Impact of Clinical Decision Support Software on the Prevalence of Drug-Drug Interactions in an Emergency Ward: A Quasi-Experimental Before-and-After Study

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Abstract

Background: Drug interactions present significant challenges in emergency departments due to the diverse patient population and the complexity of medical conditions. These interactions threaten patient safety and increase healthcare costs. Strategies such as Clinical Decision Support Systems (CDSS) and audit-and-feedback mechanisms are essential for alerting physicians to potential medication risks.

Methods: A quasi-experimental before-and-after study was conducted in the emergency department of Ghaem Hospital in Mashhad. Phase 1 (June–August 2024) retrospectively analyzed drug interactions for 482 patients using Lexidrug 2024. To ensure comparability and minimize ascertainment bias, the Phase 1 analysis was restricted to interactions involving the 150 most commonly used medications in the emergency ward, which were included in the Phase 2 software. Phase 2 (October–December 2024) assessed 482 patients using a locally developed software (Idea Pardazan Asr Hoshmand Etminan) combined with a weekly audit-and-feedback intervention sent to physicians. Major interactions, classified as Category X (life-threatening) and Category D (clinically significant), were compared using the Chi-square test in SPSS version 12.

Results: Phase 1 recorded 42 Category X interactions (8.7%) and 118 Category D interactions (24.5%). In Phase 2, Category X interactions decreased to 32 (6.6%), but this reduction was not statistically significant ($P = 0.276$). However, Category D interactions significantly decreased to 45 (9.3%) in Phase 2 ($P < 0.01$). There were no significant differences in interaction rates between academic and non-academic specialists.

Conclusion: The implementation of the software, combined with weekly feedback reports, significantly reduced clinically significant (Category D) interactions. However, the lack of a statistically significant reduction in life-threatening (Category X) interactions suggests that weekly feedback may be insufficient for critical alerts requiring immediate action. Future iterations should focus on real-time integration into clinical workflows to address urgent patient safety threats.

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Keywords: Drug Interactions; Emergency Department; Software; Lexidrug; Clinical Decision Support System; Audit and Feedback

Introduction

One of the primary functions of medical centers is to promote and restore patient health. However, this objective faces numerous challenges, particularly in public health institutions where healthcare providers—including

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nurses, physicians, and pharmacists—are significantly outnumbered by patients. Overcrowding is especially severe in emergency departments (EDs). Many patients presenting to the ED have complex conditions, and their unpredictable arrivals often result in long queues, making the emergency unit the busiest area in hospitals. Consequently, these high-pressure environments lead to reduced standards of care and an increased likelihood of medical errors, particularly those related to time constraints during patient evaluation (1,2).

Drug interactions in hospital settings can lead to serious complications, including treatment failures, adverse effects, increased healthcare costs, and prolonged hospital stays. Common causes include inappropriate medication selection, lack of awareness of existing medications, and inadequate dose adjustments, all of which are exacerbated in the fast-paced environment of an ED (3). To mitigate these risks, various tools are available for screening drug interactions, including Medscape (4), Drugs.com (5), and Lexidrug (6) (formerly Lexicomp). Among these, Lexidrug is noted for its comprehensive database and user-friendly interface. These tools categorize interactions by risk level, assisting healthcare providers in making informed medication management decisions.

In recent years, Clinical Decision Support Systems (CDSS) have been implemented to enhance patient safety and support physician decision-making (7). Specifically, Medication Decision Support Systems (MDSS) utilize artificial intelligence (AI)-driven recommendations to manage barriers and reduce medication errors. These systems can suggest overlooked tests, remind clinicians of potential side effects, or alert them to dangerous drug interactions (8). In many cases, they have been shown to save costs and improve patient safety (9). However, barriers to the widespread adoption of MDSS persist. Initial implementation can be prohibitively expensive, especially in under-resourced areas where basic health needs take priority (10). Additionally, physician adherence to CDSS recommendations is often inconsistent (11). A major challenge is "alert fatigue," wherein a high volume of low-relevance alerts causes clinicians to ignore warnings, potentially resulting in critical safety alerts being overlooked (10,12,13). Therefore, it is imperative to design systems that prioritize clinically significant alerts and deliver them effectively.

Despite advancements in technology, there is limited data on drug interactions in busy emergency departments in regions such as Mashhad, Iran. This gap underscores the necessity for cost-effective, locally adapted systems to monitor and manage drug interactions without contributing to alert fatigue. The present study aims to evaluate the effectiveness of a locally developed decision support software combined with a weekly audit-and-feedback mechanism. This system was designed to identify potentially dangerous interactions among commonly used medications in the emergency department of Ghaem Hospital, Mashhad, with the ultimate goal of improving clinical outcomes and reducing drug-related complications.

Methods

Study Design

The present study employed a quasi-experimental before-and-after design to evaluate the efficacy of locally developed decision support software combined with an audit-and-feedback intervention. The study aimed to identify and mitigate drug interactions in the emergency department of Ghaem Hospital in Mashhad, Iran, and was conducted from April 2024 to December 2024. Phase 1 (pre-intervention) data collection took place from June to August 2024; September 2024 was utilized for software setup and data analysis, and Phase 2 (intervention) was conducted from October to December 2024.

This study was approved by the Ethics Committee of Mashhad University of Medical Sciences (IR.MUMS.REC.1401.205). Since the study involved reviewing de-identified medical records and implementing a general audit-and-feedback intervention for physicians, the ethics committee waived the requirement for individual patient informed consent. All data were anonymized to protect patient privacy.

The study population consisted of patients admitted to the emergency department of Ghaem Hospital. The inclusion criteria were: 1) patients admitted as inpatients to the emergency department, and 2) patients prescribed at least five medications concurrently (polypharmacy) or at least one high-alert medication, as defined by the Institute for Safe Medication Practices (ISMP) (14). High-alert medications are drugs that carry a heightened risk of causing significant harm if used in error. Patients with incomplete medical records were excluded. A total of 964 patients were enrolled, with 482 patients allocated to each phase of the study.

The sample size was calculated to detect a difference in interaction rates between two independent groups using the Chi-square test. The parameters included a significance level of 5%, a power of 80%, and an effect size derived

from a previous study by Alavi-Moghaddam et al. (15). The calculation indicated a minimum sample size of 964 patients (482 per phase). Sample size estimation was performed using PASS statistical software (version 21.0.9).

Study Protocol

In Phase 1 (pre-intervention), medication charts for 482 patients were retrospectively reviewed by a pharmacy student and a clinical pharmacist. A list of prescribed medications was extracted and analyzed using Lexidrug® (formerly Lexicomp) drug interaction software, a well-established and widely used clinical decision-support tool in hospitals for checking drug interactions (6). The analysis focused on major interactions classified as Category D (consider therapy modification) and Category X (avoid combination).

To ensure a valid comparison between phases and eliminate ascertainment bias, the data from Phase 1 were rigorously filtered. Phase 2 utilized a specific database comprising the 150 most frequently prescribed medications, identified from hospital pharmacy data over the previous six months. Therefore, for the final Phase 1 analysis, only interactions involving these same 150 medications were retained.

In Phase 2 (intervention), a custom software program was developed by Idea Pardazan Asr Hoshmand Etminan®. This software was programmed with interaction rules for the top 150 medications, derived directly from the Lexidrug database.

A parallel run validation was conducted during the first week of Phase 2. All prescriptions generated during this period were processed simultaneously by the software and manually reviewed using Lexidrug online. The software achieved 100% concordance with the manual checks for the targeted medications, ensuring that no Category D or X interactions were missed or falsely flagged.

In the intervention phase (Audit and Feedback), the software imported data from the Hospital Information System (HIS) to identify Category D and X interactions. Unlike real-time alert systems, this intervention utilized an audit-and-feedback approach. Data for the weekly reports were extracted every weekend, and feedback emails detailing the identified interactions, their severity, frequency, and practical mitigation strategies were generated and sent to all 25 emergency medicine physicians within 24 hours of data processing. These emails contained general information about all identified drug-drug interactions (DDIs) within the department for that week, rather than individualized reports.

Outcomes

The primary outcome was the difference in the incidence of Category D and Category X interactions between Phase 1 and Phase 2. Incidence was calculated as the proportion of patients experiencing at least one such interaction. Secondary outcomes included the weekly trend of interactions during the intervention phase to assess changes in physician behavior over time.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics version 12. The primary comparison of interaction rates (categorical data) between Phase 1 and Phase 2 was performed using the Chi-square test. For the weekly trend analysis in Phase 2, a linear-by-linear association test was used to determine whether there was a statistically significant decrease in interactions over the seven-week period. A p-value of less than 0.05 was considered statistically significant.

Results

Patient and Physician Characteristics

A total of 964 patients admitted to the emergency ward of Ghaem Hospital were included in the study, with 482 patients assigned to the pre-intervention phase (Phase 1) and 482 to the intervention phase (Phase 2). Of the total study population, 507 (52.6%) were male and 457 (47.4%) were female. The gender distribution was consistent with the typical patient intake of the department. The study involved 25 physicians, consisting of 8 non-academic physicians and 17 academic emergency specialists (7 specialists and 10 residents). Crucially, the physician roster and staffing shifts remained constant throughout both phases. This stability in the prescriber workforce minimizes the confounding effects of physician variability or individual prescribing habits on the study outcomes.

Drug Interactions in Phases 1 and 2

Phase 1 (pre-intervention): Among the 482 patients reviewed (limited to the top 150 medications for valid comparison), 42 Category X and 118 Category D interactions were identified. The most prevalent Category X interaction was Quetiapine + Ipratropium (n = 8, 19.05%), followed by Spironolactone + Potassium Chloride (n = 5, 11.90%), and Salbutamol + Carvedilol (n = 4, 9.52%). The most frequent Category D interaction was Ceftriaxone + Calcium Gluconate (n = 17, 14.41%), followed by Meropenem + Valproic Acid (n = 10, 8.47%) (Figure 1).

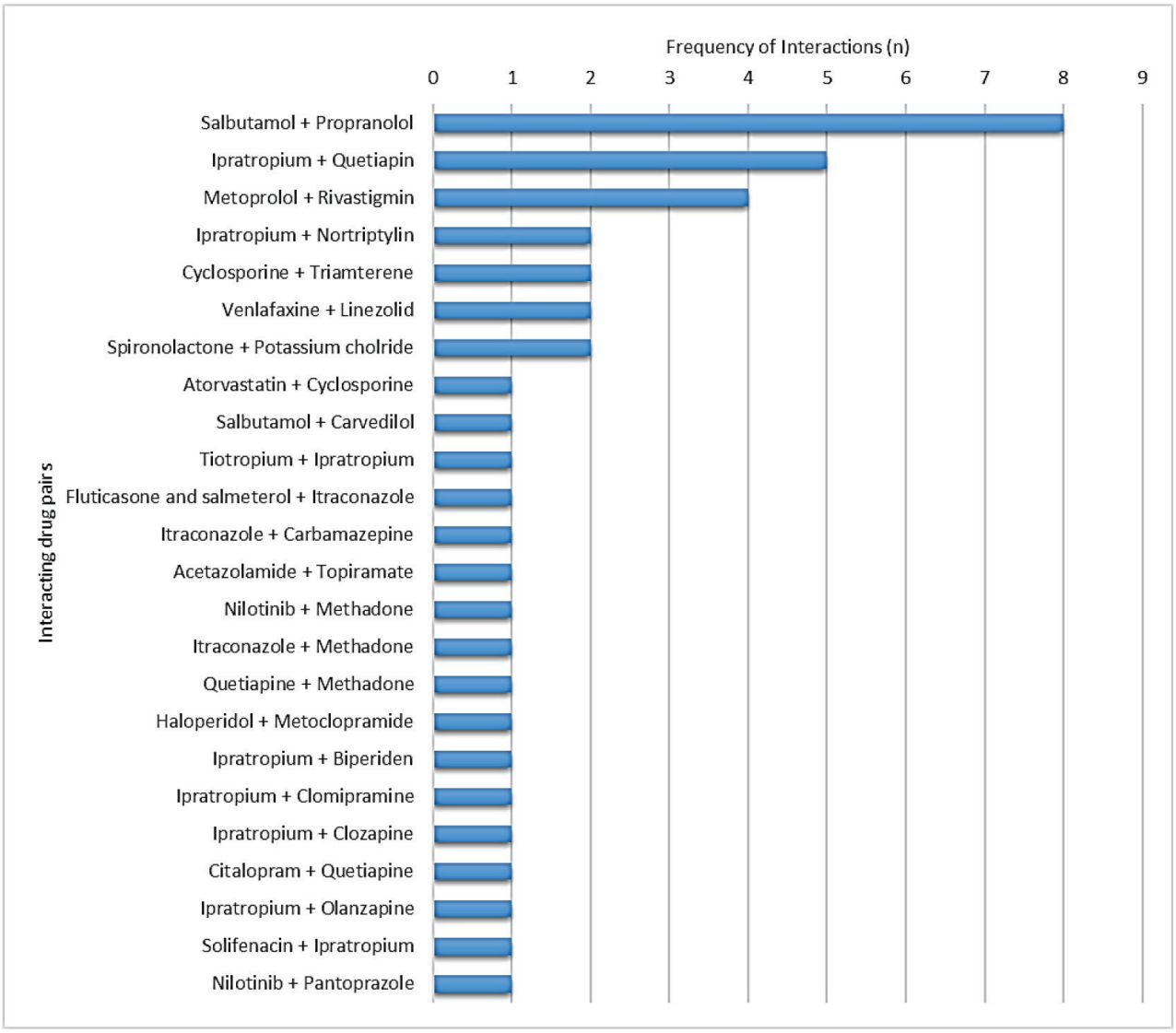

Figure 1. Category X interactions during the first phase of the study (Category X interactions: avoid combination)

Phase 2 (intervention): Following the implementation of the audit-and-feedback intervention, the incidence of interactions decreased. The number of clinically significant Category D interactions dropped significantly from 118 (24.48%) in Phase 1 to 45 (9.34%) in Phase 2 ($P < 0.01$) (Table 1). Additionally, the number of life-threatening interactions (Category X) decreased from 42 (8.71%) to 32 (6.64%). However, unlike Category D, this reduction did not reach statistical significance ($P = 0.276$) (Table 1).

Table 1. Comparison of Category X and Category D interactions in two phases of the study

Type of interactions	Phase 1 n (%*)	Phase 2 n (%*)	P-value**
Category X	42 (8.71)	32 (6.64)	0.276
Category D	118 (24.48)	45 (9.34)	<0.01

*Frequency of interactions/482 (number of patients included in each phase) × 100. **Chi-square test.

The most common interactions in Phase 2 remained similar to those in Phase 1. For Category X, Ipratropium + Quetiapine occurred 8 times (25%) (Figure 2). For Category D, Ceftriaxone + Calcium Gluconate remained the most frequent interaction (n = 14, 31.11%).

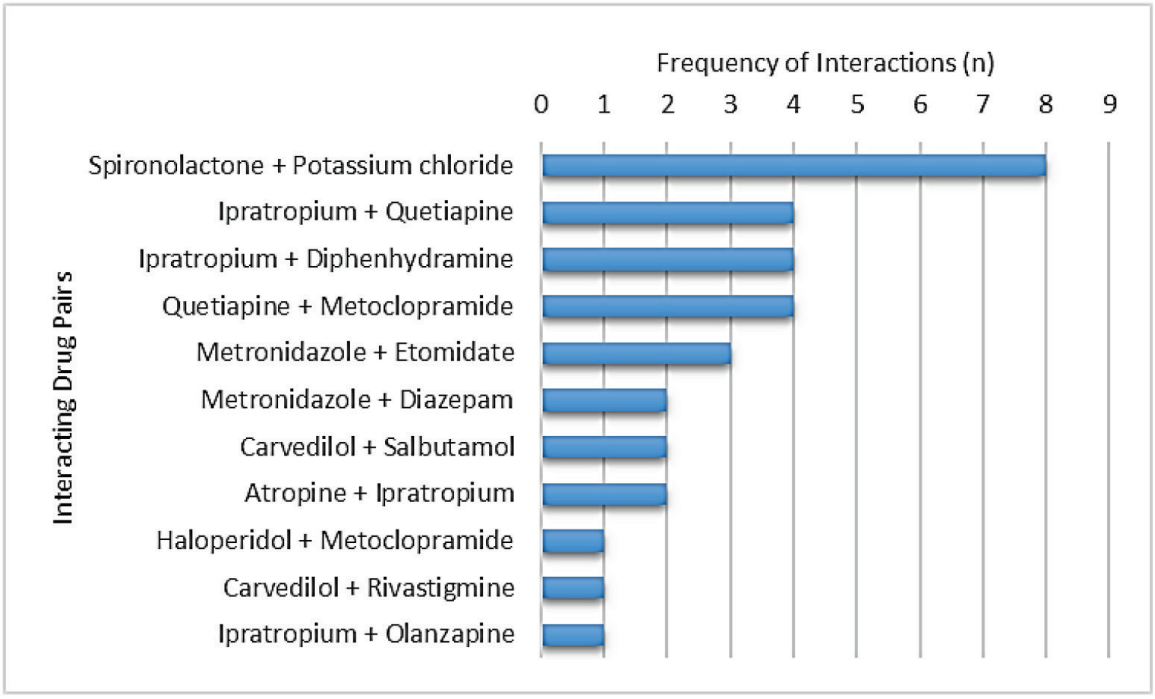

Figure 2. Category X interactions during the second phase of the study (Category X interactions: avoid combination)

Drug Interactions by Physician Groups

The impact of the intervention was analyzed across different prescriber types. In Phase 2, the incidence of both Category D and X interactions decreased in both academic and non-academic groups compared to Phase 1. However, the difference in interaction rates between the two physician groups was not statistically significant in either phase (Table 2). This suggests that the intervention had a similar effect on both academic specialists and non-academic physicians.

Table 2. Comparison of Category X and Category D interactions between two groups of prescribers in the emergency department

Phase of study	Interaction category	Non-academic specialists	Academic specialists	P-value*
Phase 1	Category X n/patients (%)	22/248 (8.87)	20/234 (8.97)	1
	Category D n/patients (%)	60/248 (24.19)	58/234 (24.79)	0.916
Phase 2	Category X n/patients (%)	17/244 (6.97)	15/238 (6.3)	0.856
	Category D n/patients (%)	19/244 (7.79)	26/238 (10.92)	0.274

*Chi-square test.

Weekly Trend of Interactions in Phase 2

During the seven-week intervention phase, weekly feedback reports were emailed to physicians. The data indicated a downward trend in interaction rates over time (Table 3). Category X interactions declined from 10% in Week one to 1.6% in Week seven, while Category D interactions declined from 10% in Week one to 7.9% in Week seven.

Table 3. Weekly report on the number of interactions during the second phase of the study

	Week 1 (n=70)	Week 2 (n=66)	Week 3 (n=71)	Week 4 (n=72)	Week 5 (n=68)	Week 6 (n=72)	Week 7 (n=63)	Total (N=482)	P-value*
Category X interactions, n (%)	7(10%)	6(9.1%)	7(9.9%)	6(8.3%)	4(5.9%)	1(1.4%)	1(1.6%)	32(6.6%)	-
Category D interactions, n (%)	7(10%)	7(10.6%)	10(14.1%)	5(6.9%)	4(5.9%)	7(9.7%)	5(7.9%)	45(9.3%)	-
Total number of interactions, n (%)	14(20%)	13(19.7%)	17(24%)	11(15.2%)	8(11.8%)	8(11.1%)	6(9.5%)	77(15.9%)	0.759

*Repeated measure test. The percentages in this table are calculated as frequency of interactions/the total number of patients enrolled in that specific week × 100.

Although a visual downward trend was observed (Figure 3), the linear trend analysis did not reach statistical significance (P = 0.759), likely due to the short duration of the intervention period.

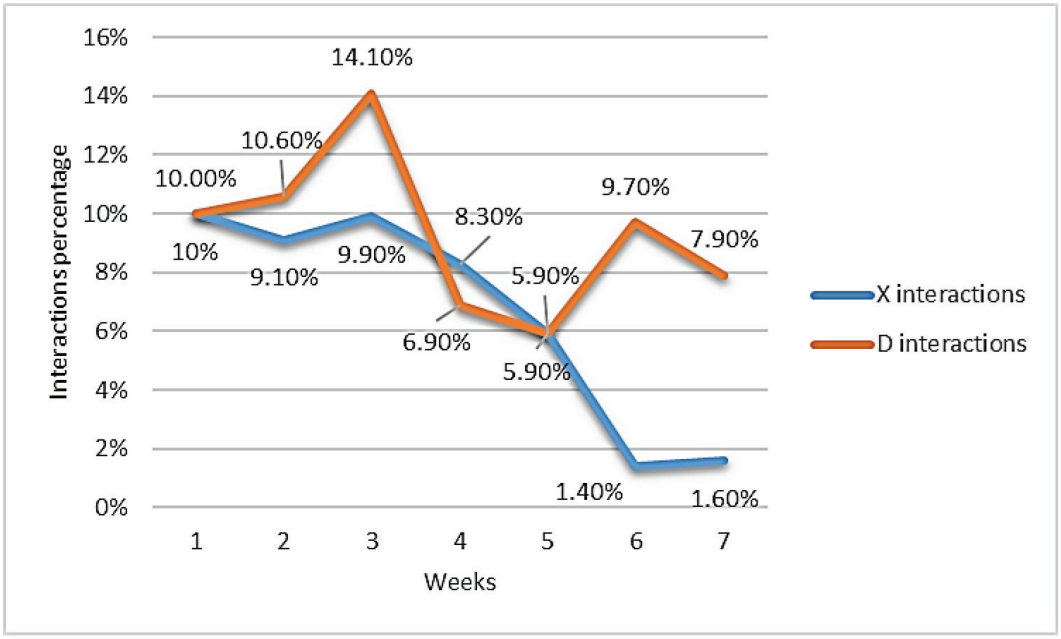

Figure 3. Weekly trends of Category X and Category D interactions during the second phase of the study (Category X interactions: avoid combination; Category D interactions: consider therapy modification)

Discussion

Addressing drug interactions in emergency settings is crucial for patient safety and optimizing treatment outcomes. Recognizing the potential for significant harm, our study aimed to evaluate the effectiveness of an audit-and-feedback intervention in reducing the incidence of potentially harmful drug interactions. In the first phase, there were 118 (24.48%) Category D drug interactions and 42 (8.71%) Category X drug interactions. These numbers decreased to 45 (9.34%) for Category D interactions and 32 (6.64%) for Category X interactions in the second phase. While the decline in Category D interactions was statistically significant (P < 0.01), the reduction in Category X interactions was not (P = 0.276). The lack of a statistically significant reduction in Category X interactions may be attributed to several factors. First, their lower baseline frequency resulted in less statistical power to detect a significant change. Second, Category X interactions, representing the highest risk, might be managed with inherent physician caution or involve complex clinical factors less responsive to general feedback. Additionally, the intervention's general nature may have been insufficient to address these severe, context-dependent risks. Although a downward trend was observed, future strategies could explore more targeted feedback or clinical decision support for these critical interactions. Moreover, in the second

phase of the study, a non-significant downward trend in the rates of both Category X and D interactions was noted.

Although there is a lack of data on the frequency of drug interactions in Iranian hospital emergency rooms, several studies conducted in various medical settings worldwide provide valuable insights. For example, a Brazilian study identified 526 interactions among 200 prescriptions, 109 of which were classified as serious, indicating a high incidence of drug interactions (79.5%) in emergency prescriptions (16). The inclusion of all interactions, regardless of their clinical significance, along with the cautious approach of the Drugs.com database used in the Brazilian study, may have contributed to the higher prevalence of interactions observed in that study compared to our investigation.

Another study conducted in the intensive care unit (ICU) of Imam Khomeini Hospital in Urmia, Iran, reported a drug interaction rate of 91%, with 15% of these interactions classified as severe (17). Although the rate of severe interactions partially aligns with the findings of the present study, the comparison lacks depth due to differences in the databases used. Similarly, Sepehri et al. found an overall interaction rate of 20.3% in various departments, including pediatrics and internal medicine, at a hospital in Zarand, Iran (18). They used custom-designed software but did not disclose the database employed, nor did they specify the severity of the interactions included in their reported 20.3% rate.

In another study by Namazi et al., 589 patients in the neurology departments of Faghihi and Namazi hospitals in Shiraz, Iran, had 403 Category D interactions and 18 Category X interactions documented (19). The rate of Category X interactions was comparable to that of the current study, but the number of Category D interactions was considerably higher, likely due to the therapeutic focus of the neurology departments, where interactions related to nervous system medications were more prevalent. These findings corroborate those of the present study.

Various studies have employed different tools to evaluate prescription medication interactions. To enhance the accuracy of their assessments, Hosseini et al., for example, used two tools simultaneously: the Micromedex program and the book "Drug Interaction Facts" (20). Similarly, Micromedex was used in an Ethiopian study to assess medication interactions in over 12,000 prescriptions (21). The Drugs.com website was used for this purpose in the aforementioned Brazilian investigation by Okuno et al. (16). In Iranian studies, Lexidrug software has become increasingly popular in recent years. Notable studies by Moradi Dirin et al. (22), Mehrpooya et al. (23), and Namazi et al. (19) have used this software. Its extensive database, frequent updates, and user-friendly interface are the primary reasons for its widespread adoption. In the current study, data were extracted using Lexidrug 2024 software (6). In the second phase, we utilized a database derived from this software, supported by a custom application developed by Idea Pardazan Asr Hoshmand Etminan. A drug interaction monitoring software must be reliable and feature a comprehensive database. It should also have access to patient information, such as demographics and medical history, to support informed clinical decisions.

Online alert systems are effective in preventing complications arising from drug interactions. Sepehri et al. used software developed by a private company; however, the original database source was not disclosed (18). Most Iranian studies have relied on established tools such as Lexidrug and Micromedex. In the present study, software based on the Lexidrug 2024 database was employed. While this software possesses several characteristics of an ideal tool, including comprehensiveness and regular updates, it currently cannot send online alerts regarding drug interactions to physicians nor integrate with the hospital's HIS to access patient data due to legal limitations. Nevertheless, this capability exists and is expected to be implemented soon with the support of the hospital's Deputy Director of Treatment and Information Technology.

A significant barrier to the effectiveness of clinical decision-making software is alert fatigue. Physicians often receive numerous alerts about drug interactions, many of which they consider irrelevant or of low importance, leading them to ignore these notifications and the software itself. This phenomenon undermines the anticipated benefits of such tools. According to Zapata et al., over 50% of drug interaction alerts generated by software are disregarded by physicians. The study suggests that addressing patients' clinical conditions may help mitigate this issue (24). Similarly, a systematic review by Felisberto et al. found that more than 90% of physicians ignore software-generated alerts, and even when alerts are adjusted to highlight more critical warnings, physician engagement does not significantly improve (25). In the current study, online warnings were not implemented, which somewhat alleviated alert fatigue. However, only clinically significant interactions (Categories X and D) were presented to physicians to minimize this problem. Weekly reports prioritized Category X interactions based on their frequency, followed by Category D interactions, and were designed to be concise while offering alternative solutions.

Active collaboration among physicians, pharmacists, and nurses is essential for reducing drug interactions in high-pressure environments such as emergency wards. Clinical pharmacists leverage their pharmacodynamics and pharmacokinetics knowledge, along with customized software alerts, to identify and manage these risks

effectively. Nurses contribute to safety by preparing medications, educating patients, and applying training in rational drug use. Promoting a team-oriented culture and incorporating training on new technologies, such as CDSS, further enhances patient safety.

This study faced several limitations. Integrating real-time drug interaction alerts with the HIS proved challenging, hindering timely decision-making. The effectiveness of weekly reports compared to immediate notifications remains uncertain, as physician engagement with warnings was not guaranteed. The lack of direct patient access prevented adjustment for demographic factors such as age and comorbidities; however, a stable physician roster helped mitigate some confounding variables. Limiting the data to the top 150 most frequently used medications may have underestimated the overall burden of drug interactions, and some flagged interactions might not represent actual clinical errors in practice. Future systems should prioritize real-time alerts, be implemented across high-risk departments (e.g., ICU, cardiology), and be supported by frequent staff training to maximize efficiency and promote teamwork.

Conclusion

This study focused on developing and evaluating an intelligent system that automatically identifies drug interactions in an emergency department. A key finding was that providing weekly reports to physicians significantly reduced the rates of Category D drug interactions. However, the reduction in life-threatening (Category X) interactions was not statistically significant. These reports increased physicians' awareness, leading to more cautious prescribing practices for clinically significant interactions. Continued advancements in technology and artificial intelligence are likely to enhance the effectiveness of these tools, underscoring the need for investment from policymakers to improve patient safety and healthcare outcomes.

Conflict of Interest

The authors declare that they have no conflict of interest.

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