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Original Article

# Drug Utilization Pattern in Chronic Kidney Disease Associated Comorbidities at a Tertiary Care Hospital

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## ABSTRACT

**Background:** Patients with Chronic Kidney Disease (CKD) with multiple Comorbidities like Hypertension, Diabetes, and Anemia require Numerous Drugs. Multiple drugs Predispose to Potential drug-drug Interactions, which increase hospital stay, health care expenses, and ultimately morbidity and mortality. So, we aim to study the drug utilization pattern in CKD-associated comorbidities at a tertiary care hospital. **Materials and Methods:** A Hospital-Based Observational and Cross-Sectional study was conducted among patients with CKD-associated comorbidities enrolling IPD, OPD, and medicine ward patients for one year. The data collection form noted details like Socio-Demographic and clinical characteristics, past medication history, Comorbidities, and current medications. Drugs were categorized according to the Food and Drug Administration (FDA) and rationality score per the World Health Organization (WHO). **Results:** A total of 100 patients were analyzed. The mean age of the patients was 55.8, out of which 69% as male maximum patients belong to stage 5 72%. Hypertension was the most prevalent comorbidity followed by diabetes and calcium channel blockers (33.3%), insulin (soluble) 33.8% and erythropoietin (51%) were the most frequently prescribed drugs for the treatment of hypertension, diabetes, and Anemia, respectively. Mainly prescribed antibiotics belong to the Beta-Lactamase (26.6%) Penicillin Class. **Conclusion:** This study's results showed that CKD was more prevalent in males and that the highest number of patients had end-stage renal disease. CKD patients are concomitantly affected by hypertension, diabetes, CVD, and Anemia. Calcium channel blockers, Insulin, and Erythropoietin were the most frequently prescribed drugs.

**Keywords:** Drug utilization pattern, Chronic Kidney Disease, Hypertension, Diabetes, Anemia, Comorbidities.

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## INTRODUCTION

A drug utilization study is defined as "the marketing, distribution, prescription, and utilization of drugs in the society with special emphasis on the resulting medical, social, and economic consequences". It has the main aim of facilitating the rational use of drugs.[1] Treatment pattern changes with disease situation, duration, and environment, which increases the need to observe drug utilization for a more extended period. The importance of drug use patterns is understood and supported by studies on drug use in CKD patients. CKD patients usually have other comorbidities and require Lifelong Medicines, which makes it very important to study the drug utilization pattern regularly.[2]

CKD is a common cause of death in persons who have comorbidities like hypertension, diabetes, and cardiovascular disease (CVD) that have been linked to poor clinical outcomes and make the condition worse and urgent to make a drug regimen for a better quality of life.[3] Another Frequent Consequence in CKD Patients is Diabetic Nephropathy, which raises the risk of Cardiovascular Disease.[4] Anemia is also a Perennial and severe complication of CKD which intensifies as the Kidney Deteriorates.[5] Understanding which drugs can be taken safely and how renal disease affects medication Metabolism is essential for Glycemic management in CKD patients.[6] A variety of symptoms including Decreased Appetite, High Blood Pressure, Frequent Urination, a Metallic Taste in the Mouth, Weight loss, pruritus, diminished mental acuity, swelling in the feet and ankles, and shortness of breath can be seen over time as dysfunction of kidney develops gradually.[7]

As many drugs are used to treat the underlying illness and any related consequences of CKD patients, many pharmaceutical interactions may happen, which also raises the risk of drug-drug interactions, drug adherence, and polypharmacy.[8] CKD patients have such a complex condition Polypharmacy the use of numerous medications- is prevalent among them. However, polypharmacy

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raises the chance of medication mistakes, Non-Adherence, and Drug issues, making it crucial to study prescribing trends and drug utilization patterns for their safety and Betterment.[9]

Understanding medication use patterns and prescribing trends in CKD patients is essential for Therapy Optimization, improving patient safety, and enhancing overall results. We aim to study the Drug utilization pattern in Chronic Kidney Disease-associated complications at a tertiary care hospital.[10]

## MATERIALS AND METHODS

The present study was a prospective and observational study conducted in a tertiary care teaching hospital. One hundred patients were Analyzed from the inpatient and outpatient departments in the Nephrology and medicine ward one year after the approval from the Institutional Ethics Committee (IEC No.2131). The patients were diagnosed according to our Inclusion/Exclusion Criteria. CKD patients of age above 18 years with comorbidities, i.e., Hypertension, Diabetes, Anemia, Bone and Mineral Deficiency, and Cardiovascular Disease Belonging to stages III, IV, or V, were included in the study. Pregnant and Lactating Women were excluded from the study if the Patients had any Surgical condition like a Kidney stone, Tumor, or Trauma. Patients were also excluded from the Study if they were unwilling to participate. A data collection form was used to collect the patient's Demographic Details (Age, Gender, and Social History), Chief Complaints, Co-Morbid Conditions, laboratory investigations, and prescribing patterns of drugs. The Glomerular Filtration Rate (GFR) was calculated with the help of the CKD-EPI equation.[11] To study the prescribing pattern, different Parameters were included in the data collection form like Drug name, Dosage, Route, Duration of the Treatment, Brand/Generic, and category of the medication according to Food and Drug Administration and rationality score as per the World Health Organization.

### Statistical Analysis

Data were presented as Mean±Standard Deviation. The distribution of various drugs across the CKD stages or in other subcategories is descriptive and presented as a number (percentage). Statistical analysis was performed using Graph pad Prism Version 6.0 (Graph pad Prism, San Diego, CA, USA).

## RESULTS

Demographic, Social, and Clinical Characteristics of Chronic Kidney Disease patients are shown in Table 1. The mean age of the Cohort participants was 55.8 years, and 69% were Male. Most of the CKD patients were 51–60 years old (43%), followed by (26%) in the age group 41-50 years. The median stay in the hospital was

**Table 1: Demographic, Social and Clinical Characteristics of Chronic Kidney Disease Patients.**

| Patient characteristics | CKD patients (*n*=100) | Missing data |
|---|---|---|
| Socio-economic factors | | |
| Male gender | 69 | -- |
| Age (Years). | 55.8 | -- |
| Education | | 18 |
| Uneducated | 25 | -- |
| Below high school | 16 | -- |
| Completed school | 34 | -- |
| College and above | 7 | -- |
| Rural residence | 58 | 12 |
| Hypertension | 78 | -- |
| Type 2 diabetes | 68 | -- |
| Cardiovascular disease | 14 | -- |
| Anaemia | 11 | -- |
| Tobacco use | 32 | 15 |
| BMI, (kg/m2) | 21.4 (21.6-27.4) | -- |
| Systolic blood pressure (mm Hg) | 130(19) | -- |
| Diastolic blood pressure (mm Hg) | 80(15) | -- |
| eGFR, mL/min/1.73m2 | <15(72) | -- |

BMI- body mass index; CKD- chronic kidney disease; eGFR- estimated glomerular filtration rate.

six days (Table 1). Most were either uneducated (25%) or had completed primary education (34%) but not graduated. 58% of patients had a Rural Background (Table 1). The study Cohort included 72% of patients in stage 5.18% in stage 4.3% in stage 3A and 7% in stage 3. Hypertension was the most commonly associated comorbidities, reported by 78% of participants. This was followed by diabetes (68%), cardiovascular disease (14%) anemia (11%).

The Concomitant Illness in CKD Patients is summarized in Table 2. Out of 100 CKD patients, Hypertension with Type 2 Diabetes Mellitus (T2DM) was more prevalent (40%), followed by patients suffering from CKD with Hypertension (HTN) (21%) and patients having CKD with T2DM (17%) (Table 2).

## Antihypertensive Treatment

Among the anti-hypertensive agents in the study, 17 different drugs were prescribed for the management of hypertension which belongs to 10 different categories. 59 patients were prescribed Calcium Channel Blockers (CCB), 46 with Diuretics, and 34 with Alpha-Blockers. Some of the patients were prescribed central Alpha-2 Agonists and a Combination of Alpha with Beta-Blockers. Angiotensin-Converting Enzyme (ACE) Inhibitors and Angiotensin Receptor Blockers (ARBs) were the least used. Combinations like ARBs with Diuretics and Diuretics with Angiotensin Type 2 (AT2) Receptor Blockers with Calcium Channel Blockers (CCBs) were also prescribed (Table 3).

## Anti-diabetic Medications

According to our prescription analysis, seven different classes of hypoglycaemic drugs were prescribed to patients with

**Table 2: Categorization based on complications.**

| Complications | No. of patient | Percentage |
|---|---|---|
| HTN + T2DM | 40 | 40% |
| HTN | 21 | 21% |
| $T_2DM$ | 17 | 17% |
| CVD + HTN | 5 | 5% |
| HTN + CVD + T2DM | 5 | 5% |
| Anaemia | 3 | 3% |
| HTN + Anemia | 2 | 2% |
| Anaemia + T2DM + CVD + HTN | 2 | 2% |
| HTN+T2Dm+Anemia | 2 | 2% |
| T2DM+CVD | 1 | 1% |
| HTN +Anemia + CVD | 1 | 1% |
| Anemia +T2DM | 1 | 1% |

HTN- hypertension; T2DM- Type 2 diabetes, CVD- cardiovascular disease.

**Table 3: Distribution of antihypertensive drugs in CKD patients.**

| Medication for Hypertension | No. of Patients | Salts |
|---|---|---|
| ACE Inhibitors | 1 | Ramipril |
| ARBs | 1 | Telmisartan |
| CCBs | 59 | Amlodipine, Cilnidipine, Nifedipine, Diltiazem |
| Beta Blockers | 20 | Atenolol, Metoprolol, Labetalol |
| Alpha Blockers | 34 | Prazosin |
| Diuretics | 46 | Metolazone, Furosemide, Torsemide |
| Central alpha 2 agonist | 9 | Clonidine, Moxonidine |
| Alpha + Beta blocker | 5 | Carvedilol |
| ARBs + Diuretics | 1 | Telmisartan+Hydrochlorothiazide |
| Diuretics+AT2 Receptor blocker + CCBs | 1 | Chlorthalidone+Telmisartan+Amlodipine |

diabetes with CKD. Short-acting insulin was mostly prescribed to 21 patients. Followed by long-acting insulin, and dipeptidyl peptidase IV (DPP-4) inhibitors were prescribed to 16 patients each. A total of 7 patients were prescribed intermediate-acting insulin, and a few patients were prescribed biguanide (Table 4).

### Anaemia treatment

A total of 11 different medications with different combinations were prescribed for the treatment of Anemia. Maximum patients i.e., 28, were administered with inj. Erythropoietin. Cap multivitamin with iron and inj. folic acid to 7 patients each. A few patients were prescribed ferric carboxy maltase. Iron sucrose, folic acid with iron with vit B12, Tab. Erythropoietin, Tab. Folic acid with Iron, Tab. Folic acid with methylcobalamin with pyridoxine hydrochloride, Darbepoetin-α, methylcobalamin (Table 5).

### Other treatment

A total of 38 different antibiotics were prescribed to the patients. Out of which, 25 patients were treated with beta-lactamase like aztreonam, Feropanem and 20 were specified with glycopeptide like Vancomycin HCl, teicoplanin, and Cephalosporin like ceftriaxone, cefuroxime axetil. Many were prescribed semisynthetic penicillin, like amoxicillin and cephalosporin plus beta-lactamase. Some other antibiotics like Clindamycin, Amikacin, Levofloxacin, etc., were also prescribed to the patient. Patients with bone and mineral disorders (51%) were prescribed medications like calcium carbonate with vitamin D3 (70%), Inj. Calcium gluconate (14%) and Tab. Folic Acid with Calcium Citrate Malate with Vitamin D 3 (12%). And a few were prescribed with Tab. Cholecalciferol.

## DISCUSSION

In this current Cohort study, we have analyzed the drug utilization pattern in Chronic Kidney Disease patients with comorbidities at a tertiary care hospital. In the present study, most patients were male (69%), and the mean age was 55.8 years. Our study results were similar to previous published research in CKD patients.[12] Male patients have a high risk of developing CKD because of increased Weight, Waist-Hip Ratio, and Increased Blood Pressure, making them more prone to develop CKD over time (Pounds *et al.*, 2013, Goldberg and Krause, 2016).[13,14]

In this CKD patients' study, a maximum number of patients had stage 5 CKD (72%). These findings were similar to previous studies by Devi *et al.* 2008 (93%) and AI-Ramahi *et al.*, 2012 (88%).[12,2] However, a study by Bajait *et al.*, 2014 has shown 42% of patients with end-stage renal disease (Stage-5).[15] The variation in the prevalence might be the difference in the stages of CKD in inclusion/exclusion criteria. In our study, we have also analyzed the co-morbidities condition with CKD patients. Hypertension was more prevalent (78%) followed by diabetes (68%), CV disease (14%), and anaemia (11%). CKD can Worsen Hypertension due to Increased Vascular Resistance and Volume Expansion.[16] various treatment guidelines have been published to manage blood pressure to Slow Down Kidney Disease and its consequences. All Antihypertensive Drugs mainly prescribed were CCB, followed by Diuretics, Alpha-Blockers, Beta-Blockers, and other drugs.

**Table 4: Distribution of hypoglycaemic drugs in CKD patients.**

| Hypoglycaemic drug | No. of Patient | Salts |
|---|---|---|
| Short-acting insulin | 21 | Insulin |
| Intermediate-acting insulin | 7 | Soluble insulin+ Isophane insulin, Isophane insulin |
| Long-acting insulin | 16 | Insulin glargine |
| DPP-4 inhibitors | 16 | Teneligliptin, Linagliptin |
| Biguanide | 2 | Metformin |

DPP – Dipeptidyl Peptidase.

**Table 5: Distribution of drugs for anemia in CKD patients.**

| Medication for Anaemia | No. of Patient |
|---|---|
| Inj. Erythropoietin | 28 |
| Inj. Folic acid | 7 |
| Cap. Multivitamin + Iron | 7 |
| Inj. Ferric Carboxy Maltase | 3 |
| Tab. Erythropoietin | 2 |
| Tab. Folic acid + Iron | 2 |

Inj- injection, Cap- capsule, Tab- Tablet.

In our study, diabetes was the 2nd most common (17%) Co-Morbidity in CKD patients. Most of the diabetic patients were treated with Inj. Insulin (70%) was followed by DPP-4 inhibitors (16%), and Biguanide was prescribed to only two patients. The result of our study was almost similar to Bajait *et al.*, 2014 study where 63% of patients were prescribed Insulin.[12] Use of metformin is Significantly less when compared to another oral Hypoglycemic agent because it may cause lactic acidosis in renal failure patients.[17]

Anaemia is another complication seen among patients (11%) due to reduced erythropoietin secretion.[16] For Anaemic patients with CKD were treated with inj. Erythropoietin (51%), followed by multivitamin with iron and folic acid (13%). The treatment pattern was similar to a previous study on CKD i.e., 69%. In contrast, in a recent study conducted by Ahlawat *et al.* 2016 and in a study by Al-Ramahi *et al.*, 2012 hematopoietic agent was reported as prescribed.[18] The reason behind the underuse of Hematopoietic agents was high cost and low patient compliance. Other drugs were Calcium Carbonate with Vitamin D 3 (70.5%), the most prescribed drug for Bone and Mineral Disorders.[19] Infections in CKD patients are Widespread. Therefore, most Antibiotics have been Prescribed to all CKD patients. Most prescribed antibiotics belong to the Beta-Lactamase (26.6%) class of Penicillin.[20]

## CONCLUSION

Our study results highlight that CKD was more prone in males and the maximum number of patients had End-Stage Renal Disease. We also observed that patients with CKD with Co-Morbid complications like Hypertension, Diabetes, CVD, and Anemia. A pattern of Drug usage was determined, and it was concluded that the most Prescribed Drug for Hypertension was Calcium Channel Blockers and Diuretics, for Diabetes Treatment, Insulin injection and use of DPP-4 inhibitors; for Anemia Treatment, Erythropoietin and for Bone and Mineral Disorder was treated with Calcium Supplement with Vitamin-D. Patients with CKD admitted to the hospital are primarily treated with the Beta-Lactamase class of Penicillin. Counseling on necessary lifestyle changes and early-stage education about the Disease, its complications, and management helps lower the occurrence of these Illnesses and Reduces the Cost, mortality, and Morbidity.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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