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ASSESSMENT OF PRESCRIBING PATTERNS AND DOSE ADJUSTMENTS IN PATIENTS WITH KIDNEY DISEASE

Dr. Beulah Milton*[1], Mohammad Fathollahi[2] and Ava Pourghannad[3]

[1]HOD and Professor, Department of Pharmacy Practice, R R College of Pharmacy.
[2,3]Pharm D. Student, R R College of Pharmacy.

***Corresponding Author: Dr. Beulah Milton**
HOD and Professor, Department of Pharmacy Practice, R R College of Pharmacy.

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ABSTRACT
Introduction: Chronic kidney disease (CKD), characterized by progressive decline in glomerular filtration rate (GFR), is a major public health issue worldwide. There is a lack of adequate data of quality of life in Indian population on the impact of therapeutic management of CKD patients**.** Earlier studied of health-related quality of life (HRQOL) in patients with CKD have focused on the end stage renal disease (ESRD) population. Objectives: To assess the prescribing pattern and dose adjustment of drugs in patients with kidney disease in a tertiary care hospital. To determine the rate of drugs requiring dosage adjustment in patients with renal failure disease according to available guidelines. Methodology: This observational study was carried out In-patient Department. It is hospital based retrospective and prospective observational study. The sample size of the study is 100 patients admitted in Sapthagiri Institute. Results: Out of 100 patient 45 (45%) patients was undergoing hemodialysis and 55 (55%) patients were non-dialysis patients. In the stage wise category of CKD, majority of patients 59 (59%) belonged to stage 5 CKD. In co-morbid condition of patient's, it was observed that hypertension 79 (42.02%). The tendency of polypharmacy with maximum number of prescriptions was having 7 (22%). Conclusion**:** In this study most of the patients were in stage V CKD and were not undergoing haemodialysis. This study reveals that most of the drugs were dosed appropriately. Drug-related problems can result in an increase in morbidity and mortality.

KEYWORDS: Chronic Kidney disease, CKD, glomerular filtration rate (GFR), kidney disease.

INTRODUCTION
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. According to World Health Organization (WHO), global burden of kidney disease contributes to nearly 8500,000 deaths/year along with urinary tract problems According to the kidney disease Outcomes Quality Initiative (K/DOQI) of the national kidney Foundation (NKF) defined CKD as a damage to the kidney or a decrease in the glomerular filtration rate (GFR) of <60ml/min/1.73 m2 for a period of three months or more. Diabetes and hypertension have been reported to be the most common risk factors for CKD. India with its huge diabetic and hypertensive population, is becoming major reservoir of CKD. The therapy of CKD and end stage renal disease (ESRD) is very expensive and out of reach of more than 90% of patients in India. CKD is usually associated with various complications and comorbidities. Secondary hyperparathyroidism and associated homeostatic control of serum calcium, phosphate and vitamin D is a critical issue in patients with CKD. Altered mineral metabolism contributes to bonedisease, cardiovasculardisease and other clinical problems in these patients. CKD is a progressive loss in kidney function over a period of time (several months to years).Severity of CKD is classified into 5 stages with stage 1being mild with few symptoms and stage 5 being the severe with poor life expectancy in untreated condition and based on its cause ,recent guidelines reclassified CKD into GFR (glomerular filtration rate) category (G1 ,G2 ,G3a, G3b,G4 and G5) and albuminuria category (A1,A2,A3). The number of renal failure patients, in need of dialysis and kidney transplantation has increased tremendously, due to which developing countries like India, with resource limited setting have a high mortality rate. Dialysis outcome study shows, uncontrolled serum concentration of phosphorous, calcium, potassium, sodium, urea and creatinine. Frequent adjustment in medications during dialysis days, unstable nature of disease, restricted lifestyle and prescription of huge number of medications make these patients at high risk of developing adverse drug events due to drug-drug interactions, suboptimal action and non-adherence to treatment plans.

MATERIALS AND METHODS

Duration of study
The study was conducted for a period of 6 months.

Site of study
The study was conducted on Sapthagiri General Medical Hospital.

Study design
This study was a hospital based observational study.

Sample size
100 patients admitted in Sapthagiri Institute of Medical Science and Research Center.

Study criteria
Inclusion criteria
All patients with chronic renal dysfunction who admitted to the hospital and prescribed with medications that are renally eliminated.

Exclusion criteria
- Patients who were not co-operative.
- Discharged patients.
- Reports were not able to collect.
- Patients with GFR >90 ml/min.
- Out Patients

Study tool
Data collected by using a self-design data collection form which consist of details like patients demographic details , pas medication history, co-morbid conditions , information regarding dialysis , stage of CKD , lab investigation and therapeutic data including name, dose , duration and frequency of drugs.

Study procedure
- All in patients with chronic renal dysfunction who admitted to the hospital and prescribed with medications that are renally eliminated were enrolled into study.
- The data will collect in a proforma which included the demographic details, past medication history, co-morbid condition, and information regarding dialysis, stage of CKD, lab investigation and therapeutic data including name, dose, duration and frequency of drugs.
- The entire data collected will entered in Microsoft excel sheet for analysis of results later.

Statistical analysis: Statistical analysis was performed using MS excel and result was statistically analyzed using appropriate statistical method (MS excel).

RESULTS

This study was conducted for a period of 6 months; the study included 100 patients from IP department of Sapthagiri Institute of Medical Science, a tertiary care hospital in Bangalore. This study was conducted for a period of 6 months; the study included 100 patients from IP department of Sapthagiri Institute of Medical Science, a tertiary care hospital in Bangalore.

Patient Demography Based on Gender
Out of 100 patients included in the study 54 (54%) were male and 46 (46%) were females [Table 1]. 45 (45%) patients were undergoing hemodialysis where 25(46.29%) were male and 20 (43.47%) females and 55 (55%) patients were non-dialysis patients where 29(53.7%) male and 26 (56.52%) were females. The number of males was comparatively high. [Table 2].

Table 1: Patient demography based on gender.

Gender	No of patients	Percentage
Male	54	54%
Female	46	46%
Total	100	100 %

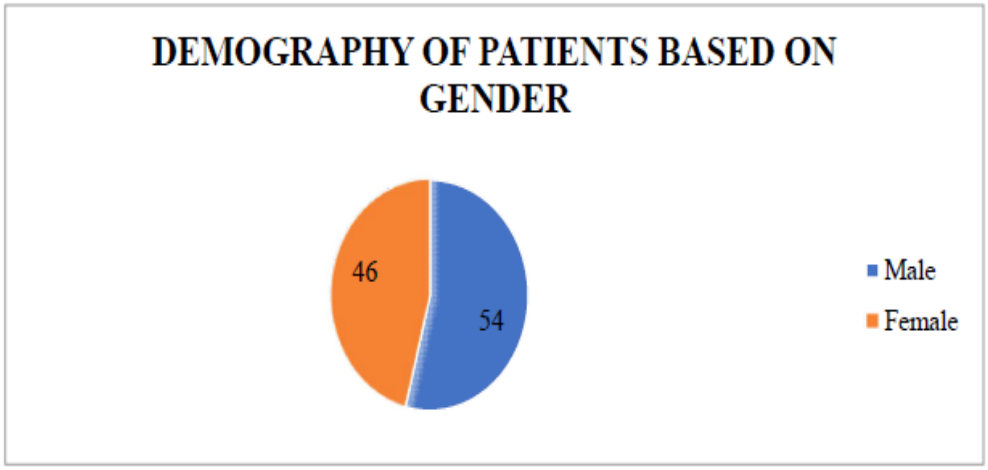
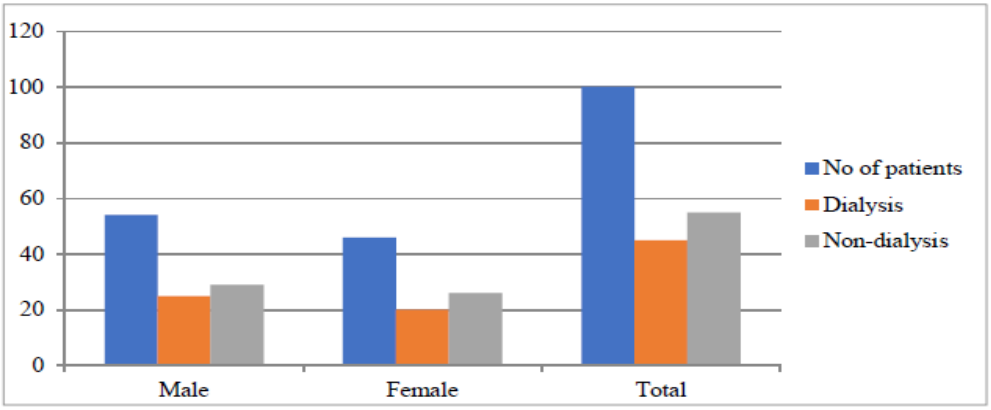


Table 2: Patient Demography Based on Gender; HD and Non-HD Patients.

	Male	Female	Total (n=100)
No of HD patients	25	20	45
No of Non-HD patients	29	6	55



Age wise Demography of Patients

Patients were categorized according to their age group. Out of 100patients majorly 43 (85.42%) were found in the age group between 41-60, followed by 40 (80.83%) in the age group between 61-80 years, 9 (17.94%) in the age group between 18-40 years, 6(11.42%) in the age groupabove 81 and 2(4.34%) in the age group below 18 years. [Table 3]

Table 3: Patient Demography With Respect To Their Age Group.

Age distribution in years	No of male Patient	No of Female Patients	Total No of Patients
<18	0	2 (4.34%)	2 (4.34%)
18-40	5 (9.25%)	4 (8.69%)	9 (17.94%)
41-60	25 (46.29%)	18 (39.13%)	43 (85.42%)
61-80	19 (35.18%)	21 (45.65%)	40 (80.83%)
81<	5 (9.25%)	1 (2.17%)	6 (11.42%)

CKD Stage wise demography of patients

Out of 100 patients, majority of patients 59 (59%) belongs to stage 5 CKD where in that 32 (59.25%) were male and 27 (58.69%) female. [Table 4]

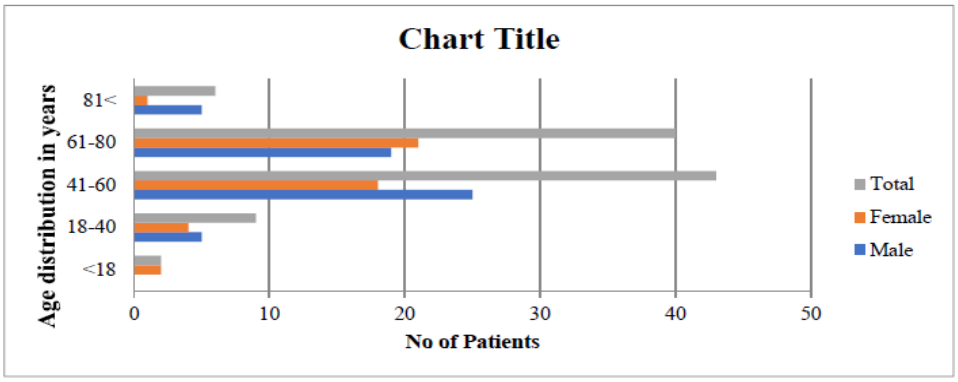
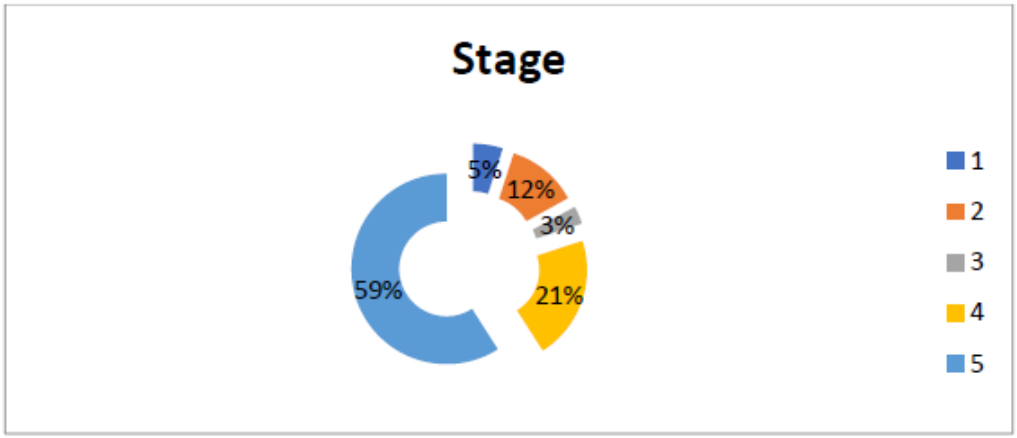


Table 4: CKD Stage wise demography of patients.

Stage	Male	Female	Total	Percentage
1	2	3	5	5%
2	5	7	12	12%
3	2	1	3	3%
4	13	8	21	21%
5	32	27	59	59%

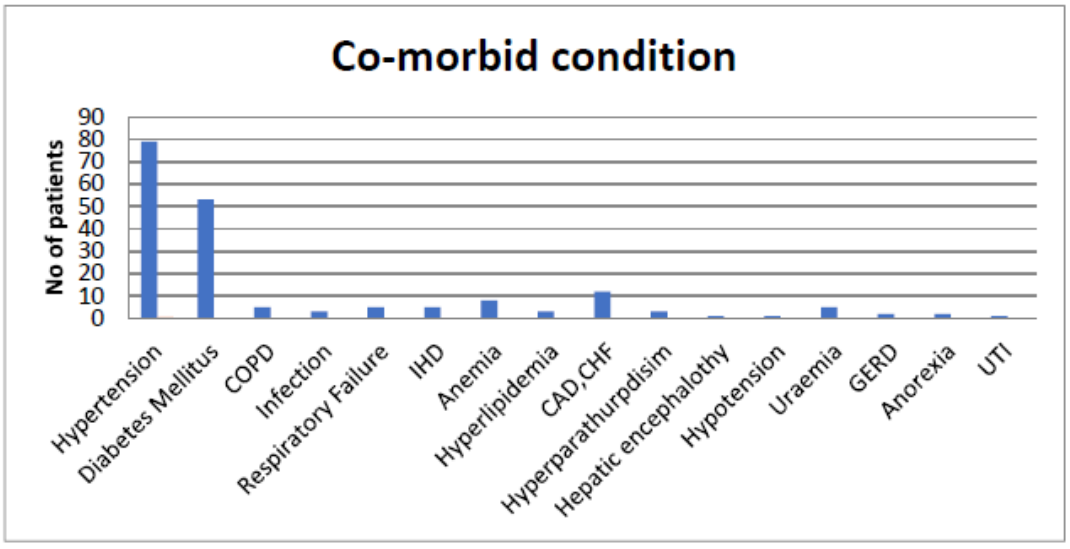


Co-Morbid Conditions of CKD Patients

Out of 100 patients enrolled in the study, it was observed that hypertension 79 (42.02%) followed by Diabetes Mellitus 53 (28.19%) and Cardiovascular disease or Cognitive Heart Failure 12 (6.38%). [Table 5]

Table 5: Co-morbid conditions of CKD patients.

Co-Morbid Condition	No of Patients(n=188)	Percentage
Hypertension	79	42.02%
Diabetes Mellitus	53	28.19%
COPD	5	2.66%
Infection	3	1.60%
Respiratory Failure	5	2.66%
IHD	5	2.66%
Anemia	8	4.26%
Hyperlipidemia	3	1.60%
CAD,CHF	12	6.38%
Hyper parathyroidism	3	1.60%
Hepatic encephalopathy	1	0.53%
Hypotension	1	0.53%
Uremia	5	2.66%
GERD	2	1.06%
Anorexia	2	1.06%
UTI	1	0.53%

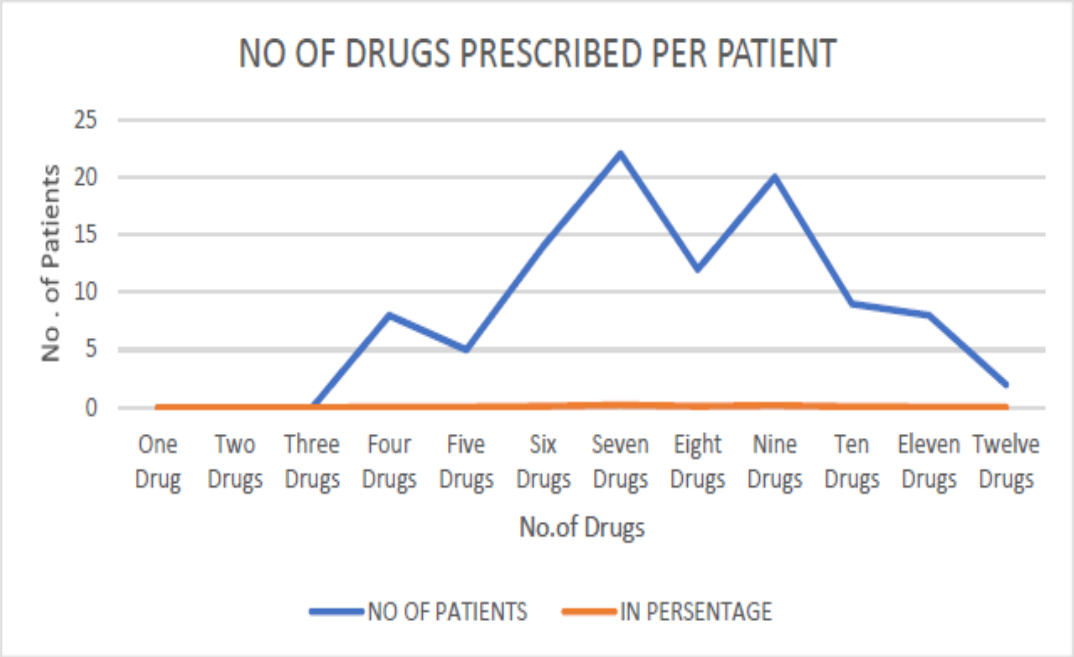


Total Number of Drugs Prescribed Per Patient

This result showed tendency of polypharmacy with maximum number of prescription were having 7 (22%). [Table 6]

Table 6: Total Number of Drugs Prescribed Per Patient.

THERAPY PATTERN	NO OF PATIENTS	IN PERSENTAGE
One Drug	0	0%
Two Drugs	0	0%
Three Drugs	0	0%
Four Drugs	8	8%
Five Drugs	5	5%
Six Drugs	14	14%
Seven Drugs	22	22%
Eight Drugs	12	12%
Nine Drugs	20	20%
Ten Drugs	9	9%
Eleven Drugs	8	8%
Twelve Drugs	2	2%

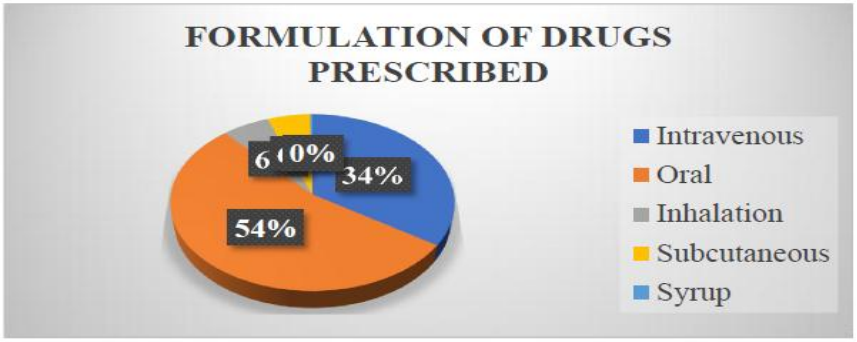


Formulation of Total Number of Drugs Prescribed

Tablets were the major formulation used for administration of drugs in this study (54.19%) followed by Intravenous injection (34.29%), Inhalation (5.89%), Subcutaneous (5.37%) and Syrups (0.26%). [Table 7]

Tablet 7: Formulation of total number of drugs prescribed.

Formulation	No of Drugs (n=764)	Percentage
Intravenous	262	34.29%
Oral	414	54.19%
Inhalation	45	5.89%
Subcutaneous	41	5.37%
Syrup	2	0.26%



Adverse drug reactions of most commonly prescribed drugs

Some drugs might show an adverse drug reaction, some reactions can cause serious damage to patients and needs to be taken care by health care providers. [Table 8]

Table 8: Adverse drug reactions of most commonly prescribed drugs.

SN	Name of drug	Adverse Drug Reaction
1	Amlodipine	Σ Swelling of legs &ankle Σ Flushing Σ Arrhythmia
2	Furosemide	Σ Diarrhea Σ Nausea Σ Vomiting
3	Piptaz	Σ skin rash Σ pruritus Σ allergic reaction
4	Ceftriaxone	Σ headaches Σ reduction of renal function Σ pseudomembranous colitis

DISCUSSION

Diabetes and hypertension have been reported to be most common risk factors for CKD. India, with its huge diabetes and hypertension population, is becoming major reservoir for CKD. The therapy of CKD and end stage renal disease (ESRD) is very expensive and out of reach of more than 90% of patients in India. This study was conducted for a period of 6months, the study included 100 patients from IP department of sapthagiri Institute of Medical Science. All patients who was admitted to the hospital with chronic renal dysfunction with GFR not more than 90 ml/min/1.73m2 and prescribed with the medications that are renally eliminated were included in this study. In this study, majority of the patients belong to the age group 41-60 years (46.29%) which was similar to the study conducted by, Ahsan Salaam, Imran Masood, where they observed that the majority of the patients belongs to the 48-64(±16.82) years. In this study, a total of 100 cases were reviewed, 45of them were undergoing haemodialysis (45%) and 55 were non haemodialysis (55%) patients. Majority of patients, HD 25(55.5%) and Non-HD patients 29(52.72%) were male and 20 (44.44%) HD patients and 26 (47.27) Non-HD patients were female.

Out of 100 patients, majority of patients 59 (59%) belongs to stage 5 CKD. Among all the co- morbid conditions hypertension was found to be the most common (42.02%) in both haemodialysis and non-haemodialysis patients. Average number of drug per person is an important index of prescription audit. The WHO recommends that the average number of drugs per prescription should be less than two. Mean number of drugs per prescription should be kept as low as possible. In this study results showed that tendency to polypharmacy with maximum number of prescriptions were having 7 drugs (22%). it could be due to in patient nature of study.Oral dosage forms were the major formulations used for administration of medication in CKD patients (54.19%). The main reason is it maybe because of easer for patients to use tablets. WHO recommends lesser use of injection as it helpful in reducing the cost of treatment and its disadvantages. The total number of prescribed in HD patients were 383 (52.01%) and in NON- HD patients were 352 (47.89%). Number of drugs dosed appropriately in HD and NON-

HD patients were 318 and 310 respectively.

From this study it is evident that, out of 735 drugs 318 (50.63%) were dosed appropriately in HD and in NON-HD it was 310 (49.36%) whereas 65 drugs (16.97%) in HD and 42 drugs (11.93%) in NON-HD were dosed inappropriately. The extend of inappropriate dosing was comparatively similar to the published literature. This may be due to increase awareness of clinicians regarding our renal dosing in our settings. According to WHO guidelines for prescribing pattern in patients with kidney failure, 107 drugs (14.55%) were found to be inappropriately prescribed. Most of them were belongs to antihypertensive drugs such as amlodipine, clonidine and prazosin which requires dose adjustment (dose reduction, prescribed alternatives) follows by antibiotic drugs which 25 drugs (28.40%) out of 88 antibiotics were prescribed additionally, in antihyperlipidemic also 8 drugs (22.85%) out of 35 prescribed drugs require for dose adjustment including switch to alternative drugs as well as therapeutic monitoring, in respiratory agents drugs 13 drugs (27.8%) out of 48 prescribed drugs require dose adjustment which mostly was omitting additional prescribed drugs.

One of the most important drug related problems in patient with renal impairment is medication dosing errors. Many medications and their metabolites are eliminated through the kidney and thus adequate renal function is important to avoid toxicity. The proper dosing of medication for patient with renal impairment can maximize therapeutic efficacy and minimize toxicity. Proper dosing can also have an economic health impact on health system. Studies have shown that an adverse drug event increase the length of hospitalization and consequently increase cost. Dosage adjustment can result in avoidance of cost associated with drug-related toxicity and in cost savings in terms of drug costs.Clinical pharmacist works directly with medical professionals and patients usually in a medical Centre like, hospital. In present scenario PHARM D should be appointed that; they can assist physicians to adjust drug dosages in patient with chronic kidney disease. The involvement of a pharmacist at the point of prescription of a drug by a physician is the most effective. The time for decision making is very important. Physician and pharmacist can work together to have safe drug prescribing that can be complex and requires stepwise approach to ensure effectiveness, minimize further damage and prevent drug nephrotoxicity.

CONCLUSION

The prevalence of chronic kidney disease is increasing and polypharmacy is common. Hence, there is a need to monitor the dosing of drugs in those patients to avoid adverse effects, to reduce the length of stay in the hospital and to control the unnecessary cost of medications. Drugs were prescribed for various co morbid conditions like hypertension, Diabetes mellitus, IHD, Infection, CAF/CHF, Anaemia, COPD, Hyperlipidaemia, GERD, Hyperparathyroidism, Uraemia, Hepatic encephalopathy, Anorexia, UTI, Hypotension. Among these 16 co-morbid condition Hypertension and Diabetes mellitus were comparatively high. Mostly, antihypertensive drugs were dosed inappropriately compared to other category of drugs. The number of drugs dosed appropriately was found to be 57 (14.88%) in HD and 47 (16.19%) in NON-HD. The number of drugs dosed inappropriately was found to be 16 (35.55%) in HD and 14 (33.33%) in NON-HD. Dose adjustment should be done mostly in antihypertensive drugs, antibiotics, hypolipidemics, analgesics and respiratory agents. Dose adjustment may be reduction of prescribed dose, prescribing alternative drugs or etc. In this study most of the patients were in stage V CKD and were not undergoing haemod ialysis. The number of male patients were comparatively high. This study reveals that most of the drugs were dose appropriately. Tablets were the major formulations used for administration of drugs in this study. Drug-related problems can result in an increase in morbidity and mortality, as well as increase in the cost of healthcare inappropriate use of medications can increase adverse drug effects that may be reflected by excessive length of hospital stay, and excessive healthcare utilization and cost. Large number of adverse drug reactions are predictable and often preventable. Preventable adverse drug events are often a result of medication errors. Prescribing errors often occur because the prescribers do not have immediate to all the needed information related to the drugs or the patient.

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