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Polypharmacy and Potential Drug Interactions in Hemodialysis Patients at Hospital X

Frida Yuli Theresia Simanjuntak[1], Rizky Farmasita Budiastuti[2]
Fridasimanjuntak97@gmail.com
[1,2]Faculty of Pharmacy, Universitas 17 Agustus 1945 Jakarta, Jakarta, Indonesia

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ABSTRACT

Chronic kidney disease (CKD) patients undergoing hemodialysis frequently receive multiple medications to manage renal complications and comorbidities, increasing the risk of polypharmacy and potential drug–drug interactions (pDDIs), which may compromise treatment safety and effectiveness. This study aimed to analyze the association between polypharmacy and the occurrence of pDDIs among CKD patients undergoing hemodialysis at Hospital X. A retrospective analytical cross-sectional study was conducted using medical records of 110 CKD patients undergoing hemodialysis between February and April 2026. Potential drug–drug interactions were identified using the Medscape Drug Interaction Checker. Data were analyzed descriptively, while the associations between polypharmacy, age, sex, comorbidity status, and pDDIs were evaluated using the Chi-square test or Fisher's Exact Test, with a significance level of $p<0.05$. Polypharmacy was identified in 71.8% of patients, while hyperpolypharmacy occurred in 24.5%. Potential drug–drug interactions were detected in 91.8% of patients, with 387 interaction events identified. Pharmacodynamic interactions accounted for 56.6% of all interactions, and Monitor Closely was the most common severity category (55.6%). Fisher's Exact Test demonstrated a significant association between polypharmacy and pDDIs ($p<0.001$), whereas age ($p=0.159$), sex ($p=1.000$), and comorbidity status ($p=0.222$) were not significantly associated with pDDIs. These findings indicate that increasing medication burden substantially elevates the risk of potential drug–drug interactions in hemodialysis patients, highlighting the importance of routine medication review and clinical pharmacist involvement to optimize pharmacotherapy and improve patient safety.

Keyword: *chronic kidney disease; hemodialysis; polypharmacy; potential drug–drug interactions; medication safety.*

Introduction

Chronic kidney disease (CKD) or Penyakit Ginjal Kronik (PGK) has become a major global public health challenge, with its prevalence increasing steadily over the past decades. According to the Global Burden of Disease Study 2021, more than 850 million people worldwide are affected by CKD, representing a 29% increase since 1990 (Mark et al., 2025) . In Indonesia, CKD also poses a substantial healthcare burden. The Ministry of Health of the Republic of Indonesia reported that the prevalence of CKD reached 3.8% of the population in 2023, corresponding to an estimated 10 million individuals across different stages of the disease (Kementerian Kesehatan Republik Indonesia, 2023) . Progressive deterioration of kidney function

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not only increases the risk of end-stage kidney disease (ESKD) requiring renal replacement therapy such as maintenance hemodialysis, but also contributes to cardiovascular morbidity, mortality, impaired quality of life, and escalating healthcare costs (Stevens et al., 2024) .

Patients with advanced CKD undergoing maintenance hemodialysis commonly present with multiple comorbidities, including hypertension, diabetes mellitus, cardiovascular disease, anemia, and mineral bone disorders. Consequently, these patients require complex pharmacological regimens involving numerous medications to manage both renal complications and accompanying chronic conditions (Al-Khulaifi et al., 2023). Managing these multiple chronic conditions simultaneously results in a heavy pill burden, which intrinsically heightens the risk of unexpected drug responses and prescribing (Chertow et al., 2023). The simultaneous use of multiple medications, commonly defined as polypharmacy, is generally characterized by the use of five or more medications concurrently. Although polypharmacy is often unavoidable in CKD management, it substantially increases the likelihood of medication-related problems, particularly potential drug–drug interactions (pDDIs) (Pramitaningastuti, 2024).

Alterations in renal function significantly affect drug pharmacokinetics and pharmacodynamics, leading to changes in drug absorption, distribution, metabolism, and excretion (Matzke et al., 2011). Because kidney impairment markedly disturbs renal excretion, non-renal clearance pathways, and drug-protein binding capacity, even subtle pharmacokinetic perturbations can significantly escalate systemic drug concentrations and toxicity risks (Verbeeck & Musuamba, 2009). These physiological changes, combined with the extensive use of multiple medications, increase patients' susceptibility to clinically significant drug interactions. Potential drug–drug interactions may reduce therapeutic efficacy, increase adverse drug reactions, prolong hospitalization, and contribute to preventable morbidity and mortality. Therefore, identifying and evaluating pDDIs constitute essential components of pharmaceutical care for patients undergoing hemodialysis.

Several studies have demonstrated the high prevalence of polypharmacy and pDDIs among hemodialysis patients. Hidayangsih et al. (2023) reported that more than 60% of patients with CKD experienced polypharmacy, while approximately 80% of hemodialysis patients received more than five medications. Similarly, Febriyani & Padmasari (2024) found that over half of CKD patients undergoing hemodialysis experienced potential drug–drug interactions with varying levels of clinical severity. Furthermore, a literature review conducted by Galistiani et al. (2025) concluded that polypharmacy is highly prevalent among hemodialysis patients and is frequently associated with moderate-to-major potential drug interactions requiring careful monitoring or therapeutic modification. In addition,

recent clinical evidence confirms that structured medication reconciliation and continuous clinical pharmacist surveillance significantly reduce drug-related problems in maintenance dialysis populations (Rama et al., 2021).

Despite growing evidence regarding polypharmacy and pDDIs in CKD, limited studies in Indonesia have specifically evaluated the association between polypharmacy and the occurrence of potential drug–drug interactions among patients undergoing maintenance hemodialysis while simultaneously considering patient characteristics such as age, sex, and comorbidity status. Understanding this relationship is essential to support rational prescribing practices, optimize medication therapy, and improve patient safety in routine clinical practice.

Therefore, this study aimed to analyze the association between polypharmacy and the occurrence of potential drug–drug interactions among patients with chronic kidney disease undergoing hemodialysis at Hospital X. In addition, the study evaluated whether demographic and clinical characteristics, including age, sex, and comorbidity status, were associated with the occurrence of potential drug–drug interactions. The findings are expected to provide evidence supporting medication review programs, strengthen clinical pharmacy services, and contribute to safer and more effective pharmacotherapy for patients undergoing hemodialysis.

Methods

This analytical observational study employed a retrospective cross-sectional design. Secondary data were collected from the medical records of patients with chronic kidney disease (CKD) undergoing maintenance hemodialysis at Hospital X, between February and April 2026. The study was conducted from February to June 2026.

Patients were selected using a purposive sampling technique based on predefined inclusion and exclusion criteria. Eligible participants were adult patients diagnosed with CKD who underwent maintenance hemodialysis during the study period and had complete medical records, including medication profiles. Patients with incomplete or unreadable medical records or insufficient medication information for drug interaction assessment were excluded. A total of 110 patients met the eligibility criteria and were included in the analysis.

Data collected included demographic characteristics (age and sex), comorbidity status, and prescribed medications. Polypharmacy was defined as the concurrent use of five or more medications, while hyperpolypharmacy was defined as the use of ten or more medications. Potential drug–drug interactions (pDDIs) were identified by reviewing each patient's medication regimen using the Medscape Drug Interaction Checker and were classified according to their mechanism and severity.

Descriptive statistics were used to summarize patient characteristics, medication use, and the prevalence of potential drug–drug interactions. The association between polypharmacy and the occurrence of pDDIs was analyzed using the Chi-square test or Fisher's Exact Test when the assumptions for the Chi-square test were not met. Additional analyses were performed to evaluate the associations of age, sex, and comorbidity status with pDDIs. Statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS), and a p-value of <0.05 was considered statistically significant.

This study was approved by the Health Research Ethics Committee of Hospital X, and all patient information was anonymized to ensure confidentiality throughout the study.

Result and Discussion

This study was conducted at Hospital X, a Type B private hospital in Central Jakarta, Indonesia. Secondary data were obtained from the medical records of patients with chronic kidney disease undergoing maintenance hemodialysis between February and April 2026. Data collection was performed from May to July 2026 and included patient characteristics, comorbidity status, medication profiles, and potential drug–drug interactions, which were identified using the Medscape Drug Interaction Checker.

1.1 Univariate Analysis

A total of 110 patients with chronic kidney disease (CKD) undergoing maintenance hemodialysis at Hospital X met the inclusion criteria and were included in this study. Univariate analysis was performed to describe the demographic and clinical characteristics of the participants, medication use, potential drug–drug interactions (pDDIs), and comorbidity profiles.

Table 1 . Demographic and Clinical Characteristics of the Study Participants

Characteristics		Frequency (n)	Percentage (%)
Age	Adult	72	65.5
	Geriatric	38	34.5
Gender	Male	50	45.5
	Female	60	54.5
Comorbidity Status	With comorbidity	99	90.0
	Without comorbidity	11	10.0
Potential Drug Interactions	Yes	101	91.8
	No	9	8.2
Polypharmacy	Non-polypharmacy (<5 medications)	4	3.6
	Polypharmacy (5–9 medications)	79	71.8
	Hyperpolypharmacy (≥10 medications)	27	24.5

As shown in Table 1, most participants were adults (65.5%), while 34.5% were geriatric patients. Female patients accounted for 54.5% of the study population, slightly exceeding male patients (45.5%). Most patients had at least one comorbidity (90.0%). Potential drug–drug interactions were identified in 91.8% of patients. Regarding medication use, polypharmacy was the most common category (71.8%), followed by hyperpolypharmacy (24.5%), whereas only 3.6% of patients received fewer than five medications.

Table 2. Distribution of Potential Drug–Drug Interactions According to Mechanism and Severity

Characteristics		Frequency (n)	Percentage (%)
Mechanism of Interaction	Pharmacodynamic	219	56.5
	Pharmacokinetic	168	43.4
Severity of Interaction	Minor	140	36.2
	Monitor Closly	215	55.6
Total		387	100.0

A total of 387 potential drug–drug interactions were identified, as presented in Table 2. Pharmacodynamic interactions were more frequent than pharmacokinetic interactions, accounting for 56.6% and 43.4% of all identified interactions, respectively. Based on severity, Monitor Closely interactions represented the largest proportion (55.6%), followed by Minor interactions (36.2%) and Serious–Use Alternative interactions (8.3%).

Table 3. Distribution of Comorbidities Among CKD Patients Undergoing Hemodialysis

Comorbidity	Frequency (n)	Percentage (%)
Hypertension	71	64.5
Anemia	39	35.5
Diabetes Mellitus	20	18.2
Coronary artery disease	11	10.0
Dyslipidemia/Hyperlipidemia	7	6.4
Vertigo	4	3.6
Arteriosclerotic heart disease	4	3.6
Functional dyspepsia	4	3.6
Others	32	29.1
Total	**387**	**100.0**

As shown in Table 3, hypertension was the most prevalent comorbidity, affecting 71 patients (64.5%), followed by anemia (35.5%), diabetes mellitus (18.2%), coronary artery disease (10.0%), and dyslipidemia (6.4%). Other comorbid conditions, including vertigo, arteriosclerotic heart disease, functional dyspepsia, electrolyte disorders, psychiatric disorders, and other less common diseases, were grouped as Others and accounted for 29.1% of the study population.

1.2 Bivariate Analysis

Bivariate analysis was performed to examine the associations between polypharmacy, age, sex, comorbidity status, and the occurrence of potential drug–drug interactions (pDDIs). The Chi-square test was used when the test assumptions were fulfilled; otherwise, Fisher's Exact Test was applied. Statistical significance was defined as a p-value of <0.05.

Table 4. Association Between Polypharmacy and Potential Drug–Drug Interactions

Polypharmacy	pDDIs Present n (%)	pDDIs Absent n (%)	Total n (%)	p-value
Non-polypharmacy	1 (25.0)	3 (75.0)	4 (100.0)	
Polypharmacy	73 (92.4)	6 (7.6)	79 (100.0)	<0.001[a]
Hyperpolypharmacy	27 (100.0)	0 (0.0)	27 (100.0)	
Total	101 (91.8)	9 (8.2)	110 (100.0)	

[a] Fisher's Exact Test.

As shown in Table 4, the majority of patients were classified in the polypharmacy group (71.8%). Potential drug–drug interactions were identified in 73 of 79 patients (92.4%) with polypharmacy and in all patients with hyperpolypharmacy (100.0%). In contrast, only one patient (25.0%) in the non-polypharmacy group experienced a potential drug–drug interaction. Fisher's Exact Test demonstrated a statistically significant association between polypharmacy and the occurrence of potential drug–drug interactions (p<0.001).

Table 5. Association Between Patient Characteristics and Potential Drug–Drug Interactions

Characteristics	pDDIs Present n (%)	pDDIs Absent n (%)	Total n (%)	p-value

Age	Adult	64 (88.9)	8 (11.1)	72 (100.0)	0.159[a]
	Geriatric	37 (97.4)	1 (2.6)	38 (100.0)	
Gender	Male	46 (92.0)	4 (8.0)	50 (100.0)	1.000[a]
	Female	55 (91.7)	5 (8.3)	60 (100.0)	
Comorbidity Status	With comorbidity	92 (92.9)	7 (7.1)	99 (100.0)	
	Without comorbidity	9 (81.8)	2 (18.2)	11 (100.0)	0.222[a]
Total		101 (91.8)	9 (8.2)	110 (100.0)	

[a]Fisher's Exact Test.

As presented in Table 5, no statistically significant associations were observed between age and the occurrence of potential drug–drug interactions (p=0.159), sex and potential drug–drug interactions (p=1.000), or comorbidity status and potential drug–drug interactions (p=0.222). Although the proportion of patients with potential drug–drug interactions was numerically higher among geriatric patients and those with comorbidities, these differences were not statistically significant.

1.3 Discussion of Participants' Characteristics

The present study included 110 patients with chronic kidney disease (CKD) undergoing hemodialysis at Hospital X. Most participants were adults (64.0%), female (54.5%), and had at least one comorbid condition (90.0%). These findings indicate that CKD patients receiving maintenance hemodialysis are predominantly individuals with multiple clinical risk factors requiring comprehensive long-term management.

The predominance of adult patients may reflect the increasing incidence of CKD among the productive-age population. This trend is largely associated with the growing prevalence of hypertension and diabetes mellitus, which are recognized as the leading causes of progressive renal impairment. In addition, lifestyle-related factors, including excessive salt intake, obesity, physical inactivity, smoking, and prolonged use of certain medications, contribute substantially to kidney damage and eventually increase the need for renal replacement therapy such as hemodialysis (Hustrini et al., 2025). Nevertheless, a considerable proportion of participants belonged to the geriatric group, which is consistent with the physiological decline in renal function associated with aging. Age-related reductions in nephron number, glomerular filtration rate, and the kidney's ability to maintain fluid and electrolyte balance increase susceptibility to CKD progression and end-stage kidney disease.

The age distribution observed in this study is consistent with previous reports indicating that most hemodialysis patients are middle-aged or older adults. Carolina et al. (2024) reported that 66.2% of CKD patients undergoing hemodialysis at RSPAL Dr. Ramelan Surabaya were between 40 and 60 years of age. Similar findings have also been reported at Universitas Sebelas Maret Hospital and Haji Jakarta Hospital, where the majority of patients were aged 55–64 years and 56–65 years, respectively. These studies suggest that CKD requiring hemodialysis is increasingly diagnosed among late-adult and early elderly populations, reflecting the cumulative effects of chronic diseases and age-related decline in renal function.

Female patients slightly outnumbered male patients in this study. This finding may be influenced by differences in the demographic characteristics of the study population, healthcare utilization, and regional epidemiological patterns. Hormonal changes following menopause, particularly the reduction in estrogen levels, have been associated with increased oxidative stress, inflammation, and renal fibrosis, potentially accelerating the decline in kidney function among older women (Stevens et al., 2024). Conversely, several studies have reported a higher prevalence of CKD progression among men due to a greater burden of modifiable risk factors, such as smoking, alcohol consumption, uncontrolled hypertension, and metabolic disorders. Therefore, the sex distribution of patients with CKD varies across studies depending on population characteristics and study settings (Ratnasari et al., 2024; Sari, 2025)

The high prevalence of comorbidities observed in this study is consistent with the clinical characteristics of CKD. Hypertension and diabetes mellitus are well-established causes of progressive renal damage leading to end-stage kidney disease and the need for hemodialysis (Stevens et al., 2024). In addition, cardiovascular disease, anemia, mineral and bone disorders, and hyperuricemia frequently coexist with CKD because of persistent deterioration in renal function (DiPiro et al., 2023). The presence of multiple comorbidities often necessitates complex pharmacotherapy, increasing the likelihood of polypharmacy and potential drug-drug interactions (Tatro, 2014). Previous studies have similarly reported that most patients undergoing hemodialysis present with one or more comorbid conditions, with hypertension being the most common (Huri & Ling, 2013; Rahman & Santika, 2022)

Although adults, females, and patients with comorbidities constituted the majority of the study population, these demographic characteristics should primarily be interpreted as reflecting the epidemiological profile of CKD patients receiving hemodialysis rather than independent predictors of potential drug interactions. The occurrence of drug interactions is more directly influenced by treatment complexity, the number of medications prescribed, and the pharmacological characteristics of the drugs used than by demographic

characteristics alone. These findings emphasize that medication review and individualized pharmacotherapy remain essential for all patients undergoing hemodialysis, regardless of age, sex, or comorbidity status.

1.4 Discussion of Potential Drug Interactions

In the present study, 91.8% of patients with chronic kidney disease (CKD) undergoing hemodialysis experienced at least one potential drug interaction, indicating that drug-drug interactions are highly prevalent in this population. This finding reflects the complexity of pharmacotherapy required for CKD management, in which patients commonly receive multiple medications to treat both the primary disease and its associated complications.

The high prevalence of potential drug interactions can be attributed to the extensive use of combination therapy in patients undergoing hemodialysis. CKD patients frequently require antihypertensive agents, antidiabetic medications, diuretics, erythropoiesis-stimulating agents (ESAs), phosphate binders, active vitamin D preparations, iron supplements, and other supportive therapies to manage complications such as anemia, mineral and bone disorders, and cardiovascular diseases. The concurrent administration of multiple medications inevitably increases the probability of drug-drug interactions, which may reduce therapeutic efficacy or increase the risk of adverse drug events (DiPiro et al., 2023).

In addition to polypharmacy, impaired renal function further contributes to the occurrence of potential drug interactions. Progressive deterioration of kidney function alters both pharmacokinetic and pharmacodynamic processes. Reduced glomerular filtration decreases the renal elimination of many drugs, prolongs drug half-life, and increases systemic drug exposure. Furthermore, alterations in protein binding, drug metabolism, and receptor sensitivity may modify therapeutic responses, making CKD patients particularly susceptible to clinically significant drug interactions (Stevens et al., 2024).

The findings of this study are consistent with previous reports. Huri & Ling (2013) found that more than 90% of CKD patients experienced potential drug interactions, largely because of complex medication regimens and the presence of multiple comorbidities requiring long-term pharmacotherapy. Similarly, Souza dos Santos et al. (2018) reported a high prevalence of potential drug interactions among hemodialysis patients, emphasizing that multidrug therapy substantially increases the likelihood of clinically relevant drug-drug interactions and highlights the importance of continuous medication monitoring.

It is important to note that the interactions identified in this study represent potential drug interactions detected using the Medscape Drug Interaction Checker rather than clinically confirmed adverse interactions. Therefore, not all identified interactions will necessarily result in adverse clinical outcomes. The clinical

significance of a drug interaction depends on several factors, including drug dosage, treatment duration, residual renal function, individual patient characteristics, and the quality of therapeutic monitoring. Nevertheless, identifying potential drug interactions remains an essential component of pharmaceutical care because it enables healthcare professionals to anticipate and prevent drug-related problems before they develop into clinically significant events.

From a clinical perspective, routine assessment of potential drug interactions should be incorporated into medication review for patients with CKD undergoing hemodialysis. Clinical pharmacists play a crucial role in reviewing prescriptions, evaluating dose appropriateness according to renal function, identifying potentially harmful drug combinations, and providing evidence-based recommendations to physicians. Interprofessional collaboration among pharmacists, nephrologists, and other healthcare professionals is essential to optimize pharmacotherapy while minimizing preventable adverse drug events.

Overall, the high prevalence of potential drug interactions observed in this study reflects the inevitable consequence of complex pharmacotherapy in patients undergoing maintenance hemodialysis. Although many identified interactions may never manifest clinically, early detection and appropriate monitoring remain fundamental strategies for promoting rational prescribing, improving medication safety, and optimizing therapeutic outcomes in this high-risk patient population.

1.5 Discussion of Mechanisms of Potential Drug Interactions

A total of 387 potential drug interactions were identified among patients with chronic kidney disease (CKD) undergoing hemodialysis. Pharmacodynamic interactions accounted for the majority of cases (219 interactions; 56.6%), whereas pharmacokinetic interactions represented 168 cases (43.4%). These findings indicate that most potential drug interactions in this study resulted from alterations in the pharmacological effects of concomitantly administered medications rather than changes in drug absorption, distribution, metabolism, or excretion.

The predominance of pharmacodynamic interactions is likely attributable to the complex therapeutic regimens commonly prescribed for patients undergoing hemodialysis. Patients with CKD frequently receive multiple medications, including antihypertensive agents, antiplatelet drugs, phosphate binders, vitamin D analogs, erythropoiesis-stimulating agents, iron supplements, and other supportive therapies for CKD-related complications. The concurrent use of medications acting on similar physiological systems may produce additive, synergistic, or antagonistic effects, thereby increasing the likelihood of pharmacodynamic interactions (DiPiro et al., 2023). Furthermore, CKD is associated with profound physiological alterations, including disturbances in fluid and electrolyte balance, anemia, mineral and bone disorders, and cardiovascular

dysfunction, which may modify drug responses and further contribute to pharmacodynamic interactions (Stevens et al., 2024).

Although less frequent, pharmacokinetic interactions also represented a substantial proportion of the identified interactions (43.4%). These interactions occur when one drug alters the absorption, distribution, metabolism, or elimination of another medication, leading to changes in drug exposure. In patients with CKD, impaired renal clearance prolongs the elimination of many drugs and their active metabolites, thereby increasing the risk of drug accumulation and toxicity. Moreover, medications commonly prescribed in hemodialysis patients, such as phosphate binders, calcium supplements, and iron preparations, may interfere with the gastrointestinal absorption of other drugs, emphasizing the importance of appropriate dosing schedules and dosage adjustments based on renal function (DiPiro et al., 2023).

The present findings are consistent with those reported by Huri & Ling (2013), who demonstrated that pharmacodynamic interactions were the most frequently identified mechanism among patients with CKD receiving multiple medications. Similarly, Patel et al. (2020) reported that pharmacodynamic interactions predominated in hemodialysis patients because of the extensive use of combination therapies targeting overlapping physiological pathways. These studies highlight the importance of identifying interaction mechanisms to facilitate appropriate clinical monitoring and reduce the risk of adverse drug events.

Despite the predominance of pharmacodynamic interactions, pharmacokinetic interactions should not be underestimated because they may significantly affect drug concentrations, therapeutic efficacy, and patient safety. Consequently, healthcare professionals should consider both pharmacodynamic and pharmacokinetic mechanisms when designing treatment regimens for patients with CKD undergoing hemodialysis. Regular evaluation of medication regimens, individualized dose adjustment according to renal function, and continuous clinical monitoring are essential to optimize therapeutic outcomes while minimizing the risk of drug-related complications.

Overall, the findings of this study demonstrate that pharmacodynamic interactions constitute the predominant mechanism of potential drug interactions among patients with CKD undergoing hemodialysis. This predominance reflects the complexity of multidrug therapy required to manage CKD and its associated comorbidities. Therefore, routine medication review and careful monitoring of patients' clinical responses remain fundamental strategies for improving medication safety and optimizing pharmacotherapy in this high-risk population.

1.6 Discussion of Severity of Potential Drug–Drug Interactions

Among the 387 potential drug–drug interactions (pDDIs) identified in this study, most were classified as Monitor Closely (215 interactions; 55.6%), followed by Minor interactions (140 interactions; 36.2%) and Serious (Use Alternative) interactions (32 interactions; 8.3%). These findings indicate that although potential drug interactions were highly prevalent among patients with chronic kidney disease (CKD) undergoing hemodialysis, the majority required close clinical monitoring rather than immediate discontinuation or replacement of therapy.

The predominance of the Monitor Closely category reflects the complexity of pharmacotherapy in CKD patients receiving hemodialysis. These patients commonly require multiple medications, including antihypertensive agents, antidiabetic drugs, phosphate binders, erythropoiesis-stimulating agents (ESAs), vitamin D analogs, iron supplements, and cardiovascular medications. Many of these drug combinations are clinically necessary despite having the potential to interact. Therefore, careful monitoring of clinical response, laboratory parameters, and adverse drug reactions is essential to ensure that the therapeutic benefits outweigh the associated risks(DiPiro et al., 2023). Furthermore, impaired renal function alters drug clearance and pharmacodynamic responses, increasing patients' susceptibility to adverse outcomes even when interactions are categorized as moderate (Stevens et al., 2024).

Minor interactions represented more than one-third of all identified pDDIs. Although these interactions generally have limited clinical significance and rarely require therapeutic modification, they should not be overlooked in patients with CKD. The cumulative effect of multiple minor interactions, particularly in individuals receiving long-term polypharmacy, may influence treatment outcomes and contribute to medication-related problems. Consequently, continuous medication review remains important to optimize pharmacotherapy and maintain patient safety (DiPiro et al., 2023).

In contrast, Serious (Use Alternative) interactions accounted for only 8.3% of the identified pDDIs. These interactions have a greater potential to compromise treatment effectiveness or cause serious adverse effects and therefore should ideally be avoided or managed using safer therapeutic alternatives. However, in nephrology practice, some high-risk drug combinations may be unavoidable because of limited therapeutic options and the complex clinical conditions of patients undergoing hemodialysis. In such situations, individualized risk–benefit assessment, dose adjustment, and intensive clinical monitoring are required to minimize adverse outcomes.

The present findings are consistent with those reported by Huri & Ling (2013), who found that most potential drug interactions among CKD patients belonged to the monitoring category, whereas serious interactions occurred less

frequently. They emphasized that many interacting drug combinations remain clinically appropriate provided that adequate monitoring is implemented throughout treatment. Similarly, Kheshti et al. (2016) reported that moderate interactions requiring clinical monitoring were the most common category among patients with CKD. The authors attributed this finding to the complexity of treatment regimens in CKD, where several potentially interacting medications are indispensable for managing multiple comorbidities and disease-related complications.

It is important to recognize that the severity classifications reported in this study were generated using the Medscape Drug Interaction Checker and therefore represent potential rather than clinically manifested drug interactions. The actual clinical consequences of these interactions depend on several patient-specific factors, including renal function, medication dosage, treatment duration, comorbidities, and the quality of therapeutic monitoring. Consequently, not all identified interactions will result in adverse clinical outcomes.

From a clinical pharmacy perspective, these findings highlight the importance of comprehensive medication review and ongoing monitoring in patients with CKD undergoing hemodialysis. Pharmacists play a critical role in identifying clinically relevant drug interactions, recommending dose adjustments or alternative therapies when appropriate, and collaborating with physicians to optimize medication safety. Routine monitoring of clinical symptoms, laboratory findings, and treatment response is particularly important for patients receiving complex multidrug regimens.

Overall, this study demonstrates that although potential drug–drug interactions are highly prevalent among patients undergoing hemodialysis, most belong to the Monitor Closely category and can be managed effectively through appropriate clinical surveillance. Strengthening pharmaceutical care services, particularly medication review and therapeutic drug monitoring, may help reduce medication-related problems while improving the safety and effectiveness of pharmacotherapy in patients with chronic kidney disease.

1.7 Association Between Patient Characteristics, Polypharmacy, and Potential Drug–Drug Interactions

The present study demonstrated that polypharmacy was the only variable significantly associated with potential drug–drug interactions (pDDIs) among patients with chronic kidney disease (CKD) undergoing hemodialysis. Fisher's Exact Test revealed a statistically significant association between polypharmacy and pDDIs ($p < 0.001$). Patients receiving polypharmacy accounted for the largest proportion of the study population (71.8%), of whom 92.4% experienced at least one potential drug interaction. Furthermore, all patients classified as having

hyperpolypharmacy experienced pDDIs, whereas only one of four patients without polypharmacy presented with potential interactions. These findings indicate that the likelihood of drug interactions increases as the number of prescribed medications increases.

The observed association is pharmacologically plausible because each additional medication increases the number of possible drug pairs capable of interacting through pharmacokinetic or pharmacodynamic mechanisms. In patients with CKD, pharmacotherapy is inherently complex because treatment aims not only to slow disease progression but also to manage multiple complications, including hypertension, diabetes mellitus, anemia, mineral and bone disorders, cardiovascular disease, and other comorbidities requiring multidrug therapy (DiPiro et al., 2023). In addition, reduced renal function alters drug absorption, distribution, metabolism, and particularly excretion, thereby increasing drug accumulation and the risk of clinically relevant interactions (Stevens et al., 2024).

The present findings are consistent with those reported by Hustrini et al. (2025), who identified the number of prescribed medications as a significant predictor of potential drug interactions in patients with CKD. Similarly, Maher et al. (2014) reported that polypharmacy is a major contributor to adverse drug events, drug interactions, medication non-adherence, and hospitalizations among patients with chronic diseases. Payne et al. (2014) further emphasized that although polypharmacy increases the risk of drug-related problems, it is often clinically appropriate in patients with multiple chronic conditions. Therefore, the primary concern should not be the number of medications itself but rather ensuring that each medication has a clear clinical indication and that the overall regimen remains rational and safe.

The high prevalence of polypharmacy and hyperpolypharmacy observed in this study likely reflects appropriate polypharmacy, as patients undergoing hemodialysis commonly require antihypertensive agents, iron supplements, folic acid, vitamin B complex, active vitamin D, phosphate binders, antiplatelet agents, and medications for associated comorbidities. Although these medications are clinically necessary, combining multiple therapies inevitably increases the probability of potential drug interactions. This finding underscores the importance of comprehensive medication review, particularly in patients receiving complex multidrug regimens. Pharmacists play an essential role in evaluating renal dose adjustments, identifying potential interactions using tools such as the Medscape Drug Interaction Checker, and collaborating with physicians to optimize medication safety.

In contrast, age, sex, and comorbidity status were not significantly associated with potential drug interactions in this study. Although geriatric patients demonstrated a higher proportion of pDDIs than adult patients (97.4% vs. 88.9%),

the association was not statistically significant (p = 0.159). Age-related physiological changes, including reduced renal function and altered pharmacokinetic and pharmacodynamic processes, may increase susceptibility to drug interactions in older adults. Nevertheless, these changes alone were insufficient to establish age as an independent predictor of pDDIs in the present study. Similar findings were reported byHidayangsih et al. (2023), who found no significant association between age and potential drug interactions among CKD patients.

Likewise, sex was not significantly associated with pDDIs (p = 1.000), with comparable proportions of potential interactions observed in male and female patients. This finding suggests that drug interaction risk is primarily determined by medication-related factors, including the number and type of prescribed drugs, rather than biological sex. This result agrees with the findings of Febriyani & Padmasari (2024), who also reported no significant relationship between sex and potential drug interactions among patients undergoing hemodialysis.

Similarly, no statistically significant association was found between comorbidity status and pDDIs (p = 0.222), although patients with comorbid conditions exhibited a higher proportion of potential interactions than those without comorbidities. Patients with multiple chronic conditions generally require more complex pharmacotherapy, thereby increasing opportunities for drug interactions. However, the present findings suggest that the presence of comorbidities alone does not independently predict pDDIs. Instead, the risk appears to be more closely related to the number and combination of medications prescribed. This interpretation is supported by Galistiani et al. (2025), who concluded that while comorbidities contribute to treatment complexity, medication burden remains the principal determinant of potential drug interactions.

Overall, these findings indicate that polypharmacy is the strongest determinant of potential drug–drug interactions among patients with CKD undergoing hemodialysis, whereas demographic characteristics and comorbidity status do not independently influence interaction risk. These results highlight the importance of routine medication review, individualized pharmacotherapy, and multidisciplinary collaboration to minimize drug-related problems while maintaining optimal therapeutic outcomes.

Conclusion

This study demonstrated that adult patients, females, individuals with comorbidities, and those receiving polypharmacy constituted the majority of patients with chronic kidney disease (CKD) undergoing hemodialysis at Hospital X. Potential drug–drug interactions (pDDIs) were highly prevalent, affecting 91.8% of patients. Pharmacodynamic interactions were the most frequently identified mechanism, while the majority of pDDIs were classified as Monitor Closely,

indicating that most interacting drug combinations can be managed safely through appropriate clinical monitoring rather than discontinuation of therapy.

A statistically significant association was observed between polypharmacy and the occurrence of potential drug–drug interactions (p = 0.001). Patients receiving a greater number of medications, particularly those with hyperpolypharmacy, had a substantially higher likelihood of experiencing pDDIs. These findings emphasize that medication burden is a major determinant of interaction risk in patients undergoing hemodialysis.

Overall, the study highlights the importance of routine medication review, renal dose adjustment, and multidisciplinary collaboration involving pharmacists and physicians to identify and manage potential drug–drug interactions. Implementing these strategies may improve medication safety, optimize therapeutic outcomes, and reduce drug-related problems in patients with chronic kidney disease receiving hemodialysis.

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