

Prevalence and Risk Factors of Chronic Kidney Disease among Hypertensive Patients in a General Medicine Outpatient Setting: A Prospective Observational Study

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Abstract

Background: Chronic kidney disease (CKD) often is hidden among the majority of patients with hypertension, and can only be diagnosed if estimated glomerular filtration rate (eGFR) and albuminuria are evaluated. Objective: To estimate the prevalence of CKD and look for risk factors associated with it in adults attending a general medicine outpatient department having hypertension.

Methods: This prospective observational study included 420 adult patients with hypertension that were followed for 6 months. Demographic information, hypertension duration, hypertension management, co-morbidities, drug use, body mass index, blood pressure, serum creatinine, eGFR and urine albumin-creatinine ratio (UACR) were documented. To confirm the diagnosis of CKD, the abnormal eGFR or albuminuria were repeated after 3 months.

Results: 408/420 patients enrolled had confirmation testing. The mean age was 58.6 +/- 11.4 years; 222 (54.4%) were male and 164 (40.2%) had diabetes. CKD was confirmed in 115 patients, giving a prevalence of 28.2% (95% CI 23.8-32.8). Reduced eGFR <60 mL/min/1.73 m² was present in 62 (15.2%), albuminuria in 103 (25.2%), and both abnormalities in 50 (12.3%). Of all the CKD patients, only 31 (27.0%) were already aware of the disease. Age ≥60 years, diabetes mellitus, hypertension duration ≥10 years, uncontrolled blood pressure, regular use of non-steroidal anti-inflammatory drugs and obesity were identified as independent risk factors by multivariable analysis.

Conclusions: CKD was present in almost one-third of patients attending the outpatient department for hypertension, with a majority of these having suspected albuminuria and low awareness. There is a need for routine combined eGFR-UACR screening in hypertensive clinics.

Keywords: Chronic Kidney Disease; Hypertension; Albuminuria; eGFR; Risk Factors; Outpatient Screening; Diabetes Mellitus.

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Introduction

Chronic kidney disease (CKD) is defined as a health-impairing condition in which kidneys have abnormalities that last for at least three months. Today, the KDIGO guidelines focus on using GFR and albuminuria for CKD assessment because either is a risk factor for progression and cardiovascular risk [1]. Hypertension is a risk factor and a consequence of CKD, and it can cause vascular and glomerular damage by increasing the intraglomerular pressure, endothelial dysfunction, arteriosclerosis, and proteinuric pathways [2].

CKD may be asymptomatic until late in the disease. The primary care and general medicine outpatient departments are thus an important

window to early detection amongst high-risk groups. A JAMA review pointed out that the prevalence of CKD ranges from 8% to 16% around the world and is often overlooked despite the existence of easy to use tests, like the eGFR with serum creatinine, and the urine albumin-creatinine ratio (UACR) [3]. The CKD-EPI equation was better at estimating GFR than previous equations and newer race-free equations have further refined clinical reporting [4,5].

The worldwide burden of CKD is high. There is a reasonable estimate that the global prevalence of CKD is approximately 11-13% [6-9] and the Global Burden of Disease (GBD) collaboration has

demonstrated a rising rate of mortality and disability due to CKD in recent decades. Some of the most powerful modifiable ones include hypertension and diabetes. Urine testing is important for early diagnosis as for patients with hypertension, persistent albuminuria can occur before overt reduction in eGFR.

Indian data indicate increasing pattern of CKD burden in both community and clinical populations. In the SEEK-India study, the prevalence of CKD was reported at 17.2% among adults screened and associated factors were found to be hypertension, diabetes, anemia and older age [8].

Some recent nationally representative ICMR-INDIAB data revealed that there is strong association between diabetes and hypertension with impaired kidney function, thus highlighting the importance of integrated screening of non-communicable diseases [9]. Regular screening for CKD in outpatient clinics of the general medical practice, however, is still underutilized, especially if UACR is not routinely used.

The present study was designed to estimate the prevalence of CKD among the adults with hypertension visiting general medicine OPD, and to find out the clinical, metabolic and medication related risk factors associated with CKD. To minimize misclassification as a result of transient abnormalities, the study used both eGFR and UACR and confirmed the results at 3 months.

Materials and Methods

Study design and setting: The study was a prospective observational study carried out in the general medicine outpatient department of a tertiary care teaching hospital for 6 months with follow up at 3 months for subjects having abnormal baseline kidney tests. The study subjects were adult patients who were known or newly diagnosed hypertensive patients visiting the clinic for routine care.

Sample size: n was calculated by the formula $n = Z^2pq/d^2$. Based on the assumption that 25% of the adult population in the area is hypertensive and the minimum sample size was 288 with 95% confidence level and absolute precision of 5%. A total of 420 participants were enrolled and underwent confirmatory testing to enable subgroup analyses, multivariable modelling and potential loss to follow-up.

Eligibility criteria: All patients aged ≥ 30 years who were diagnosed as having hypertension or blood pressure $\geq 140/90$ mmHg on two occasions within the visit were included. Hypertension was diagnosed based on the standard clinical definition or based on currently taking antihypertensive medications. Patients were excluded if they had an acute febrile illness, known end-stage kidney

disease, dialysis, kidney transplantation, pregnancy, suspected urinary tract infection, acute kidney injury, an ongoing hospital stay, malignancy, or refusal to return for repeat testing.

Structured case record form was used to collect data for the following parameters: age, sex, residence, socioeconomic status, smoking, alcohol consumption, physical activity, dietary salt intake, duration of hypertension, antihypertensive treatment, adherence, diabetes mellitus, cardiovascular disease, family history of CKD, NSAID use and previous knowledge of kidney disease. Standardized seated blood pressure, BMI, height, weight, and waist circumference were measured. Hypertension was considered to be uncontrolled if the systolic BP at the study visit was ≥ 140 mmHg or/and the diastolic BP was ≥ 90 mmHg.

Laboratory assessment: Serum creatinine was measured by an enzymatic method calibrated to isotope-dilution mass spectrometry traceability if available.

The eGFR was derived from the institutional laboratory-reported CKD-EPI equation. UACR was obtained from the measurement of spot urine albumin and creatinine. Other parameters recorded included fasting glucose, HbA1c, lipid profile, hemoglobin and serum uric acid. The participants who had an eGFR < 60 mL/min/1.73 m² or UACR ≥ 30 mg/g at baseline were retested for creatinine and UACR after three months.

Definitions: CKD was defined as UACR ≥ 30 mg/g for duration of ≥ 3 months and/or eGFR < 60 mL/min/1.73 m² for ≥ 3 months. Albuminuria categories were A1 (< 30 mg/g), A2 (30-300 mg/g), and A3 (> 300 mg/g). eGFR categories were classified as G1 (≥ 90), G2 (60-89), G3a (45-59), G3b (30-44), G4 (15-29), and G5 (< 15 mL/min/1.73 m²). Diabetes mellitus was determined by previous diagnosis, current diabetes therapy, fasting plasma glucose level ≥ 126 mg/dL or HbA1c level $\geq 6.5\%$. The definition of obesity used for the Indian population context was BMI ≥ 25 kg/m².

Data analysis: Statistical analysis was done using SPSS version 26. Continuous variables were summarized as mean \pm standard deviation and compared using independent t-test.

The categorical variables were summarized as frequencies and percentages and compared with chi-square test or Fisher exact test.

Univariate analysis of the variables significant at $p < 0.10$ and clinically important variables were entered into multivariable logistic regression to determine the independent risk factors for CKD. The odds ratios (ORs) were reported with 95%

confidence intervals (CIs). A p value of <0.05 was taken as statistically significant.

Results

A total of 420 hypertensive patients were enrolled. Twelve did not complete repeat testing after an abnormal baseline result, leaving 408 participants for final analysis. The mean age was 58.6 +/- 11.4 years and 222 (54.4%) were male. The mean duration of hypertension was 8.7 +/- 6.1 years.

Diabetes mellitus was present in 164 (40.2%), obesity in 174 (42.6%), and uncontrolled blood pressure at the study visit in 232 (56.9%).

Compared with participants without CKD, those with CKD were older, had longer hypertension duration, higher prevalence of diabetes, higher systolic blood pressure, greater NSAID use, and lower hemoglobin. Baseline characteristics are shown in Table 1.

Table 1: Clinical profile of hypertensive outpatients according to CKD status (n=408)

Variable	CKD present (n=115)	No CKD (n=293)	p-value
Age (years), mean +/- SD	64.1 +/- 10.2	56.4 +/- 10.9	<0.001
Male sex, n (%)	67 (58.3)	155 (52.9)	0.327
Hypertension duration (years)	11.2 +/- 6.8	7.7 +/- 5.5	<0.001
Diabetes mellitus, n (%)	63 (54.8)	101 (34.5)	<0.001
Obesity, n (%)	58 (50.4)	116 (39.6)	0.046
Uncontrolled BP, n (%)	78 (67.8)	154 (52.6)	0.006
Mean systolic BP (mmHg)	151.8 +/- 17.6	143.6 +/- 15.2	<0.001
Current smoker, n (%)	24 (20.9)	45 (15.4)	0.181
Regular NSAID use, n (%)	33 (28.7)	46 (15.7)	0.003
Hemoglobin (g/dL), mean +/- SD	11.8 +/- 1.7	12.9 +/- 1.5	<0.001

CKD was confirmed in 115 participants, giving a prevalence of 28.2% (95% CI 23.8-32.8). Reduced eGFR <60 mL/min/1.73 m² was present in 62 (15.2%), while albuminuria was present in 103 (25.2%). Both reduced eGFR and albuminuria were present in 50 (12.3%). Among confirmed CKD

cases, 53 (46.1%) had preserved eGFR with persistent albuminuria, demonstrating the added value of UACR screening.

Only 31 (27.0%) CKD patients were previously aware of kidney disease (Table 2).

Table 2: Prevalence and staging pattern of CKD among hypertensive patients

Kidney parameter/category	Number (%) among total n=408	Number (%) among CKD n=115
Confirmed CKD	115 (28.2)	115 (100.0)
eGFR <60 mL/min/1.73 m ²	62 (15.2)	62 (53.9)
Albuminuria (UACR >=30 mg/g)	103 (25.2)	103 (89.6)
Both low eGFR and albuminuria	50 (12.3)	50 (43.5)
G1-G2 with albuminuria	53 (13.0)	53 (46.1)
G3a	42 (10.3)	42 (36.5)
G3b	15 (3.7)	15 (13.0)
G4	5 (1.2)	5 (4.3)
A2 albuminuria	82 (20.1)	82 (71.3)
A3 albuminuria	21 (5.1)	21 (18.3)
Previously aware of CKD	31 (7.6)	31 (27.0)

Multivariable logistic regression identified age >=60 years, diabetes mellitus, hypertension duration >=10 years, uncontrolled blood pressure, regular NSAID use, and obesity as independent predictors of CKD. Sex, smoking, and family history of CKD were not independently associated after adjustment (Table 3).

Table 3: Multivariable logistic regression for risk factors associated with CKD

Risk factor	Adjusted OR	95% CI	p-value
Age >=60 years	2.46	1.54-3.92	<0.001
Diabetes mellitus	2.21	1.35-3.62	0.002
Hypertension duration >=10 years	1.94	1.17-3.21	0.010
Uncontrolled BP at visit	1.82	1.11-2.99	0.018
Regular NSAID use	1.69	1.02-2.83	0.041
Obesity	1.55	1.00-2.42	0.049
Male sex	1.18	0.73-1.91	0.500
Current smoking	1.31	0.72-2.39	0.377

Discussion

In this outpatient study, 28.2% of the adults with hypertension were confirmed to have CKD using the combined markers of eGFR and UACR, and repeat testing after 3 months. This is clinically relevant because there was a significant proportion of CKD cases who were previously aware of kidney disease (more than one-fourth) suggesting that a significant proportion of CKD cases were under-detected in routine care. A large proportion of patients with preserved eGFR but continued kidney damage were identified, regardless of whether the patients had albuminuria or not.

The prevalence observed matches with previous studies which have demonstrated a high burden of CKD in populations with hypertension. In a hospital setting, Fiseha et al. observed that 19.0% had impaired eGFR, 30.9% had albuminuria, and 33.9% had overall CKD among individuals with diabetes and hypertension [10]. The prevalence of hypertension-related CKD was estimated at ~29% in sub-Saharan Africa in a recent meta-analysis, which was similar to our results despite the geographical differences [11]. Overall, the prevalence of CKD in the SEEK study in India was 17.2% in an adult population screened for the study, and hypertension was one of the common associated factors reported [12]. The prevalence that we found is higher than what is seen in other studies, given that all the participants were people with hypertension and many had other risk factors like diabetes, obesity and uncontrolled blood pressure levels.

We will take it to a stage where we will show the importance of UACR. Almost half of these cases of CKD were found to have an eGFR that was preserved, and the presence of albuminuria would not have been detected if only creatinine had been used for screening. Given that in addition to being a useful tool for refining prognosis, urine albumin measurement can be used to direct renoprotective therapy and urine albumin measurement is useful to predict cardiovascular events independent of eGFR, KDIGO 2024 recommends assessing urine albumin. In addition, because of its possible association with systemic endothelial dysfunction, intraglomerular hypertension, and early nephrosclerosis, prior to rises in serum creatinine, albuminuria is also important in hypertension [13].

Gender (age \geq 60 years) was the strongest independent predictor. With aging, there is loss in nephrons, increased vascular stiffness and greater cumulative exposure to hypertension and metabolic insults. In line with the known contribution of hyperglycemia to glomerular basement membrane thickening, mesangial expansion and albuminuria, there was a doubling of the risk of CKD in patients with diabetes. The ICMR-INDIAB results

corroborate with the findings of the close association between diabetes, hypertension and impaired kidney function in India [14].

Lower education level, longer duration of hypertension, and uncontrolled hypertension were independent risk factors for CKD. These results are in line with KDIGO blood pressure recommendations, which focus on standardized measurement of blood pressure and intensive risk reduction in CKD if tolerated [15]. The SPRINT trial demonstrated cardiovascular benefit of intensive lowering of systolic BP in certain high-risk patients without diabetes and later interpretations of the results based on CKD have affected guideline BP targets [16]. Outpatient implementation, however, should be made on a case-by-case basis and monitored closely for hypotension and frailty, diabetes, and polypharmacy.

In this study, the use of NSAIDs was found to be associated with CKD. NSAIDs may decrease afferent arteriolar dilation in the kidneys mediated by prostaglandins, lead to acute kidney injury due to hemodynamic changes, and can exacerbate hypertension or edema. Observational data cannot establish causality, but a medication review is a pragmatic intervention in the hypertensive clinic. Obesity was also independently associated, presumably via glomerular hyperfiltration, insulin resistance, inflammation, and the presence of diabetes and sleep-disordered breathing. Metabolic risk factors have been highlighted by global CKD reviews as a major factor in the burden of kidney disease in the future [17].

Poor knowledge and awareness on the topic of CKD is a public health problem. The awareness about CKD is especially low in early stages, during which intervention is useful. Further, Chen et al. highlighted that primary care providers should perform early CKD diagnosis, risk stratification, use renin-angiotensin system (RAS) blockers if appropriate, control glycemic levels, manage cardiovascular risk factors, and avoid nephrotoxic drugs to alleviate the burden of CKD [18]. Integrated hypertension-CKD care pathways are thus appropriate to be deployed in general medicine OPDs.

This study is subject to certain limitations. It was conducted at hospitals, and may overestimate prevalence in comparison to community samples. Spot UACR was used to measure albuminuria and re-testing increased specificity but an exercise, diet and illness-induced residual variability remains a possibility. Cystatin C was not measured and eGFR was calculated in terms of creatinine. Observational design only detects associations not cause and effect. However, there are some strengths to the study, such as the prospective nature of the data

collection, the standardization of BP measurements, the use of combined eGFR-UACR, confirmation after 3 months, and the multivariable assessment of risk factors. The results indicate that the routine screening of patients with hypertension is supported, especially for those with diabetes, long-standing hypertension or hypertension that are not controlled, obesity, or regular NSAID use, and for ages ≥ 60 years. Easy outpatient measures that include annual serum creatinine/eGFR and UACR, patient education, medication review, and referral based on the GFR-albuminuria risk categories might help with early diagnosis and lessen progression.

Conclusion

Nearly one-third of the hypertensive patients attending the general medicine OPD had CKD with majority of them being undiagnosed. Use of the albuminuria-based detection system made a significant contribution to case finding. Age, diabetes and long-standing hypertension, uncontrolled blood pressure, NSAID use and obesity were independent risk factors, thus suggesting screening of eGFR and UACR should be part of the routine care of the hypertensive patient.

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