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Literature Study: Evaluation of Potential Drug-Related Problems (DRPs) in Patients with Chronic Kidney Disease

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Abstract: Chronic kidney disease (CKD) is defined as a persistent kidney disorder lasting for ≥3 months, characterized by structural or functional abnormalities of the kidneys with or without a decline in glomerular filtration rate (GFR <60 mL/min/1.73 m²). The aim of this study was to evaluate the potential occurrence of drug-related problems (DRPs) in CKD patients based on previous research findings through a systematic literature review. This study employed a systematic literature review design. The classification of DRPs was conducted using Cipolle et al.'s Classification for drug-related problems (DRPs). From the literature search that met the inclusion criteria, four articles were obtained, involving a total of 311 patients as research samples. The results were presented in both narrative and tabular form to provide an overview of the potential occurrence of DRPs in CKD patients. The distribution of CKD patients showed gender variation but was often dominated by males, with most patients aged from pre-elderly to elderly (>46 years). Hypertension and diabetes mellitus were identified as the most dominant comorbidities. Based on the analysis of the four reviewed articles, the potential occurrence of DRPs in CKD patients varied across categories and percentages. The findings indicated that the most frequently identified DRPs were "ineffective drug" (69.30%), "dose too high" (60%), "ineffective drug" (21.2%), and "dose too low" (68.18%).

Keywords: Chronic Kidney Disease (CKD); Cipolle; Drug-Related Problems (DRPs)

Introduction

Chronic kidney disease (CKD) is a progressive disorder of kidney function characterized by a decrease in glomerular filtration rate (GFR) <60 mL/min/1.73m² for more than three months or the presence of permanent structural and functional kidney damage. CKD is a serious health issue that requires serious attention because it is chronic, progressive, and associated with an increased risk of complications and mortality (Yasmin et al., 2025). In Indonesia, based on the 2023 Indonesian Health Survey published by the Health Development Policy Agency of the Ministry of Health of the Republic of Indonesia, the prevalence of CKD based on doctor's diagnosis in people aged ≥15 years was 0.18% (95% CI 0.16%–0.19%) (Kemenkes RI, 2023). Although the national prevalence appears relatively low, CKD remains a public health burden because it requires long-term therapy and significant healthcare costs, especially for advanced-stage patients undergoing hemodialysis. Patients with advanced CKD generally receive various drug regimens to treat the main condition and comorbidities such as hypertension, diabetes mellitus, anemia, and electrolyte disturbances. This condition leads to a high incidence of polypharmacy, which is the use of five or more drugs simultaneously, which is one of the main risk factors for drug related problems (DRPs).

DRPs are defined as any issue related to drug therapy that has the potential or actuality to interfere with achieving optimal therapeutic outcomes. In addition to polypharmacy, changes in pharmacokinetics

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and pharmacodynamics due to decreased kidney function also increase the risk of dosage inaccuracy, drug interactions, adverse drug reactions, and inappropriate therapeutic indications (Kurniawan, 2024). In clinical pharmacy practice, the identification and evaluation of DRPs is an important part of ensuring the safety and effectiveness of medication use. Various methods have been used globally to classify DRPs, such as The ABC of DRPs, Granada Consensus, Hepler-Strand classification, (Cipolle et al., 2012) and pharmaceutical care network europe (PCNE). The PCNE method is considered more systematic and representative in describing DRP events because it has a comprehensive classification structure (Utami et al., 2022).

However, the Cipolle et al. approach has advantages in clinical applicability because it is simpler, does not require complex subcategories, and is directly oriented towards pharmacist interventions. This approach is widely used and has been adapted in various countries, including Indonesia (Adian & Maulina, 2022).

Various studies on DRPs in CKD patients have been conducted in a number of health care facilities in Indonesia and internationally. However, most of these studies are descriptive and conducted on limited populations and settings, with variations in DRP identification methods. To date, there are still limited literature reviews that comprehensively summarize and evaluate the potential for DRPs in CKD patients. In fact, CKD patients are a high-risk group for DRPs due to renal dysfunction, polypharmacy, and accompanying comorbidities.

Based on this urgency, a literature study is needed to synthesize the results of previous studies in order to provide a comprehensive overview of the potential, types, and trends of DRPs in CKD patients. This study is expected to strengthen the scientific basis for the development of safer, more effective, and evidence-based clinical pharmacy services for patients with chronic kidney disease.

The purpose of this study was to evaluate the potential for drug-related problems (DRPs) in patients with chronic kidney disease (CKD) based on the results of previous studies reviewed through a literature study.

Method

This study is a systematic literature review that aims to evaluate the potential for drug related problems (DRPs) in patients with chronic kidney disease (CKD) based on published research results. The study was conducted from July to August 2025 through online electronic database searches. This study used a single variable, namely the potential for DRPs in CKD patients. The identification and classification of DRPs referred to Cipolle et al. (2012), which includes seven categories: unnecessary drug therapy; need for additional therapy; ineffective drugs; underdose; overdose; adverse drug reactions; and patient noncompliance.

The population in this study was all scientific articles discussing DRPs in CKD patients according to predetermined criteria. The sample in this study was scientific articles selected after screening based on inclusion and exclusion criteria. The sampling technique used non-probability sampling with a purposive sampling approach, namely the deliberate selection of articles that met the criteria and relevance predetermined to answer the research questions.

Inclusion criteria: articles discussing DRPs in CKD patients as the primary or secondary diagnosis; studies involving CKD patients with a GFR category of <15 mL/minute/1.73m² (stage G5) and/or patients undergoing renal replacement therapy such as hemodialysis; articles in Indonesian and/or research conducted in Indonesia; use the DRP classification based on Cipolle; and published between 2020 and 2025, available in full-text and open access. Exclusion criteria articles that are not available in full-text or cannot be accessed freely (non-open access).

Result and Discussion

A literature search was conducted using Google Scholar with a combination of keywords Chronic Kidney Disease (CKD), Drug Related Problems (DRPs), Cipolle et al, limited to the years 2020–2025, which yielded 20 articles in the initial identification stage. After screening the titles, abstracts, and established inclusion and exclusion criteria, a total of four articles met all criteria and were relevant to this study. These four articles were then further analyzed in this study, with each article discussing the identification of DRPs in CKD patients in several hospitals in Indonesia. The four articles involved a total of 311 CKD patients, most of whom underwent treatment in hospitals or hemodialysis units in Indonesia.

The gender distribution shows a tendency for male patients to dominate in most studies (Juwita et al., 2022; Megawati et al., 2024; Siahaan & Tobing, 2024), although one study reported a higher proportion of females (Diputra et al., 2020). This trend is consistent with the report by Delima et al. (2017), which states that the prevalence of CKD in Indonesia is higher in males, which is associated with risk factors such as smoking and alcohol consumption. Clinically, this predominance of male patients may have implications for different comorbidity profiles and treatment patterns, thereby potentially affecting the types of DRPs that arise.

Table 1. Overview of Research Articles

Research Title*	Researcher (Year)	Research Design	Sample Size
Identification of Drug Related Problems (DRPs) in Chronic Kidney Failure Patients in the Inpatient Unit of Dr. Sitanala Tangerang General Hospital	(Megawati et al., 2024)	Non-experimental descriptive, retrospective	92 Patients
Drug Related Problems (DRPs) in Chronic Kidney Disease (CKD) Patients at Dr. M. Djamil General Hospital	(Juwita et al., 2022)	Descriptive, retrospective	74 Patients
Analysis of drug related problems (DRPs) in chronic renal failure end stadium patients that are taking hemodialization in RSUD 45 Kuningan	(Diputra et al., 2020)	Non-experimental descriptive, prospective	85 Patients
Analysis of Drug-Related Problems (DRPs) in Chronic Kidney Disease Patients in the Inpatient Unit of Imelda Indonesian Workers General Hospital, Medan	(Siahaan & Tobing, 2024)	Non-experimental descriptive observation, retrospective	60 Patients

Table 2. Distribution of Patients by Gender

Researcher (Year)	Gender	Frequency	Percentage (%)
(Megawati et al., 2024)	Male	48	52.17
	Female	44	47.83
Total		92	100
(Juwita et al., 2022)	Male	44	59.46
	Female	30	40.54
Total		74	100
(Diputra et al., 2020)	Male	36	42
	Female	49	58
Total		85	100
(Siahaan & Tobing, 2024)	Male	33	55
	Female	27	45
Total		60	100

Table 3. Distribution of Patients by Age

Researcher (Year)	Age Range (Years)	Frequency	Percentage (%)
(Megawati et al., 2024)	17-25	1	1.09
	26-35	10	10.87
	36-45	10	10.87
	46-55	21	22.83
	56-65	28	30.43
	>65	22	23.91
Total		92	100
(Juwita et al., 2022)	18-25	6	8.11
	26-35	6	8.11
	36-45	18	24.32
	46-55	22	29.73
	56-65	19	25.67
	>65	3	4.06
Total		74	100
(Diputra et al., 2020)	17-25	5	6
	26-35	5	6
	36-45	15	18
	46-55	26	30
	56-65	19	22
	> 65	15	18
Total		85	100
(Siahaan & Tobing, 2024)	17-25	1	1.6
	26-35	0	0
	36-45	6	10
	46-55	17	28.3
	56-65	18	30
	> 65	18	30
Total		60	100

The majority of patients were in the pre-elderly and elderly age groups (≥46 years), with the peak distribution in the 56–65 age range (Diputra et al., 2020; Juwita et al., 2022; Megawati et al., 2024; Siahaan & Tobing, 2024). This pattern is consistent with the findings of (Maharianingsih & Putri, 2024), which show that increasing age correlates with progressive decline in kidney function. Physiologically, aging causes a decrease in glomerular filtration rate, which worsens drug elimination and increases the risk of drug accumulation. This condition explains why the elderly are more vulnerable to DRPs, especially those related to dosage inaccuracy.

Table 4. Distribution of Patients Based on Comorbidities

Researcher (Year)	Comorbidities	Frequency	Percentage (%)
(Megawati et al., 2024)	Hipertensi	57	40.14
	Anemia	57	40.14
	Bakteri Infeksi	7	4.93
	Edema Paru	5	3.52
	Pneumonia	5	3.52
	Diabetes Mellitus	4	2.82
	Asidosis Metabolik	2	1.41
	Dislipidemia	1	0.70
	Gagal Jantung Kongestif	1	0.70
	Tuberkulosis (TBC)	1	0.70
	Hiperkalemia	1	0.70
	Hipoalbumin	1	0.70
		1	0.70
(Juwita et al., 2022)	Not specified/Data not available	-	-
(Diputra et al., 2020)	Hipertensi	77	90.6
	Diabetes Mellitus tipe 2	26	30.6
	CHF (Congestive Heart Failure)	14	16.5
	Anemia	5	5.9
	Gout	5	5.9
	Stroke iskemik	1	1.2
	Dislipidemia	1	1.2
	BPH	1	1.2
(Siahaan & Tobing, 2024)	Pneumonia	15	6.55
	Hipertensi	17	7.42
	CKD stage 5	12	5.24
	PPOK	7	3.06
	Hyponatremia	15	6.55
	Asidosis	5	2.18
	Hypoglikemia	6	2.62
	Hypertiroid	1	0.44
	CHF ec HHD	5	2.18
	Anemia	24	10.48
	Sequele of cerebral infark	1	0.44
	Hemiparese	1	0.44
	PJK	1	0.44
	TB Paru	12	5.24
	Spondylosis Cervicalis	1	0.44
	ec DN	8	3.49
	DM Type II	5	2.18
	Gastritis	5	2.18
	Polip Medial Esofagus	1	0.44
	CHF ec HHD	3	1.31
	CKD stage 5D	2	0.87
	CHF ec CAD HHD	3	1.31
	Tension asites	1	0.44
	Volume Overload	5	2.18
	Metabolik	3	1.31
	Ascites	1	0.44

Researcher (Year)	Comorbidities	Frequency	Percentage (%)
	Sirosis Hepatis	1	0.44
	Cerebral Infark	2	0.87
	Hemiparase	2	0.87
	Striktur Uretra	1	0.44
	BPH	4	1.75
	PJA	1	0.44
	Oedem paru	1	0.44
	Post ALO	1	0.44
	Eksaserbasi	1	0.44
	edem paru	1	0.44
	Post op repair Pseudoaneurisma	1	0.44
	Hiponatremia	3	1.31
	Peptic Ulcer	1	0.44
	Pnuemonia	1	0.44
	DM tipe 2	1	0.44
	Effusi Pleura Bilateral	1	0.44
	Hydropyonefrosis gr IV (D)	1	0.44
	Nefrolitiasis (D)	1	0.44
	Urosepsis	1	0.44
	Moderate HI	1	0.44
	PSA	1	0.44
	ec PGOI	2	0.87
	SVT	1	0.44
	CKD stage 4	9	3.93
	Kardia Korpus Antrum Pylorik	1	0.44
	CKD stage 3B ec DN	1	0.44
	ec ND	1	0.44
	PGOI	1	0.44
	Tumor Buli	1	0.44
	Hydronefrosis Bilateral	1	0.44
	Batu Ureter Distal (D)	1	0.44
	Hidroneforsis (D)	1	0.44
	Hydropneumothoraks	1	0.44
	CHF ec CAD	1	0.44
	APS	1	0.44
	CKD Stage 3A	1	0.44
	ec HN	2	0.87
	Effusi Pleura	1	0.44
	Hypoalbumin	1	0.44
	Spondylitis	1	0.44
	CKD Stage 3	3	1.31
	Efusi pleura bilateral	1	0.44
	Pneumotoraks	1	0.44
	DM Thype II	1	0.44
	Vertigo	1	0.44
	CKD stg 4	1	0.44
	HHD	1	0.44
	GGK Stage 5	1	0.44
	Hipotiroid	1	0.44
	TBC	1	0.44

Description: 1 patient has ≥ 1 comorbid condition

The most dominant comorbidities are hypertension, followed by anemia and diabetes mellitus (Diputra et al., 2020; Megawati et al., 2024; Siahaan & Tobing, 2024). The high prevalence of hypertension confirms the bidirectional relationship between kidney disorders and blood pressure. The presence of comorbidities increases the complexity of therapy and encourages polypharmacy, which directly increases the potential for drug interactions, duplication of therapy, and dosage adjustment errors. Thus, conceptually, the higher the burden of comorbidities, the greater the risk of DRPs in CKD patients.

Table 5. Distribution of Potential DRPs in Patients with Chronic Kidney Disease

Researcher (Year)	DRPs Categories (Cipolle et al., 2012)*	Number of Incidents	Percentage (%)
(Megawati et al., 2024)	1	19	16.67
	2	15	13.16
	3	79	69.30
	4	0	0
	5	1	0.88
	6	-	-
	7	-	-
Total		144	
(Juwita et al., 2022)	1	0	0
	2	7	35
	3	0	0
	4	1	5
	5	12	60
	6	-	-
	7	-	-
Total		20	
(Diputra et al., 2020)	1	17	20
	2	5	5.9
	3	18	21,2
	4	-	-
	5	-	-
	6	17	20
	7	-	-
Total		57	
(Siahaan & Tobing, 2024)	1	10	22.73
	2	0	0
	3	0	0
	4	30	68.18
	5	0	0
	6	0	0
	7	4	9.09
Total		44	

Analysis of DRP categories based on the classification by Cipolle et al. (2012) shows variations in distribution between studies. The ineffective drug category dominates in the study by Megawati et al. (2024) (69.30%) and is also the highest category in the study by Diputra et al. (2020) (21.2%). These findings indicate that inappropriate therapy selection or regimen mismatch with the patient's clinical condition remains a major challenge in CKD management. Pharmacokinetically, changes in renal function can affect drug concentrations in plasma, preventing therapy from achieving optimal therapeutic effects.

The category of excessive dosage was the dominant finding in Juwita et al. (2022) (60%), indicating a risk of toxicity due to insufficient dosage adjustment based on glomerular filtration rate values. Conversely, underdosing dominated in the study by Siahaan & Tobing (2024) (68.18%), which has the potential to cause treatment failure. This difference shows that dose adjustment in CKD patients remains a crucial issue, both in the context of over-dosing and under-dosing.

Unnecessary drug therapy and adverse drug reactions were also found in fairly high proportions in several studies (Diputra et al., 2020). Unnecessary therapy is often associated with drug duplication or administration without strong indications, especially in patients with multiple comorbidities. Meanwhile, not all DRP categories were consistently studied in every study, such as patient non-compliance and adverse drug reactions, indicating variations in research focus among researchers.

This study used a systematic literature review method, which has the advantage of providing a broader and more comprehensive picture of DRPs in CKD patients from various populations and periods, with stronger conclusions than single studies. However, the results of the study depend on the quality and completeness of the data in the articles analyzed. Differences in methods and classification of DRPs between articles can affect the consistency of results. The limited number of articles and the lack of details on regimens and treatment duration also limit the depth of the analysis.

Conclusion

Based on the results of an analysis of four scientific literature reviews, the potential for drug-related problems (DRPs) in patients with chronic kidney disease (CKD) varies in terms of both category and percentage. The study results show that the most common DRPs found in each scientific literature are ineffective drugs (69.30%), excessive doses (60%), ineffective drugs (21.2%), and insufficient doses (68.18%). The conclusion of this study shows that the main problems in treating CKD patients lie in drug selection and dosage accuracy. In the future, treatment should focus on eGFR-based dosage adjustments, periodic effectiveness evaluations, and the involvement of clinical pharmacists in the care team to reduce the risk of DRPs and improve clinical outcomes.

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Conflicts of Interest
The authors declare no conflict of interest.

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