Acta Scientific Pharmaceutical Sciences (ISSN: 2581-5423)

Volume 4 Issue 11 November 2020

Research Article

A Cross Sectional Observational Study on Prescribing Patterns of Drugs in Chronic Kidney Disease Patients in a Tertiary Care Teaching Hospital

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Received: September 02, 2020

Published: October 08, 2020

Abstract

The prevalence of Chronic Kidney Disease are enormously increasingly world wide due to gradual rise in hypertension, diabetes, cardiovascular diseases. As kidney is a major eliminating organ, its function decreases in CKD resulting in accumulation of drugs which leads to toxic effects. Use of poly pharmacy in co- morbid conditions results in drug - drug interactions and adverse effects which may cause serious and long term illness and decrease quality of life of patient. The aim is to assess the prescribing patterns of drugs in chronic kidney patients in a tertiary care teaching hospital. Objectives are to assess the prescribing drug doses in CKD patients. To identify the risk factors in CKD. To predict the GFR by using Modified diet in renal failure formulae. To evaluate the comorbidities involved in CKD. To determine the number of drugs prescribed belong WHO essential list. To analyse the drug interactions involved in prescriptions. To assess the prescribing patterns of prescribers in CKD patients. To determine the usage of drugs by using WHO prescribing indicators. A prospective observational study carried out in Sri Venkateswara Ramnarayan Ruia Government General Hospital (SVRRGGH) during December 2016 to March 2017 (6 months). A total of 125 patients diagnosed with CKD are included in study. Patients who are not willing, below 18 years, special population including pregnant, lactating women were excluded from study. Predesigned proforma was used to collect data. Total of 125 patients were included in study, men constituted 68% of total population. Most effected age group was 51-60 years. Hypertension was major risk factor 48.20% observed in study population. Most of patients are in stage 4, 35.20%. 1163 drugs were prescribed to 125 patients. Percentage of drugs prescribed from WHO EDL was 62.90%. Prevalence of polypharmacy was very high in patients with CKD. Medication prescribing patterns suggest a high number of medications used in CKD patients with increased possibility of drug interactions. Continuous medical education of physicians and collaboration with clinical pharmacist is an important issue for quality improvement regarding renally impaired patients.

Keywords: Chronic Kidney Disease; WHO; Drugs

Introduction

Prescription pattern studies are drug utilisation studies which explains about prescribing, dispensing and administering of drugs. They explain about drug use, quality of drugs, trends and compliance with standard treatment guidelines, usage of drugs from essential medicine list and use of generic drugs [1]. The main aim of Prescription pattern studies is to promote the rational use of drugs in a public. According to WHO more than half of the medicines are prescribed and dispensed inappropriately. Chronic Kidney Disease is a world wide public health problem with an increasing incidence, prevalence, poor outcomes and high cost. Outcomes of CKD include kidney failure, complications of decreased kidney function and cardiovascular disease. Chronic kidney disease decreases kidney function, resulting in decrease in elimination of drugs which leads to

accumulation of drugs and precipitation of adverse drug reaction. Chronic kidney disease affects the elimination of renally excreted drugs and other pharmacokinetic processes involved in drug disposition (e.g. absorption, drug distribution, metabolism). In renal ill patients dosing error are common and can lead to adverse effects and poor outcomes. The Kidney Disease Outcomes Quality Initiative (K/DOQI) of the National Kidney Foundation (NKF) defines CKD as either kidney damage or a decreased glomerular filtration rate of less than 60 mL/min/1.73m^2 for 3 or more months [2].

Aim of the Study

To assess prescribing patterns of drugs in chronic kidney disease patients in a tertiary care teaching hospital.

Objectives of the Study

- To assess the prescribing drug doses in chronic kidney disease patients.
- To identify the risk factors associated in CKD patient.
- To evaluate the comorbidities involved in chronic kidney disease.
- To determine the number of drugs prescribed belong WHO essential list.
- To analyze drug interactions involved in prescription.
- To assess the prescribing patterns of prescribers in CKD patients.
- To determine the prescribing indicators involved according WHO prescribing indicators.

Methodology

Study design: Cross sectional observational study.

Study place: Sri Venkateswara Ramnarayan Ruia Government General Hospital. (SVRRGGH).

Study duration: 6 months.

Study population: 125 prescriptions.

Study site: Department of General Medicine.

Inclusion criteria

- All patients with diagnosis of CKD in general medicine department both male and female medical wards.

Exclusion criteria

- Patients below 18 years.
- Patients who were not willing.
- Special population including pregnant women and lactating women.

Data collection

A designed proforma and informed consent form was used for collection of data. The proforma contain patient demographics, diagnosis, admission complaints, past medical history, past medication history, family and surgical history, laboratory investigation reports and drugs prescribed. Evaluation proforma was used to evaluate data from proforma. Evaluation proforma contain information on co-morbidities, risk factors in CKD patients, estimation of GFR, CKD stage, drug interactions.

Results

Gender wise distribution of study population

Sex	No. of patients (n = 125)	Percentage
Male	85	68%
Female	40	32%

Table 1

Age wise distribution of study population

Age	Female (n = 39)	Male (n = 86)	Total (n = 125)	Percentage
20-30	1	3	4	3.20%
31-40	7	4	11	8.80%
41-50	8	18	26	20.80%
51-60	12	25	37	29.60%
61-70	4	27	31	24.80%
71-80	7	8	15	12%
81-90	0	1	1	0.80%

Table 2

Chronic kidney disease with comorbidities

Comorbidities	No. of patients (n = 259)	Percentage
Hypertension	67	25.80%
Diabetes mellitus	41	15.80%
Anaemia	22	8.49%
congestive cardiac failure	19	7.30%
Acute kidney injury	10	3.86%
coronary artery disease	9	3.47%
Ischemic Cardiomyopathy	7	2.70%
Cerebrovascular accident	7	2.70%
Gastro enteritis	6	2.31%
Lower respiratory tract infections	5	1.93%
Pulmonary tuberculosis	5	1.93%
Chronic obstructive pulmonary disease	5	1.93%
Acid peptic disease	4	1.54%
Hepatitis B virus	4	1.54%
Stroke	4	1.54%
Diabetic neuropathy	4	1.54%
Chronic liver disease	3	1.15%
Decompensated chronic liver disease	3	1.15%
Dilated cardiac myopathy	3	1.15%
Pulmonaryoedema	3	1.15%
Filariasis	2	0.77%
Left ventricular disease	2	0.77%
Diabetic foot	2	0.77%
Emphysema	2	0.77%
OTHERS	20	7.77%

Table 3

Risk factors in study population

Risk factor	No. of patients (n = 147)	Percentage
Hypertension	71	48.20%
Diabetes mellitus	32	21.70%
Acute kidney injury	6	4%
Others	38	25.80%

Table 4

Stages of CKD in study population

CKD Stage	No. of patients (n = 125)	Percentage
Stage-1	5	4%
Stage-2	9	7.20%
Stage-3a	13	10.40%
Stage-3b	7	5.60%
Stage-4	44	35.20%
Stage-5	43	34.40%
None	4	3.20%

Table 5

Hemoglobin levels in female study population

Hemoglobin (g/dl)	Female (n = 40)	Percentage
>11	1	2%
<11	39	98%

Table 6

Hemoglobin levels in male study population

Hemoglobin (g/dl)	Male (n = 85)	Percentage
>13	6	7%
<13	79	92.85%

Table 7

Distribution of erythropoietin in study population

Gender	Erythropoietin (n = 125)	
	Yes	No
Male	16	69
Female	9	31
Total	25	100
Percentage	20%	80%

Table 8

Pattern of antihypertensive therapy in CKD patients

Anti hypertensive drugs		
Drugs	**Number of patients**	**Percentage**
	Monotherapy (29.91%)	
Furosemide	30	85.70%
Amlodipine	4	11.43%
Enalapril	1	2.85%
Total	35	100%
	Two drug therapy (29.91%)	
Furosemide+amlodipine	26	74.28%
Furosemide+spironolactone	6	17.14%
Furosemide+metolazone	2	5.71%
Amlodipine+prazosin	1	2.85%
Telmisartan+atenolol	1	2.85%
Total	35	100%
	Three drug therapy (30.7%)	
Furosemide+amlodipine+prazosin	11	30.50%
Furosemide+amlodipine+metolazone	5	13.80%
Furosemide+amlodipine+ Spironolactone	2	5.50%
Furosemide+amlodipine+clonidine	2	5.50%

Furosemide+amlodipine+atenolol	2	5.50%
Furosemide+amlodipine+enalapril	2	5.50%
Furosemide+metoprolol+ Spironolactone	2	5.50%
Furosemide+spironolactone+ Propranolol	2	5.50%
Furosemide+spironolactone+ Enalapril	2	5.50%
Furosemide+metolazone+prazosin	3	8.30%
Furosemide+enalapril+ Metoprolol	1	2.70%
Furosemide+amlodipine+ Propranolol	1	2.70%
Metoprolol+enalapril+ Spironolactone	1	2.70%
Total	36	100%
	Four drug therapy (7.69%)	
Furosemide+amlodipine+ Metolazone+metoprolol	2	22.20%
Furosemide+amlodipine+ Spironolactone+atenolol	1	11.10%
Furosemide+amlodipine+ Labetalol+enalapril	1	11.10%
Furosemide+amlodipine+prazosin+ Enalapril	1	11.10%
Furosemide+prazosin+metolazone+ nifedipine	1	11.10%
Furosemide+amlodipine+ Spironolactone+enalapril	1	11.10%
Furosemide+spironolactone+ Enalapril+metoprolol	1	11.10%
Frosemide+prazosine+amlodipine+ Metolazone	1	11.10%
Total	9	100%
	Five drug therapy (1.7%)	
Furosemide+amlodipine+enalapril+ Metolazone+prazosin	2	

Table 9

Overall patterns of antihypertensive drugs prescribed in CKD patients

Drug group	Frequency (n = 235)	Percentage
Diuretics		
Spironolactone	18	7.65%
Metolazone	11	4.68%
Furosemide	97	41.27%
Ace inhibitors		
Enalapril	13	5.53%
CCBS		
Amlodipine	58	24.68%
Nifedipine	1	0.42%
Alfa blokers		
Prazosin	14	5.95%
Beta blokers		
Propranolol	3	1.27%
Metoprolol	7	2.97%
Atenolol	4	1.70%
Labetalol	1	0.42%
ARBS		
Telmisartan	1	0.42%
Alpha agonist		
Clonidine	3	1.27%

Table 10

Pattern of antidiabetics in CKD patients

Antidiabetic Drugs	No of Drugs (N = 51)	Percentage
Oral Hypoglycemic Agents		
One Drug Therapy	Total 4 (7.84%)	100%
Metformin	2	50%
Glimepride	1	25%
Glibenclamide	1	25%
Total	4	
Two Drug Therapy	Total 5	
Metformin+Glimepride	5(9.8%)	
Insulin Therapy		
Single Insulin Therapy	Total 34 (66.6%)	100%
Plain insulin	22	64.70%
NPH insulin	12	35.29%
Total	34	
Two Insulin Therapy	Total 3	
Plain insulin+NPH insulin	3 (5.8%)	
Oral Hypoglycemic Agents+Insulin Therapy	Total 5 (9.8%)	100%
(Metformin+Glimepride)+NPH insulin	3	60%
(Metformin+Glimepride)+Plain insulin	2	40%

Table 11

Distribution of prescribed drugs based on category

Drug category	No. of drugs (n = 1163)	Percentage
Antihypertensives	235	20.20%
Vitamins and minerals	188	16.10%
Antibiotics	136	11.69%
Antiulcer drugs	114	9.80%
Anaemic Drug	83	7.10%
Antiplatelets	53	4.50%
Antidiabetics	51	4.48%
Bronchodilators	44	3.78%
Lipid lowering agents	40	3.43%
Alkalisers	22	1.89%
Laxatives	12	1.03%
Cardiac glycosides	12	1.03%
Antitubercular therapy	12	1.03%
Corticosteroids	11	0.94%
Analgesics	7	0.60%
Nitrates	6	0.51%
Anticoagulants	5	0.42%
Antifungals	2	0.73%
Thyroid drugs	1	0.08%
Others	129	11.09%

Table 12

Possible drug – drug interactions in study population

Severity	No. observed (n = 282)	Percentage
Major	138	48.90%
Moderate	117	41.40%
Minor	27	9.57%

Table 13

Prescribing indicators

Indicators	Value
Total number of prescriptions	125
Total number of drugs prescribed	1163
Average number of drugs per prescription	9.3 (1.6-1.8)
Percentage of drugs prescribed by generic name	52.27% (100%)
Percentage of prescriptions with an injections prescribed	95.20% (13.4-24.1%)
Percentage of prescriptions with an antibiotics prescribed	47.72% (13.4-24.1%)
Percentage of drugs prescribed from WHO EDL 2015	62.90% (100%)

Table 14

Discussion

The prevalence of CKD cases are enormously increasingly world wide due to gradual rise in hypertension, diabetes, cardiovascular diseases and also inappropriate drug use and polypharmacy make people prone to drug induced renal disease in India. Most of drugs are extensively excreted by kidneys, in renal failure condition the drugs are accumulated and causes toxic or adverse effects.

The total of 125 patients were included in our study. Among total study population 85 patients were male and 40 patients are female. This explains that majority of a males population over females. This may be due to various risk factors like smoking, consumption is commonly high in men compared with women. These findings are similar to that of Tamilselvan T, Veerapandiyan AK., *et al*. study [3].

In the study, more number of patients are seen between age of 51 - 60 years (37 patients, 29.60%), followed by 61 - 70 years (31 patients, 24.80%). Age may be also one of risk factor for development of CKD, which is similar to Tamilselvan T, Veerapandiyan AK., *et al*. study [3].

The kidney plays a major role in the control of blood pressure by regulating sodium retention, extracellular fluid volume, and the renin-angiotensin system. Alteration in these mechanisms leads to hypertension in CKD. Hypertension (67, 25.80%) was the major co-morbidity in study population, followed by diabetes mellitus (41,15.80%), followed by anaemia (22, 8.49%). Most of the patients were are to be having more than one co-morbidity.

In present study major risk factor found to be hypertension (71,48.20%), followed by diabetes mellitus (32,21.70%), followed by acute kidney injury (6,4%). A patient may have more than one risk factor.

The study population with stage-4 (44,35.20%) were higher followed by Stage-5 (43,34.40%). These findings reveals that most of study population are with end stage renal disease.

Most of female patients are anaemic with haemoglobin less are than 11 g/dl (39,98%) out of 40 female study population. In total of 85 male patients 79 were anaemic with haemoglobin less than 13 g/dl (79,92.85%) out of 85 male study population. According to National kidney foundation females with haemoglobin less than 12 g/dl and males with haemoglobin less are than 13 g/dl are anaemic. The occurrence of anaemia in CKD patients is due to reduced production of erythropoietin in CKD patients. Erythropoietin is produced by kidneys which is one of its function.

Out of 125 study population, only (25,20%) received erythropoietin even though majority are anaemic. Most of patients in government hospital are unable to get erythropoietin.

Multiple drug therapy was usually followed by CKD patients due to their comorbid conditions such as hypertension, diabetes, cardiovascular disorders, phosphate retention, anaemia, dyslipidaemia, thyroid disorders, mineral imbalance etc. Hence along with antihypertensive and antidiabetic drugs the patients have to take other drugs based their comorbidity such as phosphate binders, vitamins, mineral supplements, antiplatelets etc.

Antihypertensives are given to reduce elevated blood pressure, to reduce cardiovascular diseases and reduce progression of Chronic kidney disease. This study shows that 35(29.91%) received monotherapy of antihypertensives, 35(29.91%) received two drug therapy, 36(30.7%) received three drug therapy, 9(7.69%) received four drug therapy and 2(1.7%) received five drug therapy. Furosemide was most commonly prescribed drug in both in mono and combination drug therapy. The reported mono and combination use of Furosemide was 97(41.27%). Majority antihypertentives were diuretics (216) followed by CCBs (59) and ACEI. Were as in Elahe Elhami and Kiran Nagaraju study [4] mostly prescribed drugs are ACEI followed by Diuretics and followed by CCBs. In Alwyn P Saju, Ankur C Edakkarayil., *et al*. study [5] CCBs are majorly prescribed drugs followed by Diuretics. ACEI and ARBs are first line choice of drugs in hypertension and with or with out diabetes according to JNC8 [6]. But in our hospital ACEI are less preferred drugs than others because its risk of hyperkalaemia and decreased GFR in patients and also need dose adjustments, as the patients are already renal impaired.

In this study majorly prescribed therapy was three drug therapy 30.7%, followed by two drug and monotherapy (29.91%). Furosemide+Amlodipine+Prazosin was mostly prescribed in three drug therapy 11 (30.50%). In two drug therapy Furosemide+Amlodipine was majorly prescribed drugs 26 (74.28%). In Elahe Elhami and Kiran Nagaraju study [4] mostly prescribed combinations were 30 (50%) Hydrochlorothiazide + Enalapril, follow by Torsemide + enalapril15 (25%) were the most commonly prescribed two-drug combination therapy in patients, Hydrochlorothiazide + Enalapril + Verapamil15 (62.50%), follow by Furosemide+ Metoprolol + Prazosin (25%) were the most commonly prescribed three-drug combination therapy in patients.

A total of 51 antidiabetic drugs were prescribed in 125 patients. The mostly prescribed antidiabetic drugs are Insulin therapy 34 (66.6%) followed by two drug oral hypoglycaemic agents and combination of Oral hypoglycemicagents+insulin therapy 5 (9.8%), followed by one drug therapy of oral hypoglycaemic agents 4 (7.84). In mono drug therapy of oral hypoglycemics metformin was mostly prescribed. According to National kidney foundation Metformin is contraindicated in male patients with a serum creatinine > 1.5 mg/dl and in female patients with serum creatinine > 1.4 mg/dl.

188 Vitamins and minerals are prescribed in study population. Vitamin B6, B9, B12 are essential in production of RBC, as the CKD patients are anaemic vitamin are very essential. Kidneys activate vitamin D, into calcitriol. Calcitriol maintain blood calcium levels and also remove extra phosphorus, to balance phosphorus and calcium levels in the blood, but in CKD the normal function is altered hence Calcium+ Vitamin D3 is given. Calcium gluconate is given to treat low calcium levels and in hyperkalaemia.

Risk of infection in CKD patients is high because of antibiotics usage. A total of 136 antibiotics were given. H_2 blockers and PPIs are mostly prescribed drugs to reduce stress induced ulcers and as symptomatic therapy. A total of 114 antiulcer drugs were given study population. Constipation is complication of CKD hence laxatives are mostly preferred drugs, 12 (1.03%) of laxatives are prescribed. Based on comorbidities with CKD the other drugs such as Antiplatelets 53 (4.50%), Bronchodilators 44 (3.78%), Lipid lowering agents 40 (3.43%), Alkalizers 22 (1.89%), Cardiac glycosides, Anti tubercular therapy 12 (1.03%), Corticosteroids 11 (0.94%), Analgesics 7 (0.60%), Anticoagulants 5 (0.42%), Antifungals 2 (0.73%) and Thyroid drugs 1 (0.08%) have been prescribed.

282 possible drug - drug interactions were found in prescriptions, among them 138 (48.90%) were major drug interactions, followed by 117 (41.40%) moderate drug interactions, and followed by 27 (9.57%) minor interactions were found. This due to polypharmacy in many prescriptions. In Alessandra Batista Marquito, Natalia Maria da Silva Fernande study [7] majority are moderate drug interactions 76.9%, followed by major drug interactions 16.8% and minor drug interactions were 5.9%.

In the present study, the total number of drugs prescribed for 125 patients is 1163 drugs, the average number of drugs per prescription was 9.3 which is higher than WHO prescribing indicators (1.6 - 1.8). The percentage of drugs prescribed by generic name was 52,27% which is less than WHO prescribing indicators (100%). The percentage of prescriptions with an injections prescribed was 95.20% which higher than WHO prescribing indicators (13.4 - 24.1%). The percentage of prescriptions with an

antibiotics prescribed was 67.2% which is also higher than WHO prescribing indicators. Percentage of drugs prescribed from WHO EDL 2016 was 62.94% which is also less than WHO prescribing indicators (100%).

Conclusion

It is concluded that the prevalence of polypharmacy was very high in patients with CKD. Diuretics, anti-hypertensives, oral hypoglycaemic drugs were more frequently used in CKD patients because of high prevalence of co morbidities. Medication prescribing patterns suggest a high number of medications used in CKD patients with increased possibility of drug interactions. Continuous medical education of physicians and collaboration with clinical pharmacist is an important issue for quality improvement regarding renal impaired patients.

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