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Review Paper

Evaluation Of Drug-Drug Interactions in A Hospitalized Patients: A Prospective Observational Study

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ABSTRACT

Background: Adverse drug reactions are largely caused by drug-drug interactions (DDIs), especially in hospitalized patients taking several medications. The risk of clinically significant interactions is greatly increased by polypharmacy, advanced age, and comorbid conditions, which can result in higher morbidity, mortality, longer hospital stays, and higher healthcare costs. Objective : To evaluate the prevalence, pattern, and severity of drug–drug interactions among hospitalized patients in a tertiary care hospital.Materials and Methods: At Sri Balaji Medical Care Hospital, a prospective observational study was carried out over a ten-month period. There were 98 hospitalized patients over the age of 15 from different departments. Every day, patient case records were examined to gather medication profiles and demographic information. A drug interaction checker was used to evaluate drug-drug interactions, and mean ± standard deviation was used to analyze the drugResults: Among the 98 study subjects, females constituted 53% and males 47%. The highest prevalence of DDIs was observed in the 61–80 years age group (33%). Combination interactions were more common than single interactions, with minor–moderate combinations accounting for 58.1% of cases. Overall, minor interactions were most frequent (48%), followed by moderate (39%) and major interactions (13%). Frequently identified interacting drug classes included antibiotics, cardiovascular drugs, and central nervous system agents. Clinically significant major interactions included combinations associated with QT prolongation, hyperkalemia, thrombogenicity, and CNS depression. Conclusion: The study demonstrates a high prevalence of potential drug–drug interactions among hospitalized patients, especially in elderly individuals and patients receiving multiple medications. Although most interactions were minor to moderate, the occurrence of major interactions highlights the importance of regular medication review, early DDI screening, and active involvement of clinical pharmacists to improve patient safety and optimize therapeutic outcomes.

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INTRODUCTION

A drug is a substance that is administered to the body in order to have a biological effect. By attaching to a receptor or changing an enzyme's activity, for example, it modifies one or more biochemical processes[1].Drug interactions may cause serious unwanted effects or decrease the effectiveness of certain medications. This risk is greatly increased by polypharmacy, which is especially common in elderly patients[2]. It is surprising to examine a patient in the modern era of medicine receiving only one or two drugs at a time. Drug interactions are influenced by the coexistence of several medical disorders as well as the necessity and practice of polypharmacy. A drug interaction occurs when one or more medications, foods, or beverages are administered simultaneously, changing the nature or effect of the drugs. One well-known factor influencing drug responsiveness and a major contributor to adverse drug responses is drug-drug interaction[3]. According to reports, between 4 and 5 percent of hospital inpatients are prescribed medications that may interfere. The majority of these possible drug interactions might not happen or might go unnoticed. Drug interactions were responsible for 234 (6.9%) of the 3600 (4.3%) adverse drug responses found in 83,000 drug exposures in a large surveillance effort[4]. Medication-related harm remains a significant issue among older adults, with nearly half experiencing adverse health outcomes linked to potential drug exposure. Of these events, approximately 35–59% are considered preventable, highlighting the need for improved prescribing practices, careful monitoring, and strategies to minimize risks associated with medication use in this population[5]. Drug interaction broadly classified into two types ;1. Pharmacokinetics interaction: Absorption interaction, Distribution interaction, Metabolism interaction, Excretion interaction

2. Pharmacodynamic interaction: Direct pharmacodynamic interaction, Indirect pharmacodynamic interaction[6].

Drug interactions can have negative impacts on quality of life, length of hospital stay, morbidity, death, and health care costs[7]. Common risk factors associated with drug–drug interactions (DDIs) include patient-related factors such as age and gender, alterations in pharmacokinetic processes, the use of multiple medications (polypharmacy), medication errors, and the presence of comorbid conditions[8]. Drug-related problems are a frequent cause of illness(morbidity) and, in severe cases it can contribute to death (Mortality)[9]. Polypharmacy can lead to a “prescribing cascade,” where an adverse drug reaction is misinterpreted, prompting the prescription of additional, potentially unnecessary medications, which in turn increases the patient’s risk of experiencing further adverse drug reactions[10].As age increases, the occurrence of multiple coexisting diseases often necessitates prescribing several medications to a single patient. Consequently, a typical 65-year-old patient is likely to be taking around five medications at the same time[11].Medications most often involved in significant potential interactions are those routinely used in the everyday clinical care of elderly patients with chronic conditions[12]. Exposure to drug–drug interactions (DDIs), especially those that heighten the risk of bleeding, significantly raises the probability of older adults being admitted to the hospital due to adverse drug reactions. Careful monitoring and management of such interactions are essential to reduce preventable hospitalizations and improve medication safety in this population[13]. Drug–drug interactions (DDIs) can lead to blood pressure fluctuations, sedation, central nervous system toxicity, cardiac arrhythmias, and other complications. Due to factors like long-term therapy and polypharmacy, preventing DDIs in these patients is challenging, posing significant

difficulties for physicians in managing their treatment safely and effectively[14]. The concomitant use of NSAIDs and warfarin should be avoided, especially in patients over 65 or those with risk factors for NSAID-induced gastropathy, such as peptic ulcer history, steroid use, heavy smoking, or high NSAID doses. One study found a 13-fold increased risk of haemorrhagic peptic ulcers in these patients[15].

MATERIALS AND METHODS:

It is a prospective study and was conducted in departments of Sri Balaji medical Care hospital (SBMHC), Renigunta, Tirupathi. The study was carried out on above 15 years age group of either sex for period of 10months

The total of 98 subjects of all departments were enrolled in the study. for the collection of the data, the case record files of all the patients admitted in the departments were thoroughly reviewed each day during the study period.

The information recorded included the demographic details of patients, details about medications being used. The drug- drug interactions were assessed by using the drug interaction checker. The data were stored in the Microsoft excel and were analyzed by using the mean ± standard deviation.

RESULTS

The demographic details and characteristics of the patients indicate a female predominance, with 52 out of 98 subjects (53%) being female and 46 (47%) males. The most common age group was 61–80 years, comprising 32 patients (33%), followed by the 21-40 and 41-60 age groups each had % of the patients (28 subjects). The 0-20years age group with 7 patients (7 %). while those above 80 years accounted for 3.1% (3 subjects). Regarding subjects noted combination of drug interactions were a majority of cases, comprising 57 subjects, showed minor to moderate interactions. Total of 17 subjects (17.3%) experienced a combination of minor, moderate, and major drug interactions. Additionally, 4(4.1%) subjects experienced moderate and major interactions while 3(3.1%) subjects experienced minor and major interactions. Among the study subjects, single drug interactions were observed with minor interactions in 12(12.2%) subjects, moderate in 4(4.1%) subjects, and major in 1(1.1%) subject. Among 98 subjects, drug interactions were predominantly minor (73) 48%, followed by moderate (60) 39%, while major interactions (19) 13% were least common.

sno	Details	Characteristics	No. of subjects	Total
1.	Gender	Male Female	46(47%) 52(53%)	98(100%)
2.	Age	0 – 20 years AGE GROUP 21 – 40 years AGE GROUP 41 – 60 years AGE GROUP 61- 80 years AGE GROUP 81 – 100 years AGE GROUP	7(7%) 28(28.5%) 28(28.5%) 32(33%) 3(3%)	98(100%)
3.	Subjects noted combination of drug interactions	Minor –Moderate – major Minor –Moderate Minor – Major Moderate – major	17(17.3%) 57(58.1%) 3(3.1%) 4(4.1%)	98(100%)
	Subjects noted single drug interaction	Minor Major Moderate	12(12.2%) 1(1.1%) 4(4.1%)	

4.	Total no. of drug interactions	Minor Moderate Major	71(48%) 58(39%) 19(13%)	148(100%)

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Sno	**description**	**Drug interaction**	**severity**	**In total**
1	One drug may decrease the excretion rate of another drug which could result in a higher serum level	Acetaminophen + levofloxacin Cefpodoxime proxetil +Acetaminophen Furosemide + levofloxacin Cefpodoxime + levocetrizine Cefpodoxime + pantoprazole Cefperazone + pantoprazole Acetaminophen + Sulbactum Pantoprazole + Sulbactam Cefperazone + acetaminophen Pantoprazole + Acetaminophen Acetylcysteine + fexofenadine Sucralfate + levosalbutamol Doxycycline + acetaminophen Aceclofenac + doxycycline Ceftriaxone + tramadol Tramadol + pantoprazole Ceftriaxone + pantoprazole Acetaminophen + amoxicillin Aceclofenac + amoxicillin Cefoperazone + tramadol Nitrofurantoin + Flavoxate Aceclofenac + Metoclopramide Aceclofenac + Pantoprazole Tazobactam + Levofloxacin Ceftriaxone + Acetaminophen Paracetamol + Ringers lactate Lorazepam + levofloxacin Furosemide + pantoprazole Acetaminophen + meropenem Pregabalin + doxycycline Furosemide + ceftriaxone Ciprofloxacin + meropenem Acetaminophen + rabeprazole Aceclofenac + rabeprazole Aceclofenac + pregabalin	**minor**	**45**

		Pregabalin + acetaminophen Pregabalin + rabeprazole Mefenamic acid + pantoprazole Pantoprazole + dicyclomine Acetaminophen + dicyclomine Aceclofenac + dicyclomine Mefenamic acid + amoxicillin Dicyclomine + amoxicillin Linezolid + aceclofenac Metformin + amoxicillin		
		Valproate + lorazepam Ticagrelor + sitagliptin Piperacillin + levofloxacin Glimepiride + Telmisartan Pantoprazole + piperacillin Pantoprazole + Tazobactum Azithromycin + deflazacort Ceftriaxone + amikacin Tramadol + Amikacin Pantoprazole + amikacin Ceftriaxone + dexamethasone Furosemide + tazobactum Ranolazine + metoprolol	**Moderate**	**13**
		Metronidazole + amiodarone	**major**	**1**
2	One drug may increase the excretion rate of another which could result in a lower serum level and potentially a reduction in efficacy.	Furosemide + Acetaminophen Spironolactone + Metformin Spironolactone + sitagliptin	**minor**	**3**
		Torsemide + folic acid	**Moderate**	**1**
3	One drug may increase the hypotensive activities of another drug	Labetalol + Furosemide Torsemide + spironolactone Chlorthalidone + Acetaminophen Chlorthalidone + Amlodipine Chlorthalidone + Telmisartan Metoprolol + nitroglycerin	**minor**	**6**
4	The risk or severity of hypertension can be increased when one drug is combined with another drug	Phenylephrine + levosalbutalmol Linezolid + mefenamic acid	**Minor**	**2**
5	The risk or severity of QTc prolongation can be increased when one drug is combined with another drug	Azithromycin + Levocetirizine Bilastine + Azitromycin	**minor**	**2**
		Pregabalin + domperidone Metronidazole + domperidone	**Moderate**	**2**
		Azithromycin + domperidone Levofloxacin + valproate sodium	**major**	**2**
6	The risk or severity of Tachycardia can be increased when one drug is combined with another drug	Ipratropium + formoterol fumarate Glycopyrronium bromide + levosalbutamol	**minor**	**2**
		Ipratropium bromide + glycopyrronium bromide	**major**	**1**
7		Torsemide + Telmisartan	**minor**	**2**

	The therapeutic efficacy of one drug can be decreased when used in combination with another drug	Torsemide + Metformin		
		Nortriptyline + domperidone Glimepiride + Torsemide	**moderate**	**2**
8	The therapeutic efficacy of one drug can be increased when used in combination with another drug	Pregabalin + nortriptyline Metoprolol + vildagliptin	**moderate**	**2**
9	The metabolism of one drug can be decreased when combined with another drug	Amlodipine + Azithromycin Montelukast + dextromethorphan Metformin + cilostazol Atorvastatin + cilastazol Ticagrelor + valsartan	**Minor**	**5**
		Montelukast + naproxen Naproxen + domperidone Metronidazole + tramadol Metronidazole + ondansetron Montelukast + domperidone Labetalol + Ondansetron Labetalol + Acetaminophen Acetaminophen + Montelukast Levofloxacin + Doxofylline Acetaminophen + Doxofylline Acetaminophen + Ondansetron Domperidone + doxofylline Acetaminophen + metronidazole Domperidone + acetaminophen Dexamethasone + tramadol Ciprofloxacin + metronidazole Ciprofloxacin + pantoprazole Clopidogrel + rosuvastatin Torasemide + rosuvastatin	**moderate**	**19**
		Tamsulosin + clonidine Ciprofloxacin + acetaminophen Ciprofloxacin + ondansetron Clopidogrel + torsemide	**major**	**4**
10.	The metabolism of Azithromycin can be increased when one drug combined with another drug	Acetaminophen + Azithromcin Hydrocortisone + tramadol Dexamethasone + metronidazole Clindamycin + acetaminophen	**moderate**	**4**
		Theophylline + hydrocortisone Dexamethasone + pantoprazole Nortriptyline + acetaminophen	**Major**	**3**
11.	The risk or severity of adverse effects can be increased when one drug is combined with another drug	Ceftriaxone + Ringers lactate Spironolactone + sacubitril	**minor**	**2**
		Calcium gluconate + ceftriaxone Mefenamic acid + aceclofenac	**Moderate**	**2**
		Dexamethasone + hydrocortisone	**Major**	**1**
12.	The risk or severity of gastrointestinal bleeding can be increased when one drug	Nortriptyline + aceclofenac	**minor**	**1**

	is combined with another drug			
13.	Pantoprazole can cause a decrease in the absorption of doxycycline resulting in a reduced serum concentration and potentially a decrease in efficacy	Pantoprazole + doxycycline	**moderate**	**1**
14.	The risk or severity of serotonin syndrome can be increased when ondansetron is combined with tramadol	Ondansetron + tramadol	**moderate**	**1**
15.	The risk or severity of CNS depression can be increased when one drug is combined with another drug	Lorazepam + levetiracetam Valproate sodium + levetiracetam Phenytoin + levetiracetam	**moderate**	**3**
16.	The risk or severity of angioedema can be increased when one drug is combined with another drug	Valsartan + sitagliptin Sitagliptin + sacubitril	**moderate**	**2**
17.	The risk or severity of hypokalemia can be increased when one drug is combined with another drug	Hydrocortisone + Furosemide Deflazacort + Doxofyllin Budesonide + levosalbutamol Deflazacort + doxofylline	**Moderate**	**4**
18.	The risk or severity of hyperkalemia can be increased when one drug is combined with another drug	Telmisartan + Spironolactone Valsartan + spironolactone	**major**	**2**
19.	Progesterone may increase the thrombogenic activities of tranexamic	Progesterone + tranexamic acid	**Major**	**1**
20.	The risk or severity of tendinopathy can be increased when Deflazacort is combined with Levofloxacin.	Deflazacort + levofloxacin	**Moderate**	**1**
21.	Levosalbutamol may increase the sympathomimetic activities of Formoterol.	Levosalbutamol + formoterol fumarate	**Moderate**	**1**
22.	Tranexamic acid may increase the thrombogenic activites of calcium	Tranexamic acid + calcium	**major**	**1**
23.	The risk or severity of sedation can be increased when drug is combined with another drug	Clonidine + nortriptyline Clonidine + gabapentin	**Major**	**2**
24.	Nortriptyline may increase the orthostatic hypotensive, hypotensive, and	Nortriptyline + tamsulosin	**major**	**1**

	antihypertensive activities of Tamsulosin			

DISCUSSION

- In the present study, the highest proportion of DDIs occurred in patients aged 61–80 years (33%), indicating that elderly patients are the most vulnerable group. This finding is aligns with Khaiser et al., who found that the 70–79-year age group had the highest prevalence of polypharmacy-associated DDIs. Both studies confirm that advancing age is strongly associated with increased DDI risk due to multiple comorbidities, altered drug metabolism, and reduced organ function**.**
- This study observed a slight female predominance (53%) in DDI occurrence, similar to Khaiser et al., where females also showed a slightly higher prevalence of polypharmacy (53.84%) than males. This similarity may reflect increased healthcare utilization and greater chronic medication exposure among women.
- Minor interactions were most frequent in the current study, while major interactions were less common but clinically significant. This trend aligns with Georgiev et al. (2022), who also reported that most hospitalized patient DDIs are minor-to-moderate, whereas severe interactions are fewer but require urgent clinical attention.
- In this study, combination interactions (especially minor–moderate combinations, 58.1%) were more common than single interactions, strongly suggesting that polypharmacy is the principal driver of DDI occurrence. Khaiser et al. similarly demonstrated that patients receiving ≥5 drugs had significantly higher DDI prevalence. This reinforces the established relationship between increasing medication count and exponential rise in interaction probability.
- In this study found frequent interactions involving:

Antibiotics (azithromycin, levofloxacin, ceftriaxone),Cardiovascular drugs (telmisartan, spironolactone, metoprolol),CNS drugs (nortriptyline, clonidine, pregabalin).This is consistent with the systematic review by Oliveira et al. (2020), which identified cardiovascular agents, diuretics, antimicrobials, and CNS drugs as the most common classes implicated in hospitalized elderly DDIs. □

CONCLUSION

The present study highlights the significant prevalence of drug–drug interactions among hospitalized patients, with a total of 98 subjects evaluated. A higher proportion of cases was observed in females, and the elderly age group (61–80 years) was most affected, emphasizing the impact of age and polypharmacy on interaction risk.

The majority of drug interactions were of minor and moderate severity, with minor interactions being the most common overall. Combination drug interactions were more frequently observed than single interactions, particularly minor to moderate combinations, indicating the influence of multiple drug use in clinical practice. Although major interactions were less frequent, their presence underscores the need for careful monitoring due to potential serious clinical outcomes.

These findings reinforce that polypharmacy and advancing age are key risk factors for drug interactions. Early identification, regular

medication review, and the use of drug interaction screening tools are essential to minimize adverse effects. Clinical pharmacists and healthcare professionals play a crucial role in improving medication safety, reducing preventable adverse drug reactions, and optimizing therapeutic outcomes.

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