A study on prescribing patterns in hemodialysis and renal transplantation patients

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Background
Patients treated with hemodialysis and renal transplant require complex therapy regimens that manage comorbid conditions such as diabetes, hypertension, and so on; as a result, they may develop drug-related issues. Inappropriate medication usage raises the risk of drug related problems, which can manifest as excessively extended hospital stays, higher expenses, and overuse of medical services. Prescribing pattern among the patients treated with hemodialysis and renal transplantation are not well characterized previously.

Objectives
The objective of the study is to investigate drug prescription trends in hemodialysis patients and to study the prescribing patterns of medications in kidney transplantation patients.

Materials and methods
The prospective observational study was conducted over a period of 8 months, i.e. from October 2021 to June 2022 in end stage CKD patients treating with maintenance hemodialysis and renal transplant. Different classes of drugs prescribed and percentage of drugs per prescription was estimated in this study. Data were analyzed descriptively.

Results
105 patients recruited have been analyzed of which 76 (72.38%) were male and 29 (27.6%) were female. Polypharmacy (use of ≥5 medications) was observed in 91.5% in hemodialysis patients and 100% in renal transplant patients. The most prescribed drugs in hemodialysis patients were Cardiovascular Drugs 72 (100%), and in renal transplant patients, immunosuppressant were highly prescribed 33 (100%).

Conclusion
This study concludes that the cardiovascular agents and immunosuppressant were the most common drugs prescribed among the hemodialysis and renal transplant patients respectively. polypharmacy among overall patients were observed and it may initiate drug related problems.

Keywords:
chronic kidney disease, hemodialysis, polypharmacy, prescribing patterns

Introduction

The persistent decline in glomerular filtration rate (GFR), which is a characteristic of chronic kidney disease (CKD), is a significant public health concern that is linked to high morbidity and mortality worldwide [1]. The prevalence of CKD was increasing globally and was found to be 9.1% [2]. In India, the prevalence of CKD was found to be 17.2% [3]. The rising prevalence and incidence of the disease cause poor health outcomes and more expensive medical care.

Hemodialysis (HD) and kidney transplantation are suitable therapeutic options for patients with later stages of CKD [4]. HD patients often take medications to treat various comorbidities such as diabetes mellitus and hypertension. Kidney transplant recipients take several drugs simultaneously, including immunosuppressive agents and other medications to manage underlying diseases such as diabetes, hypertension, and dyslipidemia [5]. Rational drug prescription is complex in CKD patients due to a higher risk of Drug-related problems (DRPs) since they need complex therapeutic regimens requiring frequent monitoring and dosage adjustments. The presence of other comorbidities such as diabetes mellitus, hypertension, coronary

artery disease, and infections make the situation more complicated. Inappropriate medication use can increase adverse drug effects as reflected in prolonged hospital stays and increased healthcare utilization and costs [6].

With an increased rate of HD and transplantation patients worldwide, the prescribing pattern of drug therapy and other major risk factors should examine. Appropriate drug selection for patients with CKD is essential to avoid unwanted drug effects and ensure optimal patient outcomes. Therefore, prescription pattern studies are needed to audit the prescription, track prescribing practices, and make recommendations for changes to achieve rational drug use of medications. It also assesses the rational prescribing skill of the physicians, and it can be done by conducting a prescription audit [7].

In India, prescribing pattern studies in HD and kidney transplantation patients are limited. Hence, this study is planned to analyze current prescribing trends in HD and kidney transplantation patients.

Material and methods

The prospective observational study was conducted over a period of 8 months, i.e., from October 2021 to June 2022, in the Department of Nephrology, Charitable Hospital, Mangalore, Karnataka. The study was approved by Institutional Ethical Committee (IEC) (Ref. No: NGSMIPS/IEC/13/2021) and registered in the Clinical Trials Registry-India (Ref. No: CTRI/2021/10/03/7084).

Informed consent was taken from each patient before enrolling and patients were explained about study details and clarified the objections raised. Based on the time-bound method, a total of 105 end-stage CKD patients, who visited the outpatient department of Nephrology and were treated either with HD or renal transplantation of both gender, ranging in age from 18 to 80 years, were enrolled. Patients undergoing peritoneal dialysis, cognitive impairment, and pregnant and lactating women were excluded from the study.

The materials and all relevant data for the study were collected using patient data collection form, patient case sheets, patient treatment charts, and laboratory charts. Socio-demographic details like age, gender, weight, height, body mass index (BMI), domiciliary status, comorbid conditions, social habits, and duration and frequency of HD, duration after renal transplantation were collected. Information regarding

the medications, like the number of drugs prescribed per patient, different classes of drugs prescribed and the percentage of drugs per prescription for HD and renal transplantation was estimated in this study.

The data were analyzed using descriptive statistics, and data were analyzed using IBM SPSS software version 20, United States.

Results

A total of 105 patients meeting inclusion criteria were enrolled in the study, of which male 76 (72.38%) predominates over females 29 (27.6%). The mean age of HD patients was found to be 52.22±13.87 which was more than the renal transplant patients 34±12.06. Among the total population, the majority of the patients 76 (72.38%) fall within the optimal BMI with the mean found to be 22.1±3.07 Kg/m^2. In the total study population, the majority of the patients were non-substance users 63 (60%). The majority of the HD patients were from rural areas 39 (54.16%)whereas renal transplantation patients were from urban areas 17(51.51%).

The clinical conditions of the study population were analyzed. The findings revealed that the majority of the overall patients had hypertension 103(93.09%) followed by diabetes 26 (24.76%), and ischemic heart disease (IHD) 18 (17.14%). Among the HD patients, the majority were found to be having 2-5 comorbities46 (63.87), whereas, among 33 renal transplant patients, the majority were found be having single comorbidity 20 (60.6%).

The duration and frequency of HD treatment and duration after renal transplantation were analyzed. Majority of the HD patients 32 (44.44%) had duration of HD treatment found to be ≤ 2 years. Majority of the patients having HD frequency twice a week 41 (56.94%). The majority of the renal transplant patients had a duration of 6 to 10 years after renal transplantation 23 (69.69%) (Table 1).

Analysis of drugs prescribed in HD and renal transplanted patients

The mean prescription among the overall population was 7.41±2.45. Among renal transplantation patients, the mean drugs prescribed per prescription was found to be 7.78 ± 2.01 which is higher than the mean prescription of HD patients 7.05 ± 2.8. Majority of the HD patients 47 (65.2%) and renal transplant patients 19 (57.57%)were prescribed with 5 to 8 drugs (Figure 1).

**Table 1 Demographic details of HD and renal transplant patients**

Characteristics	Total patients ($N=105$)	Number. of HD patients ($N=72$)	Number of renal transplant patients ($N=33$)
Sex			
Male	76 (72.38)	51 (70.83)	25 (75.76)
Female	29 (27.6)	21 (29.16)	8 (24.24)
Age group wise			
18–40	36 (34.28)	15 (20.83)	21 (63.63)
40–60	50 (47.61)	38 (52.77)	12 (36.36)
60–70	13 (12.38)	13 (18.05)	–
Above 70	6 (5.71)	6 (8.33)	–
Mean age±SD	43.11±12.96		
BMI			
Underweight (<18.5 kg/m^2)	10 (9.5)	7 (9.72)	3 (9.09)
Optimal (18.5–24.9 kg/m^2)	76 (72.38)	53 (73.61)	23 (69.69)
Overweight (25–29.9 kg/m^2)	17 (16.19)	11 (15.27)	6 (18.18)
Obese (>30 kg/m^2)	2 (0.095)	1 (1.38)	1 (3.03)
Mean BMI±SD	22.1±3.07	21.9±2.75	22.31±3.4
Domiciliary status			
Urban	50 (47.61)	33 (45.83)	17 (51.51)
Rural	55 (52.38)	39 (54.16)	16 (48.48)
Social habits			
Smoking	16 (15.23)	12 (16.6)	4 (12.12)
Alcohol	5 (4.76)	3 (4.16)	2 (6.06)
Both	21 (20)	10 (13.8)	11 (33.33)
No substance uses	63 (60)	47 (65.27)	16 (48.48)
Duration of dialysis			
≤2 years	–	32 (44.44)	–
3–5 years	–	25 (34.72)	–
6–9 years	–	10 (13.88)	–
≥10 years	–	6 (8.33)	–
Frequency of dialysis			
Once a week	–	2 (2.77)	–
2 times a week	–	41 (56.94)	–
3 times a week	–	30 (41.66)	–
Duration after renal transplant	–	–	
<2 years	–	–	3 (9.09)
2–6 years	–	–	7 (21.21)
6–10 years			23 (69.69)
Comorbidities: mean (SD)	1.89±1.16	2.1±1.15	1.69±1.18
Comorbidities			
Hypertension	103 (93.09)	72 (100)	31 (93.93)
Diabetes	26 (24.76)	16 (22.22)	10 (30.3)
Dyslipidemia	11 (10.4)	8 (11.11)	3 (9.09)
Hypothyroidism	4 (3.8)	4 (5.55)	–
IHD	18 (17.14)	15 (20.83)	3 (9.09)
COPD	7 (6.6)	7 (9.7)	–
Asthma	4 (3.8)	–	4 (12.12)
Number of comorbidities			
No comorbidities	1 (0.95)	–	1 (3.03)
Single comorbidity	45 (42.85)	25 (34.72)	20 (60.6)
2–5 comorbidities	58 (55.23)	46 (63.87)	12 (36.36)
>5 comorbidities	1 (0.95)	1 (1.38)	–

IHD- Ischemic heart disease; COPD- Chronic obstructive pulmonary disease

Different classes of drugs prescribed among HD and renal transplant patients were analyzed. A total of 23 classes of drugs were prescribed for overall patients. Amo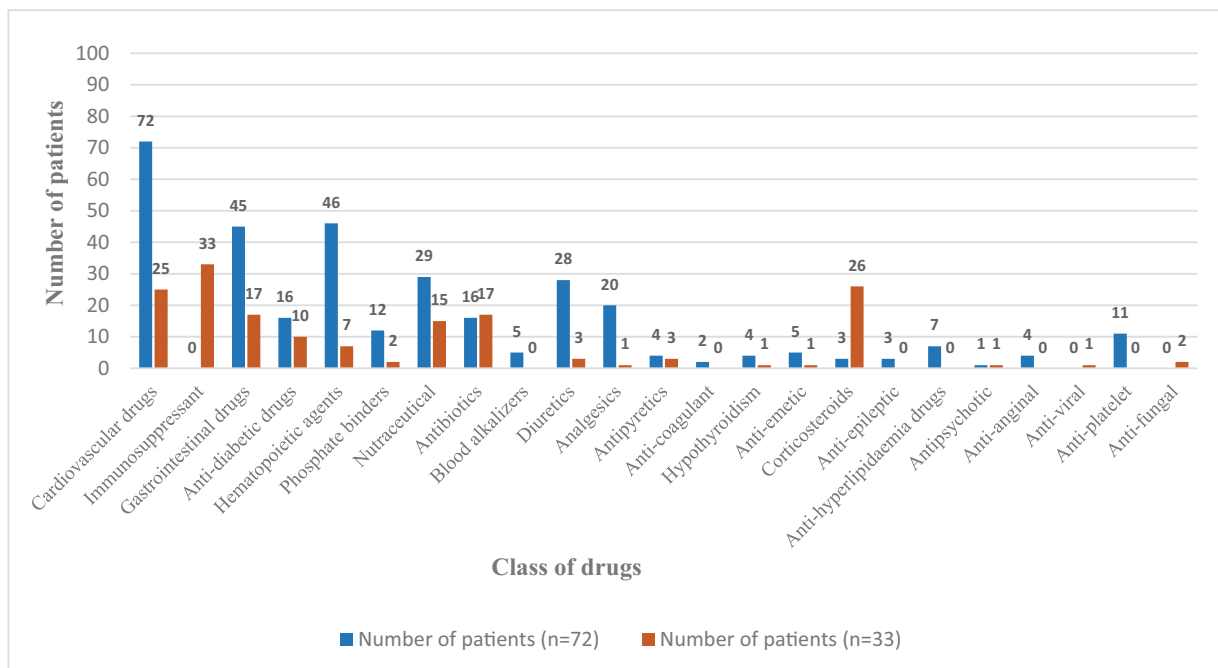ng HD patients, 20 classes of drugs were prescribed which is more than the renal transplant patients 17. The most prescribed class of drugs in HD patients were cardiovascular drugs 72 (100) followed by hematopoietic agents 46 (63.88%) and gastrointestinal

Figure 1
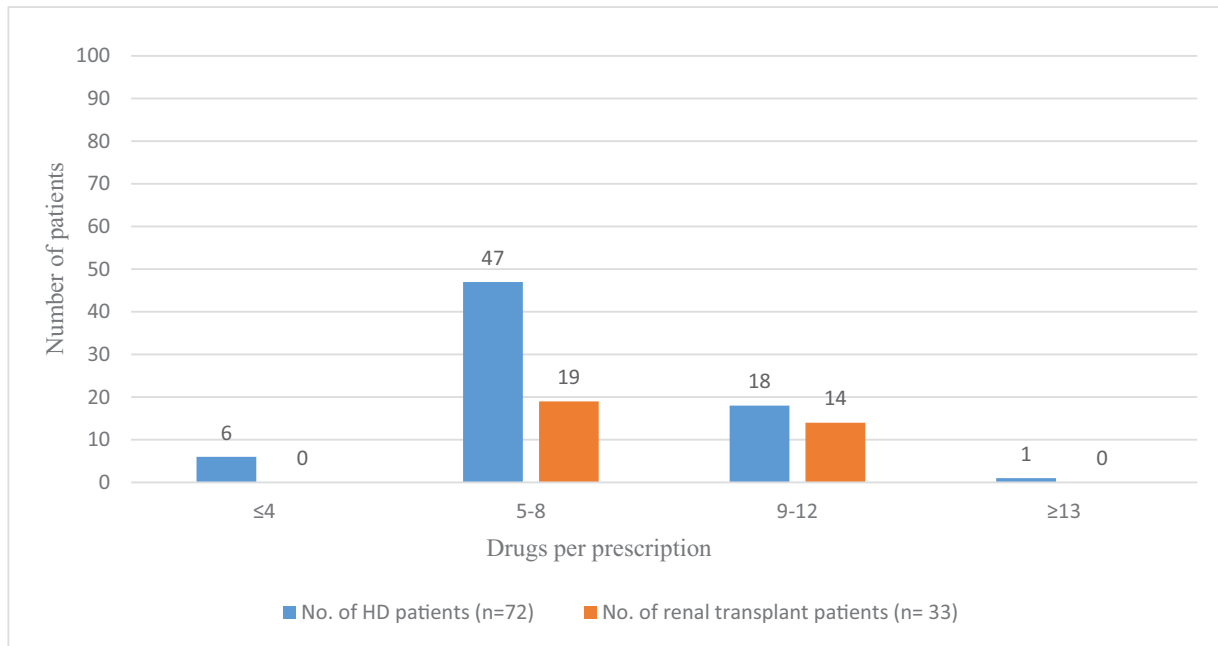
Number of drugs prescribed per prescription in HD and renal transplant patients. HD, hemodialysis.

Figure 2

Classes of drugs prescribed.

(GI) drugs 45 (62.5%)(Figure 2). In HD patients, cardiovascular drugs such as alpha 2- agonist 37 (51.38%) were highly prescribed followed by calcium channel blockers (CCBs) 34 (47.22%). The most prescribed class of drugs in renal transplant patients were immunosuppressants 33 (100%) followed by cardiovascular drugs 25(75.75%), and nutraceuticals 25 (75.75). Amongimmunosuppressants, tacrolimus was majorly prescribed 33 (100%) followed by mycophenolatemofetil 28 (84.84%) (Table 2).

Discussion

CKD has emerged as one of the leading causes of mortality and morbidity in the twenty-first century.

Table 2 Most commonly prescribed drugs in HD and renal transplant patient

Drugs	Individual drugs	No. of HD patients %(n= 72)	No. of renal transplant patients % (n= 33)
CCBs	Amlodipine	13 (18%)	7 (21.21%)
	Cilnidipine	11 (15.2%)	10 (3.0.3%)
	Nifedipine	11 (15.2%)	4 (12.12%)
Beta blockers	Carvedilol	3 (4.1%)	3 (9.09%)
	Metoprolol succinate	4 (5.5%)	3 (3.09%)
	Atenolol	4 (5.5%)	-
Alpha 2- agonist	Clonidine	37 (51.3%)	16 (48.48%)
Calcineurin inhibitors	Tacrolimus	-	33 (100%)
Mycophenolate	Mycophenolate mofetil	-	28 (84.84%)
	Mycophenolate sodium	-	3 (9.09%)
PPIs	Pantoprazole	36 (50%)	13 (39.39%)
H2 receptor blocker	Ranitidine	-	8 (24.24%)
Sulfonylureas	Gliclazide	2 (2.77%)	-
Insulin	Biphasic isophane insulin	6 (8.3%)	7 (21.21%)
	Human insulin regular	-	3 (9.09%)
	Soluble insulin injection	9 (12.5%)	-
Hematopoietic	Recombinant human erythropoietin	63 (87.5%)	5 (15.15%)
	Iron sucrose	43 (59.72%)	2 (6.06%)
Phosphate binders	Calcium acetate	10 (13.8%)	-
	Sevelamer	3 (4.16%)	2 (6.06%)
	Calcium carbonate	19 (26.3%)	12 (36.36%)
Nutraceutical	Vitamins and minerals*	18 (25%)	15 (45.45%)
	Vitamin B complex*	11 (15.27%)	-
Blood alkalizers	Sodium bicarbonate	5 (6.9%)	-
Diuretics	Furosemide	13 (18.05%)	-
	Torsemide	14 (19.4%)	2 (6.06%)
Corticosteroids	Prednisolone	1 (1.38%)	26 (78.78%)
	Budesonide	2 (2.77%)	-
Antibiotics	Cephalosporins	14 (19.4%)	4 (12.12%)
	Sulfamethoxazole – trimethoprim	-	13 (39.39%)
Analgesics	Tramadol-Acetaminophen	14 (19.4%)	-

CCB, calcium channel blocker; *CB, calcium cha; PPI, proton pump inhibitor. *Vitamins and minerals (HD patients): Folic acid, calcitriol, alfacalcidol, folic acid+methylcobalamin+pyridoxine hydrochloride, vitamin B complex+Vitamin C+zinc, vitamin B complex+vitamin C, ferrous ascorbate+folic acid, levocarnitine+vitamin E; vitamin B complex: thiamine nitrate, riboflavin, pyridoxine hydrochloride, cyanocobalamin, nicotinamide, pantothenic acid calcium salt. Vitamin and minerals (renal transplant patients): alpha-ketoanalogue, calcitriol, calcium with alfacalcidol, folic acid+methylcobalamin+pyridoxine hydrochloride, mecobalamin+alpha lipoic acid+vitamin D3 +pyridoxine+folic acid, benfotiamine.

The prevalence of CKD patients has also been rising, impacting millions people globally [8]. This increase is partly due to the rise in comorbidities. Generally, CKD patients will take multiple medications to manage the disease and other comorbidities, and this practice has been linked to adverse consequences. Polypharmacy is associated with a high economic burden in terms of drug-related complications, frequent hospitalizations, morbidity, mortality, and health care costs. Therefore, there is a need for prescribing pattern studies to assess the prescribing and distribution of drugs in patients treated with HD and renal transplantation, and this will facilitate optimal management of disease and other comorbidities through rational use of drugs.

The reports of this study showed high incidence of renal impairment in males 76 (72.38%) over females 29 (27.6%), this similar results were found in previously conducted study, [9] where reported male predominance (57%) but as per the recent epidemiological study published in 2022 females are having more prevalent to get CKD than males [8]. The mean comorbidity in the study population was found to be 1.89±1.16. Among the overall patients, majority of the patients with 2-5 comorbidities 58 (55.23%), which shows that there is a need of more drugs to manage disease and comorbidities. The average number of the drugs prescribed per patients was found to be 7.41±2. It shows that there is polypharmacy among the end stage CKD patients, which is parallel to the study reported previously, where they reported polypharmacy among CKD patients [10].

Among HD and renal transplantation patients, cardiovascular drugs were mostly prescribed. Out of cardiovascular drugs, alpha 2- agonist were highly prescribed in HD patients which was contrast to the study conducted previously, where CCBs were highly prescribed for the treatment of hypertension in HD patients [11]. CCBs were highly prescribed for the

treatment of hypertension in renal transplant patients 16 (48.48%), which was similar to the study conducted earlier, where CCBs were mostly prescribed for hypertension in renal transplant patients [12].

In present study, renal transplant patients mostly prescribed with more than one Immunosuppressant. Among immunosuppressant drugs, tacrolimus was commonly prescribed to all the patients 33 (100%), followed by mycophenolate mofetil 28 (84.84%) this is similar to the study conducted earlier, where tacrolimus was mostly prescribed at the rate of 87.7% [13].

In this study, even independent of GI diseases, proton pump inhibitors (PPIs) were mostly prescribed after anti-hypertensive and hematopoietic agents. GI drugs such as PPIs, H2 receptor blockers and other GI drugs were prescribed. PPIs were prescribed probably to prevent drug induced gastritis. Even though PPIs are thought to be safe, there remains a danger, particularly in conditions where there is renal impairment. According to study, using them increases the incidence of adverse outcomes like bone fractures, renal problems, microscopic colitis, and hypomagnesaemia [14].

Conclusion

This study concludes that the cardiovascular agents such as alpha 2 agonists followed by CCBs and immunosuppressant such as tacrolimus followed by mycophenolate mofetil are the most common class of drugs likely to be prescribed among the hemodialysis and renal transplant patients respectively. Further this research highlights the practice of polypharmacy among the hemodialysis and renal transplant patients which needs to be taken into account when treating the patients as they are likely to initiate drug related problems such as adverse drug reactions and drug interactions. Thus, there is vital role of clinical pharmacologists/ pharmacists in the medication therapy management in the CKD patients which could be milestone towards the achieving appropriateness of therapy.

Conflicts of interest
There are no conflicts of interest.

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