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Evaluation of High-Risk Medications Interpretation in hospitals

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ABSTRACT

Background: medications interpretation are a significant contributor to preventable adverse drug events and associated health complications, especially in patients receiving polypharmacy. DDIs have been shown to contribute to hospital admissions and adverse drug reactions, making their identification and management crucial. This study aimed to assess the frequency, severity, and associated factors of potential DDIs in patients admitted to internal medicine wards of a large teaching hospital.

Methods: A cross-sectional study was conducted at a large teaching hospital. Patients admitted to various internal medicine wards were included, and data on prescribed medications, patient demographics, and hospital stay were collected from medical records. The severity of potential medications interpretation was assessed using Lexi-Comp and Micromedex databases. Logistic regression was employed to analyze associations between medications interpretation and factors such as age, gender, length of hospital stay, and the number of medications prescribed.

Results: A total of 448 patients were included, with 73.3% prescribed more than four medications. A total of 3,350 potential medications interpretation were identified, with moderate interactions being the most common (60.9%), followed by major interactions (48.8%) and minor interactions (28.8%). The average patient was exposed to 7.6 potential medications interpretation, and 11.8% of patients had at least one medications interpretation. A significant association was found between the occurrence of medications interpretation and the prescription of seven or more medications (OR: 0.048, $p < 0.0001$). No significant associations were observed with age, gender, or length of hospital stay.

Conclusion: Polypharmacy is a key risk factor for potential DDIs in hospitalized patients, with moderate and major interactions being the most common. Efforts to reduce the prescription of multiple medications and implement clinical pharmacy

systems are essential to mitigate the risk of DDIs and improve patient safety in hospital settings.

KEYWORDS: medications interpretation, polypharmacy.

1. Introduction

Medications interpretation are a significant contributor to preventable adverse drug events and related health complications (1). Polypharmacy is frequently used in the treatment of various medical conditions, which increases the potential for medications interpretation. Research has shown that medications interpretation account for 1% of all hospital admissions and represent 16% of all patients hospitalized due to adverse drug reactions (ADR) (2, 3). At least 15% of patients admitted to hospitals have at least one medications interpretation at the time of admission (4). The clinical outcomes of potential medications interpretation often unpredictable, and epidemiological data on this issue are limited. A study conducted in internal medicine wards found that 56.2% of patients were exposed to one or more major or moderate potential medications interpretation (5). Another study identified 221 cases of interactions among 160 patients in an internal medicine ward, including 24 major interactions, 15 moderate ones, and 82 minor interactions. The likelihood of drug interactions increases with conditions such as renal failure or when more than six medications are prescribed (6). In many healthcare settings, professionals, including doctors, are often overburdened with patient care responsibilities (8). Medication therapy is one of the most common forms of treatment, with the number of items per prescription varying across specialties. For example, cardiologists may prescribe an average of 3.68 items, while dermatologists typically prescribe 2.06 items, which is higher than the global average (9).

In numerous hospitals, there is no established clinical pharmacy system to monitor and optimize medication use, leading to widespread irrational use of medicines. This has been identified as a significant issue in many healthcare systems, with several studies indicating that patients in these settings are at higher risk for potential DDIs (10-14). Despite the increasing recognition of this issue, data on the occurrence and consequences of DDIs, particularly in hospital inpatient settings, remains scarce.

The objective of this study was to assess the frequency and severity of potential DDIs in internal medicine wards of a large hospital and explore their association with patient age, length of hospital stay, and the number of prescribed medications.

2. Methods

A cross-sectional study was conducted at a large teaching hospital with 850 beds, serving a population of approximately 1.7 million people. The study was approved by the Ethics Committee of the affiliated university's Pharmacy Faculty. patients admitted consecutively to various internal medicine wards (including Pulmonary, Nephrology, Hematology, Cardiovascular, and Gastrointestinal departments) were included in the study. These patients were admitted with a range of diagnoses across the field of internal medicine. Permission was obtained from hospital authorities to

review patients' medical records for research purposes.

Medications prescribed during the hospital stay and at discharge were retrieved from the medical records and drug Kardex. The data collected included patient age, gender, length of hospital stay, reasons for admission, details of the medication therapy provided during hospitalization, and the severity and significance of any drug interactions. Both regular and as-needed (PRN) medications were included. All data were recorded on a standardized form.

The severity and significance of drug interactions were assessed using Lexi-Comp's desktop drug interaction software (Lexi-Comp, Inc., Ohio, USA), which classifies interactions into five categories (A to X) . Additionally, the Micromedex database® (Thomson Reuters Healthcare Inc., Greenwood Village, Colorado, USA) was used to analyze medications interpretation, categorizing interactions based on severity (contraindicated, major, moderate, or minor). The database also provided information on the mechanism of the interaction, the onset of adverse drug reactions (rapid, delayed, or unspecified), and the potential adverse outcomes of the interaction.

Data were presented as proportions, means, standard deviations, or medians. Logistic regression was used to identify associations between the occurrence of potential medications interpretation) and variables such as age, gender, length of hospital stay, and the number of prescribed medications.

Exposure to medications interpretation was the dependent variable in the model (0 = absent, 1 = present). Predictor variables included patient age (1 = below 60 years, 2 = 60 years or older), gender (1 = male, 2 = female), hospital stay (1 = less than 6 days, 2 = 6 days or more), and number of prescribed medications (1 = fewer than 7, 2 = 7 or more). Odds ratios (OR) and respective confidence intervals (CI) were calculated for each predictor. A p-value of <0.05 was considered statistically significant. All statistical analyses were performed using SPSS for Windows Version 20 (SPSS, Inc., Chicago, IL, USA).

3. Results

Among the 448 patients included in the study, 263 (58.7%) were male and 185 (41.3%) were female. The majority of patients were between 61 and 80 years old (35.7%), with a mean age of 57.8 ± 20.2 years. The median age was 61 years. The median duration of hospital stay was 9 days (mean: 13.1 ± 14.4, range: 2-220 days). The number of medications prescribed concurrently ranged from 1 to 28 (mean: 9.1 ± 4.3), and 73.3% of patients were prescribed more than four medications. Table 1 provides a summary of the general characteristics of patients in the internal medicine wards. The number of potential medications interpretation for each patient ranged from 0 to 61, with the average patient having 7.6 ± 8.8 potential DDIs. In total, 3,350 potential DDIs were identified. Overall, 11.8% of patients experienced at least one potential medications interpretation, regardless of severity. Moderate interactions were the most common (60.9%), followed by major interactions (48.8%) and minor interactions (28.8%). Only 9.2% of patients had contraindicated potential DDIs. Table 2 shows the distribution of DDIs by severity category (A to X). The most

frequent category of interactions was category C (78.6%).

Over 25% of patients were exposed to more than 10 potential DDIs during their hospital stay. In 22.3% of cases, patients had one or two potential medications interpretation. Among the 386 identified potential DDIs, most had a delayed onset (56.5%), followed by rapid onset (42%), with 38.4% having an unspecified onset. Table 3 outlines the characteristics of patients and the type of interactions in different internal medicine wards. More than 90% of patients in the pulmonary ward were exposed to at least one potential DDI. Major and moderate interactions accounted for 27% of all potential medications interpretation (907 out of 3,350). Table4 provides details on the frequency, severity, onset, and potential adverse outcomes of these interactions.

In the logistic regression analysis, a significant association was found between the occurrence of potential DDIs and the prescription of seven or more medications (OR: 0.048; 95% CI: 0.02-0.12, $p < 0.0001$). However, no significant association was found with patient gender (OR: 1.02; 95% CI: 0.56-1.81, $p = 0.94$), age (under or over 60 years) (OR: 0.94; 95% CI: 0.51-1.7, $p = 0.85$), or length of hospital stay (less than or more than 6 days) (OR: 0.82; 95% CI: 0.4-1.5, $p = 0.54$).

Table 1. General characteristics of patients in internal medicine wards

Characteristics	Frequency	
Gender	Patient:	N(%)
Male	263	(58.7)
Female	185 (41.3)	
Age (years)		
<20	15	(3.3)
21-40	82	(18.3)
41-60	126	(28.1)
61-80	160	(35.7)
81-100	65 (14.5)	
Hospital stay (days)		
≤3	2	(0.4)
3-7	144	(23.1)
>7	302 (67.4)	
Prescribed medications per patient		
<3	15	(3.3)
3-6	130	(29)
> 7	303 (67.6)	

Table 2. Prevalence of potential drug-drug interactions medications interpretation in internal medicine wards

Type of prevalence	Frequency	
Overall prevalence *	Patient: 386 (86.2)	N(%)
Severity of pDDIs		
A	71	(15.8)
B	243	(54.2)
C	352	(78.6)
D	168	(42)
X	41 (9.2)	
Major	217	(48.4)
Moderate	273	(60.9)
Minor	129	(28.8)
Rapid	188	(42)
Delayed	253	(65.5)

Unspecified	172 (38.4)	
Number of pDDIs per patient		
1-2	100	(22.3)
3-5	89	(19.9)
6-9	82	(18.3)
≥ 10	115 (25.7)	

*Overall prevalence means presence of at least one medications interpretation regardless of type of severity.

Table 3. Patients' characteristics and prevalence of potential drug-drug interaction (DDI) in different internal medicine wards

Wards	Age Means±SD	Hospital stay (Days)	Prescribed medications per patient	PDDIs severity (N (%))					
				Total	A	B	C	D	X
Pulmonary	61.7±19.8	18.4±23	10.1±4.3	123 (97.6)	14 (10.3)	86 (63.2)	114 (83.8)	61 (44.9)	15 (11)
Cardiovascular	56.3±20.7	12.1±7.6	8.9±4.4	145 (87.3)	44 (26.5)	95 (57.2)	137 (82.5)	76 (45.8)	18 (10.8)
Gastroenterology	57.3±18.9	7.9±3.7	7.2±3.4	54 (76.4)	1 (1.4)	23 (32.4)	43 (60.6)	12 (16.9)	0
Nephrology/ hematology	54.8±20.3	10.2±5.9	9.5±3.9	64 (85.3)	12 (16)	39 (52)	58 (77.3)	39 (52)	9 (12)

Table 4. Most frequently identified major or moderate interactions, their levels and potential adverse outcomes.

Interaction	Frequency	Severity	Onset	Potential adverse outcome
Aspirin + heparin	51	Major	Rapid	Increase risk of bleeding
Aspirin + clopidogrel	33	Major	Delayed	Increase risk of bleeding
Enoxaparin + warfarin	28	Major	Unspecified	Increase risk of bleeding
Aspirin + warfarin	22	Major	Delayed	Increase risk of bleeding
Digoxin + furosemide	16	Major	Delayed	Risk of digoxin toxicity
Ciprofloxacin + insulin	14	Major	Rapid	Hypoglycemia
Clopidogrel + enoxaparin	13	Major	Unspecified	Increase risk of bleeding
Atorvastatin + azithromycin	9	Major	Delayed	Increase risk of myopathy
Midazolam + morphine	8	Major	Delayed	Increase sedation
Ceftazidim + warfarin	7	Major	Unspecified	Increase risk of bleeding
Clopidogrel + warfarin	6	Major	Unspecified	Increase risk of bleeding
Ciprofloxacin + warfarin	5	Major	Delayed	Increase risk of bleeding
Losartan + spironolactone	4	Major	Delayed	Hyperkalemia
Diazepam + morphine	4	Major	Unspecified	Increase sedation
Pantoprazole + warfarin	51	Moderate	Unspecified	Increase effect of warfarin
Atorvastatin + clopidogrel	33	Moderate	Delayed	Risk of blood clotting
Aspirin + enoxaparin	28	Moderate	Rapid	Increase risk of bleeding
Aspirin + captopril	25	Moderate	Rapid	Decrease effect of captopril
Digoxin + pantoprazole	22	Moderate	Delayed	Digoxin toxicity
Losartan + warfarin	18	Moderate	Delayed	Decrease effect of warfarin
Levofloxacin + prednisolone	17	Moderate	Delayed	Increase risk of tendon rupture
Atorvastatin + digoxin	16	Moderate	Delayed	Digoxin toxicity

Diazepam + valproic acid	14	Moderate	Delayed	Excessive sedation
Digoxin + spironolactone	12	Moderate	Rapid	Digoxin toxicity
Captopril + furosemide	11	Moderate	Rapid	Acute hypotension, insufficiency
Levothyroxine + warfarin	8	Moderate	Delayed	Increase risk of bleeding
Phenytoin + valproic acid	7	Moderate	Delayed	increase effect of phenytoin
Cyclosporine + diltiazem	7	Moderate	Delayed	Increase cyclosporine toxicity
Ciprofloxacin + prednisolone	6	Moderate	Delayed	Increase risk of tendon rupture
Ciprofloxacin + methadone	5	Moderate	Delayed	Increase QTc interval
Meropenem + valproic acid	5	Moderate	Delayed	Decrease level of valproic acid
Ciprofloxacin +Magnesium Oxide	4	Moderate	Rapid	Decrease level of ciprofloxacin
Lamotrigin + valproic acid	4	Moderate	Delayed	Increase level of lamotrigin
Gentamycin+ vancomycin	4	Moderate	Delayed	Nephrotoxicity, ototoxicity

4. Discussion

This study showed that almost all the patients admitted to internal medicine wards developed at least one potential drug-drug interaction during their stay in the hospital, and an average of 7.6 medications interpretation per patient. Also, about 67% of the studied patients took a prescription of more than six drugs, which was the sole factor that had significant relation with the occurrence of medications interpretation. Other studies similarly showed this trend in that the prevalence of potential medications interpretation increases with an increase in the number of medications prescribed (16-19). Global studies have reported that polypharmacy, or the use of five or more drugs, contributes to the heightened risk for potential DDIs (20, 21). The mean number of prescribed drugs in our study was higher compared to other studies that were carried out in similar settings (5, 16, 22). This is partly because of the practice at our center where the same patients are being managed by many physicians and also, we do not have a system to alert healthcare providers about the potential DDIs.

The implementation of COPE systems with DDI alerts could foster rational prescribing and help reduce the actual incidence of DDIs in medical wards (23, 24). Rijkom et al., identified that the computerized DDI alerts might be an effective tool in preventing adverse drug events in hospitals. Ismail et al., showed that among 400 medical inpatients, 52.8% had at least one medications interpretation, whereas major and moderate pDDIs were determined among 23% and 63.6% of patients respectively. Our study demonstrated a higher overall prevalence of medications interpretation 86.2%, particularly major medications interpretation. The prevalence of moderate medications interpretation, category C, in our study was in agreement with findings in a study by Ismail. Other studies in the internal medicine wards also reported prevalence rates of medications interpretation that ranged from 43% to 56.2%, consistent with high prevalence in this study.

The most frequent category in our study was Category C interactions with 78.6% of the total. Generally, these interactions usually do not lead to toxic or life-threatening

situations but require rigorous monitoring to prevent any possible adverse outcomes. However, type X interactions, demonstrating a risk to potential harm or life threat, were observed in 41 patients representing 9.2% of the patients. The prevalence of type X interactions in the literature ranges between 0.2 and 2.4% (12, 22, 25, 26). Although in our study the frequency of type X interactions was higher, the difference might be due to differences in study design and population characteristics. As mentioned above, type X interactions can be harmful; therefore, physicians and pharmacists should show caution and closely monitor the patients for the risk of such interaction types. Age, gender, and length of stay were not significantly associated with the occurrence of medications interpretation confirming several studies on gender (17, 27) but differing from other findings where a positive association between older age, longer length of stay, and medications interpretation was shown (19, 28). For instance, one study reported that Ismail et al. identified medications interpretation significantly associated with the age of the patient ≥ 60 years [OR: 2.1, P value: 0.003], duration of hospitalization ≥ 6 days [OR: 2.6, P value: 0.001], and taking ≥ 7 medications [OR: 5.9, P value < 0.001]. Our research indicates that polypharmacy is significantly associated with increased exposure to medications interpretation.

The two most common drugs implicated in clinically significant medications interpretation were ciprofloxacin and aspirin. Ciprofloxacin, a quinolone antibiotic, exhibits two important medications interpretation: impairment of the absorption of magnesium, calcium, iron, and zinc; and inhibition of certain cytochrome P-450 enzymes involved in metabolizing a large number of drugs, including methylxanthines. The latter interaction increases the plasma levels of these drugs, which can be life-threatening for theophylline. One of the common interactions of ciprofloxacin is with insulin either by raising or lowering the blood sugar levels; hence, it is essential to monitor the blood glucose closely. Aspirin also has some well-documented medications interpretation, especially with antiplatelet or other anticoagulant medications. Examples include heparin, warfarin, enoxaparin, and clopidogrel, which raise the risk of bleeding (30). These combinations of medicines are commonly used; however, the patients need close follow-up.

5. Conclusion:

Our study determined a high prevalence of medications interpretation in internal medicine wards; moderate severity was the most prevalent class, though major medications interpretation were also frequently seen. These data are in concordance with international studies that showed a progressive and significant increase of major medications interpretation. Taking four or more prescription drugs was found to be a significant predictor for medications interpretation. Thus, in order to minimize medications interpretation -related harm, drugs with lower risks of interactions have to be prescribed, and having careful ADR monitoring is advised. Further, we recommend the development and implementation of computerized medications interpretation alert systems to avoid ADRs within the hospital setting.

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