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Exploring potential drug-drug interactions in discharge prescriptions: ChatGPT's effectiveness in assessing those interactions

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ABSTRACT

Background: Potential drug-drug interactions (pDDIs) pose substantial risks in clinical practice, leading to increased morbidity, mortality, and healthcare costs. Tools like Micromedex drug-drug interaction checker are commonly used to screen for pDDIs, yet emerging AI models, such as ChatGPT, offer the potential for supplementary pDDI prediction. However, the accuracy and reliability of these AI tools in a clinical context remain largely untested.

Objective: This study evaluates pDDIs in discharge prescriptions for medical ward patients and assesses ChatGPT-4.0's effectiveness in predicting these interactions compared to Micromedex drug-drug interaction checker.

Method: A cross-sectional study was conducted over three months with 301 discharged patients. pDDIs were identified using Micromedex drug-drug interaction checker, detailing each interaction's occurrence, severity, onset, and documentation. ChatGPT-4.0 predictions were then analyzed against Micromedex data. Binary logistic regression analysis was applied to assess the influence of predictor variables in the occurrence of pDDIs.

Results: 1551 drugs were prescribed to 301 patients, averaging 5.15 per patient. pDDIs were detected in 60.13 % of patients, averaging 3.17 pDDIs per patient, ChatGPT-4.0 accurately identified pDDIs (100 % for occurrence) but had limited accuracy for severity (37.3 %) and moderate accuracy for onset (65.2 %). The most frequent major interaction was between Cefuroxime Axetil and Pantoprazole Sodium. Polypharmacy significantly increased the risk of pDDIs (OR: 3.960, $p < 0.001$).

Conclusion: pDDIs are prevalent in internal medicine discharge prescriptions, with polypharmacy heightening the risk. While ChatGPT 4.0 accurately identifies pDDI occurrence, its limitations in predicting severity, onset, and documentation underscore healthcare professionals' need for careful oversight.

1. Introduction

In managing various diseases and comorbid conditions, the concurrent use of two or more medications is often necessary. However, when multiple drugs are administered simultaneously, there is always a potential for pharmacokinetic or pharmacodynamic interactions, where the drugs may alter each other's effects.[1] Potential drug-drug interactions (pDDIs) are defined as "a clinical response to the administration of drug combinations that is different from the expected effects of the individual agents when administered alone".[2]

Inpatients who are discharged from the hospital are in the healing stage and are prescribed various drugs for the treatment of the disease. Patients discharged from the medicine ward are more prone to polypharmacy because of comorbid conditions, constant change of dose regimen, and the critical nature of their disease; this heightened the risk of pDDI.[3,4] In hospitalized patients, the risk of potentially interacting drug combinations may further escalate due to the frequent addition of new medications to their existing treatment regimen.[3] Patients discharged from these wards face an increased risk of pDDIs due to complex medication changes during the transition from hospital to home, often without sufficient monitoring or follow-up.[3,4] Therefore, anticipating pDDIs is critical for ensuring patient safety and effective treatment post-discharge. Drug-drug interactions (DDIs) is the major cause of drug therapy problems leading to adverse drug events (ADR) and increases the risk of treatment failure, hospitalization, higher healthcare costs, and even morbidity and mortality.[5–8] Fortunately, considerable portions of ADR caused by DDI are preventable through early detection through drug-drug interactions screening software and clinical judgment of

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healthcare teams, including clinical pharmacists.[8,9]

The prevalence of potential drug-drug interactions (pDDIs) in developing countries remains significantly high, with hospital-based studies reporting rates between 23 % and 86 % in countries such as Uganda, Ethiopia, Pakistan, and Iran.[10] Further research indicates that 2.2 % to 65 % of hospitalized patients are susceptible to one or more pDDIs, while 41.1 % to 69.7 % face the risk of interacting drug combinations upon discharge.[8] Notably, a study from Nepal found an even higher prevalence, with 78.3 % of hospital discharge prescriptions involving pDDIs.[4]

Implementing computerized screening like Micromedex drug-drug interactions checker is the most effective way of identifying pDDIs since identifying and addressing DDIs can be difficult for pharmacist interns, newly licensed professionals, and even some experienced pharmacists because of the large number of interacting pairs.[11] The Micromedex Drug-Drug Interaction Checker is a comprehensive, evidence-based tool that helps healthcare professionals identify and assess potential drug interactions, providing severity ratings and actionable recommendations.[12] Previous studies have demonstrated that the Micromedex drug interaction checker outperformed other interaction checkers in completeness and consistency of pDDI information, resulting in superior sensitivity and specificity.[12,13] Not only the occurrence of interactions but also their severity, onset, and documentation are very crucial in making clinical decisions of their clinical significance and assessing patient harm. Severity denotes the magnitude of the interaction outcome; onset signifies the time the interacting effect occurs, and documentation denotes reliability, quantity and nature of documentation. Micromedex categorizes drug interactions based on the quality of documentation into four levels: excellent, good, fair and not specified. Interactions are classified as “excellent” when supported by controlled clinical trials, “good” when based on less rigorous studies, and “fair” when evidence is limited or insufficient.[13,14] Micromedex drug interaction checker can provide all these crucial pieces of information, which helps in informed decision-making. This program combines a user-friendly interface, regular updates, and seamless electronic health record integration for real-time, high-sensitivity detection of pDDIs, making it a top choice among pDDIs screening tools.[15] However, it requires a paid subscription, may generate excessive minor alerts, sometimes misses true positive pharmacodynamic interactions and can be overwhelming for non-professionals.[11,16] The subscription cost of the Micromedex interaction checker poses a significant barrier to its use in developing countries like Nepal, where limited budgets and low resources predominate in most hospitals.[17] Additionally, it may not account for patient-specific factors and does not consider the dosing of drugs and also requires internet access, making it less accessible in remote areas.[16] Despite these limitations, it is a highly valuable resource for informed clinical decision-making.

Since the advent of ChatGPT, various AI models such as Gemini, Microsoft Copilot, Claude, Scite, SciSpace, Paperpal, Jenni AI, Yomu AI, and CoWriter AI have been developed to perform specialized tasks. For example, Scite, SciSpace, Paperpal, Jenni AI, and CoWriter AI are specifically designed and optimized for tasks like writing research papers and extracting high-quality information from the scientific literature. In contrast, ChatGPT stands out for its versatility, widespread recognition, and accessibility as a free tool. ChatGPT in drug-drug interaction prediction represents an innovative application of artificial intelligence in healthcare. By leveraging natural language processing and large datasets, ChatGPT can assist healthcare professionals in identifying potential drug interactions more efficiently.[18] It has the potential to complement traditional drug interaction tools by analyzing vast amounts of medical literature, clinical guidelines, and real-world data to provide insights and predictions. Although not a substitute for dedicated clinical databases like Micromedex drug-drug interaction checker, ChatGPT can enhance decision-making by providing explanations, simplifying complex interactions, and offering suggestions for further investigation.[19] This integration of AI could help streamline the detection of drug interactions and improve patient safety in clinical settings. Using ChatGPT for drug-drug interaction prediction is fast and user-friendly, offering insights from vast medical data. It can supplement traditional tools but lacks real-time updates and clinical validation, which may lead to inaccuracies in complex cases.[20] Over-reliance without consulting specialized databases could pose risks in critical healthcare decisions.

Few studies have evaluated the efficacy of ChatGPT in predicting potential drug-drug interactions (pDDIs).[18,19] These studies relied on previously published pDDI literature and used an earlier, less advanced version of ChatGPT. However, they had notable limitations, including the inability to comprehensively evaluate critical parameters such as severity, onset, and documentation. Prior research on pDDIs in Nepal, often limited to specific drug groups and combined with studies on prescription errors, has relied on free interaction checkers with low sensitivity and specificity, resulting in a less comprehensive exploration of pDDIs.[21,22] To date, no research has utilized real-world interacting drug pairs to assess the advanced models of ChatGPT 4.0 ‘s predictive capabilities, particularly in key areas such as interaction severity, onset, and supporting documentation. This gap in knowledge leaves healthcare professionals uncertain about whether ChatGPT can be reliably used for pDDIs prediction, especially in terms of these critical factors. Therefore, this study aims to investigate real-world pDDIs in hospital discharge patients from a medical ward using the Micromedex interaction checker and assess the effectiveness of ChatGPT 4.0 in predicting these interactions, including their severity, onset, and documentation.

2. Method

2.1. Ethics approval

The Institutional Review Committee of Purbanchal University School of Health Sciences (PUSHS-IRC Ref. No.: 031) granted the study's ethical approval. Authorization for data collection at the hospital was secured from the hospital board (Koshi Hospital Ref. No.: 2196). Participation was entirely voluntary, and written informed consent was obtained from the patients prior to the initiation of data collection.

2.2. Study design, sample size, and selection criteria

A cross-sectional study was conducted upon the discharge of patients from the General Medicine Ward at Koshi Hospital in Biratnagar, Nepal, between January 2024 and April 2024. Koshi Hospital is a government-managed tertiary care facility with 350 beds, offering specialized services in areas such as Medicine, Pediatrics, Psychiatry, Radiology, and Dermatology, among others. The hospital serves approximately 1000 to 1200 patients daily across its various departments.[23] The sample size for the study was determined using a prevalence-based calculation,[24] targeting a 95 % confidence interval and a 5 % margin of error. Based on previous research showing a 78.3 % prevalence of pDDI,[4] the estimated sample size was 262 participants. A consecutive sampling method was applied to select eligible participants. The inclusion criteria for the study were hospitalized inpatients of any age and gender who provided informed consent, were prescribed two or more medications upon discharge, and received a confirmed diagnosis. Exclusion criteria included patients who declined to participate, those who left against medical advice, mortality cases, and patients who were transferred without a discharge prescription or prescribed only topical medications (e.g., creams, eye drops, ointments, sprays). Ultimately, 301 patients met the inclusion criteria and were included in the analysis.

2.3. Procedure

A clinical pharmacist conducted daily visits to the hospital's medicine department to collect discharge summaries of patients. Patients were discharged after the physician conducted ward rounds in the day time, mostly at 11 AM. After the physician wrote discharge summaries

with dose regimens, we screened the discharge summaries for inclusion criteria, including criteria of two or more drugs prescribed. Patients whose discharge summaries met the inclusion criteria were enrolled in the study after obtaining their consent. The primary source of data was the patient discharge summaries, which provided sociodemographic details, diagnoses, and discharge drug regimens. Medicines were prescribed using their brand names; however, their generic names, doses, and frequencies were documented. This information was systematically recorded in a specially designed patient profile form. Most of the prescribed drugs were oral dosage forms except a few, like insulin, which is subcutaneous. Since the Micromedex Drug Interaction Checker[14] operates exclusively with the generic names of drugs and does not account for dosage or frequency, these parameters were excluded from the analysis conducted using this tool. Therefore, the clinical relevance of potential drug-drug interactions (pDDIs) was not assessed in this study. Each patient's discharge medications in generic names were then entered into the Micromedex drug interaction checker[14] to identify interacting drug pairs, along with their severity, onset, and documentation. Nutraceuticals and topical preparations, such as creams and lotions, were excluded from the Micromedex drug interaction analysis.

This study used ChatGPT advanced model 4.0[25] to evaluate previously detected interacting pairs by the Micromedex drug interaction checker.[14] To assess the accuracy of ChatGPT[25] in predicting potential drug-drug interactions (pDDIs), the identified interacting drug pairs by Micromedex drug interaction checker[14] were also evaluated using ChatGPT 4.0[25] with the following standardized prompt to ensure consistent and reliable results:

"Determine if a potential drug-drug interaction (pDDIs) occurs between [Drug interacting pairs identified by Micromedex interaction checker, e.g., Cefuroxime Axetil and Pantoprazole Sodium] by responding 'Yes' or 'No.' If 'Yes,' also specify:

- Severity (choose from: Contraindicated, Major, Moderate, Minor).
- Onset (choose from: Rapid, Delayed, Not Specified).
- Documentation quality (choose from: Excellent, Good, Fair, Not Specified)."

In order to make the procedure comparable with the Micromedex interaction checker,[14] only the generic names of the medicine were entered in ChatGPT 4.0.[25]

The responses generated by ChatGPT 4.0[25] were then compared to the results from Micromedex[14] to evaluate the model's accuracy in predicting drug interactions, including their severity, onset, and documentation quality.

2.4. Data analysis

The recorded data for pDDIs were entered into Excel and imported into SPSS V.27 software, and descriptive analyses were performed to analyze the data. The results were presented in frequency and percentage for categorical data and mean for continuous variables. Univariate and multivariate Binary logistic regression analysis was used to determine the influence of predictor variables on the occurrence of pDDI. A confidence interval of 95 % and p-value <0.05 was considered significant. Those significant variables at $p < 0.05$ in univariate analysis were incorporated in multivariate logistic regression mode to assess the influence of multiple predictors.

3. Results

A total of 476 diseases were diagnosed in 301 patients, resulting in an average of 1.58 diseases per patient (±0.8). The number of diagnosed diseases per patient ranged from a minimum of 1 to a maximum of 5. Table 1 classifies diseases according to ICD-11, with the highest percentage of diagnoses in "Diseases of the respiratory system" (26.05 %) and the lowest in "Neoplasms" and "Symptoms, signs or clinical findings, not elsewhere classified" (0.63 % each). The majority of participants (58.1 %) were diagnosed with a single disease, while only a small fraction (0.3 %) had five diagnoses.

Table 1
International Classification of Diseases 11th Revision (ICD 11) level one classification of diagnosed disease.

ICD 11 level one classification of diagnosed disease	Frequency	Percentage (%)
Certain infectious or parasitic diseases	21	4.41 %
Diseases of the blood or blood-forming organs	7	1.47 %
Diseases of the circulatory system	85	17.86 %
Diseases of the digestive system	39	8.19 %
Diseases of the genitourinary system	76	15.97 %
Diseases of the nervous system	17	3.57 %
Diseases of the respiratory system	124	26.05 %
Endocrine, nutritional or metabolic diseases	89	18.70 %
Extension Codes	5	1.05 %
Mental, behavioural or neurodevelopmental disorders	7	1.47 %
Neoplasms	3	0.63 %
Symptoms, signs or clinical findings, not elsewhere classified	3	0.63 %
Total	**476**	**100.00 %**

A total of 1551 drugs were prescribed to 301 patients, resulting in an average of 5.15 drugs per patient (±2.13). The maximum number of drugs prescribed to a single patient was 12. Table 2 presents the classification of drugs prescribed at discharge according to the Anatomical Therapeutic Chemical (ATC) system. The most frequently prescribed drugs fall under "Alimentary tract and metabolism" (32.62 %), while the least prescribed are "Antiparasitic products, insecticides, and repellents" (0.64 %).

A total of 574 drug interactions were identified in 181 out of 301 patients, resulting in a prevalence of 60.13 %. The average number of potential drug-drug interactions (pDDIs) per patient was 3.17 (±2.66), with a maximum of 14 pDDIs observed in one patient.

The results of the potential drug-drug interactions (pDDIs) as assessed by the Micromedex Drug Interaction Checker are summarized in Table 3. Among the potential drug-drug interactions (pDDIs), only one interaction (0.2 %) was classified as contraindicated in terms of severity, while a significant portion, 55.6 %, was classified as major. Regarding onset, 7.1 % of interactions were identified as having a rapid onset. For documentation quality, only a small fraction (4.4 %) of interactions had "excellent" documentation.

The effectiveness of ChatGPT-4.0 in predicting potential drug-drug interactions (pDDIs) that were identified by the Micromedex interaction checker is summarized in Table 4 as follows: 100 % for occurrence, 37.3 % for severity, 65.2 % for onset, and 20.6 % for documentation quality.

Table 5 presents the top twenty contraindicated and major severity

Table 2
Level one ATC classification of drugs prescribed at discharge.

Level one ATC classification	ATC Code	Frequency	Percentage
Alimentary tract and metabolism	A	506	32.62 %
Blood and blood forming organs	B	146	9.41 %
Cardiovascular system	C	296	19.08 %
Genito urinary system and sex hormones	G	16	1.03 %
Systemic hormonal preparations, excl. Sex hormones and insulins	H	29	1.87 %
Antiinfectives for systemic use	J	259	16.70 %
Musculo-skeletal system	M	13	0.84 %
Nervous system	N	44	2.84 %
Antiparasitic products, insecticides and repellents	P	10	0.64 %
Respiratory system	R	219	14.12 %
Various	V	13	0.84 %
Total		**1551**	**100.00 %**

Table 3
Severity, onset, and documentation of pDDI as per micromedex drug interaction checker.

Variables	Category	Frequency	Percentage (%)
Severity	Contraindicated	1	0.2
	Major	319	55.6
	Moderate	215	37.5
	Minor	39	6.8
Onset	Rapid	41	7.1
	Delayed	128	22.3
	Not Specified	405	70.6
Documentation	Excellent	25	4.4
	Good	125	21.8
	Fair	422	73.5
	Not Specified	2	0.3

Table 4
Effectiveness of ChatGPT 4.o in predicting pDDI parameters.

Variables	Correct		Incorrect	
	Frequency	Percentage	Frequency	Percentage
Occurrence	574	100	0	0
Severity	214	37.3	360	62.7
Onset	374	65.2	200	34.8
Documentation	118	20.6	456	79.4

drug interaction pairs. Only one contraindicated pair of Flavoxate Hydrochloride and Potassium Citrate was found, which can cause gastrointestinal irritation. Cefuroxime Axetil and Pantoprazole Sodium was the most frequent major interaction pair (8.4 %), with decreased cefuroxime exposure as a probable effect.

Table 6 showed that the prevalence and risk of pDDI were significantly higher in female patients, patients over the age of 65, patients with comorbid conditions, and patients taking five or more drugs ($p < 0.05$). Furthermore, multivariate binary logistic regression analysis indicated that polypharmacy (taking five or more drugs) was a significant predictor of pDDI, with an adjusted odds ratio of 3.960 (2.265-6.924) at p-value <0.001.

4. Discussion

This study reveals a significant prevalence of potential drug-drug interactions (pDDIs) in discharge prescriptions, with 60.13 % of patients experiencing at least one pDDI. Diseases of the respiratory system were the most commonly diagnosed conditions in our study, largely due to a high proportion of elderly patients with chronic obstructive pulmonary disease (COPD), community-acquired pneumonia (CAP), and asthma during the study period. This finding contrasts with a study conducted in Switzerland, where cardiovascular diseases predominated among discharged inpatients.[3] Such variations underscore the influence of geographic location on disease patterns and healthcare needs.

Despite respiratory diseases being the most prevalent, the majority of prescribed drugs belonged to the "Alimentary Tract and Metabolism" category according to the Anatomical Therapeutic Chemical (ATC) classification. This suggests a considerable use of medications related to gastrointestinal and metabolic functions in discharged patients. On average, patients were prescribed 5.15 ± 2.13 drugs, aligning with

Table 5
Top 20 contraindicated and major severity pair of potential drug-drug interactions.

Major category Interacting Drugs	Frequency	Percent	Onset	Documentation	Probable Clinical effect
Flavoxate Hydrochloride: Potassium Citrate (Contraindicated)	1	0.2	Not Specified	Fair	Gastrointestinal irritation
Cefuroxime Axetil: Pantoprazole Sodium	27	8.4	Not Specified	Fair	Decreased cefuroxime exposure
Aspirin: Spironolactone	15	4.7	Not Specified	Good	Reduced diuretic effectiveness, hyperkalemia, or nephrotoxicity
Aspirin: Furosemide	13	4.1	Not Specified	Fair	Risk of salicylate toxicity, reduced diuretic effectiveness and possible nephrotoxicity
Cefuroxime Axetil: Rabeprazole Sodium	13	4.1	Not Specified	Fair	Decreased cefuroxime exposure
Insulin Glargine, Recombinant: Metformin Hydrochloride	13	4.1	Not Specified	Fair	Risk of hypoglycemia
Metformin Hydrochloride: Sitagliptin Phosphate	11	3.4	Not Specified	Fair	Risk of hypoglycemia
Aspirin: Torsemide	10	3.1	Not Specified	Good	Reduced diuretic effectiveness and possible nephrotoxicity
Isoniazid: Rifampin	10	3.1	Delayed	Good	Risk of hepatotoxicity
Pyrazinamide: Rifampin	10	3.1	Delayed	Good	Severe hepatic injury
Insulin Glargine, Recombinant: Linagliptin	9	2.8	Not Specified	Fair	Risk of hypoglycemia
Furosemide: Losartan Potassium	8	2.5	Not Specified	Fair	Severe hypotension and deterioration in renal function, including renal failure
Insulin Glargine, Recombinant: Sitagliptin Phosphate	8	2.5	Not Specified	Fair	Risk of hypoglycemia
Aspirin: Fluticasone Propionate	7	2.2	Not Specified	Fair	Risk of salicylism subsequent to withdrawal of corticosteroids.
Cefuroxime Axetil: Ranitidine Hydrochloride	7	2.2	Not Specified	Fair	Decreased cefuroxime exposure
Furosemide: Levothyroxine Sodium	6	1.9	Not Specified	Fair	Increased risk of free thyroid hormones, followed by an overall decrease in total thyroid hormone levels
Budesonide: Ranitidine Hydrochloride	5	1.6	Not Specified	Good	Increased budesonide exposure
Furosemide: Telmisartan	5	1.6	Not Specified	Fair	Severe hypotension and deterioration in renal function, including renal failure
Insulin Glargine, Recombinant: Linagliptin	5	1.6	Not Specified	Fair	Increased risk of hypoglycemia.
Levofloxacin: Prednisolone	5	1.6	Delayed	Excellent	Increased risk of tendon rupture.
Formoterol Fumarate: Torsemide	4	1.3	Not Specified	Fair	Increased risk of ECG changes or hypokalemia.

Table 6
Results of univariate and multivariate binary logistic regression analysis between selected predictor variables with pDDI.

Variables	Category	pDDI		COR (95 % CI)	*P*-value	AOR (95 % CI)	P-value
		Yes ($n = 181$)	No ($n = 120$)				
Gender	Female	109 (60.2 %)	52 (43.3 %)	1.98 (1.24–3.161)	0.004*	1.632(0.983-2.710)	0.058
	Male	72 (39.8 %)	68 (56.7 %)	1			
Age Group	>65	97 (53.6 %)	50 (41.7 %)	1.617 (1.015–2.576)	0.043*	1.170 (0.696–1.967)	0.555
	≤65	84 (46.4 %)	70 (58.3 %)	1		1	
Comorbidities	≥1	150 (82.9 %)	74 (61.7 %)	3.008 (1.764–5.130)	<0.001*	1.499 (0.802–2.801)	0.205
	0	31 (17.1 %)	46 (38.3 %)	1		1	
No of Drug	≥5	134 (74 %)	43 (35.8 %)	5.105 (3.098–8.414)	<0.001*	3.960 (2.265–6.924)	<0.001*
	<5	47 (26 %)	77 (64.2 %)	1			

AOR: Adjusted odds ratio; COR: Crude odds ratio; CI: Confidence Interval.
* Shows significant at p-value < 0.05.

findings from a Nepalese study where the average number of prescribed drugs was 6.2 ± 2.7.[4] This consistent pattern highlights the issue of polypharmacy, which elevates the risk of pDDIs and emphasizes the importance of careful medication management, especially at discharge.[26]

The average number of pDDIs per patient was 3.17, which is somewhat lower than the 5.08 ± 3.89 reported in a similar Nepalese study,[4] yet still substantial. This discrepancy may reflect differences in study settings, population characteristics, or prescribing practices. While the high prevalence of pDDIs suggests a potential for adverse effects, not all interactions necessarily lead to harm. The clinical significance of pDDIs depends on patient-specific factors, including physiological, biochemical, and disease characteristics.[8,11] Although interaction-checking software provides essential guidance, healthcare professionals should use these tools as aids rather than absolute indicators. Determining the clinical relevance of pDDIs requires a multidisciplinary approach, especially involving clinical pharmacists who can assess patient-specific factors such as sociodemographics, disease profile, and drug administration duration.[27]

Our study also revealed that major-severity pDDIs represented the highest proportion of interactions, unlike a previous study in Nepal where moderate-severity interactions predominated.[4] Major-severity pDDIs are more likely to result in patient harm, underscoring the need for vigilant monitoring by healthcare providers. A contraindicated interaction between Flavoxate Hydrochloride and Potassium Citrate was identified, a combination that poses a risk of gastrointestinal irritation due to Flavoxate's ulcerogenic effect.[28] Additionally, the most frequent major interaction involved Cefuroxime Axetil and proton pump inhibitors (PPIs). Since PPIs reduce gastric acidity, they may decrease Cefuroxime's bioavailability, suggesting that these drugs should not be co-administered without careful consideration.[28]

In assessing the effectiveness of ChatGPT-4.0 in identifying pDDIs, our study found that the advanced AI model could accurately detect the occurrence of interactions of drug-interacting pairs identified by the Micromedex interaction checker. However, ChatGPT's performance was less reliable in predicting critical parameters such as severity, onset, and documentation quality. These parameters are essential for clinical decision-making; for example, minor pDDIs may not necessitate therapeutic changes, as they are unlikely to cause harm and could sometimes even be beneficial, as in the case of probenecid with penicillin.[1] Prior studies have highlighted ChatGPT-3.5's low sensitivity in identifying DDIs,[20] and our findings indicate that, while ChatGPT-4.0 shows improvement, it still has limitations in accurately assessing the severity, onset, and documentation quality of pDDIs. This underscores the need for further optimization of AI models to support clinical decision-making effectively.

Furthermore, our study supports the well-established association between polypharmacy and pDDIs. Patients prescribed more than four medications were significantly more likely to experience pDDIs, consistent with prior research linking multiple medications with increased risks of drug interactions and adverse effects.[29] A study by Bamagous et al. (2023) revealed that 97.2 % of elderly patients were on polypharmacy, and 85.3 % of them experienced at least one pDDI.[30] Viktil et al. found a linear relationship between polypharmacy and drug-related problems (DRPs), with drug-drug interactions (DDIs) being a major contributing factor. Their study revealed that each additional medication resulted in an 8.6 % increase in the number of DRPs, highlighting the significant role of DDIs in this association.[31] Rigorous studies have established the fact that polypharmacy is the major cause of DDIs, leading to higher rates of Adverse drug reactions, higher healthcare costs, and medication noncompliance.[1] Additionally, our analysis identified advanced age, comorbid conditions, and female gender as significant factors associated with pDDIs. Treating comorbid conditions often necessitates complex medication regimens, increasing the likelihood of pDDIs.[32] Elderly patients are particularly susceptible due to physiological changes, weakened immune systems, and altered pharmacokinetic and pharmacodynamic profiles, which frequently result in polypharmacy and a higher risk of pDDIs.[33,34] Female patients also exhibit a higher susceptibility, likely due to a combination of physiological, metabolic, hormonal, and sociocultural factors.[35] This finding aligns with research by Jazbar et al., which found higher rates of DDIs among women and individuals aged 65 and above.[8]

4.1. Strengths and limitations

Our study benefits from several strengths that enhance its relevance and impact. With an adequate sample size and the use of consecutive sampling, the study captures a comprehensive view of pDDIs occurring over a three-month period, providing a robust representation of clinical practice. Additionally, it leverages real-world interacting pairs to assess the advanced model ChatGPT-4.0's effectiveness in predicting clinically relevant pDDIs, offering valuable insights into AI's potential in healthcare. Beyond merely identifying interactions, the study also delves into critical factors like severity, onset, and documentation quality, which are essential for informed clinical decision-making. However, certain limitations exist in our study. One major limitation is that we only analyzed interacting pairs detected by the Micromedex interaction checker when evaluating ChatGPT-4.0's effectiveness. This approach, while efficient for true positives, does not account for the possibility of false positives that may arise if all possible combinations of prescribed medications for individual patients were analyzed in ChatGPT. Likewise, conducting the study within a single hospital setting may limit the generalizability of findings to other healthcare environments with varying prescribing patterns. Moreover, while the study identifies potential interactions, it does not measure their clinical relevance or outcomes in individual patients, leaving the true impact of pDDIs on patient health unassessed. Additionally, the study does not account for interactions between drugs and herbal or nutraceutical products, which could be significant in a real-world, holistic assessment of patient safety.

5. Conclusion

This study highlights the prevalence and potential risks of drug-drug interactions (pDDIs) in discharge prescriptions, emphasizing the need for vigilant medication management during the hospital-to-home transition. The findings reveal a notable presence of major-severity interactions, underscoring the importance of careful monitoring and the role of clinical judgment in assessing patient-specific factors. ChatGPT-4.0 demonstrated high accuracy in identifying pDDI occurrences but showed limitations in assessing critical parameters like severity, onset, and documentation quality. While the advanced model of ChatGPT holds promise as an adjunct tool, it is not a substitute for specialized interaction checkers like Micromedex drug-drug interaction checker, especially for critical decision-making. Future advancements in AI could further enhance its application, but healthcare providers must continue to rely on established databases and clinical expertise to ensure patient safety. This research provides a foundation for optimizing AI-assisted tools in clinical practice, particularly in settings prone to polypharmacy and complex medication regimens.

Impacts on practice

- Implementing drug interaction screening software for all discharge prescriptions, with clinical pharmacists and the healthcare team reviewing and communicating clinically relevant interactions to prescribing physicians, can improve patient safety and optimize medication management.
- While ChatGPT effectively identifies potential drug-drug interactions, its limited accuracy in predicting parameters like severity and onset means it cannot be solely relied upon. Clinical pharmacists should verify pDDIs through established sources and interaction-checking software to ensure reliable and safe decision-making in patient care.

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CRediT authorship contribution statement

Rahi Bikram Thapa: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Subash Karki:** Writing – review & editing, Investigation, Formal analysis, Conceptualization. **Sabin Shrestha:** Writing – review & editing, Investigation, Formal analysis.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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