

Medication Prescribing Pattern in Patients with Chronic Kidney Disease Attending Nephrology OPD in a Tertiary Care Hospital

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Received: 01-06-2026 / Revised: 15-07-2026 / Accepted: 21-08-2026

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Conflict of interest: Nil

Abstract

Background: Chronic Kidney Disease (CKD) represents a major global health burden often complicated by multiple co-morbidities requiring complex pharmacological management. Polypharmacy and altered pharmacokinetics predispose CKD patients to drug accumulation, adverse reactions, and drug interactions. This study aimed to assess the medication prescribing pattern, adherence to the World Health Organization (WHO) essential medicines list, and the prevalence of co-morbidities among CKD patients attending the nephrology outpatient department of a tertiary care hospital.

Methods: A descriptive observational study was conducted over an 18-month period at the Nephrology OPD of Government T D Medical College, Alappuzha. A total of 195 CKD patients aged 18–75 years who met the eligibility criteria were evaluated. Data on demographics, CKD staging (Cockcroft-Gault formula), co-morbidities, and prescribed drugs were gathered and analyzed using SPSS version 16. Drugs were classified according to the WHO Anatomical Therapeutic Chemical (ATC) system.

Results: Among 195 patients, 67.2% (n=131) were male and 32.8% (n=64) were female, with a mean age of 58.59±11.35 years. Most patients presented in Stage 5 (39.5%) and Stage 4 (33.3%) CKD. A total of 1,337 drugs were prescribed across 195 prescriptions, with a mean of 6.86±2.10 drugs per prescription (range: 2–14), highlighting prevalent polypharmacy. Only 42.7% (n=571) of prescribed drugs were from the WHO Model List of Essential Medicines. Based on ATC classification, cardiovascular system drugs were the most frequently prescribed (38.7%), followed by alimentary tract and metabolism agents (22.5%), and drugs acting on blood and blood-forming organs (21.9%). The oral route accounted for 91.3% of drug administrations. The most common co-morbidities were hypertension (87.7%), dyslipidemia (48.2%), and diabetes mellitus (46.2%).

Conclusion: Polypharmacy is common among CKD patients, particularly those in advanced stages with multiple co-morbidities. Cardiovascular agents constitute the predominant drug class prescribed. Rational drug selection, dose adjustments based on renal function, and adherence to essential medicine guidelines are imperative to minimize adverse drug events and improve patient outcomes.

Keywords: Chronic Kidney Disease, Prescription Pattern, Polypharmacy, ATC Classification, Essential Medicines.

DOI: 10.25258/ijcpr.18.9.170

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Introduction

Chronic Kidney Disease (CKD) is a major global health burden due to its high prevalence, associated risk of End-Stage Renal Disease (ESRD) and Cardio Vascular Disease (CVD).[1]

The Kidney Disease Outcomes Quality Initiative (KDOQI) of the National Kidney Foundation (NKF) define “CKD as either kidney damage or a decreased Glomerular Filtration Rate (GFR) of less than 60 mL/min/1.73 m² for at least 3 months”.[3] Co- morbidities of CKD include diabetes mellitus, hypertension, coronary artery disease, risk of infections and recurrent hospital admissions. Hence

polypharmacy or use of more than 5 drugs at a time is unavoidable.

These patients are at high risk for developing drug related problems due to the medically unstable nature of the disease.[4] Pharmacokinetics in renal compromised patients is altered and often results in drug accumulation and toxicity. Appropriate drug selection for patients is required in chronic kidney disease to avoid unwanted drug effects and to ensure the effectiveness of medication and to prevent drug induced nephrotoxicity.[5]

The Rational Use of Medicines (RUM) is defined as "Patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community.[6] Rational drug prescription is a difficult task in CKD patients because these patients need complex therapeutic regimens that require frequent monitoring and dose adjustments.

Prescription Pattern Monitoring Studies (PPMS) are drug utilization studies with main focus on prescribing, dispensing and administering of drugs. They promote appropriate use of drugs and prevents misuse of drugs. Prescription patterns explain the extent and profile of drug use, quality of drugs, and compliance with regional, state or national guidelines like standard treatment guidelines. It also explains the usage of drugs from essential medicine list and use of generic drugs.[7]

This study can illustrate the present day scenario of CKD patients and the prescribing trends of physicians in managing these patients with co-morbidities. It will provide an outline for management strategies and healthcare decision making.

CKD is classified into five stages on the basis of GFR: more than 90 mL/min per 1.73 m² (stage 1), 60–89 mL/min per 1.73 m² (stage 2), 30–59 mL/min per 1.73 m² (stage 3), 15–29 mL/min per 1.73 m² (stage 4), and less than 15 mL/min per 1.73 m² (stage 5).[8]

Early diagnosis and treatment of the underlying cause are imperative in patients with chronic kidney disease. The administration of multiple medications as well as poor compliance with drug regimens and drug interactions may contribute to drug-related problems.[9] According to the study conducted by Rama et al on assessment of drug-drug interactions among renal failure patients it was found that the frequency of Drug-Drug Interaction (DDI) in medications of CKD patients was 76.09%.[4]

If the patient is in CKD stage 3 or higher, certain drugs may tend to be insufficiently be eliminated by poorly functioning kidneys. This will lead to accumulation of drug in the body and cause toxic side effects. Hence the dose of drugs must be adjusted according to the patient's degree of renal insufficiency.[10] In a study by Murthy B V and V, hypertension was the most commonly associated co- morbidity seen in CKD patients. The drugs used were CCB's (Amlodipine, Nifedipine) 08.48%, and ACE 4.46%/ ARB's 2.67% (Enalapril and Telmisartan).[11]

According to a prospective study conducted by Chawla et al on assessment of drug utilization and quality of life in 100 patients with CKD, it was

found that most common anti-hypertensive group prescribed was diuretics (98% of patients). [12].

In the study by Murthy B V and V diabetes was the 2nd common co- morbidity with most of them suffering from type 2 diabetes. Oral Hypoglycemic Agents (OHAs) have been used in majority of patients and insulin in few patients. Use of Metformin was very less when compared to other OHA because it may cause lactic acidosis in renal failure patients. Fixed Drug Combination (FDC) and poly therapy by using at least two OHA's together or an Insulin and OHA's together were noted.[11]

In a cross sectional study conducted in India on drug utilization pattern in patients with CKD with special emphasis on antibiotics, it was found that the average number of drugs utilized per patients was 8.1 ± 3.2 . As per this study CKD patients are at higher risk of infections and had recurrent hospital admissions. Respiratory tract infections was the most common among infections. Urinary tract infections were more common in females. [13]

A prospective study was conducted by Al ramahi in Nephrology department of a Malaysian hospital on 600 CKD patients. The study was conducted in two phases with 300 patients in each phase. During the first phase, the patients were prescribed 2814 medication orders. There were 2981 medications during the second phase. The mean number of medications in the first and second phases was 9.38 ± 3.63 and 9.94 ± 3.78 respectively.[14]

A multicentre prospective cohort study of patients with moderate to advanced CKD (stages 3–5) conducted by Bailie et al in which 619 patients were recruited from four academic nephrology centres reported the mean number of medications prescribed per patient as 8 ± 4 . The proportion of patients prescribed with different classes of medications included erythropoietin (20%), intravenous iron (13%), HMGCoA reductase inhibitors (16%), ACEIs (44%), ARBs (13%), Beta blockers (46%), CCBs (52%) and Aspirin (37%). [15]

According to a retrospective study by Fasipe et al, which reviewed the medical case records of CKD patients the most common co-morbid conditions were hypertension (112 [91.10%]) and diabetes mellitus 45 (36.60%). A total of 1264 prescriptions were made, and the mean number of prescribed medications per patient was 10.28 ± 3.85 . [16]

According to a study by Kantanavar et al on prescription pattern in CKD patients done in 188 prescriptions it was found that hypertension was the most common co-morbidity (82%) observed, followed by anaemia (54.8%) and type 2 diabetes (43%). A total of 1436 drugs were prescribed to 188 CKD patients. Each patient received an

average of 7.6 drugs. Polypharmacy was seen in all patients. Drugs acting on the cardiovascular system constituted the bulk of the prescriptions (31%). Other important categories of drugs prescribed included antimicrobials (5.8%), antiplatelets and hypolipidaemic agents (5%), antidiabetic drugs (4.7%) and phosphate binders (4%).[17]

Previous studies shows that CKD patients suffer from multiple co-morbidities and are prescribed large number of medications. Hence pharmacotherapy of CKD is complex and inevitably requires poly pharmacy with frequent monitoring of drugs and their dosage adjustments.

Method

Study Design: Descriptive study.

Study Duration: Within 18 months of obtaining Ethics Committee approval.

Study Setting: Nephrology Department of Government T D Medical College Alappuzha.

Inclusion Criteria: Patients diagnosed with chronic kidney disease within age group of 18-75 years of both sex attending Nephrology OPD who gave consent for study.

Exclusion Criteria

Patients with malignancy and infections like HIV, HBsAg and HCV.

Patient planned for renal transplant and post renal transplant patients.

Pregnant ladies and breast feeding mothers.

Sample Size Calculation: All patients diagnosed with chronic kidney disease fulfilling the inclusion criterion attending Nephrology out Patient Department (OPD) during the study period were taken. Minimum sample size was determined by the formula $n = \frac{4pq}{d^2}$,

Where 'n' = sample size, p = prevalence, q= 100-p

According to a previous study prevalence of cardiovascular drugs used in CKD patients was 33.9%.[18]

Hence p taken as 33.9%. Applying in the formula

$$4 \times 33.9 \times (100-33.9)$$

$$6.78 \times 6.78 = 194.9 = 195 \text{ cases}$$

Study Variables

Independent variables:

- Age
- Sex
- Staging

The different stages of CKD form a continuum. The stages of CKD are classified as follows:

- Stage 1: Kidney damage with normal or increased GFR ($>90 \text{ mL/min/1.73 m}^2$)
- Stage 2: Mild reduction in GFR ($60-89 \text{ mL/min/1.73 m}^2$)
- Stage 3a: Moderate reduction in GFR ($45-59 \text{ mL/min/1.73 m}^2$)
- Stage 3b: Moderate reduction in GFR ($30-44 \text{ mL/min/1.73 m}^2$)
- Stage 4: Severe reduction in GFR ($15-29 \text{ mL/min/1.73 m}^2$)
- Stage 5: Kidney failure (GFR $<15 \text{ mL/min/1.73 m}^2$ on dialysis)

GFR was calculated using the Cockcroft-Gault formula [19]

$$\text{For Males, GFR} = \frac{(140 - \text{Age in years}) \times \text{Wt. in Kg}}{72 \times \text{Sr. Creatinine}}$$

$$\text{For Females, GFR} = \frac{(140 - \text{Age in years}) \times \text{Wt. in Kg} \times 0.85}{72 \times \text{Sr. Creatinine}}$$

$$72 \times \text{Sr. Creatinine}$$

Co-morbidities seen in CKD patients:

Determined based on patients having drugs for Hypertension, Diabetes mellitus, Coronary artery disease, Dyslipidaemia, Anaemia and Hyperuricemia.

Infections Seen in CKD Patients: Infections will be determined by evaluating blood routine and urine routine results.

Ethical Consideration: The study was initiated after getting clearance from the institutional research committee and institutional ethics committee. A prescriber's consent and written informed consent was sought from the study participants.

Study Procedure: Study was conducted in Nephrology OPD of Govt TD Medical College Alappuzha. After getting prescriber's consent and written informed consent from the patients, data was collected by interviewing and from patient's case record using pre structured proforma. Data collected include age, gender, weight, medical history, any co morbidities, various drugs prescribed, its strength, dose and route of administration. All prescribed drugs were classified into categories based on Anatomical Therapeutic Chemical (ATC) system main group recommended by the World Health Organization (WHO).[20] Medication prescribing pattern in terms of indication, average number of drugs prescribed per prescription, commonly prescribed class of drugs and antibiotics used was determined. Confidentiality of the information obtained was assured. Data obtained was analysed and conclusions drawn.

Data Entry and Statistical Analysis: The data of all chronic kidney disease patients was tabulated

using Microsoft excel and presented with the help of descriptive statistics using SPSS software version 16.

Results

This study was conducted over a period of 18 months. Within the study period 195 prescriptions of patients having chronic kidney disease were analysed for prescribing pattern in terms of indication, average number of drugs prescribed, classification and route of administration.

Sex distribution of CKD: Out of 195 CKD cases, 131 (67.2%) were males and 64(32.8%) were females.

Male to female ratio was 2.04: 1. Age of the patients included in the study was between 18-75years. According to the study mean age was 58.59 ± 11.354 years with minimum age being 20

years and maximum being 75year. Number of patients belonging to stage 5 CKD is 77(39.5%), stage 4 CKD is 65 (33.3%), stage 3B CKD is 28 (14.4%), stage 3A is 12 (6.2%), stage 2 is 11 (5.6%) and stage 1 CKD is 2 (1%).

Analysis of Drugs Prescribed in CKD: A total of 1337 drugs were prescribed in 195 prescriptions. Out of 1337 only 571 drugs (42.7%) were from the WHO essential drug list.^[21]

Distribution of drugs per prescription: Minimum number of drugs prescribed was 2 and maximum was 14 per prescription with mean 6.86 ± 2.101 drugs and median 7.

Distribution of drug according to ATC classification: 1337 drugs were classified based on ATC classification main group. Distribution of drugs in various classes is given below

Table 1: Distribution of drug according to ATC classification

ATC classification	Class	Number of drugs prescribed	Percentage of drugs prescribed
Alimentary tract and metabolism	A	301	22.50%
Blood and blood forming organs	B	293	21.90%
Cardiovascular system	C	517	38.70%
Dermatologicals	D	3	0.20%
Genitourinary system and sex hormones	G	31	2.30%
Systemic hormonal preparation(excluding sex hormones)	H	9	0.70%
Antiinfectives for systemic use	J	31	2.30%
Antineoplastic and immunomodulating agents	L	0	0.00%
Musculoskeletal system	M	73	5.50%
Nervous system	N	44	3.3%
Antiparasitic, insecticides and repellants	P	2	0.15%
Respiratory system	R	31	2.30%
Sensory organs	S	0	0.00%
Various	V	2	0.15%

Discussion

The present study was conducted in Nephrology OPD of Government T D Medical College during over the period of 18 months. Prescription of 195 patients diagnosed with CKD were assessed for prescription pattern and co-morbidities.

Out of 195 patients, 67.2% were males and 32.8% were females. Male to female ratio was 2.04: 1. This was higher than the results found in a prospective, cross-sectional observational study by Santra et al conducted in 185 CKD patients where in 108 (58%) were males and 77 (42%) were females with male to female ratio 1.4:1 [13] CKD was found to be more common in males in both the studies. The incidence of ESRD seems to be higher in men, indicating that the progression rate of renal disease may be faster in men than women.[22]

According to this study mean age was 58.59 ± 11.354 years. This can be compared with the results of the study conducted by Ahlawat et al where

mean age of the patients was 53.8 years and the study by Bajait et al where mean age was 51.40 ± 14.29 years.[18,23] In the study by Santra et al mean age of CKD patients was 45.81 ± 11.16 . [13] According to a study by Manley et al mean age of patients with CKD was reported as 60.2 ± 15.6 . [24]

In the present study 39.5% had stage 5 CKD and 33% had stage 4 CKD which is comparable to the study by Ahlawat et al where 42% had CKD stage 5 followed by CKD stage 4 with 22%. [18] A study by Adibe et al on 169 CKD patients, reported that more than half of the patients (56.2%) in their study were in CKD stage 4 or 5. [25]

High incidence in stage 5 and 4 CKD in these studies can be due to the fact that, they were conducted in Nephrology department and patients with CKD are referred to a nephrologist when there is progression to stage 4 and 5. Prevalence of large number of comorbidities in the later stages of CKD and regular dialysis in stage 5 CKD could be the

reasons for this finding.[17] On analyzing the drugs prescribed for all CKD patients included in this study, it was found that a total of 1337 drugs were prescribed to 195 patients. Mean number of drugs prescribed per prescription was 6.86 ± 2.101 with median 7. These results were comparable with the study by Ahlawat et al where in a total of 2,681 drugs were prescribed in 408 prescriptions and mean number of drugs per prescription was 6.57.[18] The study by Chakraborty et al on 'prescribing pattern of medicines in CKD patients on maintenance hemodialysis, reported a total of 1098 drugs prescribed for 100 patients. The median number of drugs per prescription was 10.[9] According to a study by Manley et al the mean number of drugs per prescription was 12.3 ± 5 with median 12. [24]

Minimum number of drugs per prescription was 2 ($n=1$) and maximum number of drugs per prescription was 14 drugs ($n=1$). 4 patients received 3 drugs each, 16 patients received 4 drugs each, 32 patients received 5 drugs each, 39 patients received 6 drugs each, 38 patients received 7 drugs each, 28 patients received 8 drugs each, 17 patients received 9 drugs each, 8 patients received 10 drugs each, 6 patients received 11 drugs each, 3 patients received 12 drugs each and 2 patients received 13 drugs each. In this study it was found that, patients with CKD stage 5 received more drugs compared to other stages.

All these results indicates polypharmacy. Polypharmacy has been defined as the use of 5 or more medications to one patient at a time. However, in view of the complex nature of CKD and coexisting co-morbidities, polypharmacy is inevitable in CKD patients.[9,23]

Out of 1337 drugs 571 drugs (42.7%) were from WHO essential drug list. Other studies which analysed this parameter were studies by Bajait et al and Devi et al. In the study by Bajait et al 41.53% of the prescribed drugs were from the WHO essential medicines list according.[23] According to Devi et al study percentage of drugs prescribed from WHO essential drug list was 53%.[26] The study by Ahlawat et al analysed the percentage of drugs from National List of Essential Medicine (NLEM) and reported as 19% of the drugs prescribed were from NLEM.[18]

In this study 1337 drugs prescribed were classified on the basis of ATC classification and it was found that drugs of the class cardiovascular system (38.7%) was most commonly prescribed followed by alimentary tract and metabolism (22.5%) class of drugs, drugs from blood and blood forming organs (21.9%) and musculoskeletal system (5.5%).

According to the study conducted by Ahlawat et al cardiovascular system (33.9%) drugs was the most commonly prescribed class followed by alimentary tract and metabolism (15.8%), musculoskeletal system (14.5%) and blood and blood forming organs (14.1%).[18] Comparing both these studies, cardiovascular system class of drugs were the most commonly prescribed drugs in CKD patients followed by alimentary tract and metabolism class of drug.

The study by Bajait et al reported percentage of drugs prescribed from alimentary tract and metabolism as 44.86% which was higher than the present study. In the same study percentage of drugs prescribed from cardiovascular system (22.05%) was lower compared to present study. Drug prescribed for treatment of disorders of blood and blood forming organs (21.38%) was similar to the present study.[23]

In this study, use of antimicrobial agents contributes to 2.6% of total drugs prescribed which is comparable to the study by Ahlawat et al (2.2%) but less than the study by Chakraborty et al (10.93%) . In this study FDCs (0.7%) were the commonly prescribed antimicrobial agents followed by Macrolides (0.5%) and Cephalosporins (0.4%) and Fluroquinolones (0.4%). Antifungals and Anthelmintics accounts for 0.2% and 0.15% respectively. In the study by Chakraborty et al antibiotics used include Ceftriaxone (1.91%) Cefoperazone (1.73%) and Levofloxacin (1.55%). [9,18]

In this study, 91.32% of drugs were given orally. Drugs prescribed by subcutaneous and intravenous route were 5.92% and 1.65% respectively 1.12% were given topically. In a study by Kantanavar et al, of the 1436 drugs prescribed, 1204 drugs (83.8%) were administered by oral route, 44 drugs (3.1%) by intravenous route, 42 drugs (2.9%) by intramuscular route and 146 drugs (10.2%) by subcutaneous route.[17] In the study by Ahlawat et al drugs prescribed parenterally were 11%.[18] Hence the commonest route of administration was oral. According to the present study, 87.7% of patients had hypertension followed by dyslipidaemia (48.2%), diabetes mellitus (46.2%), hyperuricemia (33.8%), coronary artery disease (31.8%), anaemia (12.3%) and hypothyroidism (3.6%). In the study by Santra et al 95% were hypertensives, 87% were diabetic, 86% were anaemic. Dyslipidaemia was associated with 83% of the patients and 52% had hypothyroidism.[13] In the study conducted by Ahlawat et al 55% of patients were found to have hypertension followed by anaemia (46%), diabetes (40%), dyslipidaemia (36%), coronary artery disease (10%) and hypothyroidism (7%).[18]

In both these studies quoted incidence of hypertension is more compared to other co morbidities which is consistent with present study.

In the present study, 14.3% had infections of which 6.2% had urinary tract infections, 4.6% had respiratory tract infections and 2.5% had skin infections and 1% had gastrointestinal tract infections. In the study by Santra et al 58% of patients were suffering from infections of which 37% patients had respiratory tract infection and 34% had urinary tract infections. High incidence of infections in the study conducted by Sandra et al can be because their study was concentrated on drug utilization pattern in patients with chronic kidney disease with emphasis on antibiotics.[13]

This study identifies the prescription pattern of patients diagnosed with chronic kidney disease and co-morbidities associated with the disease. The results obtained were comparable to previous studies with respect to male female ratio, stages of CKD, prescription pattern and co- morbidities. According to this study, prescribing pattern depends upon the stage of CKD and co-morbidities associated with the disease.

Conclusion

The present study was undertaken to find out the medication prescribing pattern in terms of indication, average number of drugs prescribed, classification and route of administration in patients with chronic kidney disease. This study also enlightens us about the common co morbidities associated with CKD.

- 195 prescriptions fulfilling the inclusion criteria were studied over a period of 18 months.
- CKD was found to be more common in males 67.2% (n=131) than in females 32.8% (n=64).
- Mean age of the patients in this study was 58.59±11.354.
- Of the 195 cases 39.5% (n=77) were in CKD stage 5, 33.3% (n= 65) were in CKD stage 4, 14.4% (n=28) were in CKD stage 3B, 6.2% (n=12) were in CKD stage 3A, 5.6% (n=11) were in CKD stage 2 and 1% (n=2) were in CKD stage 1
- A total of 1337 drugs were prescribed in 195 prescriptions with mean number of drugs prescription being 6.86± 2.101.
- Patients with CKD stage 5 received more drugs compared to other stages.
- 571 drugs (42.7%) were from WHO essential drug list.
- Drugs were classified on the basis of ATC classification and it was found that drugs belonging to cardiovascular system (n=517, 38.7%) were most commonly prescribed in this study. Drugs falling in Alimentary tract and

metabolism class (n=301, 22.5%) and blood and blood forming organs class (n= 293, 21.9%) were the next commonly prescribed drugs.

- Most common route of administration was oral route (n=1221), followed by subcutaneous (n=79) and intravenous (n=22). 15 drugs were given topically.
- Co - morbidities associated with CKD were hypertension in 87.7% (n=171), dyslipidaemia in 48.2% (n=94), diabetes mellitus in 46.2% (n=90), hyperuricemia in 33.8% (n=66), coronary artery disease in 31.8% (n=62), anaemia in 12.3% (n=24) and hypothyroidism in 3.6% (n=7) .
- Common infections associated with CKD are urinary tract infection (n=12), respiratory tract infection (n= 9), skin infections (n=5) and gastro intestinal tract infections (n=2).

To conclude, this study analysed the wide variety of drugs prescribed for patients with CKD. The number of medications significantly increases with declining kidney function and associated co-morbidities. The prescription of multiple drugs reflect the severity or multiplicity of co- morbid conditions. Hence rational drug prescription is required in CKD patients to avoid drug interaction and adverse effects.

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