

AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: http://www.ajptr.com/

A Prospective Observational Study On Prescribing Patterns Of Drugs Used In Chronic Kidney Disease Management At Secondary Care Hospital

SK. Farahan Subahan^{1,2}, J.N. Suresh Kumar³, M. Bhavani¹, G. Anitha¹, G. Vyshnavi¹, P. Sirisha¹

1.Department of Pharmacy Practice, Narasaraopeta Institute of Pharmaceutical Sciences, Narasaraopet, Palnadu (Dt), Andhra Pradesh, India-522601.

2.Research Scholar, Faculty of Pharmacy, Bharath Institute of Higher education and Research, Chennai-600073

3. Department of Pharmaceutics, Narasaraopeta Institute of Pharmaceutical Sciences, Narasaraopet, Palnadu (Dt), Andhra Pradesh, India-522601.

ABSTRACT

One significant systemic ailment is chronic renal disease. Co-morbid illnesses combined with declining renal function cause patients to take more than one medication. Choosing the right medications is essential to preventing side effects. This study has a prospective observational design in which all patients with chronic kidney disease (CKD) are included in the analysis. Relevant data was acquired through the use of patient data collection forms, which were filled out and examined. In this study, 120 patients who had prescriptions for medications were reviewed prospectively; of these, 76 (63.33%) were men and 44 (36.66%) were women. According to demographic data, men are more likely to develop CKD. According to demographic information, patients between the ages of 41 and 60 were found to be high in 62 middle-aged individuals (51.66%) and low in young adults (7.83%) in the 19–30 age group. Anti-hypertensive medications were the most commonly prescribed class of pharmaceuticals, followed by cardiovascular, hematinic, and anti-diabetic medications. A total of 1.16% of prescriptions were written under their generic names. 10.96% of prescriptions included an injectable products. Antibiotic prescriptions made up 54.16% of all prescriptions. Ninety-three percent of the medications prescribed came from the WHO Essential medicines list. The study shows that the prescription of brand-name medications was frequently noticed using WHO core indicators, which were used to monitor the drug prescribing trend. This study concludes that CKD patients were more likely to be treated with diuretics, antihypertensives, oral hypoglycemic medications, and hematinic agents. CKD, prescribing patterns, antihyperetensives, hypoglycemic, prevalence, Keywords:

Polypharmacy.

*Corresponding Author Email: pidugurallasirisha9@gmail.com Received 05 May 2024, Accepted 02 June 2024

Please cite this article as: Sirisha P *et al.*, A Prospective Observational Study On Prescribing Patterns Of Drugs Used In Chronic Kidney Disease Management At Secondary Care Hospital. American Journal of PharmTech Research 2024.

INTRODUCTION

Chronic kidney disease (CKD) is characterized by structural or functional abnormalities of the kidney that have persisted for three months or more and have a negative impact on health. The Centers for Disease Control and Prevention (CDC) 2021 predicts that the prevalence of chronic kidney disease (CKD) is higher in individuals 65 years of age or older (38%) compared to those 45–64 years (12%) and 18–44 years (6%). Men are slightly more likely than women (12%) to have CKD (14%). An estimated 37 million persons in the US, or more than one in seven, have chronic kidney disease [1].

End-stage renal disease can result from a number of causes. While some illnesses affect more immediately, others cause kidney damage over time. Diabetes, hypertension, polycystic kidney disease, renal vascular disease, renal artery stenosis (RAS), lithium nephropathy, analgesic nephropathy, and glomerular disorders, including glomerulonephritis and glomerulosclerosis [2].

Kidney failure may result from certain kidney-related disorders that are risk factors for chronic kidney disease (CKD). Obesity, Diabetes, and Glomerulonephritis heart-related conditions, renal cancer, acute renal injury, smoking, polycystic kidney disease, autoimmune illness [3].

If kidney damage advances slowly, signs and symptoms of chronic renal disease appear gradually. Changes in urination, swelling, fatigue, skin rash/itching, metallic taste in mouth/ammonia, breath, nausea, vomiting, shortness of breath, and feeling cold can all result from renal failure, depending on how bad it is [4].

Numerous consequences, such as metabolic acidosis, pulmonary edema, anemia, uremic encephalopathy, cardiovascular illness, hyperkalemia, and bone-mineral disorders, are linked to the reduction in kidney function [5].

Need of the study

The World Health Organization (WHO) estimates that 5–10 million people worldwide lose their lives to renal disease each year as a result of improper prescription and dispensing practices for more than half the available medications [6].

A global public health concern, chronic kidney disease is marked by rising incidence, prevalence, and unfavorable consequences. Drug utilization studies that provide information on prescribing, dispensing, and administering medications are known as prescription pattern studies.

Prescription pattern studies' primary goal is to encourage the public's responsible use of medications. Patients with chronic kidney disease (CKD) are prescribed several kinds of medicines for different co-morbidities [7].

As a result of decreased kidney function brought on by chronic renal disease, medicines accumulate and drug-related issues progress more quickly. The right medication must be chosen to minimize side effects and to provide the best possible outcomes for the patient. This calls for regular monitoring and dosage adjustments [8-9].

The purpose of the study is to identify prescription trends for patients with CKD, make recommendations for strategies to encourage drug use, reduce prescription errors, and enhance treatment outcomes.

Expected outcome of the study

After analyzing the cases the outcome we expected is to increase appropriate dosing and frequency of drugs used in CKD to reduce drug interactions to improve therapeutic outcome to promote rational use of drugs.

MATERIALS AND METHOD

Study Design: A prospective observational study.

Study Site: This study was carried out at the secondary care facilities in Narasaraopet, including Kosuru Kidney and Skin Care Hospital. Most of the patients that come to these facilities are from the Narasaraopet area.

Study Period: The investigation was carried out for six months.

Sample Size: 120 patients from the Department of Nephrology's inpatient and outpatient clinics who met the study's inclusion and exclusion requirements were chosen.

Study Criteria: The following criteria will be taken into consideration when conducting the study: 1. Criteria for inclusion; 2. Criteria for exclusion

Inclusion Criteria:

- 1. The age range of 20 to 80 years old was covered.
- 2. Both the inpatient and outpatient departments are included in the study.
- 3. Patients with CKD who are open to taking part.
- 4. Patients undergoing hemodialysis [10-15].

Exclusion Criteria:

1. Patients who were younger than 20 or older than 80 years old were not accepted.

2. Breastfeeding and pregnant women were not included.

Ethical Clearance:

The Narasaraopet Institute of Pharmaceutical Sciences' Institutional Ethics Committee gave its approval to this investigation (IEC-NIPS/PPP/2022-23/002).

Source of Data:

Every day, information from the patient's medical records and other relevant sources was documented, along with data on their demographics, clinical status, prescribed medications, and other pertinent and essential information. Data collection and analysis: Patient medical records are consulted to get structured data collecting forms containing information on the patient's demographics (age, sex, gender, etc.), cause for admission, medical history, medication history, prescribed medications, their dosage, and frequency of administration. The results are analysed by using appropriate tools.

Study Procedure:

After prior genuine approval from authorized research authorities of the institution and approval from Ethical committee, study was conducted maintaining a strict confidentiality about patient information (Ref No: IEC-NIPS/PPP/2022-23/002). Every day, all of the patients who were hospitalized to the nephrology department were examined in order to evaluate their drug usage using WHO indicators.

Based on the inclusion and exclusion criteria, patients are enrolled. The study was disclosed to the subjects who were part of the current investigation. Prior to the subjects' involvement in the study, their consent was obtained. An appropriate patient data collection form was created to gather all pertinent and required data. By looking over the case files, treatment charts, and patient interviews, particular information on each patient was gathered, including age, gender, diagnosis, recommended treatment (including dosage form, ROA, frequency), drug interactions, and other pertinent information. Every patient who was enrolled in the study received a personal visit in order to gather any additional data. Their prescriptions and the treatment plan were compared.

RESULTS AND DISCUSSION

Demographic details as per ICH classification:

When the demographic information for CKD patients (n=120) was examined based on the ICH classification, 7 (5.83%) of them were young adults, followed by 16 (13.33%) adults, 62 (51.66%) middle-aged adults, and 35 (29.16%) elderly adults.

According to the demographic information below, patients between the ages of 41 and 60 were found to be high, with 62 (51.66%) middle-aged adults, while those over 60 were found to be 35 (29.16%) old adults. The same was presented in Figure 1.



Figure 1: Demographic details as per ICH classification

Distribution based on gender:

A total of 120 sample population members were included and reviewed, as indicated by the sample distribution based on gender as indicated below. Of them, 36.66% (n=44) were women and 63.33% (n=76) were men. According to demographic statistics, men were more likely to have CKD. The data was represented in Figure 2 [11].





Staging of CKD patients based on GFR:

The staging of CKD patients according to GFR rate is displayed below. Nine (7.5%) were in stage 3, 23 (19.16%) were in stage 4, and 87 (72.5%) were in stage 5. Of them, 1 (2.5%) was in stage 2. Stage 5 patients were more numerous than stage 4 patients based on GFR. The data was presented in Figure 3 [12].



Figure 3: Staging of CKD patients based on GFR

Comorbidities Associated with CKD:

Following hypertension with diabetes mellitus 39(32.5%), hypertension + diabetes mellitus + hypothyroidism 5(4.16%), hypertension + hypothyroidism 3(2.5%), and hypertension + diabetes mellitus + cardiovascular disease 3(2.5%), the most common co-morbidity associated with patients with chronic kidney disease (CKD) was hypertension 66(55%). The data was presented as Figure 4 [13-14].



Figure 4: Distribution based on Co-morbidities

Pattern of anti-hypertensive agents:

The antihypertensive medication regimen among CKD patients, Of the 120 study participants, 41 underwent monotherapy, followed by 34 receiving dual drug therapy, 21 receiving triple drug therapy, 5 receiving quadruple drug therapy, 3 receiving five drug therapy, and 1 receiving six drug therapy, according to the report.

As indicated below (Table 1), in monotherapy, the most frequently prescribed class of medications is diuretics 28 (23.3%), whereas in two-drug therapy, the least frequently prescribed class is ACE Inhibitors 1 (0.83%) [15].

Anti-Hypertensive Agents	Number of	Percentag
	Patients	e (%)
MONOTHERAPY		
Beta Blockers	5	4.16
CCBs	4	3.33
Diuretics	28	23.3
Vasodilators	1	0.83
Alpha Antagonists	3	2.5
DUAL DRUG THERAPY		
ACE + Diuretic	1	0.83
Alpha Antagonist + CCB	1	0.83
Alpha Antagonist + Diuretic	7	5.83
ARB + Beta Blocker	1	0.83
Beta Blocker + CCB	1	0.83
Beta Blocker + Vasodilator	1	0.83
Beta Blocker + Diuretic	2	1.66
CCB + Diuretic	17	14.16
Diuretic + Vasodilator	3	2.5
TRIPLE DRUG THERAPY		
Alpha Agonist + Diuretic + Vasodilator	2	1.66
Alpha Antagonist + ARB + Diuretic	1	0.83
Alpha Antagonist + Beta Blocker + CCB	2	1.66
Alpha Antagonist + Beta Blocker + Diuretic	3	2.5
Alpha Antagonist + Beta Blocker + Vasodilator	1	0.83
Alpha Antagonist + Diuretic + CCB	3	2.5
ARB + CCB + Diuretic	1	0.83
ARB + CCB + Vasodilator	1	0.83
Beta Blocker + CCB + Diuretic	4	3.33
Beta Blocker + CCB + Vasodilator	1	0.83
Beta Blocker + Diuretic + Vasodilator	1	0.83
Alpha Antagonist + Diuretic + Vasodilator	1	0.83
QUADRUPLE DRUG THERAPY		
Alpha Antagonist + CCB + Diuretic + Vasodilator	1	0.83
ARB + Beta Blocker + Diuretic + Vasodilator	1	0.83
Beta Blocker + CCB + Diuretic + Vasodilator	3	0.83
FIVE DRUG THERAPY		
Alpha Agonist + Alpha Antagonist + Beta blocker + Diuretic +	1	0.83
Vasodilator		
Alpha Agonist + Alpha Antagonist + CCB + Diuretic + Vasodilator	1	0.83
Alpha Antagonist + ACE + ARB + CCB + Diuretic	1	0.83
SIX DRUG THERAPY		
Alpha Agonist + Alpha Antagonist + Beta Blocker + CCB +	1	0.83
Diuretic + Vasodilator		

Table 1:	Pattern	of A	Anti-Hy	pertensi	ive Agents
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Pattern of cardiovascular agents:

Among the 120 individuals in the sample with chronic kidney disease, 7 underwent monotherapy, 14 underwent dual medication therapy, and 2 underwent triple medication therapy. The information shows that among CKD patients listed in the table, dual medication therapy that is, anti-platelet + anti-hyperlipidaemics was most frequently recommended. Data was shown in Figure 5.



Figure 5: Pattern of Cardiovascular Agents

Pattern of anti-diabetic agents:

The use of anti-diabetic medications in CKD patients' patterns, fifteen individuals in the sample population of 120 underwent monotherapy, five underwent dual medication therapy, and one underwent quadruple drug therapy. In monotherapy, the most often prescribed class of medications was Sulfonyl Urea 6 (5%), followed by 4 (3.33%). Data was presented in Figure 6.



Figure 6: Pattern of Anti-Diabetic Agents

Pattern of hematinic agents:

The pattern of hematinic agents: 120 patients received prescriptions for 39 different hematinic drugs. Among the CKD patients listed below, iron supplements were the most often given medication, accounting for 35 (29.16%) of prescriptions in monotherapy and 3 (2.5%) in combined drug therapy (iron supplements with erythropoietin stimulating agents). The data shown in Figure 7.





Pattern of gastric acid suppressing & anti emetic agents:

The distribution of gastric acid suppressors among patients with chronic kidney disease (CKD) is shown below. Of the 120 sample patients, PPIs and D2 receptor antagonists were administered the most frequently (71 out of 59.16%) in dual medication therapy, followed by PPIs (33 out of 27.5%) in monotherapy. Data presented in Figure 8.





Pattern of various other agents:

The distribution of additional drugs among 120 sample patients with CKD. As indicated below, the recommended medicine classes were thyroid medications (11) followed by calcium supplements (30), phosphate-removing agents (31) and laxatives (4). Data shown in Figure 9.



Figure 9: Pattern of various other agents

Distribution of drugs based on anatomical therapeutic chemical (atc) classification:

Medication distribution among CKD patients according to ATC categorization. 120 research participants received prescriptions for a total of 868 medications. In the sample population listed below, out of 868, the most often prescribed class of medications was cardiovascular system 223 (25.63%), followed by alimentary tract and metabolism 122 (14.02%). Data shown in Figure 10.



Figure 10: Distribution of drugs based on ATC classification

Drug - drug interactions through prescription analysis:

The substance-drug Prescription analysis revealed 40 potential drug interactions among 868 medications; of these, 4 were serious, 33 were moderate, and 3 were minor interactions. This information was obtained from the prescriptions of CKD patients. According to the data below, the majority of medication interactions in the study population were mild. Data presented in Table 2.

S. No	Drug Interaction	Interaction type	Effect	No of cases (40)
1.	Hydrocortisone +Levofloxacin	Major	Tendinitis or Tendon rupture	1
2.	Amiodarone +Levofloxacin	Major	Increases QTC interval	1
3.	Pregabalin + Tapentadol	Major	Respiratory depression, Sedation	1
4.	Levothyroxine + Calcium carbonate	Moderate	Decrease the effects of levothyroxine	2
5.	Bisacodyl +Torsemide	Moderate	Increase the risk of dehydration	1
6.	Calcitriol +Sevelamer	Moderate	Decrease the effects of calcitriol	3
7.	Torsemide +Carvedilol	Moderate	Lower blood pressure and slow heart rate	4
8.	Torsemide +Esomeprazole	Moderate	Hypomagnesaemia	2
9.	Metoprolol +Prazosin	Moderate	Increases blood Pressure	1
10.	Aspirin +Insulin Regular	Moderate	Hypoglycemia	1
11.	Torsemide +Escitalopram	Moderate	Hyponatraemia	1
12.	Cefoperazone +Torsemide	Moderate	Kidney problems	1
13.	Tolvaptan +Telmisartan	Moderate	Hyperkalaemia	1
14.	Prazosin +Carvedilol	Moderate	Irregular Heart beats	2
15.	Clopidogrel +Esomeprazole	Moderate	Reduce the Effectiveness of Clopidogrel	2
16.	Torsemide +Metformin	Moderate	Increase blood sugar levels	1
17.	Sucralfate +Furosemide	Moderate	Decreases effect of furosemide by inhibition of absorption	1
18.	Enalapril +Pregabalin	Moderate	Increases toxicity	1
19.	Furosemide +Ceftriaxone	Moderate	Nephrotoxicity	1
20.	Pantoprazole +Levothyroxine	Moderate	Increasing gastric PH	1
21.	Metoprolol +Furosemide	Moderate	Decrease serum potassium	1
22.	Glimepiride +Dapagliflozine	Moderate	Increases effect of the pharmacodynamic synergism	1
23.	Torsemide +Metolazone	Moderate	Decreases serum potassium	1
24.	Esomeprazole+ Ferrous Fumerate	Moderate	Increasing gastric PH	1
25.	Prazosin +Nifedipine	Moderate	Increase anti-hypertensive channel blocking	1
26.	Aceclofenac +Torsemide	Moderate	Aceclofenac increases & torsemide decreases serum potassium	1
27.	Aspirin +Calcium & Vit D3	Moderate	Reduce serum salicylate concentrations	1
28.	Torsemide +Sulfamethoxazole	Moderate	Increase the blood levels of torsemide	1
29.	Aspirin +Furosemide	Minor	Decrease effect of furosemide by pharmacodynamic antagonism	1
30.	Carvedilol +Aspirin	Minor	Increase serum potassium	1
31.	Clipidogrel +Torsemide	Minor	Decreasing metabolism	1

Table 2: Drug - Drug interactions through prescription analysis

Assessment of prescribing patterns using WHO core indicators:

WHO prescribing indicators were utilized to evaluate the drug use pattern. It was discovered that the range of medications per encounter was 1-6. The findings showed that of the 868 medications prescribed in the research group, 120 contained 54.16% antibiotics and 1.16% generic name prescriptions. The findings showed that injections were included in 10.96% of prescriptions. As indicated below, the data showed that 93.7% of prescriptions were written from the Essential Drug List, whereas 6.3% of prescriptions were not written from the list. Data was summarised in Table 3.

WHO DRUG USE INDICATORS	AVG/PERCENTAGE
Prescribing indicators	
Total number of prescriptions	120
Total number of drugs prescribed	868
Percent medicines prescribed by generic name	1.16
Percent encounters with an antibiotic prescribed	54.16
Percent encounters with an injection prescribed	10.96
Percent medicines prescribed from EDL or formulary	93.7
Patient-care indicators	
Average consultation time (minutes)	5 min
Average dispensing time (seconds)	7 -10 min
Percent medicines actually dispensed	100%
Percent medicines adequately labelled	100%
Facility-specific indicators	
Availability of EDL or formulary to practitioners	YES
Percent key medicines available	90%

 Table 3: Assessment of prescribing patterns using WHO core indicators

DISCUSSION

A six-month prospective observational study carried out at the nephrology department of Kosuru Kidney and Skin Care Hospital, (secondary care hospitals), Narasaraopet. In all, 120 prescriptions were monitored over the course of the six-month trial period. When the demographic information for CKD patients (n=120) was examined based on the ICH classification, 7 (5.83%) of them were young adults, followed by 16 (13.33%) adults, 62 (51.66%) middle-aged adults, and 35 (29.16%) elderly adults.

According to demographic information, patients between the ages of 41 and 60 were found to be high among 62 (51.66%) middle-aged adults, while those above 60 were found to be 35 (29.16%) old adults in the same age range. Our study had 120 patients in total. Out of the entire study population, 44 (36.66%) and 76 (63.33%) of the patients were female.

According to demographic data, men outnumber women in the population due to a number of risk factors, including age, smoking, and alcohol use, which is often higher in men than in women.

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Patients in the research population who were admitted had CKD stage V (87, 72.5%), which was greater than stage IV (23, 19.16%) and stage III (9, 7.5%). In the study population, Stage II (1, 0.83%) was determined to be the least. These results indicate that end-stage renal disease (ESRD) affects the majority of study populations. 66(55%) of the co-morbidities in our study were hypertension, followed by 39(32.5%) and 5(4.16%) of the co-morbidities with CKD being hypertension + diabetes mellitus. The primary co-morbidity was hypertension, as the kidneys regulate extracellular fluid volume, salt retention, and the renin-angiotensin-aldosterone system (RAAS) to a large extent.

In CKD, alterations in these pathways result in hypertension. Antihypertensives are prescribed to lower blood pressure, lower cardiovascular disease, and slow the advancement of chronic kidney disease. According to this study, of the 120 study participants, 41 had monotherapy, followed by 34 dual drug therapies, 21 triple drug therapies, 5 quadruple drug therapies, 3 five drug therapies, and 1 six drug therapies. Diuretics were the most often prescribed medication class (23.3%). In that instance, the most often given medication for both monotherapy and combination drug therapy was torsemide. Diuretics made up the majority of anti-hypertensives (88,45.12%), followed by calcium channel blockers (28,14.35%), beta blockers (26, 13.33%), and alpha agonists (27, 13.84%). Angiotensin-converting enzyme inhibitors (2.02%) were the least prescribed class of medications due to the risk of hyperkalemia and decreased GFR in patients, as well as the need for dose adjustments. Triple medication therapy (beta blocker + CCB + diuretic), 4(3.33%) was the most commonly given treatment in this study, followed by dual drug therapy (CCB + diuretic), 14(14.16%). Of the 120 sample members in this study, 7 underwent monotherapy, 14 underwent dual drug therapy, and 2 underwent triple medication therapy. According to this data, the most common dual medication therapy administered to patients with chronic kidney disease (CKD) was anti-platelet + anti-hyperlipidaemics. Cardiovascular disease is also one of the co-morbidities associated with CKD. For a total of 120 patients, 31 anti-diabetic medications were prescribed. In monotherapy, Sulfonyl Urea 6 (5%), followed by Insulin Analogue 4 (3.33%), was the most prescribed medication class. Meglitinide 2 (1.66%) plus competitive alpha glucosease inhibitors were the most often recommended class of medications for dual drug therapy in the study population.

For a total of 120 patients, 39 hematinic agents were prescribed. In CKD patients receiving dual pharmacological therapy, the most often given medications are Iron Supplements 35 (29.16%) in monotherapy and Iron Supplements + Erythropoietin Stimulating Agents 3 (2.5%). Only 4 of the

120 study participants received erythropoietin; the majority of patients were unable to obtain it because of socioeconomic issues.

In our study, 111 gastric acid suppressants were administered out of a sample group of 120. D2 Receptor Antagonist 71 (59.16%) in combination medication therapy, followed by Proton Pump Inhibitors 33 (27.5%) were the most frequently recommended class of medications in monotherapy to lessen ulcers caused by stress and as symptomatic treatment.

CKD patients have a higher risk of infection due to the use of antibiotics such aminoglycosides. 65 antibiotics in all were administered. The research population is also prescribed a variety of additional medications. Thyroid medications made up 11(9.16%) of the prescribed class of medications because hypothyroidism is one of the co-morbidities associated with chronic kidney disease (CKD). Calcium supplements, or calcium and vitamin D3, made up 30(25%) of the prescribed medications because kidneys convert vitamin D into calcitriol. It keeps the blood's levels of calcium and phosphorus in equilibrium, but because CKD affects normal function, calcium and vitamin D3 are given.

Because phosphate retention can happen in CKD, 31 (or 25.83%) phosphate-removing medicines were given. Phosphate binders were therefore advised. Since constipation is a CKD consequence, laxatives are typically prescribed medications. Of the laxatives, 4 (3.33%) were prescribed.

A total of 120 study participants received prescriptions for 868 different medications. Cardiovascular system medications accounted for 223 (25.63%) of the 868 prescriptions, followed by medications for the gastrointestinal tract and metabolism (122, 14.02%), musculoskeletal system (88, 10.11%), anti-infectives for systemic use (65, 7.47%), blood and blood-forming agents (55, 6.32%), genito-urinary and sex hormones (39, 4.48%), and anti-parasitic medications (least prescribed).

This study uses prescription analysis to display drug-drug interactions among patients with chronic kidney disease. 40 potential drug interactions were discovered in prescriptions out of 868 medications; four of these were serious, 33 were moderate, and three were mild. Due to polypharmacy in many prescriptions, the majority of medication interactions in the research group were found to be moderate.

120 participants in the current study received prescriptions for a total of 868 medications. A total of 1.16% of prescriptions were written under their generic names. 10.96% of prescriptions included an injectable recommendation. Antibiotic prescriptions made up 54.16% of all prescriptions. Ninety-three percent of the medications prescribed came from the WHO Essential medicines list.

CONCLUSION

The current study offers prescribing trends for the use of CKD medications in the nephrology department. There were 120 patients in our study. Males in the 41–60 age range were more likely to have CKD than females. The maximum number of patients in our study have stage 5 chronic kidney disease (CKD), which is accompanied by co-morbidities such as hypertension, diabetes mellitus, hypothyroidism, and cardiovascular diseases, as well as risk factors like age, obesity, smoking, and alcohol use. The study shows that the prescription of brand-name medications was frequently noticed using WHO core indicators, which were used to monitor the drug prescribing trend. The practice of prescribing generic names should be started in order to save costs. Data analysis revealed that the most commonly prescribed medicine class was anti-hypertensive agents, which was followed by anti-diabetic, hematinic, and cardiovascular agents. Medication-related issues were tracked, and it is not necessary to downplay insignificant medication interactions. It was necessary to switch to an alternate treatment plan and stop therapy in the event of moderate or severe drug interactions. Our research led us to the conclusion that patients with CKD had a very high prevalence of polypharmacy. In individuals with CKD, diuretics, antihypertensives, and oral hypoglycemic medications were used more frequently.

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