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Study of drug utilization pattern in chronic kidney disease patients undergoing haemodialysis

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Abstract

Introduction: Chronic kidney disease (CKD) is a global threat to health, especially for developing countries because of an increasing incidence and poor outcome. Careful selection of drugs while prescribing in patients with CKD is necessary and the drug and its dose should be selected appropriately to avoid drug interactions, renal damage, adverse drug reactions and poor outcomes. However, errors in prescription in patients with CKD do occur. Hence it is important to study the drug utilization pattern in chronic kidney disease patients undergoing haemodialysis.
Materials and methods: A cross sectional, prospective observational study was carried out in the haemodialysis unit at a tertiary care hospital. Patient details like registration number, age, gender and medications were recorded in the Case Record Form. Prescribing indicators were evaluated as per WHO criteria.
Results: Out of 361study population 319 (88.37%) patients were having comorbidities and 42 (11.63%) patients were without any comorbidities. In total 2933 drugs were prescribed to study population and 8.12 drugs were prescribed per patient. Furosemide was the most commonly prescribed drug followed by amlodipine and sodium bicarbonate. Out of total prescribed drugs, 335 (11.4%) were antibiotics. Most commonly prescribed antibiotic was ceftriaxone. About 54.3% of drugs were prescribed by generic name. Out of total prescribed drugs, 2263 (77.2 %) drugs were listed in NELM.
Conclusion: This study provides an insight regarding utilization pattern of a wide variety of drug classes in CKD patients undergoing haemodialysis in a tertiary care hospital and suggests a possible improvement in prescribing practices in CKD patients.
Keywords: Chronic Kidney disease, haemodialysis, drug utilization, WHO criteria, comorbidities.

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1. Introduction

Chronic kidney disease encompasses a spectrum of different pathophysiological processes associated with abnormal kidney function and a progressive decline in glomerular filtration rate. Chronic renal failure is the process of continuous decline in nephron number and typically corresponds to chronic kidney disease stage 3-5 (Stage 3: 30-59 ml GFR/min/1.73m^2, stage 4:15-29 ml GFR/min/1.73m^2, stage 5: <15 ml GFR/min/1.73m^2).[1] Chronic kidney disease is a global threat to health in general specially for developing countries because of an increasing incidence and poor outcome. In India prevalence of stage 3 and above stage of chronic kidney disease is 6%. [2] The prevalence of renal failure can be attributed to changes in diet, physical inactivity, increased cases of diabetes, hypertension, and infectious diseases. Renal failure leads to end stage renal disease (ESRD) that requires expensive renal replacement therapies that includes dialysis and renal transplantation. However, the availability of these procedures is limited in India due to high cost.

Management of renal failure includes treatment of the comorbid conditions while considering the renal insufficiency. [3] Evidence shows that appropriate treatment of these comorbid conditions by appropriate use of the drugs delay progression of CKD and development of complications.

In addition to hypertension, diabetes mellitus, dyslipidemia and other comorbidities like coronary artery disease, anemia and infection affect clinical course of chronic kidney disease and increases the cost of treatment. [4-5] Its treatment includes vitamin preparations, phosphate binders, antihypertensives, hypoglycemics, diuretics, iron supplements and variety of other medications.[6] Chronic kidney disease patients are more susceptible to infections and likely to be prescribed antibiotics. The dosing of all drugs including antibiotics should be optimized and monitored so as to prevent adverse drug reactions, avoid further renal injury and to facilitate treatment outcomes. Because of the multiple medications, chronic kidney disease patients are at higher risk of developing drug-related problems. They require frequent monitoring. Inappropriate use of drugs in these patients can lead to adverse drug reactions; increase in hospital stays and increased cost of treatment.

Therefore, careful drug choice while prescribing for patients with renal failure and dosage adjustment has to be done to make safe and optimized therapy. [7] This study intended to find out the type of drugs used by patients with renal failure, their appropriateness, and consequences of irrational treatment. This is expected to significantly contribute to safe treatment of patients with renal failure and avoidance of progression of renal damage.

Hence this study of drug utilization pattern was planned to assess the drug utilization pattern in chronic kidney disease patients with or without comorbidities and to evaluate the prescriptions of drugs for rationality on the basis of WHO prescribing indicators in the patients of chronic kidney disease.

2. Materials and methods

2.1 Study design

This is a cross sectional, prospective observational study carried out in chronic kidney disease patientsin the haemodialysis unit at tertiary care hospital. The duration of the study was one and half years (November 2017 to April 2019). The study was started after getting approval from Institutional Ethics Committee.

2.2 Sample size

The study population included 361 cases of chronic kidney disease.

2.3 Inclusion criteria:

- Patients of chronic kidney disease undergoing haemodialysis aging 18 to 70 years of either sex.
- Patients who were willing to participate in the study.

2.4 Exclusion Criteria:

- Patients who were in acute renal failure
- Patients with poisoning and snake bite requiring haemodialysis
- Unconscious and pregnant patients
- Patients having psychiatric illness
- Illiterate patients who have major hearing impairment and not able to speak
- Not ready to give informed consent

Permission was obtained from head of the department of Medicine to conduct the study. Patients, who were admitted to Medicine ward and dialysis unit for haemodialysis and fulfilled the eligibility criteria, were approached and counselled about the study. The patients were assessed for eligibility as per the inclusion/exclusion criteria. Demographic details like registration number, age, gender and medication details as listed in the case notes were recorded in the Case Record Form. Study assessed demographic data and WHO prescribing indicators.

WHO Prescribing indicators include average number of drugs per encounter, percentage of drugs prescribed by generic name, percentage of encounters with an antibiotic prescribed, percentage of encounters with an injection prescribed, percentage of drugs prescribed from essential drugs list.

Formulae for prescribing indicators:

(a) Average number of drugs per encounter (C)

C = B/A where

B is total number of different drug products prescribed
A is the number of encounters surveyed

Purpose: To measure the degree of polypharmacy

(b) Percentage of drugs prescribed by generic name (E)

E = D/B x 100 where

D is the number of drugs prescribed by generic name
B is the total number of drugs prescribed

Purpose: To measure tendency to prescribe by generic name

(c) Percentage of encounters with antibiotic/s prescribed (G)

G = F/A x 100 where

F is the number of patients encounters with one or more antibiotic/s prescribed
A is the total number of encounters surveyed

Purpose: To assess the prescribing frequency of these often inappropriately used agents

(d) Percentage of encounters with an injection prescribed (K)

K = J/A x 100 where

J is the total number of patients who received 1 or more injections
A is total number of encounters

Purpose: To measure overall level of use of this commonly overused and expensive form of drug therapy

(e) Percentage of drugs prescribed from essential drugs list (M)

M = L/ B x 100 where

L is the number of products prescribed from National List of Essential Medicines
B is the total number of drugs prescribed

Purpose: To measure the degree to which practices conform to the national drug policy

Adverse drug reactions were recorded in suspected adverse drug reaction reporting form. Causality relationships of adverse drug reactions with suspected drug were assessed as per Naranjo's ADR probability scale.

2.5 Statistical methods:

The detail data was entered into Microsoft excel sheet and subsequently analyzed statistically by using descriptive statistics. SPSS Software version 21 was used for analysis. Whenever possible results were expressed as mean ± standard deviation [SD] and percentage.

3. Results

Total number of 361 chronic kidney disease patients with or without comorbidities were included in the study. Out of 361 patients 319 (88.37%) patients were having co-morbidities like diabetes mellitus, hypertension, anemia etc. and 42 (11.63%) patients were without any co-morbidities. Overall average age of the study population was 46.13 years.

In study population, 236 (65.37 %) were male patients and 125 (34.63%) were female patients.

Average comorbidities per patient were 1.43. The most common comorbidities were hypertension (63%), anemia (40.72%) and diabetes mellitus (29.36%)**[Table 1]**

Table 1: Types of comorbidities in study population

Sr. No.	Comorbidity	No of patient affected (%)
1	Hypertension	228 (63.16%)
2	Anemia	147 (40.72%)
3	Diabetes mellitus	106 (29.36%)
4	Hepatitis B / C	11 (3.05%)
5	Ischemic heart disease	11 (3.05%)

Total 2933 drugs were prescribed to study population**.** Average numbers of drugs prescribed per patient were 8.12. Numbers of drugs required in patients with comorbidities were more as compared to number of drugs required for patients without comorbidities. However, this difference was not statistically significant. (p value- 0.1731) **[Figure 1]**

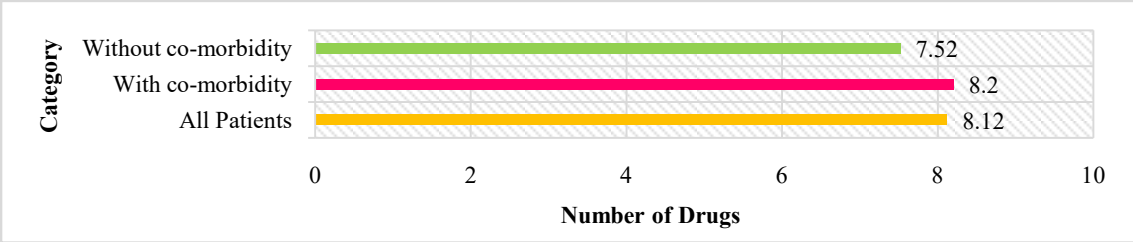

Figure 1: Number of drugs prescribed per patient in study population

Furosemide was the most commonly prescribed drug followed by amlodipine and sodium bicarbonate **[Figure 2].**

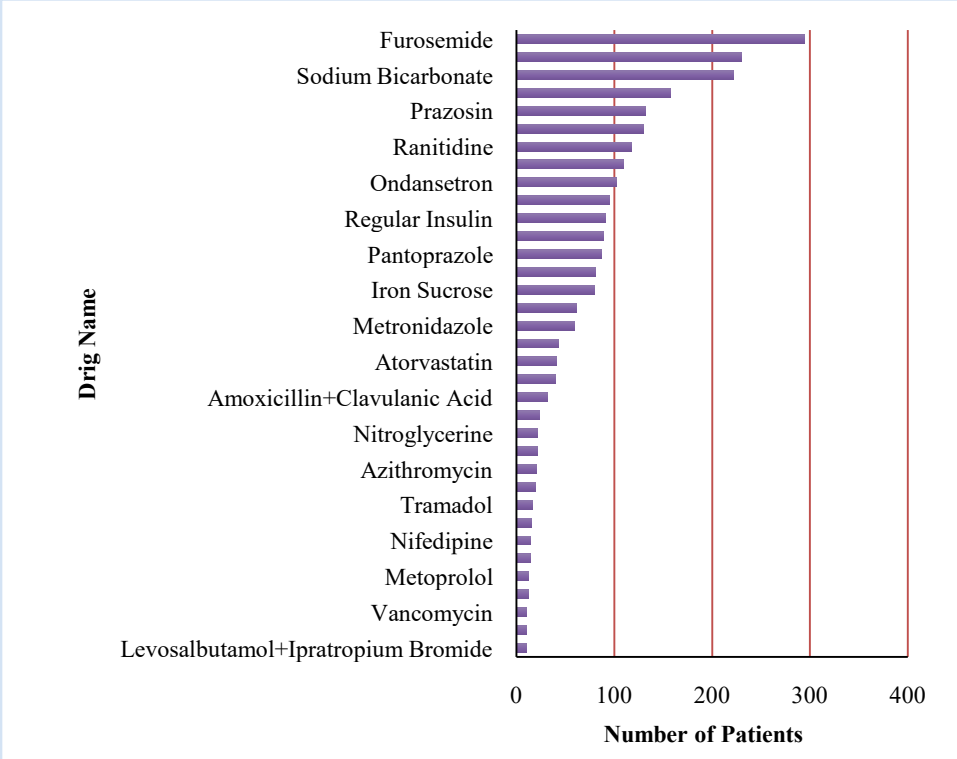

Figure 2: Drug utilization pattern in study population

In study population, 39 drug classes were prescribed to the patients. Common drug classes given in table among 39 drug classes.

The most common classes of drugs prescribed were antihypertensive (18.6%), antacid (13.5%) and antimicrobial agents (12.1%) **[Table 2]**

Table 2: Various drug classes used in study population

Sr No.	Drug Class	No. of drugs (%)
1	Antacid	393 (13.5%)
2	Antidiabetic	138 (4.7%)
3	Antiemetic	123 (4.2%)
4	Antihypertensive	547 (18.6%)
5	Aldosterone antagonist	5 (0.2%)
6	Antimicrobial	356 (12.1%)
7	Antiplatelet	51 (1.7%)
8	Bronchodilator	38 (1.3%)
9	Bile salts	5 (0.2%)
10	Calcium preparation	263 (9%)
11	Corticosteroid	22 (0.8%)
12	Diuretic	324 (11%)
13	Hematinic	255 (8.7%)
14	Hypolipidemic drugs	44 (1.5%)
15	Miscellaneous	225 (7.7%)

Number of drugs prescribed by brand name and generic name were 1339 (45.7%) and 1594 (54.3%) respectively **[Figure 3].**

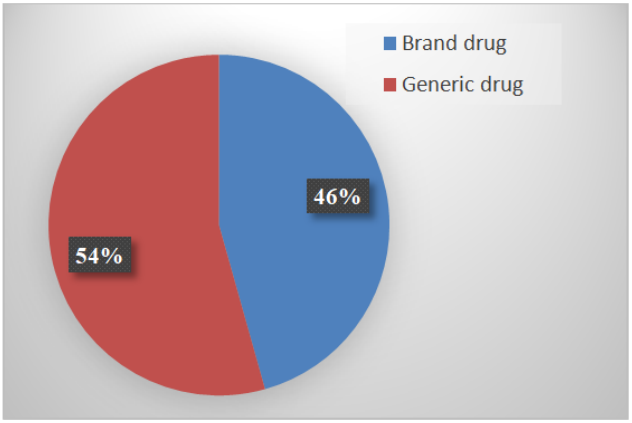

Figure 3: Use of Generic name versus brand name in study population

Out of total prescribed drugs, 356 drugs (12.13 %) were antibiotics **[Figure 4].** The most commonly prescribed antibiotic was ceftriaxone (47.19%) followed by metronidazole (15.16%).

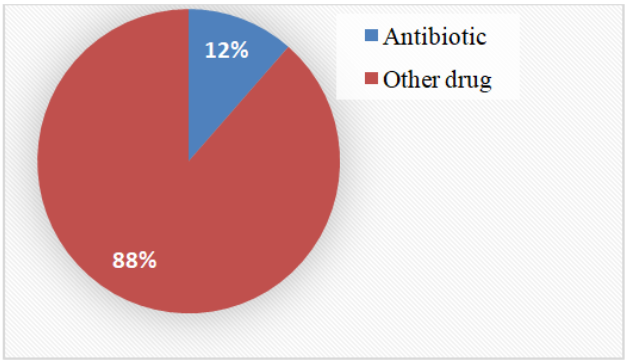

Figure 4: Percentage distribution of antibiotics in study population

Out of total prescribed drugs, 2263 (77.2 %) drugs were listed in NLEM **[Figure 5].**

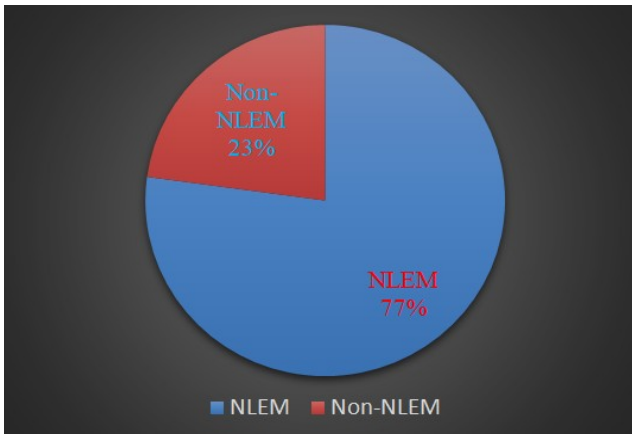

Figure 5: Distribution of drugs based on NLEM in study population

WHO Prescribing indicators

1. Average no. of drugs per encounter: 8.12
2. Percentage of drugs prescribed by generic name: 54.34%
3. Percentage of encounters with antibiotic/s prescribed: 12.13%
4. Percentage of encounters with an injection prescribed: 41.28%
5. Percentage of drugs prescribed from essential drugs list: 77.15%

Adverse Drug Reactions

In total four incidences of adverse drug reactions were reported in this study. Hyperkalemia was reported with the use of enalapril and telmisartan which was managed by stopping drug or reducing dose respectively **[Table 3].**

Table 3: Adverse drug reaction and causality assessment in study population

No.	Drug	ADR	Causality	Management
1.	Enalapril	Hyperkalemia	Possible	Enalapril was stopped and Clonidine started
2.	Telmisartan	Hyperkalemia	Possible	Telmisartan dose reduced to half
3.	Iron sucrose	Itching & chills	Probable	Iron sucrose stopped. Hydrocortisone and Pheniramine administered parentally
4.	Insulin mixtard	Hypoglycemia episode	Possible	Insulin mixtard stopped and dextrose 25% given I.V.

4. Discussion

This study showed Polypharmacy due to the prevalence of co-existing illnesses. Average drugs prescribed per patient were 8.12 which is almost similar to study by Narayana *et al*[8] Use of generic drugs varied compared to previous studies, but still it was more than fifty percentage of total drug prescribed. Drugs prescribed from NLEM were more compared to previous studies. The gender distribution and mean age of patients in our study was similar to that reported in an earlier study.[9] Greater number of middle-aged individuals were affected which may be related to natural aging of the kidneys and many conditions that damage the kidneys such as diabetes, high blood pressure, and heart diseases.

Male predominance may be due to higher prevalence of risk factors such as elevated blood pressure, diabetes mellitus, smoking, hyperlipidemiain them. [10]

In the present study antihypertensive class of drugs was prescribed more commonly as hypertension is commonly associated with CKD. Drug utilization pattern in the study by Chakraborty *et al* [11] was found to be similar to the present study where antihypertensives (23.41%) antacids (15.76%) antimicrobials (10.93%), diuretics (9.29%), phosphate binders (11.2%) and antidiabetics (2.73%) were used. Previous study had showed diuretics use in 9.15% of patients which is nearly similar to present study.[8] High ceiling diuretics were required to maintain urine output and avoid fluid overload.[14]

In present study haematinics were used in 8.7% patients. Haemodialysis patients lack iron due to loss of small amount of residual blood discarded in the dialyzer and tubing after each dialysis session. Erythropoietin is not produced in sufficient amount, which leads to renal anemia. Hence iron supplements and erythropoietin should be administered in patients undergoing haemodialysis. The use of erythropoietin in anemic CKD patients subsequently reduces blood transfusion requirement. Utilization of antacids in present study which is slightly less as compared to their use in Chakraborty *et al* [11] study and more than that in Narayan *et al* study. [8] Incidence of peptic ulcers, gastro-esophageal reflux disease, dyspepsia is more in chronic kidney disease patients. So, antacids were used to prevent peptic ulcers, gastro-esophageal reflux disease and for the symptomatic relief of dyspepsia.

Furosemide was one of the commonly used drugs in present study as well as in Oommen *et al* [12] study. Loop diuretics are recommended in patients with GFR<30 ml/min/1.73m^2 as per KDOQI guidelines. Amlodipine was most commonly prescribed calcium channel blockers in present study as well as in Oommen *et al* [12] study. Hyperphosphatemia is a frequently seen complication in patients with end stage renal disease. In present study, calcium lactate and calcium acetate were maximally prescribed as phosphate binders, similar trend is observed in Oommen *et al* [12] and Abhisek *et al* [13] studies. Large observational studies identified hyperphosphatemia as an independent risk factor for cardiovascular disease and mortality in patients on dialysis. Administration of dietary phosphorus binders to block intestinal phosphorus absorption is the cornerstone of therapy for hyperphosphatemia. In CKD patient's phosphorus should be maintained within the target range with dietary restrictions and use of phosphate binders. Aluminium based phosphate binders use is currently restricted because of their tissue accumulation. Hence calcium-based phosphate binders are preferred. In addition, calcium salts are more affordable for poor patients as compared to sevelamer hydrochloride and lanthanum carbonate. Adverse drug reactions reported in present study are very few as compared to those reported by Chakraborty *et al* [10] in their studies. In our study all the WHO prescribing indicators were assessed. Similarly, Rajeshwari *et al* [9] study also assessed all the WHO prescribing indicators. While Abhisek *et al* [13] and Narayana *et al* [6] not considered all these prescribing indicators in their studies.

In present study 54.34% drugs were prescribed by generic name while no drug was prescribed by generic name in Narayana *et al* [8] study. It is clearly evident that prescribing by generic name in the present study was better as compared to previous studies. Increasing generic prescribing would rationalize the use and reduce the cost of drugs. [15]

World health organization (WHO) highly recommends prescribing by generic as safety precaution for patients, because it identifies the drug clearly and enables better information exchange.[16] Thus, prescribing by generic names should be promoted, as it would help in reduction of chances of drug duplications, drug interactions and provide cheaper treatments.

The percentage of antibiotics prescribed was 12.13% which was higher than the study by Rajeshwari *et al* [9] study. Study by Chakraborty *et al* [11] showed similar antibiotic prescribing. However, since many antibiotics are eliminated by kidneys and some may be nephrotoxic in nature, careful antibiotic drug and dose selection are necessary.

The antibiotic use should be done judiciously which is quite necessary to prevent the emergence of antibiotic resistance, arising due to uncontrolled use of antibiotics. Also, the controlled use will reduce the cost of treatment. The higher percentage of injectables used in present study might be due to requirement of insulin, erythropoietin, iron sucrose etc. which are available in parenteral dosage forms.

Similar results showed by Abhisek *et al* [13] study in which 72.62% of prescribed drugs were from NLEM while in Narayana *et al* [6] and Rajeshwari *et al* [9] studies much lesser drugs, 39.75% and 41.5% were from NLEM respectively. Essential medicines are intended to be available within the context of functioning health care systems at all times in adequate amount, in appropriate dosage forms, with assured quality and adequate information and at price the individual and community can afford. For optimum utilization of resources, government should concentrate on these drugs identifying them as essential. Adoption of NLEM for procurement and supply of medicines especially in public sector is necessary. Prescribing of drugs as per NLEM in health care system results in improvement in availability of medicines, cost saving and more rational use of drugs. [17] Patient compliance and cost analysis were not assessed and possible drug-drug interactions were not reported in the present study. Larger drug utilization studies should be conducted at more than one tertiary care hospitals. So that we can get strong evidence about drug utilization trends and magnitude of irrationalities in prescribing.

This study provides an insight regarding utilization pattern of a wide variety of drug classes in CKD patients undergoing maintenance haemodialysis in a tertiary care teaching hospital setting and suggests a possible improvement in prescribing practices in CKD patients. Certain areas like potential drug interactions, adverse drug reactions and adherence are required to be explored further.

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References

[1]. Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, Loscalzo J. Harrison's Principles of Internal Medicine,20th ed. New York: McGraw Hill;2018

[2]. Verma PP, Prevalence of chronic kidney disease in India- where we are heading, *Indian journal of Nephrology*, 2015; 25(3): 133-135.

[3]. Perazella MA. Renal Vulnerability to Drug Toxicity. *Clin J Am Soc Nephrol*. 2009; 4(7): 1275–83.

[4]. Agarwal SK, Srivastava RK. Chronic kidney disease in India: challenges and solutions. *Nephron Clin Pract*. 2009; 111(3): c197-203.

[5]. Rajapurkar MM, John GT, Kirpalani AL, Abraham G, Agarwal SK. What do we know about chronic kidney disease in India: first report of the Indian CKD registry? *BMC Nephrology*, 2012; 13(10):1- 8.

[6]. 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.

[7]. Decloedt E, Leisegang R, Blockman M, Cohen K. Dosage adjustment in medical patients with renal impairment at Groote Schuur Hospital. *South African Medical Journal*. 2010; 100(5): 304–6.

[8]. Murthy N, Satyanarayana V. Prescribing pattern of drugs in chronic kidney disease patients on hemodialysis at a tertiary care hospital. *IJBCP*, 2017; 6(4): 928.

[9]. 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 Pharmacol and Clin Sci*. 2016; 5(3): 65-72.

[10]. Chandel Ritesh Kumar. A Descriptive Analysis of Prescribing Patterns of Drugs in Chronic Kidney Disease Patients on Maintenance Hemodialysis. *JMSCR* 2019; 07(05).

[11]. Chakraborty S, Ghosh S, Banerjea A, Hazra A, Mandal S. Prescribing patterns of medicines in chronic kidney disease patients on maintenance haemodialysis. *Indian Journal of Pharmacology* 2016; 48(5): 586-590.

[12]. Oommen JM, Nerurkar DP, Sajith M, Jawale S, Ambike SM. Prescription Pattern of Chronic Kidney Disease Patients undergoing Hemodialysis in Tertiary and Private Hospital. *J Young Pharm.* 2019; 11(2): 202-6.

[13]. Abhisek P A, Rajendra Panda R, Samal R, Mohapatra N, Mohanty S. Drug Utilisation Pattern and Adverse Events in Patients with Chronic Kidney Disease on Maintenance Haemodialysis. *Journal of Clinical and Diagnostic Research*. 2017; 11(10): 11-16.

[14]. Arnoff GR, Berns JS, Brier ME. Drug Prescribing in Renal Failure, 5 edn. Philadelphia, PA: American College of Physicians; 2007.

[15]. Quick JD, Hogerzeil HV, Velasquez G, Rago L. Twenty-five years of essential medicines. *Bull World Health Organ*. 2002; 80: 913-14.

[16]. Guidelines on the use of international nonproprietary names (INNs) for pharmaceutical substances. Geneva, World Health Organization, 1997 (http://apps.who.int/medicinedocs/ en/d/Jh1806e)

[17]. Adibe M.O., Prof Aguwa C.N., Ukwe C.V., Okonta J.M., Udeogaranya P.O. Outpatient Utilization of anti-diabetic drugs in the South Eastern Nigeria; *Int J. Drug Dev. & Res.* I 2009; 1(1): 27-36.