

Drug Interactions Prevalence: A Review

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Abstract

Aim: To study the prevalence of drug interactions in hospital settings and its comparison in various countries of the world by literature survey.

Method: A review was carried out of the articles published between 2003 and 2013. Various search terms with different combinations were used like Drug interactions, Prevalence, Hospital and ICU.

Results: The percentage of interactions varied greatly between patients admitted in the critical units as compared to the patients admitted in general wards of the hospital from 70 - 73% potential drug interactions being reported in critical care units as compared to general wards having a maximum of upto 50% potential drug interactions. Also, there was seen a slight increase in the percentage of potential drug interactions at the time of discharge of patients from the hospitals as compared to those reported at the time of admission.

Conclusion: Many studies have been conducted on the prevalence of drug interactions with reports varying widely. Also, the incidence of drug interactions seems to be low in countries having advanced health care monitoring systems.

Keywords: Drug Interactions; ICU

Introduction

Advancements in medical technology has provided drugs which are important for the provision of treatment and care to the population. Pharmacotherapy has become very complex due to the co-administration of many drugs of different therapeutic classes in order to treat these diseases. This has led to the use of many drug combinations which interact with each other [1,2]. A drug interaction, thus is an interaction between a drug and another substance (which may be a drug, a food substance or any other substance used with the drug) that prevents the drug from performing as expected [3]. In terms of mechanism, drug interactions are often characterized as being either pharmacokinetic or pharmacodynamic. Pharmacokinetic interactions influence the disposition of a drug in the body and involve the effect of one drug on absorption, distribution, metabolism and excretion of another one. Pharmacodynamic interactions are related to the pharmacological activity of the interacting drugs. They do not involve changes in serum concentration of drugs [4]. Potential for drug-drug interaction arises when a patient consumes two or more drugs. These kind of multiple drug regimens are on rise due to which the risk of adverse interactions has increased [5,6]. Similarly drug interactions have been reported to be more frequent in elderly patients, in patients who have longer stay in hospitals and patients who receive many drugs [7]. Martinbiancho, *et al.* [8] reported that drug interactions appear in 3 to 5% of patients who receive few drugs but when 10 or more drugs are prescribed, the frequency of interactions increases significantly.

An intensive care unit (ICU) of a hospital has high frequency of medications received by patients because the physicians target on treating the critical condition of the patient. Therefore, it's rational to expect a high probability of pharmacokinetic interactions in ICU prescriptions [9]. In ICU, studies have disclosed that potential drug interactions may occur in 44.3 to 95% of patients [10-13].

Methods

The authors conducted a review of the literature focusing on drug interaction studies in hospitals using Science Direct and Pubmed database published from 2003 to 2013 using relevant keywords. (drug interactions in hospital, drug interactions in critical care units, prevalence of drug interactions in hospitals, prevalence of drug interactions in critical care units, prevalence of drug interactions in ICU, drug interaction in ICU, irrational use of drugs in critical care). All the results which were available free were screened and review articles and abstracts were excluded. Abstracts were not considered as they did not contain complete results. Furthermore, the bibliographies of review articles were also screened for other relevant literature.

This review was done to get an overall picture of the prevalence and incidence of drug interactions at tertiary care hospitals in various countries.

Prevalence of drug interactions and the drug pairs involved in interaction varies greatly in different countries due to the variation in factors like different population, prescribing habits of prescribers, variation in nature of diseases, variation in drugs prescribed and difference in treatment strategies.

Drug interactions at hospital admission, stay and discharge

According to various studies, drug interactions increase after admission to hospital and at the time of discharge as compared to the time of admission (Figure 1). This may be due to change of medication during stay at the hospital. A study reported that the percentage of patients presenting a potential drug-drug interaction increased from 48% to 60% from the time of admission to the time of discharge of the patient. This study included 500 patients and at the time of admission 240 patients had a potential drug interaction while at discharge 300 patients had a potential drug interaction. This study reported a median of 2 potential drug interactions per patients [14]. Another study also reports a rise in drug interactions at the time of discharge. This study reported that at the time of admission 68.7% patients had potential drug-drug interactions where the maximum number of drug interactions per patient were 16, while at the time of discharge this increased to 69.6% and the maximum number of drug interactions per patient also rose to 17. Although this is only a slight increase but there was a significant rise in drug interactions during the patient's stay at the hospital. It was reported that 73.9% patients had some potential drug-drug interactions during the stay at the hospital. During the patient's stay at the hospital the maximum number of drug interactions reported were 22 [15].

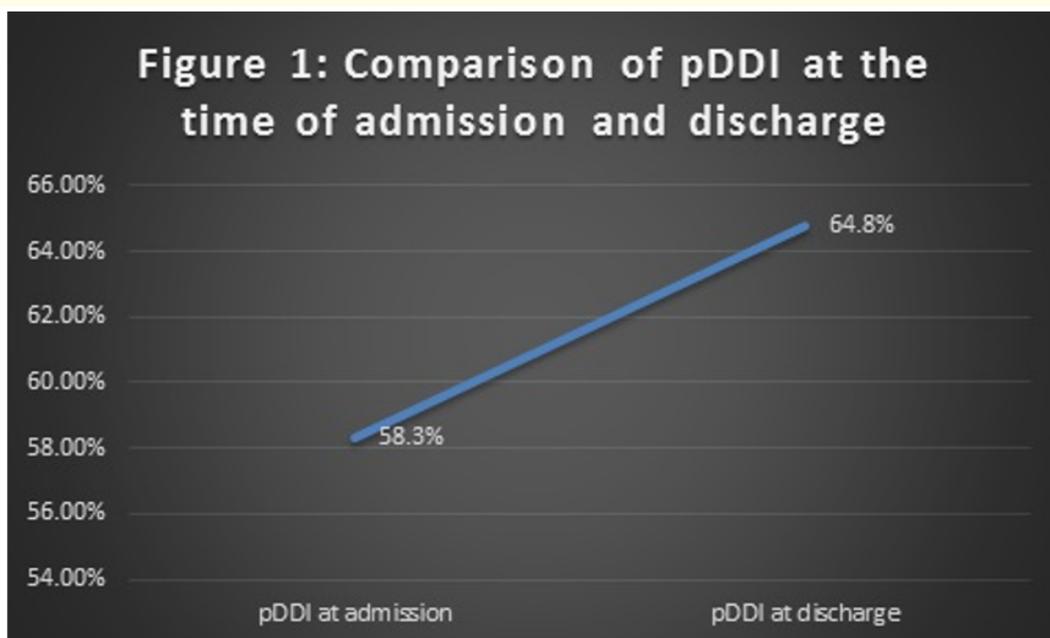


Figure 1: Comparison of pDDIs at the time of admission and discharge.

Drug interactions in critical care units

Critical care units reported a higher incidence of drug-drug interactions (Figure 2). A Brazilian study of critical care units, in which 1069 prescriptions were analyzed, reported 775 (72.5%) prescriptions had drug interactions with 419 (39.2%) having at least one significant drug interaction. Of these interactions 51.6% had a delayed onset of action while 48.4% had an early onset. 39.7% of the interactions had a minor severity while 50.4% had moderate and 9.8% had major severity [16]. Andriano, *et al.* [15] also reported in a study conducted at an ICU of a university teaching hospital in Brazil that drug interactions occurred in 70% of the prescriptions of which interactions having delayed onset were most prevalent. In another study which was conducted in the ICU of seven teaching hospitals in Brazil, 70.6% patients had at least 1 potential drug interaction with 36.5% interactions were of major severity and 50.1% of moderate severity [30]. A study in Iran also showed similar results. This study involving 567 prescriptions reported that 72% of prescriptions (413 prescriptions) had an interaction, with 61% having a delayed onset, 17.4% were having a severity of major interactions and 73.6% had moderate severity (Table 1). Moreover, a positive relationship between number of prescribed drugs and frequency of interactions was reported in this study. ($P < 0.0001$) [9]. Giti Hajebi, *et al.* [17] also reported in their ICU study that in 3130 prescriptions, a total of 3960 interactions were found in which 55.8% interactions were of delayed onset of the total interactions and 47.2% interactions had moderate severity. While a complete opposite result was found in a cancer center in USA which showed the incidence of major drug interactions to be only 7.3% in the 275 patient studied at their ICU [29].

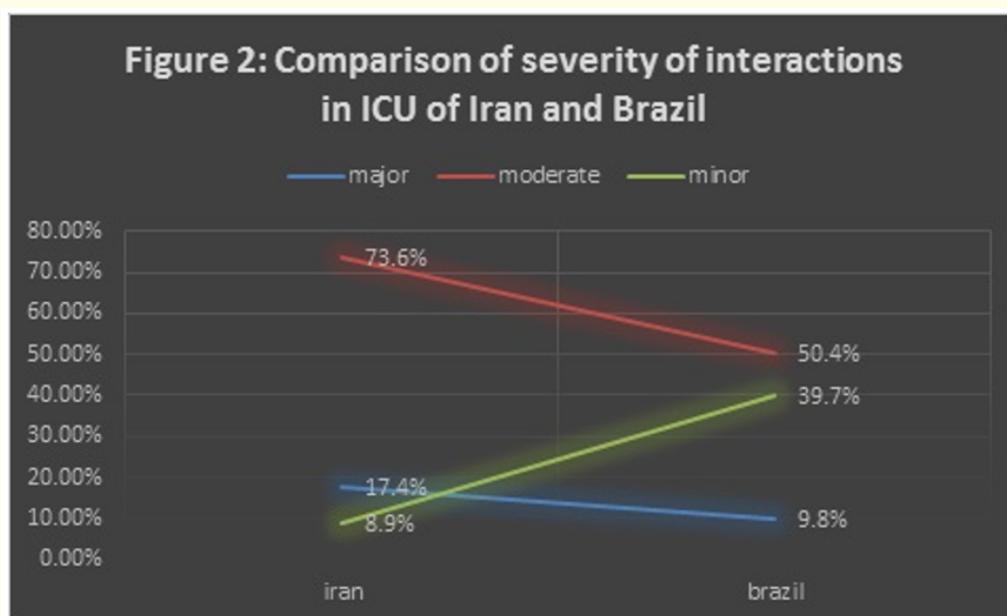


Figure 2: Comparison of severity of interactions in ICU of Iran and Brazil.

	Brazil	Iran
Total Interactions	72.5%	72%
Delayed onset	51.6%	61%
Major severity	9.8%	17.4%
Moderate severity	50.4%	73.6%

Table 1: Interactions in critical care units.

Drug interactions in hospital wards

Moving away from the critical care units of a hospital, a different picture of prevalence of drug interactions come into view (Figure 3). According to a study in a hospital in Brazil, 49.7% prescriptions reported drug interactions. 1785 prescriptions were analyzed in this study. Of these 234 (26.4%) prescriptions had only one potential drug interaction while 653 (73.6%) had more than one DDI. Prevalence of drug interactions increased with the age of the patient and the number of prescribed drugs [18]. A study conducted in Uganda identified 75 potential drug-drug interactions in 235 prescriptions. This study showed almost similar results with 41 (17.4%) prescriptions having one potential drug interaction [19]. While prescriptions of a hospital in Italy reported only 5.5% drug interactions [20]. Another study in Italy reported that among 11% drug interactions in hospitalized patients with 9.5% having 2 interactions and 1.3% having three interactions. Age was a major contributor to the chances of exposure to drug interactions, where the risk of drug interaction increased at old age [21]. Potential drug interactions were reported to be 54% in study in Switzerland. Interactions were reported to be higher at the time of discharge of patients from hospital compared to the time of admission in this study [14]. Another study in Switzerland backed this result showing that potential drug interactions rise during stay of the patient in hospital and at the time of discharge as compared to the time of admission. Statistical analysis showed that only 30% of the patients had drug interactions at the time of admission to hospital, while this value raised to 56% during hospitalization and was 31% at the time of discharge [22]. A study in Thailand involving a total of 258951 prescriptions reported potential drug interactions in 72296 (27.9%) of the prescriptions [1]. A study involving 1000 prescriptions in an Iranian hospital, the overall prevalence of drug interactions was 20.3% [23]. Sajid Bashir, *et al.* [7] reported that interactions were found in 66.9% of prescriptions, with public sector showing much higher percentage of drug interactions as compared to the private sector. A total of 1420 prescriptions were collected in which 950 drug interactions were found.

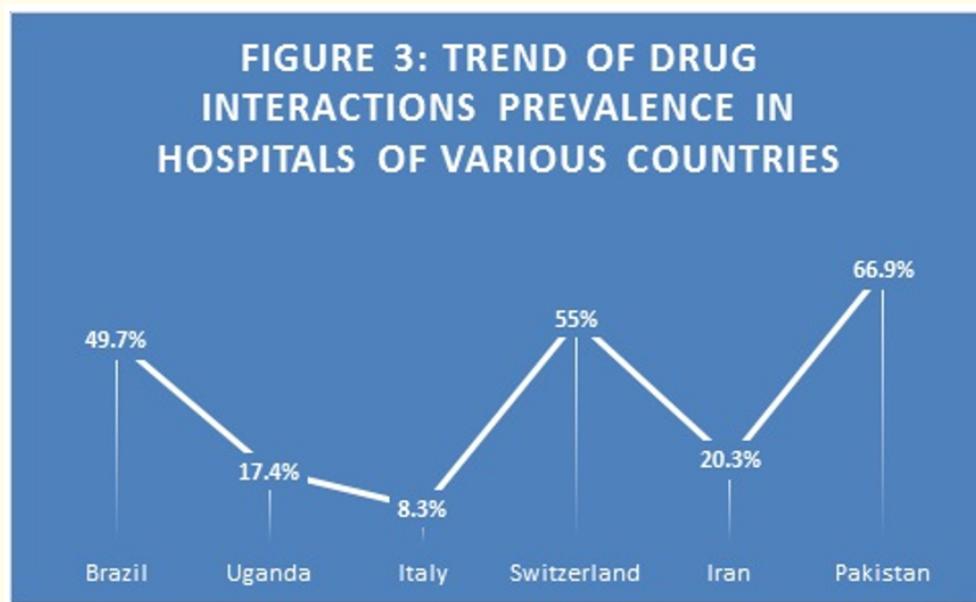


Figure 3: Trend of Drug-interactions prevalence in hospitals of various countries.

In HIV patients the incidence of drug interactions were also similar to the interactions found in hospitals. Two studies showed that potential drug interactions occurred in 40% and 65.2% in Switzerland and India respectively [24,25]. The study in Switzerland showed

that 599 of the total 1497 patients had a potential drug-drug interaction, while the Indian study showed that in 118 patients 77 patients suffered a drug interaction and a total of 175 drug interactions were detected in this study. In Singapore 4.7% drug interactions were found in prescriptions of oral anti-cancer agents, study included 8837 patients and 478 patients suffered a drug interaction [26]. The Eli Lilly safety database reported that 5.4% interactions occurred in patients who were given gemcitabine (anti-cancer drug) and anticoagulants concomitantly [27].

Commonly interacting drug pairs

Drugs which pertain the most risk to potential interactions include cardiovascular drugs, NSAID's, rifampicin, amikacin, diuretics, midazolam, anti depressants, phenytoin and anticoagulants [31-37]. As far as gender was considered there was a slight rise in potential drug interactions in the female population [29,30]. Age was also a factor contributing to the increase in potential drug interactions. People over the age of 55 years experienced more potential drug interactions as compared to other age groups.

Conclusion

Drug interactions are reported worldwide with varying percentages with many countries showing a high percentage of drug interactions. Critical care units have shown higher percentages of drug interactions as compared to general wards in hospitals. Similarly, elderly population also shows a high incidence of drug interactions owing to the fact that polypharmacy is higher due to the complexity of the disease condition of these patients. These drug-drug interactions lead to decreased therapeutic effectiveness, toxicity and other adverse effects. Most of these drug-drug interactions are usually preventable only by careful monitoring and intervention of pharmacists by making patient and situation specific decisions. Therefore, it is essential that health professionals be able to evaluate the potential for DDIs and, when detected, to determine appropriate prevention or management strategies.

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