Introduction

Drug utilization research is defined by the World Health Organization (WHO) as, "the marketing, distribution, prescription, and use of drugs in a society, with special emphasis on the resulting medical, social, and economic consequences."[1]

Chronic kidney disease (CKD) is now recognized as a major medical problem worldwide.[1] The global burden of disease (GBD) study 2015 ranked CKD 17th among the causes of deaths globally (age-standardized annual death rate of 19.2 deaths per 100,000 population).[1] In many countries, CKD is now among the top five causes of death. In India, GBD 2015 ranks CKD as the eighth leading cause of death.[1]

CKD represents a progressive irreversible decline in the glomerular filtration rate. A common phenomenon in renal failure is progressive renal function loss irrespective of the underlying cause of the kidney disease. Most chronic nephropathies lack a specific treatment and progress relentlessly to end-stage kidney disease, whose prevalence is increasing worldwide.[4] A reason for increasing prevalence of CKD is the rapidly increasing worldwide incidence of diabetes[5] and hypertension.[6] In India, given its population >1 billion, the rising incidence of CKD is likely to pose major problems for both health care and the economy in future years. Indeed, it has been recently estimated that the age-adjusted incidence rate of end-stage renal disease (ESRD) in India to be 229 per million population[7] and >100,000 new patients enter renal replacement programs annually in India.[8] A vast proportion of kidney failure patients in the developing world, including India, died without receiving renal replacement therapy (RRT).[9] In India, due to scarce resources, only 10% of the ESRD patients receive any RRT.[10]

ABSTRACT

Background: Chronic kidney disease (CKD) patients receive many medications with multiple doses per day rendering them at high risk for developing drug-related problems. Materials and Methods: A observational prospective study was carried out among the indoor patients of internal medicine wards and hemodialysis unit at Medical College Baroda and SSG Hospital, Vadodara, for 6 months. Patients of both sexes and of any age who were diagnosed to have chronic renal disease and on maintenance hemodialysis were included. Approval of IEC and informed consent was taken before initiation of the study. Data were analyzed using Microsoft Excel. Results: A total of 302 patient included in the study were analyzed, of which 185 were male and 117 were female with mean age of patient of 51.78 ± 8.93 years. Of these 302 patients, 17.88% of the patients were on maintenance hemodialysis and anemia was the most commonly occurring comorbid (95%) condition among them. Alimentary tract and metabolism class were the most commonly utilized class of drugs (41.87%) from anatomic therapeutic chemical classification and the average number of drugs prescribed was 9.35 ± 2.5. Drugs prescribed by generic name contributed to 64% of the lot and 76.6% from the national list of essential medicine. Fixed-dose drug combinations (FDCs) prescribed were 17.03%. Of total drugs prescribed, 84.91% of drugs were actually dispensed from the hospital drug store free of cost. Conclusion: Variety of drug classes was prescribed in a cohort of CKD patients who contributing to polypharmacy and substantially increasing risk of drug interactions.

Keywords: Chronic kidney disease, drug utilization research, hemodialysis, polypharmacy
Polypharmacy is common in CKD patients. ESRD patients who are on hemodialysis have complex drug regimens and receive many medications with multiple doses per day render these patients at high risk for developing drug-related problems and non-adherence to treatment.[11]

Although several drug utilization studies in CKD patients have been done worldwide, there is a lack of data which can shed light on the most common drugs prescribed in practice to these patients. Hence, the present study was carried out with the aim to study the drug utilization pattern in CKD inpatients of Medicine Department and hemodialysis unit at S. S. G. Hospital, Vadodara.

**Materials and Methods**

An observational prospective study was conducted among the indoor patients of internal medicine wards and hemodialysis unit at Medical College Baroda and SSG Hospital, Vadodara, during January 2017–June 2017.

Data of 302 patients were collected. Patients of either sex and of any age who were diagnosed to have chronic renal disease undergoing treatment in internal medicine wards and hemodialysis unit and patients on maintenance hemodialysis were included in the study. Patients diagnosed with acute renal failure and patients not willing to participate in the study were excluded from the study.

Approval of the Institutional Ethics Committee for Human Research was taken before initiation of the study and patients were given information about the nature of study in their own language and written informed consent was obtained from them before obtaining the required information from their indoor case file.

Patient’s demographic data, detailed medical history including drugs prescribed, its dosage forms, route of administration, frequency of administration, indications and duration of therapy, and biochemical parameters were recorded from the patient’s file and treatment chart on a predesigned case record form.

**Statistical analysis**

The data were entered into Microsoft Excel Spreadsheet and analyzed using the WHO core indicators with application of suitable statistical tests (such as mean ± standard deviation, percentage).

**Results**

**Demographic profile of patients according to their age and gender distribution**

A total of 302 patients were included, of which 185 (61.26%) were male patients while female patients were 117 (38.74%), with male-to-female ratio of 1.58:1 (185:117). Maximum number of patients (34.44%) belonged to the age group of 41–50 years followed by a very less margin in age the group of 51–60 years of age (33.44%). Mean age calculated was 51.78 ± 8.93 years.

**Comorbid conditions associated with CKD patients**

Of all the patients, 95.36% were found to be anemic followed by hypertension (80.79%), infective illness (45.03%), dyslipidemia (28.81%), diabetes mellitus (22.19%), ischemic heart disease (7.62%), and hypothyroidism (0.99%). Only 17.88% of the patients were found to be on maintenance hemodialysis.

**Drugs prescribed per patient**

The total numbers of drug products prescribed to patients were 2823. During the study, the number of drugs per prescription varied from 1 to 18 and majority of the patients 63.57% were prescribed 6–10 drugs per prescription followed by 27.15% were prescribed 11–15 drugs per prescription and 8.27% were prescribed 1–5 drugs per prescription. Sixteen–eighteen drugs per prescription were prescribed to only 0.99% of patient.

**Drugs prescribed according to formulations**

Drugs were prescribed mainly in five different dosage forms. Tablet was the most commonly prescribed dosage form (69.15%), followed by injectable (23.20%), capsule (6.98%), syrup (0.53%), and granules (0.14%).

**Anatomic therapeutic chemical (ATC) classification**

According to ATC classification, drugs for alimentary tract and metabolism (41.87%) were the most commonly prescribed class of drugs, followed by drugs for cardiovascular system (25.97%), drugs for blood and blood-forming organs (21.18%), anti-infectives for systemic use (6.09%), drugs classified under various group (2.62%), drugs for nervous system (1.02%), drugs for respiratory system (0.39%), systemic hormonal preparations (0.18%), and drugs for musculoskeletal system (0.11%) [Table 1].

**The WHO/international network for rational use of drugs core drug use prescribing indicators**

The average number of drugs prescribed per patient was 9.35 ± 2.5. Of the total (2823) prescribed drugs, 64.08% of drugs were prescribed by generic name and 35.92% of drugs were prescribed by brand name. The percentage of patients with antimicrobials prescribed was 44.37%. The percentage of drugs prescribed from national essential drug list was 76.62%. The percentage of patients prescribed with an injection was 77.81%. The percentage of patients prescribed with calcium-based phosphate binders and non-calcium-based phosphate binders was 76.49% and 24.50%, respectively. The percentage of patients prescribed with oral iron and erythropoietin was 57.62% and 17.88%, respectively. A total of 481 drug products (17.03%) were prescribed as fixed-dose combinations (FDCs). Of 2823 drugs, 2397 drugs were supplied from hospital while 426 drugs were purchased by patients from outside pharmacies [Table 2].
Drug group-wise distribution

A total of 2823 drugs were prescribed in 302 patients. Of these, antihypertensive group was the most commonly prescribed drug group and constituted 20.40% of total drugs. In this drug group, diuretics were the major contributors (8.11%), followed by calcium channel blockers (4.99%), centrally acting agents (4.96%), nitrates (2.09%), beta-blockers (1.63%), and angiotensin-converting enzyme inhibitors (0.7%). Hematopoietic agents were the second most common group of drug prescribed (16.61%) followed by vitamins and minerals (16.29%). Other groups of drugs prescribed were phosphate binders (10.8%), antiulcer agents (7.76%), antiemetics (6.77%), antibacterial agents (6.09%), antiplatelet (4.14%), hypolipidemic agent (3.08%), antidiabetics (2.37%), laxatives (0.64%), and miscellaneous group (2.94%) Table 3.

Prescribing frequency of antibacterial agents

A total of 172 antibacterial agents were prescribed out of total 2823 drugs. Cephalosporins were the most commonly prescribed antibacterial agents. They accounted for 49.41% of the total prescribed antibacterials followed by penicillins (17.44%) and nitroimidazoles (11.63%).

Drugs prescribed as FDCs

A total of 11 commonly prescribed FDCs were given in 302 patients who accounted for 17.03% of the total drugs prescribed. Out of these majorities, 50.10% were multivitamin B complex followed by Vitamin A + Vitamin D (33.06%), soluble insulin 30% + isophane insulin 70% (5.82%), and piperacillin + tazobactam (3.33%). Other FDCs prescribed were amoxicillin + clavulanic acid (2.91%), calcium + Vitamin D (1.87%), trimethoprim + sulfamethoxazole (1.25%), liquid paraffin + milk of magnesia (0.62%), bromhexine + chlorpheniramine + dextromethorphan (0.62%), cefpodoxime + clavulanic acid (0.21%), and ferrous fumarate + folic acid + zinc (0.21%). All the FDCs prescribed were included in the list approved by CDSCO except combination of bromhexine + chlorpheniramine + dextromethorphan and soluble insulin 30% + isophane insulin 70% Table 4.

Discussion

CKD patients are at high risk of infections and land up in recurrent hospital admissions. Reduced or absence excretion by kidneys in renal failure causes alteration in pharmacokinetics of drug, leading to accumulation of drug metabolites resulting in toxicity. The presence of comorbid conditions may also lead to administer more drugs which further increase chance of drug interactions.

In this study, data from 302 patients were collected over a period of 6 months. The male patients (61.26%) were found to be higher than the female patients (34.74%) in this study with the ratio of male:female coming to 1.8 times. This finding is in concurrence with the results of Ahlawat et al. and Bajait et al.

The mean age of the patients in the present study was 51.78 ± 8.93 years. It was similar to the results of Bajait et al. (51 years) but lower than reported by Ahlawat et al. (53.8 years) and Devi and George (55.1 years).

Of the comorbidities that we observed in the present study, anemia was found to be the most commonly occurring comorbidity.
and dyslipidemia. In another similar study carried out by Al-Ramahi, 84% of the CKD patients were affected by hypertension followed by anemia in 80% of patients. While in studies carried out by Ahlawat et al. and Bajait et al., hypertension was observed in 55% of the patients which was quite lower than the present study. The most likely reason for the hypertension occurring as most common comorbidity after anemia can be well explained by the fact that renin-angiotensin system is affected in the patients of CKD which also is responsible for controlling blood pressure.

Out of the total CKD patients studied, only 17.88% were on maintenance hemodialysis. These numbers were similar as the study by Ahlawat et al. (18%) compared to the study carried out by Bajait et al. (3%) and Al-Ramahi (9.3%). This number is quite higher than reported by Ahlawat et al. (6.5) and Devi and George (7.4%). Polyparmacy is defined as prescription of five or more medications to one patient within a period of one year. However, considering the requirement of drugs in CKD patients, it may not be considered as polyparmacy. However, it is a well-known fact that over-the-counter use of medicines is common in this country. This further increases the chances of drug interactions and ADRs and is accountable for the fact that average number of drugs per patient could be well above 9.35.

In the present study, percentage of drugs prescribed by generic name was 64% which was higher compared to the study carried out by Bajait et al. where only 12% of drugs were prescribed by generic name. While the studies carried out by Devi and George and Ahlawat et al. had all the drugs prescribed by brand name.

Percentage of drug prescribed from the national list of essential drugs in the present study was 76.6% which is similar to the study carried out by Ahlawat et al. (80%), but much higher than that reported in studies carried out by Devi and George (53%) and Bajait et al. (42%). This suggests good adherence to the essential drug list in our set up.

According to ATC classification system, drugs from the alimentary tract and metabolism class were the most commonly utilized class of drugs (41.87%) followed by cardiovascular drugs and blood-forming agents contributing to 26% and 21%, respectively. This is similar to the findings in the study by Bajait et al. which reported 45%, 23%, and 21%, respectively, for the three classes of drug mentioned above.

In the present study, 44% of patients were prescribed either one or more antibacterial agents which are much higher than reported by Ahlawat et al. which was 15%. The antibacterial agents contributed to 6.09% of total drug prescribed which is higher than that reported by Ahlawat et al. (2.2%) and Bajait et al. (0.9%). The misuse of antibiotics is an impending threat to health of population worldwide. Irrational prescribing of antibiotics can lead to adverse reactions,
leading to hospital admissions, cost, and risk of emerging resistant strains.

The number of drugs prescribed by parenteral route was 23% which was higher compared to 11% recorded in the study conducted by Ahlawat et al.

Of total prescribed drugs (2823), most of the drugs were prescribed from antihypertensive group (20.40%) followed by hematopoietic agents (16.61%), and vitamins and minerals (16.29%). Diuretics (8.1%) were the most commonly used antihypertensive agents in the study followed by calcium channel blockers (4.9%) and centrally acting antihypertensive agents (4.9%). Ahlawat et al. in their study reported 8.2%, 6.3%, and 2.8% of total drugs prescribed belonging to diuretics, calcium channel blockers, and angiotensin II receptor blockers, respectively.

In CKD patients, erythropoietin is not produced in sufficient amount, which leads to renal anemia. Hence, iron supplements and erythropoietin are routinely prescribed in patients of CKD.

In the present study, hematopoietic agents contributed to 16.6% of total drugs prescribed which is similar to observed in the study by Ahlawat et al. Of these agents, folic acid (7.9%) was the most commonly utilized drug followed by iron supplements (6.7%). This is much lower compared to results seen in the study by Tamilselvan et al. which is 44.4% and 41.4%, respectively. The use of erythropoietin in the present study was 1.9% which is higher to the study carried out by Ahlawat et al. (1.1%) and lower than Bajait et al. (2.94%). In the present study, vitamins and minerals contributed to 16.29% of total drugs prescribed which are lower to the study carried out by Bajait et al. (24.71%). The use of hypolipidemic agents (3%) in the present study was found parallel to the study carried out by Ahlawat et al. (5%). However, these results are stark in contrast of the study by Tamilselvan et al. where hypolipidemic agents contributed 41% of total drug prescribed.

Phosphate binders are one of the most commonly prescribed medicines in CKD patients. In the present study, 76.49% of the patients were prescribed with calcium-based phosphate binders followed by non-calcium-based phosphate binders 24.5%. This finding is similar to the study by Navaneethan et al. which reported the use of calcium-based phosphate binder and non-calcium-based phosphate binder to 75% and 25%, respectively.

Percentage of FDCs prescribed was 17.03%. Among these combinations, multivitamin B complex was the most commonly prescribed FDCs (50.10%). We were not able to compare the data on this parameter, as we could not find any other study reporting on the same.

Although all efforts have been made to make the study explanatory, it still goes with the limitations of having relatively smaller sample size and short duration of the study. There is a need to conduct other such studies in multiple centers, as well as with larger sample size and for a longer duration to get a broader and comprehensive idea of drug use pattern.

Conclusion

This study identified a wide variety of drug classes prescribed in a cohort of CKD patients indicative of prevailing morbidity. It has identified some areas of concerns like polypharmacy which may cause high incidence of drug interactions and adverse reactions. There is a need to conduct other such studies in multiple centers, as well as with larger sample size and for a longer duration to get a broader and comprehensive idea of drug use pattern.

References


