Prospective observational study on the prescription pattern of medications in chronic kidney disease patients at tertiary care hospital

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Abstract— **Background: The kidney is the structural and functional unit responsible for regulating homeostasis, equilibrium(acid-base) and electrolytes, also kidney plays a major role in the disposition of many drugs. CKD patients were commonly present with several other comorbidities of which HTN and DM are the most common. a large number of medications usually prescribed to CKD patients that are complicated and require dosing and frequent monitoring. The objective of the study is to analyze the prescription pattern of medications in CKD patients Method: a prospective observational study on the prescription pattern of medications in chronic kidney disease patients which is based on the collection of data on a daily visit to the department of nephrology, medicines and HICU in tertiary care hospital. The patient who met the criteria were involved in the study. WHO Prescribing Indicator, ATC classification of drugs and therapeutic class drug distribution were used for the analysis of drugs. Result: Out of 60 collected cases, 70% were male and 30% were female. The study population were also having comorbidities along with CKD in which HTN was the highest among CKD patients with 75% followed by DM (68%), Anemia (30%), Respiratory Disorder (27%), CVD (18%), Thyroid Disorder (15%) and UTI (13%). WHO drug prescribing indicator showed that the average number of drugs prescribed per patient was 12, the percentage of drugs prescribed by generic name was (390) 54%, the percentage of a patient with an injection prescribed was (246) 34%, the percentage of drugs prescribed from essential medicine list was (580) 80%. Antihypertensive drugs (163) 22.5% were commonly used drugs followed by vitamins (141)19.44%, minerals (99) 13.65%, antimicrobial (93) 13.2%, hemopoietic agents (53) 7.3%, anti-diabetic agent (52) 7.2% and hypolipidemic agent (39) 5.4%. Conclusion: An overall understanding of medications used in CKD management, their complications and comorbidities associated with it, helps physicians and prescriber in better control and management of CKD patients, adverse effects and toxicities of the drugs, which in turn leads to improving patient compliance to treatment therapy. After the analysis of all the CKD cases, it was found that symptoms along with the comorbidities were managed accordingly. Meanwhile, the rationality of prescribing was followed.**

Key words— **Chronic kidney disease, comorbidities, prescription pattern, dialysis.**

I. INTRODUCTION

The kidney is the structural and functional unit responsible for regulating homeostasis, equilibrium(acid-base) and electrolytes, also kidney plays a major role in the disposition of many drugs. Almost half of all medicines as well as their metabolites are excreted by the kidneys and about 30% of all the adverse reactions have either renal cause or renal effect [1]. Chronic Kidney Disease is a condition which is characterized by a decrease in the function of the kidney explained by a reduction in the Glomerular filtration rate below 60ml/min/1.73m^2 in a period not less than 3 months or biomarkers that shows kidney damage explained by urine sediments abnormalities, kidney image/biopsy [2]. The process of removing waste of toxins and extra water from blood is nothing but Dialysis. It is a mechanical replacement of Kidney function especially when the kidney is not functioning properly. However, dialysis cannot perform the function of a kidney. But to some extent can manage its activities by the mechanism of diffusion and ultrafiltration. Dialysis is performed in CKD when the GFR rate falls below 15ml/min/1.73m^2 (ESRD) [3]. According to the eGFR score, there are five stages of chronic kidney disease, with the fifth stage considered renal failure(GFR less than 15ml/min) [4]. CKD is a worldwide common non-communicable disease with a prevalence estimated as 9.1% and almost 18% among those elderly above 65 years of age, this increases the rate of morbidity and mortality all over India. CKD patients were commonly present with several other comorbidities such as HTN, DM, infection and coronary artery disease in which HTN and DM is the most prevailing risk factor [4,5]. The common etiologies of chronic kidney disease are diabetic nephropathy, elevated blood pressure, intestinal nephritis, pyelonephritis, polycystic kidney disease, and obstructive nephropathy. Also, chronic kidney disease can be the result of untreated acute kidney injury caused due to either infections or drugs or some toxic substances such as heavy metals.   A patient in countries with high income are commonly associated with diseases like DM, and HTN. Whereas in low and middle-income countries it has additional potential causes like infectious diseases and environmental toxins, but most remain unknown [6,7] CKD complications or symptoms are initially or continuously managed during the dialysis process. But for the comorbidities associated with CKD, different drugs are used for their management. However, some of these drugs are removed during the dialysis process which reduces their therapeutic effects in the management of comorbidities associated with it. Lower molecular weight drugs with low protein binding and smaller volume of distribution are drugs that are considered to be dialysable. Whereas drugs with high molecular weight, high protein binding and a large volume of distribution are poorly dialysable drugs [8].

Patients with chronic kidney disease are at risk of developing drug-related problems as they required complex drug therapy with frequent monitoring as well as dose adjustment [9]. The combination of both multiple drug regimens and appropriate dosage

considerations make the pharmacological care of chronic kidney disease patients challenging, due to the alteration of both pharmacokinetic and pharmacodynamic parameters [10]. A drug evaluation study is an approved, trusted and effective tool for the evaluation of drugs prescribed to critically ill patients and has the objective of achieving the rational use of drugs which plays an important role in healthcare decision-making [11]. According to the World Health Organization (WHO), rational drug use is when individuals take pharmaceuticals that are appropriate for their clinical needs, take them for an adequate amount of time, and do so at the least expensive cost [12]. A large number of medications usually prescribed to CKD patients that are complicated and require dosing and frequent monitoring. Therefore, we attempted to conduct this study to evaluate the prescription pattern for the rational use of medication in CKD patients.

II. MATERIALS AND METHOD

A prospective observational study on the prescription pattern of medications in chronic kidney disease patients which is based on the collection of data on a daily visit to the department of nephrology, medicines and HICU in tertiary care hospital. The patient who met the criteria were involved in the study. WHO Prescribing Indicator, ATC classification of drugs and therapeutic class drug distribution were used for the analysis of drugs. This study also included the analysis of drugs that are dialysable. Standard references like Micromedex, Medscape, and standard books like Pharmacotherapy by Joseph Dipiro were referred.

Inclusion criteria
- All CKD patients with or without decreased GFR levels.
- All CKD patients above 18 years old.
- Both in and out CKD patients.
- CKD patients on MHD
- CKD patients not on MHD

Exclusion criteria
- A patient was admitted with Acute Kidney Injury.
- A patient below 18 years old
- Pregnancy patient
- The patient admitted with drug-induced Kidney Injury
- The patient underwent Renal Transplantation.

Determination of prescribing pattern

For patients who were newly diagnosed with CKD or previously diagnosed with CKD based on the inclusive criteria, the entire relevant details were obtained by observing the patient's case sheet. The patient's demographic details like age, gender, weight, past medical history, laboratory parameters along with currently prescribed medications were collected and documented in a suitable designed data collection form.

III. RESULT

In this current study prescriptions of 60 CKD patients were analyzed during the study period of 3 months.

Demographic Data

A total of 60 cases of CKD patients were analyzed in this study both inpatient and outpatient. Out of 60 patients, 42 (70%) were male and 18 (30%) were female which indicates that the male is more prone to develop CKD as compared to females.

Fig no. 1: Gender distribution of CKD patients.
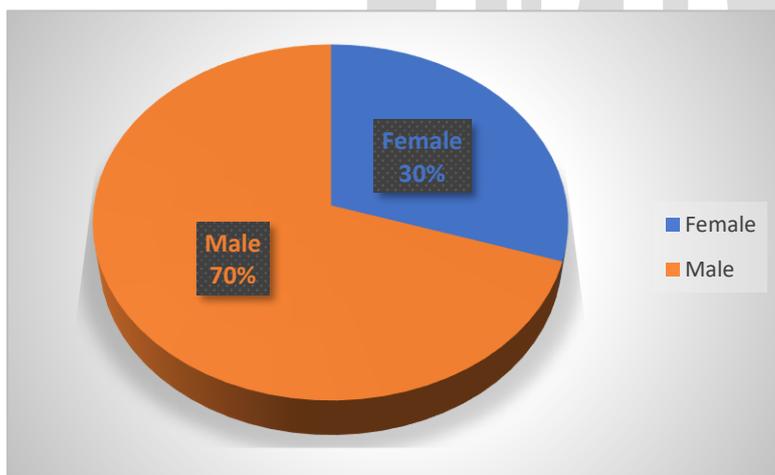
The age of the patients varies from 20-100 years and a majority of the patients were falling under the age of 60-80 years whereas the least number of patients were falling under the age of 0-20. The mean age calculated was 57.6.

The following figure describes the age distribution of the study population.
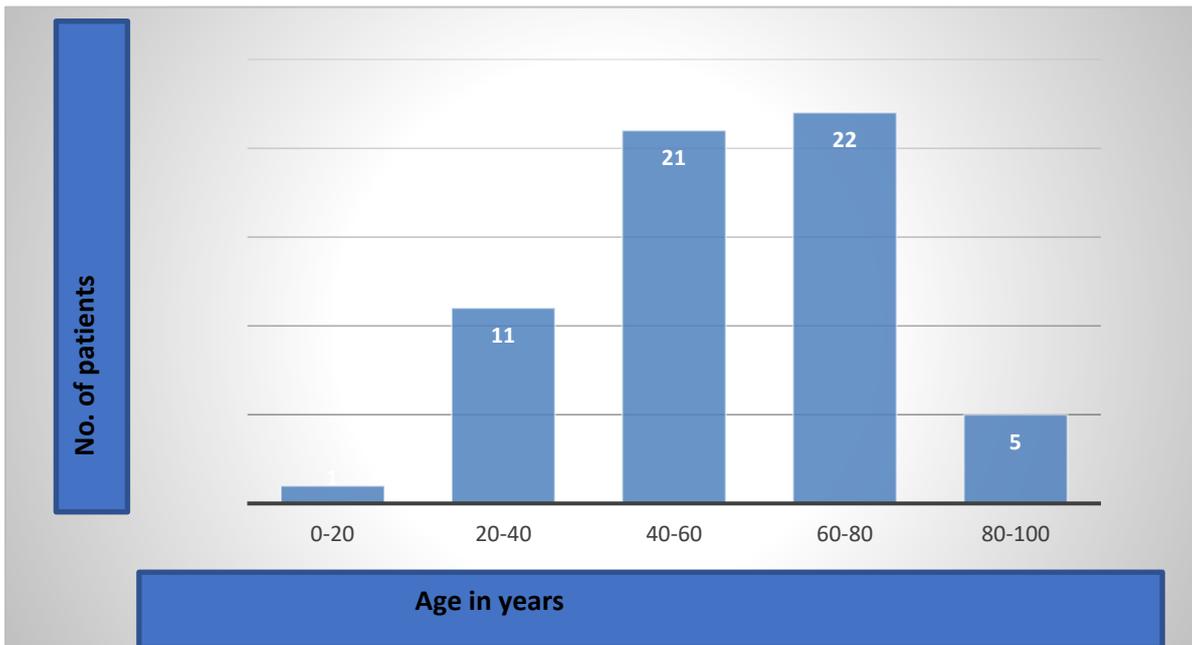
Fig no.2: Age distribution of CKD patient

Comorbidities

The study population were also having comorbidities along with CKD in which HTN was the highest among CKD patients with 75% followed by DM (68%), Anemia (30%), Respiratory Disorder (27%), CVD (18%), Thyroid Disorder (15%) and UTI (13%).
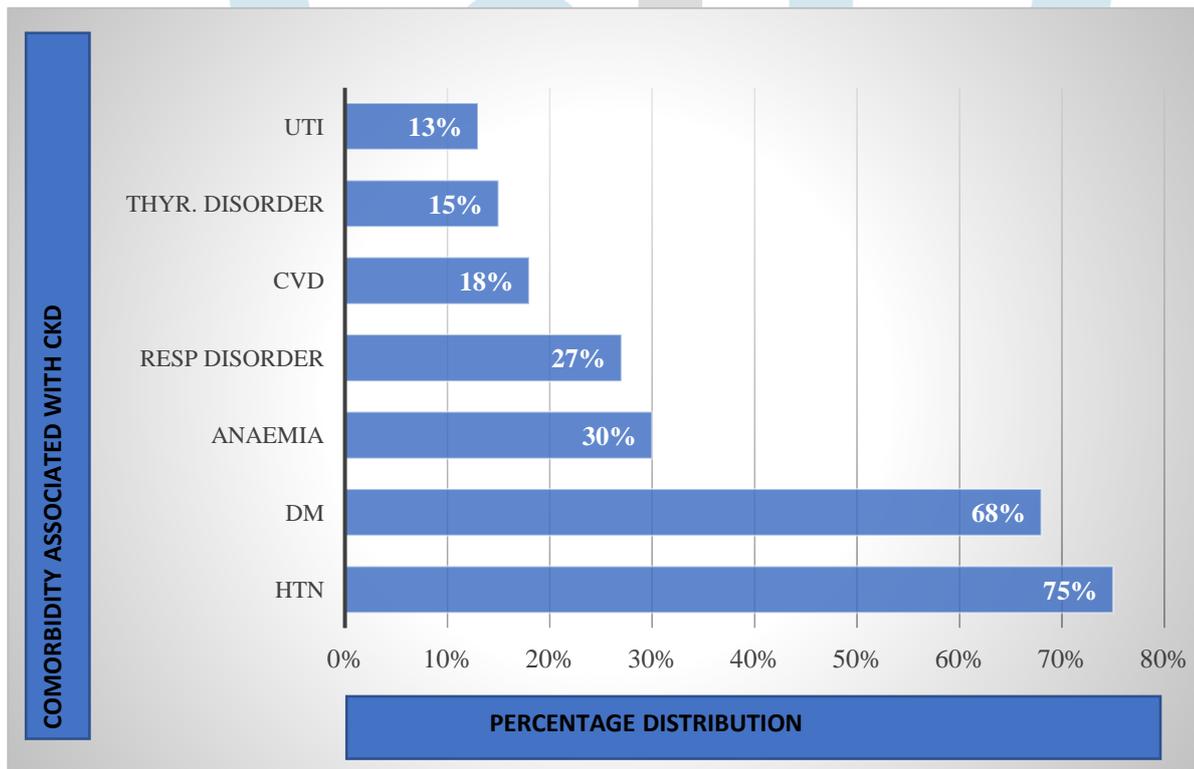

Fig no. 3: Comorbid disease along with CKD

CKD stage distribution

The CKD stages of the patients according to the creatinine clearance at the time of data collection are as follows:
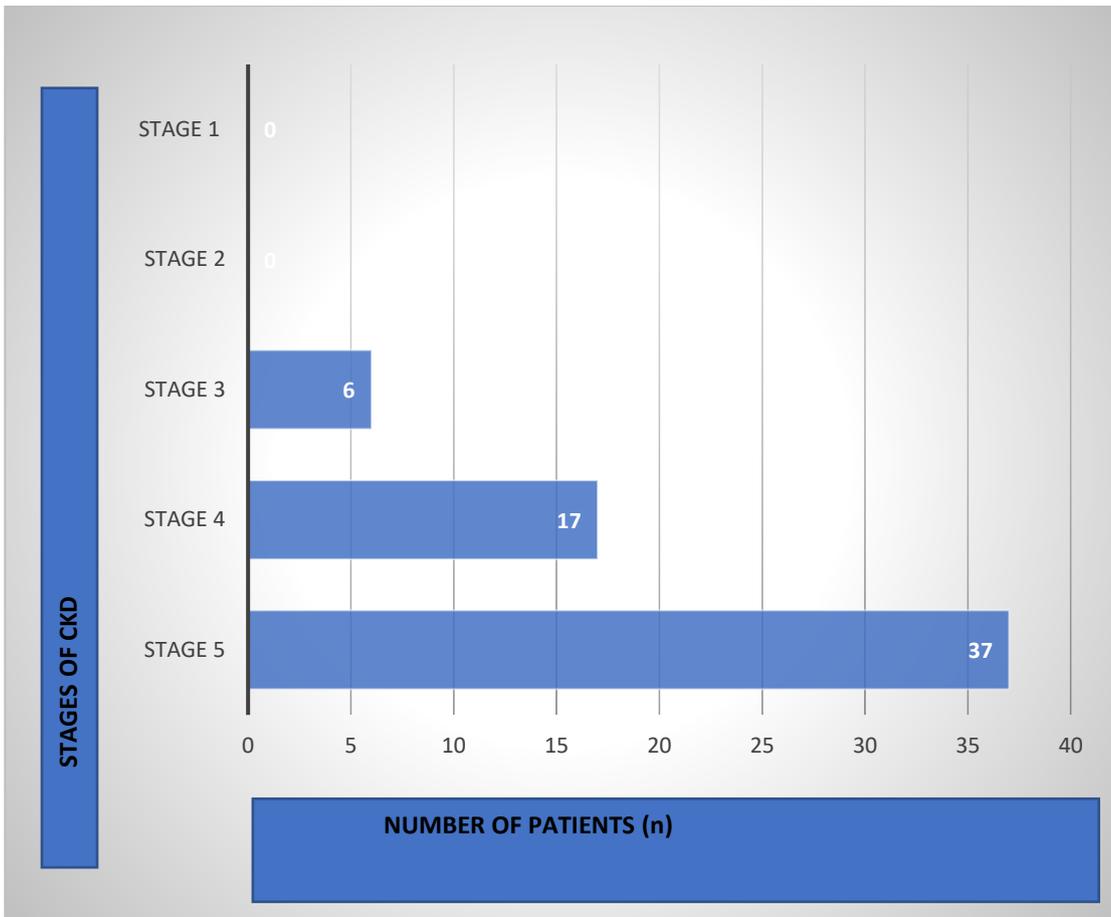
Fig no. 4: Stages of CKD patients

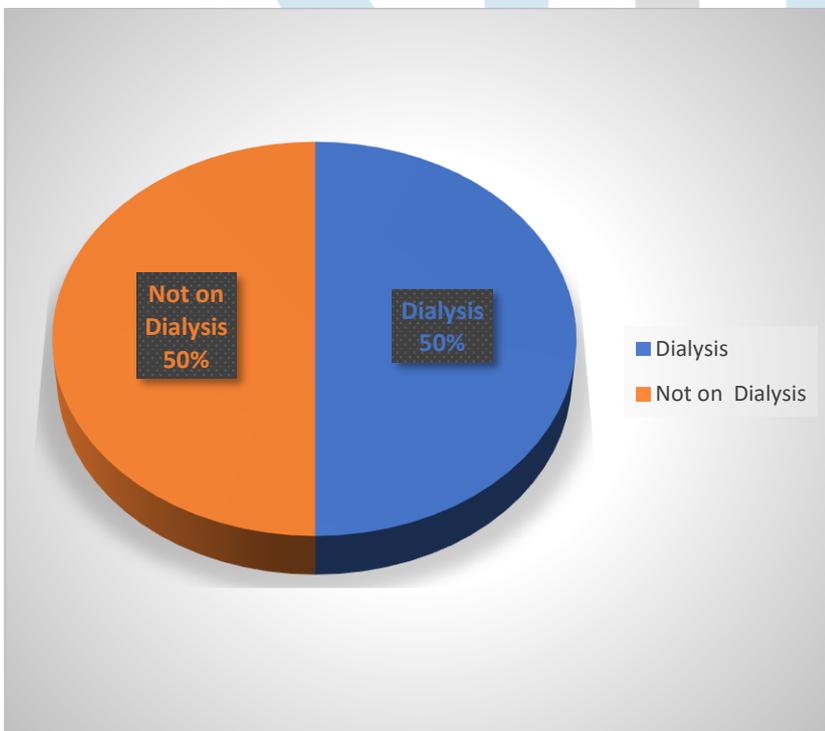50% of patients were on Dialysis and 50% of patients were not on dialysis.

Fig no. 5: Percentage distribution of dialysis among CKD patients
Prescription Pattern observations

Table no. 1: WHO Prescribing Indicator

WHO prescribing indicator	Number (n)
Case analyzed	60
Total number of Drugs prescribed	725
Average number of Drugs per prescription	12
Total number of drugs prescribed by generic name	390
Total number of patients with an injection prescribed	246
Total number of drugs prescribed from Essential Medicine List	580

The total number of drugs prescribed in overall cases that had been analyzed was 725 drugs. In which the average number of drugs prescribed per case was 12. The total number of drugs prescribed by generic name was 390 (54%), the total number of patients with an injection prescribed was 246 (34%), the total number of drugs prescribed from Essential Medicine List was 580 (80%).
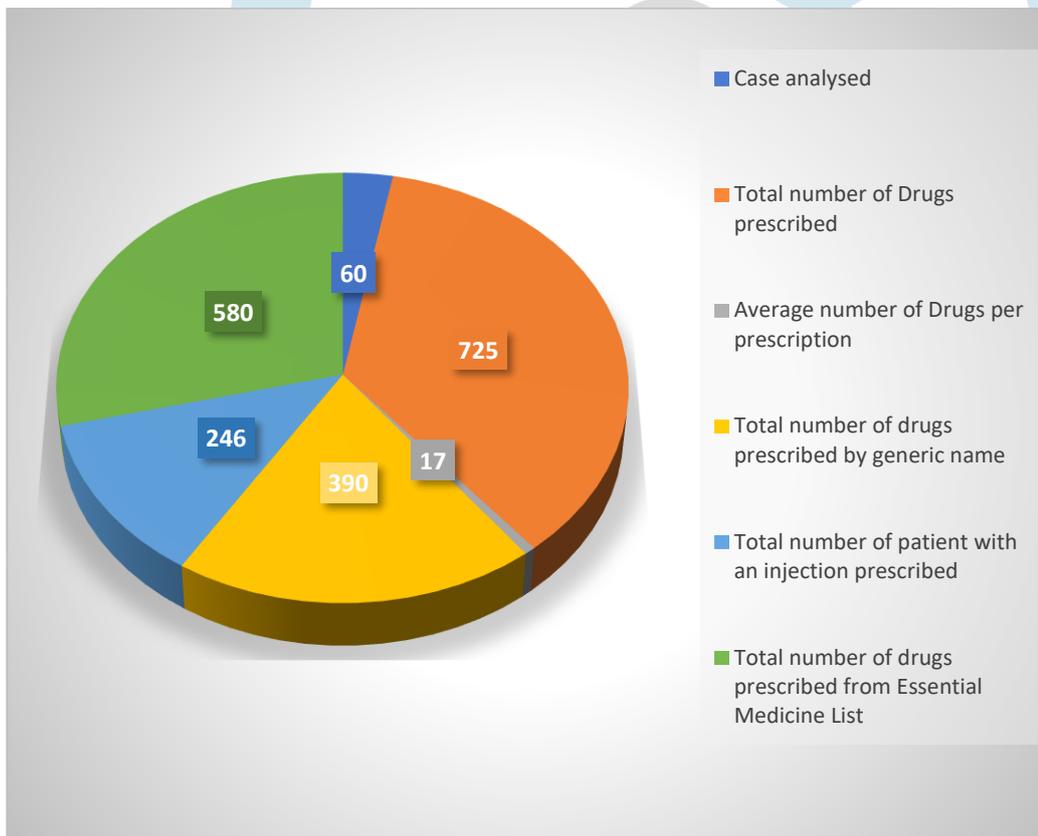

Fig no.6: WHO Prescribing Indicator

Table no. 2: Drug distribution according to ATC classification

ATC class code	ATC class	No. of Drugs (n=725)	Percentage (%)
A	Alimentary tract and metabolism	309	43
B	Blood and Blood forming Product	102	14

C	CVS	185	25.5
D	Dermatology system	0	0
G	Genitourinary system and sex hormone	0	0
H	Systemic hormone Preparation	0	0
J	Anti-infective for systemic use	93	13
L	Anti-Neoplastic and immunomodulatory agent	3	0.41
M	Musculoskeletal system	4	0.5
N	Nervous system	18	2.5
P	Anti-parasitic products, insecticides and repellents	0	0
R	Respiratory system	9	1.2
S	Sensory organ	2	0.3
V	Various	0	0

The current study showed that according to the ATC classification, drugs belonging to the class of Alimentary tract and metabolism 309 (43%) were the most commonly prescribed followed by Cardiovascular 185 (25.5%) drugs followed by Blood and blood-forming products 102 (14%) followed by Anti-infective drugs 93 (13%).
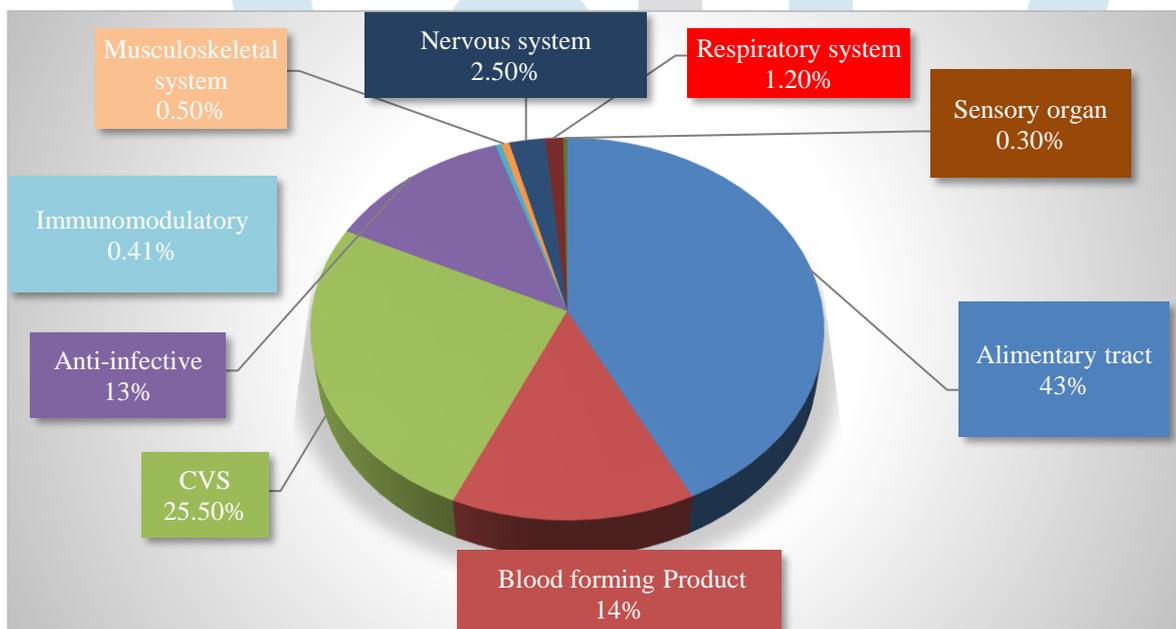

Fig no. 7: Drug distribution according to ATC classification

Table no. 3: Therapeutic class-wise drug distribution.

Drug class	Number	Percentage
Antihypertensive	163	22.5%
Calcium channel blocker	15	2.06%

Diuretic	59	8.13%
Beta blocker	68	9.37%
Alpha blocker	9	1.24%
Others(Isolazine & nitrite)	12	1.65%
Hypolipidemic drugs	39	5.4%
Statins	22	3.03%
Statin +aspirin	8	1.10%
Statin +Clopidogrel	9	1.10%
Anti-Diabetic	52	7.2%
Insulin	52	7.2%
Vitamin	141	19.44%
Vitamin D	23	3.17%
Thiamine	58	7.72%
Multivitamin	60	8.27%
Mineral	99	13.65%
Sodium bicarbonate	45	6.2%
Uric Acid Binders	12	1.65%
Calcium	42	5.79%
Haemopoietic	53	7.31%
Iron	27	3.72%
Folic Acid	15	2.06%
Erythropoietin	11	1.51%
Antimicrobial	93	13.2%
Antithyroid	9	1.04%
Others (Antacids, Antiepileptic, Analgesic, Probiotic Antihistamine)	76	10.4%

And therapeutically class wise the Antihypertensive class of the drugs (163) were the highest prescribed with a percentage of 22.5% followed by Vitamins (141) at 19.44%, Minerals (99) at 13.65%, Antimicrobials (93) at 13.2%, haemopoietic agents (53) with 7.31%, Antidiabetic agents (52) with 7.2%, hypolipidemic agents (39) with 5.4%, etc.
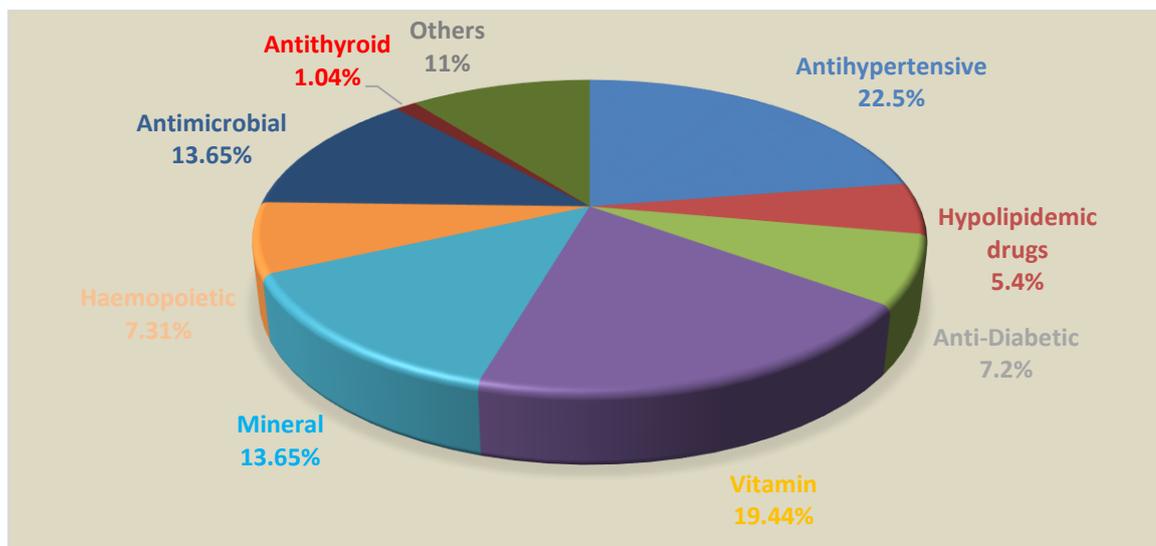
Fig no. 8: Therapeutic class-wise drug distribution.

Table no. 4: Dialysable Drugs

Drug name	No. of cases	Conventional Dialysis	Peritoneal Dialysis
Amoxicillin	15	Yes	No
Aspirin	8	Yes	Yes
Cefuroxime	4	Yes	No
Metoprolol	9	Yes	No
Atenolol	11	Yes	No
Azathioprine	4	Yes	No
Acyclovir	6	Yes	No
Tazobactam	15	Yes	No
Piperacillin	15	Yes	No
Metronidazole	12	Yes	No
Clavulanic Acid	15	Yes	Yes
Meropenem	15	Yes	No
Colistin	3	Yes	No
Sulbactam	8	Yes	No
Fluconazole	9	Yes	Yes
Gentamycin	5	Yes	Yes

After analyzing all the medications that have been prescribed in all cases, the following drugs were found to be Dialysable during conventional Hemodialysis whereas some of them are not dialysable during Peritoneal Dialysis.

IV. DISCUSSION

In our current study, the mean age of patients was found to be 57.6 years. This was found to be higher than that found in the studies done by Latha Kamath et.al and Purna Atray et.al (47.56 years and 51.51 years respectively) [11,13]. The majority of patients in the current study were falling in the age group of 60-80 years. There was a male preponderance over the female patient. Out of 60 patients studied 42 (70%) patients were male and 18 (30%) were female. This finding is in concurrence with Latha Kamath et.al and Purna Atray et.al [11,13]. Studies have shown that male patients substantially have a higher prevalence of CKD and incidence rate of end-stage renal disease than that observed in female patients. In our study, men showed higher prevalence than women because of comorbidities that men had along with CKD such as DM, HTN and infections whereas most of the women were with no comorbidities associated.

Some studies suggest that African American men have a higher risk of CKD progression than African American females because of poorly controlled HTN among these males as well as men with Diabetes have a higher incidence of albuminuria and decreases in the eGFR than compared to women [14]. This could be one of the reasons for men having preponderance over women.
The majority of the patients in our study were falling under stage 5 whereas the study conducted by Latha Kamath et.al and Purna Atray et.al [11,13] showed that the majority of patients were falling under stage 4 of CKD. In the present study, HTN (75%) was the highest among CKD patients followed by DM, Anemia and others. These findings were similar to the study conducted by Latha Kamath et.al and Purna Atray et.al [11,13].

According to the ATC classification of the drug, the current study showed that drugs belonging to the Alimentary tract and metabolism were the commonly prescribed drugs with 43% followed by Cardiovascular drugs (25.5%), Blood forming products (14%). The reason was that Vitamins and Minerals were prescribed in almost all the cases for the management of CKD complications in which, drugs from Cardiovascular class and Blood Forming products were the second and third highest respectively due to the higher prevalence of HTN and Anemia among the collected cases as comorbidity associated with CKD. The study conducted by Latha Kamath et.al [13] showed that drugs belonging to the cardiovascular class (43.8%) were the commonest prescribed class of drug followed by Alimentary tract and metabolism (35.4%), Blood and blood forming products (16.07%) whereas the study conducted by Purna Atray et. al [13] showed that drugs from Blood forming agents were highly recommended class of drugs (20.15%) followed by cardiovascular agent (19.08%), Alimentary tract and metabolism (17.94%).

In the present study, the average number of drugs per prescription was 12 which is different from the average number of drugs reported by Latha Kamath et.al, Purna Atray et.al and Janet Mary Ommen et.al (5.13, 7.83, 7.51 respectively) [11,13,15]. The differences in the average number of drugs might be due to the size of the study population, comorbidities and behavior of the prescriber. The percentage of drugs prescribed by generic name was 54% which is higher than the study conducted by Latha Kamath et.al (33.3%). Drugs prescribed from Essential Medicine List in this present study was 80% which is higher than the reported percentage by studies conducted by Latha Kamath et.al, and Purna Atray et.al (65.8%, 55.63% respectively) [11,13]. The percentage of patients with an Injection prescribed was 34% which is higher than the study conducted by Latha Kamath et.al, and Purna Atray et.al. (16.6%, 9.71% respectively) [11,13].

Among the Cardiovascular class of medications, Beta blockers were commonly used in the present study followed by Diuretics and Calcium Channel Blockers. (9.37%, 8.13% and 2.06% respectively). Latha Kamath et.al reported that Calcium Channel Blockers were the most commonly prescribed among the CVS group of drugs followed by Diuretics and alpha Blockers (18%, 8.28% and 4.22% respectively) [13]. Among all the prescribed drugs Antihypertensive class, drugs were the highest prescribed medication with a percentage of 22.5% followed by Vitamins at 19.44%, Minerals at 13.65%, Antimicrobials at 13.2%, haemopoietic agents at 7.31%, Antidiabetic agents with 7.2%, hypolipidemic agents with 5.4%, etc. among which multivitamins with Thiamine was almost given to all CKD patients. Whereas sodium bicarbonate, uric acid binders and calcium-based binder were highly prescribed. The study was similar to the study conducted by Latha Kamath et.al, and Purna Atray et. al [11,13] as the Antihypertensive class of medication was the highest prescribed medications among all the prescribed drugs whereas there was a slight percentage difference with the remaining class of drugs. This study also evaluated the drugs which are dialysable during either conventional or Peritoneal dialysis. Some of these drugs were prescribed and noted as explained in table no. 4.

Time-to-time evaluation of prescribing patterns in CKD patients plays an important role in ensuring and maintaining the rationality of prescribing patterns. The information obtained from the studies can be evaluated and utilized in preventing errors related to medications by monitoring the drug therapy and its effectiveness in managing CKD complications along with the comorbidities associated with it. As well as, make changes in the treatment regimen for the patient's benefit if necessary. For overall CKD management, laboratory assessment as well as frequent clinical monitoring is required. The main aim of CKD pharmacotherapy is to prevent Kidney disease progression along with the management of the ongoing disease process. CKD treatment is not just targeted towards the disease but also focuses on the management of comorbidities associated with CKD. An overall understanding of medications used in CKD management, their complications and comorbidities associated with it, helps physicians and prescribers in better control and management of CKD patients, adverse effects and toxicities of the drugs, which in turn leads to improving patient compliance to treatment therapy. Further large-scale studies at different multiple centers with large sample size, is needed from time to time, which will help and contribute to analyzing, comparing and rationalizing the prescribing pattern trends in CKD patients, which leads to a proper finding on a larger population.

V. CONCLUSIONS

This study elucidates the prescribing pattern of medications in CKD patients. A total of 60 cases were analyzed out of which males and females were enrolled to study, the male majority over females were noticed, and the age distributions of a patient were from 20 years and above in which the majority of a patient were falling between the age of 60-80 years. The study population was also having comorbidities along with chronic kidney disease in which HTN was the highest followed by DM, Anemia, Respiratory disorder, CVD, Thyroid disorder and UTI. All the stages of CKD were enrolled to study however majority of the patients were found in stage 5 and no patient was found in stages 1 and 2.

The prescription pattern of medication in CKD patients was analyzed according to WHO criteria assessment and based on the ATC classification of drugs it was found that the Alimentary tract and metabolism were the most commonly prescribed medications followed by cardiovascular drugs, blood-forming agents and anti-infective drugs. Therapeutic class wise of the prescribed medication in CKD patients were also done in which antihypertensive class of medications were the highest prescribed medications followed by vitamins, minerals, antimicrobial and haemopoietic agents. Drugs which are dialysable through conventional and peritoneal dialysis were observed and noted while analyzing the prescribed medications. After the analysis of all the CKD cases, it was found that symptoms along with the comorbidities were managed accordingly. Meanwhile, the rationality of prescribing was followed.

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