

Chronic Kidney Disease: A Review of Drug Related Problems and Medication Management in Chronic Kidney Disease Patients

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Abstract: Chronic kidney disease (CKD) is a progressive condition characterized by abnormalities in kidney structure or function that persist over time. The kidneys play an essential role in the elimination of drugs and their metabolites; therefore, impairment of kidney function can significantly affect drug pharmacokinetics and pharmacodynamics. CKD patients are at increased risk of DRPs because of altered renal function, polypharmacy, multiple comorbidities and complicated medication regimens. Common DRPs in CKD include inappropriate drug selection, incorrect dosage, inappropriate dosing frequency, untreated indications, unnecessary drug therapy, drug-drug interactions, adverse drug reactions, medication duplication and non-adherence. Polypharmacy is common among CKD patients because several diseases may need to be treated simultaneously. Although multiple medicines may be clinically necessary, increasing medication burden can increase the possibility of drug-drug interactions, adverse effects, medication errors and poor adherence. Chronic kidney disease (CKD) is a major public health concern due to its high morbidity, mortality, hospitalization rates, healthcare costs, and reduced life expectancy. Globally, Chronic Kidney Disease (CKD) is one of the leading causes of mortality. Patients with any degree of renal disease are at risk of altered drug metabolism and impaired renal excretion. Comprehensive medication management involving physicians, pharmacists, nurses and patients can contribute to safer and more effective pharmacotherapy. Regular medication review, appropriate renal dosing, monitoring, patient counselling and identification of potentially harmful medicines should be considered integral components of CKD care. Toxicity resulting from the accumulation of drugs or metabolites and ineffective dosing due to inappropriate dose adjustment can significantly affect the clinical outcomes of critically ill patients. The care of patients with CKD is complex and involves multiple healthcare providers and multidisciplinary CKD clinics, as well as various inpatient and outpatient services. Appropriate management of CKD therefore requires coordinated care and individualized treatment strategies. Randall Russell provided a contextual framework by describing the patient journey from the primary nephrologist in the community to the progressive renal insufficiency clinic and hospital-based care. Patients may experience shock related to diagnosis, uncertainty about disease progression, and concerns regarding the need for dialysis. Therefore, individualized care that considers patients' values, preferences, and overall well-being is important for improving patient satisfaction and quality of care.

Keywords: Chronic Kidney Disease (CKD); Renal Insufficiency; Drug Metabolism; Renal Excretion; Dose Adjustment; Drug Toxicity; Individualized Care; Dialysis; Patient Satisfaction.

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I. INTRODUCTION

Chronic kidney disease (CKD) is an important public health problem due to its high morbidity and mortality risk.[2] Hospitalization rates are high among CKD patients. Clinical pharmacy services have been established to provide care for

CKD patients, especially those experiencing a complicated course of treatment.[2] CKD is a major global health concern, affecting over 33 million people worldwide and contributing to approximately 5–10 million deaths annually.[3]

Patients with kidney disease often require multiple medications to manage their underlying illnesses and complications.[3] Moreover, inappropriate dosing can have a significant impact on clinical outcomes, such as mortality, the need for dialysis, and progression of kidney disease.[3] This problem is particularly important in low-resource settings.[3] In Ethiopia, where diagnostic and therapeutic resources are limited, the burden of renal disease is high. Data on medication dosing practices and their impact on patient outcomes are scarce.[3] Currently, efforts have been made to better understand the progression of kidney disease. In 2002, the Kidney Disease Outcomes Quality Initiative (KDOQI) of the National Kidney Foundation developed practice guidelines for CKD. [4] A number of epidemiological studies assessed the prevalence of CKD in different populations and regions to estimate kidney function.[4] Two systematic reviews recently published data on the prevalence of CKD in population-based study samples. These studies used the standardized definition from the KDOQI practice guidelines and particularly focused on the performance of equations for estimating GFR, such as the MDRD equation and the C-G equation, and provided a summary of the burden of CKD. [4] The past 10 years have shown increased interest in the treatment of CKD. A significant relationship exists between health-related quality of life and appropriate treatment, particularly regarding medication dosing practices and their impact on patients.[5] Currently, limited efforts have been made to better determine the progression of kidney disease. The KDIGO 2012 CKD guidelines was built on the united state-based CKD outcomes Quality Initiative, in 2002 guidelines on definition, classification and evaluation of CKD.[11] Pharmacokinetic and pharmacodynamic properties of many medicines are generally affected by kidney disease. When prescribing medications to patients with kidney disease, multiple factors should be taken into account including drug absorption, distribution, metabolism, and excretion. Active or toxic metabolites may also be affected by kidney disease and uremia.[7] Therapeutic drug monitoring may be necessary to ensure adequate drug levels while assessing the potential for drug accumulation. [7] Commercially available database that include administrative and laboratory data can be used to assess prescribing patterns among physicians treating individuals with advanced CKD (stage 4-5) who are not on dialysis or who have not received a transplant. Treatment should be based on appropriate guidelines and patient-specific requirements.[10]

II. METHODS

➤ Operational Definition:

- Renal drug dose adjustment practice: The clinical practices of optimising doses of drugs that are metabolised, excreted or pose a burden on the kidney to avoid toxicities. Practice was measured based on the FPA's usual dose adjustment guidelines which should use the Cockcroft-Gault equation (<https://globalrph.com/renal/>) as the applicable preferable tool for this study.

- Chronic Kidney Disease: Kidney damage or decreased glomerular filtration rate (GFR) below 60 mL/min/1.73 m² for three months or more [3].
- Cockcroft-Gault equation: It is a formula used to estimate creatinine clearance and helps in deciding the appropriate dose of some medicines in patients with reduced kidney function [3].
- eGFR calculation for renal drug dose adjustment: Calculated as $(140 - \text{Age}) \times \text{body weight} / \text{Plasma creatinine} \times 72$
- Acute Kidney Injury: Acute kidney injury that full fills KDIGO criteria that is increase in serum creatinine by 0.3 mg/dL or increase in serum creatinine to 1.5 times baseline or more.
- Estimated GFR: eGFR is an estimated value used to assess kidney function based on certain patient-related factors.
- Creatinine Clearance: A measure of the volume of blood plasma that the kidneys clear of creatinine per unit of time, used to assess overall kidney function.[11]
- Creatinine Clearance: A measure of the volume of blood plasma that the kidneys clear of creatinine per unit of time, used to assess overall kidney function.
- Polypharmacy is probiotic for older adults with CKD: Polypharmacy can lead to inappropriately high doses of medications, drug–drug interactions, and adverse events (NIHMS 332). In older adults with CKD, medication adherence is critical to slow kidney disease progression and reduce mortality. Medication adherence is also an important element in mitigating cardiovascular risks and preventing cardiovascular events
- Medication Compliance Tool: Medication management situation was investigated using a unique questionnaire from [1]. This form contained items of “medication management”, “medication storage”, “medication safety step”, “medication administration situation”, “knowledge of side effects.” The number of medication being taken and the frequency of administration were extracted from patient's electrical medical charts.

➤ Medication Management Situation:

• Question-1 What is your Current Occupation

- ✓ Unemployed
- ✓ Part-time
- ✓ Full-time employed
- ✓ Other

• Question-2 Who is Managing your Medication?

- ✓ The Patient themselves
- ✓ Husband or wife
- ✓ Other family member
- ✓ Individual other than family

• Question 3- How is your Medication Being Stored?

- ✓ Storage in medicine bag from the pharmacy
- ✓ Storage in a different container
- ✓ Storage in medicine specific container

✓ Other

• *Question 4- When the Storing the Medication, what State is it in?*

✓ In the sheet that it was received in, popping the pills out each time

✓ In the sheet but cut into small pieces

✓ Storage after removal from sheet

✓ Had pharmacy package it individually

✓ Other

• *Question-5 What is your Medication Administration Situation?*

✓ Take it without forgetting

✓ Some times forget to take it

✓ Often forget to take it

✓ Almost never take it in line with physician instruction

➤ *Factor Affecting Medication Compliance in CKD Patient:*

Table 1 Factor Affecting Medication Compliance in CKD Patient

S. No.	Factors	Examples
1.	Patients-relate factors	Forgetfulness, lack of knowledge, lack of motivation
2.	Treatment-related factors	Polypharmacy, complete dosing schedule, Adverse effect
3.	Disease-related factor	Multiple comorbidities, long term treatment
4.	Socioeconomic factors	Cost of medicines, financial difficulties
5.	Health-related factors	Poor patient counselling, inadequate follow-up
6.	Psychological factors	Anxiety, depression, Treatment burden

• Medication adherence measurement and tools: 43 qualifying articles, 6 (14.0%) studies used multiple method to measure medication adherence. The most common measures used for assessing medication adherence were MMAS-8 (n=11[25.6%], MPR (including MPR modified) (n=10 [23.3%]), PDC (n=8 [18.6%]), and MEMS (n=6 [14.0%]).

• Quality assessment: The quality assessment found that all included studies were at “low” concern regarding applicability for this review. Among studies that used subjective tools, eleven studies were deemed to be at risk of bias due to “unclear” assessments in the QUADAS-2 domain of “patient selection” [22,23,24] Four studies had “unclear” assessments in the domain of “index test” [10, 41, 43, 65], and ten studies were found to have “unclear” assessments in the domain of “flow and timing” [22, 23]. On the other hand, among studies that utilized objective measures for assessing medication adherence, one study was judged to have “unclear” assessments in the QUADAS-2 domain of “patient selection”, three studies had “unclear” assessments in the “index test” domain, and three studies were found to have “unclear” judgment in the domain of “flow and timing”.

• Result: factors associated with medication adherence While the overwhelming majority of patients were aware of their CKD diagnosis. The majority of participants reported receiving preventive counselling on CKD-related content and those with lower medication adherence were significantly more likely to endorse receiving counselling from their provider, specifically salt consumption if they

had hypertension than those with higher medication adherence.

Those with lower medication adherence were more likely than participants with higher medication adherence to report putting off seeing a provider and to report putting off filling a medication during times when they did not have health insurance (n=296).

➤ *Adverse Safety Effect:*

• Participants found to have lower medication adherence had higher frequencies of Class I events and composite Class I or II events than those with higher medication adherence [n = 77296].

• After multivariable adjustment, individuals with lower medication adherence were more likely to have a Class I safety event than those with higher medication adherence. PR: 1.39; 95% confidence interval [CI], (1.2-1.75) 20% more likely to have a Class I or II safety event than those with higher medication adherence [77296].

• Lower medication adherence was significantly associated with:

✓ Major multiple (2) Class I safety events (PR, 1.71; 95% CI, 1.18–2.49).

✓ Multiple (2) composite Class I or II safety events (PR, 1.35; 95% CI, 1.04–1.76).

✓ Multiple (2) potential [PPS?] (PR, 2.44; 95% CI, 1.08–2.69) [77296]. [34]

Table 2 Adverse Safety Effect

S. No.	Tool	Main purpose	Assessment method
1.	Morisky Medication Adherence scale (MMAS-4)	Medication-taking assessment behaviour	4-items questionnaire
2.	Morisky Medication Adherence Scale (MMAS-8)	To assess medication adherence	8-items questionnaire
3.	Medication Adherence Rating scale (MARS)	To assess the patient medication-taking behaviour& adherence	Self- report
4.	Brief Medication Questionnaire (BMQ)	To identify medication adherence barriers	Structured questionnaire

5.	Pill Count estimate	To estimate actual medication use	Actual medication use
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Table 3 Study-Specific Characteristics of the Studies Included in the Systematic Review

Study and Country	Sample/Population	Medication adherence measure
Ada and Ozcan [21] -Turkey	198; HD + PD	MMAS-8 (Turkish)
Afsar et al. [22] - Iran	405; Non-dialysis CKD + HTN	MMAS-8
Alkatheri et al. [23] - Saudi Arabia	89; HD	MMAS-8 (Arabic)
Amado et al.- Portugal	122; HD	MTA (Adapted for Portugal)
Bandiera et al.- Switzerland	73; DKD	MEMS
Bandiera et al.- Switzerland	31; DKD	MEMS
Jense et al. [28]-Sweden	31,688; CKD + HF	PDC
Kaakubo et al [29] - Japan	483; HD	ASK-12 (Japanese)
Kaul et al. [30] - India	120; Non-dialysis CKD + HD	MMAS-8
Kronish et al. [32] -USA	30; CKD +HTN	MEMS
Lassen et al. [33] - Denmark	2,199; T2DM + CKD	MPR

III. CONCLUSION

Thank You.

Chronic Kidney Disease (CKD) is a progressive condition that significantly affects drug elimination, pharmacokinetics, and overall patient safety. Drug-related problems such as inappropriate drug selection, incorrect dosing, drug–drug interactions, adverse drug reactions, and medication non-adherence are common among CKD patients and may contribute to poor therapeutic outcomes. Effective medication management plays an important role in preventing and identifying these problems. Appropriate dose adjustment according to renal function, regular monitoring of patients, identification of potential drug interactions, patient counselling, and proper adherence to prescribed therapy can improve the safety and effectiveness of treatment. Pharmacists and other healthcare professionals have an important role in optimizing pharmacotherapy and reducing medication-related risks in CKD patients. A multidisciplinary approach, supported by regular monitoring and individualized treatment, can improve patient outcomes, reduce complications, and enhance the overall quality of care. Therefore, systematic identification and management of drug-related problems should be an essential part of CKD management.

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