammarly.com) to refine grammar points and language style in writing. Subsequently, the authors thoroughly reviewed and edited the content as necessary, assuming full responsibility for the publication's content.

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