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Original Research Article

A study of drug utilisation pattern in patients of chronic kidney disease at a tertiary care hospital

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ABSTRACT

Background: Chronic kidney disease (CKD) is a major public health issue and widely prevalent non-communicable disease in India. CKD has a complex pharmacotherapy and it inevitably requires poly-pharmacy. CKD patients require to take medications for a lifelong period, which makes it very important to study the prescribing trends on a regular basis. The main objective of the study was to analyse current prescribing trends in the management of CKD patients and to know whether the prescribing rationality was maintained.

Methods: After Institutional Ethics Committee approval, a prospective Cross-sectional study was carried out at Nephrology department of a tertiary care hospital for a period of six months from 1st June 2017 to 30th November 2017. Patients diagnosed with CKD by treating Nephrologist were included and their prescriptions were analysed to study the prescribing patterns.

Results: A total of 120 cases were analysed during the study, of which 81.7% were males and 18.3% were females. Analysis of WHO core drug prescribing indicators showed that the average number of drugs prescribed per patient was 5.13, percentage of drugs prescribed by generic name was 30.03%, percentage of patients with an injection prescribed was 16.6%, percentage of drugs prescribed from essential medicine list was 65.8% and percentage of patients prescribed with an antibiotic was 10.8%. Antihypertensive drugs (39.9%) were the most commonly used drugs, followed by, calcium salts (12.01%), multi-vitamins (7.6%), oral iron supplements (6.8%), erythropoietin (6.3%) and ulcer protectives (6.1%).

Conclusions: Maximum number of drugs were prescribed from cardiovascular class of drugs. Calcium channel blockers and diuretics were the commonest group of antihypertensives prescribed. The principle of rational prescribing was followed.

Keywords: Chronic kidney disease, Drug utilization, Prescribing pattern, Pharmacoepidemiology

INTRODUCTION

Chronic kidney disease (CKD) is a major public health problem due to its increasing incidence, prevalence and associated economic burden. CKD has an estimated global prevalence of 11%-13%.[1] According to the World Health Organization (WHO), CKD contributes to nearly 850,000 deaths worldwide annually.[2]

CKD is characterized by multiple disorders affecting the morphology and functioning of kidneys.[3] CKD patients present with several co-morbidities such as hypertension, diabetes mellitus, coronary artery disease and infection. The presence of these co-morbidities has a twofold impact on the patients - firstly, it increases the cost of treatment and secondly, it poses a challenge for the treatment of CKD patients.[4]

Due the prescription of multiple medications, CKD patients are at higher risk of developing drug-related problems. They need complex therapeutic regimen which require frequent monitoring on a regular basis. Inappropriate use of drugs in these patients can lead to

adverse drug reactions, increased hospital stays and increased cost of treatment.[4,5]

Drug utilization in CKD changes with time period, physician, disease conditions and population, which makes it important to study the drug utilization continuously over a period of time.[6] Drug utilization studies in CKD patients help to understand pattern of drug use. As CKD patients need lifelong therapy, it is very important to study the prescribing trends on a regular basis.

In India, given its population of more than 1billion, and the rising incidence of CKD is likely to pose major problems for both healthcare and the economy in future years.[7] So, understanding the drug utilisation pattern in CKD patients is very important to know about the current prescribing trends, to understand common co-morbidities associated with CKD and to study their impact on overall health condition of the patient on a long run.

World Health Organization (WHO), has defined Drug utilization study (DUS) as "The marketing, distribution, prescription and uses of drugs in a society with special emphasis on the resulting medical, social and economic consequences." The principle aim of the drug utilization research is to facilitate the rational use of the drugs. It is very difficult to improve prescribing habits, without knowing about the pattern of drug use in the patients.[8]

Conducting DUS on a regular basis is beneficial in the following ways i.e. firstly it will give an overall overview regarding the actual pattern of drug use for a particular disease condition, in a given population, over a given period of time. Secondly, it will help in detecting early signals of irrational drug use. Thirdly, the data obtained from these studies can be used to improve drug use on long term. Fourthly, it will also help to ensure a quality control of drug use.[9]

Currently there is very limited evidence from India on the prescribing trends in CKD patients.[4] Hence this study was undertaken with the objective to analyse current prescribing trends in the management of CKD patients and to know whether the prescribing rationality was maintained.

METHODS

A prospective, cross sectional, observational study was carried out at the Nephrology OPD of Krishna Rajendra Hospital, Mysore for a period of 6 months from 1st June 2017 to 30th November 2017. Sample size was calculated to be 120 using estimation technique.

Inclusion criteria

- Patients of either sex, age 18 years or more
- Diagnosed by the clinician to have chronic kidney disease and currently on drug treatment.

Exclusion criteria

- Surgical conditions like kidney stone
- Tumors and trauma
- Pregnant and lactating women
- Patients not willing to participate.

After obtaining clearance from the Institutional Ethics Committee, subjects attending Nephrology department at Krishna Rajendra Hospital, attached to Mysore Medical College and Research Institute, Mysore, diagnosed with CKD by the treating Nephrologist, were included in the study after obtaining a written informed consent.

The socio-demographic data along with other relevant details of the study subjects were collected from patient's OPD card and their prescriptions were analysed.

Prescriptions were analysed for studying the prescribing trends in patients of CKD. Drugs were classified into different groups on the basis of Anatomic Therapeutic Chemical (ATC) classification.

Rationality of prescription was analysed by comparing with WHO core prescribing indicators i.e.[10]

- Average number of drugs per encounter,
- Percentage of drugs prescribed by generic name,
- Percentage of encounter with an antibiotic prescribed,
- Percentage of encounter with an injection prescribed,
- Percentage of drugs prescribed from the essential medicine list or formulary.

Statistical analysis

Data on utilisation of different classes as well as individual drugs were subjected to statistical analysis. Statistical Package for Social Sciences (SPSS) software version 20 was used for the descriptive analysis. Descriptive statistics like mean and median was used for continuous variables and frequency and percentage for categorical variables. Probability (p) value of less than 0.05 was considered to be statistically significant for all analysis.

RESULTS

In the current study prescription of 120 CKD patients was analyzed during the study period of 6 months.

Demographics

Out of 120 patients studied, 98 (81.7%) were male and 22 (18.3%) were female patients (Figure 1). In present study there was a male preponderance over the female patients.

Majority of patients were in the age group of 41-50 years (41.7%), with a mean age of 47.56years (Figure 2) and majority of patients were belonging to stage 4 and more of CKD.
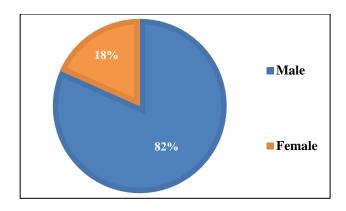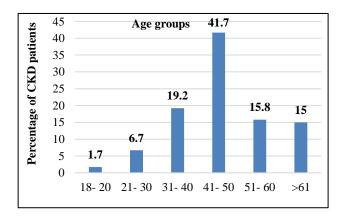
Figure 1: Gender distribution of CKD patients.

Figure 2: Age distribution of CKD patients.

Co-morbidities

Most frequently encountered co-morbidity in CKD patients was hypertension (40%); followed by combination of hypertension and diabetes (7.5%), diabetes (4.2%), anaemia (4.2%) and a combination of ischaemic heart disease (IHD) and hypertension (4.2%) (Figure 3).
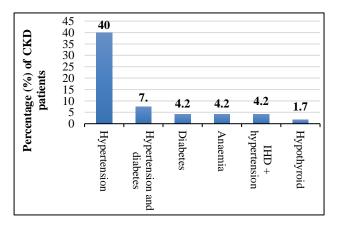

Figure 3: Co-morbid diseases seen in CKD patients.

WHO rational prescribing criteria assessment

The total number of drugs prescribed in the study was 616 drugs. Average number of drugs per prescription was 5.13. Percentage of drugs prescribed by generic name was 30.03%, percentage of patients with an injection prescribed was 16.6%, percentage of drugs prescribed from essential medicine list was 65.8% and percentage of patients prescribed with antibiotic was 10.8% (Table 1).

Table 1: WHO prescribing indicators.

WHO prescribing indicators	Number
Total number of drugs prescribed	616
Average number of drugs per prescription	5.13
Percentage of drugs prescribed by generic name	30.03%
Percentage of patients with an injection prescribed	16.6%
Percentage of drugs prescribed from essential medicine list	65.8%
Percentage of patients prescribed with antibiotic	10.8%

Drug utilisation pattern

Table 2: Drug classification according to ATC classification.

ATC Class code	ATC Class	No. of drugs (n= 616)	Percentage (%)
A	Alimentary tract and metabolism	218	35.4%
B	Blood and blood forming products	99	16.07%
C	CVS	270	43.8%
D	Dermatology system	0	0
G	Genitourinary system and sex hormones	0	0
H	Systemic hormonal preparation	2	0.3%
J	Anti- infectives for systemic use	13	2.11%
L	Anti-neoplastic and immunomodulatory agent	0	0
M	Musculoskeletal system	1	0.16%
N	Nervous system	9	1.46%
P	Anti-parasitic products, insecticides and repellents	0	0
R	Respiratory system	4	0.65%
S	Sensory organ	0	0
V	Various	0	0

The current study showed that, according to the ATC classification of drugs, cardiovascular (CVS) drugs were the commonly prescribed (43.8%), followed by drugs

belonging to the class of alimentary tract and metabolism (35.4%) (Table 2).

Antihypertensive class of drugs were commonly prescribed (39.9%) class of drugs, followed by haematopoietic agents (15.4%), calcium-based phosphate binders (12%), and vitamins and mineral class of drugs (8.9%) (Table 3).

Table 3: Therapeutic class wise drug distribution.

Drug class	ATC code	No.	%
Antihypertensives		246	39.94
Diuretics	C03CA	51	8.28
Calcium channel blockers	C08CA	111	18.02
CCB-BB		0	0.00
Beta blockers	C07AB	17	2.76
Alpha blockers	C02CA	26	4.22
ACE Inhibitors	C09AA	3	0.49
ARBs	C09CA	2	0.32
ARB + DU		0	0.00
Others (Nitrates, ARB+CCB, ACE inhi+ diuretics)		36	5.84
Hypolipidemic drugs		28	4.55
Statins	C10AA	13	2.11
Fibrates		1	0.16
Statins + aspirin		8	1.30
Aspirin + clopidogrel		6	0.97
Antidiabetic		21	3.41
Insulin	A10A	15	2.44
DPP-4 inhibitors	A10B	3	0.49
Sulphonylureas	A10B	1	0.16
Metformin		2	0.32
Vitamins and minerals		55	8.93
Vitamin D	A11HA	1	0.16
Vitamin B12	A11EA	3	0.49
Multivitamins		47	7.63
Sodium bicarbonate		4	0.65
Phosphate binders		74	12.01
Calcium	V02AA04	74	12.01
Selvamer	V03AE02	0	0.00
Hematopoietic agents		95	15.42
Iron (oral)	B03A	42	6.82
Iron (inj.)		6	0.97
Folic acid	B03B	8	1.30
Erythropoietin	B03XA01	39	6.33
Antimicrobials	J01	13	2.11
Others		84	13.64

Others- antithyroid drugs, antacids, lactulose, analgesics, probiotics, anti-histaminic etc.

Among the prescriptions that were analysed during the study, number of antihypertensive drugs per prescription was 2.05. Number of patients prescribed with an antimicrobial, calcium-based phosphate binder, diuretics, oral iron were 10.83%, 61.66%, 40% and 35% respectively (Table 4).

Table 4: Prescription analysis in CKD patients.

Prescription details	No. (%)
Total number of drugs prescribed	616
No. of drugs per prescription	5.13
No. of anti-hypertensives drugs per prescription	2.05
Drugs prescribed by generic name	185 (30.3)
Drugs prescribed from NLEM	405 (65.57)
Drugs prescribed as injections	70 (11.36)
patients prescribed with anti-microbials	13 (10.83)
patients prescribed with calcium based phosphate binders	74(61.66)
Patients prescribed with diuretics	48 (40)
Patients prescribed with oral iron	42 (35)

DISCUSSION

Chronic kidney disease (CKD) is a widely prevalent non-communicable disease that is responsible for increasing morbidity in India.[7] It is a global threat to health in general and for developing countries in particular, as a result of an increase in incidences of lifestyle diseases like diabetes and cardiovascular diseases. Due to these co-morbid diseases along with CKD, patients invariably end up with a complex pharmacotherapy for CKD involving multiple drugs.[11,12]

In our current study the mean age of patients was found to be 47.56years. This was found to be lower than that found in studies done by Ahlawat et al, Devi et al, and Al Ramahi et al.[4,13,14] (53.8years, 55.1years and 55.6years respectively). Majority of patients in current study were in the age group of 41-50years. In India incidence of diabetes is highest in the age group of 45-60years.[15] Even the incidence of hypertension increases after 45 years of age.[16] Diabetes and hypertension being important comorbidities seen to be associated with CKD, might be one of the reasons for majority of CKD patients being in the 41-50 years age group in our study.

There was a male preponderance over the female patients. Out of 120 patients studied, 98 (81.7%) were male and 22 (18.3%) were female patients. This finding is in concurrence with Ahlawat et al, Devi et al, and Al Ramahi et al.[4,13,14] Studies have shown that male patients show a substantially higher prevalence of CKD and incidence rate of ESRD than those observed in female patients. There are also studies which suggest that, men with diabetes have a higher risk of nephropathy than women with diabetes do.[17] This might be one of the reasons for male preponderance in present study.

Majority of patients belonged to stage 4 and more of CKD, this was also consistent with the studies conducted by Ahlawat et al, Devi et al, and Al Ramahi et al.[4,13,14]

In present study hypertension (40% of cases) was the commonest co-morbidity; followed by combination of hypertension and diabetes, diabetes, anaemia and a combination of ischaemic heart disease (IHD) and hypertension. These findings were similar to Ahlawat et al.[4] where hypertension was found to be common co-morbidity (55%), followed by diabetes, and anemia. However, the incidence of hypertension as comorbidity with CKD was higher (84%) in studies conducted by Al Ramahi et al. [14]

According to the ATC Classification system of drugs, cardiovascular class of drugs (43.8%) were the commonest prescribed class of drugs. This was higher than the study carried out by Ahlawat et al, and Devi et al, which reported it to be 33.9% and 28% respectively.[4,13] The reason for this might be due to high incidence of hypertension as a comorbidity in most of the patients in present study.[4,13]

Alimentary tract and metabolism class of drugs and blood forming agents were the next commonly prescribed group of drugs. This was in concurrence with studies conducted by Ahlawat et al.[4]

In the present study average number of drugs per prescription was 5.13., which is smaller than the average number of drugs reported by Ahlawat et al, Devi et al, Bajait et al, and Al Ramahi et al.[4,13,14,18] (6.57, 7.4, 9.4 and 9.3 respectively). This difference in the average number of drugs may be due to the study population size, co-morbid conditions and physician prescribing behaviour. Percentage of drugs prescribed by generic name was 30.03%, which is higher than Bajait et al, (12%).[18]

Drugs prescribed from essential medicine list in present study was 65.8%, which is higher than reported by studies conducted by Devi et al, and Bajait et al, (53% and 42% respectively).[13,18] But is lower than the study conducted by Ahlawat et al, which was 81%.[4] Percentage of patients with an injection prescribed was 16.6%, which is lower than Devi et al, (32%).[13]

Among the cardiovascular class of drugs calcium channel blockers were commonly used in the present study, followed by diuretics and alpha blockers (18%, 8.28% and 4.22% respectively). Ahlawat et al, reported that diuretics were the most commonly prescribed CVS group of drugs followed by calcium channel blockers, and Angiotensin II Receptor Blockers (ARBs) (8.2%, 6.3% and 2.8% respectively).[4] Sonawane et al, and Jessani et al, reported that beta blockers were the commonly used antihypertensives.[19,20] Calcium based phosphate binders were prescribed in 61.66% of patients, which was lower than that of study conducted by Ahlawat et al, (91%) and Navaneetan et al, (75%).[4,21] Commonly used phosphate binder in our study was Calcium carbonate.

Multivitamins were also commonly prescribed in our study, Haematopoietic agents constituted 15.42 % of drugs given to CKD patients. This was consistent with the results reported by Ahlawat et al, (15.2%).[4]

Among all the prescribed drugs, antihypertensive agents were the most predominantly used. Followed by calcium salts (12.01%), multi-vitamins (7.6%), oral iron supplements (6.81%), erythropoietin (6.3%) and ulcer protectives (6.1%). The findings were similar to study conducted by Rajeshwari et al.[10] Haematinics and multivitamins are commonly prescribed drugs as CKD patients are more prone to develop anemia and weakness due to the disease. They are also more susceptible to stress ulcers and dyspepsia, so antacids are also commonly prescribed to CKD patients.

It is very important to evaluate the prescribing pattern in CKD patients on a time to time basis, so as to identify potential Drug-drug interactions (pDDIs), try to prevent it, thereby improving patient condition and compliance to therapy. Identifying, categorising of DDIs is very essential to understand the adverse effects of drugs given to CKD patients.

Drug utilization evaluation in CKD patients from time to time will help to ensure that the rationality of prescription is maintained, and the information obtained from the study can be utilised in preventing problems related to medications, in evaluating effectiveness of drug therapy and in making any changes in the treatment regimen for the patients if required.

For overall management of CKD, patients need to undergo frequent clinical and laboratorial assessment as well. Prevention of progression and treatment of the ongoing disease process is the main aim of pharmacotherapy of CKD. Treatment of CKD not only is targeted towards the disease per say, but also involves management of co morbid diseases associated with CKD.

There is a need for conducting further, large scale studies at multiple centres, with a larger sample size from time to time, which will help to analyse, compare and rationalise prescribing trends in CKD patients., which will also give a proper perspective to these findings on a larger population.

In current study drugs from cardiovascular system class were the commonly utilised class of drugs according to ATC classification of drugs. A fair proportion of drugs were prescribed from NLEM. Calcium salts, multi-vitamins, oral iron supplements, erythropoietin and ulcer protectives were found to be commonly utilised drugs in the current study.

Present study illustrates the current day scenario of CKD patients attending Nephrology OPD in a tertiary care hospital, prescribing trends of the physicians in managing these patients with co-morbidities and disease related complications. Present study provides the baseline data and would help build data for carrying out further drug utilization studies. An overall understanding of various

drugs used in the management of CKD, its complications and other comorbid diseases associated with it, will help the physicians in better management of patients, as far as adverse effects, toxicities etc of the drugs are concerned. Thereby improving patient compliance to therapy and overall outcome of CKD pharmacotherapy.

REFERENCES

1. Hill NR, Fatoba ST, Oke JL, Hirst JA, O'Callaghan CA, Lasserson DS, et al. Global prevalence of chronic kidney disease - a systematic review and meta-analysis. PLoS One. 2016 Jul;11(7).
2. World Health Organization: Burden of Disease Project. Available at: http://www3.who.int/whosis/menu.cfm. Accessed 22 October 2018.
3. Santra S, Agrawal D, Kumar S, Mishra SS. A study on the drug utilization pattern in patients with chronic kidney disease with emphasis on antibiotics. J Integrative Nephrol Androl. 2015 Jul 1;2(3):85.
4. Ahlawat R, Cruz SD, Tiwari P. Drug utilization pattern in chronic kidney disease patients at a tertiary care public teaching hospital: Evidence from a cross-sectional study. J Pharma Care Health Sys. 2015 Dec;3:149-53.
5. Pavitra R Y, Geetha M, Aggarwal R and Somashekar H S. Drug utilization pattern of antihypertensive drugs in chronic kidney disease patients in a tertiary care hospital. IOSR J Dental Med Sci. 2014 Nov;13(11):23-7.
6. Laporte JR, Orme ML. Drug utilization and the teaching of rational drug use. WHO Reg Publ Eur. 1993;45:183-91.
7. Singh AK, Farag YM, Mittal BV, Subramanian KK, Reddy SR, Acharya VN, et al. Epidemiology and risk factors of chronic kidney disease in India–results from the SEEK (screening and early evaluation of kidney disease) study. BMC Nephrol. 2013 Dec;14(1):114-92.
8. Piparva KG, Parmar DM, Singh AP, Gajera MV, Trivedi HR. Drug utilization study of psychotropic drugs in outdoor patients in a teaching hospital. Indian J Psychol Med. 2011 Jan;33(1):54-8.
9. Drug Use Evaluation. World Health Organization. Available at: http://www.who.int/medicines/technical_briefing/tbs/

11-PG_Drug-Use-Evaluation_final-08.pdf. Accessed 25 October 2018.
10. Rajeshwari, Nagabushan H, Prakash GM, Rekha MC. Assessment of quality of life and drug usage among hemodialysis patients at a tertiary care hospital. Int J Pharm Clin Sci. 2016 Sept;5(3):65-72.
11. Chawla S, Ranjan A, Singh N.P, Garg N and Kumar A. Assessment of drug utilization and quality of life in patients of chronic kidney disease in a tertiary care hospital. World J Pharm Pharm Sci. 2016;5(9):1214-26.
12. Tamiselvan T, Veerapandiyan AK. Study of drug utilisation pattern of chronic renal failure patients in a tertiary care hospital. Int. J Pharm Pharm Sci. 2014;6(9):482-84.
13. Devi DP, George J. Diabetic nephropathy: prescription trends in tertiary hospital. Indian J Pharm Sci. 2015;70:374-78.
14. Al Ramahi R. Medication prescribing patterns among chronic kidney disease patients in a hospital in Malaysia. Saudi J Kidney Dis Transpl. 2012;23:403-8.
15. Tripathy JP, Thakur JS, Jeet G, Chawla S, Jain S, Pal A, et al. Prevalence and risk factors of diabetes in a large community-based study in North India: results from a STEPS survey in Punjab, India. Diabetol Metabol Syndrome. 2017 Dec;9(1):8.
16. Prabhakaran D, Jeemon P, Ghosh S, Shivashankar R, Ajay VS, Kondal D, et al. Prevalence and incidence of hypertension: results from a representative cohort of over 16,000 adults in three cities of South Asia. Indian Heart J. 2017 Jul 1;69(4):434-41.
17. Chang PY, Chien LN, Lin YF, Wu MS, Chiu WT, Chiou HY. Risk factors of gender for renal progression in patients with early chronic kidney disease. Med. 2016 Jul;95(30):1-19.
18. Bajait CS, Pimpalkute SA, Sontakke SD, Jaiswal KM, Dawari AV. Prescribing patterns of medicines in chronic kidney disease with emphasis on phosphate binders. Indian J Pharmacol. 2014;46:35-9.
19. Sonawane KB, Qian J, Hansen RA. Utilization patterns of antihypertensive drugs among the chronic kidney disease population in the United states: a cross-sectional analysis of the national health and nutrition examination survey. Clin Ther. 2014:15:802-4.
20. Jessani S, Bux R, Jafar TH. Prevalence, determinants, and management of chronic kidney disease in Karachi, Pakistan - a community based cross-sectional study. BMC Nephrol. 2014;15:1471-92.
21. Navaneethan SD, Sakhuja A, Arrigain S, Sharp J, Schold JD. Practice patterns of phosphate binder use and their associations with mortality in chronic kidney disease. Clin Nephrol. 2014;82:16-25.