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No funding was received for this study. The authors declare no conflict of interest. The study received ethical approval. All participants provided informed consent.

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Evaluation of Drug-Related Problems in Non-Dialysis Chronic Kidney Disease at Northwest General Hospital Peshawar: A Cross-Sectional Study

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ABSTRACT
Background: Chronic kidney disease (CKD) is a progressive condition associated with substantial morbidity, polypharmacy, and altered drug pharmacokinetics, placing patients at high risk of drug-related problems (DRPs). Non-dialysis CKD (ND-CKD) patients, in particular, face increased vulnerability to adverse drug events and drug–drug interactions (DDIs), necessitating proactive pharmaceutical care. Objective: This study aimed to evaluate the prevalence, causes, and clinical outcomes of DRPs in ND-CKD patients, assess the nature and acceptance of pharmacist-led interventions, and identify associations between Pharmaceutical Care Network Europe (PCNE) domains and DRP outcomes. Methods: A cross-sectional study was conducted among 157 ND-CKD inpatients at Northwest General Hospital, Peshawar. DRPs were identified and classified using PCNE version 9.1, and DDIs were analyzed via Lexicomp®. Data were analyzed using descriptive statistics and multivariate logistic regression. Results: A total of 254 DRPs were identified, predominantly due to inappropriate drug selection (42.91%) and patient-related factors (26.77%). Lexicomp® detected 157 DDIs, with Category C interactions most common (68.8%). Of 278 pharmacist interventions, 80.21% were accepted, and 44.96% of DRPs were completely resolved. Significant associations were found between DRP causes, intervention acceptance, and outcomes ($p<0.05$). Conclusion: DRPs are frequent in ND-CKD and predominantly preventable. Pharmacist-led interventions significantly improve therapeutic safety, highlighting the need for their integration into renal care.

Keywords
Chronic Kidney Disease, Drug-Related Problems, Non-Dialysis, Pharmacist Interventions, Drug–Drug Interactions, PCNE Classification

INTRODUCTION
Chronic kidney disease (CKD) is a progressive disorder of renal structure and function that confers substantial cardiovascular and mortality risk and demands careful long-term pharmacotherapy (1,6). Clinically, CKD is defined by a sustained reduction in estimated glomerular filtration rate (eGFR <60 mL/min/1.73 m² for ≥3 months) and/or markers of kidney damage, which provides the basis for staging and longitudinal management (5). Distinguishing CKD from acute kidney injury (AKI) is essential because AKI is often reversible and requires different diagnostic pathways and treatment priorities (7).

The global burden of CKD has risen markedly and now constitutes a major public health priority, with wide geographic and demographic heterogeneity, including within South Asia (9,3). In Pakistan, service delivery pressures and multimorbidity patterns mirror international trends, creating a growing population of non-dialysis CKD (ND-CKD) patients who require complex medication regimens over prolonged periods (3,9). Polypharmacy and altered pharmacokinetics in ND-CKD heighten vulnerability to drug-related problems (DRPs)—events or circumstances involving drug therapy that actually or potentially interfere with desired outcomes (12,13). In older and multimorbid patients, inappropriate prescribing and therapeutic cascades are common, amplifying preventable adverse drug reactions (ADRs) and avoidable utilization (17,18,20,21). Adherence challenges further compound risk in CKD, contributing to disease progression and poorer clinical trajectories (16).

Within CKD care, DRPs typically arise from suboptimal drug selection, dosing errors relative to kidney function, and clinically significant drug–drug interactions (DDIs) (23,11). The likelihood of harmful DDIs increases steeply with the number of co-prescribed agents, underscoring the value of systematic interaction screening in routine practice (19). Evidence suggests that pharmacist-delivered medication review and reconciliation can detect and resolve many DRPs, improve adherence, and reduce downstream utilization in CKD, including after hospitalization (14,25).

Despite this, contemporary data on the epidemiology and resolvability of DRPs in ND-CKD within Pakistani tertiary settings remain limited (23,24). To address this gap, we evaluated the prevalence, typology, and determinants of DRPs among ND-CKD inpatients at a tertiary hospital in Peshawar, characterized DDIs using a standardized interaction database, and quantified the uptake and outcomes of pharmacist-led interventions. Our objective was to generate actionable evidence to inform integrated, pharmacist-enabled models of ND-CKD pharmacotherapy in comparable resource settings (23–25,14).

MATERIALS AND METHODS

This cross-sectional observational study was conducted in the nephrology ward of Northwest General Hospital, a tertiary care centre in Peshawar, Pakistan. The study aimed to characterize the prevalence, causes, and outcomes of drug-related problems (DRPs) in patients with non-dialysis chronic kidney disease (ND-CKD). Ethical approval was obtained from the Institutional Review Boards of Kohat University of Science and Technology and Northwest General Hospital prior to data collection, and all participants provided written informed consent.

Patients with a confirmed diagnosis of CKD stages 3a to 5 were eligible, as defined by the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines (5). Staging was determined using the CKD-EPI equation, classifying patients into stage 3a (eGFR 45–59 mL/min/1.73 m²), stage 3b (30–44 mL/min/1.73 m²), stage 4 (15–29 mL/min/1.73 m²), and stage 5 (<15 mL/min/1.73 m²). Patients with eGFR ≥60 mL/min/1.73 m², a history of kidney transplantation, or pregnancy were excluded.

A total of 198 consecutive patients admitted between [insert study period if available] were screened. Of these, 157 met inclusion criteria and were enrolled in the final analysis. Sample size was estimated a priori using Daniel's formula for cross-sectional studies, assuming a prevalence rate of DRPs based on published literature and a 95% confidence interval with 5% precision (23).

Demographic, clinical, and pharmacological data were extracted from electronic medical records and bedside charts using a standardized case-report form. Variables collected included age, sex, CKD stage, comorbidities, laboratory parameters, and full medication history.

Drug-related problems were identified and classified according to the Pharmaceutical Care Network Europe (PCNE) classification system, version 9.1, which categorizes DRPs across seven domains, including treatment effectiveness, adverse reactions, and cost-effectiveness (12). Each DRP was linked to one or more potential causes (e.g., inappropriate drug selection, dosing error, or patient non-adherence).

All prescribed medications were screened for potential drug–drug interactions (DDIs) using the Lexicomp® Interact database. Interactions were categorized from A to X, where A denotes no known interaction and X indicates contraindicated combinations that should be avoided (23). Each identified DDI was further evaluated for clinical relevance and recommended management actions.

Pharmacist-initiated interventions were recorded at three levels: prescriber (e.g., therapy modification or substitution), drug (e.g., dosing adjustment or discontinuation), and patient (e.g., counseling and adherence support). Outcomes were documented as accepted, rejected, or unknown based on prescriber response. The resolution status of each DRP was classified as totally solved, partially solved, not solved, or unknown.

Data was entered and analysed using SPSS (version 25.0; IBM Corp., Armonk, NY, USA). Categorical variables were summarized as frequencies and percentages, while continuous variables were expressed as means ± standard deviations (SD) or medians with interquartile ranges, as appropriate. Associations between PCNE domains and DRP outcomes were assessed using multivariate binary logistic regression, with variables selected based on clinical relevance and prior evidence (11,14). Statistical significance was defined as a two-tailed $p < 0.05$.

RESULTS

A total of 157 ND-CKD patients were included. Males were 83 (52.9%) and females 74 (47.1%). Most patients were aged ≥60 years (56.1%). Hypertension (79.6%) and diabetes mellitus (50.3%) were the most common comorbidities (Table 1).

Table 1. Demographic and clinical characteristics of the study population (n=157)

Variable	Category	n	%
Age (years)	10–29	22	14.0
	30–59	47	29.9
	≥60	88	56.1
Gender	Male	83	52.9
	Female	74	47.1
Comorbidities	Hypertension	125	79.6
	Diabetes mellitus	79	50.3

Across the cohort, 157 DDIs were identified. Most were Category C (monitor therapy) (68.8%), followed by Category B (no action needed) (15.9%), Category D (consider therapy modification) (10.2%), Category X (avoid combination) (3.2%), and Category A (no known interaction) (1.9%). Corrected examples and spellings are shown in Table 2.

Table 2. Drug–drug interactions by Lexicomp® category (n=157 interactions)

Category	Lexicomp® description	n	%	Representatives*
A	No known interaction	3	1.9	Omeprazole + Vancomycin; Heparin + Meropenem
B	No action needed	25	15.9	Aspirin + Sodium bicarbonate; Paracetamol + Tramadol
C	Monitor therapy	108	68.8	Furosemide + Aspirin; Humulin R + Tramadol
D	Consider therapy modification	16	10.2	Dexamethasone + Sodium bicarbonate; Calcium gluconate + Ceftriaxone
X	Avoid combination	5	3.2	Alfacalcidol + Calcitriol; Omeprazole + Clopidogrel

A total of 254 DRPs were recorded. The leading causes were drug selection problems (42.9%), patient-related factors (26.8%), and dispensing errors (22.8%) (Table 3). There were 278 planned interventions; multiple interventions could address a single DRP (hence totals across types exceed 100%). Most were at the prescriber level (66.9%). Overall acceptance was 80.2% (95% CI: 75.5–84.9). DRP resolution status is summarized in Table 4. Multivariate analyses evaluated domain-level associations. Significant associations were observed for Causes ↔ Planned interventions,

Causes ↔ Intervention acceptance, Causes ↔ DRP status, and Intervention acceptance ↔ DRP status (all p=0.001). By contrast, Planned interventions ↔ Intervention acceptance and Planned interventions ↔ DRP status were not significant (p=0.933 and p=0.187, respectively) (Table 5). Drug selection errors were the leading cause of DRPs, accounting for 42.91%, followed by patient-related factors (26.77%) and dispensing errors (22.83%), while dose selection (1.96%) and drug use problems (5.51%) were less frequent.

Table 3. Causes of drug-related problems (n=254 DRPs)

Cause	n	%
Drug selection problems	109	42.9
Patient-related factors	68	26.8
Dispensing errors	58	22.8
Drug use problems	14	5.5
Dose selection errors	5	2.0

Table 4. Interventions (types and acceptance) and DRP resolution

Parameter	Category	n	%	Notes / Inference
Intervention type (n=278)	Prescriber level	186	66.9	Non-mutually exclusive categories
	Drug level	105	37.8	
	Patient level	78	28.1	
Intervention acceptance (n=278)	Accepted	223	80.2	Proportion 95% CI: 75.5–84.9†
	Rejected	42	15.1	
	Unknown	13	4.7	
DRP status (n=254)	Totally solved	114	44.9	
	Partially solved	28	11.0	
	Not solved	10	3.9	
	Unknown	102	40.2	

† Normal (Wald) 95% confidence interval for a single proportion.

Note: Intervention categories are overlapping; more than one intervention could be recorded per DRP.

Table 5. Associations between PCNE domains and outcomes (multivariate models)

Domain pair	p-value
Causes ↔ Planned interventions	0.001
Causes ↔ Intervention acceptance	0.001
Causes ↔ DRP status	0.001
Planned interventions ↔ Intervention acceptance	0.933
Planned interventions ↔ DRP status	0.187
Intervention acceptance ↔ DRP status	0.001

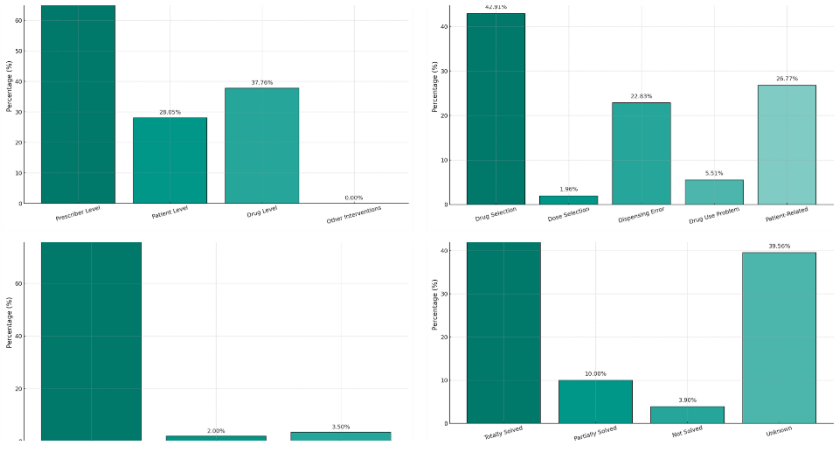

Figure 1 Drug-related problem (DRP) among non-dialysis chronic kidney disease (ND-CKD) patients

Most pharmacist-led interventions targeted prescriber decisions (66.90%), with substantial activity also at the drug (37.76%) and patient (28.05%) levels. Intervention proposals were accepted in the majority of cases (80.21%), indicating strong interprofessional collaboration, while approximately 2% were not accepted and ~3–5% remained undocumented. Following interventions, 44.96% of DRPs were completely resolved and 10.00% partially resolved, whereas 3.90% remained unsolved and 39.56% had unknown outcomes, underscoring the need for improved follow-up and documentation.

DISCUSSION

This study provides one of the few comprehensive evaluations of drug-related problems (DRPs) among non-dialysis chronic kidney disease (ND-CKD) patients in a tertiary care setting in Pakistan. Among 157 patients, a total of 254 DRPs were identified, a prevalence comparable to previous studies reporting rates between 12% and 87% across different CKD populations (11). The high DRP burden observed underscores the clinical vulnerability of ND-CKD patients, who are frequently exposed to polypharmacy, altered pharmacokinetics, and multiple comorbidities such as hypertension and diabetes, all of which increase medication-related risk (6,9,23).

The leading causes of DRPs in this study were inappropriate drug selection (42.91%) and patient-related issues (26.77%), aligning with earlier findings from India and other regions where suboptimal treatment choice, therapeutic duplication, and non-adherence were frequently implicated (24). These results emphasize the critical importance of individualized prescribing and patient education in CKD care, where inappropriate drug choice can exacerbate renal decline, compromise therapeutic efficacy, or precipitate adverse drug reactions (13,17). Additionally, dispensing errors and drug use problems—though less frequent—represent preventable contributors to medication-related morbidity, highlighting the need for robust safety checks and interdisciplinary communication (18).

The high prevalence of clinically significant drug–drug interactions (DDIs) further reflects the complexity of pharmacotherapy in this population. Category C interactions, which require monitoring, accounted for the majority (68.8%), a finding consistent with previous reports emphasizing the importance of ongoing clinical surveillance in patients receiving multiple agents (23,25). These interactions often involve agents with narrow therapeutic windows or renal clearance dependence, reinforcing the need for integrated DDI screening in clinical workflows (14).

Pharmacist-led interventions demonstrated substantial clinical impact in this cohort. More than two-thirds of interventions targeted prescriber-level decisions, and the overall acceptance rate was 80.21%. This figure, though slightly lower than the ~90% reported in some international studies (25), nonetheless indicates strong collaborative practice and recognition of pharmacists' clinical contributions. The lower acceptance rate may reflect context-specific factors such as prescriber autonomy, institutional prescribing protocols, or differing perceptions of clinical relevance. Interestingly, the lack of a significant association between planned interventions and their acceptance ($p=0.933$) suggests that the quality and contextual appropriateness of recommendations may outweigh sheer quantity.

Despite these findings, nearly 40% of DRP outcomes remained unknown, reflecting a persistent challenge in follow-up documentation and longitudinal monitoring in real-world practice. Improving feedback loops between prescribers, pharmacists, and nursing teams may enhance DRP resolution tracking and clinical decision-making in future interventions. The significant associations observed between most PCNE domains ($p < 0.05$) further illustrate the multifactorial nature of DRP management, where causative factors, intervention strategies, and patient outcomes are closely interlinked. Collectively, these results support the integration of clinical pharmacists as core members of the multidisciplinary renal care team. Their involvement in medication reconciliation, dosage adjustment, DDI monitoring, and patient counseling has consistently been shown to reduce inappropriate prescribing, improve adherence, and optimize clinical outcomes (14,25). Moreover, pharmacist participation may contribute to cost savings by preventing hospitalizations and reducing medication-related complications (19).

CONCLUSION

This study demonstrates a substantial burden of DRPs among ND-CKD patients, predominantly driven by inappropriate drug selection, patient-related issues, and clinically significant DDIs. Pharmacist interventions were frequently accepted and associated with improved outcomes, highlighting their pivotal role in optimizing therapy and enhancing patient safety. These findings underscore the importance of incorporating pharmacist-led services into standard CKD care pathways. Future multi-centre studies with larger and more diverse populations are warranted to validate these findings, evaluate long-term patient outcomes, and inform evidence-based national guidelines for DRP prevention and management.

REFERENCES

1. Levey AS, Coresh J. Chronic Kidney Disease. Lancet. 2012;379(9811):165–80.
2. Evans M, et al. A Narrative Review of Chronic Kidney Disease in Clinical Practice: Current Challenges and Future Perspectives. Adv Ther. 2022;39(1):33–43.
3. Jha V, et al. Chronic Kidney Disease: Global Dimension and Perspectives. Lancet. 2013;382(9888):260–72.
4. Kazancioglu R. Risk Factors for Chronic Kidney Disease: An Update. Kidney Int Suppl. 2013;3(4):368–71.
5. Inker LA, Levey AS. Staging and Management of Chronic Kidney Disease. In: National Kidney Foundation Primer on Kidney Diseases. 6th ed. Elsevier; 2018. p. 476–83.
6. Ammirati AL. Chronic Kidney Disease. Rev Assoc Med Bras. 2020;66(Suppl 3):s03–9.
7. Yoon SY, et al. Acute Kidney Injury: Biomarker-Guided Diagnosis and Management. Medicina. 2022;58(3):340.
8. He L, et al. AKI on CKD: Heightened Injury, Suppressed Repair, and the Underlying Mechanisms. Kidney Int. 2017;92(5):1071–83.
9. Francis A, et al. Chronic Kidney Disease and the Global Public Health Agenda: An International Consensus. Nat Rev Nephrol. 2024;20(7):473–85.
10. Gregg LP, et al. Fatigue in CKD: Epidemiology, Pathophysiology, and Treatment. Clin J Am Soc Nephrol. 2021;16(9):1445–55.
11. Kyomya J, et al. Drug-Related Problems and Associated Factors Among Patients With Kidney Dysfunction at a Tertiary Hospital in Southwestern Uganda. BMC Nephrol. 2023;24(1):375.
12. Yla-Rautio H, Siissalo S, Leikola S. Drug-Related Problems and Pharmacy Interventions in Non-Prescription Medication. Int J Clin Pharm. 2020;42(2):786–95.
13. Ayele Y, Tesfaye ZT. Drug-Related Problems in Ethiopian Public Healthcare Settings: Systematic Review and Meta-Analysis. SAGE Open Med. 2021;9:20503121211009728.
14. Tuttle KR, et al. Medication Therapy Management After Hospitalization in CKD: A Randomized Clinical Trial. Clin J Am Soc Nephrol. 2018;13(2):231–41.
15. Westphal JF, Brogard JM. Drug Administration in Chronic Liver Disease. Drug Saf. 1997;17(1):47–73.
16. Cedillo-Couvert EA, et al. Self-Reported Medication Adherence and CKD Progression. Kidney Int Rep. 2018;3(3):645–51.

17. Alhumaidi RM, et al. Risk of Polypharmacy and Its Outcome in Terms of Drug Interaction in an Elderly Population. J Clin Med. 2023;12(12):3960.
18. Gallagher P, Barry P, O'Mahony D. Inappropriate Prescribing in the Elderly. J Clin Pharm Ther. 2007;32(2):113–21.
19. Goldberg RM, et al. Drug-Drug and Drug-Disease Interactions in the Emergency Department: Analysis of a High-Risk Population. Am J Emerg Med. 1996;14(5):447–50.
20. Pirmohamed M, et al. Adverse Drug Reactions as Cause of Admission to Hospital: Prospective Analysis of 18,820 Patients. BMJ. 2004;329(7456):15–9.
21. Lazarou J, Pomeranz BH, Corey PN. Incidence of Adverse Drug Reactions in Hospitalized Patients: A Meta-Analysis of Prospective Studies. JAMA. 1998;279(15):1200–5.
22. Bero LA, Lipton HL, Bird JA. Characterization of Geriatric Drug-Related Hospital Readmissions. Med Care. 1991;29(10):989–1003.
23. Alruqayb WS, et al. Drug-Related Problems in Hospitalized Patients With Chronic Kidney Disease: A Systematic Review. Drug Saf. 2021;44(12):1345–63.
24. Shouqair TM, et al. Evaluation of Drug-Related Problems in Chronic Kidney Disease Patients. Cureus. 2022;14(4):e24019.
25. Susilawati NM, Halimah E, Saidah S. Pharmacists' Strategies to Detect, Resolve, and Prevent DRPs in CKD Patients. Pharmacia. 2021;68(3):619–26.