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A Study on Prescribing Pattern of the Drugs in Chronic Kidney Disease; a Tertiary Care Hospital

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ABSTRACT
Chronic kidney disease (CKD), characterized by progressive decline in glomerular filtration rate (GFR), is a major public health issue worldwide and is associated with high morbidity and mortality. India, with its huge diabetic and hypertensive population, is becoming a major reservoir of CKD. The therapy of CKD andendstagerenal disease(ESRD) is very expensive and out of reach of more than 90% of patients in India. Appropriate drug selection for patients with CKD is important to avoid unwanted drug effects and to ensure optimal patient outcomes.

KEYWORDS: Chronic kidney disease; creatinine; comorbidities; medication; prescribing patterns.

I. INTRODUCTION

[1]Kidney is the major organ for maintaining homeostasis of fluid and electrolytes and in particular, plays an important role in the disposition of many drugs. Chronickidney disease affects renal drug elimination and other pharmacokinetic processes involved in drug disposition (e.g., absorption, drug distribution, non-renal clearance [metabolism]). About half of all drugs or their metabolites are excreted by the kidneys, and 30% of all adverse effects of medication have a renal cause or a renaleffect.

KDIGO guidelinesfocus on topicsrelatedto the preventionor management of individuals with kidney diseases. Criteriaused by KDIGO for topic prioritization include the burden of illness based on prevalence and scope of the condition or clinical problem; amenability of a particular condition to prevention or treatment and expected impact; existence of a body of evidence of sufficient breadth and depth to enable the development of evidence-based guidelines; potential of guidelines to reduce variationsin practices, improve health outcomes, or lower treatmentcosts.

The Kidney Disease: Improving Global Outcomes (KDIGO) 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease (CKD) serves to update the 2002 KDOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification, and Stratification following a decade of focused research and clinical practice in CKD. The document aims to provide state-of-the-art guidance on the evaluation, managementandtreatmentforallpatientswithCKD.Specifically,theguideline retainsthedefinitionofCKDbutpresentsanenhancedclassificationframework for CKD; elaborates on the identification and prognosis of CKD; discusses the management of progression and complications of CKD; and expands on the continuum of CKD care: timing of specialist referral, ongoing management of peoplewithprogressive CKD,timing of the initiation of dialysis,and finally the implementation of a treatment program which includes comprehensive conservative management. The development of the guideline followed an explicit process of evidence review and appraisal.

According to kidney disease improving global outcomes guidelines (KDIGO), chronickidneydiseaseisdefinedasabnormalitiesofkidneystructureorfunction, present for greater than 3 months with implications for health. CKD is classified based on cause, GFR category (G1-G5), albuminuria category (A1-A3) abbreviated asCGA.

Based on GFR, the KDIGO classifies chronic kidney disease as G1 (normal or high >90 ml/min/1.73 m^2), G2 (mildly decreased 60-89 ml/min/1.73 m^2), G3a (mildly to moderately decreased 45-59 ml/min/1.73 m^2), G3b (moderately to severely decreased 30-44 ml/min/1.73 m^2), G4 (severely decreased 15-29 ml/min/1.73 m^2), G5 (kidney failure < 15 ml/min/1.73 m^2).Based on albuminuria, KDIGO classifies chronic kidney

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disease as A1 (normal to mildly increased <30 mg/g or 3 mg/mmol), A2 (moderately increased30-300 mg/g or 3-30 mg/mmol), A3 (severely increased >300 mg/g or >30mg/mmol).

II. MATERIALS AND METHODS

STUDY DESIGN: The study involves both Prospective and Retrospective Observational study.

STUDY SITE: This study is going to be conducted at Mallige hospital. Mallige hospital is a multispecialty tertiary care hospital with over 126 beds conveniently located in the heart of Bengaluru, the capital of Karnataka state of India. Mallige hospital consist of many departments like Nephrology, Cardiology, Radiology, General Medicine, Surgical, Pediatrics, Obstetrics & Gynecology, etc.

STUDY DURATION: The study was conducted for a duration of 6 months from January 2021 to June 2021.

STUDY METHOD: Patient data collection form, Patient inform consent form

SAMPLE SIZE: The study was limited for a sample of 150 based on the time schedule allotted for the project including further circumstances.

STUDY CRITERIA

Inclusion Criteria: All adult patient having the age of 18 years and above with chronic renal dysfunction with creatinine clearance of less than 50 ml /min.

Exclusion Criteria: Pregnantwomen,patients who aren't willing to participate in thestudy, patients with GFR > 50 ml/min, patients who are not receiving any pharmacologicalagents, out-patientdepartment.

SOURCE OF DATA

Prescription of patient / medicationchart, Patient data collectionform, Patient casesheet, Laboratorydata, Investigationaldata, Nursing and doctorsnote

STUDY METHOD

Preparation of Informed Consent Form:

Informed consent form was prepared in English and Kannada and same were used. Prior to the selection of subjects, the consent form was orally explained to the participants before filling it and non-verbally by taking help of caregiver (when needed) and staffs who are well known to the patients and made them understood. In the study, only the contributors desired to fill ICF were included.

Data(s) Collection: Data(s) was collected using data collection form.

III. RESULTS

a) DIALYSIS DISTRIBUTION OFPATIENTS

Out of 150 patients included in the study, 138 patients (92%) were undergoing Hemodialysis and 12 patients (8%) were non-Hemodialysis patients.

Table 1: Dialysis distribution of patients

Dialysis distribution	No. of patients	Percentage
HD Patients	138	92%
Non-HD Patients	12	8%
Total	**150**	**100%**

b) AGE DISTRIBUTION OFPATIENTS

Out of 150 patients, majority of patients 78 HD patients (56.52%) and 5 non patients (41.66%) belong to age group of 61-80 years.

Table 2: Age distribution of patients

Age in Years	No. of HD Patients	Percentage	No. of non HD patients	Percentage
18-40	8	6%	2	17%
41-60	31	22%	1	8%

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61-80	78	56.52%	5	41.66%
>80	21	15.21%	4	33.33%

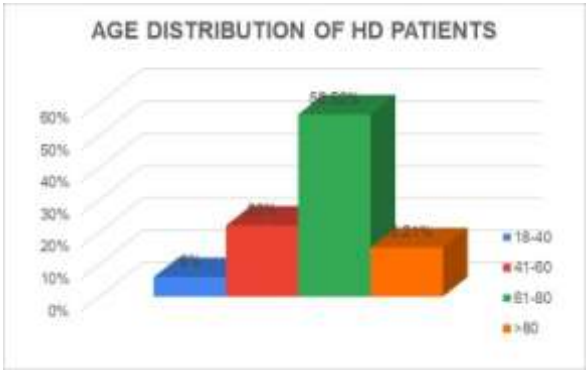

Figure 1

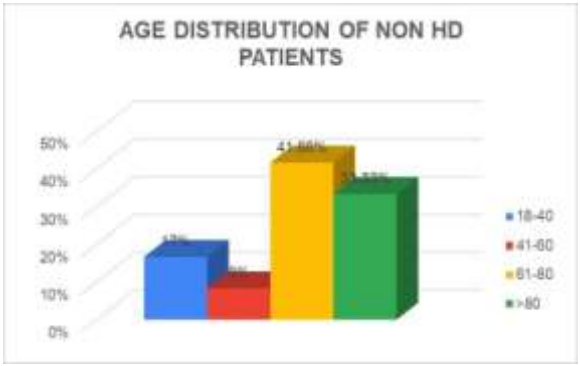

Figure 2

c) GENDER DISTRIBUTION OFPATIENTS

Out of 150 patients included in the study, 92 Hemodialysis patients (67%) and 6 non-Hemodialysis patients (50%) were male and 46 Hemodialysis patients (33%) and 6 non-Hemodialysis patients (50%) were female. The number of males was comparatively high in Hemodialysis cases and equal in non-Hemodialysis cases.

Table 3: Gender distribution of patients

Gender	No. of HD patients	Percentage	No. of non-HD patients	Percentage
Male	92	67%	6	50%
Female	46	33%	6	50%
Total	138	100%	12	100%

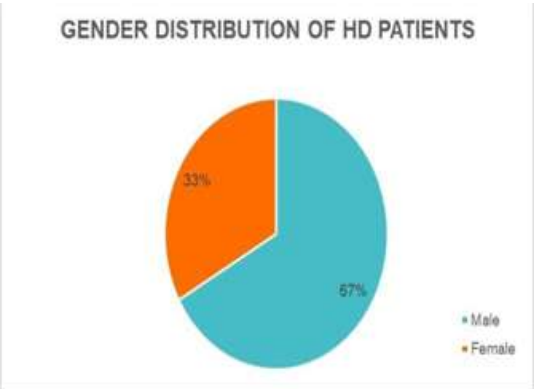

Figure 3

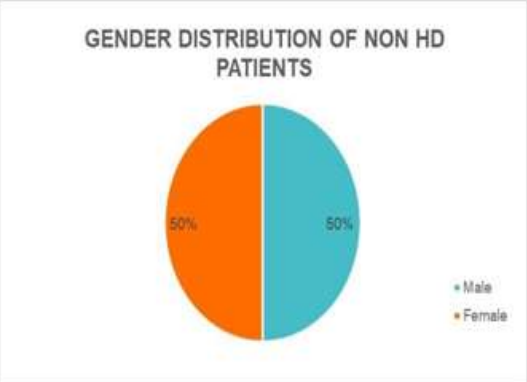

Figure 4

d) STAGE DISTRIBUTION OFPATIENTS

Out of 150 patients, majority of patients 85 (56.66%) belong to Stage 5 CKD.

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Table 4: Stage distribution of patients

Stage	No. of patients	Percentage
Stage 1	0	0%
Stage 2	1	0.66%
Stage 3	31	20.66%
Stage 4	33	22%
Stage 5	85	56.66%
Total	150	100%

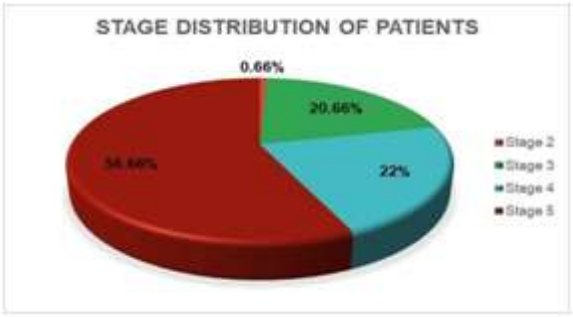

Figure 5

e) GFR CLASSIFICATION BASED ON KDIGOGUIDELINE

According to KDIGO guideline, we found out that G5 (52.17% in HD and 50% in non-HD) has greater percentage distribution in both HD and non-HD

Table 5: Percentage distribution of GFR (ml/min/1.73m^2) in HD and non-HD patients

GFR Range	HD	Percentage	NON-HD	Percentage
G1	0	0%	0	0%
G2	0	0%	0	0%
G3a	2	1.449%	1	8.33%
G3b	23	16.67%	5	41.67%
G4	41	29.71%	0	0%
G5	72	52.17%	6	50%

f) COMORBID CONDITIONS OFPATIENTS

In CKD patients, the most common comorbid conditions observed were hypertension, diabetes mellitus, ischemic heart disease, cerebrovascular accident, thyroid illness, COPD/ asthma/ bronchitis and kidney disease. Among these, hypertension and diabetes mellitus were comparatively high in both HD and non-HD cases.

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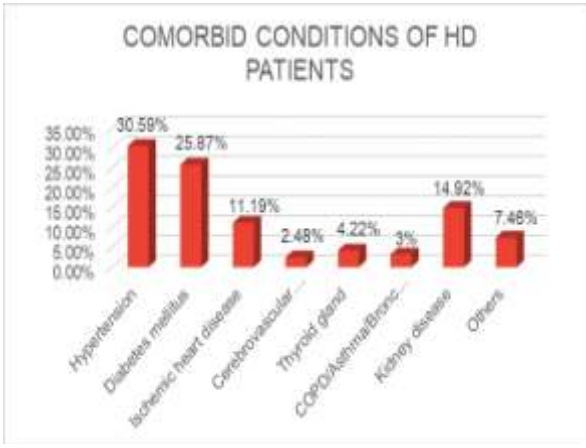

Figure 6

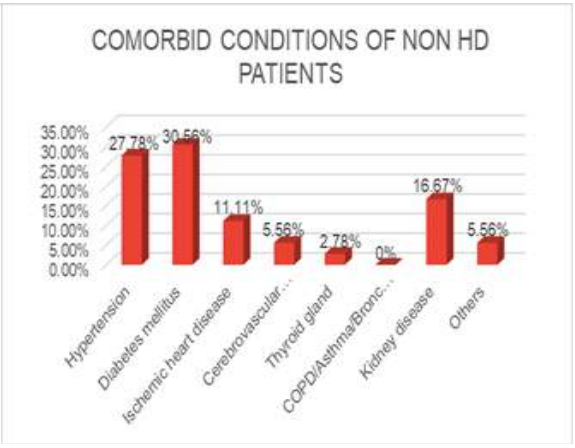

Figure 7

g) DISTRIBUTION OF LENGTH OF STAY INHOSPITAL

The average length of stay of patients in the hospital was found to be between 1-5 days.

Table 6: Length of stay in hospital

Length of stay	No. of patients	Percentage
1-5	98	67.58%
6-10	36	24.82%
11-15	9	6.2%
>16	2	1.37%

Figure 8

h) NUMBER OF MEDICATIONS PRESCRIBED IN STUDY POPULATION

Out of 150 prescriptions, the number of prescriptions in HD patients were 138 (92%) and non-HD patients were 12 (8%). The total number of drugsprescribed in HD patients were 1811 and non-HD patients were 145. Average number of drugs per prescription in HD patients were 13.12 and non-HD patients were 12.08.

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i. DISTRIBUTION OF CARDIOVASCULAR DRUGS

Table 7: Distribution of cardiovascular drugs

CV drugs	HD	Percentage	Non-HD	Percentage
Anti- hypertensive	199	45%	20	51%
Anti- arrhythmic	39	9%	3	8%
Anti-platelet	40	9%	1	3%
Anti-coagulant	37	8%	1	2%
Anti- hyperlipidemic	14	3%	3	8%
Other CV drugs	117	26%	11	28%

ii. MOST COMMONLY PRESCRIBED CARDIOVASCULAR DRUG IN EACH CLASSAnti-hypertensive drugs: The highest prescribed anti-hypertensive drug was Lasix (12.33% in HD and 12.82% in non HD) given in the form of intravenous (7.84% in HD and 10.25% in non HD) and oral (4.48% in HD and 2.56% in non HD) preparations followed by Amlong (8.52% in HD and 7.69% in non HD) and Cilacar (3.13% inHD).

Anti-coagulant drugs: Clexane (4.93% in HD) was the most widely prescribed anti-coagulant drug.

Anti-hyperlipidemic drugs: Among the anti-hyperlipidemic drugs, Atorva (0.89% in HD) is themost prescribed drug.

Anti-arrhythmic drugs: Cordarone (6.27% in HD) is the most frequently prescribed anti-arrhythmic drug.

Anti-platelet drugs: The highest prescribed anti-platelet drug was ecosprin (2.46% in HD)

Other cardiovascular drugs: Isolazine (3.36% in HD) which belongs to a class of drug called vasodilator is the most commonly prescribed drug.

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i) CORRELATION

Table 8: Correlation between total number of cardiovascular drugs and number of HD patients.

T**Correlations**			NO. OF HD PATIENTS
TOTAL NO. OF CV DRUGS	Pearson Correlation	1	.314**
	Sig. (2-tailed)		<.001
	N	138	138
NO. OF HD PATIENTS	Pearson Correlation	.314**	1
	Sig. (2-tailed)	<.001	
	N	138	138

**. Correlation is significant at the 0.01 level (2-tailed).

From the table no.8, the correlation coefficient between total number of cardiovascular drugs prescribed and number of HD patients is having positive correlation as r=0.314 and correlation coefficient is significant at the p<0.01 obtained by 2-tailed test. (If the P value is <0.05 it is said to be significant).

j) DRUG INTERACTIONS

Out of 150 cases, drug-drug interactions were found in 25 cases and percentage was16.67%.

IV. DISCUSSION

[2]In this study, a total of 150 patients were reviewed diagnosed with any stagesof CKD. 138 of them were undergoing HD (92%) and 12 were non-HD (8%) patients.Majorityofpatients,HD92(67%)andnon-HD6(50%)weremaleand 46 (33%) HD patients and 6 (50%) non-HD patients were female. The results of these studies revealed male predominance which was similar to a study conducted by Sourav Chakraborty et.al, which also shows male predominance ofHDinCKDpatients.Themeanserumcreatininelevel

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wasfoundtobe4.79 mg/dl.

[3]Out of 150 patients, majority of patients 78 (56.52%) HD patients and 5 (41.66%) non-HD were belonging to age group of 61-80 years. Majority of patients 85 (56.66%) were in stage 5 CKD. Among all the comorbid conditions, hypertension and diabetes mellitus was found to be most common in both HD (30.59% and 25.87% respectively) and non-HD patients (27.78% and 30.56% respectively). These results were similar to a study conducted in a tertiary care hospital by Buddhavarapu Murthy et.al, where large number patient was suffering from hypertension and diabetes mellitus.

[4]Out of 150 prescriptions, the number of prescriptions in HD patients were 138 and non-HD patients were 12. The total number of drugs prescribed in HD patientswere1811andnon-HDpatientswere145.Averagenumberofdrugsper prescription in HD patients were 13.12 and non-HD patients were 12.08 which indicates polypharmacy. Average number of drugs per prescription and polypharmacy results were similar to a cross-sectional study conducted by Viswam K Subeesh et.al. Polypharmacy has been defined as the use of 5 or moremedicationstoonepatientatatime.However,inviewofthecomplexnature and coexisting comorbidities of CKD, some researchers suggest the use of more than 9 drugs at a time to be considered polypharmacy.

From this study, out of 150 patients, 25 (16.67%) major drug interactions were found and average drug-drug interaction per prescription was 0. 1667.One ofthe drug interactions from our study was Clarithromycin+Atorvastatin which was supported by the article "Interaction potential between clarithromycin and individual statins-A systematic review conducted by Mette Marie Hougaard Christensen et. al. Polypharmacy is a likely contributor to the potential drug- drug interactions perprescription.

We did Pearson correlation using IBM SPSS Statistics 28.0.0.0 (190). We proved that correlation is significant at 0.01 level as the P value obtained by 2- tailed test is <.001 which is highly significant.

Clinical pharmacist works directly with medical professionals and patients usually in a medical center like hospital. The involvement of apharmacist at the point of prescription of a drug by a physician is the most effective. The time for decision-making is very important. Physicians and pharmacists can work togethertohavesafedrugprescribingthatcanbecomplexandrequiresstepwise approach to ensure effectiveness, minimize further damage and prevent drug nephrotoxicity. Our study is limited by its sample size, unicentric nature and hospital-based evaluation. However, it has generated a profile of drug use in Indian CKD patients that can serve as the basis for future comparisons. It has also identified some areas of concern such as polypharmacy and incidence of potential drug-drug interactions. There is a need for exploring these issues in detail through future drug-use surveys in CKDpatients

V. CONCLUSION

The prevalence of chronic kidney disease is increasing and polypharmacy is common. Hence, there is a need to monitor the prescribing pattern of drugs in those patients to avoid the adverse effects, to reduce the length of stay in the hospital and to control the unnecessary cost ofmedications. In this study, most of the patients were in stage five CKD and most of them were undergoing hemodialysis. The number of male patients were comparatively higher than females. Most of the CKD patients belong to the age group of 61-80years. Drugs were prescribed for various comorbid conditions like hypertension, diabetes mellitus, ischemic heart disease, cerebrovascular accident, thyroid disorder, COPD/asthma/bronchitis, kidney disease and others. Among these comorbidconditions,hypertensionanddiabetesmellituswerecomparatively high in both HD and non-HDpatients.

Cardiovasculardrugswerethemostprescribeddrugbothin HDandnon-HD cases followed by antibiotic and vitamin and nutritional supplements. Anti- hypertensive was most commonly prescribed cardiovasculardrug. Drug-related problems (DRP) such as drug-drug interactions were seen which can result in an increase in morbidity and mortality, as well as an increase in the cost ofhealthcare. Based on KDIGO guideline, most of the patients were categorized into G5 (kidney failure <15ml/min/1.73m^2). Clinical pharmacists who have developed confidence and skill in using pharmacotherapeutics as a clinical tool, will be able to participate in this interdisciplinary approach to individualized patientcare.

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