ISSN: 0975 -8542

Journal of Global Pharma Technology

Available Online at: www.jgpt.co.in

RESEARCH ARTICLE

Assessment of Drug Utilization Pattern in Chronic Kidney Disease Patients in A Tertiary Care Hospital Based on Who Core Drug Use Indicators

Maitha Mohammed Al-Jabri, C. S. Shastry*, Sharad Chand

Department of Pharmacy Practice, NGSM Institute of Pharmaceutical Sciences, Paneer, Nitte (Deemed to be University), Deralakatte, Mangaluru- 575018.

***Corresponding Author: C. S. Shastry**

Abstract

Introduction: Chronic kidney disease (CKD) is defined as any decrease in the glomerular filtration rate (GFR) with an abnormality in the kidney structure or its function. CKD patients are presented with multiple co-morbidities and compromised pharmacokinetics resulting in compromised quality of life and considerable economic burden. Aim: To study the drug utilization pattern in Chronic Kidney Disease (CKD) patients by using the World Health Organization (WHO) core drug use indicators. Materials and Method: A prospective observational drug utilization study was carried out in out-patients of Department of Nephrology of Justice K S Hegde Charitable Hospital, Mangalore, for period of 8 months. CKD patients with an age of 18 years and above were included with consent. Data was collected using data collection forms, patients case notes, prescriptions sheet and personal interviews. Result: A total of 256 patients were recruited. Of which, 192 (75%) patients were males and 64(25%) were females with a mean age of 54.5 years. Average consultation time was 6.5 minutes. A total of 1374 drugs were prescribed to these patients with an average of 5.3 drugs per prescription. The most common prescribed class of drugs were for the cardiovascular system (42.6%) followed by the hematopoietic system (16.7%). Further, 65% of the drugs were prescribed from the national list of essential medicines (NLEM) whereas 8.7% of drugs were prescribed by generic name. Conclusion: Utilizing the WHO's core drug use indicators in this special patient population will strengthen the current hospital drug use policies and improve the drug usage pattern, saving the precious life years and monetary resources.

Keywords: *Drug utilization, Chronic kidney disease, WHO Indicators, Prescription.*

Introduction

Chronic kidney disease (CKD) is characterized by a decrease in the glomerular filtration rate (GFR) of less than 60 ml/min/1.73 m^2 for three or more months and abnormality in the kidney structure or its function [1]. With a prevalence of 10-13.5% worldwide, CKD is considered as one of the major non-communicable diseases [2].CKD is a significant contributor to comorbidities such as cardio vascular diseases and end stage renal disease (ESRD) [3].

CKD was ranked 27th in the number of deaths in 1990 (annual death rate 15.7 per 100,000), rose to 18th position in 2010 (annual death rate 16.3 per 100,000) [4]. In India, the prevalence of CKD is 17.2% and it was more in male than females as a result of chronic alcoholism, diabetes mellitus, smoking, hypertension and chronic vascular diseases (CVD) [5]. Pharmacokinetics parameters in these patients are often compromised and result in drug accumulation, toxicity and adverse drug events (ADEs) [6, 7]. Furthermore, CKD patients carry heightened risk for ADEs due to multiple co-morbidities, use of many medications, and being cared for by many practitioners [8]. Co-morbidities such as hypertension, infections, diabetes mellitus, and coronary artery disease can be present in CKD patients.

Such co-morbidities can increase treatment cost as well as treatment challenges. The need for prescribing multiple medications can increase the chance of developing adverse outcomes in CKD patients [9].World health organization (WHO) has defined rational

drug use as "patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements for an adequate period of time and at the lowest cost to them and their community." [10]. Drug utilization is defined as "the marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences".

The study of utilization pattern in a specific setting helps in providing an idea about how the drugs are prescribed which detect the presence of irrational use of medicines [11]. Specific method of assessment is must in order to achieve the rationality of medicines. From this point WHO have developed core drug use indicators in Utilization studies [12, 13]. The current study aims to evaluate the utilization pattern in Chronic Kidney disease patients using WHO core drug use indicators.

Materials and Methods

Study Design and Study Center

This is a prospective observational study conducted in the out-patient department of Nephrology of Justice K S Hegde Charitable Hospital, Mangalore, India.

Duration

Eight months from August 2018 to April 2019

Ethical Approval

Study approval was taken from the Institutional Ethics Committee (IEC) of Justice K S Hegde Charitable Hospital, Mangalore, India.(Ref. No. NGSMIPS/ IEC/ 15/2018-19)

Sample Size

256 patients

Inclusion Criteria

CKD patients above 18 years of either gender with a minimum two drugs per prescription

Exclusion Criteria

Patients not willing to participate in the study

Data Sources

- Patient case sheets, drugs prescription charts, interview with patients/care takers for demographic details

Materials Used

- Patient data collection form, informed consent forms, WHO core drug use indicators, national list of essential medicines, SPSS 16.0 software.

The WHO Core Drug use Indicators: 13

Prescribing Indicators

- Average number of drugs Per encounter $= \frac{\text{Total number of drugs}}{\text{Total number of the prescription}}$
- Percentage of drugs prescribed by generic name $= \frac{\text{No.drugs prescribed by generic name}}{\text{Total No.of drugs prescribed}} \times 100$
- Percentage of encounters with an antibiotic $= \frac{\text{No.Prescription with antibiotic}}{\text{Total No.Prescription}} \times 100$
- Percentage of encounters with an injection prescribed $= \frac{\text{No.Prescription with injection}}{\text{Total No.Prescription}} \times 100$
- Percentage of drugs prescribed from essential drugs list or formulary $= \frac{\text{No.of drugs prescribed from NLEM}}{\text{Total No.drugs}} \times 100$

Patient Care Indicator

- Average consultation time $= \frac{\text{Total time of a series of consultation}}{\text{Total No.Consultations}}$

Health Facility Indicator

- Availability of copy of essential drugs list or formulary. (Yes or no, per facility)

Complementary Indicator

- Average of cost per prescription $= \frac{\text{Total cost of the prescribed drugs}}{\text{Total No.Prescription}}$

Analysis of the data was carried out by using statistical package for social science (SPSS) 16.0 for windows.

Results

A total of 256 patients were included in the study. Patients were categorized based on their stage of CKD into five groups, namely stage 2, stage 3, stage 4, stage 5 and stage 5D (stage five with dialysis).

Stage Wise Distribution of CKD Patients

Out of 256 patients, 123 patients belonged to stage 5D (48.04%), followed by stage 5 which had 86(33.59%) patients. Patients with impaired kidney function and GFR less than 15 ml/min/1.73 m^2 constituted about 82% of the total sample size. The stage wise distribution of CKD patients is summarized in Figure 1.

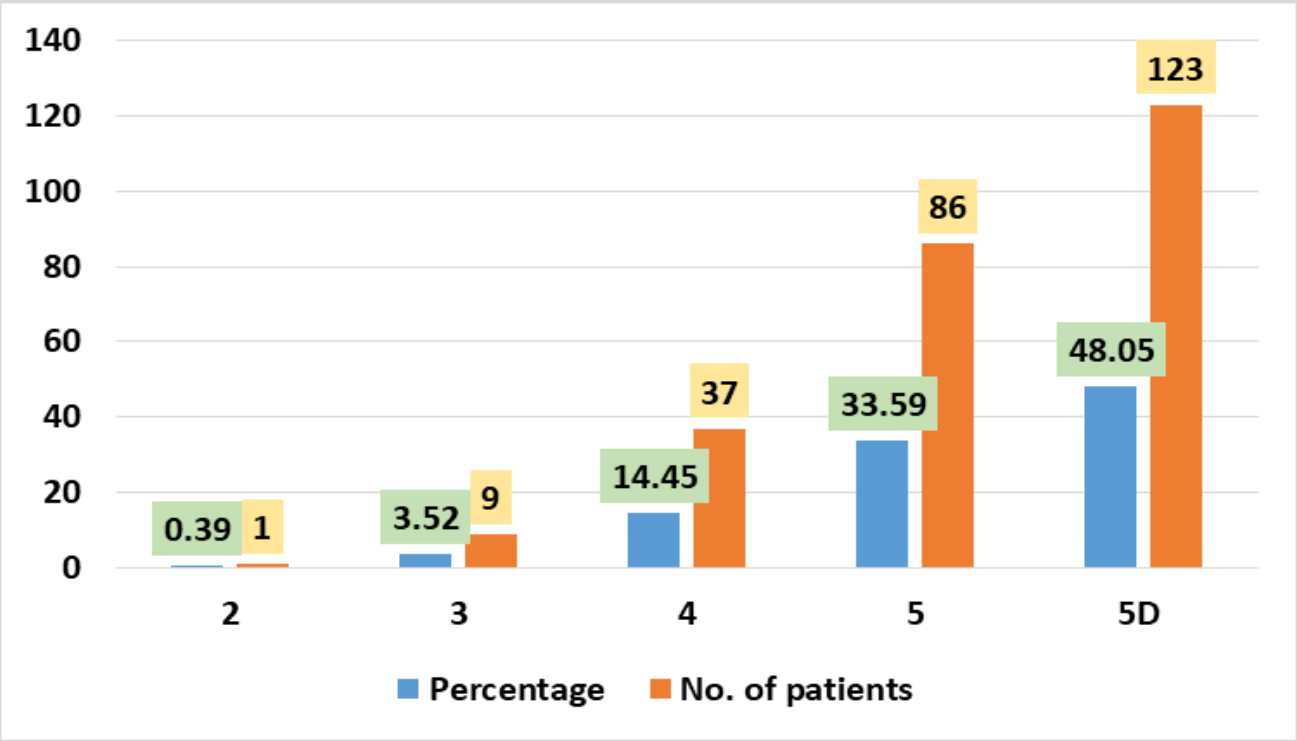

Figure 1: Stage wise distribution of CKD patients

Demographics Details of the Patients

In the present study, the number of male patients 192(75%) outnumbered the female patients 64 (25%). Out of 192 male patients, 153 (79.7%) were in stage 5 & 5D. Similarly 87.5% of female patients were in stage 5.

Table1: Gender wise distribution of patients

Gender	CKD stages										Total	
	2		3		4		5		5D			
	Nos.	%	Nos.	%	Nos.	%	Nos.	%	Nos.	%	Nos.	%
Male	1	100	7	77.8	31	83.3	67	77.9	86	69.9	192	75
Female	-	-	2	22.2	6	16.2	19	22.1	37	30.1	64	25
Total	1		9		37		86		123		256	

Age Wise Distribution

Among the study population, the age ranged from 18-81 years.

The mean age of population was 54.5 ± 13.43. Age wise distribution of the patients is summarized in Table 2.

Table 2: Age wise distribution of patients in different stages of CKD

Age group(year)	CKD stages										Total	
	2		3		4		5		5D			
	Nos.	%	Nos.	%	Nos.	%	Nos.	%	Nos.	%	Nos.	%
18-35	0	0	3	33	8	21.6	5	5.8	10	8.1	26	10.2
35-55	1	100	1	11.1	11	29.7	35	40.7	48	39.0	96	37.5
>55	0	0	5	55.6	18	48.6	46	53.5	65	52.8	134	52.3
Total	1	0.39	9	3.52	37	14.45	86	33.6	123	48.04	256	100

Domiciliary Status

The domiciliary status of the patients was also analyzed. 71.9% of the patients were from rural areas surrounding the study center. The domiciliary background had no bearing on the percentage of patients in stage 5 of CKD. The relevant data is presented in Table 3.

Table 3: Domiciliary status of patients in different stages of CKD

Domiciliary status	CKD stages										Total	
	2		3		4		5		5D			
	Nos.	%	Nos.	%	Nos.	%	Nos.	%	Nos.	%	Nos.	%
Rural	10	100	8	88.9	22	59.5	61	70.9	92	74.8	184	71.9
Urban	0	0	1	11.1	15	40.5	25	29.1	31	25.2	72	28.1
Total	1		9		37		86		123		256	

Distribution Based on Co-morbidities

Almost all the patients recruited in the study had at least one co morbid condition. The occurrence of co-morbidities in CKD patients are depicted in Figure 2.

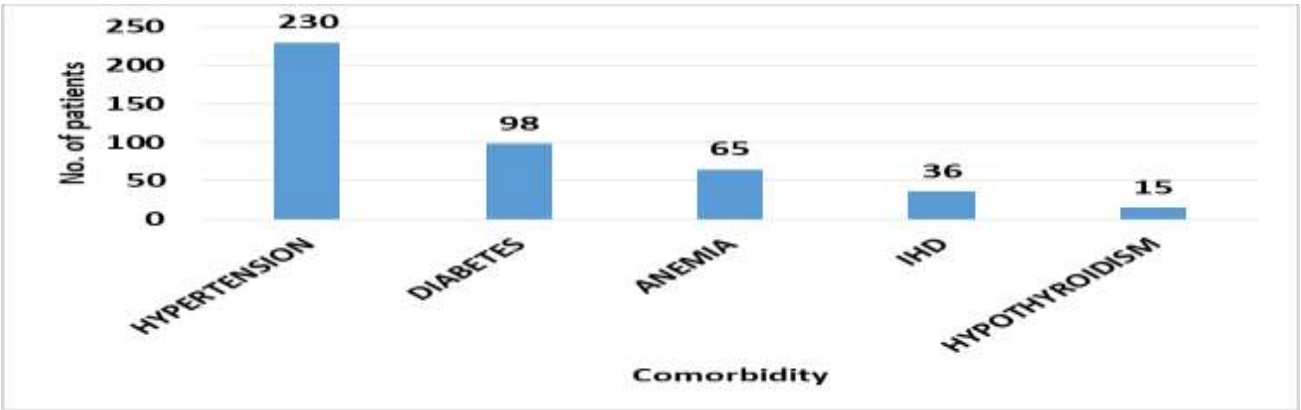

Figure 2: Co morbidities in CKD

Drug Utilization Pattern

Out of 1374 prescribed drugs only 8.7% were prescribed by generic name, 65% of the drugs were prescribed from the Indian national list of essential medicines. The mean cost of prescription was found to be 2,357.25 INR for two weeks prescription. A total of 256 prescriptions were analyzed with a total of 1374 drugs, out of which drugs acting on cardiovascular system were the most prescribed drugs (586 drugs, 42.6%).

Table 4: Drug usage pattern in patients suffering from CKD

Drug class	Frequency	Percentage (%)
Cardiovascular drugs (n=586, 42.6%)		
Calcium Channel Blockers	162	27.6
Diuretics	115	19.6
Centrally Acting alpha 2 agonist	95	16.2
Anticoagulant, antiplatelet, hypolipidemic	97	16.6
Beta Blockers	50	8.5
Alpha- adrenergic blockers	32	5.5
Vasodilators	11	1.9

Angiotensin II Receptor Blockers (ARBs)	11	1.9
Nitrates	11	1.9
Angiotensin Converting Enzyme inhibitors	2	0.3
Haematinics (n=229, 16.7%)		
Epoetin alfa	106	46.3
Intravenous Iron Sucrose	84	36.7
Darbepoetin	15	6.5
Oral Elemental Iron	15	6.5
Folate	9	4
Gastrointestinal Drugs (n=140,10.2%)		
Proton Pump Inhibitors	82	58.6
Dopamine Antagonist	32	22.9
H2 Blockers	21	15
Others	5	3.6
Vitamins and Minerals (n=131, 9.5%)		
Calcium carbonate + Vitamin D3	66	50.4
Vitamin D3 derivatives	39	29.8
Vitamin B complex	26	19.8
Acid Base disorder drugs (n=82, 6%)		
Sodium bicarbonate	63	77
Febuxostat	19	23
Anti-diabetic Drugs (n=81, 5.9%)		
Insulin	50	61.7
Oral Hypoglycemic Agents	31	38.3
Phosphate Binders (n=35, 2.5%)		
Calcium Acetate	18	51.4
Sevelamer	17	48.6
Drugs for Respiratory System (n=19, 1.4%)		
Xanthine Alkaloid	14	53.8
Others	5	19.2
Drugs for Nervous System (n=15, 1.09%)		
Antidepressant	7	46.7
Antiepileptic	3	20
Antipsychotic	3	20
Other	2	13.3
Antibiotics (n=12, 0.9%)		
Cefixime	5	41.6
Linezolid	2	16.7
Rifaxmine	1	8.3
Amoxicillin+Clavulinic Acid	2	16.7
Ceftriaxone	2	16.7
Analgesic (n=19, 1.4%)		
Acetaminophen+ Tramadol	11	57.9
Paracetamol	7	36.8
Naproxen	1	5.3
Thyroid medication (n=11, 0.8%)		
Levothyroxine	11	100
Others (n=7, 0.5%)	7	0.5

Table 5: WHO core drug use indicator

INDICATORS		DATA
Prescribing indicators	Average number of drugs per prescription	5.3 drugs per prescription
	Percentage of drugs prescribed by generic name	8.7%
	Percentage of encounters with an antibiotics	3.9%
	Percentage of encounters with injections	56.25%

	Percentage of drugs prescribed from essential drugs list or formulary	65%
Patient care indicator	Average consultation time	6.5 minutes
Facility care indicator	Availability of copy of essential drugs list or formulary.	No
Complementary indicators	Average of cost per prescription	2,3 57.25 INR

Discussion

A total number of 256 CKD patients were included in the present study which revealed that 75% of them were male patients this is similar to the observation made by several other researcher. Bharani *et al* [14], Abhisek *et al* [15] And Bajait *et al* [16].Reported the involvement of 68.2%, 71.3% and 63.06% of male in their study of CKD patients. The higher incidence in CKD observed in male patients may be due to the role of sex hormone in the progression of the disease. Animal in-vitro studies showed that testosterone has harmful influence, while estrogen has a protective influence on kidney injury process. Also, human in-vitro studies showed that testosterone can induce apoptosis of kidney's proximal tubular cell.

On the other hand, males tend to have high protein and calories intake in comparison with the females. Higher protein intake is associated with the initiation and progression of kidney diseases [17]. Demographic analysis shows maximum number of patients in the older adult age group >55 years (51.6%) with a mean age of 54.5 ± 13.4. This result is in consistence with the study conducted by Fespie *et al* [18]. CKD is higher in older age due to the increase in the main risk factors such as Hypertension, diabetes mellitus and cardiovascular diseases [17].

A cohort study showed, there is a decline in GFR with age. This decline increased significantly from 0.82 ± 0.22 in age-group 20–30 years to 0.84 ± 0.08, 1.07 ± 0.08 and 1.15 ± 0.12 ml/min/year/1.73 m^2 in age groups 31–40, 41–50 and above 50 years age respectively, which conformed the decline in kidney function with age [19]. In this study, maximum of the patients were ESRD (81.54%), same is reported in other studies conducted by Fespie *et al* [18].

And Ahlawat *et al* [9].Where ESRD patients constituted the maximum number of patients which was 69.9% and 42% respectively. CKD patients enrolled in the study were presented with co-morbidities, of which, hypertension was the most common co-morbidity 230 (89 %). Other comorbidities like diabetes mellitus (38 %), anemia of CKD (25%), ischemic heart disease (IHD) (14%), and hypothyroidism (5.6%). In the studies conducted by Santra *et al* [20].And Ahlawat *et al* [9].Discussed similar association of co-morbidities, hypertension was common co-morbidity. It might be due to the fact that hypertension is the most common leading cause of CKD [4]. We summarized that the co-morbid condition and CKD normally co-exist especially in the elderly.

CKD patients with multiple co-morbidities may require poly-pharmacy. 166 patients were prescribed with more than 5 drugs per prescription because of the co-morbid condition which indicate the poly-pharmacy. The mean number of drugs per prescription was found to be 5.3 ± 1.4. These results were similar to the studies conducted by Kantanavar *et al* [21].And Deepan *et al* [11].

7.6 and 5.8 drugs per prescription respectively. The study by Fasipe *et al* [18].Showed mean drugs per prescription of 10.28 ± 3.85 which is significantly higher than what we have observed in our study, this may be due to the physician preference, higher co-morbid condition or hospitalization. Out of the different medications prescribed to the patients, cardiovascular drugs were most commonly prescribed 586(42.6%).This is what we expected because as stated above 89% of the patients were hypertensive and obviously have to be treated with anti-hypertensive.

Calcium channel blockers 27.6% are the most prescribed anti-hypertensive, followed by diuretics and centrally acting alpha 2 agonist 19.6% and 16.2% respectively. These results were similar to a study conducted by Chakraborty *et al* [22].Where cardiovascular drugs were more commonly prescribed. In our study, the utilization of cardiovascular drugs is more than the later study which is 23.41% of the total drugs, compared to 42.6%

of the total drugs in the present study. One of the most important ways to prevent medications errors and promote cost effective prescribing, is prescribing by generic name. It varies from 13.3%-93% all over the world [23].

In the present study the percentage of drugs prescribed by generic name is 8.7%. However, study conducted by Chawla *et al* [24]. Has showed 34% of the drugs were prescribed by generic name, whereas, in the study by Bajait *et al* [16]. And Ahlawat *et al* [9]. Revealed none of the drugs were prescribed by generic name. The wide variation in the prescription pattern of generic drugs is mainly due to the fact that the doctor preferred to prescribe branded medicines. The recent guidelines to prescribe the drugs by generic name will change the scenario in future. National list of essential medicines (NLEM) it's prepared in reference to the WHO list of essential medicines.

Essential medicines are those that are selected depending on the clinical need of the population. It will promote prescribing by generic name, which will result in cost effective prescribing [25]. In present study, 65% of the total drugs were prescribed from NLEM. This finding is lower than the study carried by Kumar *et al* [26].

In similar setting where in 90.9% of the drugs were prescribed from NLEM. This is might be due to the unavailability of the NLEM in our study setting. Further, the percentage of prescriptions with at least one injection or antibiotic was 56.25% and 3.9% respectively. This high percentage of injection is due to the high number of patients having co-morbidities such as anemia of CKD or type 2 diabetes mellitus, which require injections in management.

In the study conducted by Kumar *et al* [26].Lower percentages of prescriptions with injection (5.55%) was reported compared to our study. This is due to under prescription of erythropoietin injections, because of poor economic status of the patients. The reported percentage of antibiotic was lower than the reported in studies conducted by Ahlawat *et al* [27].And Kumar S *et al* [26]. CKD patients are present with multiple co-morbidities, which require multiple medications. This will increase the cost burden in CKD patients. In our study the average cost per prescription was found to be 2,357.25 INR. Contrary to the study conducted by Kumar *et al* [26].Which was 178 INR, lower than the reported in our study.

The analysis of the data of prescriptions that cost more than 5000 INR, revealed that the major expense is due to the prescription of more than 5 drugs including erythropoiesis stimulating agents which are relatively high in cost starting from 1000 INR and above per injection, with frequency of one injection per week. The high mean age which is 54.5 years in our study is another factor that increases the pharmaceutical expenditure of patients due to the high co-morbidities.

Conclusion

Utilizing the WHO's core drug use indicators in this special patients population will strengthen the current hospital drug use policies and improves the drug usage pattern, saving the precious life years and monetary resources. It's important to conduct a periodic drug utilization studies and presenting the results to the health care professionals (HCPs). Owing to the scarcity of these studies in outpatient settings, Clinical Pharmacists as drug therapy managers can play an excellent role in optimizing the drug therapy regimens supporting other HCPs. To conclude based on the present study on drug utilization pattern, the following may be implemented in the study center

- Displaying the national list of essential medicines and circulating it among the health care professional.
- Encouraging the use of drugs from NLEM which are considered more cost effective.
- Use of generic drugs to minimize the errors in prescription writing and dispensing.

References

1. Marriot J, Cockwell P, Stringer S (2012) Chronic kidney disease and end‐stage renal disease. In: Walker R, Whittlesea C, editors. Clinical Pharmacy and therapeutics. UK: Churchill living stone, 272.

2. Tsai W, Wu H, Peng Y, Ko M, Wu M, Hung K, *et al (2016)* Risk factors for development ad progression of chronic kidney disease. Medicine, 95: 11.

3. Nugent RA, Fathima SF, Feigel AB, Chyung D (2011) The burden of chronic kidney disease on developing nations: A 21st century challenge in global health. Nephron. Clin. Pract., 118: 269-277.
4. Jha V, Garcia C, Iseki K, Naicker S, Plattner B, Saran R, Wang A, Yang C (2013) Chronic kidney disease: global dimension and perspectives. Lancet., 382:260-272.
5. Murthy B, Satyanarayana V (2017) Prescribing pattern of drugs in chronic kidney disease patients on hemodialysis at a tertiary care hospital. Int. J Basic. Clin. Pharmacol., 6(4): 928-932.
6. Hudson JQ, Wazny LD (2008) Chronic Kidney Disease. In: DiPiro, J. T., Talbert, R. L., Yee, G. C., *et al.,* eds. Pharmacotherapy: A Pathophysiologic Approach. 7th ed. New York: McGraw-Hill, 634
7. Roberts JA. Lipman J (2009) Pharmacokinetic issues for antibiotics in the critically ill patient. Crit. Care. Med., 37: 840-51.
8. Philips M, Wilson JA, Aly A (2017) An evaluation of medication reconciliation in an outpatient nephrology clinic. Cannt. J., 26(2):29-33.
9. Ahlawat R, D'cruz S, Tiwari P (2015) 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., 3: 1.
10. WHO (1985) The rational use of drugs. Report of a conference expert, Nairobi, 25-29 Geneva: World Health Organization, 1987.
11. Dheepan BN, Sarala N, Raghavendra BN (2015) Drug utilization study in hemodialysis unit in a tertiary care Centre in kolar. Int. Pharm. Bio. Sci., 5(1):72-78.
12. Shalini S, Ravichandran V, Mohanty B K, Dhanaraj SK, Saraswathi R (2010) Drug utilization studies- An overview. International Journal of pharmaceutical sciences and Nanotechnology, 3(1): 803-810.
13. How to Investigate Drug Use in Health Facilities: Selected Drug Use Indicators - EDM Research Series No. 007: Chapter 2: Core Drug Use Indicators: Prescribing Indicators [Internet]. World health organization.1993 [cited 5 feb 2019]. Available from http://apps.who.int/medicinedocs/en/d/Js2289e/.
14. Bharani K, Bharani R, Vohra R, Goyal C (2003) Drug utilization pattern of antihypertensive drugs in chronic kidney disease stage 5 patients in a tertiary care hospital of central India. International journal for basic & clinical pharmacology, 7(7):1411-1414.
15. Abhisek P, Panda R, Samal R, Mohapatra N, Mohanty S (2017) Drug utilization pattern and adverse events in patients with chronic kidney disease undergoing maintenance haemodialysis at a tertiary care hospital of Odisha. Journal of clinical and diagnostic research, 11(10):11-16.
16. Bajait C, Pimpalkhute S, Sontakke S, Jaiswal K, Dawrl A (2014) Prescribing pattern of medicines in chronic kidney disease with emphasis on phosphate binders. Indian journal of pharmacology, 46(1): 35-39.
17. Goldberg I, Krause I (2015) The role of gender in chronic kidney disease. Eur. Med. J., 1(2):58-64.
18. Fesipe O, Akhideno P, Nwaiwu O, Adelosye A (2017) Assessment of prescribed medications ans pattern of distribution for potential drug-drug interactions among chronic kidney disease patients attending the Nephrology clinic of Lagos university teaching hospital in sub-Saharan west Africa. Clinical pharmacology: Advances and applications, 9: 125-132.
19. Cohen E, Nardi Y, Krause I, Goldberg E, Milo G, Garty M *et al* (2014) A longitudinal assessment of the natural rate of decline in renal function with age. J. Nephrol., 27(6):635-41.
20. Santra S, Agrawal D, Kumar S, Mishra S (2015) A study on the drug utilization pattern in patients with chronic kidney disease with emphasis on antibiotics. J. Nephrol. Androl., 2(3):85-89.
21. Kantanavar K, Holla R, Rao S (2017) A study of prescription pattern in the drug therapy of chronic kidney disease. International journal of pharmacological research., 7(04): 81-87.

22. Chakraborty S, Ghosh S, Banerjea A, Raman R, Hazra A, Mandal S (2016) Prescribing patterns of medicines in chronic kidney disease patients on maintenance hemodialysis. Indian journal of Pharmacology, 48(5): 586-590.

23. Swamy N, Mateti U, Bairi R, Sivva D, Ans Martha S (2014) Drug utilization pattern in south Indian pediatric population: A prospective study. Perspective in clinical research, 5(4):178-183.

24. Chawla S, Ranjan A, Singh N, Garg N, Kumar A (2016) Assessment of drug utilization and quality of life in patients of chronic kidney disease in a tertiary care hospital. World journal of pharmacy and pharmaceutical sciences., 5(9): 1214-1226.

25. National List of Essential Medicines (NLEM) (2015) India [Internet]. World health organization. 2015 [cited in 21st March 2019]. Available from: http://apps.who.int/medicinedocs/en/m/abstract/Js23088en/.

26. Kumar V Nagesh, Kumar G (2013) A prospective study on prevalence, dialysis, and drug utilization of chronic renal failure patients. International Journal of pharmacology research, 3(2):45-52.

27. Ahlawat R, Tiwari P, D'Cruz S (2017) Direct cost for treating chronic kidney disease at an outpatient setting of a tertiary hospital: Evidence from a cross-sectional study. Value in health regional issues, 12: 36-40.

