A STUDY ON IDENTIFICATION & ASSESSMENT OF MEDICATION INAPPROPRIATNESS IN CHRONIC KIDNEY DISEASE PATIENTS AT A TERTIARY CARE HOSPITAL

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ABSTRACT

Elderly individuals with chronic kidney disease (CKD) often face the added burden of multimorbidity, making them vulnerable to inappropriate prescription practices. This study focused on evaluating such practices within this demographic and contributed to the implementation of the Ambulatory Kidney Care model to improve prescribing behaviors. In hospitalized CKD patients, improper medication use can lead to extended hospital stays, increased healthcare costs, and elevated morbidity and mortality risks. Hence, the careful selection of pharmaceutical agents is essential in this population. The study was a six-month observational analysis conducted at the Medicine and Nephrology departments of a tertiary care hospital in Vijayapura. A total of 114 hospitalized CKD patients (81 males and 33 females) were assessed. The most frequent comorbidities identified were hypertension, anemia, and diabetes mellitus. Among 1103 prescribed drugs, 71 were found inappropriate, 85 had drug-drug interactions, and 19 were contraindicated in CKD. The study highlights the critical need for vigilant medication management in CKD patients to prevent adverse outcomes. Clinical pharmacists play a crucial role in contributing to renal drug cost management by prescribing and modifying medications tailored to individual patients. The promotion of rational drug use is essential to eliminate polypharmacy, inappropriate prescriptions, drug-drug interactions, and contraindications, particularly in CKD patients. Pharmacists have taken on an emerging role in prescribing and modifying medications. Moreover, their role in educating patients about the hazards of self-medication, excessive drug use, and polypharmacy cannot be understated, as it ensures patients adhere to proper medication practices.

KEYWORDS: Chronic Kidney Disease (CKD), KDIGO Guidelines, Glomerular Filtration Rate (GFR), Drug-Related Problems (DRP's).

INTRODUCTION:

Chronic kidney disease can be defined by lasting structural or functional irregularities within the kidneys, spanning 3 months or beyond. The hallmark is a reduction in the GFR to below 60 mL/min/1.73 m^2, sustained for a minimum of 3 months. Individuals receiving hospital care are notably vulnerable to challenges arising from medication-related issues. This susceptibility is attributed to prolonged treatment regimens and extended stays in medical facilities, resulting in escalated healthcare expenditures. Within the population affected by chronic kidney disease, key risk factors are hypertension (HTN), diabetes mellitus (DM), coronary artery disease, and susceptibility to infections.

CKD is often referred to as a 'silent disease' because patients may not experience noticeable symptoms until the disease has progressed significantly. However, when symptoms do occur, they may include:

- Difficulty maintaining focus.
- Reduced desire to eat.
- Nocturnal muscle cramps.
- Enlarged feet and ankles.
- Inflammation around the eyes.
- Dry and irritated skin.
- Fatigue.
- Increased frequency of urination.

Diabetes including hypertension emerges as the primary instigators of CKD, with the natural progression of aging also heightening the susceptibility to this enduring ailment.

Approximately 6% of U.S. adults have stage 2 chronic kidney disease (CKD), with many progressing to stages 3 and 4. Globally, over 90% of CKD cases are attributed to five main causes, with regional variations. Diabetic nephropathy, especially from type 2 diabetes, is a leading cause in North America and Europe. Hypertension is commonly seen in newly diagnosed CKD patients, often indicating either latent glomerular disease or systemic vascular disorders like nephrosclerosis.

In older adults, chronic renal ischemia and systemic vascular diseases are significant contributors to CKD. The rising CKD prevalence in the elderly is linked to longer life spans due to reduced cardiovascular mortality. Importantly, early-stage CKD often presents with

heart, brain, or lung complications and even mild declines in kidney function or proteinuria are now seen as key risk factors for cardiovascular disease.1

Medication-related issues (MRIs)

This encompasses any event or situation tied to medication therapy that obstructs or has the potential to impede patients from attaining ideal medical care results. In the realm of healthcare systems, multimorbidity—where multiple medical conditions coexist—affects roughly 70% of the senior demographic, presenting notable clinical and financial complexities. Notably, a substantial portion of hospital admissions among older adultsstems from chronic illnesses. To effectively cater to the expanding requirements of multimorbidity patients, a comprehensive strategy is imperative, encompassing social dimensions, nutritional considerations, and pharmacotherapy.

Eight classes of medication-related problems.

1. Untreated symptoms.
2. Inappropriate drug selection.
3. Suboptimal dosage.
4. Excessive dosage.
5. Inadequate consideration of adverse drug reactions.
6. Missed doses or treatment.
7. Drug interactions.
8. Unjustified drug usage.3

The mechanism for pharmacokinetic interactions:

Interactions that affect drug absorption predominantly occur in the gastrointestinal tract. Nevertheless, some interactions can be beneficial when used with parenteral formulations. For instance, adrenaline as a vasoconstrictor can prolong analgesia when combined with local anesthetics. However, long-acting molecules like bupivacaine are preferable to avoid exposing patients to unnecessary risks associated with additional drugs.

In the gastrointestinal tract, various mechanisms can modify drug absorption:

1. Chelation: Certain heavy metal ions, including iron, calcium, and magnesium, and zinc, can bind with anionic medications, resulting in the formation of poorly soluble salt forms that

diminish the absorption of the drugs. Similarly, ion exchange resins like cholestyramine can attach to drugs, leading to reduced absorption.

2. Alterations in gastrointestinal motility: Specific medications can influence the motility of the gastrointestinal (GI) tract, impacting the pace at which drugs pass through the GI tract and consequently affecting their absorption rate. For instance, metoclopramide can enhance GI motility and facilitate the opening of the pyloric sphincter, expediting the transit of drugs. However, its impact on the overall quantity absorbed might not be significant.

3. Effects on bowel flora: Medicines can bring about changes in the composition of microorganisms within the large intestine, subsequently influencing the kinetics and effects of drugs. Broad-spectrum antibiotics, for instance, can modify the bacterial population, thereby influencing the metabolism of specific drugs such as combined oral contraceptives and coumarin anticoagulants.

Interactions that influence drug distribution often involve instances where drugs bound to plasma proteins are displaced by others with stronger binding affinities.

4. Displacement of protein binding: Although historically deemed important, the displacement of protein-bound drugs as a mechanism for drug interactions is now rarely of clinical significance. While displacement can occur, it usually increases the concentration of free drugs in the plasma, subsequently undergoing rapid elimination through normal metabolic processes.

Interactions impacting drug metabolism are particularly critical and intriguing:

5. Metabolic induction: The metabolism of one drug (inducer) can be augmented by another (substrate), resulting in decreased substrate levels and elevated metabolite concentrations. This phenomenon can diminish the effect of the parent drug or give rise to the production of toxic metabolites, as observed with paracetamol and CYP2E1 inducers.

6. Metabolic inhibition: Inhibition amplifies the levels of a drug in the plasma, potentially leading to toxicity or heightened side effects if the parent drug is active. It can also delay the action of prodrugs, exemplified by diltiazem and cyclosporine.

7. Interactions involving drug transporters: Drug transporters play a crucial role in ferrying drugs across cell membranes. One well-known transporter is P-glycoprotein (P-gp), which is implicated in various interactions. For example, P-gp expels digoxin from intestinal cells, influencing its absorption. Certain drugs can inhibit or induce P-gp, further complicating the interaction landscape.

8. Genetic polymorphism and drug interactions: Genetic variations in certain cytochrome P450 isoenzymes (CYP2D6, 2C9, and 2C19) can affect drug metabolism. Differences in metabolic status can explain inter-individual variations in drug interactions. For instance, patients with different metabolic statuses of CYP2C19 may respond differently to diazepam or its inhibitor, omeprazole.2

MATERIALS AND METHODOLOGY:

An observational study was conducted in the Nephrology and Medicine departments of a well-known tertiary care hospital at Bijapur city. The study included a sample size of 114 patients. Ethical approval was collected before conducting the study, reference number IEC/BLDECOP/2022/02.Data was collected through patient interviews and thorough review of individual case records. Information for the study was sourced from multiple references, including patient case files, direct interviews, KDIGO guidelines, and the Micromedex online drug database.

Work Procedure:

Socio-demographic and other relevant details of the patients were recorded. The individual patient data included age, sex, serum creatinine, blood urea nitrogen levels, co-morbid conditions, reasons for admission, and medications prescribed during hospitalization. The GFR was computed using the Chronic Kidney Disease EPI formula, as recommended by the KDIGO guidelines for chronic kidney disease assessment and management, and a suitable GFR category was allocated to each patient.

To determine the ill-suited drugs in CKD patients the calculated GFR rate was considered, and KDIGO guidelines were consulted. Additionally, multiple drug references, including Micromedex and the drug handbook, were utilized to verify inappropriate drug use. A pre-validated list of contraindicated drugs, approved by the Department Physician, was employed as a method to study. The presence of pharmacodynamic interactions was checked in every

prescription using Micromedex version 9.1. All collected information was recorded and managed in Microsoft Excel sheets.

We conducted the statistical analysis using SPSS Software version 20, with a significance level established at a p-value of less than 0.05. The outcomes were represented using mean + SD (standard deviation) values, percentage tables, and diagrammatic presentations. Descriptive analysis was conducted on demographic data, such as age, body weight, creatinine value, blood urea nitrogen levels, and the number of drugs per prescription.

RESULTS

Table no: 1 Distribution of Gender

Gender	Number of patient(N=114)	Percentage
Male	81	71
Female	33	29

Table No: 2 Distribution of age ranges

Age	Number of patients (N=114)	Percentage
18-25	3	3
26-35	8	7
36-45	18	16
46-55	30	26
56-65	31	27
66-75	22	19
76-85	2	2

Table no: 3 Length of Hospitalization

No of days	No of patients (N=114)	Percentage
1-5	68	59.64
6-10	29	25.43
11-15	14	12.28
16-20	2	1.75
>20	1	0.87

Table No: 4 Distributions of patients according to Departments

Department	No of patients (N=114)	Percentage
Medicine	74	65
Nephrology	40	35

Table No: 5 Distribution of the count of coexisting medical conditions

Number of diseases	Quantity of individuals (N=114)	Percentage
0	6	5.26
1	36	31.57
2	45	39.47
3	27	23.68

Table no: 6 Categorization of different stages

Phases	Number of patients (N=114)	Proportion
Phase 1	2	1.75
Phase 2	6	5.26
Phase 3	14	12.28
Phase 4	32	28.07
Phase 5	60	52.63

Table No: 7 Number of Drugs prescribed

Sl.no	Number of drugs	No of patients	Percentage
1	1-5	19	16.6
2	6-10	60	52.63
3	11-15	30	53.5
4	16-20	8	7.01
5	>21	2	1.75

Table No: 8 categorizations of selected DRPs

Sl.NO	Drug-related problem	Total no of drugs (N=1103)	Percentage
1	Inappropriate drug	71	40.57
2	Contraindication	19	10.85
3	Drug-drug interaction	85	48.57

Fig No: 1 Categorization of Selected DRPs

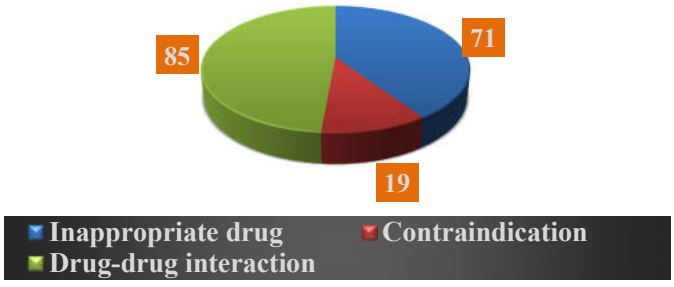

Table No: 9 Number of inappropriate drugs

Inappropriate drugs found?	No.of patients (N=114)	Percentage
Yes	71	62.28
No	43	37.71

Fig No: 02 Number of inappropriate drugs

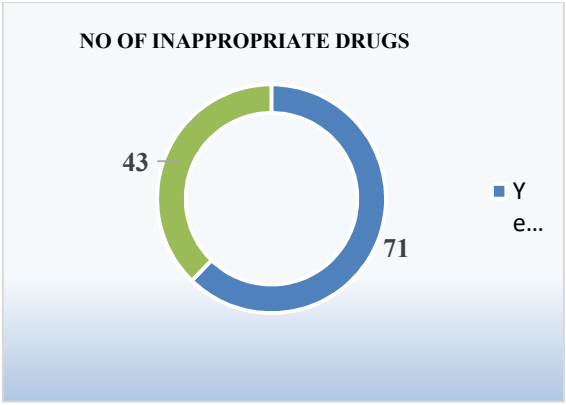

Table no: 10 Total number of contraindication drugs

Contraindication found	No of patients (N=114)	Percentage
Yes	19	16.66
No	95	83.33

Fig no:3 Total number of Contraindications

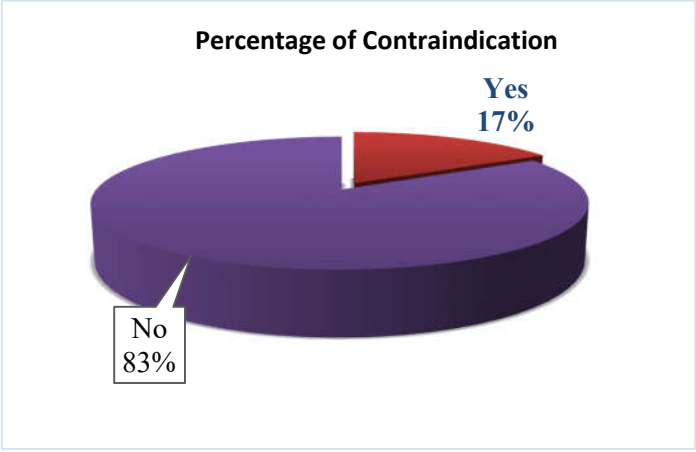

Table no:11 Severity of Drug-Drug Interaction

Severity	No. of patients (N=85)	Percentage
Major	28	32.94
Moderate	49	58.57
Minor	8	11.42

Fig No: 4 Interaction between drugs

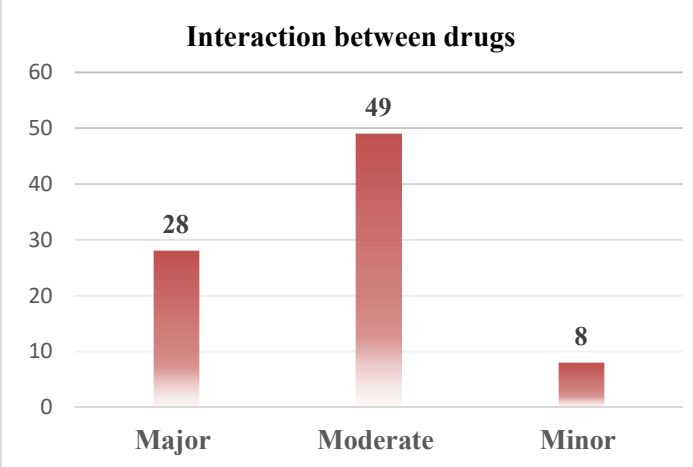

Table no:12 Inappropriate drugs list

Sl.no	Drug name	Generic name	Class of drug	No of patients (N=71)	Percentage
1	Inj.Lasix	Furosemide	Anti-hypertension	16	22.53
2	Tab. Lasix	Furosemide	Anti-hypertension	38	53.52
3	Tab.Dytor	Torsemide	Anti-hypertension	7	9.85
4	Tab.Demadex	Torsemide	Anti-hypertension	2	2.81
5	Tab. Frusoleca	Furosemide	Anti-hypertension	3	4.22
6	Tab.Glycomet	Metformin	Anti-diabetic	1	1.40
7	Tab.Metoz	metolazone	Anti-hypertension	2	2.81
8	Tab.Telista	Telmisartan	Anti-hypertension	1	1.40
9	T.Tenepen	Teneligliptin	Anti-hypertension	1	1.40

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Fig No:5 Inappropriate drugs

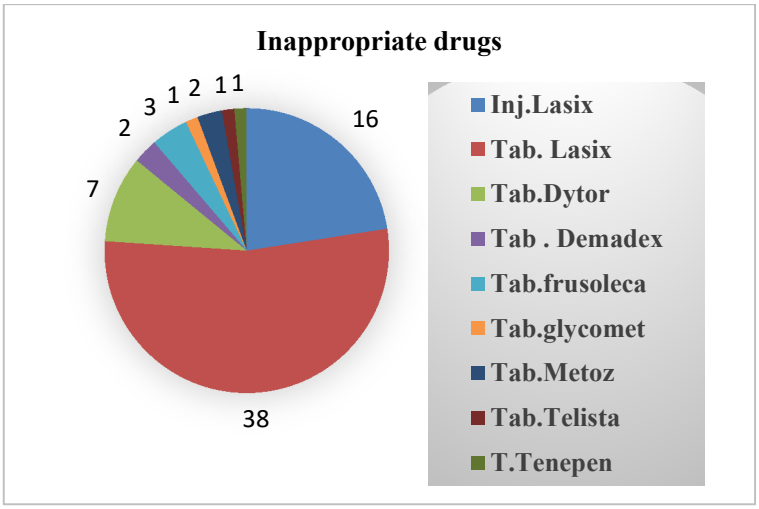
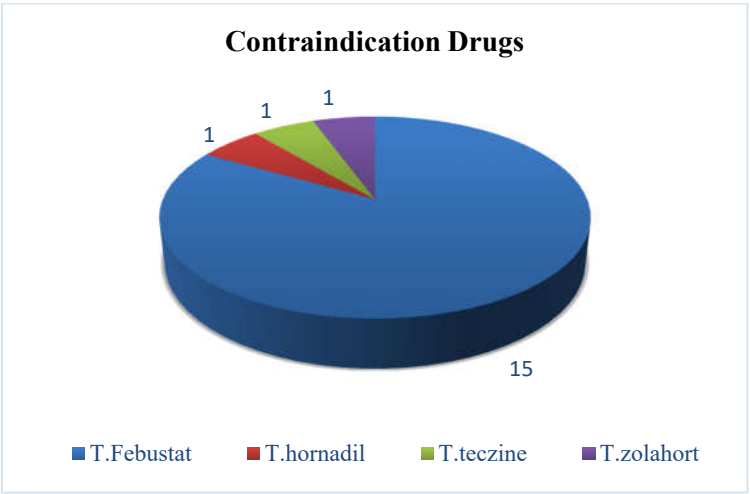


Table no: 13 Contraindicated drugs

Sl.no	Drug Name	Generic name	Class of Drug	No of patients	Percentage
1	Inj. Metrogyl	Metronidazole	Antibiotics	15	78.94
2	T. Febustat	Febuxostat	NSAID's	1	5.2
3	T. Hornadil	Nicorandil	Anti-Hypertension	1	5.2
4	T. Teczine	Levocetirizine	Anti-Histamine	1	5.2
5	T. Zolahort	Azilsartan	Anti-Hypertension	1	5.2

Fig No: 6 Contraindication drugs



DISCUSSION:

The study included a total of 114 CKD patients, with 81 being male and 33 being female, indicating a higher prevalence of CKD in males. The result is consistent with similar research carried out by S Rakshana and Preetha Selva on the prescription pattern within patients with chronic kidney disease who are being treated at a tertiary care hospital. Most CKD individuals participating in the study were in the age range of 56-65 years while the lowest incidence was observed in the age range of 76-85 years, aligning with previous research.3

Hospital admission data revealed that most CKD patients were admitted for 1-5 days, with findings studied by Hesty U. Ramadaniati et al. on medication-related issues in CKD individuals receiving medical care at a hospital in Indonesia. The study also showed that the medicine department had the highest number of admissions (74 patients), followed by the nephrology department (40 patients)4

Regarding socio-economic status, the study found that most CKD patients were from the middle class (82 patients), while 19 and 13 patients belonged to the upper and lower classes, respectively. This data can be attributed to cost-effectiveness concerns among patients about medication prescription, and it correlates with research carried out by Aster WakjiraGaredow et al. on medication-related issues within CKD patients admitted at a medical center in Ethiopia.5

The prevalent coexisting health conditions detected in CKD patients were hypertension, anemia, and diabetes mellitus, suggesting a causal connection with CKD. It is worth noting that most patients were likely in stage 5 CKD, while the minority were categorized under stage 1 CKD. This alignment corresponds with a study conducted by Clare MacRae et al., which explored potentially inappropriate prescribing practices in individuals with CKD within the context of primary care.6

The study also assessed medication use within CKD patients and found that most patients were on 2 medications (47 patients), followed by 1 medication (25 patients). The most prescribed medications were anti-hypertensive drugs, with fewer patients being prescribed anti-diabetic agents. However, a considerable number of patients received medications in injectable form, highlighting the need to encourage the prescription of medication by generic name and promoting oral administration.

Inappropriate medication uses and potential interaction between drugs were identified in the study. Overall, 71 medications were prescribed inappropriately, alongwith anti-hypertensive

drugs being the most common offenders. Interaction between drugs was observed in 85 drugs, with moderate interactions being the most prevalent. Contraindicated drugs were also found in 19 cases, mainly in the anti-diabetic class.

Proton pump inhibitors and antibiotics were commonly prescribed for prophylaxis in hypertension and hyperglycemic agents, which may lead to interaction between drugs and risk factors in CKD individuals. Monitoring and drug therapy modifications were deemed necessary for CKD patients to ensure appropriate medication use.

Overall, this study provides valuable insights into the improper utilization of medications in CKD patients, highlighting the importance of implementing guidelines, and interventions to optimize medication practices and improve patient outcomes.

CONCLUSION:

Chronic Kidney Disease (CKD) is a long-term condition marked by structural or functional kidney abnormalities lasting over three months, commonly indicated by a glomerular filtration rate (GFR) below 60 mL/min/1.73 m^2. Often asymptomatic in early stages, CKD may present later with symptoms like fatigue, cognitive decline, appetite loss, edema, dry itchy skin, and increased urination.

Beyond its clinical effects, CKD patients frequently face drug-related problems (DRPs) due to complex medication regimens. These issues can lead to poor health outcomes, more hospitalizations, higher treatment costs, and increased mortality risk. A major concern is the use of inappropriate medications, especially in the elderly, where reduced renal function makes them vulnerable to drug toxicity.

Drug-drug interactions (DDIs) are also common in CKD patients due to polypharmacy and can negatively impact drug safety and effectiveness. Some medications are completely contraindicated in CKD due to their potential to worsen kidney function or other comorbidities.

Clinical pharmacist obsereved 19 contraindicated drugs prescribed in our study . Few drugs were replaced, drug dose alteration and few drugs were stopped by considering the safety and efficacy of the drug in CKD patients. The study helps to develop a standard drug chart list where, it will have the list of all safety drugs for CKD patients and also list of contraindicated

drugs which were not safe for CKD patients. The role of pharmacist in drug related problems was highlighted by identifying, assessing, using KDIGO, Micromedex and the observed DRP's were communicated to the physicians, and necessary changes were made as the end result.

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