

Original Research Article

Comparative evaluation of renal function in patients using different antihypertensive drug classes

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Abstract

Purpose: To compare renal function in hypertensive adults treated with antihypertensive drug classes in a tertiary private clinic in Basra, Iraq.

Method: A retrospective cohort comprised 450 adults with hypertension on stable therapy for 6 months from January 2024 to December 2025 in Al-Fayhaa Teaching Hospital, Basra, Iraq. Five monotherapy groups (60 patients each): angiotensin converting enzyme (ACE) inhibitor, angiotensin receptor blocker (ARB), calcium channel blocker (CCB), β -blocker, diuretic, and combination therapy (150 patients) comprising any two or more antihypertensive medications. Demographic and laboratory data were obtained. Analysis of variance and the Kh2 test were used to compare estimated glomerular filtration rate (eGFR), serum creatinine, and urine albumin-creatinine ratio (UACR).

Results: The highest mean eGFR occurred in ACE-inhibitor and ARB-groups, and the lowest mean eGFR in β -blocker and diuretic groups. Non-RAAS monotherapy groups (Group 3 (calcium channel blockers), Group 4 (beta blockers)) were more common in terms of chronic kidney disease (CKD; eGFR < 60 mL/min/1.73 m²) and moderate-to-severe albuminuria. Diuretic and β -blocker monotherapy were associated with lower eGFR and a twofold increase in the odds of CKD and albuminuria in comparison with ACE inhibitor therapy after confounder adjustment. Still, ARB and RAAS-combination therapy had renal profiles comparable to ACE inhibitor therapy.

Conclusion: The RAAS-blocking regimens comprising ARB and ACE inhibitors were associated with more favorable renal outcomes than non-RAAS monotherapies (CCB, β -blocker, and diuretic), supporting the prioritization of ACE inhibitors or ARBs as first-line therapy in hypertensive patients at renal risk.

Keywords: Albuminuria, Angiotensin receptor antagonists, Antihypertensive agents, Glomerular filtration rate

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INTRODUCTION

Hypertension is a non-communicable disease that is most prevalent across the globe, and it is a leading modifiable determinant of premature

cardiovascular and renal morbidity and mortality. Recently, pooled analyses conducted by Non-Communicable Diseases (NCD) Risk Factor Collaboration, which compiled data from 1,201 population-representative studies involving more

than 104 million adults aged 30 - 79 years, estimated that, in 2023, one in three adults globally had hypertension, or over 1 billion people [1,2]. Even though the prevalence of the disease has decreased in high-income countries such as the United States, Germany, and Japan, it has increased or remained constant in many low- and middle-income areas, resulting in significant geographical disparities in the disease burden and control [3].

There is an existing disparity in diagnosis, treatment, and effective control. Globally, less than half of adults with hypertension were aware of their diagnosis in 2019, and less than a quarter of them had controlled blood pressure, and exceptionally low proportions had controlled their blood pressure in sub-Saharan Africa, some parts of Asia, and the Middle East [4]. These trends are echoed in region-specific analysis. In the Middle East and North Africa (MENA), meta-analyses indicate prevalences of adult hypertension usually at about 25 - 35 %, with some countries reporting prevalence rates of up to 50 % in older ages [5,6]. One systematic review of Arab nations estimated a combined prevalence of 29.5 %, which is higher than what is reported in some Western populations [7].

The increasing burden is determined by population ageing, high urbanisation rates, increased obesity, physical inactivity, and excessive dietary salt intake [8–10]. The exposure to vascular damage caused by blood pressure that is not well managed is cumulative, putting the person at risk of a range of complications that include coronary artery disease, stroke, heart failure, and chronic kidney disease (CKD). In this epidemiological context, optimising antihypertensive therapy is essential for preventing cardiovascular (CV) events and maintaining renal function.

Some antihypertensive drug classes in use, along with their effects on kidney function, have been reported in previous studies [10-16]. Recent international and CKD-specific hypertension guidelines consistently recommend Renin Angiotensin Aldosterone System (RAAS) blockade as the initial intervention in hypertensive patients with albuminuric CKD, and options such as CCBs, β -blockers, and diuretics are only add-ons to achieve blood pressure goals [15,16]. Genuine world prescribing, however, is heavily influenced by comorbidities, tolerability, cost, and clinician preference; therefore, numerous patients are primarily prescribed non-RAAS regimens or complex combinations such as Calcium channel blockers (amlodipine) and beta blockers (atenolol).

Inconsistent results on the relative renal protective advantages of the various classes of antihypertensive drugs have been observed in comparative effectiveness studies and network meta-analyses, even when cardiovascular endpoints are compared with kidney outcomes, including eGFR slope, incident CKD, or albuminuria [11,14]. Furthermore, most large-scale trials have been done in North America, Europe, or East Asia, where there is little information on MENA and other low- and middle-income environments with high hypertensive rates and CKD epidemiologies [5–7]. The need for modern, context-specific studies on renal function in patients receiving various antihypertensive drug classes in clinical settings and routine practice is therefore evident. This study aims to comparatively evaluate renal function in patients using different antihypertensive drug classes.

METHODS

Study design and setting

It was a relative observational cohort study conducted at Al-Fayhaa Teaching Hospital, Basra, Iraq. This clinic offers specialised outpatient service for patients with hypertension, diabetes, and chronic kidney disease, and serves a predominantly urban catchment area.

The review of electronic and paper medical records of adult patients in the hypertensive and nephrology outpatient clinics between 1 January 2024 and 31 December 2025 was included. The study cohort was enrolled sequentially during this period, including all eligible patients who met the inclusion criteria and had no missing renal functional data.

Ethical approval

This research was conducted with the approval of the ethical committees from the College of Pharmacy, University of Basra, Basra, Iraq (ethical approval number EC107), and the Iraqi Medical Research Centre (ethical approval number 284/2023), in accordance with the Declaration of Helsinki regarding human subjects [17].

Study population

All 612 adult patients with a documented diagnosis of primary hypertension and at least one recorded visit to the clinic during the study period were screened.

Inclusion criteria

Participants were included if they were ≥ 18 years at the time of visit, had a diagnosis of primary (essential) hypertension recorded in the medical file by a treating physician, had been on a stable antihypertensive regimen (no change in drug class and no $> 50\%$ dose change) for at least 6 months prior and had at least one complete set of renal function tests (serum creatinine, estimated glomerular filtration rate (eGFR), and urine albumin measurement) within 3 months of the index visit.

Exclusion criteria

Patients were excluded if they had evidence of acute kidney injury (AKI) at baseline ($\geq 50\%$ increase in serum creatinine over 7 days or clinical diagnosis of AKI), end-stage kidney disease (maintenance dialysis or kidney transplantation), pregnancy at any time during the 6 months preceding the index visit, documented secondary causes of hypertension (e.g., renal artery stenosis, endocrine hypertension such as Cushing's syndrome or primary aldosteronism, coarctation of the aorta), missing or incomplete key laboratory data: baseline serum creatinine or urine albumin-creatinine ratio (UACR).

Study groups

Patients were divided into six groups according to the types of antihypertensive drug classes at the first visit to the outpatient clinic. For patients prescribed multiple agents, the regimen was audited to determine which drug the treating physician considered the primary agent (first-line) or the highest daily dose class otherwise. In order to maintain clinical interpretability and have a sufficient number of participants per group, combinations between a renin-angiotensin system blocker and another class were clustered independently (Table 1). Patients who were placed on fixed-dose combinations were grouped based on their constituents (e.g., ACEi/diuretic was placed in the RAAS + diuretic group). Combinations to which mineralocorticoid receptor

antagonist (MRA) regimens were assigned were held in the combination group due to small expected sizes, but will be presented in sensitivity analyses.

Sample size calculation

Sample size was calculated to determine a clinically meaningful difference in mean eGFR between antihypertensive groups. Based on previous regional clinic data and published literature [7], the following assumptions were made: expected mean eGFR in the reference group (RAAS-based therapy) of 75 mL/min/1.73 m², minimum clinically important difference between groups of 5 mL/min/1.73 m², common standard deviation (SD) of eGFR across groups of 15 mL/min/1.73 m², type I error (α) of 0.05, two-sided, and power ($1 - \beta$) of 80 %. Using these parameters and a one-way ANOVA framework in G*Power software (version 3.1), the minimum required sample size was estimated at 360 participants (60 per group) to determine the specified difference with adequate power. To account for an anticipated 20 % rate of missing or unusable data (e.g., incomplete laboratory results, loss to follow-up for longitudinal measures), the target sample size was inflated to 450 participants. The larger target size for the combination group reflects its higher expected prevalence in routine practice and allows exploration of subgroup patterns (e.g., RAAS + CCB vs RAAS + diuretic).

Data collection

Data were extracted from the clinic's electronic health record system and, where necessary, supplemented by reviewing paper files. A standardised data abstraction form was used to ensure uniform collection across all patients.

Clinical and demographic variables

Variables recorded at the index (first) visit include: demographic data, anthropometric measures, lifestyle factors, medical history and comorbidities.

Table 1: Grouping of participants by antihypertensive regimen

Group	Antihypertensive regimen	Notes	No. of patients
1	ACE inhibitor monotherapy	Any ACEi at a stable dose	60
2	ARB monotherapy	Any ARB at a stable dose	60
3	CCB monotherapy	Dihydropyridine or non-dihydropyridine	60
4	β -blocker monotherapy	Cardio-selective or non-selective	60
5	Diuretic monotherapy	Thiazide or loop diuretic	60
6	Combination therapy (RAAS $\pm$ other classes, including MRAs)	Two or more agents; RAAS-based and non-RAAS-based combinations	150

Blood pressure measurements were taken after 5 minutes of rest in the seated position, with an appropriately sized cuff, and recorded as the mean of two readings taken 1 – 2 minutes apart. Where available, home or ambulatory blood pressure monitoring data within the preceding 3 months were recorded.

Medication data

Medication data obtained from prescription records and clinic notes included antihypertensive agents: drug name, class, daily dose, dosing frequency, and duration of continuous use (months), therapy pattern: monotherapy vs combination therapy; presence of RAAS inhibitor; exposure to MRAs, other cardiovascular and renal medications: statins, antiplatelet agents, sodium–glucose cotransporter-2 (SGLT2) inhibitors, and other nephroprotective agents where applicable, concomitant potential nephrotoxic drugs: non-steroidal anti-inflammatory drugs (NSAIDs), certain antibiotics, contrast agents, and traditional remedies when documented.

Laboratory measurements

Laboratory data closest to the index visit (within $\pm$ 3 months) were recorded. If multiple results existed in this window, the value closest in time to the index visit was selected. The parameters collected were serum creatinine, blood urea nitrogen (BUN), estimated glomerular filtration rate (eGFR), and urine parameters (spot urine albumin–creatinine ratio (UACR) or 24-hour urinary protein excretion, and serum electrolytes.

Other biochemical parameters

Fasting blood glucose, glycated haemoglobin (HbA1c) for patients with diabetes, and lipid profile (total cholesterol, LDL, HDL, triglycerides) [18]. For patients with available longitudinal data, serum creatinine and eGFR values at least 12 months after the index visit were also extracted to permit assessment of change in renal function over time.

Statistical analysis

Data were analyzed using descriptive and inferential statistics. Continuous variables were expressed as mean $\pm$ standard deviation (SD), while categorical variables were presented as frequencies and percentages. Differences in continuous variables among antihypertensive groups were assessed using one-way analysis of variance (ANOVA). Categorical variables were compared using Chi-square (χ^2) test. To evaluate

the independent association between antihypertensive regimen and renal outcomes, multivariate linear regression and multivariate logistic regression analyses were performed after adjusting for potential confounding variables. $P < 0.05$ was considered statistically significant.

RESULTS

Study population flow

Eligibility was screened among 612 patients with a recorded diagnosis of primary hypertension who visited the hypertension and nephrology clinics during the study period, of whom an initial 528 were eligible on the basis of complete records. Seventy-eight patients were rejected following secondary screening due to acute kidney injury at baseline (14), end-stage kidney disease on dialysis or post-transplant (19), documented secondary hypertension (11), pregnancy (7), and missing key renal laboratory data (serum creatinine or UACR; 27). A total of 450 patients were therefore included in the final analysis. According to their predominant antihypertensive regimen at the index visit.

Baseline characteristics

Table 2 shows that the average age of the entire group was 59.4 ± 11.1 years, and 52.9 % were females. The age differences between groups were not significant ($p > 0.05$). The overall mean body mass index was in the overweight-to-obese range (30.1 ± 4.7 kg/m²) across all groups, and between-group differences were not significant ($p > 0.05$). The β -blocker and diuretic monotherapy groups had the longest duration of hypertension and indicated a higher cardiovascular risk profile. There was general similarity in office systolic and diastolic blood pressures; the differences were also not significant ($p > 0.05$).

Diabetes mellitus and preexisting cardiovascular disease prevailed most in the combination therapy group, which was in agreement with more complicated or advanced disease needing multidrug regimens. The use of Sodium–Glucose Cotransporter-2 (SGLT2) inhibitors like Dapagliflozin and Empagliflozin was also higher when compared with other groups and it is not significant in combination and RAAS-based monotherapy groups ($p > 0.05$). Regular use of non-steroidal anti-inflammatory drugs like mefenamic acid and ibuprofen (NSAIDs) was slightly higher compared with other groups, and it is not significant in patients receiving diuretic monotherapy (Table 2).

Table 2: Baseline demographic and clinical characteristics of participants by antihypertensive regimen (n = 450)

Characteristic	ACEi (n = 60)	ARB (n = 60)	CCB (n = 60)	β -blocker (n = 60)	Diuretic (n = 60)	Combination (n = 150)	P-value*
Age (years)	58.4±10.7	59.1±11.0	60.3±0.9	61.0±11.3	62.5±10.2	57.0±11.5	0.08
Female (n; %)	32 (53.3)	31 (51.7)	34(56.7)	27 (45.0)	35 (58.3)	89 (59.3)	0.19
BMI (kg/m ²)	29.7±4.5	30.0±4.6	30.3±4.9	30.4±4.4	30.8±4.8	30.0±4.7	0.76
Duration of hypertension (years)	9.1±5.2	9.5±5.0	10.2±5.4	11.1±5.7	11.5±6.1	9.8±5.3	0.04
SBP (mmHg)	137.4±11.6	136.9±11.2	138.6±12.1	139.1±11.9	141.3±12.4	137.5±11.8	0.09
DBP (mmHg)	83.1±7.6	82.7±7.4	83.9±8.1	84.2±7.9	85.0±8.3	83.4±7.7	0.28
Diabetes mellitus (n; %)	23 (38.3)	24 (40.0)	22 (36.7)	25 (41.7)	21 (35.0)	74 (49.3)	0.09
Dyslipidaemia (n; %)	29 (48.3)	31 (51.7)	30 (50.0)	32 (53.3)	28 (46.7)	83 (55.3)	0.63
Established CVD (n; %)	14 (23.3)	15 (25.0)	16 (26.7)	18 (30.0)	17 (28.3)	55 (36.7)	0.12
History of CKD/proteinuric kidney disease (n; %)	13 (21.7)	14 (23.3)	15 (25.0)	16 (26.7)	16 (26.7)	46 (30.7)	0.48
SGLT2 inhibitor use (n; %)	7 (11.7)	8 (13.3)	5 (8.3)	6 (10.0)	4 (6.7)	29 (19.3)	0.07
Regular NSAID use (n; %)	9 (15.0)	10 (16.7)	11 (18.3)	12 (20.0)	15 (25.0)	26 (17.3)	0.32

Values are mean $\pm$ SD. *P-value between-group comparison (ANOVA or χ^2 as appropriate), cardiovascular disease (CVD)

Renal function across drug classes

There was a significant difference in baseline eGFR between groups ($p < 0.001$). The mean eGFR was highest in patients on ACEi or ARB monotherapy. It was closely followed by the combination therapy group, with the lowest in the diuretic and β -blocker monotherapy groups. The same occurred with serum creatinine and BUN, in the reverse direction. ACEi and ARB had the lowest median UACR, and β -blockers and diuretics had the highest median UACR. In combination groups, median UACRs were intermediate, although still lower than those of non-RAAS monotherapies ($p < 0.001$). The ratio of patients with moderate to severe albuminuria (A2 - A3) was between about one in three in ACEi-ARB groups and more than half in the diuretic group.

Incidence and prevalence of renal impairment

One hundred and twenty-two out of four hundred and fifty patients (27.1 %) had CKD criteria, i.e., eGFR < 60 mL/min/1.73 m². The prevalence of CKD varied significantly between the antihypertensive groups (kh2; $p = 0.003$) as indicated in Table 4, with a prevalence of CKD of 18.3 % in the ACEi group, and 38.3 % in the diuretic group. In 197 patients (43.8%), moderate to severe albuminuria (A2 - A3) was found. The ACEi and ARB groups had the lowest prevalence (35.0 and 36.7 %, respectively), while the diuretic (55.0 %) and β -blocker groups (51.7 %) had the highest prevalence. The intermediate rates were observed again in the combination therapy group (40.0 %).

RAAS-based therapy (ACEi and ARB groups) was found to have a lower incidence of CKD

(23.0% vs 33.9%), and A2-A3 albuminuria (38.4 vs 50.6) (both $p < 0.01$) in exploratory analyses that combined all RAAS-based regimens (ACEi, ARB and any regimen containing ACEi/ARB) compared to purely non-RAAS regimens (CCB, β -blocker, and diuretic monotherapy).

Multivariable analysis

Interaction between non-RAAS monotherapies and lower eGFR was significant in both stratified subgroups when patients were divided based on the presence of diabetes mellitus; the strength of interrelationships was slightly greater in the presence of diabetes ($p < 0.001$). Adjusted eGFR change of -9 to -10 mL/min/1.73 -1.73 m² versus ACEi with diabetic subgroup with Diuretic and β -blocker monotherapy were associated with increased odds of CKD and albuminuria. The trend was also similar, albeit with low values, in non-diabetic patients, and confidence intervals (CIs) were wider, since they were smaller. There was no significant interaction between drug class and diabetes status (p -interaction > 0.10) in CKD, although trends of the hi same showed that the participants with diabetes were at higher risk.

Sensitivity and subgroup analyses

Several predefined subgroup analyses were performed to assess the robustness of the main findings.

Stratification by diabetes status

The interaction between non-RAAS monotherapies and lower eGFR was significantly greater in patients with diabetes mellitus, but the strength of the association was slightly greater in patients without diabetes.

Table 3: Baseline renal function of participants by antihypertensive regimen (n = 450)

Parameter	ACEi (n = 60)	ARB (n = 60)	CCB (n = 60)	β -blocker (n = 60)	Diuretic (n = 60)	Combination (n = 150)	P-value*
eGFR (mL/min/1.73 m ²)	78.2±18.1	76.4±17.3	71.0±19.0	69.5±19.6	67.8±20.4	74.0±18.5	<0.001
Serum creatinine (mg/dL)	1.02±0.32	1.05±0.34	1.18±0.40	1.22±0.42	1.27±0.45	1.10±0.36	<0.001
BUN (mg/dL)	18.7±6.1	19.3±6.4	21.1±7.0	21.6±7.2	22.4±7.6	20.2±6.7	0.01
UACR (mg/g, median (IQR))	24 (11–51)	27 (13–58)	45 (19–110)	49 (21–120)	55 (24–135)	36 (15–89)	<0.001
CKD (eGFR <60), n (%)	11 (18.3)	12 (20.0)	18 (30.0)	20 (33.3)	23 (38.3)	38 (25.3)	0.003
Albuminuria A2–A3, n (%)†	21 (35.0)	22 (36.7)	30 (50.0)	31 (51.7)	33 (55.0)	60 (40.0)	0.002

eGFR: estimated glomerular filtration rate, BUN: blood urea nitrogen, UACR: urine albumin–creatinine ratio, CKD: chronic kidney disease. *From one-way ANOVA (continuous variables) or χ^2 test (categorical variables). A2–A3 is defined as UACR ≥ 30 mg/g or equivalent proteinuria.

Table 4: Association between antihypertensive regimen and renal outcomes in participants (multivariable models)

Regimen (vs ACEi)	Adjusted β for eGFR (mL/min/1.73 m ²)* (95% CI)	P-value	Adjusted OR for CKD† (95% CI)	P-value	Adjusted OR for A2–A3 albuminuria‡ (95% CI)	P-value
ARB monotherapy	-1.8 (-5.3 to 1.7)	0.31	1.12 (0.64–1.97)	0.69	1.08 (0.63–1.84)	0.78
CCB monotherapy	-5.4 (-9.0 to -1.8)	0.003	1.72 (1.01–2.94)	0.045	1.64 (1.00–2.69)	0.049
β -blocker monotherapy	-6.3 (-9.9 to -2.7)	0.001	1.91 (1.10–3.30)	0.021	1.78 (1.07–2.97)	0.026
Diuretic monotherapy	-7.9 (-11.7 to -4.1)	<0.001	2.30 (1.33–3.99)	0.003	2.05 (1.22–3.44)	0.007
Combination therapy	-2.5 (-5.5 to 0.5)	0.10	1.35 (0.84–2.18)	0.21	1.21 (0.77–1.89)	0.41

*From multivariable linear regression with eGFR as the dependent variable. From multivariable logistic regression with CKD (eGFR < 60 mL/min/1.73 m²) as the outcome. From multivariable logistic regression with A2–A3 albuminuria as the outcome. All models were adjusted for age, sex, BMI, duration of hypertension, Systolic blood pressure (SBP) and diastolic blood pressure (DBP), diabetes, dyslipidaemia, baseline CKD history, smoking, regular NSAID use and SGLT2 inhibitor therapy

Adjusted eGFR change of -9 to -10 mL/min/1.73 m² versus ACEi, with diabetic subgroup, with Diuretic and β -blocker monotherapy, was associated with increased odds of CKD and albuminuria. The trend was also similar, albeit with lower values, in non-diabetic patients, and CIs were wider because they were smaller. There was no significant interaction between drug class and diabetes status (p -interaction > 0.10) in CKD, although trends of the same showed that the people with diabetes were at higher risk.

Stratification by baseline renal function

Increment from mild albuminuria (A1) to moderate to severe albuminuria (A2 - A3) exhibited a lower risk of incident at 12 months of follow-up in RAAS-based regimens (ACEi, ARB, and combinations) compared to non-RAAS monotherapy, but the occurrences were relatively minor. The direction of association between drug class and eGFR slope at 12 months is

comparable in patients who received CKD at baseline (eGFR < 60), yet in patients who received CKD at baseline (eGFR < 60), the variations are not invariably statistically significant due to limited follow-up and events.

Stratification by age

In aged patients, a stronger association between non-RAAS monotherapies and decreased eGFR was observed. In patients aged 65 years, diuretic monotherapy resulted in adjusted change of eGFR closer to 10 mL/min/1.73 m² than ACEi, whereas in patients aged under 65 years, the difference was closer to 5 mL/min/1.73 m². Even though interaction between age group and regimen was not significant ($p > 0.05$). The trend indicates that older patients might be specifically vulnerable to side effects of non-RAAS monotherapies that affect the kidneys, particularly diuretics.

DISCUSSION

The main finding that ACEi and ARB regimens are associated with more favourable renal outcomes is consistent with current international recommendations. ACE inhibitors or ARBs have been shown to lower intraglomerular pressure, reduce albuminuria, and slow CKD progression, which explains why they are first-line antihypertensive medications recommended for patients with CKD and moderate-to-severe albuminuria [19]. The article by Georgianos and Agarwal also highlights RAAS blockade as the basis of treatment in CKD patients with hypertension, especially in those with albuminuria. These recommendations are reflected in the improved eGFR and albuminuria characteristics observed among users of ACEi or ARB in this study [15]. Fu *et al* [13] demonstrated that the introduction of RAAS inhibitors, compared with CCBs, is associated with a much lower risk of kidney replacement therapy, with no excess mortality or significant cardiovascular events. More recently, a meta-analysis in advanced CKD found that RAAS blockade reduced the risk of end-stage kidney disease compared with non-RAAS strategies, but did not affect mortality or cardiovascular events [20]. The two analyses agree with the more favourable renal status in RAAS-treated groups in this study.

The near parallel effects of ACEi and ARB also reflect the findings from prior comparative studies, which indicate that, at recommended doses, both drugs provide similar long-term effects in high-risk groups with regard to the prevention of CKD progression. Recent studies indicate that diuretics are effective in controlling volume and reducing blood pressure in CKD. However, evidence of a renoprotective effect as first-line treatment is scarce, and overdiuresis may worsen kidney function and electrolyte balance [21,22].

Clinically, the results further support the idea that the choice of antihypertensives in patients with high renal risk should be based on blood pressure rather than differences in the outcome of kidney function. The stable relationship between RAAS blockade and more favourable renal indices supports the continued use of ACE inhibitors or ARBs as initial treatment in patients with hypertension and albuminuria or low eGFR, as recommended by Kidney Disease: Improving Global Outcomes (KDIGO) and other guidelines [12,15]. This translates in clinical practice in Iraq into a need to review and standardise the established antihypertensive regimens in such patients, and where it is not contraindicated,

RAAS blockade should be added as a therapeutic cornerstone.

Secondly, the poorer renal profile of diuretic and β -blocker monotherapy implies that they should not be used as long-term treatment in high-risk individuals more often. Instead, they are more appropriate as adjunctive drugs to RAAS blockade to treat specific indications: diuretics for volume overload and resistant hypertension, and β -blockers for cardiovascular indications, e.g., coronary artery disease or heart failure. Considering the identified risks of volume depletion, prerenal azotaemia, and hyperkalaemia in patients on combined RAAS blockers, MRAs and diuretics, such agents should be accompanied by increased monitoring of renal activity and electrolytes, especially at high doses that are more intensive [16].

Third, the presence of a high-unrecognised CKD and albuminuria prevalence in this cohort highlights the need to conduct systematic kidney evaluation in hypertensive clinics. Regular measurement of eGFR and urinary albumin-creatinine ratio should be adopted to achieve risk stratification [22], and these data indicate that such measures should be adopted in Iraqi practice to identify a significant proportion of patients that may warrant an increase in RAAS-based and, in some cases, MRA- or SGLT2-based renoprotective measures.

Considering the foregoing, RAAS-blocking agents, such as ACE inhibitors or ARBs, should be given as first-line antihypertensive treatment to patients with primary hypertension and those with elevated renal risks in Iraq, unless there are any known contraindications. The primary role of diuretics, CCB and β -blockers as low-efficacy agents is as add-on therapy to RAAS-based regimens, depending on clinical symptoms, and with thorough kidney function and serum potassium monitoring. In available cases, protocols that include SGLT2 inhibitors and, in some diabetic CKD patients, non-steroidal MRAs such as finerenone should be used to supplement the existing renal and cardiovascular protection, as suggested by recent European Renal Best Practice and KDIGO recommendations [12,16].

Limitations of this study

Although causality cannot be established (due to the retrospective study design and possible residual confounding), the findings are valuable for providing much-needed context-specific data from Iraq, where published evidence on patterns of antihypertensive use and kidney outcomes is

scarce. Through a combination of local data and international trials and practice documents, such as those on RAAS blockade, diuretics, and emerging MRAs, clinicians and policymakers will be able to optimise treatment algorithms to focus on renoprotective measures and reduce the increasing burden of hypertensive kidney disease in the area.

Future studies require incorporating more sophisticated statistical and computational modelling methods, such as predictive regression and machine learning-based systems, to determine the antihypertensive regimens with the strongest association with renal protection and CKD progression across varied patient groups [23,24]. Concepts from immunometabolism emphasise how metabolic pathway regulation influences disease outcomes, which may provide a valuable framework for future studies exploring metabolism-linked renal responses to antihypertensive therapies [25].

CONCLUSION

This study demonstrates that in the Iraqi population with primary hypertension, antihypertensives are significantly associated with renal condition of the patient. The RAAS blockade via either ACE inhibitor or ARB monotherapy, and combinations with RAAS, is consistently associated with increased eGFR and decreased proteinuria. In contrast, diuretic and β -blocker monotherapies are associated with increased CKD and proteinuria burden, even after blood pressure control and adjustment for key clinical covariates. Calcium channel blockers effectively reduce blood pressure in hypertensive patients; however, their renal protective effects appear to be less pronounced compared with RAAS inhibitors. Therefore, they are often more beneficial when used in combination therapy to achieve optimal blood pressure control.

Directions for future studies should be to confirm and expand these findings in larger, multicentre cohorts in both Iraq and neighbouring countries, preferably with follow-up and standardised measurement of blood pressure and albuminuria using eGFR. Residual confounding would be addressed by pragmatic randomised or well-matched comparative-effectiveness research comparing RAAS-based strategies with non-RAAS strategies in the local context, thereby enhancing causal inference. Also, specific assessments of the uptake, safety, adherence, and cost-effectiveness of SGLT2 inhibitors, MRAs, and new antihypertensive combinations such as RAAS inhibitors + calcium channel blocker, like perindopril + amlodipine, in

populations with CKD in Iraq are required to inform policy and reimbursement decisions.

DECLARATIONS

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Use of Artificial intelligence/Large language models

The authors confirm that AI-based tools were used solely for language editing and manuscript polishing purposes (e.g., grammar, phrasing, and clarity). No AI tools were used to generate content, interpret data, or influence study design, results, or conclusions. All intellectual contributions, study analyses, and interpretations reported in the manuscript are the original work of the authors.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of interest

No conflict of interest is associated with this work.

Contribution of authors

We declare that this work was done by the author(s) named in this article, and all liabilities relating to claims about the content of this article will be borne by the authors.

Ethical approval

This research was conducted with the approval of the ethical committees from the College of Pharmacy, University of Basra, Basra, Iraq (ethical approval number EC107), and the Iraqi Medical Research Centre (ethical approval number 284/2023).

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