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Research Article

POLYPHARMACY INDUCED DRUG-DRUG INTERACTIONS- AN OBSERVATIONAL AND INTERVENTIONAL STUDY

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A B S T R A C T

Aims and Objectives:

- To study the incidence and pattern of drug-drug interactions
- To identify and minimise preventable drug-drug interactions as far as possible.
- To minimize health care cost burden on patients and health care system.
- To improve the patients quality of life
- To improve the rationality of drug therapy
- To decrease the hospitalization of patients

Methodology: An observational and interventional study was conducted for a period of 6 months in the various departments of VishwaBharathi super specialty hospital, Kurnool. A total of 60 patients/ prescriptions were included in this study. A total of 102 DDIS were identified from 27 prescriptions.

Results: Our study concluded that a high percentage of 54(52.94%) DDIs were found in patients of age group >60 years and whereas distribution of drug-drug interactions based on severity showed many major drug-drug interactions (59.80%). Further the study concluded that a high number of DDIs were found in cardiology department (32 DDIS) followed by General Medicinedepartment (28 DDIs).

Conclusion: Hence, monitoring of prescriptions with polypharmacy is highly necessary in order to reduce the occurrence of DDI's and other drug related problems. In this aspect, Clinical pharmacist play an important role in healthcare system by assisting the physicians in dosage and duration adjustments, in discontinuation of unnecessary and inappropriate medications, in establishing a balance between risks and benefits of multiple drug therapies, thereby preventing the occurrence of DDIs, and thus improving the rationality of drug therapy, patients quality of life, decreasing the hospitalization of patients and health care cost burden to the patient and society.

INTRODUCTION

Polypharmacy is the main issue of patient safety in all healthcare settings in world wide.[1] Polypharmacy can be defined as the use of multiple drugs or increase in number of drugs that are medically necessary[2] or sometimes Polypharmacy, means the use of 7 or more than 7 drugs per day. The word Polypharmacy is derived from two Greek words 'Poly' meaning 'more than one' and Pharmacy meaning 'drug'. Polypharmacy is more common in older ambulatory care, hospital inpatients department, and nursing home patients. [2] Unfortunately, this increased use of multiple medications or Polypharmacy is associated with the increase of negative consequences such as increased risk of adverse drug reactions, Drug interactions, reduced functional capacity, poor quality of life and multiple geriatric syndromes. As a result of this negative consequences, Polypharmacy sets up a barrier to treatment adherence by creating a complex therapeutic regimens. Polypharmacy increases the risk of numerous negative consequences mainly in the elderly patients due to changes in biochemical composition of tissue, progressive decrease in physiological capacity, reduced ability to adopt to stimuli, increased susceptibility and vulnerability to disease and increased risk of death. [3, 2]

Polypharmacy is the main cause of many potential drug interactions in prescriptions in day to day practice. [4] A drug-druginteraction (DDI) occurs when one substance (usually another drug) alters the pharmacological effect of other drug when both administered simultaneously. The pharmacological effect of both the drugs may be increased (synergistic action) or decreased (antagonistic action) or a new or unanticipated adverse or toxic effect may be produced. Usually, in hospital

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or in clinical settings drug interactions not only exist with the drugs (drug-drug interactions) but also with the food products (drug food interactions)**.** Drugs interact in two major ways. Pharmacokinetically and pharmacodynamically. A pharmacokinetic drug-drug interaction occurs when one drug causes a change in other drugs serum concentration by altering its absorption, distribution, metabolism or elimination. A pharmacodynamics drug-drug interaction (interaction at drug receptors) occurs when the clinical effect is altered by administering the two drugs concomitantly such as those yielding synergistic or antagonistic therapeutic effect and those yielding overlapping or additive toxicities.[5]

The incidence of drug-drug interactions increases exponentially as the number of drugs co-prescribed increases for a individual patient.[4,6] Critically ill or chronically ill patients are mainly at increased risk of drug-drug interactions due to polypharmacy as well as impaired homeostatic mechanisms. [6]

By using Micromedex 2.0® software, drug.com and STOCKLEY's book, Potential drug-drug interactions were categorized into different levels as follows:

Onset

- Rapid: The effect of interaction occurs within 24 hours of administration.
- Delayed: The effect occurs if the interacting combination is administered for more than 24 hours i.e., days to week(s)
- Unspecified: The occurrence of effect of interaction is not specified.

Severity

- Contraindicated: The drug-combination is contraindicated for concurrent use.
- Major: There is risk of death and/or medical intervention is required to prevent or minimize serious negative outcomes.
- Moderate: The effect of interaction can deteriorate patient's condition and may require alteration of therapy.
- Minor: Little effects are produced that don't impair therapeutic outcome and there is no need of any major change in therapy. [4]

Polypharmacy and its negative consequences like drug interactions imposes a healthcare cost burden on both the patient and the health care system. [2]

Incidence of DDIs is estimated to vary from 6%-30% in hospitalized patients which leads to an increase on risk to the patients health outcomes and an increase in health care cost burden to patient and healthcare system.[7]

The probability of DDIs increases to 50% in patients taking 5-9 medications where as the risk/probability increases to 100% in patients taking 20 or more medications.[2]Therefore, based on the above incidence and prevelance of DDIs ,we hypothesis the need for careful monitoring of prescriptions with polypharmacy.

Prescriptions containing polypharmacy can be accepted as long as they are clinically appropriate or meet the criteria for the need of the patient condition, but monitoring is required for the occurrence of drug related problems.[4] .This creates the need of adopting some successful interventions to optimize prescribing multiple drugs or polypharmacy.[3] One of the most best intervention for improving/optimizing polypharmacy is involving an interprofessional approach which often includes a clinical pharmacist.[2]

Therefore, the clinical pharmacist have a potential role in the healthcare setting in assisting medical practitioner / physician in altering or reducing the number of medicines taken, in reducing the frequency of doses to be taken, reducing the no: of ADRs, DDI's, improving health related quality of life and decreasing the health care cost burden on the patient and health care system.[4]

Thus, the purpose of the present study was to conduct a broader integrated review aimed at identifying and summarizing studies examining drug-drug interactions in patients who are polymedicated.

Aims and Objectives

- To study the incidence and pattern of drug-drug interactions in our hospital and to identify whether the drug interactions are associated with polypharmacy
- To identify and minimise preventable drug-drug interactions as far as possible.
- To minimise health care cost burden on patients and health care system.
- To improve the patients quality of life
- To improve the rationality of drug therapy
- To decrease the hospitalization of patients.

MATERIALS AND METHODS

Place of the study

The study was conducted in the various departments (General medicine, Psychiatry, Neurology, Diabetology, Cardiology) of a territory hospital, Vishwa Bharathi superspeciality hospital, Kurnool, after obtaining the ethical clearance.

Duration of the study

The study was conducted for a period of 6 months during September 2016 to Feb 2017

Study population

Patients prescribed with seven or more than seven drugs from all the departments of hospital

Sample size

60 Patients

Study design

An Interventional and observational study

Patients Eligibility criteria

Patients are enrolled in the study based on inclusion and exclusion criteria.

Inclusion Criteria

- Patients of both gender from all the departments (General medicine, psychiatry, neurology, diabetology, and cardiology) of hospital receiving seven or more than seven drugs were included.
- Both new and old patients who are on polypharmacy.
- Patients from both inpatient and outpatient departments.

- Patients who are willing to participate in the study

Exclusion Criteria

- The patients from departments other than those mentioned in inclusion criteria.
- Pregnant and lactating females, Paediatrics.
- Cases of therapeutic failure: intentional or accidental poisoning, with a history drug abuse.
- Patients taking oncological drugs, ointments (topical medications) eye drops, vitamin supplements, mineral supplements, homeopathic medications and herbal treatments.
- Patients who are not willing to participate in the study.

METHOD OF STUDY

Sources of Data

A separate data entry format was specially designed including the drug chart and Pharmacist intervention column. The data was collected during routine ward rounds from various sources such as patient's case sheets, treatment charts and patient interviews and/or care takers interviews and transferred to specially designed data entry format for evaluation

Methods of detecting drug interactions

Patient who met the study criteria were included in the study.The first step in the detection of Drug interactions is collection of data. The data to be collected include patient's demographic data; presenting complaints; past medication history; drug therapy details including current medications and medication on admission; and lab data. All the cases were reviewed retrospectively and monitored extensively for the pattern of drug uses like their category, indication, and rationality of the prescription, concurrent drugs prescribed and/or number of drugs in prescriptions. Drug-drug interactions were identified and documented by using MICROMEDEX 2.0® software. Potential drug-drug interactions were categorized on the basis of gender, age, severity, department, number of DDIs per prescription.

RESULTS AND DISCUSSION

As per the patient demographic data obtained, a total of 60 patients prescriptions (35males (58.33%) and 25(41.77%) females) were included in this study. Out of 60 patients, 27 patients (9 females (33.33%) and 18(66.66%) males) were found to have drug-drug interactions in their prescriptions. A total of 102 DDIs were identified from 27 prescriptions.

In this study, a maximum of 19 patients belongs to an age group of above 60 years followed by 12 patients belongs to an age group of 51-60 years .This data shows that , geriatric patients are more prone to diseases, for which multiple drugs will be prescribed.

Age wise distribution of DDIs

Table 1 Age wise distribution of DDIs

Age group	No of prescriptions	No of prescriptions with DDIs	Total number of DDIs	% of DDIs
11-20	3	1	1	0.9803
21-30	6	4	10	9.803
31-40	10	0	0	0
41-50	10	4	25	24.50
51-60	12	5	12	11.76
>60 yrs.	19	13	54	52.94
Total	60	27	102	100

A maximum of 54(52.94%) DDIs were found in patients belonging to age group of above 60 years followed by 25(24.50%) drug- drug interactions among patients belonging to age group of 41-50 years and then 12(11.76%) drug interactions among patients belonging to age group of 51-60 years. The results of our study are in correlation with results of the study conducted by Kumar Swamy R.C., Jignesh U Ramani and Bushipaka Ramesh, *et al*. in which a high incidence of DDIs (175) were found in patients belonging to age group of >60 years followed by 160 DDIs in patients of 41-60years age group. [7]

This data suggests that geriatric patients are more prone to diseases and may be having concomitant disease conditions for which multiple drugs will be prescribed and thus making the patient more prone to DDIs.

Gender wise distribution of Drug-drug interactions

Table 2 Gender wise distribution of Drug-drug interactions

Gender	No of patients prescriptions	Number of prescriptions with DDIs	No of DDIs	% of DDIs
Female	25	9	28	27.45
Male	35	18	74	72.54
Total	60	27	102	100

Among 102 Drug interactions, a high incidence of 74(72.54%) Drug-drug interactions were found in male population and 28(27.45) drug-drug interactions were found in female population.

Severity of Drug-drug interactions

Based on severity, Drug-drug interactions were classified into minor, moderate and major. Minor drug interactions will be having very little clinical effect and hence not considered in this study. Only major and moderate drug interactions were considered in this study.

Table 3 Severity of Drug-drug interactions

Severity	Number of drug-drug interactions	% of drug interactions
Major	61	59.80%
Moderate	41	40.19%
Total	102	100

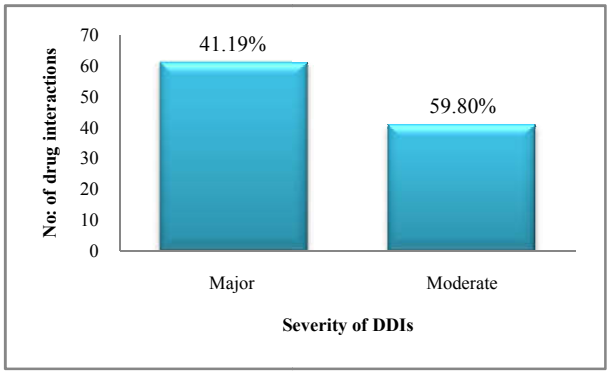

Figure 1 Severity of Drug-drug interactions

In this study we found that most of the patient prescriptions were having major drug-druginteractions. A total of 61(59.80%) major DDIs were found followed by 41(41.19%) moderate DDIs. Thus this discrepancy in prevalence may be due to patient's expectation and demand of quick relief, incorrect diagnosis and the influence of the attractive

promotional programs by the pharmaceutical companies. A study by Kumar Swamy R.C., Jignesh U Ramani, Bushipaka Ramesh, etal.Showed 155 moderate DDIs, 123 major DDIs and 122 minor DDIs whose results are in contrast to our study[7]. A study by Nimmy N. John, R.H. Udupi and K.M.Binu on Incidence of Polypharmacy induced DDIs in a tertiary care hospital showed a high number of moderate DDIs (66.2%) followed by 20.1% of minor DDIs and 13.63% of major DDIs. [6]A study by Ashok Kumar Malpani, RiyazMiya showed a high number of 37 moderate DDIs, 5 major DDIs and 23 minor DDIs. [8]

Department wise distribution of drug-drug interactions

Table 4 Department wise distribution of drug-drug interactions

Department	No of drug-drug interactions	% of drug-drug interactions
Cardiology	32	31.37
Neurology	27	26.47
General medicine	28	27.45
Pulmonology	4	3.92
Nephrology	7	6.86
Gynecology	4	3.92
Total	102	100

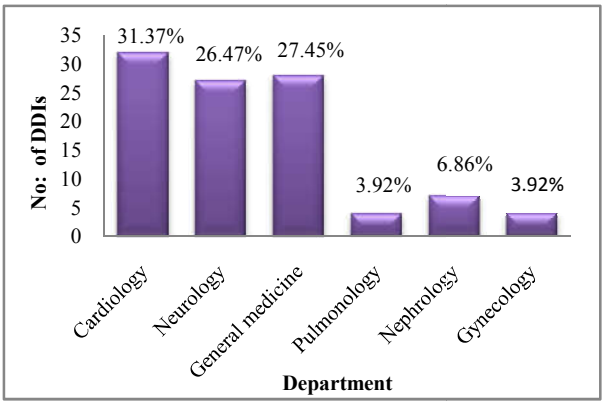

Figure 2 Department wise distribution of drug-drug interactions

Out of 102 drug-drug interactions, a majority of 32(31.37%) drug-drug interactions were from cardiology department followed by 28 drug interactions from general medicine and 27 drug-drug interactions were from neurology department.
This data confirms that patients admitted in cardiology department have high exposure to polypharmacy and thus are more prone to drug interactions.

The results of our study are in correlation with the results of the study conducted by Nimmy N. John, R.H. Udupi, and K.M. Binu who reported a high incidence of 38 DDIs from Pulmonology department followed by 34 DDIs from Gastroenterology department, 29 DDIS from Cardiology department and 14 DDIs from Neurology department. [6]

Effect of drug-drug interactions on P^K and P^D parameters

Table 5 Effect of drug-drug interactions on $P^{K \text{ and}}$ P^D parameters

Effect of DDIs	No of DDIs	% of DDIs
On Pharmacokinetics	2	1.96
On Pharmacodynamics		
• Drug action increased	68	66.66
• Drug action decreased	30	29.41
• Either increased or decreased	2	1.96
Total	102	100

Drug-drug interactions can alter or have effect on P^K and P^D of interacting drugs. In this study, 2(1.96%) drug-drug interactions were found to alter the pharmacokinetics of interacting drugs. 100 (99.4%) DDIs were found to alter (either increase or decrease the action of drugs) pharmacodynamics of interacting drugs.

Distribution of drug-drug interactions based on management

Management of drug-drug interactions is very important in order to improve the patient's quality of life, to decrease the adverse effect of drug-drug interactions on patients, to decrease cost burden due to drug interactions to the patients to society, to improve rationality of treatment

Table 6 Distribution of drug-drug interactions based on management

Management of drug-drug interaction	No of drug-drug interactions	% of drug-drug interactions
By close monitoring	52	50.98
By changing duration of drug administration	44	43.13
By drug discontinuation	1	0.98039
By using alternative drug	5	4.901
Total	102	100

A majority of 52(50.98%) drug-drug interactions were managed by close monitoring of either vitals, electrolytes, ECG, laboratory parameters of patients. About 44(43.13%) drug-drug interactions were managed by changing the duration of administration of interacting drugs. only 1 drug-drug interaction was managed by discontinuation of drug due to serious issue of major bleeding by concomitant administration of enoxaparin and NSAID (diclofenac)

Number of drug-drug interactions per individual patient

Around 6 patients were found to have at least 1 potential to drug-drug interaction, followed by 3 patients with 2 drug-drug interactions, 5 patients with 3 drug-drug interactions , 6 patients with 4 drug-drug interactions , 2 patients with 6 drug-drug interactions , 2 patients with 7 drug-drug interactions and 2 patients with 10 drug-drug interactions.

Drug-drug interactions encountered in the study

Clopidogrel+ Aspirin (8 DDIs), Clopidogrel+ Rabeprazole (5 DDIs), Amlodipine+ Clopidogrel (7 DDIs) are most commonly encountered major DDIs in this study. Atorvastatin+ Clopidogrel (9 DDIs) are the more commonly encountered moderate DDIs in the study.A study by Kumar Swamy R.C., Jignesh U Ramani, Bushipaka Ramesh, et al. showed Ofloxacin+ On dansetron (31DDIs), Metformin+Ofloxacin (19 DDIs) as the most common major DDIs and Azithromycin+Ondansetron (43 DDIs), Metronidazolr+Theophylline (37 DDIs) as the most common moderate DDIs. [7]

Aspirin (Antiplatelet), Clopidogrel (Antiplatelet), Atarvostatin (Dyslipidemic), Rabeprazole (Antacid), Ondensetron (5 -HT receptor antagonist), Ofloxacin (antibiotic) are most common drugs involved in drug drug interactions.

Severity of DDIs	Interacting Drugs	Class of Interacting Drugs	Mechanism of DDI	Effect of DDI		Management of DDIs	Frequency of DDIs	% of DDIs
				On Pharmacokinetics(P^K)	On Pharmacodynamics(P^D)			
Major	Oflaxacin +Ondensetron	Quinolones+ 5 -HT receptor antagonist	Increased Q-T interval prolongation	-	Increased	Closely monitor of ECG	3	2.94%
Major	Aceclofenac +Furosemide	NSAIDs +Diuretic	Decreased diuretic effect and possible nephrotoxicity	–	Decreased	Avoid concomitant use or change duration of drugs administration.	1	0.98%
Major	Aceclofenac+ Spironolactone	NSAIDs +Diuretic	Decreased diuretic effect and possible nephrotoxicity	–	Decreased	Avoid concomitant use or change duration of drugs administration	1	0.98%
Major	Aceclofenac+ Aspirin	NSAIDs+ Antiplatelet	Increased risk of bleeding	–	Increased	Monitor blood count	1	0.98%
Major	Aceclofenac+Clopidogrel	NSAIDs+Antiplatelet	Increased risk of bleeding	–	Increased	Monitor blood count	1	0.98%
Major	Amlodipine+Clopidogrel	Antihypertensive+Antiplatelet	Increased risk of thrombotic events and decreased anti platelet effects	–	Increased	Avoid concomitant use or change duration of drugs administration	7	6.86%
Major	Aspirin+Furosemide	Antiplatelet +Diuretic	Reduced diuretic effect and possible nephrotoxicity	–	Decreased	Monitor renal function test	2	1.96%
Major	Artemether/Lumefentrine +Ondansetron	Anti malarial +5 HT receptor antagonist	Increased Q-T interval prolongation	–	Increased	Closely monitor ECG	1	0.98%
Major	Aspirin+ Enoxaparin	Antiplatelet +Anticoagulant	Decrease the risk of major bleeding events	–	Increased	Discontinuation of an NSAID prior to initiation of LMWH therapy	1	0.98%
Major	Aspirin+Eplerenone	Antiplatelet+Diuretic	Decreased diuretic effect and possible nephrotoxicity	–	Decreased	Monitor renal function test	1	0.98%
Major	Aspirin+Piracetam	Antiplatelet +Cognitive Enhancers	Increased risk of bleeding	–	Increased	Monitor blood count	1	0.98%
Major	Aspirin+Spironolactone	Antiplatelet +Diuretic	Reduced diuretic effect and possible nephrotoxicity	–	Decreased	Monitor renal function test	1	0.98%
Major	Aspirin+Telmisartan/ Hydrochlorothiazide	Antiplatelet +Antihypertensive	Increased risk of bleeding	–	Increased	Monitor blood count	1	0.98%
Major	Atarvostatin +Diltiazem	Antiplatelet +Calcium channel blocker	Increased risk of rhabdomylosis	–	Increased.	Avoid concomitant use or change duration of drugs administration	1	0.98%
Major	Ciprofloxacin+Insulin	Quinolones + Antidiabetic	Increased risk of thrombosis	–	Increased.	Avoid concomitant use or change duration of drugs administration	2	1.96%
Major	Ciprofloxacin+ Ondansetron	Quinolones + 5 HT receptor antagonist	Increased risk of QT interval prolongation	–	Increased.	Closely monitor ECG	1	0.98%
Major	Clopidogrel +Aspirin	Antiplatelet+Antiplatelet	increased risk of bleeding	–	Increased.	Monitor blood count	8	7.84%
Major	Clopidogrel+Dilitiazem	Antiplatelet +Calcium channel blocker	Decreased anti platelet effect and increased risk of thrombotic events	–	Decreased	Avoid concomitant use or change duration of drugs administration	1	0.98%
Major	Clopidogrel+Enoxaparin	Antiplatelet +Anticoagulant	Increase the risk of bleeding	–	Increased	Monitor patients closely for signs or symptoms of bleeding	1	0.98%
Major	Clopidogrel+ Rabeprazole	Antiplatelet +H2 receptor blocker	Increase the risk of thrombosis	–	Increased	Use of H2 blockers	5	4.90%
Major	Clopidogrel+Piracetam	Antiplatelet +Cognitive Enhancers	Increased risk of bleeding	–	Increased	Monitor blood count	1	0.98%
Major	Aspirin+Heparin	Antiplatelet +Anticoagulant	Increased risk of bleeding		Increased	Monitor blood count	2	1.96%
Major	Dexemethasone+ Diclofenac	Corticosteroids+NSAIDs	Increased risk of GIT ulcer bleeding		Increased	Avoid concomitant use or change duration of drugs administration	1	0.98%
Major	Diclofenac +Naproxen	NSAID+ NSAID	Increased risk of bleeding		Increased	Monitor blood count	1	0.98%

Major	Domperidone+ Ondensetron	Antiemetics+5 -HT receptor antagonist	Increased Q-T interval prolongation		Increased	Closely monitor ECG	2	1.96%
Major	Eplerenone+Metoprolol	Diuretic +Beta blocker	Result in hyperkalemia		Increased	Monitor electrolytes	1	0.98%
Major	Escitalopram+Ofloxacin	Antidepressant +Quinolones	Increased Q-T interval prolongation		Increased	Closely monitor ECG	1	0.98%
Major	Furosemide+Aspirin	Diuretic +Antiplatelet	Decreased diuretic effect and possible nephrotoxicity		Decreased	Avoid concomitant use or change duration of drugs administration	1	0.98%
Major	Heparin+Clopidogrel	Antiplatelet +Anticoagulant	Increased risk of bleeding	–	Increased	Monitor blood count	3	2.94%
Major	Heparin+Nitroglycerin	Antiplatelet +Antianginal	Decreased in partial thromboplastintime	–	Decreased	Careful monitoring of partial thromboplastin time	1	0.98%
Major	Insulin +Oflaxacin	Antidiabetic +Quinolones	Increased risk of hypo or hyperglycemic effect	–	Increased	Monitor blood glucose levels	1	0.98%
Major	Labetalol+Diltiazem	Anti hypertensive +Calcium channel blocker	Increased risk of hypotension ,bardycardiaand conduction disturbances	–	Increased	Avoid concomitant use or change duration of drugs administration	1	0.98%
Major	Metaprolol+ Diltiazem	Beta blocker + Calcium channel blocker	Increased risk of hypotension ,bardycardiaand conduction disturbances	–	Increased	Avoid concomitant use or change duration of drugs administration	1	0.98%
Major	Metronidazole +Ofloxacin	Nitroimidazole+ quinolones	Increased Q-T interval prolongation	–	Increased	Closely monitor ECG	2	1.96%
Major	Metronidazole +Ondensetron	Nitroimidazoles +5 - HT receptor antagonist	Increased Q-T interval prolongation	–	Increased	Closely monitor ECG	1	0.98%
Moderate	Aspirin+ Sodium bicarbonate	Antiplatelet +Gastric acid neutralizers	Decreased aspirin effectiveness	–	Decreased	Avoid concomitant use or change duration of drugs administration	1	0.98%
Moderate	Aspirin+ Insulin	Antiplatelet +Antidiabetic	Increased risk of hypoglycemia	-	Increased	Monitor blood glucose levels	3	2.94%
Moderate	Aspirin+Metoprolol	Antiplatelet +Beta blocker	Increased Blood pressure	–	Increased	Monitor Blood pressure	2	1.96%
Moderate	Aspirin+Nitroglycerin	Antiplatelet +Antianginal	Increase in nitroglycerin concentration and additive platelet function depression	–	Increased	Avoid concomitant use or change duration of drugs administration	2	1.96%
Moderate	Aspirin+Ramipril	Antiplatelet +Antihypertensive	Decreased ramipril effectiveness	–	Decreased	Avoid concomitant use or change duration of drugs administration	1	0.98%
Moderate	Aspirin+Sorbitrate	Antiplatelet +Antianginal	Increased nitroglycerin concentration and additive platelet function	–	Increased	Avoid concomitant use or change duration of drugs administration	1	0.98%
Moderate	Atenolol +Glimepiride	Beta blocker + Anti diabetic	Result in hypoglycemia or hyperglycemia	–	Increased or Decreased	Monitor blood glucose levels	1	0.98%
Moderate	Atenolol +Metformin	Beta blocker + Anti diabetic	Result in hypoglycemia or hyperglycemia	–	Increased or Decreased	Monitor blood glucose levels	1	0.98%
Moderate	Atarvostatin + Clopidogrel	Hypolipidaemic+ Antiplatelet	Decreased formation of Clopidogrel active metabolite resulting high on treatment platelet reactivity	Decreased	–	Avoid concomitant use or change duration of drugs administration	9	8.823
Moderate	Dexemethasone+ Phenytoin	Corticosteroids+ Antiepileptic	Decreased Dexomethasone effectiveness		Decreased	Avoid concomitant use or change duration of drugs administration	1	0.98%
Moderate	Hydrocortisone +Phenytoin	Corticosteroid +Antiepileptic	Decreased hydrocortisone effectiveness		Decreased	Avoid concomitant use or change duration of drugs administration	1	0.98%

Moderate	Insulin+Telmisartan/Hydrochlorothiazide	Antidiabetic +Antihypertensive	Increased risk of hypoglycemia		Increased	Monitor blood glucose levels	2	1.96%
Moderate	Labetalol+Aspirin	Antihypertensive +Antiplatelet	Increased blood pressure		Increased	Avoid concomitant use or change duration of drugs administration	2	1.96%
Moderate	Lorazepam+Telmisartan	General Anaesthetic +Antihypertensive	Decreased BP	–	Decreased	Monitor BP	1	0.98%
Moderate	MemantineHcl+Sulfamethaxazole	Cognition Enhancers +Sulfonamide	Increased memantine effect	–	Increased	Avoid concomitant use or change duration of drugs administration	1	0.98%
Moderate	Metronidazole +Phenytoin	Nitroimidazole+ Anti-epileptic	Increased risk of phenytoin toxicity	–	Increased	Avoid concomitant use or change duration of drugs administration	1	0.98%
Moderate	Midazolam+Ranitidine	General Anaesthetic +H2 receptor blocker	Increased midazolam bioavailability	Increased	–	Avoid concomitant use or change duration of drugs administration	1	0.98%
Moderate	Midazolam+ Theophylline	General Anaesthetic +Bronchodilator	Decreased benzodiazepine formation	–	Decreased	Avoid concomitant use or change duration of drugs administration	1	0.98%
Moderate	Ondensetron+ Magnesium Hydroxide	5 -HT receptor antagonist +Antacids	Increased heart rhythm	–	Increased	Closely monitor ECG	1	0.98%
Moderate	Phenytoin+ Sulfamethaxazole	Anti epileptic +Sulfonamide	Increased phenytoin exposure	–	Increased	Avoid concomitant use or change duration of drugs administration	1	0.98%
Moderate	Quinine-+Magnesium Hydroxide	Antiarrhythmic +Antacid	Increased the risk of irregular heart rhythm	–	Increased	Closely monitor ECG	1	0.98%
Moderate	Quinine+Ondansetron	Antiarrhythmic + 5 -HT receptor antagonist	Increased the risk of irregular heart rhythm	–	Increased	Closely monitor ECG	1	0.98%
Moderate	Ramipril+Aspirin	Ramipril+Aspirin	Decreased ramipril effectiveness	–	Decreased	Avoid concomitant use or change duration of drugs administration	1	0.98%
Moderate	Tramadol+Ondansetron	CNS Analgesic+ Opioid Analgesics	Decreased the effect of Tramadol	–	Decreased	Avoid concomitant use or change duration of drugs administration	3	2.94%
			Total				102	100%

CONCLUSION

Prescription of more drugs i.e., polypharmacy to treat multiple comorbid conditions (or) to gain quick patient satisfactorial response and prescription of additional drugs to treat side effects increases the risk of drug- drug interactions. Our study concluded that a high percentage of DDI were found in patients of age group >60 years and whereas distribution of drug-drug interactions based on severity showed many major drug-drug interactions (59.80%). Further the study concluded that cardiology department followed by General medicine department are more prone to polypharmacy, so more drug-drug interactions were noted in those departments. Hence, monitoring of prescriptions with polypharmacy is highly necessary in order to reduce the occurrence of DDI's and other drug related problems. In this aspect, Clinical pharmacist play an important role in healthcare system by assisting the physicians in dosage adjustments, in discontinuation of unnecessary and inappropriate medications, in establishing a balance between risks and benefits of multiple drug therapies, thereby preventing the occurrence of DDIs, ADRs and thus improving the rationality of drug therapy, patients quality of life, decreasing the hospitalization of patients and health care cost burden to the patient and society.

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