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### A retrospective evaluation of prescription pattern on chronic kidney disease patients in a tertiary care hospital

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#### ABSTRACT

**Background:** CKD is known as abnormalities in structure of kidney or functioning of Glomerular Filtration Rate (GFR) <60 ml/min./1.73m<sup>2</sup> for at least three month duration. Various complications include hypertension, anemia, diabetes mellitus and bone mineral related disorders. The objective of work is to study the prescription pattern, compare prescribing indicators with standard and evaluate of rational prescribing of drugs. **Methods:** A retrospective observational analysis conducted on chronic kidney disease (CKD) patients from the department of general medicine, of Government District Headquarters Hospital, Virudhunagar.

**Result:** Study included 102 prescriptions, of which 895 drugs were totally given. Average number of drugs per encounter was 8.77. Percentage of drugs in generic name was 88.83; percentage of drug prescribed from national list of essential medicine was 92.96. Percentage of encounters with antibiotic and injection were 47.06, 83.33 respectively. **Conclusion:** Antihypertensive drugs are prescribed more commonly for the patients, in which Calcium Channel Blockers are given frequently than ACE inhibitors or Angiotensin – II Receptor blockers. The prescribing indicators deviate from WHO optimal values which should be rectified to improve the standards of treatment and patient care. A better counseling would alleviate the clinical conditions of the community to improve quality of care.

**Keywords:** CKD, Co-morbidities, Prescribing Indicators, Prescription Pattern

#### INTRODUCTION

Chronic kidney disease (CKD) is notable and spectacular in high risk of having complications like cardiovascular abnormalities, hyperlipidemia, anemia and bone related disorders. It is defined as abnormalities in kidney structure or function, present for more than 3 months, with implications for health. It is also referred as the presence of either kidney damage or Glomerular Filtration Rate (GFR) <60 ml/min./1.73m<sup>2</sup> for atleast three month duration. It is a risk multiplier of diseases like diabetes and hypertension. Hence it is primarily important in maintaining the renal health by many ways of avoiding exposed to risk factors. A Global study in 2017 reports that, around 1.2 million people

died by CKD, of which all age mortality rate was increased by 41.5% (1-4).

Another study by Coresh and colleagues depicts the information that prevalence of hypertension is high in CKD patients rising with age. In India, diabetes and hypertension accounts for about 40-60% of CKD cases. It can be reversed from the end stage renal disease by early detectment of kidney failure. The highly developed countries have the highest rate of incidence of end stage renal failure. They generally suffer economically for the expense required in implicating therapy for diabetes and cardiovascular diseases (5).

Considering the **etiology** of Chronic Kidney disease; In India, diabetes, hypertension, chronic glomerulonephritis are the most common etiologies of CKD. PAN India registry

reports that there is 30% diabetes and 16% of undetermined etiologies in 48% cases with stage-V younger patients than those under stage - III,IV (6).The unknown form of chronic kidney disease is denoted by CKDu, it is CKD which is uncommon to any traditional factors. The co-morbidities are

caused by etiological factors like sedentary lifestyle, food pattern, smoking, chronic alcohol consumption etc.(7).

The different **stages** of Chronic Kidney Disease, as per KDIGO guidelines for kidney diseases is determined by assigning glomerular filtration rate and albuminuria (8-10).Based on glomerular filtration rate, its classified as;

**Table-1 GFR categories in CKD**

STAGE	ESTIMATED GFR (ml/min/1.73m <sup>2</sup> )	CONDITION
G1	More than and equal to 90	Normal or high
G2	60-89	Mildly decreased
G3a	45-59	Mildly to moderately decreased
G3b	30-44	Moderately to severely decreased
G4	15-29	Severely decreased
G5	Less than 15	Kidney failure

Chronic Kidney Disease is a progressive condition, associated with various complications related to high prevalence and decreased kidney functioning leads to death. Several complications of CKD are;

1. Hypertension in CKD patients is called as 'resistant hypertension' as it requires treatment for 3 or more antihypertensive agents at maximally tolerated doses and one must be a diuretic. Pulse pressure may be increased in hypervolemic patients be treated with diuretics. Another study demonstrated the hypertension remains the important risk factor for developing severe cardiovascular complications in stage II and stage III kidney disease patients (11).
2. When the GFR decreases to less than 60ml/min the chances of development of cardiovascular abnormalities like coronary syndrome increases gradually and patients under stage III and IV have high risk in CVS diseased conditions. The risk factors are found to be hypercholesterolemia, uremia-related risk factors such as inflammation, oxidative stress and atherosclerosis. Coronary artery calcification is more prevalent among CKD patients (12).
3. Anemia increases mortality and morbidity by deteriorating the renal function called as 'cardio-renal anemia syndrome'. This common complication in CKD patients is basically due to erythropoietin deficiency, blood loss and decreased  $t_{1/2}$  of RBC and iron deficiency. The high rate of iron loss (1-3 g/year) is due to gastrointestinal bleeding from the combination of gastritis and platelet dysfunction in both dialysis and non-dialysis CKD patients. The Hemoglobin concentration should be measured only when clinically indicated, or at least annually in CKD stage III, twice per year in CKD stage IV, V non-dialysis cases, or every 3 months in CKD stage- V dialysis (13-15).
4. In people with diabetes, CKD is potentially devastating and increases the cardiovascular risk which leads to kidney failure requires dialysis or kidney transplant. Yearly screening of assessment of urine albumin excretion and e-GFR is mandatory for CKD patients. Patients with diabetes and CKD have an 8-fold higher risk of cardiovascular complications

and all-cause of mortality compared to those without diabetes and CKD (16-22).

5. CKD associated bone and mineral disorders comprises of abnormalities in bone and mineral metabolism and extra skeletal calcification. Renal phosphate excretion is reduced. Four types of renal osteodystrophy can be diagnosed; osteitis fibrosa cystica, osteomalacia, adynamic bone disorder and mixed osteodystrophy (23).

According to KDIGO guidelines, treatment of CKD with common pharmacological interventions includes angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs),  $\beta$ -blockers, diuretics, statins (HMG Co-A reductase inhibitors) and calcium channel blockers (CCBs). There are additional specific therapies including medications and non pharmacological interventions that target control of blood pressure, hyperglycemia, hypocalcemia, hyperphosphatemia, cholesterol and obesity. Special attention must be paid to the risk of hyperkalemia and other cardiovascular drugs.

This a retrospective study of analyzing the prescription pattern and utilization of drugs in chronic kidney disease patients using various key prescribing indicators approved by World Health Organization.

Though multiple medications were given, making a rational prescription is an effortful task for prescribers. Inappropriate use of medications can increase adverse drug effects and cause excessive length of hospital stays, health care utilization, and costs. It is essential to provide them evidence based treatment to improve the outcomes. Patients with end-stage kidney disease (ESKD) receiving dialysis treatment are complex and are prone to poly pharmacy. The prescribing pattern will be more effective when instructed by considering KDIGO guidelines (24-26).WHO indicators are widely used to evaluate the rationality of drugs prescribed to patients. It includes the following such as average number of drugs prescribed per encounter, percentage of drugs prescribed by generic name, percentage of encounters with antibiotics prescribed, percentage of encounters with an injection prescribed, percentage of drugs prescribed from an essential drug list. These parameters would reflect whether the pattern of prescribing is rational or not. Other complementary indicators are average

consultation time, average dispensing time, percentage of drug actually dispensed, patients knowledge about correct usage of drugs promotes the rational prescribing of drugs in CKD patients (27, 28). The aim and objective of this study,

- To carry out a retrospective study for determining the pattern of prescription and drug utilization on Chronic Kidney Disease patients in a Government Tertiary care hospital.
- To study the pattern of drugs prescribed in Chronic Kidney Disease patients.
- To compare the prescribing indicators with World Health Organization (WHO) indicators.
- To evaluate the rationale of the prescriptions obtained.

## MATERIALS AND METHODS

### Study Design

This is a retrospective observational study.

### Study Site

This study is conducted in Government District Headquarters Hospital, Virudhunagar, which is now upgraded to Government Medical College Hospital, Virudhunagar. All the cases were collected from the case sheets of General Medicine wards of this tertiary care hospital.

## RESULT

**Table – 2: Demographical classification of patients in study**

DEMOGRAPHICS		
AGE (Years)	GENDER	
	MALE	FEMALE
20-40	7	4
41-60	39	22
61-80	17	12
81-100	1	-

### Study Duration

The cases studied are collected from the hospital during 2018 February to 2020 March.

### Sample Size

A total of 102 Chronic Kidney Disease patients were included in the study.

### Inclusion Criteria

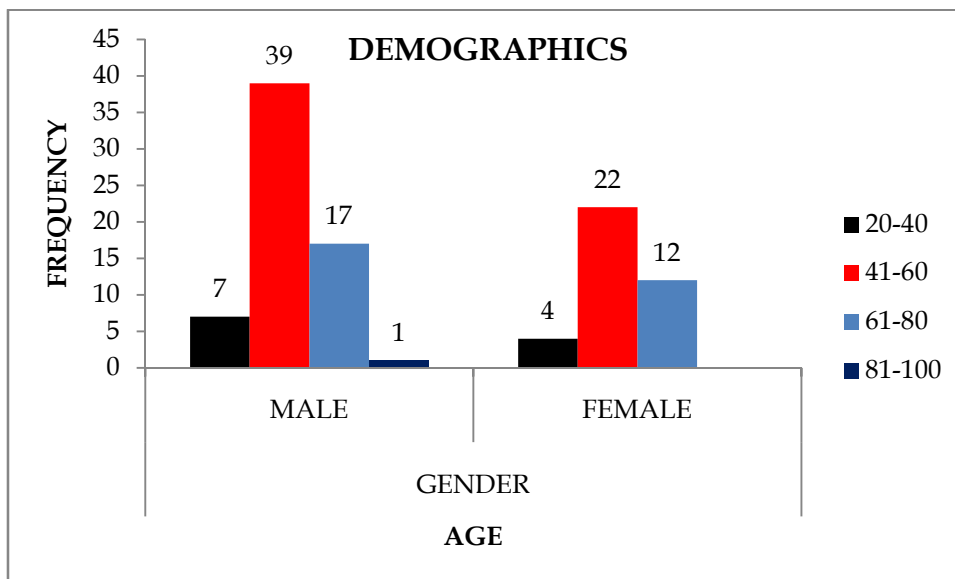
- Patients age >20 years of both male and female.
- Patients with associated co morbidities and disease conditions.
- Patients who are taking multiple drug regimen.

### Exclusion Criteria

- Patients of age <100 years.
- Patients who are not willing to undergo the study.
- Emergency and Intensive care unit patients.
- Death of patient before being discharged.

### Study Procedure

- Patient information's like age, gender, laboratory data and diagnosis along with medication information like name, dose, dosage and frequency of prescribed drugs were obtained from case sheets of the hospital.
- The data are analyzed on basis of WHO prescribing indicators, other standard treatment guidelines and protocols.



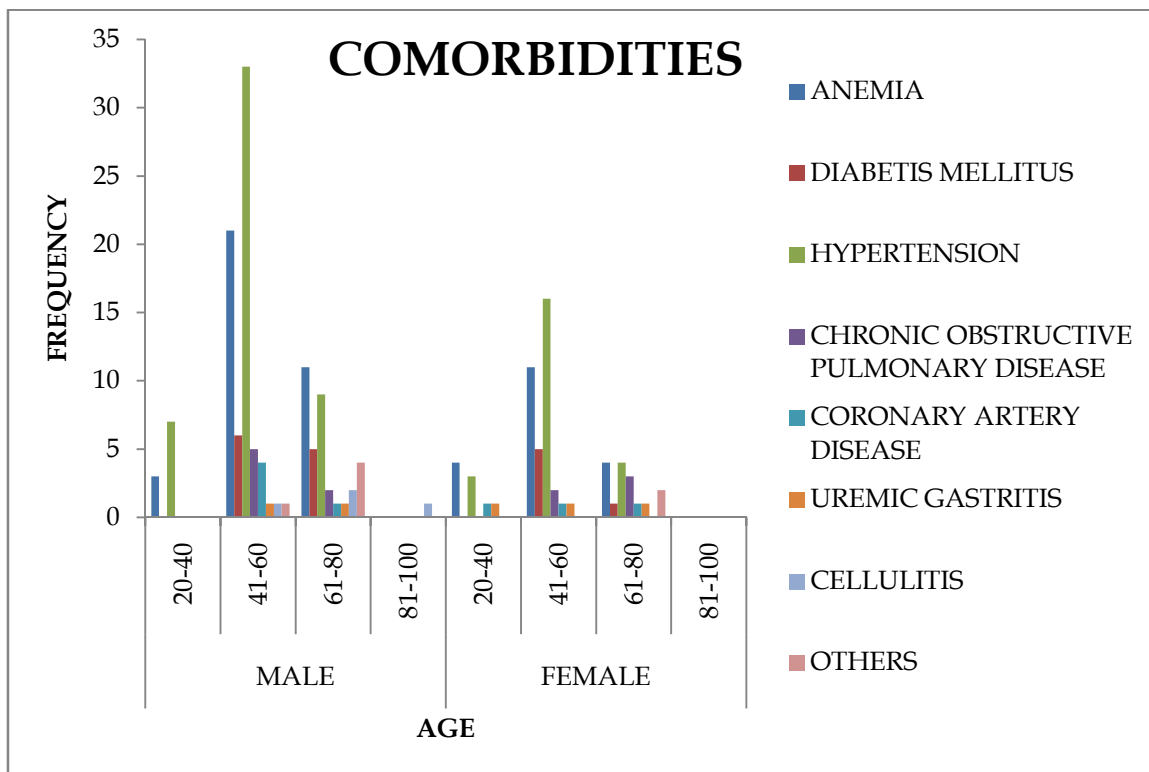
**Graph-1**

The demographic details of CKD patients; age and gender wise distribution of patients were demonstrated in **Table-2 and Graph-1**. It was observed that 62.74% of patients were male; patients of the age group 41-60 were predominant with 39 male and 22 female.

**Table – 3 Co-morbidities of CKD**

COMORBIDITIES	TOTAL	PERCENTAGE
ANEMIA	54	68.35
HYPERTENSION	72	91.14
DIABETES MELLITUS	17	31.48
CAD	8	10.13
COPD	12	15.19
UREMIC GASTRITIS	5	6.33
CELLULITIS	4	5.06
OTHERS	7	8.86

The co-morbidities associated with the study population were emphasized in Table-3 and Graph-2. Hypertension was found to be the most prevalent among other co-morbidities 91.14%.The prevalence of co-morbidities of the patients observed with respect to their age and gender was represented in Graph-2



Graph-2 Co-morbidities of CKD with respect to age and gender

The prescription indicators were given in Table-4. Totally we have analyzed 102 prescriptions having 895 drugs. The average number of drugs per encounter was 8.77. But the optimal value should range between 1.6 - 1.8. This may result in poly pharmacy and also serious adverse reactions.

Table-4 Prescription indicators analysis in ckd patients (29, 30)

PRESCRIPTION INDICATOR	FREQUENCY	VALUE	OPTIMAL VALUE
Total number of patients prescriptions analyzed		102	
Total number of drugs prescribed		895	
Average number of drugs per encounter		8.77	1.6-1.8
Percentage of drugs prescribed in generic name	795	88.83	100
Percentage of encounters with antibiotic prescribed	48	47.06	20-26.8
Percentage of encounters with injection Prescribed	85	83.33	13.4-24.1
Percentage of drug prescribed from national essential medicine list	832	92.96	100

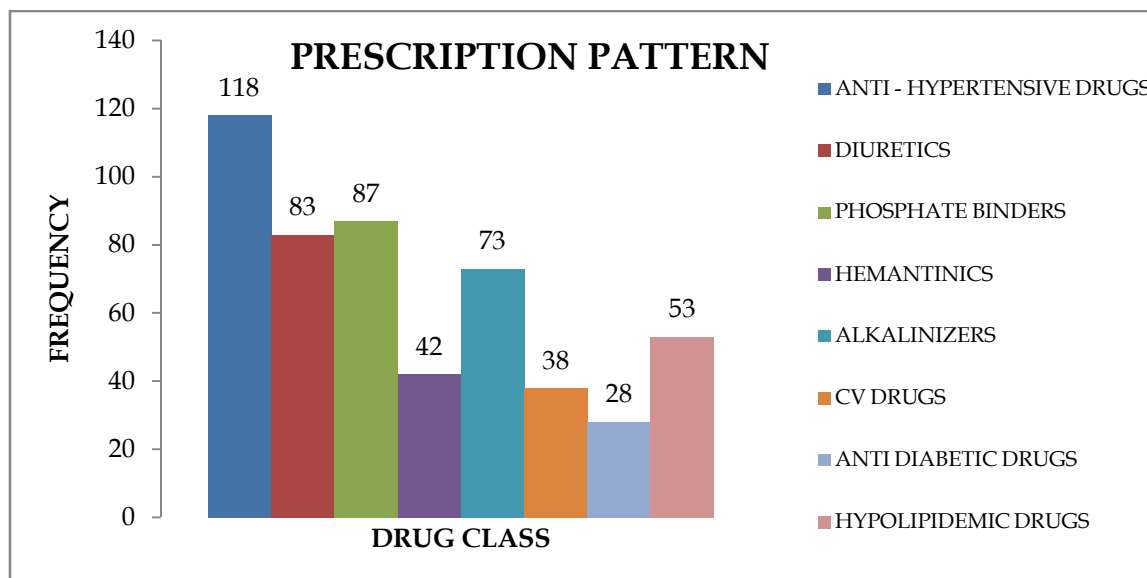
Table – 5 Prescription pattern of ckd patients in this study

CLASS	DRUGS	FREQUENCY
CARDIOVASCULAR DRUGS	<b>1. Antihypertensive Drugs</b>	
	<b>i) Calcium Channel Blockers</b>	
	Amlodipine	33
	Nifedipine	28
	Cilnidipine	5
	<b>ii) <math>\alpha</math>-Blockers</b>	
	Prazosin	6
	Clonidine	5
	Methyldopa	12
	<b>iii) <math>\beta</math>-Blockers</b>	
	Metoprolol	11
	Carvedilol	4
	Bisoprolol	3
	Atenolol	2
<b>iv) ACE Inhibitors</b>		
Enalapril	7	

	Ramipril	1
	<b>v) ARBs</b>	
	Telmisartan	1
	<b>2. Antiplatelet Drugs</b>	
	Aspirin	15
	Clopidogrel	10
	<b>3. Vasodilators</b>	
	Isosorbide Dinitrate	5
	Isosorbide Dinitrate + Hydralazine	6
	<b>4. Cardiotonic</b>	
	Digoxin	2
<b>DIURETICS</b>	Furosemide	76
	Torsemide	5
	Spirinolactone	2
	Calcium Carbonate	79
<b>PHOSPHATE BINDERS</b>	Calcium Acetate	5
	Sevelamar Hydrochloride	3
<b>ALKALINIZER</b>	Sodium Bicarbonate	73
<b>HEMANTINICS</b>	Ferrous Sulphate	37
	Iron Sucrose	1
	Epoetin- $\alpha$	4
<b>HYPOGLYCEMIC DRUGS</b>	Insulin	17
	Metformin	6
	Glipizide	4
	Glibenclamide	1
<b>HYPOLIPIDEMIC DRUGS</b>	Atorvastatin	53

The prescription pattern of the study population was portrayed in **Table-5 and Graph-3**.

The various classes of drugs provided in treating these Chronic Kidney Disease patients were listed effectively. From Graph-3, it has been clearly stated that calcium channel blockers was prescribed among anti-hypertensive's, followed by others phosphate binders, diuretics.



**Graph – 3**

## DISCUSSION

CKD is an abnormality in kidney structure or function present for more than 3 months, with implications for health generally characterized with reduced glomerular filtration rate (GFR)  $<60\text{ml}/\text{min}/1.73\text{m}^2$ . It is a risk multiplier of diseases like diabetes and hypertension. CKD is mostly

associated with other co-morbidities like anemia, COPD and bone related disorders. The CKD and its complications are treated effectively using some standard treatment guidelines like K/DOQI, JNC. This study aimed to evaluate the prescription pattern on CKD patients retrospectively. As per the literature review, there were difficulties in diagnosing the disease and following up for the standard treatment

guideline or protocol due to co morbidities and also in application of the treatment methods other than conventional therapy. Anti-hypertensive drugs were the most prescribed and their pattern should be assessed and evaluated in accordance with the standard treatment guidelines. There was a persistent clinical inertia in nephrology management of renal anemia. The assessment of socioeconomic status of the patients plays a major role in providing patient care. A delineated requisite for pertinent changes in current prescribing trends with WHO prescribing indicators would be necessary.

The retrospective observational study was carried out the prescription pattern and drug utilization on Chronic Kidney Disease was determined.

The demographic details of CKD patients; age and gender wise distribution of patients were observed in which 62.74% of patients were male and 37.26% were female; patients of the age group 41-60 were predominant with 39 male and 22 female. The different stages of CKD based on Glomerular Filtration Rate (GFR) were classified. It showed that majority of hospitalized patients were in stage-V of CKD. The distribution of staging of CKD in accordance with both the genders was enlisted, among this Stage-V of CKD was highly observed in 19 male and 11 female patients.

The co-morbidities associated with the study population were emphasized. In that hypertension was found to be the most prevalent among other co-morbidities 91.14%. The prevalence of co-morbidities of the patients observed with respect to their age and gender. In which hypertension was the most associated co-morbidity in age group 41-60 with 33 male patients and 16 female patients. Anemia was the second most prevalent co-morbidity having 21 male patients and 11 female patients in the same age group.

The prescription indicators were determined. Totally 102 prescriptions having 895 drugs were analyzed. The average number of drugs per encounter was 8.77, the optimal value should range between 1.6 - 1.8. This may result in poly pharmacy and also serious adverse reactions. The percentage of drugs prescribed in generic name was 88.83 (795) which should be 100. Because it can positively affects the cost minimization of drug regimens (31). Percentage of prescription with an antibiotic was 47.06; the standard value is 20.0 - 26.8. The percentage of prescription with an injection prescribed was 83.33; the reference value is 13.4 -

24.1. The percentage of drug prescribed from national list of essential medicines was 92.96, should be 100 to increase the rational prescribing pattern.

Antihypertensive drugs were the most prescribed, in which Calcium Channel Blockers were prescribed more than ACE inhibitors and ARB, but according to JNC-7, the first line agents are Angiotensin Converting Enzyme Inhibitors (or) Angiotensin –II Receptor Blockers and the Calcium Channel Blockers may increase the cardiovascular risks (32). Loop diuretics (Furosemide) were the most given diuretic drug. So serum potassium levels should be monitored carefully. Calcium Carbonate was the most administered phosphate binders and it is more safe and cost effective than Sevelamar hydrochloride (33). Anemia was the second most prevalent co morbidity and it has to be treated appropriately. The other cardiovascular drugs like Aspirin, Digoxin and Isosorbide dinitrates were used to treat other risks like Coronary Artery Disease.

In future, study can be further elaborated to determine the drug related problems associated with poly pharmacy and patient non-compliance. Pharmacotherapeutic Drug Monitoring can also be carried out to individualize the drug regimen for the patients having drug related problems due to poly pharmacy. As we adapt to changes in the health care, it will remain important to follow these patients for changes in issues impacting practice to preserve access for patient care.

## CONCLUSION

The observed prescription pattern shows that antihypertensive drugs are prescribed more commonly for the patients, in which Calcium Channel Blockers are given frequently than ACE inhibitors or Angiotensin – II Receptor blockers. The prescribing indicators deviate from WHO optimal values which should be rectified to improve the standards of treatment and patient care. This study intends the incorporation of standard treatment guidelines and protocols for the patients. Patient counseling would be expedient for the health prospective of the patients; a better counseling would alleviate the clinical conditions of the community. These can be made possible with the help of a clinical pharmacist which will drastically improve the quality of patient care.

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