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Original Article

Prevalence of potential drug interactions among outpatients' prescriptions of community pharmacies in Nineveh Governorate, Iraq

[Prevalencia de posibles interacciones farmacológicas entre las recetas de los pacientes ambulatorios de las farmacias comunitarias de la gobernación de Nínive, Iraq]

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Abstract

Context: Management of chronic diseases requires the use of various drugs and dietary supplements. Their use is a potential source of drug interactions that interfere with therapeutic responses.

Aims: To determine the prevalence of potential drug interactions, severity levels, and related risk factors in outpatient prescriptions submitted to community pharmacies.

Methods: A cross-sectional study was conducted using convenience sampling. From August to December 2021, outpatient prescription data were collected from 16 community pharmacies within the Nineveh Governorate-Iraq. Recorded data included age (≥18 years), gender, and prescribed drugs and/or dietary supplements. Two online software programs were used for assessing drug interactions: Medscape.com and Drugs.com. Potential drug interactions were classified as minor, moderate/significant, or major/serious.

Results: Among the 1000 prescriptions, the total interactions were 1373. More than half of the prescriptions (57.6%, 576/1000) had potential drug interactions. These interactions were mainly observed among the drugs (89.9%, 518/576). The severity of the interactions was mostly (50%) moderate/significant. A significant association ($p \leq 0.001$) was reported for numerous prescribed items with the occurrence of potential interactions. Nonsteroidal anti-inflammatory drugs/aspirin (44%), and calcium/magnesium-containing products (approximately 20%) contributed to the most frequent potential drug interactions.

Conclusions: A high prevalence of potential drug interactions, mostly of moderate severity, was reported among outpatient prescriptions. These interactions are significantly associated with the number of prescribed items. The vital role of pharmacists in adopting strategies for monitoring potential drug interactions is essential for ensuring safe therapeutic regimens for patients.

Keywords: dietary supplements; Iraq; outpatients; potential drug interactions; prescriptions.

Resumen

Contexto: El tratamiento de las enfermedades crónicas requiere el uso de diversos fármacos y suplementos dietéticos. Su uso es una fuente potencial de interacciones farmacológicas que interfieren con las respuestas terapéuticas.

Objetivos: Determinar la prevalencia de interacciones farmacológicas potenciales, los niveles de gravedad y los factores de riesgo relacionados en las recetas de pacientes ambulatorios enviadas a las farmacias comunitarias.

Métodos: Se realizó un estudio transversal mediante muestreo de conveniencia. Desde agosto a diciembre de 2021, se recopilaron datos de prescripciones de pacientes ambulatorios de 16 farmacias comunitarias dentro de la gobernación de Nínive-Irak. Los datos registrados incluyeron la edad (≥18 años), el sexo y los medicamentos y/o suplementos dietéticos prescritos. Se utilizaron dos programas informáticos en línea para evaluar las interacciones farmacológicas: Medscape.com y Drugs.com. Las posibles interacciones farmacológicas se clasificaron como leves, moderadas/significativas, o importantes/graves.

Resultados: Entre las 1000 prescripciones, el total de interacciones fue de 1373. Más de la mitad de las prescripciones (57,6%, 576/1000) presentaban interacciones farmacológicas potenciales. Estas interacciones se observaron principalmente entre los fármacos (89,9%, 518/576). La gravedad de las interacciones fue mayoritariamente (50%) moderada/significativa. Se notificó una asociación significativa ($p \leq 0{,}001$) para numerosos artículos prescritos con la aparición de interacciones potenciales. Los antiinflamatorios no esteroideos/aspirina (44%) y los productos que contienen calcio/magnesio (aproximadamente 20%) contribuyeron a las interacciones farmacológicas potenciales más frecuentes.

Conclusiones: Se notificó una alta prevalencia de interacciones farmacológicas potenciales, en su mayoría de gravedad moderada, entre las prescripciones de los pacientes ambulatorios. Estas interacciones están significativamente asociadas con el número de artículos prescritos. El papel fundamental de los farmacéuticos en la adopción de estrategias de control de las posibles interacciones farmacológicas es esencial para garantizar regímenes terapéuticos seguros para los pacientes.

Palabras Clave: Iraq; pacientes ambulatorios; posibles interacciones farmacológicas; prescripciones; suplementos dietéticos.

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INTRODUCTION

Adopting multiple-drug treatment regimens increases the risk of hospitalization, the emergence of medication mistakes, adverse drug reactions, and drug interactions (Chatsisvili et al., 2010). Drug interactions occur when there is a change in a patient's response to a particular drug due to other drugs, dietary supplements (DS), disease, food, formulation excipients, or environmental factors (Snyder et al., 2012). Recently, DS have been widely used in addition to the diet (Perlman et al., 2013). Mostly, their usage remains a personal decision, and only about a quarter of DS are used based on the advice of healthcare providers (Ronis et al., 2018). Generally, these supplements are safe, but most consumers are unaware of their pharmacological activity and their involvement in adverse drug interactions (Patel and Beckett, 2016; Perlman et al., 2013).

Drug interactions can occur in any practical setting, whether in a hospital setting or among outpatients (Nusair et al., 2020). In outpatients, interactions among drugs are responsible for over 38% of adverse drug reactions and 1.1% of hospital admissions (Nusair et al., 2020). These interactions are either of pharmacokinetic or pharmacodynamic mechanisms, which may cause desired effects, decrease efficacy and effectiveness, or increase toxicity (Becker et al., 2007; Gardiner et al., 2008). However, various severities of drug interactions can occur, either in minor and unnoticeable or severe forms, resulting in detrimental health effects (Nusair et al., 2020).

Despite the existence of many drug interactions, only a small portion of these are clinically relevant, and actual drug interactions result in adverse patient outcomes (Chatsisvili et al., 2010; Jazbar et al., 2018). Potential drug interactions (pDIs) occur when uncertainty exists regarding adverse patient outcomes (Jazbar et al., 2018). Based on the selected study population and specific location, the proportion of actual interactions among potential drug-drug interactions (pDDIs) ranges from 0.25% to 25% (Jazbar et al., 2018). Various reports are available on the prevalence of pDIs for both drugs and DS (Gardiner et al., 2008; Ren et al., 2020). This could vary considerably depending on the patient's specific risk factors, such as age, gender, comorbid conditions, and a number of prescribed medications and supplements (Dirin et al., 2014; Gardiner et al., 2015; Mousavi et al., 2015; Nusair et al., 2020).

To our knowledge, no published reports are available on pDIs among outpatient prescriptions in Nineveh Governorate-Iraq. Therefore, the present study aimed to investigate the prevalence of pDIs among prescribed items, taking into account the severity of interactions and associated risk factors.

MATERIAL AND METHODS

Design, period, and location of the study

This cross-sectional study of outpatient prescription data was conducted from August 2021 to December 2021. Using a convenience sampling method, written prescriptions were collected from 16 pharmacies located in diverse geographical areas within Nineveh Governorate, Iraq. These pharmacies were either small independent pharmacies or belonged to non-governmental medical establishments. They had part-time work and received regular handwritten prescriptions, with only one pharmacy among the 16 pharmacies receiving typed prescriptions from the physicians. Information about the types and sales of over-the-counter (OTC) drugs in these pharmacies was beyond the scope of this study. As these drugs are not controlled by the pharmacies. Community pharmacists, with the help of one or more pharmacy assistants, were responsible for running the pharmacies and dispensing prescriptions.

Nineveh Governorate in Iraq has a population approaching four million, making this governorate the second largest in population in Iraq (Ninewa, 2010). Approximately 61% of Nineveh's population lives in urban areas (Ninewa, 2010). Nineveh Governorate has institutions for primary, secondary, and university education (CSO, 2021). After 2017, the inhabitants of Mosul City, which is the provincial capital of Nineveh governorate, suffered from a fragile healthcare system with inadequate healthcare resources for every patient (Mosul, 2020; Ninewa, 2010).

According to the report by World Health Organization - Eastern Mediterranean (2023), non-communicable diseases, such as diabetes, cancer, chronic lung diseases, and heart diseases, account for 55% of all mortalities in Iraq. Therefore, chronic management with multiple medications can be a source of pDIs that necessitate monitoring of therapeutic regimens (Ismail et al., 2013).

Ethical considerations

The study was approved in writing by the Collegiate Committee for Medical Research Ethics at the University of Mosul, Mosul, Iraq (date:8/8/2021; Code: CCMRE-phA-21-10). Furthermore, written consent through WhatsApp messages was obtained from pharmacists to take the permission of patients to have their prescriptions involved in the study after

explaining the aims of the study to them and assuring them that their privacy will be preserved.

Inclusion/exclusion criteria

The details of the patients' prescriptions were collected, including age (more than 18 years) and gender (male/female). The drugs and/or DS (minimum two items) in the prescriptions were also recorded, regardless of the dose and route of administration. The prescribed DS were either vitamins, minerals, or nutraceuticals.

The exclusion criteria were as follows: Prescriptions with incomplete patient information. Herbal drugs, as these drugs exhibit increased compositional variability and uncertainty (Ren et al., 2020). Drugs that were not covered by either drug interaction screening tool; Drug.com or Medscape.com. Both screening tools may not include drugs licensed for use outside the United States of America (USA).

Screening tools for pDIs

Using the online drug interaction checker software programs Medscape.com and Drugs.com, the prescribed items of either the drug or DS, which may result in pDIs, were detected.

Medscape from WebMD is part of the WebMD health professional network (https://reference.medscape.com/drug-interaction) checker. According to their criteria, drug interactions were categorized as minor (no change needed), significant (close monitoring), or serious (consider an alternate).

Medscape interaction checkers might separately check each interacting pair with more than one mechanism attributed and report more than one severity score for each drug interaction (Sancar et al., 2019). Therefore, the highest severity score was recorded for the detected drug interactions that showed multiple scores.

The Drug.com interactions checker (https://www.drugs.com/drug_interactions.html) was supported by several free leading medical information suppliers. Drug interactions on Drug.com were categorized as major, moderate, and minor depending on the severity of clinical significance.

The compounded products were individually examined according to the content of the pharmacologically active ingredients. The exception is multivitamin products, because of the diversity of available products. Therefore, such products were considered (multivitamins with minerals) by using Drug.com and (iron/folic acid/vitamin/mineral) by using Medscape.com. The prevalent pDIs, their extent of severity, potential adverse outcomes, and the mechanism of interactions of either pharmacokinetics, pharmacodynamics, or unknown were recorded (Snyder et al., 2012).

Statistical analysis

Using SPSS vs.24 (IBM, New York, NY, USA), quantitative and qualitative variables were presented using frequency, percentage (%), mean, standard deviation (SD), and the range as appropriate. Binary logistic regression analysis was performed to detect the association between the occurrence of pDIs (dependent variable) and the specified risk factors (independent variables). The adjusted odds ratio (OR) was reported, and the confidence interval (CI) was 95%. The statistical significance level was set at p less than 0.05.

RESULTS

Overall, 1000 outpatients' prescriptions were gathered from different community pharmacies in Nineveh Governorate-Iraq. Table 1 shows that the total number of interactions was 1373, with a mean of 1.37 ± 1.9. More than half (57.6%) of the prescriptions had pDIs and most (80.7%) had only one to three interactions. The type of pDIs was mostly (89.9%) among the drugs, compared to only 10.8% among the DS. The severity of interactions found using drug.com was more than half (57.2%) of moderate severity and 6.4% of major severity (Table 1). However, moderate-severity interactions (46%) and serious-severity interactions (4%) were found using Medscape.com.

General outpatient characteristics are reported in Table 2, where the mean age was 42.3 ± 16.4 years. Most of them (39.3%) were older adults (>45 years), and females comprised the largest proportion (68.7%). The majority of prescriptions (75.2%) were found using one to three drugs, and about (40%) of prescriptions contained DS.

Regarding risk factors for the presence of pDIs (Table 2), the existence of numerous prescribed items revealed a significant association, with the absence of such an association concerning the age and gender of patients. However, the odds of prescriptions with pDIs were higher for middle-aged adults (adjusted OR = 1.4; 95% CI = 0.99-1.97) compared to old-aged adults (adjusted OR = 1.1; 95% CI = 0.83-1.56). In addition, female patients vs. male patients had an elevated risk of developing pDIs (adjusted OR 1.03; 95% CI = 0.77-1.38).

Table 3 shows the most common moderate to major pDDIs. The most frequent potential interaction (44%) was contributed by nonsteroidal anti-

Table 1. Characteristic of potential drug interactions (pDIs) in prescriptions.

The overall pDIs = 1373		
Average ± SD (1.37 ± 1.9)		
Range (1-15)		
Items	**Frequency**	**(%)**
Number of prescriptions with pDIs		
Yes	576	57.6
No	424	42.4
Total	**1000**	**100**
Number of pDIs per prescription		
1-3	465	80.7
4-6	82	14.2
7-9	20	3.5
≥10	9	1.6
Total	**576**	**100**
Type of pDIs*		
Potential drug-drug interactions	518	89.9
Potential drug-dietary supplement interactions	117	20.3
Potential interactions among dietary supplements	62	10.8
Interaction severity according to drug.com	**Sum.**	**%**
Minor	132	9.6
Moderate	785	57.2
Major	88	6.4
Not found by drug.com database	368	26.8
Total	**1373**	**100**
Interaction severity according to Medscape	**Sum.**	**%**
Minor	225	16.4
Monitor closely	631	46
Serious	56	4 %
Not found by Medscape database	461	33.6
Total	**1373**	**100**

*In prescriptions with potential interactions, N = 576. SD: Standard deviation, Sum: summation.

inflammatory drugs (NSAIDs), including aspirin, mostly of pharmacodynamic interactions. The most prevalent major -moderate interaction (4.5%) was between fluoroquinolones and corticosteroids, whereas the potential interaction between fluoxetine and risperidone was only 1.7%.

By examining potential DS interactions (Table 4), 20% were attributed to calcium-and/or magnesium-containing products. The severity of the interaction was moderate, and the mode of interaction was either pharmacokinetics or pharmacodynamics in nature. Only 2% of the interactions were contributed by omega-3 fatty acids and NSAIDs in an unknown mode of interaction.

DISCUSSION

Healthcare providers should know about the classification of pDIs, the mechanism of interactions, the higher-risk drugs and DS, and the most exposed patient groups (Diksis et al., 2019; Haq et al., 2020). In the present study, among 1000 prescriptions from community pharmacies in Nineveh Governorate, Iraq, the prevalence of pDIs in both drugs and/or DS was 57.6%, mostly pDDIs (89.9%). This high prevalence of pDDIs can be attributed to the consideration of all the severity grades allocated to pDIs. Compared with the prevalence of pDDIs in other countries, it was 96% in Jordan (Nusair et al., 2020), whereas it was low in China (30.29%) (Ren et al., 2020), Pakistan (22.3%) (Ismail et al., 2018), and Greece (18.5%) (Chatsisvili et

Table 2. General patients' characteristics and the associated factors with potential drug interactions in prescriptions (N = 1000).

Data	Number of prescriptions (%)	Number of prescriptions with potential drug interactions (%)	Adjusted odd ratio (95% CI)	P-value
	Total No.	**Total No.**		
	1000 (100%)	576 (57.6%)		
Age group (years)				
Mean ± SD	42.3 ± 16.4			
18 - 30	311 (31.1)	166 (28.8)	Reference	-------
31 - 45	296 (29.6)	183 (31.8)	1.4 (0.99-1.97)	0.06
More than 45	393 (39.3)	227 (39.4%)	1.1 (0.83-1.56)	0.43
Gender				
Male	317 (31.7%)	180 (31.3%)	Reference	------
Female	683 (68.3)	396 (68.7)	1.03 (0.77-1.38)	0.84
Number of prescribed medications				
0	17 (1.7)	7 (1.22)	Reference	--------
1-3	752 (75.2)	370 (64.24)	2.4 (0.81-7.20)	0.115
4-5	211 (21.1)	181 (31.42)	16.8 (5.25-53.79)	<0.001
>6	20 (2.0)	18 (3.12)	23.7 (3.81-147.19)	0.001
Number of prescribed dietary supplement				
0	568 (56.8)	313 (54.3)	Reference	-------
1-2	404 (40.4)	244 (42.4)	1.6 (1.20-2.11)	0.001
3-4	28 (2.8)	19 (3.3)	3.5(1.38-8.87)	0.008

CI: confidence interval; SD: standard deviation.

al., 2010). The reported different prevalence of pDDIs among studies may be due to multiple factors, such as variations in the study population, sample size, research design, prescribed drugs and DS, and different drug interaction checkers used (Nusair et al., 2020; Ren et al., 2020). These factors ultimately affect the severity and predictors of pDIs (Aljadani and Aseeri, 2018; Nusair et al., 2020).

In the present study, drug interaction checkers (Drugs.com and Medscape) were conveniently used because they are readily available online for practical applications (Sancar et al., 2019). Interactions of moderate severity were the most prevalent in the present study. This means that relevant drugs should be used with careful clinical monitoring (Ismail et al., 2018). The least-reported severity was categorized as a major interaction. These results are comparable to those of previous studies (Cruciol-Souza and Thomson, 2006; Das et al., 2019; Nusair et al., 2020). However, de Oliveira et al. (2021) stated in their systemic review that results should be interpreted based on the clinical knowledge. Major drug interactions may not produce harmful effects, whereas significant adverse effects can occur owing to moderate drug interactions (Chatsisvili et al., 2010).

Risk factor analysis for the presence of pDIs in the present study revealed a significant association when there were high numbers of prescribed drugs and/or DS. Similar results were reported in previous studies (Gardiner et al., 2015; Murtaza et al., 2016; Ren et al., 2020). The likelihood of interaction increases from 50% to 100% when there is an increase in the use of five to seven drugs (Secoli et al., 2010). The present study showed that outpatient age and gender were not significantly associated with the presence of pDIs, a finding similar to those of other reports (Murtaza et al., 2016; Shafiekhani et al., 2019). However, Cruciol-Souza and Thomson (2006) and Egger et al. (2007) reported that elderly patients form a significant risk factor. As the age of patients increases, they become more susceptible to comorbid conditions and polypharmacy (de Oliveira et al., 2021; Shafiekhani et al., 2019). With age-related physiological changes and alterations in the kinetic characteristics of drugs, there is a greater risk of developing adverse drug interaction outcomes (Diksis et al., 2019; Sánchez-Fidalgo et al., 2017). Females had an elevated rate of pDIs, as

Table 3. Examples of most common moderate- major potential drug–drug interactions (pDDIs).*

pDDIs	Interaction severity/prevalence (%)**	Mechanism of pDDIs	Potential adverse effects
Corticosteroids + NSAIDs/aspirin	Moderate/minor (18.6%)	Pharmacodynamics: Increases toxicity of each other Pharmacokinetics: An increase in the renal clearance and/or induction of hepatic metabolism of aspirin caused by corticosteroids	Increase the potential of serious gastrointestinal toxicity (inflammation, bleeding, ulceration, perforation)
NSAIDs/aspirin + fluoroquinolone	Moderate (8.3%)	Unknown: This may be by displacement of gamma-aminobutyric acid from receptors in the brain	Risk of central nervous system stimulation/seizure
Famotidine + fluoroquinolone	Moderate (6.4%)	Pharmacodynamics: Additive effect on prolongation of QT interval	Raise the danger of ventricular arrhythmias, including Torsade de Pointes and sudden death
Bemiparin + NSAIDs/aspirin	Moderate (5.2%)	Pharmacodynamics: Both increase anticoagulation	Potentiate the risk of bleeding complications
Fluoroquinolone + corticosteroids	Major/moderate (4.5%)	Unknown	It may increase the risk of tendon rupture
More than one NSAIDs, including topical preparations	Major/moderate (3.6%)	Pharmacodynamics: Increased NSAIDs adverse effects, even with topical administration, which may be absorbed systemically	The possibility of severe gastrointestinal toxicity may increase, which includes inflammation, bleeding, ulceration, and perforation
NSAIDs + methotrexate	Major (1.9%)	Pharmacokinetics: Possibly by inhibition of renal elimination of methotrexate and its metabolite. The secondary role of certain NSAIDs by displacement of methotrexate binding to serum albumin	Increase the plasma concentrations and toxicities of methotrexate
Fluoxetine + risperidone	Major/moderate (1.7%)	Pharmacokinetics/Pharmacodynamics: The level or effect of risperidone is raised by affecting (inhibiting) hepatic enzyme CYP2D6 metabolism Both drug increase QTc interval	Enhance the risk of extrapyramidal adverse effects

*Based on both Medscape and Drug.com databases. **Prevalence (%) = (number of pDDIs/ total number of prescriptions with potential drug interactions) × 100. NSAIDs: Nonsteroidal anti-inflammatory drugs.

Table 4. Most common moderate potential dietary supplement interactions.*

Potential interactions	Interaction severity/prevalence (%)**	Mechanism of potential interactions	Potential adverse effects
Vitamin D analog + calcium salts	Moderate (9.0%)	Pharmacodynamics: Additive calcium-sparing effects	Increasing the risk of hypercalcemia
Vitamin D analog + magnesium-containing products	Moderate (6.6%)	Pharmacodynamics: Additive magnesium-sparing effects	Increasing the risk of hypermagnesemia, particularly in the presence of renal impairment
Calcium/magnesium-containing products + aspirin	Moderate/minor (4.9%)	Pharmacokinetics: Raising renal salicylate clearance by the reduction in salicylate renal tubular reabsorption due to urinary alkalization	Analgesic and anti-inflammatory effects are potentially reduced or inadequate
Fish oils/omega-3 fatty acid + NSAIDs/aspirin	Moderate (1.9%)	Unknown	Possibly potentiate the pharmacologic effects of anticoagulants and other drugs that affect hemostasis, such as NSAIDs

* Based on both Medscape and drug .com database. ** Prevalence (%) = (number of potential dietary supplement interactions / total number of prescriptions with potential drug interactions) × 100. NSAIDs: Nonsteroidal anti-inflammatory drugs.

reported by Cruciol-Souza and Thomson (2006) and Obreli Neto et al. (2012). The reason for this could be related to the longer lifespan of females, making them more susceptible to comorbid diseases (Shafiekhani et al., 2019). This raises the possibility of pDIs by using additional medications (Shafiekhani et al., 2019).

Both physicians and pharmacists could benefit from the list of the most frequently reported major or moderate pDDIs in the present study. As these interactions have potentially important clinical outcomes and severities, careful monitoring is necessary to avoid harmful clinical consequences (Ismail et al., 2013). The most frequently reported major/moderate

interaction in the present study (4.5%) was between fluoroquinolones and corticosteroids. Fluoroquinolone can contribute to an increased risk of tendon rupture by approximately 14-fold among males and elderly patients (> 60 years), and with the use of concomitant corticosteroid therapy (Drug.com, 2023; Fish, 2001). Therefore, it is recommended that any patient suffering from tendon pain or inflammation during the use of fluoroquinolone to discontinue the drug and avoid exercise until the presence of tendinitis is adequately assessed (Drug.com, 2023; Fish, 2001).

In this study (Table 3), NSAIDs, including aspirin, were the most common drugs causing pDIs. Similar results have been previously reported (Murtaza et al., 2016; Nabovati et al., 2014; Obreli Neto et al., 2012). A high prevalence of NSAIDs use in elderly patients with concomitant use of known potential interacting drugs such as warfarin, corticosteroids, and methotrexate can result in harmful effects (Ljung et al., 2011; Vandraas et al., 2010). As NSAIDs are known to cause adverse gastrointestinal, renovascular, and cardiovascular effects (Ljung et al., 2011). In addition, NSAIDs affect coagulation and homeostasis of blood vessels with proven susceptibility to bleeding or thromboembolic complications (Vandraas et al., 2010). Therefore, whenever possible, it is necessary to avoid using NSAIDs or at least to use them cautiously with these previously mentioned medications (Al-Azayzih et al., 2020).

This study reported low (1.7%) but of considerable importance with regard to major/moderate severities of the interaction between fluoxetine (a selective serotonin-reuptake inhibitor antidepressant) and risperidone (an atypical antipsychotic). As a result, these interactions either reduce efficacy and/or adherence to the therapeutic regimen in psychiatric patients (Kennedy et al., 2013). Atypical antipsychotics are used to manage patients with psychotic conditions, such as schizophrenia and bipolar disorders, often in combination with other psychotropic drugs, such as antidepressants and antiepileptics (Kennedy et al., 2013). Consequently, psychiatric patients are at high risk of pDDIs because of presence of comorbid conditions and the need for chronic management with multiple medications (Aburamadan et al., 2021; AlRuthia et al., 2019; Liu et al., 2022). The pharmacokinetic and pharmacodynamic mechanisms of pDDIs could be involved (Aburamadan et al., 2021). Pharmacokinetic interactions are mediated by co-prescribing antipsychotic drugs with inducers or inhibitors of hepatic cytochrome P450 enzymes (Aburamadan et al., 2021; Kennedy et al., 2013). These enzymes are responsible for the extensive metabolism of antipsychotics, thus contributing to the high frequency of pDDIs among psychiatric patients (Aburamadan et al., 2021). In clinical practice, pharmacodynamic interactions are commonly involved and may precipitate severe complications, such as seizures, extrapyramidal symptoms, serotonin syndrome, and QTc interval prolongation (Aburamadan et al., 2021; Kennedy et al., 2013). Therefore, psychiatrists should be aware of the probability of clinically significant drug interactions with careful monitoring of patients to ensure maximum efficacy and minimal adverse events of the therapeutic regimen (Kennedy et al., 2013; Liu et al., 2022).

The available evidence supporting drug-DS interactions, as with drug-drug interactions, differs widely (Karny-Rahkovich et al., 2015; Ronis et al., 2018). Ronis et al. (2018) stated in their review article that multivitamin/mineral supplements, calcium supplements, and fish oils/ omega-3 fatty acids were among the most commonly used supplements, to improve and maintain general health. Ultimately, most potential DS interactions reported in the present study were of moderate severity, particularly those contributed by these supplements.

The main potential DS interactions were between calcium/magnesium-containing products and vitamin D (Table 4). Similar results were noted by Levy et al. (2016), as vitamin D was found to increase calcium absorption in the small intestine and can contribute to hypercalcemia when taken with calcium-containing products. However, the actual occurrence of hypercalcemia is unclear because of calcium or vitamin D intake alone or due to their interaction. Therefore, it is essential to examine the potential interaction between these two supplements (Levy et al., 2016).

There are limited studies on the interaction of magnesium with calcium and vitamin D (Shahsavani et al., 2021). Although using magnesium supplementation can increase and maintain vitamin D levels and prevent its toxicity, vitamin D can increase the absorption of magnesium in the intestine (Shahsavani et al., 2021). Therefore, it is critical to closely monitor patients and refrain from using magnesium-containing products by those on chronic renal dialysis and receive treatment with a vitamin D analog (Drug.com, 2023). Chronic hypermagnesemia may contribute to the etiology of adynamic bone disease in dialysis patients owing to possible additive pharmacological effects (Drug.com, 2023). Furthermore, the potential interaction of fish oil/omega-3 fatty acid supplements with NSAIDs/aspirin was reported in this study (Table 4). This supplement could exacerbate anticoagulation and promote bleeding, particularly with the use of anticoagulants and platelet inhibitor drugs (Ronis et al., 2018; Spanakis et al., 2021).

Adopting the most commonly used strategies for recognizing pDIs can be helpful, such as educational mediation, easy access to drug interaction checker sources, and the use of computer-based alerting systems (Nabovati et al., 2017). Pharmacists perform an essential role, whether in hospitals or outpatient clinics, in selecting proper drug combinations (Nusair et al., 2020). These combinations should provide minimum drug interactions and adverse drug reactions (Nusair et al., 2020).

Study strength and limitations

Despite living in the twenty-first century, medication errors continue to be an important issue. Additional studies are required to further understand the prevalence of pDIs. This would help to identify issues and potential clinical outcomes to guarantee medical safety. In outpatient settings, community pharmacists are the only individuals with the legal authority to dispense secure medications with minimal risks to patients.

In this study, most screened prescriptions were handwritten by physicians, without considering the OTC medications that the patients had used. Therefore, the introduction of electronic prescriptions and barcodes can be helpful in identifying patients and their medications, while ensuring safe prescribing and dispensing (Chatsisvili et al., 2020; Somogyi-Végh et al., 2019). Although two screening tools were used in this study, there were still some medications that were not involved in drug interaction analysis, in addition to omitting herbal medications that may contribute to such interactions. This can lead to under-reporting of pDIs. Using a convenience sampling method, the possibility of generalizing the results is limited.

CONCLUSION

A high prevalence of pDIs among outpatient prescriptions for community pharmacies has been reported. Strong evidence is available regarding the number of prescribed items and the development of pDIs. Most pDIs were of moderate severity; therefore, clinical monitoring of patients is of utmost importance. The effective role of pharmacists in adopting strategies for monitoring pDIs may be helpful in ensuring a safe therapeutic regimen for patients.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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