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PRESCRIPTION PATTERN OF MEDICINES IN CHRONIC KIDNEY DISEASE PATIENTS IN NEPHROLOGY DEPARTMENT OF A TERTIARY CARE TEACHING HOSPITAL: AN OBSERVATIONAL STUDY

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Abstract

Objectives: Chronic Kidney Disease patients required lifelong multiple therapy. Multitudinous medication increases risk of irrational drug use and drugs related problems in CKD patients. This study was done to estimate the current trends of prescribing pattern of medicines in chronic kidney disease patients and to assess the rationality of prescriptions.

Methods: A prospective observational study was conducted at a tertiary care teaching hospital. All the prescribing details of study participants including patient's demographic details, diagnosis, drug name, dose, duration and frequency were recorded in specially designed performa and rationality of prescription was assessed using WHO core prescribing indicators.

Results: Demographic analysis showed males predominance with 54% and females were 46%. Most of the study population belongs to the age group more than 40 years (50%). Anemia and Hypertension were the main co morbidities associated with CKD followed by diabetes. Most commonly prescribed drugs were cardiovascular drugs (18.24%) in which anti-hypertensive i.e. calcium channel blockers (24%) and diuretics (20%) were commonly used.

Conclusions: The present study concluded that further improvements are needed in prescribing practices of CKD patients mainly in average number of drugs per prescription, prescription of drugs with generic names and prescription of drugs from the National essential medicines list.

Keywords: Chronic Kidney Disease; Drug Utilization Pattern; Rationality; WHO Core Prescribing Indicators

Introduction

Chronic Kidney Disease (CKD) is characterized by progressive decline in glomerular filtration rate (GFR).[1] CKD is an eternity of kidney disease fluctuating from mild stage of kidney damage to end-stage renal disease (ESRD). [2] CKD is distinguished by several disorders altering the morphological structure and functions of kidneys.[3] There are several co-morbidities are associated with CKD patients such as hypertension, diabetes mellitus, coronary artery disease and infection. Co-morbidities possess binary influence over the CKD patients like it increases the cost of treatment plus CKD patients also possesses the challenging aspect towards the treatment. [4]

Chronic Kidney Disease (CKD) is increasing worldwide associated with high mortality and morbidity. Around 10% of the adult population are affected by CKD.[5] If left untreated CKD can progress to End Stage of Renal Disease (ESRD).At global level the annual growth rate of ESRD is about 8% while in India 100,000 patients of ESRD are seen every year.[6]

Several research articles of CKD concluded that hypertension and diabetes are the two most prevalent issues in India. Prolongation or long standing of these illness causing two-thirds of the cases of CKD. CKD patients required lifelong multiple therapy. Multitudinous medication increases risk of irrational drug use and drugs related problems in CKD patients. So, to maintain the rationality it is necessary to provide appropriate therapeutic regimen with dosage adjustments and frequent drug monitoring and analysing the prescription pattern on a regular interval.[7] The purpose of therapeutic regimen is to prevent, cure, or control various disease conditions and states.[8] Appropriate medication for CKD patients is necessary to avoid undesired drug effects or side effects, drug-drug interactions and to obtain optimal patient outcomes. Inappropriate drug selection may cause the risk of side effects or adverse drug reactions. [9]

World Health Organization (WHO) and National Health Policy of India emphasized on the treatment of diseases by the use of medicines from the National essential medicine list (NEML) and prescribed by their generic names. [10] The World Health Organization (WHO) has created a set of "core prescribing indicator" for advancement in the concept of rationalization. It incorporates the prescribing indicators, the patient care indicators and the facility indicators.[11] These prescribing indicators analyse the performance of health care practitioners related to the appropriate uses of drugs. These prescribing indicators explains static prescribing characteristics related to poly pharmacy, percentage level of antibiotics and injection used per prescription and the average number of prescribed drugs from National Essential Medicine list.[12]

The pattern of drug prescription, consumption and variation in the pattern emphasized the importance of prescription analysis in CKD patients. Drug utilization and prescription pattern monitoring, finds out the issues resulting in to create awareness among practitioners. [13] Prescription pattern depends on the different factors and these factors influence the behaviour of prescribing trend and it will get modify only after knowing the causative factors behind it. [14] Prescribing faults and errors effect patients' health regarding safety and quality.[15] Prescription errors are related to the way of prescription writing, whereas prescribing faults refers irrational prescribing, inappropriate prescribing, under prescribing, overprescribing and ineffective prescribing that results in inaccurate medical conclusions with respect to treatment and its monitoring. [16, 17]

The clear picture of prescription pattern of medication in CKD patients still required to be studied. And it is necessary to find out the CKD associated co morbidities, current prescribing pattern and identify the area for improvement.[7] The Drug utilization studies perform a significant action in rational drug use.[18] Drug pattern of CKD changes over period of time, prescriber, disease conditions and population, which makes it important to do prescription pattern monitoring on regular basis.[19]

Hence, the present study was planned in Mahatma Gandhi Medical College & Hospital which is a multispecialty teaching hospital. This study was needful to identify the prescription pattern of CKD patients and evaluate the rationality of prescriptions in accordance with WHO Core Prescribing indicators and also focused on the factors responsible for problems associated with irrational prescribing.

Methodology

A prospective observational study was conducted in the Department of Pharmacology in collaboration with the Department of Nephrology in Mahatma Gandhi Medical College and Hospital, Jaipur Rajasthan from June to December 2019. The study was conducted after obtaining Institutional Ethics Committee approval and informed consent from the participants for registering them in to the study. Over a period of 6 months, 100 CKD patients of either sex and aged over 18 years, meeting the inclusion and exclusion criteria who had given written informed consent were included in the study.

Terminally ill patients who were not in a position to be interviewed were excluded from the study. According to non- probability purposive Sampling technique we have selected first 100 CKD participants based on the characteristics that we need in our study.
Patients of either sex and age of patients>18 years and <70 years diagnosed with Chronic Kidney Disease admitted in the department of Nephrology, Mahatma Gandhi Medical College, Jaipur from June 2019 to December 2019 were included in the present study except those patients who are terminally ill, pregnant and lactating women or not willing to participate in the study.
All the details of study participants like patient's demographic details (name, age, sex) diagnosis, pharmacotherapy details (drug name, dose, duration and frequency) were recorded in the specially designed performa.

Rationality of prescription was analysed by using WHO core drug prescribing indicators including- Average number of drugs per prescription, percentage of drugs prescribed by generic name, percentage of antibiotics prescribed per prescription, percentage of injection prescribed per prescription, percentage of drugs prescribed from essential medicine list.[11]
Data collection and analyzation was done in MS Excel 2007and result of data taken interpreted and represented in percentages and proportions.

Result
Totally 100 CKD patient's prescriptions were included in the study after screening for inclusion and exclusion criteria.

Demographics Details of the Patients
Out of total 100 CKD patients, the number of males were 54 and females were 46. The male female ratio was 54:46 (Table no.1).Out of 100 patients, 50% patients belong to > 40 years age group (Table no.2).

Table no. 1: Shows the gender wise distribution of study population

Gender	N	%
Males	54	54%
Females	46	46%
Total Number of Patients	100	100%

Table no 2: Age wise distribution in study population

Age Groups	N	%
20-29 Years	24	24%
30-40 Years	26	26%
>40 Years	50	50%

Stage Wise Distribution of CKD Patients
Out of total 100 CKD patients, the 29 % of males & 20% of females were belongs to CKD stage 3 and 13% males & 17% female belongs to CKD stage 4 &12% males & 09% female belongs to CKD stage 5 (Table no.3).

Table no.3: Description of patients belongs to CKD stage 3, 4& 5

CKD STAGE	CKD STAGE 3 GFR 30-59 ml/min/1.73m^2		CKD STAGE 4 GFR 15-29 ml/min/1.73m^2		CKD STAGE 5 GFR <15ml/min/1.73m^2	
Gender	N	(%)	N	(%)	N	(%)
Males	29	29%	13	13%	12	12%
Females	20	20%	17	17%	9	09%
Total Number of Patients	49	49%	30	30%	21	21%

Co-morbidities based distribution of patients

In present study anaemia (84%) was the commonest co morbid condition associated with CKD followed by hypertension (54%) and diabetes (10%) (Table no.4)

Table no.4: Description of Comorbidities associated with CKD among study participants

Comorbidities	**N**	**%**
Anemia	84	84%
Hypertension	54	54%
Diabetes	10	10%
Others(seizure, hypothyroidism, hepatitis C, renal septicemia, tubercular ascitis, polycystic kidney damage, erythma multiforme, obstructive uropathy, pelvic ureteric junction obstruction, renal cellulitis, focal segmental glomerulosclerosis, acute erosive gastropathy, cervical spondylosis).	34	34%

Drug Utilization Pattern

The total number of drugs prescribed were 274 out of which 50 (18.24%) were Cardiovascular drugs, 46 (16.7%) Multivitamins, 44 (16.05%) Antibiotics, 26 (9.48%) Gastrointestinal Drugs,10 (3.64%) Anti diabetic Drugs, 4 (1.45%) Hematopoietic Agents (Table no.5).

Among the 18.24% of cardiovascular drugs, 24% calcium channel blockers (mainly Nifedipine SR and Amlodipine) followed by 20 % diuretics(mainly Torsemide and Spironolactone), 8% alpha$_2$ agonists(Clonidine), 8%beta-blockers(mainly Metoprolol succinate ER),8% alpha+beta blockers (Carvedilol), 4%alpha blockers (Prazosin Hydrochloride SR) and 4%calcium channel blockers + angiotensin converting enzyme inhibitors (Amlodipine+Lisinopril) were prescribed (Table no.6, Fig 2).

Table no.5: Prescription pattern of drugs for CKD among study participant

Drug Class	**(n)**	**(%)**
Cardiovascular Drugs	50	18.24%
Antibiotics	44	16.05%
Multivitamins, mineral Supplements &Phosphate binders	46	16.7%
Gastrointestinal Drugs	26	9.48%
Anti diabetic Drugs	10	3.64%
Hematopoietic Agents	4	1.45%
Others	100	36.49%

Table no.6: Overall Distribution of Cardiovascular Drugs

Drug Class	**(n)**	**(%)**
Calcium Channel Blockers	12	24%
Diuretics	10	20%
Alpha$_2$ agonists	4	8%
Beta blockers	4	8%
Alpha+Beta blockers	4	8%
Alpha blockers	2	4%
Calcium Channel Blockers+Angiotensin Converting Enzyme Inhibitor	2	4%
Others	12	24%

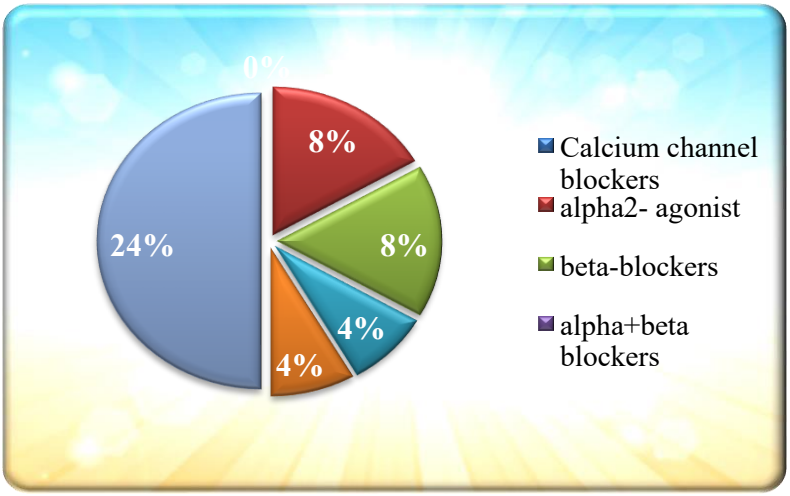

Fig 1: Overall Distribution of Cardiovascular Drugs

WHO Core Drug Prescribing Indicators Analysis:

According to WHO Core drug prescribing Indicators analysis of 100 prescriptions it was observed that only 24 (8.75%) drugs were prescribed by generic name. About 54(19.70%) of parenteral preparations were used. Most commonly prescribed injections were Pantoprazole, sulbactam + cefoperazone and Ondansetron. (Fig. 1)

Around 5.47% prescriptions contained Fixed Dose Combinations (Amoxicillin + clavulanic acid), (Sulbactam + Cefoperazone), (EC Pantoprazole + SR Domperidone) and (Torsemide + Spironolactone) were the most commonly prescribed FDCs.

A total of 274 drugs were prescribed in 100 patients. 58.39% of drugs prescribed from the National Essential Medicines List 21st list amended in 2019. (Fig. 2)

.[21] Average number of drugs per prescription was 2.74. Only 8.75% (n=24) drugs were prescribed by their generic name where as 91.24% (n=250) drugs belongs to trade names. 16.05% (n=44) antibiotics were administered to the 86% of selected population. 84% of these patients received 19.70% (n=54) parenteral route of drug administration. About 80% of study population were prescribed 5.47% (n=15) of Fixed Dose Combinations.

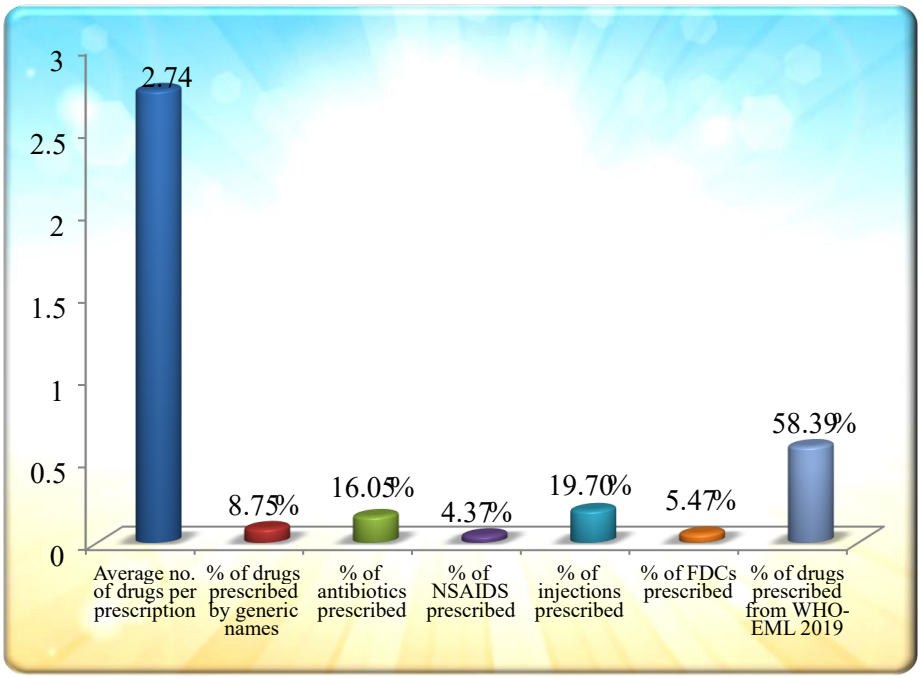

Fig 2 : WHO Core Drug Prescribing Indicators

Discussion

The results of the study showed slight predominance of male population compared to female population with a ratio of 54:46 which correlates with previous study [3]

Co-morbid conditions like hypertension, diabetes, and anemia were most common among CKD patients and found relevant with concomitant studies. [3] In our study, only the patients of CKD stages III-V were recruited however in previous study [4] the patients from all stage of CKD were included. In the present study out of total 274 drugs were prescribed in which average number of drugs per prescription was 2.74, which is smaller than that reported in older studies i.e (6.57 and 9.4 respectively). [4], [20]

In contrast to other studies Calcium Channel Blockers (18.24%) were most commonly prescribed cardiovascular drugs however, a previous study reported that Diuretics (9.29%) were most commonly prescribed cardiovascular drugs followed by the another study of which also indicated that Diuretics (9.50%) were most commonly prescribed cardiovascular drugs. [20], [9]

Out of 274 prescribed drugs 9.30% (n=24) belongs to generic names whereas 91.24% (n=250) were brand drugs this data vary from other study where no drug was prescribed by its generic name showing irrational prescription pattern.[20] Clinicians must be encouraged to prescribe more Generic drugs rather than brand drugs.

In contrast to other studies overall result indicates that only 58.39% (n=160) drugs were prescribed from NEML 21st list amended in 2019 however in other studies 41.53% of the prescribed drugs were from the WHO essential medicines list. [20]

Despite anemia (84%) being most common co morbid condition associated with CKD only (1.45%) haematopoietic agents (erythropoietin) were used at limited extent. These results are similar to a previous study [20]. This erythropoietin stimulating agent (ESA) reduces the requirement of blood transfusion in anemic patients.

A previous study showed Diabetic nephropathy (36.9%) as an etiology of CKD patients [2].Whereas in this study around 10% of study population had a diabetes as a co morbidity, treated with anti diabetic drugs (3.64%) in which 2% of patients were received Insulin whereas 8% of diabetic population were administered with other anti diabetic drugs [Saroglitazar, (Myoinositol 600mg+Metformin Hydrochloride SR), Linagliptin] which may improve kidney damage along with control on high blood sugar level whereas in previous studies indicated that Oral antidiabetic drugs were not used. They can precipitate serious hypoglycemia or metabolic acidosis in CKD patients. [9]

In contrast to other studies wherein out of total prescribed drugs (1052), most commonly prescribed were vitamins and minerals (24.71%) [9]. In our study out of 274 total prescribed drugs, 46 (16.07%) were Multivitamins, mineral Supplements & Phosphate binders such as Calcium salts (Calcium Acetate), (Calcium and vit D supplements), iron supplements (Ferrous Ascorbate and Folic acid), (vitamin supplements tablets with iron), phosphate binders [Calcitriol]. In previous study 91% of the patients were prescribed with calcium based phosphate binders followed by non-calcium based phosphate binders (4%) whereas in another studies Calcium carbonate was the most frequently prescribed phosphate binders, followed by calcium acetate however in present study calcium acetate & Calcitriol are commonly prescribed. [4], [20]

Respiratory tract infections and urinary tract infections in female patients, renal cellulites and septicaemia were commonly expected similar to other study[3]. In contrast to previous study A very high percentage of study population (86%) were exposed to antibiotics (16.05%) during hospitalization (Amoxicillin + Clavulanic acid), (Azithromycin) and Levofloxacin (oral antibiotics), (Sulbactam + Cefoperazone), (Piperacillin + Tazobactam) {parenteral antibiotics}.[20] Other antibiotics such as metronidazole and linezolid prevent the emergence of bacterial resistance. Anti-tubercular drug therapy (Isoniazid), Rifampicin and Pyrazinamide were initiated in the patients and careful indication required regarding antibiotic renal dose selection, whereas in other study Anti-

tubercular therapy was initiated in 6 patients with normal adult doses of isoniazid and rifampicin and a renal adjusted dose of pyrazinamide.[3]

Limitations

The study sample in the present study was relatively small and unicentric. Only indoor patients were included. More data to be required from other medical centres to evaluate the underuse of generic drugs, Erythropoiesis - stimulating agents, phosphate binders and also justify the use of antibiotics. The results of my study provide a reference data with other similar studies in the future and more studies are in the future required to improve prescription pattern or practices.

Conclusion

The conclusion of this study demonstrates the current prescription trends in which wide variety of drug classes were prescribed by brand names (91.24%) whereas less number of drugs were prescribed by generic names (8.75%) which indicated the irrational prescription practices and this study also indicated that only (58.39%) of drugs were taken from the national essential drug list which suggests continuous prescription audit and education of health care professionals regarding rational use of medicines in accordance with WHO Core drug use indicators to improve the quality of life of CKD patients and advised early diagnosis and medication of CKD to prevent it from getting worsened and also suggest long term follow up in CKD patients.

This study also demonstrated that the management of CKD patients possesses a challenge to physicians and provided present day condition and baseline data in managing renal compromised patients with co-morbidities. Despite of all efforts taken by government and the WHO, the prescription pattern in terms of rationality remains inadequate so more rational approaches are necessary to improve prescription patterns and there is urgent need of developing prescribing guidelines for CKD patients.

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Conflict of Interests

In relation to the publishing of this paper, the author hereby certifies that there are no competing interests.

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