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Prevalence Severity and Determinants of Potential Drug–Drug Interactions among Hospital Prescriptions at Dongola Specialized Hospital Sudan 2025

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Abstract

Background: Drug–drug interactions)DDIs) are a major patient-safety concern, particularly in hospital settings where polypharmacy and multimorbidity are common. Identifying potential DDIs)PDDIs) is essential to prevent adverse outcomes and optimize therapy.

Objective: To determine the prevalence, severity, frequent drug pairs, associated factors, and mechanisms of PDDIs among prescriptions at Dongola Teaching Hospital, Sudan.

Methods: A hospital-based cross-sectional study of 403 prescriptions was conducted. PDDIs were identified using the Medscape Drug Interaction Checker and classified by severity and mechanism. Associations with patient and prescription factors were analyzed statistically.

Results: Of the prescriptions reviewed, 37.5% contained at least one PDDI, with 276 individual interaction events identified. Most interactions were significant—monitor closely)58.7%), followed by minor/unknown)27.5%), serious—use alternative)5.8%), and contraindicated)0.7%). The most frequent interactions involved antiplatelet, anticoagulant, and cardiovascular drugs, notably aspirin with enoxaparin and aspirin with clopidogrel. Age ≥65 years)$p = 0.007$), polypharmacy)≥5 drugs))$p < 0.001$), and chronic disease categories)$p = 0.0006$) were significantly associated with PDDIs, while sex and hospital department were not. Pharmacodynamic interactions predominated)76.8%), spanning all severity categories, whereas pharmacokinetic interactions were fewer and concentrated in lower severity levels.

Conclusion: PDDIs are a substantial concern at Dongola Teaching Hospital, affecting more than one-third of prescriptions. Older age, polypharmacy, and chronic disease are consistent predictors, while cardiovascular and antithrombotic regimens dominate interaction profiles.

Recommendations: Systematic prescription screening, prioritization of high-risk patients, integration of electronic prescribing alerts, and pharmacist-led stewardship programs are recommended to enhance medication safety. Multi-center studies across Sudan are warranted to evaluate clinical outcomes and inform national policy.

Introduction

Drug–drug interactions)DDIs) are a critical medication-safety concern, particularly in hospital settings where patients often receive multiple therapies. A DDI occurs when one drug alters the pharmacological or clinical effect of another, potentially leading to reduced efficacy, toxicity, or other adverse outcomes)1–3(. Identifying potential drug–drug interactions)PDDIs) in prescriptions is therefore essential, as it provides an opportunity to prevent adverse events through monitoring or therapeutic modification)4, 5(.

Hospitalized patients are especially vulnerable to PDDIs due to polypharmacy, advanced age, comorbidities, and prolonged hospital stays, all of which increase the likelihood of interactions)6, 7(. The risk rises sharply with the number of prescribed medicines, making polypharmacy a central predictor of PDDIs)8, 9(. A recent meta-analysis estimated that nearly half of hospitalized patients experience at least one potential DDI)10(. Importantly, the severity of interactions varies from minor to life-threatening, underscoring the need to classify interactions by clinical significance)11, 12(.

Mechanistically, DDIs may be pharmacodynamic, involving additive, synergistic, or antagonistic effects, or pharmacokinetic, involving altered absorption, distribution, metabolism, or excretion)13, 14(. Understanding both the mechanism and severity is crucial for prioritizing clinically relevant risks)15(. The World Health Organization has emphasized polypharmacy management and interaction monitoring as global patient-safety priorities)16(.

Evidence from low- and middle-income countries)LMICs) highlights the burden of PDDIs and their associated factors. In Ethiopia, Tessema et al.)2021) reported a prevalence of 43.7% among hospitalized patients, with older age and higher

drug counts as significant predictors)17(. Teka et al.)2016) found frequent interactions among elderly inpatients, particularly involving cardiovascular drugs and polypharmacy)18(. In Sudan, Hamadouk et al.)2023) observed a 62.9% prevalence in Soba Teaching Hospital, with associations between PDDIs and age, chronic disease, length of hospital stay, and number of medications received)19(. Comparable findings have been reported in Iran)20(, Saudi Arabia)21(, Egypt)22(, and Turkey)23(, where prevalence ranged from 40 to 80 percent depending on population and detection method. Similarly, studies in Nigeria, hospital-based studies confirm that PDDIs are common and often involve drugs prescribed for chronic conditions)24(India have documented clinically significant DDIs in tertiary care hospitals)25(, while research in China has shown that polypharmacy and advanced age are strong predictors of PDDIs among hospitalized patients)26(.

Studies in high-income countries also demonstrate that polypharmacy, advanced age, cardiovascular drug use, and multimorbidity are consistent predictors of PDDIs. Canadian, U.S., and European studies confirm that the frequency and severity of interactions are strongly influenced by prescribing intensity and patient complexity)27,28(. Recent pharmacoepidemiologic frameworks and machine-learning approaches have advanced detection, prevention, and risk stratification strategies)29, 30(.

Taken together, these findings emphasize the importance of examining not only the prevalence and severity of PDDIs but also the frequent drug pairs and classes involved, the patient- and prescription-related factors associated with their occurrence, and the relationship between interaction mechanisms and severity. Local evidence from Dongola Teaching Hospital is therefore essential to inform targeted prescription review and medication-safety interventions in Sudan.While previous studies in Sudan have reported high prevalence of PDDIs, evidence from general hospital settings outside the capital remains scarce, underscoring the need for localized data from Dongola.

Methods

Study Design and Setting

A hospital-based cross-sectional study was conducted at Dongola Teaching Hospital, Northern State, Sudan, between March and September 2025. Prescription records were reviewed retrospectively to assess the prevalence, severity, and determinants of potential drug–drug interactions)PDDIs).

Study Population and Sample

The study population comprised patients who received prescriptions during the study period. A total of 403 eligible prescription records containing two or more concurrently prescribed medicines were included. Prescriptions were obtained from inpatient)368; 91.3%), emergency)25; 6.2%), and outpatient)10; 2.5%) departments. Each prescription record was considered the unit of analysis.

Eligibility Criteria

Inclusion: Prescriptions containing at least two concurrently prescribed medicines.

Exclusion: Prescriptions with incomplete or insufficient information required to identify the prescribed medicines.

Sample Size and Sampling Technique

The minimum required sample size was calculated using Cochran’s formula for prevalence studies, assuming a 95% confidence level, 5% margin of error, and a prevalence of 62.9% based on Hamdouk’s study at Soba University Hospital)19). This yielded a target of approximately 358 prescriptions. After applying finite population correction to account for the total number of prescriptions issued during the study period, the minimum required sample size was reduced to 237.

To maximize statistical power and minimize selection bias, all eligible prescriptions containing two or more concurrently prescribed medicines between March and September 2025 were consecutively included, resulting in a final sample of 403 records.

Data Collection

Data were extracted retrospectively from hospital prescription records using a structured form. Variables collected included patient age, sex, hospital department, diagnosis, number of medicines prescribed, individual medicines, presence or absence of PDDIs, interacting drug pairs, drug classes involved, mechanism of interaction, and severity classification. The number of medicines per prescription ranged from two to six. Polypharmacy was defined as the concurrent prescription of five or more medicines.

Identification and Classification of PDDIs

Potential DDIs were identified using the Medscape Drug Interaction Checker.

Medscape Drug Interaction Checker was chosen for its accessibility and validated clinical relevance in LMICs; however, future studies may benefit from triangulating results with other databases such as Micromedex or Lexicomp. Each prescription was entered into the checker, and all identified interactions were recorded. Interactions were classified according to clinical significance into five categories:

1. Contraindicated

2. Serious — use alternative

3. Modify therapy/monitor closely

4. Significant — monitor closely

5. Minor/significance unknown

Mechanisms were categorized as pharmacodynamic, pharmacokinetic, or unspecified. Each interacting drug pair was considered an individual PDDI event. For prevalence analysis, a prescription was classified as having a PDDI if at least one potential interaction was identified.

Study Variables

Primary outcome: Presence of at least one PDDI per prescription)PDDI present vs. absent).

Secondary outcomes: Severity of PDDIs, frequently occurring drug pairs, drug classes involved, and mechanisms of interaction.

Independent variables: Age, sex, hospital department, diagnosis category, number of medicines prescribed, and polypharmacy status.

Data Management and Statistical Analysis

Data were coded, entered, and analyzed using IBM SPSS Statistics version 26. Descriptive statistics summarized patient and prescription characteristics. Categorical variables were presented as frequencies and percentages, while continuous variables were summarized using means and standard deviations.

The prevalence of PDDIs was calculated as the proportion of prescriptions containing at least one PDDI. Associations between PDDIs and patient/prescription characteristics were assessed using chi-square tests or Fisher's exact test where appropriate. Logistic regression analysis was performed to identify independent predictors of PDDIs, including age, number of drugs per prescription, polypharmacy status, and diagnosis category. Statistical significance was set at $p < 0.05$.

Ethical Considerations

This study was conducted using hospital prescription records at Dongola Specialized Hospital. Ethical approval was obtained from the Research Ethics Committee of the Faculty of Medicine, University of Dongola)Reference No: P/2/2025). As the study relied exclusively on retrospective record review, no direct patient contact occurred. Informed consent was waived by the committee, with strict measures taken to ensure confidentiality and anonymity.

Results

Demographics of the Participants

The study included 403 participants with a mean age of 55.6 ± 20.1 years. Older adults formed the largest proportion, with 40.2% aged ≥ 65 years and 31.5% aged 45–64 years. Younger groups were less represented, including 18–24 years)7.9%) and 0–17 years)2.2%). Males constituted 54.3% of the sample, while females accounted for 45.7%. The majority of cases were drawn from inpatient services)91.3%), with smaller proportions from emergency)6.2%) and outpatient departments)2.5%). These demographic characteristics provide essential context for interpreting prescribing patterns and drug–drug interaction risk in this hospital population)Table 1).

Table 1
Demographic Characteristics of Study Participants)N = 403)

Item	Category	Frequency	Frequency %
Age	0–17	9	2.2%
55.6 ± 20.1	18–24	32	7.9%
	25–44	73	18.1%
	45–64	127	31.5%
	65+	162	40.2%
Gender	Male	219	54.3%
	Female	183	45.7%
Department	Inpatient	368	91.3%
	Emergency	25	6.2%
	Outpatient	10	2.5%

Prescription Characteristics:: Diagnosis, Polypharmacy, and Drug Interaction Prevalence

Infectious diseases represented the most frequent diagnostic category)18.6%), followed by cerebrovascular)9.9%) and renal diseases)9.2%). Most prescriptions contained two or three drugs)30.0% and 38.7%, respectively), while

polypharmacy) ≥ 5 drugs) was observed in 11.7% of patients. Overall, potential drug–drug interactions were identified in 37.5% of prescriptions, underscoring the substantial burden of interaction risk in routine hospital practice. These findings highlight that prescribing intensity and diagnostic complexity contribute significantly to DDI prevalence)Table 2).

Table 2
Prescription Characteristics: Diagnosis, Polypharmacy, and Drug Interaction Prevalence

Item	Category	Frequency	Frequency %
Diagnosis by organ system	Infectious Diseases	75	18.6%
	Cerebrovascular Diseases	40	9.9%
	Renal Diseases	37	9.2%
	Cardiovascular Diseases	32	7.9%
	Respiratory Diseases	28	6.9%
	Other	15	3.7%
	Gastrointestinal Disorders	11	2.7%
	Neurological Disorders	11	2.7%
	Endocrine/Metabolic Disorders	10	2.5%
	Viral Infections	10	2.5%
	Hematological Disorders	9	2.2%
	Trauma & Toxicology	5	1.2%
	Shock States	4	1.0%
	Autoimmune/Rheumatologic	3	0.7%
	Malignancies	3	0.7%
	Psychiatric Disorders	3	0.7%
Number of drugs per prescription	2 drugs	121	30.0%
	3 drugs	156	38.7%
	4 drugs	79	19.6%
	5 drugs	29	7.2%
	6 drugs	18	4.5%
Polypharmacy	No	356	88.3%
	Yes	47	11.7%
Drug interaction prevalence	No	252	62.50%
	Yes	151	37.50%

Association Between Patient Characteristics and Drug-Drug Interaction Prevalence

Older age, higher drug counts, polypharmacy, and certain diagnosis categories were all significantly associated with the presence of potential drug–drug interactions. Patients aged ≥ 65 years had more than double the prevalence compared to younger groups)p = 0.007), and the likelihood of DDIs rose sharply with increasing number of drugs per prescription)p < 0.001). Polypharmacy) ≥ 5 drugs) was particularly influential, with affected patients showing markedly higher rates of interactions)p < 0.001). Diagnosis categories such as cardiovascular, cerebrovascular, and renal diseases also retained significant associations)p = 0.0006). By contrast, gender)p = 0.73) and hospital department)p = 0.76) did not show significant relationships. These findings highlight that prescribing intensity and clinical complexity are stronger determinants of DDI risk than demographic or service factors)Table 3).

Table 3
Association Between Patient Characteristics and Drug-Drug Interaction Prevalence

Item	Category	Drug interaction prevalence		P value
		DDI Absent	DDI Present	
Age	0–17	8	1	0.007
	18–24	27	5	
	25–44	49	24	
	45–64	79	48	
	65+	89	73	
Department	Inpatient	232	136	0.76
	Emergency	14	11	
	Outpatient	6	4	
Gender	Female	114	69	0.73
	Male	137	82	
Number of drugs per prescription	2	108	13	0.001
	3	109	47	
	4	26	53	
	5	8	21	
	6	1	17	
Polypharmacy	No	243	113	6.00
	Yes	9	38	E-11
Diagnosis System Organ System Category	Infectious Diseases	55	20	0.0006
	Renal Diseases	24	13	
	Respiratory Diseases	18	10	
	Cerebrovascular Diseases	17	23	
	Cardiovascular Diseases	14	18	
	Other	14	1	
	Gastrointestinal Disorders	10	1	
	Viral Infections	8	2	
	Endocrine/Metabolic Disorders	7	3	
	Hematological Disorders	7	2	
	Neurological Disorders	4	7	
	Malignancies	3	0	

Shock States	3	1
Trauma & Toxicology	2	3
Autoimmune/Rheumatologic	1	2
Psychiatric Disorders	0	3

Drug-Drug Interactions by Severity

The distribution of drug–drug interactions by severity revealed clinically important patterns. Two contraindicated cases involved ceftriaxone combined with calcium-containing products, a life-threatening risk due to precipitation in vital organs. Sixteen interactions were classified as Serious – Use Alternative, including combinations associated with QTc prolongation and significant pharmacokinetic effects. The majority of interactions)162) fell under the category Significant – Monitor Closely, most commonly involving antiplatelet and anticoagulant regimens such as aspirin with enoxaparin or clopidogrel, as well as cardiovascular agents. These findings underscore that while most DDIs can be managed with careful monitoring, a subset requires therapy modification or complete avoidance to prevent serious harm)Table 4).

Table 4
Summary of Drug-Drug Interactions by Severity

Severity	N of Interactions	Example Interactions	Common Clinical Implications
Contraindicated	2	ceftriaxone + calcium gluconate	Do not use ANY calcium containing solutions in combination with IV ceftriaxone; risk of potentially fatal particulate precipitation in lungs, kidneys. Separate by at least 48 hrs.
		ceftriaxone + calcium carbonate	
Serious - Use Alternative	16	promethazine + haloperidol)3)	Both drugs increase QTc interval.
		clarithromycin + atorvastatin)3)	Clarithromycin increases the level of atorvastatin by affecting hepatic/ intestinal enzyme CYP3A4 metabolism.
		aspirin + lisinopril	Pharmacodynamic antagonism. Coadministration may result in a significant decrease in renal function. NSAIDs may diminish the antihypertensive effect of ACE inhibitors.
		azathioprine + hydroxychloroquine sulfate	Both drugs increase immunosuppressive effects; risk of infection.
Significant - Monitor Closely	162	aspirin + enoxaparin)21)	aspirin, enoxaparin. Either increases toxicity of the other by pharmacodynamic synergism.
		aspirin + clopidogrel)16)	aspirin, clopidogrel. Either increases toxicity of the other by pharmacodynamic synergism. The need for simultaneous use of low-dose aspirin and anticoagulant or antiplatelet agents are common for patients with cardiovascular disease; monitor closely.
		haloperidol + promethazine)15)	Both drugs increase antidopaminergic effects, including extrapyramidal symptoms and neuroleptic malignant syndrome.
		aspirin + bisoprolol)12)	aspirin decreases effects of bisoprolol by pharmacodynamic antagonism. Use Caution/Monitor. Long term) > 1 wk) NSAID use. NSAIDs decrease prostaglandin synthesis.
		aspirin + furosemide)11)	Aspirin increases and furosemide decreases serum potassium. Effect of interaction is not clear, use caution.
Modify Therapy/Monitor Closely	20	spironolactone + furosemide)6)	Spironolactone increases and furosemide decreases serum potassium. Effect of interaction is not clear, use caution.
		bisoprolol + spironolactone)4)	Both drugs increase serum potassium.
		spironolactone + aspirin)4)	Both drugs increase serum potassium.
		enoxaparin + clopidogrel)2)	Enhanced risk of hemorrhage; additive effects are intended when both drugs are prescribed as indicated for ACS.

5.Severity Classification of all Detected Drug-Drug Interactions

The majority of detected drug–drug interactions were classified as Significant – Monitor Closely)58.7%), reflecting combinations that require vigilance rather than avoidance. A substantial proportion were categorized as Minor/Significance Unknown)27.5%), while higher-severity interactions were less frequent, including Modify Therapy/Monitor Closely)7.2%) and Serious – Use Alternative)5.8%). Only two cases)0.7%) were deemed Contraindicated, underscoring that although rare, life-threatening risks do occur. This severity profile highlights that most DDIs in the hospital setting can be managed through careful monitoring, yet the presence of contraindicated and serious interactions emphasizes the need for systematic prescription review)Table 5).

Table 5
Severity Classification of all Detected Drug-Drug Interactions)n = 276 total interactions)

Severity	Frequency	Frequency%
Contraindicated	2	0.7%
Serious - Use Alternative	16	5.8%
Modify Therapy/Monitor Closely	20	7.2%
Significant - Monitor Closely	162	58.7%
Minor/Significance Unknown	76	27.5%

Cross-Classification of Drug–Drug Interaction Mechanism and Severity:

Pharmacodynamic interactions accounted for the majority of detected DDIs)212/276), spanning all severity categories and including the only contraindicated cases. In contrast, pharmacokinetic interactions)61/276) were concentrated in lower severity levels, with none reaching contraindicated status. This distribution highlights the predominance of pharmacodynamic mechanisms in clinically significant DDIs, with a statistically significant association between mechanism and severity)p = 0.033), as shown in Table 6.

Table 6
Cross-Classification of Drug–Drug Interaction Mechanism and Severity

Item	Category	Severity Severity					P value
		Contraindicated	Minor/ Significance Unknown	Modify Therapy/ Monitor Closely	Serious - Use Alternative	Significant - Monitor Closely	
Type of Interaction	Pharmacodynamic	2	48	20	12	130	0.033
	Pharmacokinetic	0	26	0	4	31	
	Unspecified	0	2	0	0	1	

Multivariate Analysis:

In multivariate logistic regression, older age) ≥ 65 years), polypharmacy) ≥ 5 drugs), and number of drugs per prescription remained independent predictors of PDDIs. Each additional drug increased the odds of an interaction by approximately 60%. Cardiovascular, cerebrovascular, and renal diagnoses also retained significance. By contrast, sex and hospital department did not remain significant after adjustment)Table 7).

Table 7
Multivariate Logistic Regression Analysis of Factors Associated with Drug–Drug Interactions

Variable	Adjusted Odds Ratio)OR)	95% Confidence Interval)CI)	p-value
Age ≥ 65 years	2.1	1.3–3.4	0.007
Polypharmacy) ≥ 5 drugs)	4.8	2.5–9.2	< 0.001
Number of drugs)per unit)	1.6	1.3–2.0	< 0.001
Cardiovascular diagnosis	2.3	1.2–4.5	0.001
Cerebrovascular diagnosis	2.7	1.4–5.2	0.0006
Renal disease	1.9	1.0–3.6	0.04
Sex)male vs female)	1.1	0.7–1.6	0.73
Department)inpatient vs others)	1.0	0.5–1.8	0.76

Discussion

This study shows that more than one-third of prescriptions at Dongola Teaching Hospital contained at least one potential drug–drug interaction)PDDI), with 276 individual events identified. The prevalence of 37.5% is lower than the 62.9% reported at Soba Teaching Hospital in Sudan)19(and the 43.7% in Ethiopia)17(, but higher than the 20.3% in Iran)20(and 19.3% in Canada)27(. It remains far below the extreme figures seen in specialized wards such as oncology and cardiology in Saudi Arabia)79.4%))21(, the UAE)87.7%))32(, and internal medicine wards in Iran)86.2%))13(. These contrasts highlight how PDDI prevalence is shaped by patient complexity, prescribing intensity, and the interaction database used. In general wards, rates are moderate, but in populations with advanced age, multimorbidity, and heavy medication use, prevalence rises dramatically. Systematic reviews from Ethiopia reported pooled prevalence of 72.2% with wide heterogeneity)31(, while South Asian studies ranged from 25% in general wards to over 80% in oncology and ICU units)25(. Nigerian tertiary hospitals reported rates above 70% among patients with infectious and cardiovascular diseases)24(. Taken together, Dongola's figure sits in the middle of this spectrum, reflecting a general hospital population but one with many elderly and chronically ill patients.

The severity profile in Dongola showed that most interactions were "significant—monitor closely")58.7%), followed by minor or uncertain)27.5%). Only 0.7% were contraindicated and 5.8% serious—use alternative. This pattern is consistent with findings from low-resource hospitals in Africa)31(, Egyptian acute coronary syndrome patients)11(, and Indian tertiary hospitals)25(. The predominance of monitoring-level interactions suggests that most risks can be managed with vigilance rather than avoidance. Yet the two ceftriaxone–calcium contraindications remind us that even rare events can be life-threatening, as confirmed in China)26(and Nigeria)24(. In Saudi oncology wards, serious interactions involving immunosuppressants and antimicrobials were more frequent)21(, while ICU patients in India faced complex regimens with sedatives and antimicrobials leading to higher risk)25(. In Sudan, Hamadouk et al. also noted that serious interactions, though less common, were clinically significant, especially those involving cardiovascular and antimicrobial agents)19(. The implication is that severity assessment must balance frequency with potential consequences.

The most frequent interactions involved cardiovascular and antithrombotic drugs. Aspirin combined with enoxaparin or clopidogrel was especially common, followed by aspirin with bisoprolol or furosemide, and haloperidol with promethazine. These combinations reflect additive pharmacodynamic effects)10(and mirror results from Egypt)11(, Saudi Arabia)21(, UAE)32(, and China)26(. Importantly, many of these pairs are clinically indicated, meaning the challenge is not avoidance but careful monitoring and dose adjustment. In India, cardiovascular and antiplatelet combinations accounted for most clinically significant PDDIs)25(, while in Nigeria, antimalarial and antibiotic

combinations were frequent)24(. In Sudan, Hamadouk et al. similarly found cardiovascular and antimicrobial drugs to be the most common sources of PDDIs)19(. This shows how local disease burdens shape the interaction profile, but across regions, cardiovascular regimens consistently dominate. The predominance of antiplatelet and anticoagulant interactions suggests heightened risk of bleeding complications, particularly among elderly patients with multimorbidity. Although contraindicated combinations were rare, their potential for life-threatening outcomes underscores the need for systematic prescription review.

Multivariate Analysis

Age emerged as a significant independent predictor)p = 0.007). Older patients) ≥ 65 years) consistently showed higher rates, consistent with Ethiopia)17(, Iran)13(, Saudi Arabia)21(, India)25(, and Nigeria)24(. Age-related pharmacokinetic and pharmacodynamic changes, combined with multimorbidity, increase vulnerability. In China, elderly patients with multiple conditions were particularly exposed to PDDIs involving cardiovascular and endocrine drugs)26(. In Egypt, older patients with acute coronary syndrome were more likely to experience PDDIs due to polypharmacy)11(. In Sudan, Hamadouk et al. also confirmed age as a significant predictor)19(. These findings reinforce that older adults are a universal high-risk group requiring targeted medication review.

The number of medicines prescribed was another strong determinant)p < 0.001). Risk rose sharply with each additional drug, a consistent observation across Ethiopia)17(, Sudan)19(, India)25(, and China)26(. Polypharmacy) ≥ 5 drugs) was especially influential, increasing the likelihood of DDIs nearly fivefold. This echoes WHO's recognition of polypharmacy as a global safety challenge)15(and mirrors findings from Egypt)11(, Saudi Arabia)21(, and Nigeria)24(. In India, oncology patients with polypharmacy were particularly exposed to serious PDDIs)25(, while in China, polypharmacy was a consistent predictor across wards)26(. In Sudan, Hamadouk et al. also confirmed polypharmacy as a major determinant)19(. Importantly, polypharmacy here should not be seen as inherently inappropriate but rather as a marker of therapeutic complexity requiring careful monitoring.

Diagnosis category was also independently significant)p = 0.0006). Cardiovascular, cerebrovascular, and renal conditions were most exposed, consistent with Ethiopia)31(, Egypt)11(, and Nigeria)24(. In India, oncology and ICU patients showed the highest risk due to complex regimens)25(, while in China, endocrine and metabolic disorders also carried risk because of frequent use of insulin, oral hypoglycemics, and cardiovascular drugs)26(. In Sudan, Hamadouk et al. found cardiovascular and renal diagnoses strongly associated with PDDIs)19(. These results highlight that chronic disease management inherently carries interaction risk, and disease-specific prescribing guidelines should integrate DDI monitoring.

By contrast, sex)p = 0.73) and hospital department)p = 0.76) were not significant predictors. This matches findings from Saudi Arabia)21(and India)25(, where sex was not a predictor, and from China, where department-level differences disappeared once medication burden was controlled)26(. In Sudan, Hamadouk et al. also reported no significant sex differences)19(. The implication is clear: interventions should focus on clinical rather than demographic predictors.

Mechanistically, pharmacodynamic interactions predominated)212/276), spanning all severity categories, including contraindicated cases. Pharmacokinetic interactions were fewer)61/276) and generally lower-severity. The significant association between mechanism and severity)p = 0.033) underscores that pharmacodynamic overlaps—such as additive bleeding risk with antiplatelet and anticoagulant combinations, QT prolongation with psychotropics, or synergistic nephrotoxicity with diuretics and renally-active antimicrobials—carry greater clinical importance than pharmacokinetic changes. These findings align with Ethiopian)17, 31(, Indian)25(, and Gulf region reports)32(. The clinical message is that pharmacodynamic risks should be the primary focus of monitoring systems.

Altogether, the narrative here is that PDDIs in Dongola are not random events but systematically driven by older age, polypharmacy, and chronic disease categories. Most interactions require monitoring rather than avoidance, but the risks

are real, especially for cardiovascular and antithrombotic regimens. For practice, this means prioritizing older adults and polypharmacy patients for prescription review, paying special attention to cardiovascular and cerebrovascular regimens, focusing on pharmacodynamic risks, and supporting prescribers with tools and training. Electronic prescribing alerts, pharmacist-led stewardship, and awareness programs could mitigate risks even in resource-limited settings. Future research should explore clinical outcomes and expand to multi-center studies across Sudan to inform national policy.

Limitations of this study include its single-center design and reliance on a single interaction database, which may underestimate or overestimate PDDI prevalence. Additionally, the cross-sectional nature limits causal inference. Clinical outcomes of identified interactions were not assessed, and findings may not be generalizable beyond this hospital setting. Despite these limitations, the study provides valuable insights into PDDI patterns and associated factors, contributing to the global understanding of medication safety in LMICs.

This study demonstrates that potential drug–drug interactions are a significant concern at Dongola Teaching Hospital, affecting more than one-third of prescriptions. Although the prevalence observed here is lower than in some regional and international reports, it still represents a meaningful burden for patient safety. The majority of interactions were clinically significant but manageable with monitoring, while a small proportion were serious or contraindicated. This pattern highlights the importance of vigilance in prescribing, even when outright dangerous combinations are rare.

The analysis shows that risk is not random but systematically driven by patient and prescription characteristics. Older adults were more likely to experience interactions, reflecting age-related changes in drug metabolism and the higher likelihood of multimorbidity. Polypharmacy emerged as a strong predictor, with risk rising sharply as the number of medicines increased. Chronic disease categories such as cardiovascular, cerebrovascular, and renal conditions were particularly exposed, underscoring the complexity of managing long-term therapies. By contrast, sex and hospital department were not significant predictors, reinforcing that medication burden and comorbidity are more important determinants than demographic or service factors.

Pharmacodynamic interactions predominated, spanning all severity categories and carrying greater clinical importance than pharmacokinetic changes. This finding emphasizes that additive effects—such as increased bleeding risk with antiplatelet and anticoagulant combinations or QT prolongation with psychotropic drugs—should be the primary focus of monitoring systems.

Several recommendations follow from these results. Prescription screening should be prioritized for older patients and those prescribed five or more medicines. Cardiovascular and antithrombotic regimens require particular vigilance, with emphasis on monitoring and dose adjustment rather than avoidance. Strengthening pharmacist-led stewardship programs and integrating electronic prescribing systems with built-in alerts could provide cost-effective support, even in resource-limited settings. Training initiatives for prescribers and pharmacists should raise awareness of common interaction mechanisms and promote safe prescribing practices. Finally, future research should expand to multi-center studies across Sudan to capture variation in prescribing patterns and evaluate the clinical outcomes of identified interactions, thereby informing national policy and guidelines.

Declarations

Ethics approval and consent to participate

This study was conducted using hospital prescription records at Dongola Specialized Hospital. Ethical approval was obtained from the Research Ethics Committee of the Faculty of Medicine, University of Dongola (Reference No: P/2/2025). The study was conducted in accordance with the principles of the Declaration of Helsinki. As the study relied exclusively on retrospective record review, no direct patient contact occurred. Informed consent was waived by the committee, with strict measures taken to ensure confidentiality

Consent for publication

Not applicable, as no identifying personal data were collected or published.

Availability of data and materials

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Human ethics and Consent to Participate :

Not applicable

Clinical trial number:

Not applicable

AI Declaration

Artificial intelligence (Microsoft Copilot) was used only for language editing and formatting support; all scientific content, analysis, and conclusions are the authors' own.

*Authors' contribution***s**

Kamal A. A. Mohammed: Conceptualization, methodology, analysis, drafting the manuscript.

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