

Original Article

STUDY OF POTENTIAL DRUG INTERACTIONS AMONG EIGHT MAJOR DEPARTMENTS- GENERAL MEDICINE, ORTHOPEDICS, GYNECOLOGY, PULMONOLOGY, GENERAL SURGERY, PSYCHIATRY, OTOLARYNGOLOGY AND DERMATOLOGY OF A TERTIARY CARE TEACHING HOSPITAL IN SOUTHERN INDIA

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ABSTRACT

Objective: To identify frequency, type, severity and predictors of potential drug-drug interactions (pDDIs), potential drug-food interactions (pDFIs), potential drug-alcohol interactions (pDAIs) and potential drug-tobacco interactions (pDTIs) and most frequently interacting drug combination pairs in hospitalized patients from departments (depts) of General Medicine (GM), Orthopedic (Ortho), Gynecology (OBG), Pulmonology (Pulmo), General Surgery (GS), Psychiatry (Psych), Otolaryngology (ENT) and Dermatology (Derm) of study population.

Methods: A Prospective Observational Study was conducted in eight major dept's of a tertiary care teaching hospital for a period of 6 mo. A sample size of 650 prescriptions reflecting admission no's for each department were used.

Results: A total of 650 patients were included in the study. Among them, 282 (43.4%) were males and 368 (56.6%) were females. The mean age of the study population was 39.67±15.23. A total of 487 pDDIs, 734 pDFIs, 586 pDAIs and 159 pDTIs were found out of 650 hospitalized episodes. OBG showed the highest pDDIs and pDAIs. Highest pDFIs and pDTIs were seen in Pulmo. The majority of DDIs were minor, DFIs and DAIs were moderate and DTIs were of major in severity. Pharmacokinetic types of interactions were seen in the majority of the depts. Logistic regression analysis showed that Polypharmacy was associated with the occurrence of DIs. Most of the DIs repeated several times in particular depts and a list of these combinations was prepared.

Conclusion: With the high occurrence of overall DIs and characteristic patterns of DIs combination pairs among different departments of the hospital, the presence of clinical pharmacists in hospitals can play a great role, especially in developing nations like India where their role in hospitalized settings is always controversial.

Keywords: Drug interactions, Drug-drug interactions, Drug-food interactions, Drug-alcohol interactions, Drug-tobacco interactions, Departments, Drug combination pairs, Clinical Pharmacist

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INTRODUCTION

Drug interactions (DIs) are one of the most common causes of adverse drug reactions and continues to be a public health challenge in both developed and developing countries in the world. These DIs can be defined as an alteration in the efficacy or toxicity of a drug caused by concomitant administration with other drugs, food, beverages, and other supplements [1]. With thousands of drugs available worldwide and a substantial increase in drug discovery processes, the range of possibilities for drug interactions is considerable. It is reported that elderly patients with their increased complexity of the disease and therapeutic regimen are more susceptible to the occurrence of DIs [2].

However, these DIs may also occur independently in patients of all age groups. As the pattern of medications received by patients of different age groups and in different departments in a hospital is more complex, it is not easy to estimate the occurrence of DIs accurately. The prescriptions having 3 or more drugs had increased from 11.8% in 1988-1994 to 20.08% in 2007-2010 and having 5 or more drugs have increased from 4% to 15.01% during the same time period in the United States [3, 4].

The mechanism implicated in the occurrences of DIs can be Pharmacokinetic (PK) with alteration in the absorption, distribution, metabolism, and excretion of object drug or Pharmacodynamic (PD) in which interaction is close to the target organ and has an additive or antagonistic effect on the pharmacological action of the object drug [5].

About 30% of all adverse drug events increasing the hospital stay and healthcare cost of patients are related to DIs [6, 7].

Therefore, reviewing the therapy by the clinical pharmacist based on the physiological conditions of the patient and considering the type of allergies, medication history, and social habits of the patient, the clinical pharmacist may play a key role in preventing different types of DIs and adverse events.

Not much data is available on the distribution pattern of DIs in different department's (dept's) of the hospital. There are several published data regarding the pattern of DIs in a particular department of the hospital or the overall interactions found in particular age groups [2, 8]. Further, the literature has mainly focused on drug-drug interactions (DDIs), while there are also risks of occurrence of DIs with food, alcohol, and tobacco [9-11]. There are some very well-known potential drug-food interactions that are potentially dangerous and may result in therapeutic failure. With an increasing population taking alcohol and tobacco, many drugs interact adversely with them. Hence this study aims to find out the frequency, type, severity, and predictors of potential drug-drug interactions (pDDIs), potential drug-food interactions (pDFIs), potential drug-alcohol interactions (pDAIs) and potential drug-tobacco interactions (pDTIs) and the most frequently interacting drug combination pairs in hospitalized patients from departments (depts) of General medicine (GM), Orthopedic (Ortho), Pulmonology (Pulmo), General Surgery (GS), Psychiatry (Psych), Otolaryngology (ENT) and Dermatology (Derm) of the study population, which will help the doctor to be aware of these

interactions when prescribing and a pharmacist working in clinical settings to gain a well-grounded knowledge in the prevention,

detection, and management of these interactions and contribute greatly to the patient's safety and wellbeing.

Table 1: Demographic profile of the patients from different departments of the hospital

S. No.	Parameters	Total no	%
1	Gender wise distribution		
	General Medicine		
	-Male	55	55%
	-Female	45	45%
	Orthopedic		
	-Male	45	45%
	-Female	55	55%
	Gynecology		
	-Male	0	0%
	-Female	100	100%
	Surgery		
	-Male	50	50%
	-Female	50	50%
	Otolaryngology		
	-Male	39	39%
	-Female	61	61%
	Pulmonology		
	-Male	35	70%
	-Female	15	30%
	Psychiatry		
	-Male	33	66%
	-Female	17	34%
	Dermatology		
	-Male	25	50%
	-Female	25	50%
2	Age wise distribution		
	General Medicine		
	18-30years	28	28%
	31-60years	60	60%
	>60years	12	12%
	Orthopedic		
	18-30years	24	24%
	31-60years	71	71%
	>60years	5	5%
	Gynecology		
	18-30years	58	58%
	31-60years	42	42%
	>60years	0	0%
	Surgery		
	18-30years	21	21%
	31-60years	68	68%
	>60years	11	11%
	Otolaryngology		
	18-30years	30	30%
	31-60years	60	60%
	>60years	10	10%
	Pulmonology		
	18-30years	10	20%
	31-60years	28	56%
	>60years	12	24%
	Psychiatry		
	18-30years	12	24%
	31-60years	33	66%
	>60years	5	10%
	Dermatology		
	18-30years	29	58%
	31-60years	19	38%
	>60years	2	4%

MATERIALS AND METHODS

Methodology

The research was conducted in a tertiary teaching hospital, Bhaskar General Hospital, for a period of 6 mo (i.e. June 2019-November 2019) in GM, OBG, Ortho, GS, Pulmo, ENT, Psych, and Derm depts.

Type of study

Prospective Observational Study.

Study design

The data was collected from the patient's medical record or medical profile sheet for a duration of 6 mo from 8 different departments in a tertiary care hospital. The data collected from the patient's medical record included demographic details of patient, chief complaint, history of present illness, lab investigations, past medical conditions, medical or any potential allergic history, final diagnosis, day-wise medication therapy with their dose, frequency, route, duration of therapy and dosage-form.

Consent was obtained from all subjects before the study. All data were collected and analyzed for this study.

Inclusion criteria were patients of both gender aged more than 18 y with complete clear data and exclusion criteria were patients with less than 18 y old and prescription with unclear data.

A total of 650 prescriptions with 100 prescriptions each were from GM, Ortho, OBG, GS, and ENT, and 50 each from Psych, Pulmo, and Derm depts reflecting admission numbers for each dept were assessed for pDIs.

As the minimum sample size recommended by the W. H. O. is 600, the current sample size was considered as an appropriate sample size for this study.

Study measures

pDDIs, pDFIs, pDAIs, and pDTIs were detected using the drug interaction checking software tool Micromedex®-2.7 and www.drugs.com database.

Statistical analysis

For categorical variables, frequency/percentages were calculated, and continuous variables were expressed as mean±SD. The binary logistic regression model was used to analyze the association of occurrence of pDIs with specified risk factors, including gender, age, and the number of drugs prescribed. P<0.05 and P<0.01 were considered statistically significant and highly significant, respectively. All statistical analyses were done using the SPSS software database. Bar diagrams, tables, and charts were created using Microsoft Excel 2010 version to depict percentages and averages.

RESULTS

A total of 650 patients from eight different departments of the hospital were included in the study. Among them, 282 (43.38%) were males and 368 (56.61%) were females. The demographic profile of the patients is shown in table 1. The mean age of the study population was 39.67±15.23. The mean number of medications received per prescription in each dept is shown in fig. 1.

The mean no of potential DIs per prescription in each dept is shown fig. 2.

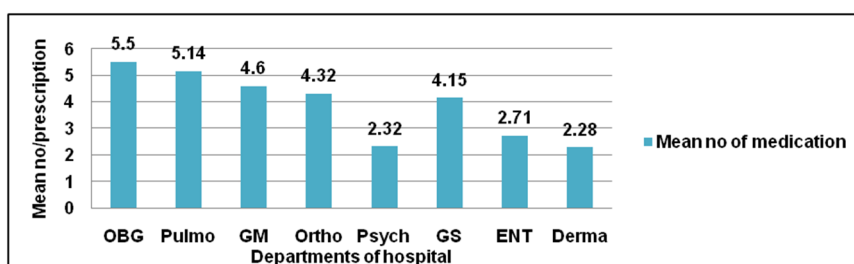


Fig. 1: Mean no of medication per prescription in each department

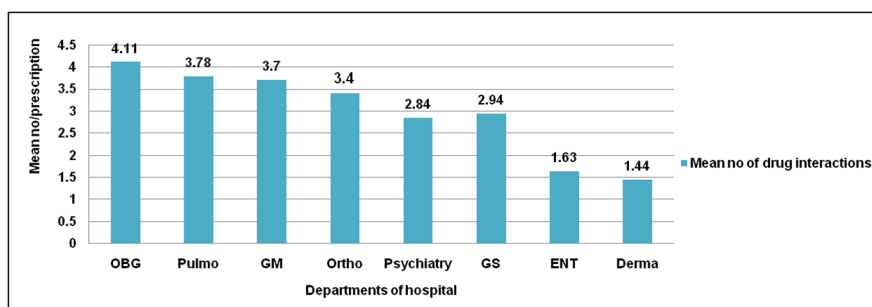


Fig. 2: Mean no of DIs per prescription in different departments of hospital



Fig. 3: An outline of the whole study

A total of 487 pDDIs, 734 pDFIs, 586 pDAIs and 159 pDTIs were seen in 650 prescriptions from GM, OBG, Ortho, ENT, GS, Psych, Pulmo and Derm depts of a tertiary care teaching hospital. Fig. 3 provided an outline of the whole study.

The fig. 4 demonstrates the occurrence of pDDIs, pDFIs, pDAIs and pDTIs among different depts of hospital. The OBG and Pulmo dept has significantly higher DIs when compared to the other 6 depts. The Derm and ENT depts have the least number of DIs.

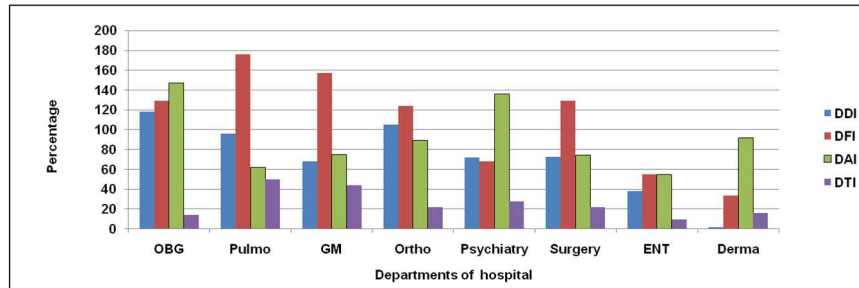


Fig. 4: Comparison of DIs in different departments of hospital

DDIs among different depts were the majority of moderate and minor types (fig. 5).

Except psychiatry, moderate type of DFI were predominantly seen in all depts (fig. 6).

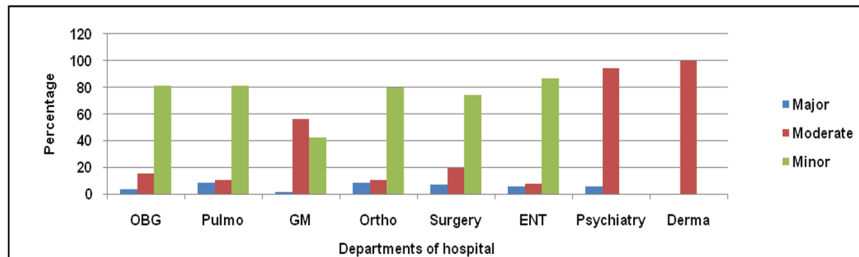


Fig. 5: Severity of DDI in different departments of hospital

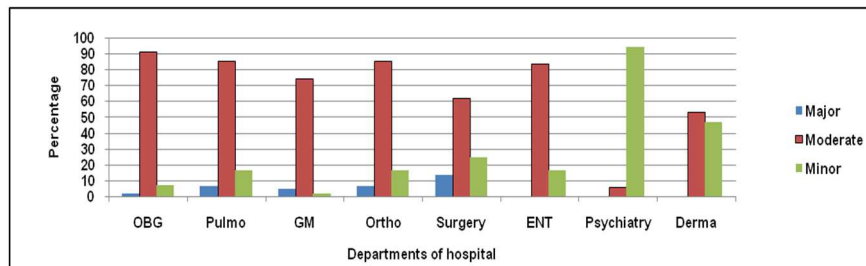


Fig. 6: Severity of DFI in different departments of hospital

The severity of DAI also followed a similar trend with moderate type predominating in all depts except medicine and surgery where

major DAI are of a major type. Many contraindicated types of interactions have also been identified in various depts (fig. 7).

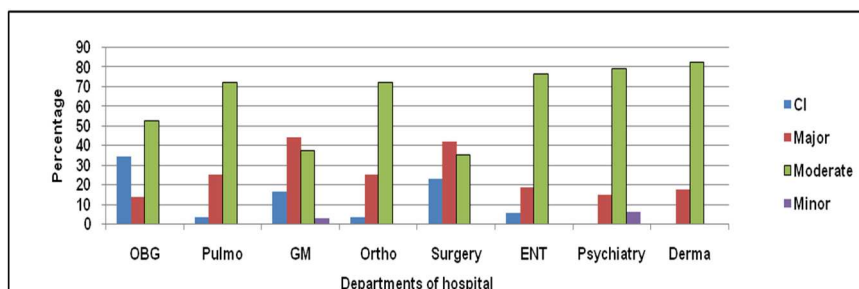


Fig. 7: Severity of DAI in different departments of hospital

All the depts had the majority of major type of DTI (fig. 8).

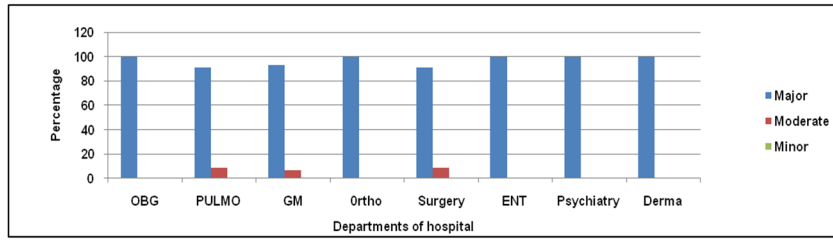


Fig. 8: Severity of DTI in different departments of hospital

No significant difference among males and females with regard to severity of DIs were observed.

The majority of DIs in different depts. of hospitals were PK in nature, except for the variations in dermatology and psychiatry (fig. 9).

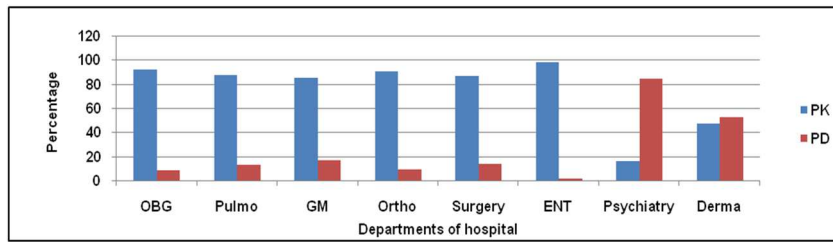


Fig. 9: Distribution of PK and PD interactions in different departments of hospital

Logistic regression analysis showed a significant correlation with regard to the mean number of medications per prescription and

mean no of potential DIs among different depts. of the hospital. (r=0.88, p=0.003488) fig. 10

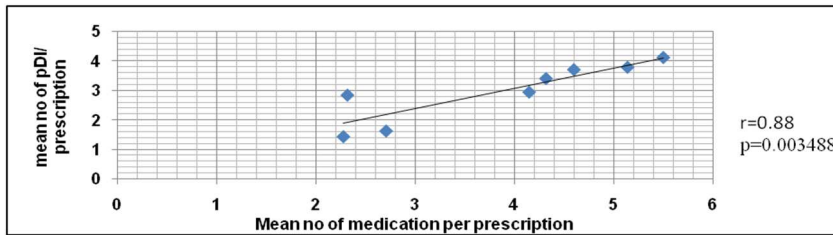


Fig. 10: Relationship between mean no of medications per prescription and mean no of DI per prescription

There were no significant differences with regard to the age of patients and gender with number of DIs seen.

Table 2,3,4, 5 shows the most common DI pairs in all the eight depts of the hospital.

Table 2: Most common DDI pairs in all the eight departments of the hospital

Department	Drug-drug combination pairs	No. of cases	Severity	Consequences of DDIs
General medicine	a.) Ceftriaxone+Diclofenac	7, 4, 4	Minor,	Increase concentrations of diclofenac,
	b.) Atorvastatin+Pantoprazole		Moderate	Increase blood levels of atorvastatin,
	c.) Clopidogrel+Pantoprazole		Moderate	Decrease effectiveness of clopidogrel
Orthopedic	a.) Ceftriaxone+Diclofenac	35, 6, 2	Minor, Major	Increase concentration of diclofenac
	b.) Diclofenac+Acetoclofenac		Moderate	Increased risk of bleeding, Increased blood levels of methotrexate
	c.) Methotrexate+Prednisolone			
Gynecology	a.) Ceftriaxone+Diclofenac	40, 2, 2	Minor,	Increase concentration of diclofenac,
	b.) Amikacin+Ceftriaxone		Moderate Major	Increases risk of kidney damage. Agitation
	c.) Tramadol+Ondansetron			
Surgery	a.) Ceftriaxone+Diclofenac	28, 4, 2	Minor Moderate	Increase concentration of diclofenac,
	b.) Amikacin+Ceftriaxone		Moderate	Increases risk of kidney damage Increase risk of bleeding
	c.) Aspirin+Clopidogral			
Otolaryngology	a.) Ceftriaxone+Diclofenac	10, 2	Minor, Major	Increase concentration of diclofenac, QT interval prolongation
	b.) Azithromycin+Moxifloxacin			
Pulmonology	a.) Azithromycin+Levalbuterol	5, 4, 4	Moderate	QT interval prolongation, Hypokalaemia and
	b.) Theophylline+Budesonide		Moderate	Increase T levels, Hypokalemia and ECG changes.
	c.) Levalbuterol+Furosemide		Moderate	
Psychiatry	a.) Olanzapine+Valproate	6, 6, 6	Moderate	Decrease in olanzapine plasma concentration,
	b.) Risperidone+Olanzapine		Moderate	Increase side effects like drowsiness, blurred vision, Increase side effects like drowsiness, blurred vision.
	c.) Clonazepam+Paroxetine		Moderate	
Dermatology	a.) Hydroxyzine+Cetirizine	1	Moderate	Increase side effects like dizziness, drowsiness

Table 3: Most common DFI pairs in all the eight departments of the hospital

Department	Drug-food combination pairs	No. of cases	Severity	Consequences OF DFIs
General medicine	a.)Pantoprazole+Cranberry	44	Moderate	Reduced effectiveness of pantoprazole
	b.)Acetaminophen+Cabbage/Food	27	Moderate, Minor	Decreased acetaminophen effectiveness.
	c.)Furosemide+Food	10	Moderate	Decreased furosemide efficacy
Orthopedic	a.)Acetaminophen+Cabbage/Food	18	Moderate, Minor	Decreased acetaminophen effectiveness.
	b.)Cranberry+Ranitidine	57	Moderate	Reduced effectiveness of ranitidine.
Gynecology	a.)Cranberry+Ranitidine	75	Moderate	Reduced effectiveness of ranitidine.
	b.)Food+Ampicillin	15	Moderate	Decreased ampicillin concentrations
Surgery	a.)Cranberry+Pantoprazole	51	Moderate	Reduced effectiveness of pantoprazole.
	b.)Cranberry+Ranitidine	22	Moderate	Reduced effectiveness of ranitidine.
	c.)Grapefruit+Tramadol	16	Major	Increased tramadol plasma concentration
Otolaryngology	a.)Cranberry+Ranitidine	25	Minor	Decreased effectiveness of ranitidine
	b.)Acetaminophen+Cabbage/Food	10	Moderate, Minor	Decreased effectiveness of acetaminophen.
Pulmonology	a.)Acetaminophen+Cabbage/Food	21	Moderate, Minor	Decrease effectiveness of acetaminophen.
	b.)Theophylline+Caffeine	12	Moderate	Increased theophylline plasma levels.
	c.)Theophylline+Food	12	Moderate	Altered theophylline concentration
Psychiatry	a.)Chlordiazepoxide+Caffeine	17	Minor	Decreased effect of chlordiazepoxide
	b.) Clonazepam+Caffeine	10	Minor	Decreased effects of clonazepam.
Dermatology	a.)Acetaminophen+Cabbage/Food	8	Moderate, Minor	Decreased acetaminophen effectiveness.

Table 4: Most common DAI pairs in all the eight departments of the hospital

Department	Drug-alcohol combination pairs	No. of cases	Severity	consequences of DAIs
General medicine	a.) Acetaminophen+Alcohol	27, 15, 12	Major	Increased risk of hepatotoxicity, Increased bioavailability of alcohol, Disulfiram like reaction
	b.) Ranitidine+Alcohol		Moderate, C. I.	
	c.) Metronidazole+Alcohol			
Orthopedic	a.) Ranitidine+Alcohol	57, 18	Moderate	Increased bioavailability of alcohol, Increased risk of hepatotoxicity
	b.) Acetaminophen+Alcohol		Major	
Gynecology	a.) Metronidazole+Alcohol	50, 75	C. I, Moderate	Disulfiram like reaction, Increased bioavailability of alcohol
	b.) Ranitidine+Alcohol			
Surgery	a.) Ranitidine+Alcohol	22, 17, 16	Moderate, C. I.	Increased bioavailability of alcohol, Disulfiram like reaction, Increased risk of respiratory depression
	b.) Metronidazole+Alcohol		Major	
	c.) Tramadol+Alcohol			
Otolaryngology	a.) Acetaminophen+Alcohol	10, 25	Major	Increased risk of hepatotoxicity, Increased bioavailability of alcohol
	b.) Ranitidine+Alcohol		Moderate	
Pulmonology	a.) Ranitidine+Alcohol	6, 21	Moderate	Increase bioavailability of alcohol. Increased risk of hepatotoxicity
	b.) Acetaminophen+Alcohol		Major	
Psychiatry	a.) Chlordiazepoxide+Alcohol	17	Moderate	Increased sedation
	b.) Olanzapine+Alcohol	12, 10	Moderate	Excessive C. N. S. depression, Increased sedation
	c.) Clonazepam+Alcohol		Major	
Dermatology	a.) Levocetirizine+Alcohol	36	Moderate	Increase nervous system side effects of levocetirizine

Table 5: Most common DTI pairs in all the eight departments of the hospital

Departments	Drug-tobacco combination pairs	No. of cases	Severity	Consequences of dtis
General medicine	a.) Acetaminophen+Tobacco	27	Major	Decreased exposure of CYP1A2 substrates
	b.) Ondansetron+Tobacco	12	Major	Decreased exposure of CYP1A2 substrates
Orthopaedic	a.) Acetaminophen+Tobacco	18	Major	Decreased exposure of CYP1A2 substrates
	b.) Ondansetron+Tobacco	6	Major	Decreased exposure of CYP1A2 substrates
Gynecology	a.) Acetaminophen+Tobacco	8	Major	Decreased exposure of CYP1A2 substrates
	b.) Ondansetron+Tobacco	6	Major	Decreased exposure of CYP1A2 substrates
Surgery	a.) Acetaminophen+Tobacco	14	Major	Decreased exposure of CYP1A2 substrates
	b.) Ondansetron+Tobacco	6	Major	Decreased exposure of CYP1A2 substrates
Otolaryngology	a.) Acetaminophen+Tobacco	10	Major	Decreased exposure of CYP1A2 substrates
Pulmonology	a.) Acetaminophen+Tobacco	21	Major	Decreased exposure of CYP1A2 substrates
	b.) Theophylline+Tobacco	12	Major	Decreased exposure of CYP1A2 substrates
Psychiatry	a.) Olanzapine+Tobacco	8	Major	Decreased exposure of CYP1A2 substrate
Dermatology	a.) Acetaminophen+Tobacco	21	Major	Decreased exposure of CYP1A2 substrates

DISCUSSION

DI, resulting in adverse drug events present a growing concern in healthcare settings. The patient requirement for multiple drug therapy, types of food intake, alcohol and tobacco habits, and the type of disease the patient is suffering from may result in decreased therapeutic benefit, adverse effect, or patient harm through a phenomenon called "Drug Interaction" [12].

In our sample size of 650 patient's medication profile, in which 282(43.38%) were males and 368(56.61) were females. An increase in the female patient's proportions could be due to n=100 female patients from the gynecology dept. The mean age of the study population was 39.67±15.23. There was no statistically significant difference among the mean age of patients in various depts and with respect to gender. Mean no of medication per prescription in different depts of the hospital are given in fig. 1, with the highest number obtained from OBG (5.5±1.38). These numbers were less

than the mean number of medications per prescriptions among geriatric patients (6.53 ± 1.15) as reported by Varsha Shetty, *et al.* [2].

In our study, a total of 487 pDDIs were found in 650 patient medication profiles, with the highest number of pDDIs from OBG dept followed by Ortho, Pulmo, GS, Psych, GM, ENT and Derm having the least pDDIs. The highest number of pDDIs from OBG is in contrast from the study conducted by Lubinga SJ, *et al.* [13] which showed the less occurrence of pDDIs in OBG. As rightly stated by Ferracini A, *et al.* [14] during hospitalization, pregnant and breastfeeding women use a complex pharmacotherapy with many drugs prescribed, and hence their prescriptions are more susceptible to pDDIs. Pulmo, the second-highest contributor for pDDIs were having 48 pDDIs in 50 patients. A total of 29 patients (58%) in the Pulmo dept were having pDDIs pair contributing to a total of 48 pDDIs. A single prescription with 8 pDDIs and two prescriptions having 6 pDDIs each were identified. The higher occurrence of pDDIs in Ortho and GS is in accordance with the study conducted by Ramya Balaprabha G, *et al.* [15] with the use of antibiotics, analgesic and polypharmacy having contributed to these significantly higher numbers of pDDIs. In our study, the GM ward was having a moderately significant higher pDDIs. These could be due to variations in the study setting, number, and type of comorbidities as well as by the prescribing culture of the physician. However, the overall interaction rate was significantly higher in these depts. A total of 30 patients had contributed to 38 pDDIs in ENT. Lack of practical data was seen in the analysis of pDDIs in the ENT dept. As stated by Woron J, *et al.* [16] concomitant use of drugs at the same time can lead to as high as 55% cases with DDIs in ENT dept. The least number of pDDIs in Derm dept were in accordance with the study conducted by Ramya Balaprabha G, *et al.* [15]. Pulmo (10%), Ortho (9%), and GS (5%) were having a higher number of major pDDIs. The majority of DDIs were moderate and minor in severity. The majority of interactions were PK in nature in accordance with the study conducted by Dais D, *et al.* [17]. Metabolism types of DDIs were predominant and were associated with the induction and inhibition of drug-metabolizing enzymes.

We noticed that many of the drugs given during the hospital stay of the patient were repeated in the discharge summary chart, which the patient takes at home. Therefore, there is a high possibility of the patient taking medicine with certain food and beverages that may result in adverse consequences.

It was observed that not much importance is given by the physician with regard to DFIs when writing a prescription. These interactions constitute a common hidden problem encountered in clinical practice. pDFIs either decrease the action of drugs or increase the action of drugs or cause adverse effects [9]. We, therefore, aim to evaluate the pDFIs occurring among different departments of hospitals.

A total of 734 pDFIs were found in 650 patient's medical records. The highest occurrence of DFIs was found in Pulmo dept with 88 pDFIs were found in 50 patient's medication chart, was in accordance with the study conducted by Ramalingam K *et al.* [16]. The GS, OBG, and Ortho had a significant higher number of pDFIs. Psych dept had moderately high pDFIs, with caffeine being the major reason for causing an additive pharmacodynamic interaction with psychiatric medications. The ENT and Derm had relatively less number of pDFIs.

The majority of pDFIs were of moderate severity (73.16%). The study conducted by an Indian author among hospitalized cardiac patients also revealed a maximum number of DFIs were of moderate severity [18]. 92.64% of DFIs were PK in nature. Every intake of food may have a significant impact on the process of absorption, distribution, metabolism, and elimination relating to the higher occurring of PK DFIs [19].

The use of alcohol is common among both young and adults, males and females. Alcohol consumption in India amounted to about 5.4 billion liters in 2016 and was estimated to reach about 6.5 billion liters by 2020 [20]. These numbers could be much higher for the rest of Asia and other countries globally. Despite this high prevalence, only a few physicians discuss alcohol use with their patients [21].

In our study, a total of 586 pDAIs were found in a total of 650 patient's medical records. The highest number of pDAIs was found in OBG. This is of significant importance since alcohol consumption by pregnant women can have serious adverse effects on both the mother and the fetus. A survey conducted by CADD among 5,000 Indian women aged between 17-80 y, revealed an increase in the rate of women drinking alcohol in India which could be due to peer pressure, exposure to a different lifestyle, and increased stress [22]. Therefore, the utmost caution should be given by the physician and pharmacist to the pregnant mother about alcohol-drug interactions that can have potential adverse life-threatening outcomes. The psychiatry department has the 2nd highest pDAIs with 46 (92%) of patients having at least 1 DAIs. As stated by Cheng C, *et al.* [23], individuals with mental health disorders are particularly vulnerable because of their psychotropic medications, which are typically taken for extended periods and are known to have PK and PD interactions with alcohol. The least number of pDAIs were found in the ENT dept. A major point to be noted is 34.01%, 22.97%, 16%, 5.45%, and 3.37% patients in OBG, GS, GM, ENT, and Ortho respectively had pDAIs which are contraindicated. The majority of pDAIs were PK type (70.81%), this could be explained by the metabolism of alcohol by the alcohol-dehydrogenase enzyme in the liver and CYP450 enzyme's mainly CYP2E1 [21]. Psych and Derm had a higher number of PD type of pDAIs involving an increased risk of ADE or an increased susceptibility to the medication effects.

Cigarette smoking remains highly prevalent in most of the countries. There are approximately 120 million smokers in India. According to WHO, India is home to 12% of the world's smoker's population [24]. Cigarette smoking induces several cytochrome enzyme's preferably CYP450 enzymes, notably, CYP1A2. Medications metabolized by CYP1A2 will have a shorter duration of action [25].

A total of 159 pDTIs were seen in a total 650 patient's medical profiles. An interesting finding is a total of only 10 pDTIs pair were seen in 650 patient's which had contributed to a total of 159 pDTIs. 98.44% of pDTIs were of PK in nature. 95.59% were found to be Major in severity. This impact of cigarette smoking needs to be considered in planning and assessing response to drug therapy.

These interactions are difficult to observe clinically in patients because of shorter hospital stays of patients, incomplete information given by the patient to the doctor or pharmacist and the complexity of PK parameters to assess.

Clinically relevant measures that can be taken to possibly avoid drug interactions

- Concurrent use of Ceftriaxone and Diclofenac in prescriptions by the physician in many departments was seen. Although the interaction is minor and clinically not observed much, the interaction has exaggerated hemodynamically mediated Acute Renal Failure in a post-surgical patient [26]. Therefore, the patient's on this combination therapy should be monitored for renal functions-particularly volume-depleted patients, and can be avoided by removing or replacing NSAID with another analgesic or renal sparing NSAIDs (non-selective or coxib's) can be preferred.
- The interaction between Atorvastatin and Pantoprazole can be prevented by replacing Pantoprazole with other PPI like Rabeprazole [27].
- The interaction between Clopidogrel and Pantoprazole can be prevented by replacing Pantoprazole with Ranitidine [27].
- Concurrent use of two NSAIDs at the same time (Diclofenac+Aceclofenac) may increase the risk of side effects reported with this class of drug i.e. stomach ulcer, GI bleeding. This interaction can be prevented by combining NSAID with Acetaminophen for mild to moderate pain [28].
- As Methotrexate and Prednisone is an effective combination for Rheumatoid Arthritis, the increased blood levels of Methotrexate and the adverse effect of this interaction can be prevented by giving low doses of Prednisone [29].
- Concurrent use of Amikacin and Ceftriaxone may result in nephrotoxicity. The patient's renal condition should be monitored particularly in volume-depleted patients and can be avoided by

replacing Ceftriaxone with an antibiotic that is not dependent on renal clearance or by reducing the dose of Ceftriaxone [30].

- Concurrent use of Aspirin and Clopidogrel may cause unusual bleeding. The monitoring of blood count should be done if co-administration is needed [31].
- Using Moxifloxacin with Azithromycin can increase the risk of an irregular heart rhythm that can be serious and life-threatening. The combination should be avoided and if suspected, immediate ECG monitoring and patient electrolyte condition or patient's previous cardiovascular conditions should be evaluated [32].
- Patients should be advised regarding cabbage and food intake with Acetaminophen [33].
- Caffeine consumption altering the therapeutic response of Psychiatric medication and Theophylline can be prevented by advising the patient to avoid the use of caffeine and caffeinated products when prescription with such drugs are written [34].
- Often, DFIs can be avoided by prescribing the drug an hour before or after meal consumption.
- Education of the patient on the potential risk factors associated with concurrent alcohol, tobacco, and medication use should be done by the Doctor and Clinical Pharmacist.

However, as the development of clinically relevant DIs is reported to be unpredictable and may vary with an individual to individual, we agree with Janchawee B, *et al.* that DIs often need not always have clinically important adverse consequences but it is important to identify the DIs in order to prevent any harm to the patient's [35].

Relating to the high prevalence of pDDIs, pDFIs, pDAIs, and pDTIs among different depts of the hospital, we recommend that Clinical Pharmacists should be posted in every hospital within India. Furthermore, a Clinical Pharmacist should have the skills and abilities to assess drug therapy, identify and prevent the medications that are having the potential to cause DIs, thereby minimizing the undesirable or adverse outcome in medical care and improving the quality of care given to the patients.

The prescription should be essentially monitored in the respective dept's of the hospital found with which high prevalence rate of DIs. The food-related choice should be advised by the Clinical Pharmacist to the patient at the time of prescription review.

As the teaching hospitals are the role models for the medical students, the prescribing behavior of the teacher can affect the students and can also influence the policymakers by informing them about the quality of drug use in health facilities.

India, being the hub for the majority of the smoker's globally, we, therefore, recommend the studies to be conducted with regard to the prevalence of alcohol and tobacco consumption among patient receiving medication, thereby preventing the DIs in this area and through education to the patient by the Clinical Pharmacist, Physician, and Health care professionals to promote safe and effective therapies.

The pDIs observed in our study warrants the careful use of medications and their strict monitoring to avoid DIs.

LIMITATIONS

Our study is a medical record-based study and focuses on potential or theoretical DIs without direct interactions with the patient. The non-prescription drugs were not taken into account. Studies based on the prevalence of actual DIs among patients may be more significant providing real-time data.

CONCLUSION

In a country like India where the role of Clinical Pharmacist in the hospitalized setting is controversial, the large fig. of pDDIs, pDFIs, pDAIs, and pDTIs indicates their essential role in optimization of therapeutic regimen and quality of care provided to the patients. A characteristic pattern of DIs combination pairs were observed

among the eight departments of the hospital. Hence these combinations should be corrected. Patient education regarding certain food choices, alcohol, and tobacco usage with medication should be given by the clinical pharmacist at the time of prescription review. The use of electronic systems for assessing DIs should be encouraged. A list of commonly used drug combination pairs found in the particular dept of the hospital can be given to the physician which helps in avoiding these DIs to the maximum and improves the quality of care provided to the patient.

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ABBREVIATIONS

pDDIs-Potential drug-drug Interactions, pDFIs-Potential drug-food Interactions, pDAIs-Potential drug-alcohol Interactions, pDTIs-Potential drug-tobacco Interactions, dept-Department, PK-Pharmacokinetic, DIs-Drug Interactions, ADE-Adverse drug event, OBG-Obstetrics and Gynaecology, GM-General Medicine, Ortho-Orthopaedics, Pulmo-Pulmonology, GS-General Surgery, Psych-Psychiatry, Derm-Dermatology, E. N. T-Ear, Nose, and Throat, PDI's-Potential Drug interactions, W. H. O-World Health Organisation, SPSS-Statistical Package for the Social Science, ECG-Electrocardiography, C. I-Contraindicated, C. N. S-Central Nervous System, CADD-Community Against Drunk Driving, PD-Pharmacodynamic, No-Number, Cyp 450-Cytochrome p 450, Cyp 2E1-Cytochrome 2E1, NSAID-Non-Steroidal Anti Inflammatory Disease, PPI-Proton pump inhibitors, G. I-Gastrointestinal

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AUTHORS CONTRIBUTIONS

This work was carried out in collaboration with all authors. Authors TJ, MAK designed the study, wrote the protocol, managed the analysis of the study, performed the statistical analysis, and managed the literature searches. Author AV KB assisted in writing the draft of the manuscript.

CONFLICT OF INTERESTS

There is no conflict of interest.

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