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Drug-Related Problems and Pharmacist Interventions in Inpatients with Chronic Kidney Disease

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ABSTRACT

Studies report poor quality and break in the care of chronic kidney disease (CKD) patients due to complex pharmacotherapy, frequent dose changes and adherence issues. The addition of clinical pharmacists on the healthcare team will enable improved quality of care. The aim of the study is to characterize drug-related problems (DRPs) among CKD patients and intervene to improve patient outcomes. This prospective, interventional study was carried out in the admitted inpatients of a tertiary care hospital during the period October 2018 to May 2019. Patients admitted to inpatient wards of nephrology, medicine, surgery and orthopedics who were diagnosed with chronic kidney disease of any stage and etiology and who gave consent to participate were included in the study. Patients diagnosed with cancer and/or receiving chemotherapy, significant liver disease, as evidenced by Child-Pugh grades B and C, and those with substance abuse disorders were excluded from the study. A clinical pharmacist reviewed the patient treatment chart to identify drug-related problems and communicated appropriate suggestions or recommendations to the nephrologist or attending physician. Identified DRPs were categorized according to 'The Pharmaceutical Care Network Europe Foundation (PCNE) classification V 6.2. Among 833 patients included in the study, a total of 250 DRPs were identified from 245 patients. DRPs occurred at a rate of 1.02 per patient in the study population. The most common drug classes involved were antibiotics, tramadol, insulin, and oral antidiabetic drugs. Dose change and the new drug started were the most common interventions made. Pharmacists can make positive contribution in caring for patients with CKD.

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INTRODUCTION

The incidence of chronic kidney disease (CKD) is increasing worldwide and is associated with poor outcomes and increased cost of disease management (Foundation, 2002). CKD is a progressive disease where a patient's kidney function slowly declines over time and during this period the normal kidney architecture dwindles and is replaced with interstitial fibrosis (Joy *et al.*, 2008).

Regardless of diagnosis specificity, the major outcomes of CKD involve progression to kidney failure, complications from decreased kidney func-

tion, along with the development of cardiovascular disease (Snively and Gutierrez, 2004; Foley *et al.*, 1998). Unfortunately, CKD is "underdiagnosed" and "under-treated," this has paved a path to improve both the detection and management of CKD patients (Foundation, 2008).

Predialysis and dialysis patients' medical management is often complex and implicated with polypharmacy, poor medication adherence, and recurrent dosage adjustments (Manley *et al.*, 2005). In turn, this may precipitate drug-related problems in pharmacotherapy and may warrant drug therapy monitoring to ensure optimal therapeutic outcomes, improved medication adherence, and digression of comorbidities and other associated risks. Achieving positive health outcomes through quality use of medicines is of utmost importance in hospitalized patients. Adverse outcomes of CKD can always be prevented or delayed. Further, diagnosing the disorder at an early stage, initiating optimized pharmacotherapy, implementing mitigation plans for associated complications, retraining patients to manage their disease and facilitating the kidney replacement therapies have all been associated with improved outcomes (Foundation, 2008).

The modern multidisciplinary health care team consisting of doctors, nurses, clinical pharmacists, and dieticians, play an important role in dampening disease progression and addressing comorbid conditions effectively in these patients. Clinical pharmacists, proven specialists in pharmacotherapy, are effectively involved in optimizing patient care. The role of clinical pharmacist in providing improved care in patients with various chronic diseases has been supported by evidence (Kaboli *et al.*, 2006; Viktil and Blix, 2008). Benefits of pharmaceutical care by hospital pharmacists has demonstrated a positive impact on rates of readmission, length of stay and hospital costs (Dooley *et al.*, 2004). Though several studies of drug-related problems in CKD have been carried out, few studies are reported from India and still fewer have reported pharmacist interventions among CKD patients. The current study was undertaken to investigate the pattern of drug-related problems occurring in CKD patients admitted to a tertiary care hospital and to record pharmacist interventions directed at solving the drug-related problems.

Aim

The aim of the study is to assess the pattern of occurrence of drug-related problems according to Pharmaceutical Network Europe Classification (PCNE) and document pharmacist interventions among CKD patients

MATERIALS AND METHODS

This prospective interventional study was conducted at a tertiary care teaching hospital for a period of nine months between October 2018 to May 2019. The institutional human ethical committee approved the study prior to its commencement. Patients admitted to inpatient wards of nephrology, medicine, surgery and orthopedics who was diagnosed with chronic kidney disease of any level and etiology and who gave consent to participate were included in the study. Patients diagnosed with cancer and/or receiving chemotherapy, significant liver disease, as evidenced by Child-Pugh grades B and C, and those with substance abuse disorders were excluded from the study.

A clinical pharmacist reviewed the patient treatment chart or dialysis case notes and laboratory reports and conducted the patient interview and interacted with healthcare professionals to gather all the required data. The pharmacist evaluated the patients' data to identify drug-related problems (DRPs) if any. Where a drug-related problem is identified, it was brought to the notice of concerned nephrologists and discussed prior to its confirmation. For the purpose of our study, a drug-related problem is defined as 'an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes.' All DRPs identified in the study was classified according to 'The Pharmaceutical Care Network Europe Foundation (PCNE) classification V 6.2 (Foundation, 2010). All the confirmed DRPs were intervened and addressed by communicating the appropriate suggestions/recommendations to the concerned physician/nephrologist. All the DRPs that were identified and suggestions/recommendations made were suitably documented.

RESULTS AND DISCUSSION

A total of 833 patients were enrolled in the selected departments. The demographic details of the study population are presented in Table 1. The average age of the study patients was 53.73(range: 41 to 66 years). The average length of hospital stay was of 6.02 days, and the average number of medications prescribed was 6.14. Most [n=326; (39.1%)] patients had stage 1 CKD; most patients had type 2 diabetes as comorbidity [n=313; (37.6%)].

A total of 250 DRPs were identified from 245 patients. DRPs occurred at a rate of 1.02 per patient in the study population. Out of 250 DRPs, 105 (42%) were Manifest problems and 145 (58%) were found to be Potential problems. The type of DRPs observed

Table 1: Demographic details of the study population

Characteristic	Total (n=833)
Males	468 (56.2%)
Females	365 (43.8%)
Average Age in years	53.73±12.76
The average length of stay in hospital in days	6.02±5.16
The average number of drugs prescribed per patient	6.14±3.14
CKD Stage	
Stage 1	326 (39.1%)
Stage 2	233 (27.9%)
Stage 3	210(25.2%)
Stage 4	41(4.9%)
End-stage renal disease	23(2.7%)
Etiology of CKD	
T2DM	313 (37.6%)
Type 2 Diabetes mellitus + Hypertension	271 (32.5%)
Hypertension	231 (27.7%)
Glomerular Disease	17 (2.0%)
Autosomal Disease	1 (0.1%)

in both test and control groups are shown in Table 2.

When classified according to PCNE, Adverse drug reactions (PCNE code - P2.1) were the most common (40.4%) DRPs observed in both test and control groups. Treatment effectiveness was the next primary problem domain (PCNE code – P1.2), with 28% of DRPs. In this domain P1.2 – C3.6 [(10.4%) – Problem: Treatment effectiveness; Cause: Dosage adjustment] followed by P1.2 – C1.3 [(7.2%) Problem: Treatment effectiveness; Cause: Drug Interaction] were commonly occurring combinations. P3.2 – C1.2, C1.4 [(6.4%, 4.4%) – Problem: Treatment Costs; Cause – Drug use without indication, Drug duplication] were other frequently occurring DRP Problem-cause combination. The most commonly implicated drugs in causing ADRs were insulin and antidiabetic drugs in the nephrology wards and Tramadol from Medicine and Surgery and NSAIDs from Orthopaedic wards.

Pharmacokinetic variability that needed dosage adjustments were the most common DRP identified after adverse drug reactions. Potential drug-drug interactions and untreated indications also were observed. Among the drug interactions, Linezolid and tramadol, when given together, can increase tramadol toxicity, Digoxin and esomeprazole can cause digoxin toxicity, and aspirin with cilostazol increasing chances of bleeding was documented. Among the untreated indications, therapy for hyperkalemia, hypokalemia, and anemia; and antihypertensives and antidiabetic agents/insulin therapy for hypertensive and type 2 diabetic patients respectively, which were inadvertently missed out from the treatment chart after admission were observed. Drug use without indication was observed among 16 patients and included medications prescribed for increasing potassium levels when serum potassium was normal (5 patients), prescribing more than two antibiotics for respiratory tract/urinary tract infection (4 patients), use of ondansetron and domperidone (4 cases), paracetamol/NSAID (3 patients) without the patient complaining of vomiting and pain/fever respectively.

Our study findings are similar to the one conducted by Langebrake C et al (Langebrake *et al.*, 2015) where inappropriate use of drugs (23.4%) and wrong dose or interval of administration (22.1%) were the most common causes for DRPs. Another study (Silva *et al.*, 2015) that evaluated the need for pharmaceutical care implementation in institutionalized, polymedicated elderly in nursing homes identified a mean of 15 DRP/patient. Our study found a mean of 1.02 DRP/patient. This could be due to the nursing home setting of the former study where polypharmacy is common in the elderly population. This could have led to an increased number of DRPs/patients in their study. Further, in their study, the most common DRPs were Adverse Drug Event, (49.51 %), Drug treatment more costly than necessary (19.11 %), Effect of drug treatment not optimal (14.82 %) and Unnecessary drug treatment (6.16 %). A study of Swiss inpatients assessing the

Table 2: Problem and Cause codes and descriptions of drug-related problems as per PCNE classification

Problem Primary Domain	Problem Code & Description	Cause Code & Description	No. of DRPs (%) Total (n=250)
Treatment Effectiveness (Potential problems with the effect of pharmacotherapy)	P1.2 Effect of drug treatment not optimal	C3.6 Dosage adjustment	26 (10.4)
		C3.4 Improper frequency	08 (3.2)
		C5.4 Administration	08 (3.2)
		C1.1 Inappropriate Drug	05 (2.0)
		C1.3 Drug Interaction	18 (7.2)
		C7.1NonCompliance	05 (2.0)
	P1.3 Wrong effect of drug treatment	C8.1Other cause, specify - Drug-induced kidney injury	04 (1.6)
	P1.4 Untreated Indication	C1.5 Indication for drug treatment not noticed	14 (5.6)
		C1.9 New indication for drug treatment presented	13 (5.2)
Adverse Drug Reactions (Patient Suffers or will suffer from the adverse event)	P2.1 Adverse drug event (non-allergic)	C8.2 No obvious cause	101 (40.4)
	P2.2 Adverse drug event (allergic)	C8.2 No obvious cause	09 (3.6)
Treatment Costs	P3.1 Drug treatment more costly than necessary	C2.1 Drug form	07 (2.8)
		C4.2 Duration of therapy	05 (2.0)
	P3.2 Unnecessary drug treatment	C1.4 Drug Duplication	11 (4.4)
		C1.2No indication for a drug	16 (6.4)

occurrence of DRPs reported 91 DRPs pertaining to treatment effectiveness and 14 DRPs relating to treatment costs among a total of 494 DRPs (Taegtmeyer *et al.*, 2012). Overall, it appears that adverse drug reactions and the selection of drugs for therapy (that affect treatment efficacy) are the most common areas where medication-related problems reportedly occur.

Langebrake C et al (Langebrake *et al.*, 2015) also found that most drug-related problems occurred in surgery, intensive care unit followed by internal medicine wards. Most problems related to inappropriate use of drugs, and dosing and drug administration problems involving systemic antibacterials, antithrombotics, pain-killers, antacids & proton pump inhibitors, and drugs indicated for the management of renin, aldosterone, angiotensin system abnormalities. Our study findings from the period included in this report corroborate with their findings. It would probably have to do with the patient population under study being really impaired, and polypharmacy leading to potential drug-drug interactions. Further, a systematic review of 21 studies concluded that the most common reported DRPs were incorrect dosing that warranted additional pharmacotherapy and resulted in increased cost of management (Stemer and Lemmens-Gruber, 2011).

Other studies have reported between three to

Table 3: Problem Codes, Cause Codes, and Interventions of DRPs

Problem Codes	Cause Codes	Intervention Codes & Description	No. of Interventions Total n=250*
P1.2 Effect of drug treatment not optimal	C3.6	I3.2 Dosage Changed to…	18
		I1.2 Prescriber asked for information	08
	C3.4	I3.4 Instructions for use changed to …..	08
	C5.4	I2.4 Spoken to family member/caregiver	08
	C1.1	I3.5 Drug Stopped	01
		I1.4 Intervention proposed, not approved by the prescriber	04
	C1.3	I3.1 Drug Changed to…	18
	C7.1	I2.1 Patient (medication) counseling	05
P1.3 Wrong effect of drug treatment	C8.1	I3.5 Drug stopped	04
P1.4 Untreated Indication	C1.5	I3.6 New drug started	14
	C1.9	I3.6 New drug started	13
P2.1 Adverse drug event (non-allergic)	C8.2	I4.2 Side effect reported to authorities	101
P2.2 Adverse drug event (allergic)	C8.2	I4.2 Side effect reported to authorities	09
P3.1 Drug treatment more costly than necessary	C2.1	I1.4 Intervention proposed, not approved by the prescriber	02
		I3.3 Formulation changed to…	05
	C4.2	I3.5 Drug stopped	05
P3.2 Unnecessary drug treatment	C1.4	I3.5 Drug stopped	11
	C1.2	I3.5 Drug stopped	16

Primary Domain Codes of Intervention for DRPs: I1 – At Prescriber level, I2 – AtPatient-level, I3 – At Drug level, I4 – Other intervention or activity
*Includes Interventions not approved by prescribers

seven DRPs identified for each patient (Stemer and Lemmens-Gruber, 2011; Grabe *et al.*, 1997; Parthasarathi *et al.*, 2003) while at our study site on an average per patient, and we had 1.02 DRPs. This could be because of the study setting, as well as the patient population included. This study was carried out at a tertiary care hospital with a good quality of care provided by multidisciplinary professionals and also the patient population was a mix of educated urban subjects and subjects from a rural background. A study (Alassaad *et al.*, 2015) carried out at general medicine wards of Uppsala University's Hospital found that patients with impaired renal function apart from other vulnerable patient populations were associated with an increased risk of DRPs. It follows that patients with impaired renal function need to have special patient care since they are at risk for adverse outcomes.

By assessing the types of DRPs occurring in a population, measures to prevent DRPs from occurring may be instituted. Also, if the outcomes for chronic diseases such as the one in this study are clearly defined, DRPs affecting patient outcomes may be identified and detailed process maps for every patient care activity in the hospital can be charted for improved patient care delivery and minimized adverse outcomes.

Among the 250 interventions made, the prescribers accepted and implemented 244 (97.6%) interventions accordingly. The details of the DRPs, causes, interventions and outcomes are outlined in Table 3. The interventions not accepted included prescribing analgesics post-surgery for postoperative pain (2 patients, health care professionals agreed to review

need for analgesic once patient's labs were available, physiotherapy was advised instead), and selection of antibiotic based on culture sensitivity reports (4 patients, patient is responding well to the antibiotic currently prescribed).

Dose changed, the drug stopped and the new drug started were the most common interventions. Most of the interventions done were at the drug level, and some were at the patient level; at the prescriber level, information was sought by the prescriber in 11 cases. The majority of drug-related problems that were identified were solved.

According to a systematic review (Raiisi *et al.*, 2019) of clinical pharmacy practice in the care of chronic kidney disease patients, various pharmacist activities in different studies included modifying drug doses, requesting and monitoring laboratory parameters, assessing the appropriateness of medications, performing medication reconciliation, patient medication counseling, and adherence motivation, and managing specific CKD complications. In our study, some of the activities like drug dose modifications, patient medication counseling and monitoring laboratory parameters were done by the pharmacist.

The kind of pharmacist intervention or activity in health care depends upon the health care set-up, the patient population, and the local health-care policies. According to the authors of this study, the setting dictates the pharmacist activity and pharmacists have to look for areas where they can contribute towards improving patient care and try to implement the same in the set-up. In this regard, the pharmacist may allude to existing guidelines for the management of disease, government policies and other such resources to achieve desired patient outcomes.

CONCLUSION

Adverse drug reactions were the most common DRPs identified among the CKD inpatients. DRPs occurred at a rate of 1.02 per patient. The most common drug classes involved in DRPs were antibiotics, tramadol, and insulin and oral antidiabetic drugs. 'Effect of drug treatment not optimal' was identified as one of the major causes of the DRPs (28%). Dose change and the new drug started were the most common interventions made. The addition of clinical pharmacists to the healthcare team would benefit the patient.

Disclosure

The authors declare that they have no conflict of interest.

Ethical Approval

The study was performed in accordance with the ethical standards of the institutional ethics committee, the Helsinki declaration (1964) and its later amendments or comparable ethical standards

Informed Consent

Informed consent was obtained from all individual participants included in the study

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