(IJRMST) 2019, Vol. No. 7, Jan-Jun **e-ISSN: 2455-5134, p-ISSN: 2455-9059**

POTENTIAL DRUG-DRUG INTERACTIONS IN PRESCRIPTIONS DISPENSED IN COMMUNITY AND HOSPITAL PHARMACIES IN DUHOK CITY

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ABSTRACT

Objectives: The goal of the present study was to assess and compare the types and the incidence of drug-drug interactions (DDIs) in prescription orders dispensed in both private pharmacy and hospital pharmacy settings. Methods: A total of 2796 previously dispensed prescriptions were obtained from private pharmacies and hospital pharmacies of Azadi Teaching Hospital/Duhok. The drug interactions were determined by processing all prescriptions using the Lexi-Comp application. The identified DDIs were sub-classified into five classes (A, B, C, D, X). Results: More than one-half of collected prescriptions had at last one DDI, of which the commonest type of interaction was type C (74.3%) and the interactions were more common in hospital settings than in private pharmacy prescriptions (P < 0.001) Conclusion: The results of the present study confirmed that patients are at high risk of adverse drug interaction and urgent follow-up is required. The study recommends potential follow-up of written prescriptions by hospital pharmacists to avoid disastrous adverse effects and this could considerably prevent the consequence of DDIs in written prescriptions.

Keywords: *interaction; community; pharmacist; hospital; pharmacokinetics, pharmacodynamics.*

INTRODUCTION

Adverse drug events (ADEs) are the most common complications related to medication therapy among patients. ADEs are common, costly, and may have life-threatening consequences. The high prevalence of drug uses in medical managements and the possibility of human mistake could increase the prevalence risk of these adverse events [1,2].

Drug-drug interactions (DDIs) are an important subgroup of ADEs [3] which are highly distributed in patients receiving multiple-drug treatment [4] and are a significant source of avoidable drug-related events (i.e., ADEs) [5].

Drug interactions takes place when the side effects of a single drug are changed by the presence of alternative agents, that is, drugs, meals, drinks, or environmental parameters [6]. Although drug interactions can be used for therapeutic effectiveness, it is known that DDIs may compromise patient safety by leading to toxicity or reducing therapeutic benefit and may increase mortality and morbidity, especially in critically-ill patients [7-11].

Pharmacokinetic interactions are interactions due to one drug's effect on the dissemination of another drug through the body. These interactions are modulation in the response of the body would normally process a drug towards eventual elimination (including the way it is metabolized). Pharmacokinetic interactions may result in delayed/prolonged onset of effect, decreased or increased action, toxicity, or altered excretion, and directly affect the plasma levels of the drug that reaches the target site. Pharmacokinetic interactions encompass modulation in absorption, distribution, metabolism, and excretion [13].

Pharmacodynamic interactions occur when physician want their patients to obtain the benefits of two or more

drugs are used that have additive or synergistic pharmacological activities or have antagonistic pharmacological activities. Pharmacodynamic interactions are more challenging for prediction than pharmacokinetic interactions. Often, drugs are used in combination to take advantage of their close pharmacodynamic effects, such as the use of sulfonylurea and metformin in diabetes mellitus. However, it is the unintentional additive or synergistic effects of medications that cause significant problems in patients [14].

When more than one physician are involved in the treatment of the same patient, the number of prescribed drugs may increase, and it may be difficult for the general practitioners to keep track of all medications. This will lead to an increased risk of potential DIs. The risk factors that are associated with potential DIs are advanced age, polypharmacy, and multiple prescribers [15-17]. Within hospitals, DDIs can lead to complications, which in turn may prolong the length of hospital admission or even lead to death [18]. The percentage of patients in primary or secondary health care that receives interacting drugs ranges from 7 to 22. In the old-age, this limits ranges from 22 to 31 [19]. A US study found that the risk of non-intended drug interactions increased from 13% for patients taking two medications to 82% for patients taking seven or more medications [20, 21].

Pharmacists play an important role in protecting the patients from the dangers posed by potential DDIs, especially concerning drugs with a narrow therapeutic index [22]. Manual review of medications in a prescription can be performed by pharmacists, but the efficiency in the detection of DDIs is approximately 70% of DDIs in a two-drug prescription, and the proportion decreases substantially as the number of medications increases [23]. By using computerized DDI screening programs we can significantly improve the identification of potentially harmful DDIs, beyond what can be achieved with manual review alone [24].

To the best of our knowledge, this is the first documented study in drug interactions here in Duhok city, we designed this study to investigate the prevalence and type of DDIs in prescriptions of both community and hospital pharmacies of Duhok city, Kurdistan Region, Iraq.

METHODS

A prospective, descriptive cross‐sectional study was conducted on prescriptions of different community pharmacies and inpatient and outpatient pharmacies of Azadi teaching hospital. During the study period, we collected an overall of 1032 prescriptions. All prescriptions from December 2016 to May 2017 were analyzed.

Prescriptions with two or more prescribed drugs were selected, and data were extracted on predesigned forms including patient characteristics (gender, age), the number of drugs, and severity and significance of drug interactions. The severity and significance of drug interactions were analyzed using the interaction application in the Lexi‐Comp website [25]. The significance of drug interactions was divided into 5 categories (A to X) according to the application, which is presented in Table 1. Demographic data of patients and other data of prescriptions were presented as mean ± standard deviation or percentage of cases. Independent sample *t*‐test and Chi square test were applied to assess differences among groups. $P < 0.05$ or less were considered statistically significant. The data were processed using SPSS software (SPSS, Inc. Chicago, IL, USA) version 23.0.

Risk Rating	Action
A	No Known Interaction
B	No Action Needed
C	Monitor Therapy
D	Consider Therapy Modification
X	Avoid Combination

RESULTS

A total number of 1031 written prescriptions were retrieved, 503 (48.7%) and were collected from private pharmacies, 264 (25.6%) from outpatient, and 264 (25.6%) from inpatient pharmacies of Azadi Teaching Hospital (Figure 1). Analysis of these prescriptions showed that 544 (52.7%) of them had at least one interaction. A total of 1573 cases of interactions were found in prescriptions of which 74.3% of interactions were classified as type C. The frequencies of drug interactions in community and hospital pharmacies are shown in Table 2.

Table 2 Frequencies of drug interactions in community and hospital pharmacies

Prescription	Community pharmacy [Number (%)]	Inpatient Hospital Pharmacy [Number (%)]	Outpatient Hospital Pharmacy [Number (%)]
With interaction	237(47)	195(73.9)	112(42.4)
Without interaction	266(52.9)	69(26.1)	152(57.6)
Sum	503(100)	264(100)	264(100)

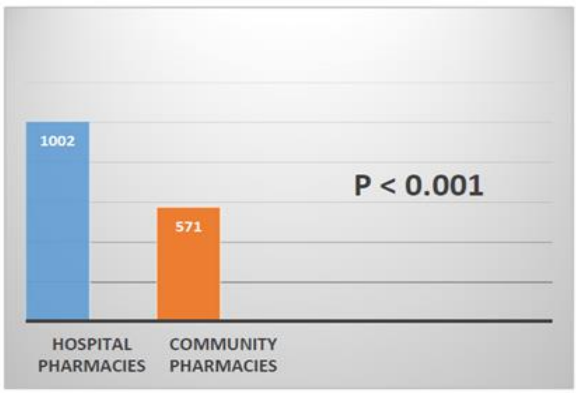

Figure 1. Prevalence of DDIs in Hospital and Community Pharmacies.

Type C interactions had the highest prevalence among community and hospital pharmacies prescriptions, Figure 2.

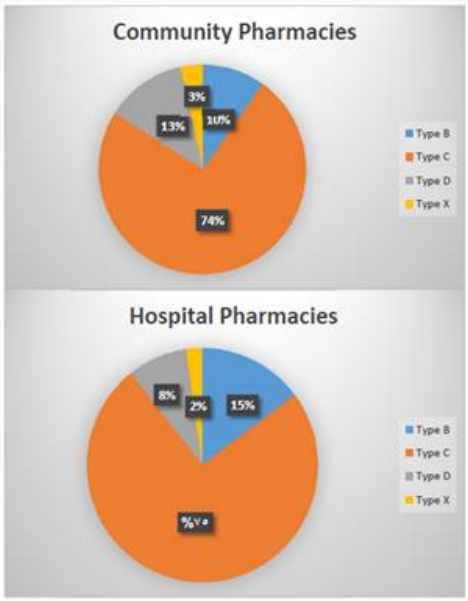

Figure 2. Prevalence of different DDIs types in Community and Hospital Pharmacies

The average number of items per prescription was 4.1; three-drug item prescriptions were the most prevalent ones (n=316, 30.6%). The mean ± standard deviation of items in prescriptions with interaction was 5.0 ± 2.3 compared to 3.09 ± 1.1 in prescriptions without interactions, and the difference was significant (P < 0.001). Increasing the number of drugs per prescription significantly increased the probability of drug interaction as shown in Figure 3.

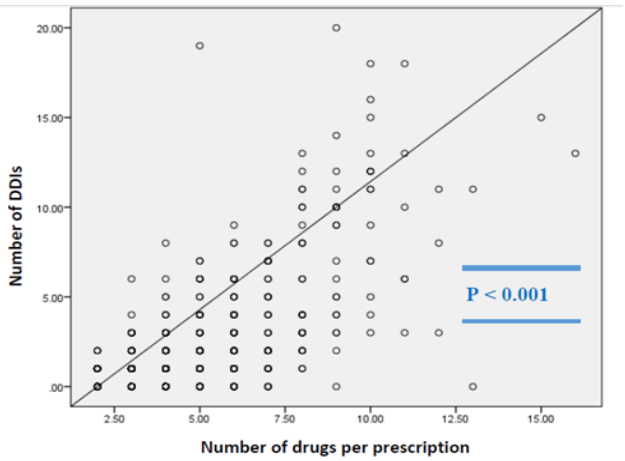

Figure 3. The correlation between the number of DDIs and the number of items per prescription.

From 264 prescriptions retrieved from the inpatient hospital pharmacy, the majority belonged to the coronary care unit (CCU) and intensive care unit (ICU), and internal medicine ward (n=81, 30) as shown in Table 3.

Table 3. Prevalence of DDI in inpatients

Ward	No. of prescription (%)
Internal Medicine	81(30.7)
CCU and ICU	86(32.6)
Gynecology	37(14)
Neurology	20(7.6)
Surgery	30(11.4)
Urology	10(3.8)
Sum	264 (100)

Figure 4 shows the different types of DDIs within each ward in Azadi Teaching Hospital. 86% of prescriptions in CCU and ICU had at least one drug interaction. The mean items per prescription were 5.9 in the prescriptions of these wards. The relationship between the number of items per prescription and the number of DDIs observed was very significant (P<0.001).

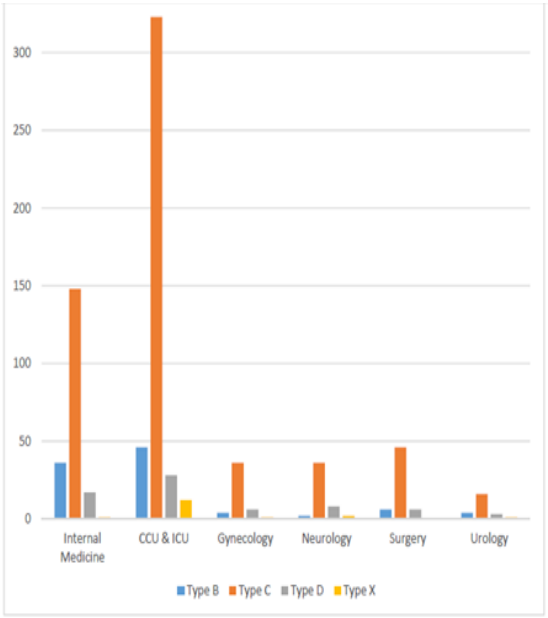

Figure 4. Types of DDIs in prescriptions from different wards

DISCUSSION

In this study, we found that the overall frequency of potential DDIs observed in prescriptions (both in community and hospital pharmacies) in Duhok city, Kurdistan Region, Iraq, was almost 53%. Which is far higher than the frequency observed in many western studies [12, 22, 26], and still higher than some studies in the neighborhood for example in eastern Iran and Kurdistan province, Iran [27, 28].

This broad range of prevalence rate may be in particular linked to factors such as study design, methodology, definitions, and characteristics of the population, number items per prescription, and corpus of drug interactions.

According to our results, the global popularity of DDIs was higher in hospital pharmacies than in community pharmacies; this potential variation may be linked to the point that in health-care unit patients usually have more critically-ill conditions and morbidities which might potentially require multiple medications, while consequently probability of drug interactions will increase. Also dealing with more severe diseases and more efficient drugs with lower therapeutic index, therefore, more serious side effects and interactions.

Polypharmacy is a pivotal agent which leads to DDIs, the more drugs per prescribed orders, the more the probability of drug-drug interactions occurrence. Our study confirmed that almost all prescriptions had 3-4 drug items per written orders (average of 4.1 items per prescription). Compared to our locality, in Iran healthcare provider settings has reported that the mean items of drug per written orders were 3.2 in 2007; [29] however, it is decreasing but is at standstill higher than other region in the world with an average of 1.3-2.1 items per prescription [29].

Correspondingly, according to the results of some studies, the occurrence potential drug interactions for patients receiving more than two drugs range from 24.3% to 42% [30], therefore, the greater the number of drugs, the higher the possibility of DDIs.

In the hospital setting, the mean items per prescription were 5.9; this number was 6.7 for ICU and CCU, which had the most drug interactions (86%). These specific results observed regarding the CCU and ICU wards are consistent with some studies like that of Askari et. al. which demonstrate that every ICU admission had on average 1.67 relevant potential DDIs [18], and the study performed by Vanham et. al. [31] which pointed to the challenge of potential DDIs in the majority of ICU patients (79%).

The commonest kinds of interaction happened in our study was type C, accounting for 74% of all interactions demonstrated regarding the settings. Type C drug interaction will not cause any comorbid or fatal complication and only need monitoring. Only 2.7% of all interactions were reported to be type X interactions but is a considerable ratio. Subsequent studies reported a high rate of major potential drug interactions, ranged from 0.83% to 17% [32].

Our results indicate that patients in Duhok city, Iraq, are in a danger of adverse drug reactions due to potential DDIs; however, we did not identify determinants of drug interactions by pharmacies in this study, but possible causes such as lack of knowledge about the DDIs or patient medication history, also lack communication between primary and secondary health care providers or between the prescribers and patients could be the reasons for the dispensing of unsuitable drug combinations.

Thus, adherence to the correct policies of writing prescriptions, reduce the number of prescribed medications, promoting physicians' awareness about potentially serious DDIs, for example, by participating in related technical courses could help reduce the percentage of drug interactions. Furthermore, an appropriate computerized surveillance programme for follow-up drug interaction should be invented. Pharmacists can also play a central role in the detection and prevention of drug‐related events and reducing the percentage of DDI and its related hazardous consequence. Patients with chronic diseases [33-36] (Cardiovascular diseases or diabetes or neurological diseases or cancers) are already on drug-use and represent the most challenging group for DDIs that's because addition of new agents could initiate or propagate the harm of the already existed drugs. Finally, some systemic diseases could vitiate the side effects especially endocrine diseases (thyroid and diabetes).

CONCLUSION

The study concluded that more than half of the dispensed prescriptions had on minimum one potential serious drug interaction, and the highest percentage of the DDIs belong to type C which requires only monitoring. However, type X interaction was also observed in a relatively high percentage. Drug interaction shown in prescriptions dispensed in the Hospital setting was significantly higher than that in the community pharmacies. The rate of DDIs is significantly correlated with the rate of items per prescription. The higher the items prescribed, the more probability for the occurrence of DDIs. CCU and ICU wards are the source of the high percentage of potential and sometimes dangerous DDIs compared with other wards.

ACKNOWLEDGMENT

The authors are very grateful to the College of the Pharmacy/University of Duhok, the Staff of Azadi Teaching Hospital, and community pharmacies for their cooperation to fulfill this research.

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