SHORT COMMUNICATION

Trends in prescribing patterns and drug related problems of kidney disease patients

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Abstract

The descriptive cross-sectional study was planned to evaluate drug-related problems, including drug-drug interactions, dose error, use of nephrotoxic drugs and polypharmacy, with special emphasis on kidney disease patients. The study was conducted from January to June 2019 in the Nephrology Ward of Ayub Teaching Hospital, Abbottabad, Pakistan. Doses of medicine and drug-drug interactions were evaluated by comparing it with standard protocols in British National Formulary and Lexicomp. Prescriptions were also evaluated for polypharmacy and use of nephrotoxic drugs. Out of 131 patients, 72 (55%) were males. Drug-drug interactions were found in 69 (52.7%) patients among whom the highest percentage was of moderate drug-drug interaction 63 (48.1%), followed by major 39 (29.8%) and minor 29 (22%) drug-drug interactions. Incidence of polypharmacy 68 (51.9%) and use of nephrotoxic drug 101 (77%) was high, while dose error was low 14 (10.7%). All drug-related problems were present with a high percentage in patients with chronic kidney diseases 29 (78.4) out of 37 (28.2%) such patients. There was significant association of chronic kidney diseases stages with drug-drug interactions, polypharmacy, dose error and prescribing drugs ($p<0.05$). The higher incidence of drug-related problems reflected irrational prescribing trends and deficiency of professional staff dealing with kidney disease patients.

Keywords: Kidney disease, Drug-drug interactions, Polypharmacy, Nephrotoxic drugs, Dose error.

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Introduction

Kidney disease (KD) is defined as a group of disorders that affect kidney function and structure. The decrease in renal function is known as renal dysfunction. Minor abnormality in kidney function and structure is associated with high risk of developing complications in kidney as well as mortality. KDs include nephrolithiasis, hydronephrosis, diabetic nephropathy, glomerulonephritis, acute renal failure (ARF) and chronic kidney disease (CKD).[1]

Pharmacotherapy in patients is becoming complex, and inappropriate prescribing can lead to increased healthcare cost, hospital admissions, prolonged hospital stay, reduced quality of life (QOL) and increased mortality and morbidity rate.[2] In case of chronic diseases, drug therapy becomes more complex, as is in case of KD, because patients are taking an average of eight medicines per day. Patients with KD are medically complex and require multiple medications. In the early stages of KD, treatment is needed for the condition that is responsible for KD, such as diabetes mellitus (DM), hypertension (HTN), nephrolithiasis etc., along with medication to stop disease progression. However, as kidney function declines, more medications are required to manage complications of the renal disease, such as anaemia, hyperlipidaemia, bone disorders and cardiovascular complications. In KD patients, it is difficult to adhere to treatment regimen and they are at high risk of developing drug-related problems (DRPs).[3]

DRPs are categorised into three groups: overuse of medicines that increase chances of adverse drug effects and drug-drug interactions (DDIs); under-use of medicines where the disease is not properly treated with the required dose of medicine; and inappropriate prescribing, such as high doses of medicines.[4]

DRPs have been categorised into different classes by different researchers. In short, DRPs deal with drug choice, dose of drugs, DDIs, adverse drug reactions (ADRs), monitoring of drug effects and polypharmacy. DRPs include potential and actual problems. Actual problems are present in different clinical forms, such as ADR and allergic reactions, or in the form of therapeutic failure. A potential problem does not present in the clinical form, but, if left untreated. it can lead to drug-related harm to patients.[5]

Common DRPs in KDs are inappropriate dose, adverse effects, DDIs and polypharmacy. Inappropriate use of drugs is harmful and can worsen the disease condition. To avoid these DRPs, the prescribed medication should be reviewed.[6]

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A DDI can be defined as "a phenomenon by which a drug potentiates or diminishes the effect of other drugs by pharmacokinetics, pharmacodynamics or various other mechanisms.[7] In KD patients, it is more challenging to avoid DDIs because of the complex nature of the disease. Prevalence of DDIs in patients with KD is very high because of polypharmacy that is involved in KD management. According to a study in developing countries, the chance of DDIs in patients taking 2 medicines was 13%, which increase to 40% if patients were taking 5 medicines, and to 80% in patients taking >5 medicines.[8] Prevalence of DDIs is also associated with the increase in length of hospital stay (LOS), healthcare cost, morbidity and mortality.[9]

Polypharmacy is a nonspecific term and there are multiple definitions of polypharmacy. The World Health Organisation (WHO) defines it as "the administration of many drugs at the same time or the administration of an excessive number of drugs".[10] Some researchers defined it as "concurrent use of multiple drugs" and some classified it into minor and major polypharmacy, with minor polypharmacy means two drugs, and major polypharmacy meaning more than four drugs. Others defined it as "taking too many inappropriate drugs or taking two medications for the same condition".[11] However, the most commonly used definition of polypharmacy is "taking five or more medications".[12] KD patients are medically complex and require multiple medications. Patients have multiple causes of developing CKD and an increase risk of developing comorbidities. For the treatment of aetiology of CKD and comorbidities, a number medications are used and this results in greater chances of DRPs in these patients.[13]

Nephrotoxic drugs are substances that are injurious to kidney and can cause pre-renal, intra-renal and post-renal damage. Nephrotoxic drugs cause renal injury by different mechanisms. Most of the renally excreted drugs exert their effects directly on renal tubules, which include cellular injury and death in tubular necrosis or inflammation in the renal interstitium in case of interstitial nephritis.[14] The use of nephrotoxic drugs causes a decline in renal function. Physicians should avoid the use of nephrotoxic drugs, or use with caution if the patient has KD. Common nephrotoxic drugs include nonsteroidal anti-inflammatory drugs (NSAIDS), antimicrobials, like aminoglycosides, beta-lactam antibiotics and quinolones, cardiovascular agents, like angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), clopidogrel and statins, chemotherapeutics, radiocontrast agents, diuretics, like loop and thiazide, proton pump inhibitors (PPIs), like omeprazole, lansoprazole and pantoprazole, ranitidine and drugs of abuse, like cocaine, heroin and methadone. Drug-induced nephrotoxicity can be avoided by correcting the risk factors for nephrotoxicity, such as assessment of renal function before prescribing drugs, adjustment of doses according to the renal function, and, if possible, avoiding prescribing nephrotoxic drugs.[15]

The current study was planned to evaluate DRPs, including DDIs, dose error, use of nephrotoxic drugs and polypharmacy in KD patients.

Materials and Methods

The descriptive cross-sectional study was conducted from January to June 2019 in the Nephrology Ward of Ayub Teaching Hospital (ATH), Abbottabad, Pakistan. After approval from the ethics review committee of the Department of Pharmacy, COMSATS University Islamabad, Abbottabad Campus, the sample was raised from among KD patients of either gender aged ≥18 years. All dialysis-dependent patients were excluded.

ATH is a 1000-bedd tertiary care hospital with different departments. In the nephrology ward, medication orders were handwritten by nephrologists on patient charts which were followed by medical officers and nurses. These patient charts included patient's demographics, chief complaints, comorbidities, diagnostic tests, diagnosis, date of admission and discharge and prescribed medicines. Prescription included brand names of medicine, dose, frequency and route of administration. These medication record/charts were reviewed for data-collection regarding daily prescribed orders, medicine administration record, laboratory test results from admission to discharge for the identification of any DRPs.

All medication orders were reviewed for proper dose calculation according to patient laboratory test results, especially estimated glomerular filtration rate (eGFR), potential DDIs, polypharmacy, use of nephrotoxic drugs and drug error. Dose of medicine and DDIs were evaluated by comparing it with standard protocols given in British National Formulary (BNF) and Lexicomp software. The 76th edition of BNF for September-March 2019 was used as a reference for evaluation of dose. Lexicomp version 4.5.1 was used for the evaluation of DDIs. Potential DDIs have been classified as major, moderate and minor according to the literature.[16] Major DDIs are interactions that have risk of death or can result in serious negative outcomes. These drug combinations should be avoided or needs therapy modification. Moderate DDIs are interactions that are unlikely to be life-threatening, but can result in harmful effects. This type of interaction requires therapy modification. Minor DDIs are interactions that produce little effects and do not interfere with therapeutic outcomes. This type of interactions does not require any change in therapy. All prescriptions were also evaluated for

polypharmacy. Medication orders having ≥5 medications for a single disease condition, excluding supplements, were considered to have polypharmacy. Use of nephrotoxic drugs was assessed by using a list of nephrotoxic drugs that was drafted in a previous study.[15] Drug dose errors were estimated by evaluating the dose in line with eGFR values.[17]

Data was analysed using SPSS 25. Descriptive statistics were used to calculate frequencies and percentages of study variables. Frequencies and percentages were used to represent gender, age group, stage of CKD patients, potential DDIs, polypharmacy, use of nephrotoxic drugs and dose error. Association between a patient's clinical characteristics and study variables was evaluated by chi-square test with a significance level of $p<0.05$. Correlation between study variables was identified by applying Spearman's rho correlation test and assessed by correlation coefficient value by using a significance level of $p<0.01$ at 99% confidence interval (CI).

Results

Out of 131 patients, 72 (55%) were males. DDIs were found in 69(52.7%) patients among whom the highest percentage was of moderate DDIs 63 (48.1%), followed by major 39(29.8%) and minor 29 (22%). Overall, 38 (28%) patients were diagnosed with CKD, 50(38%) with nephrolithiasis, 10 (7.6%) with hydronephrosis and 34 (25.9%) with ARF. Among CKD patients, 23(62.2%) were at CKD stage V, 10(27%) stage IV and 4 (10.8%) were at CKD stage III. Common co-morbidities among these patients were HTN and DM (Table-1).

There were 72 (55%) prescriptions having DDIs, while 59 (45%) prescriptions had no DDI. Polypharmacy was observed in 68 (51.9%) patients, while the use of nephrotoxic drugs and dose error was observed in

Table-1: Demographic and clinical data.

Demographics	Groups	n (%)
Gender	Male	72 (55)
	Female	59 (45)
Age groups (mean age 48.82 ±18.502 years)	18–27	15 (11.5)
	28–37	24 (18.3)
	38–47	23 (17.6)
	48–57	34 (26)
	≥58	35 (26.7)
Clinical presentation		
Diagnosis	CKD	37 (28.2)
	Nephrolithiasis	50 (38)
	Hydronephrosis	10 (7.6)
	ARF	34 (25.9)
CKD Stage	Stage V	23 (62.2)
	Stage IV	10 (27)
	Stage III	04 (10.8)
Comorbidities	HTN	17 (13)
	DM	13 (9.9)
	IHD	1 (0.8)
	HTN+DM	11 (8.4)
	HTN+DM+IHD	1 (0.8)
	IHD+HTN	1 (0.8)
	Enlarged Prostate	2 (1.5)
	HTN+Enlarged prostate	1 (0.8)
	None	84 (64.1)

CKD: Chronic kidney disease, ARF: Acute renal failure, HTN: Hypertension, DM: Diabetes mellitus, IHD: Ischemic heart disease.

Table-2: Prevalence of DRPs and DDIs in KD Patients.

All drug related problems	n (%)
DDIs in total prescriptions	72 (55%)
Polypharmacy	68 (51.9)
Use of nephrotoxic drugs	101 (77)
Dose error	14 (10.7)
Severity of DDIs	
Major DDIs	39 (29.8)
Moderate DDIs	63 (48.1)
Minor DDIs	29 (22)
DDIs in CKD (Total Patients number of CKD=37)	29 (78.4)
Severity of DDIs in CKD	
Major DDIs	16 (12.4)
Moderate DDIs	27 (20.9)
Minor DDIs	13 (10.1)
DDI in Other KDs (Total Patients number of other KDs=94)	39 (41.5)
Severity of DDIs in other KDs	
Major DDIs	23 (17.8)
Moderate DDIs	36 (27.9)
Minor DDIs	14 (10.9)
Number of DDIs per prescription (mean=2.07±2.957)	
No DDI	59 (45)
1 to 2	31 (23.7)
3 to 5	23 (17.6)
≥6	18 (13.7)
Major DDI	
Alfacalcidol + Vitamin D3	16 (23)
Amikacin + Na-Picosulfate	1 (1.4)
Amoxicillin clavulanate + Na-Picosulfate	1 (1.4)
Atorvastatin + Carbamazepine	1 (1.4)
Bisoprolol + Carbamazepine	1 (1.4)
Ca-Acetate + Ca-Carbonate	17 (24.3)
Ca-Acetate + Ca-Gluconate	2 (2.9)
Ca-Acetate + Ceftriaxone	6 (8.6)
Ca-Gluconate + Ceftriaxone	5 (7.1)
Cefixime + Na-Picosulfate	1 (1.4)
Cefoperazone + Na-Picosulfate	1 (1.4)
Clopidogrel + Omeprazole	2 (2.9)
Codeine + Tramadol	1 (1.4)
Ibuprofen + Ketorolac	2 (2.9)
Ketorolac + Na-phosphate	1 (1.4)
Metoclopramide + Thioridazine	7 (10)
Pheniramine + Tramadol	1 (1.4)
Thioridazine + Tramadol	4 (5.7)

DRPs: Drug-related problems, KD: Kidney disease, DDIs: Drug-drug interactions, CKD: Chronic kidney disease.

101 (77%) and 14 (10.7%) patients respectively. In all prescriptions, there were 39(30.2%) having major, 63 (48.8%) moderate and 27 (20.9%) minor DDIs. Out of 37 (28.2%) CKD patients, 29(78.4%) prescriptions had DDIs, whereas in other 94 (71.8%) KD patients, DDIs were 39 (41.5%). There were 56 DDIs found in CKD patients; 16(28.6%) major, 27 (48.2%) moderate, and 13 (32.2%) minor. In other KD patients, there were 73 DDIs; 23 (31.5%) major, 36 (49.3%) moderate, and 14(19.2%) minor. Mean DDI per prescription was 2.07±2.957, and frequencies of major DDIs were noted (Table-2). Likewise, frequencies of moderate (Table-3) and minor DDIs (Table-4) were also noted.

There were 68(51.9%) prescriptions having polypharmacy; 27 (39.7%) in CKD patients and 41(60.3%) in other KD patients (Table-5). The most common prescribing drug groups were antibiotics, narcotic/prokinetic agent and NSAIDs (Figure-1A), and there were 72 different

Table-3: Frequency of moderate DDIs.

Drug-drug interaction	n (%)
Alfacalcidol + Ca-Acetate	13 (8.1)
Alfacalcidol + Ca-Carbonate	16 (10)
Alfacalcidol + Ca-Gluconate	2 (1.3)
Amikacin Sulfate + Diclofenac	1 (0.6)
Aminophylline+ Caffeine	1 (0.6)
Amlodipine + Ca-Acetate	1 (0.6)
Amlodipine + Ca-Carbonate	4 (2.5)
Amlodipine + Ca-Gluconate	2 (1.3)
Amlodipine + Clopidogrel	1 (0.6)
Amlodipine + Tamsulosin	3 (1.9)
Amlodipine + Thioridazine	2 (1.3)
Aspirin + Clopidogrel	2 (1.3)
Aspirin + Furosemide	2 (1.3)
Aspirin + Glyceryl trinitrate	1 (0.6)
Atorvastatin + Clopidogrel	1 (0.6)
Bisoprolol + Glyceryl trinitrate	1 (0.6)
Bisoprolol + Nifedipine	1 (0.6)
Bisoprolol + Tamsulosin	1 (0.6)
Bisoprolol+ Thioridazine	2 (1.3)
Ca-Acetate + Levothyroxine	1 (0.6)
Ca-Acetate + Nifedipine	3 (1.9)
Ca-Acetate + Vitamin D	14 (8.8)
Ca-Carbonate + Captopril	1 (0.6)
Ca-Carbonate + Levothyroxine	1 (0.6)
Ca-Carbonate + Nifedipine	3 (1.9)
Ca-Carbonate + Rosuvastatin	1 (0.6)
Ca-Carbonate + Thioridazine	1 (0.8)
Ca-Carbonate + Vitamin D3	20 (12.5)
Ca-Gluconate + Ciprofloxacin	1 (0.6)
Ca-Gluconate + Nifedipine	1 (0.6)
Ca-Gluconate + Vitamin D	4 (2.5)
Clopidogrel + Furosemide	1 (0.6)
Clopidogrel + Rosuvastatin	2 (1.3)
Dexamethasone + Furosemide	1 (0.6)
Dexamethasone + Moxifloxacin	1 (0.6)
Dimenhydrinate + Itopride	1 (0.6)
Dimenhydrinate + Metoclopramide	4 (2.5)
Dimenhydrinate + Thioridazine	2 (1.3)
Diphenhydramine + Metoclopramide	1 (0.6)
Diphenhydramine + Thioridazine	1 (0.6)
Domperidone + Thioridazine	3 (1.9)
Ferrous Sulfate + Omeprazole	1 (0.6)
Ferrous Sulfate + Ranitidine	4 (2.5)
Furosemide + Thioridazine	1 (0.6)
Furosemide + Tamsulosin	1 (0.6)
Glyceryl trinitrate + Nifedipine	1 (0.6)
Hydrochlorothiazide + Valsartan	1 (0.6)
Metoclopramide + Orphenadrine	1 (0.6)
Metoclopramide + Tramadol	21 (13.1)
Nifedipine + Tamsulosin	1 (0.6)
Nitroglycerin + Ramipril	1 (0.6)
Tamsulosin + Valsartan	1 (0.6)
Thioridazine + Valsartan	1 (0.6)

DDIs: Drug-drug interactions.

Table-4: Frequency of minor DDIs.

Drug-drug interaction	n (%)
Amlodipine + Ketorolac	2 (4.3)
Aspirin + Ca-Carbonate	2 (4.3)
Aspirin + Ferrous Sulfate	1 (2.1)
Ca-Carbonate + Ferrous Sulfate	9 (19.1)
Ca-Carbonate + Ranitidine	5 (10.6)
Domperidone + Salbutamol	1 (2.1)
Furosemide + Levothyroxine	1 (2.1)
Metoclopramide + Paracetamol	13 (27.7)
Paracetamol+ Tramadol	12 (25.5)
Tamsulosin + Thioridazine	1 (2.1)

DDIs: Drug-drug interactions.

Table-5: Frequency of polypharmacy, nephrotoxic drugs and dose errors.

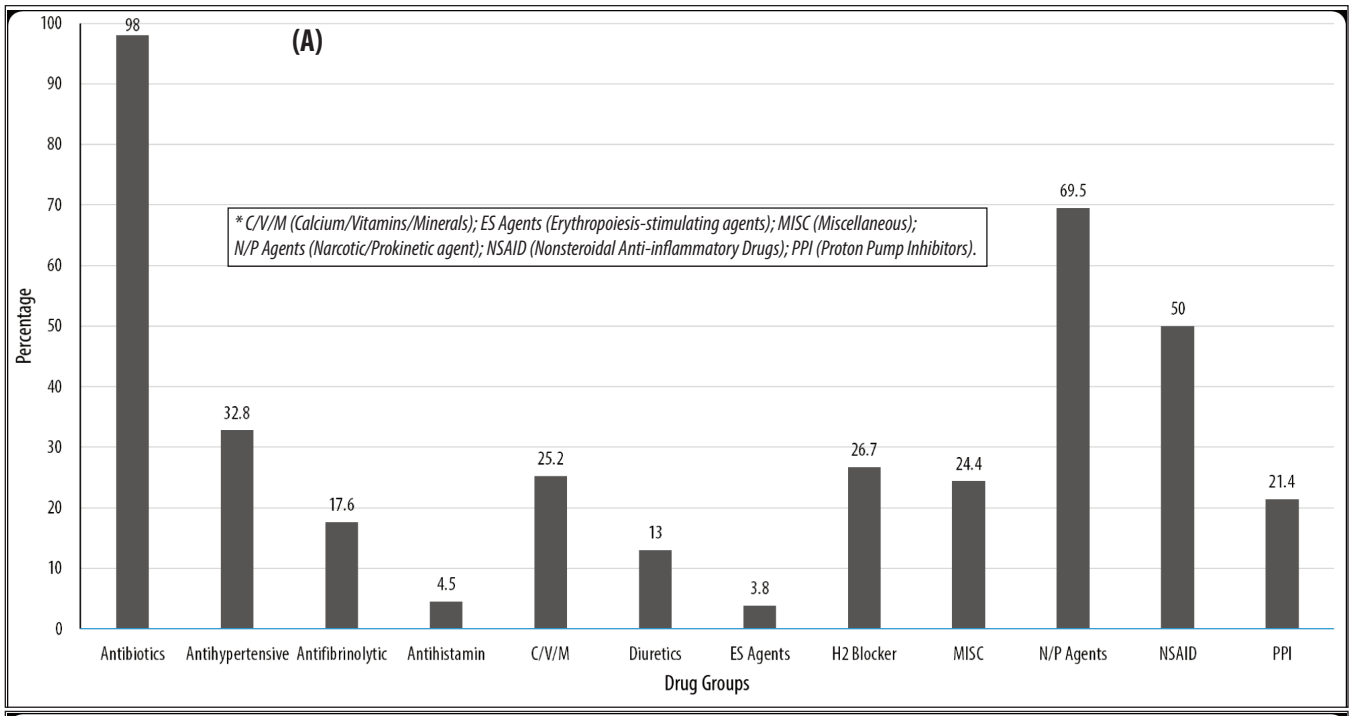
Polypharmacy	n (%)
CKD Patients (n=37)	27 (73)
Other KDs (n=94)	41 (43.6)
No. of Drugs per Prescription	
2 to 4 Drugs	65 (49.6)
≥5 Drugs	66 (50.4)
Nephrotoxic Drugs	
Analgesics	23 (17.6)
Antimicrobials	23 (17.6)
Antihypertensive	06 (4.6)
Diuretics	07 (5.3)
PPI	13 (9.9)
H2 Blocker	26 (19.8)
Miscellaneous	03 (2.3)
No Nephrotoxic drugs	30 (22.9)
Dose Error	
Ranitidine	10 (7.6)
Diclofenac sodium	1 (0.8)
Metformin	1 (0.8)
Solifenacin succinate	2 (1.5)
No Dose Error	117 (89.3)

CKD: Chronic kidney disease, PPI: Proton pump inhibitors, H2: Histamine2

combination of drugs used (Figure-1B).

Age group had significant association with study variables DDIs, polypharmacy, nephrotoxic drugs and dose error ($p>0.05$) except prescribing drug groups ($p<0.05$). Co-morbidities and CKD stages showed significant association with all study variables except nephrotoxic drugs (Table-6)

DDIs had significant strong positive correlation with polypharmacy and strong positive correlation with the number of drugs prescribed ($p<0.01$). DDIs also showed a positive correlation with nephrotoxic drugs prescribed and negative correlation with dose error, but both were not significant ($p>0.01$). Polypharmacy had statistically significant ($p<0.01$) positive correlation with nephrotoxic



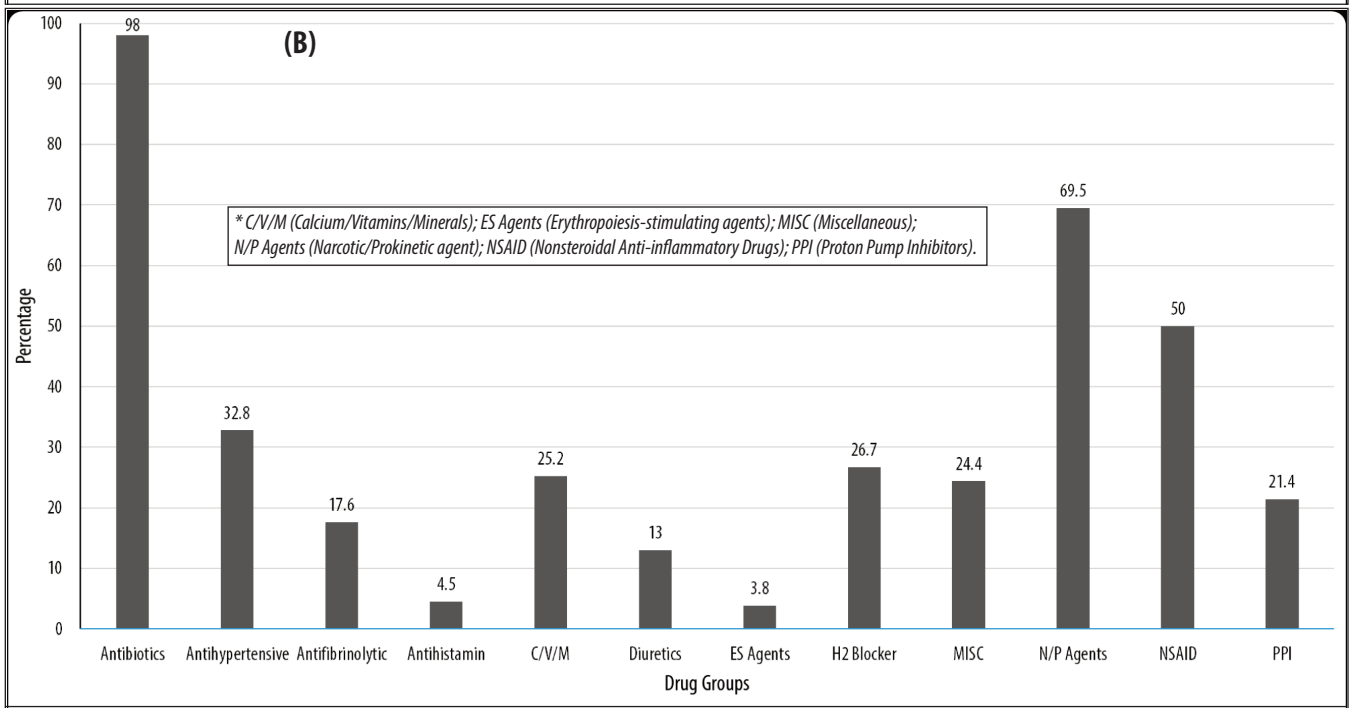


Figure-1: (A) Frequency of different drug groups in prescriptions;(B) Different drug combinations in the prescriptions.

Table-6: Frequency of polypharmacy, nephrotoxic drugs and dose errors.

Patient Characteristics	DDIs Chi sq. (p-value)	Polypharmacy Chi sq. (*p*-value)	Nephrotoxic drugs Chi sq. (*p*-value)	Dose error Chi sq. (*p*-value)	Prescribing drugs Chi sq. (*p*-value)
Age groups	6.644 (0.156)	8.741 (0.068)	9.341 (0.053)*	6.393 (0.172)	15.831 (0.003)*
Comorbidities	6.440 (0.036)*	16.690 (0.034)*	8.734 (0.365)	31.285 (0.001)*	18.301 (0.019)*
CKD stage	12.90 (0.005)*	9.215 (0.027)*	1.505 (0.681)	18.629 (0.001)*	13.388 (0.004)*

* Significance level p-value ≤0.05; DDIs: Drug-drug interactions, CKD: Chronic kidney disease.

Table-7: Correlation between study variables.

Correlation	Correlation Coefficient (r)	*p*-value
DDIs–Polypharmacy	0.388**	0.001
DDIs–Nephrotoxic drugs	0.018	0.840
DDIs–Dose error	-0.034	0.696
No. of DDIs– No. of Drugs Prescribed	0.561**	0.001
Polypharmacy–Nephrotoxic drugs	0.348**	0.001
Polypharmacy–Dose error	0.135	0.124
Polypharmacy–Prescribing Drug Groups	0.848**	0.001
Nephrotoxic drugs–Dose error	0.71	0.421
Nephrotoxic drugs–Prescribing Drug Groups	0.331**	0.001
Dose error–Prescribing Drug Groups	0.195*	0.026

** Correlation is significant at the 0.01 level (2-tailed); * Correlation is significant at the 0.05 level (2-tailed); DDIs: Drug-drug interactions.

drugs and prescribing drug group. Polypharmacy's correlation with dose error (p=0.124) was also positive, but not statistically significant. Nephrotoxic drugs had positive correlation with dose error (p>0.01) and prescribing drug group (p<0.01). Lastly, the dose error had positive, but non-significant correlation with prescribing drug groups (Table-7).

Discussion

The current study focussed on trends of prescribing patterns and DRPs in patients with KDs. DRPs can complicate the nature and severity of disease. The study had majority male patients, while the overall mean age was 48.82±18.502 years. Similar findings of male majority and high mean age were reported earlier.[9] The current study highlighted all KDs, while the earlier study was only on CKD patients.

Incidence of different KDs showed more nephrolithiasis patients (38%), followed by CKD (28.2%) and ARF (25.9%), with more frequent comorbidities being HTN and DM. Nephrolithiasis incidences was much higher compared to a previous report.[18] Possible reason might be the limitation of the study to a single hospital. The present study showed slight difference in the prevalence of CKD and ARF than some previous studies conducted in Pakistan.[19,20] CKD stage V patients were more (62.2%) in the current study, but still much less compared to a previous research.[21]

The incidence of potential DDIs and polypharmacy in the study population was high, with more incidences of moderate interactions. Incidence of potential DDIs was more in patients with CKD than other KD patients. The high incidence of potential DDIs in patients with CKD might be due to complex nature of the disease. One more reason may be the multiple medicines which are required for CKD management and its complication or comorbidities.[9] However, other KDs, like nephrolithiasis and hydronephrosis, had low incidence of potential DDIs. Possible reason for this could be the symptomatic treatment of the disease to control the pain, or, in severe cases, surgery is preferred over medication.[22] Incidence of potential DDIs in patients with CKD in the current study was almost the same as was reported in an earlier study conducted in Punjab, Pakistan.[17] Similarly, studies conducted in India and West Africa reported potential DDIs in CKD patients as 76% and 78% respectively.[9,23]

In terms of DDI severity, moderate DDIs were more both in CKDs and other KDs compared to major and minor DDIs with mean DDIs of 2.07±2.957 per prescription in the current study. A Nigerian research reported similar findings, but with high incidence of CKD and moderate DDIs.[9] This big difference in reports might be due to irrational and different prescription trends for treating KD in the previous study.[9] The most frequent major DDI in the current study related to Ca-Acetate+Ca-Carbonate, in moderate DDIs it related to Metoclopramide+Tramadol, and in minor DDIs it related to Metoclopramide+Paracetamol. These interactions were different compared to a study showing different prescription patterns.[9]

In the current study, the most commonly prescribed medicines in all KDs, especially CKDs, were antibiotics, narcotic/prokinetic agents and NSAIDs. An earlier study reported furosemide and calcium carbonate being the most frequently used medication.[9] The difference might indicate irrational use of antibiotics in the current study, or different prescribing trends in the selected region of the previous study.

The present study reported a high burden of polypharmacy in CKD patients. This was in line with literature.[24]

A statistically significant association between polypharmacy and DDIs was found in the current study, implying that as the number of prescribed medicines increased, the risk of DDI also increased. A significant association between the two elements has been reported earlier as well.[9,13]

A positive and significant correlation was seen in the current study between the number of DDIs and the number of drugs prescribed, indicating that as the number of prescribed drugs increased, there was an increase in DDIs. This has also been reported earlier.[24]

In the present study, a high number of patients were exposed to nephrotoxic drugs. On evaluation of individual nephrotoxic drugs prescribed in patients with KDs, analgesics and antimicrobials were found to be the most frequently used drugs. A previous report indicated a relatively high use of nephrotoxic drugs in CKD patients.[25] The same study also highlighted a more frequent use of diuretics (37%) and proton pump inhibitors (PPIs) (15%) which was contrary to the present study. A study conducted in Italy reported low (49%) use of nephrotoxic drugs in patients with CKD compared to the present study.[15] The most commonly prescribed class of drugs was NSAIDs (47%), which was same as in the current study.

In the current study, the incidence rate of dose error in patients with KDs was low. Previous studies on dose error in patients with renal insufficiency reported an incidence of dosing errors ranging from 5-24% showing high trend of dose errors, indicating irrational prescribing practices by the physicians.[25,26]

The current study has its limitations. The duration and single-centre setting could not produce a broader picture of the problem. Large-scale, multi-centre studies are needed to reflect the actual sale of DRPs in CKD patients.

Conclusion

The prevalence of DDIs and polypharmacy was high in KD patients. However, the prevalence of nephrotoxic drug and dose error was relatively low. Among the KDs, DRPs were common in CKD patients. The determinants of polypharmacy and DDIs were comorbidities, CKD stage and age. The higher occurrence of DRPs reflects a lack of professional staff that can help in reducing and managing DRPs. A collaboration work of all medical professionals along with clinical pharmacists can identify and eliminate DRPs.

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