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STUDY ON DRUG-DRUG INTERACTIONS IN DIFFERENT POPULATION IN TERTIARY CARE TEACHING HOSPITAL OF WARANGAL REGION

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ABSTRACT

Aims and Objectives: To study the drug-drug interactions in prescriptions of inpatients in a tertiary care teaching hospital and to assess the age group and department more prone to DDIs. **Methodology:** This prospective study was conducted over a period of six months in 2016 to identify the drug-drug interactions in different population tertiary care teaching hospital of Warangal region. **Results:** A total of 816 cases were reviewed from which 1261 DDIs were identified, age group more prone to DDIs is 36-54 years (66.03%) and department is neurology (71.39%) with moderate DDIs in severities resp., the highest is the single DDI prescriptions in the age group of 55 or more (48) and department general medicine (58), the pharmacokinetic interactions are more in the age group of 13-18years (82.35%) and pharmacodynamic interactions are more in neurology department (62.61%), single diagnosis and co-morbidities patients are more prone to DDIs in the age group 55 years or more(32.32% and 32.31% resp.) and department cardiology (31.72 and 30.89% resp.), the fixed dose combination of Ampicillin+Amikacin (48%) frequently involved in DDIs most appeared in the all over departments, prescriptions with minor polypharmacy (321) involved mostly in DDIs, most frequent interacting drug identified is Digoxin (54%) when compare with other drugs. **Conclusion:** Elderly people were more prone to drug-drug interactions due to age related physiological changes, multiple diseases, polypharmacy and immunosupression. Hence special care must be taken while prescribing drugs to elderly patients especially in co-morbid conditions.

KEYWORDS: Tertiary care teaching hospital, major polypharmacy and moderate polypharmacy.

INTRODUCTION

Recent developments in pharmacotherapy have contributed considerably to improve patient's safety and quality of life. As a result of such developments, the number of available medications and their uses is increasing. Although drugs are used to achieve beneficial therapeutic effects, they can also lead too many undesirable consequences. One of such consequences is the development of drug-drug interactions (DDI). DDI is a specific type of Adverse Event (AE) that occurs when the effects of the drug is modified. Evidence from epidemiologic is that the study suggests that DDIs contribute to 6-30% of AEs with significant hospitalizations (or) death. In spite of DDIs, prescribes the two or more drugs simultaneously is sometimes intentional with the aim of obtaining a specific pharmacological synergism.[1]

DRUGS	MECHANISM OF ACTION	MANAGEMENT
Clopidogrel + Aspirin	clopidogrel with aspirin either increases toxicity of other by PD synergism (Increased risk of bleeding)	Use low dose aspirin (or) closely monitor the clopidogrel (half-life 6 hours), aspirin (half-life15-20 minutes).[2]

According to WHO severity assessment of drug-drug interactions is classified as: Mild, Moderate, and severe.

1.1 Mild: Examples include metformin decreases levels of furosemide by unspecified interaction mechanism[3] and Ceftriaxone increases toxicity of furosemide by PD synergism.

1.2 Moderate: Examples of this includes Proton pump inhibitors such as omeprazole, ianoprazole, pantoprazole (or) rabeprazole inhibit cytochrome P4502C19 to varying degrees.[3]

1.3 Severe: Examples of this include the combination of ACE inhibitors with potassium-sparing diuretics such as amiloride can increase potassium retention so strongly that life-threading hyperkalemia. Fluoroquinolone are combined with microlidess such as erythromycin this may be results in QT prolongation.[3]

Some of the drugs with long half-life are: Phenytoin (12-42hours), clonazepam (18-50hours), fluoxetine (4-6days), active lipophilic metabolite (4-6days), Diazepam (20-100hours), Digoxin (39hours), and Digitoxin (168 hours).[4]

The combined effect of drugs taken concurrently the results may be antagonism (or) synergism and may be lethal in some cases, it is important for the patient, pharmacist, physician and nurse to be aware of the potential drug - drug interactions that are prescribed as well as those that the patient may be self-administering, many patients especially the elderly may take several medicines each drug. The chances of developing an undesired drug interaction increases rapidly with number of drugs used. A clinically relevant drug-drug interaction occurs when the effectiveness (or) toxicity of one medication is attended by the administration of another medication (or) a substance that is administered for medical purpose (to be distinguished from drug-food interaction). Adverse consequence of drug-drug interaction may result from either diminished therapeutic effect (or) toxicity. Among various types of medical errors the occurrence of drug-drug interaction is one that is usually preventable. It is therefore essential that a health professional is able to evaluate the potential drug-drug interaction and when detected, determine the appropriate prevention (or) management- a strategy of patient's health care.

Adverse drug reactions resulting from drug-drug interactions can be prevented by making patient specific assessments and it is appropriate avoiding concomitant administration by implementing alternative therapeutic strategies (or) taking precautions such as dosage adjustment, increased monitoring. Dosing needs to be considered as a factor which might have some effect on the development of ADRs.[5] Before starting any new prescription drug (or) OTC drug, healthcare provider should known the patient information regarding past medical history, past medication history food habits and social habits and choose the correct medication according to patients need and if for any warnings pharmacist look for the "*DRUG INTERACTION REACTION*[6] ".

Major reason for choosing this project is to identify one of the major challenges in drug administration that is potential drug-drug interactions. when several drugs are being administered there is a possibility of adverse drug reactions (ADEs) as one drug can increase (or) decreased the effect of another drug may lead to serious consequences even leads to death. Recognition of drugs that have a narrow therapeutic index and the major perpetrators of pharmacokinetic interactions will help identify most of the pharmacokinetic interactions.[7]

MATERIALS AND METHODS

The study was a prospective observational study, conducted over a period of six months. This study was conducted in inpatients of tertiary care teaching hospital which contain

departments such as General medicine, Cardiology, Neurology, Pediatrics, General surgery and auxiliary departments. Patients of all age groups admitted as inpatients in General medicine, Cardiology, Neurology, Pediatrics, General surgery departments. Selection of only those prescriptions of inpatients which containing more than four medications in a prescription are taken into the study. Exclusion criteria include prescription which contains less than four medications. The prescriptions of patients of outpatient department of the hospital.

RESULTS

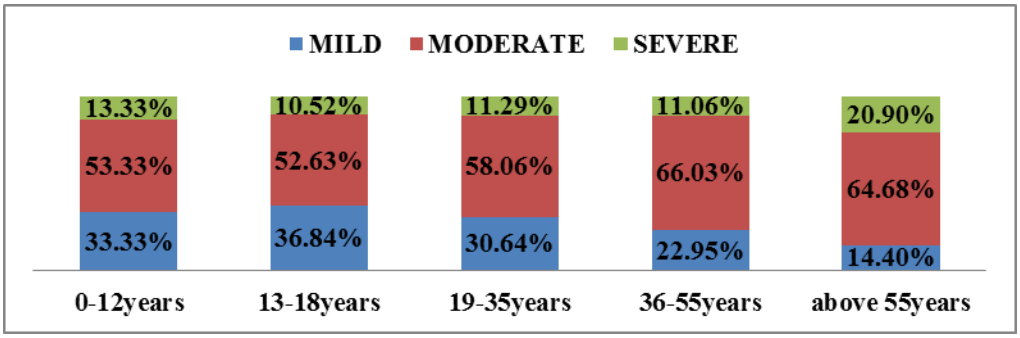

Figure 1.1: Graph shows severity DDI comparing within age groups.

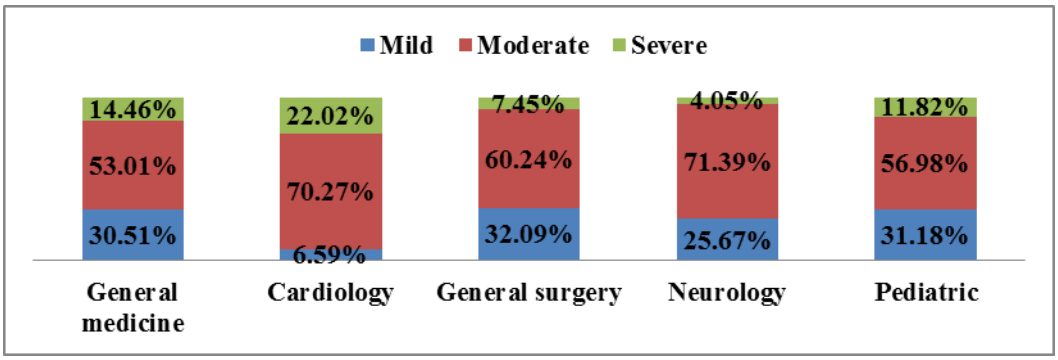

Figure 1.2: Graph shows severity of DDI comparing within departments.

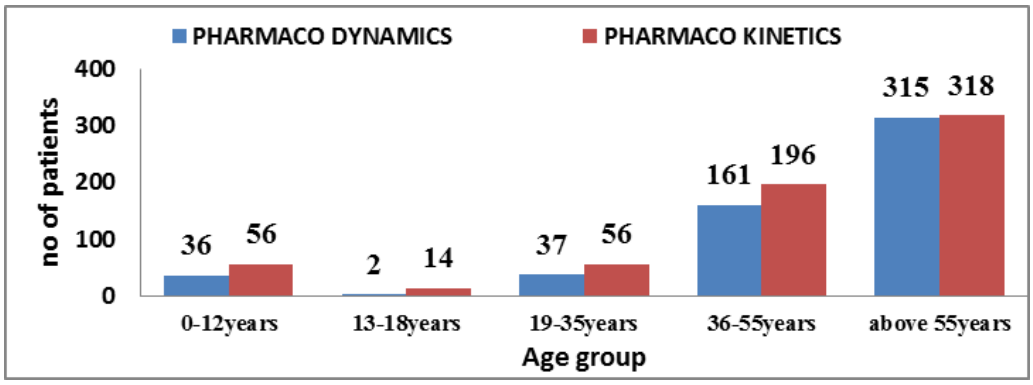

Figure 2.1: Graph shows type of DDI in different age groups.

Table 2.1: Type of DDI in different departments.

DEPARTMENT	PHARMACO DYNAMIC	PHARMACO KINETIC	OTHERS
GENERAL MEDICINE	198	140	3
CARDIOLOGY	217	260	55
GENERAL SURGERY	72	103	5
NEUROLOGY	67	39	1
PEDIATRICS	38	60	3

Table 3.1: DDI in Single Diagnosis and Co-morbid prescriptions comparing within age groups.

Age	DDIs in single diagnosis prescriptions	DDIs in co-morbid prescriptions
0-12 years	13.67%	12.02%
13-18 years	4.54%	2.96%
19-34 years	24.20%	23.88%
35-54 years	25.25%	28.91%
55 years or more	32.32%	32.21%

Table 3.2: DDIs in Single Diagnosis and Co-morbid prescriptions comparing within departments.

Departments	DDIs in single diagnosis prescription	DDIs in co-morbid prescriptions
General medicine	16.17%	17.85%
Cardiology	31.72%	30.89%
Genera surgery	22.62%	15.62%
Neurology	15.37%	25.87%
Pediatric	14.09%	10.55%

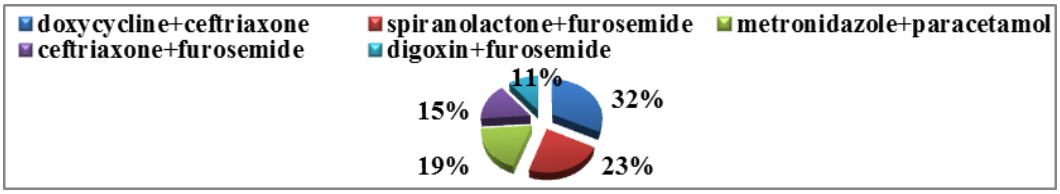

Figure 3.1: Frequent drug combinations causing DDIs in general medicine.

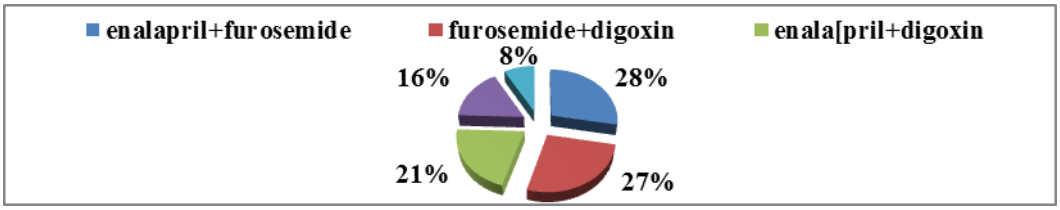

Figure 3.2: Frequent drug combinations causing DDIs in Cardiology

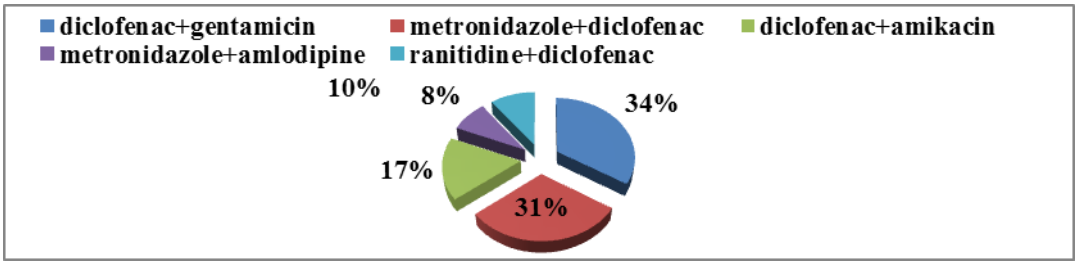

Figure 3.3: Frequent drug combinations causing DDIs in General surgery.

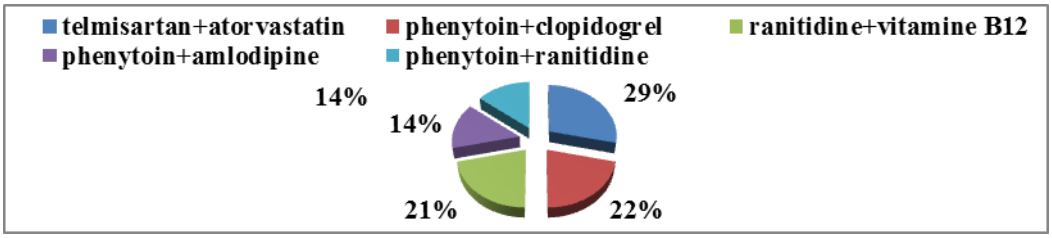

Figure 3.4: Frequent drug combinations causing DDIs in Neurology.

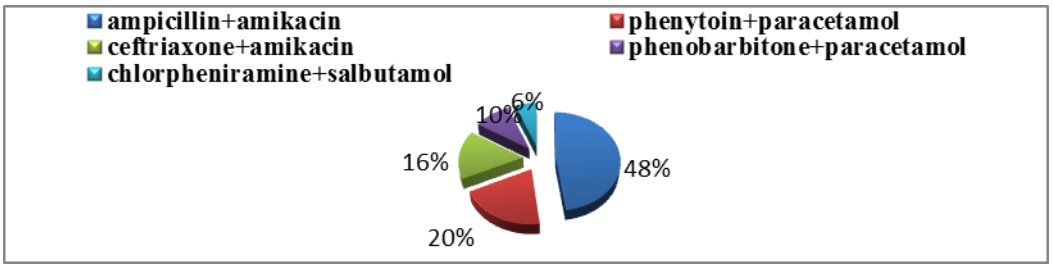

Figure3.5: Frequent drug combinations of DDIs in Pediatrics.

Table 4.1: DDIs due to polypharmacy.

Prescription Containing Drugs	Total Prescriptions	Interacting Cases	Non Interacting Cases
4-10 DRUGS	722	321	401
11-15 DRUGS	114	99	15
15 DRUGS OR MORE	17	16	1

DISCUSSION

Drug-drug interaction is a situation in which a substance affects the activity of other drug when both are administered together, this can be synergistic (when drugs effect is increased) or antagonistic (when drugs effect is decreased).

This is the study to evaluate the management and prevalence of drug-drug interactions which is collected from patient clinical data. Now a day's drug-drug interactions are most common in elderly patients. It is also one of the reasons to choose this project is, to educate the people

regarding the drug-drug interactions and this project may help physicians and health care providers to promote better patient health care and outcomes.

Raman sripada, Sv.Suresh kumar. et al., done a study on the prevalence and severity of possible drug-drug interactions in the inpatient department of internal medicine during the study period a total of 437 cases were screened for drug-drug interactions by using the software's, among them drug interactions and the prevalence was observed in 51.9%. Out of 437 cases a total of 675 possible drug-drug interactions were observed. The prevalence of possible drug-drug interactions in the age group 51-60 years (27.8%) was found to be high, followed by the age group 61-70 years (22.9%). Severity of drug-drug interactions based on age wise were categorized in the study with 6.8% of the minor severity interactions and 63.3% with moderate severity and with 29.9% major severity. Majority of interactions were of moderate severity followed by major and minor severities. Minor, moderate, major interactions are highly prevalent in the age group 61-70 years2.

In the present study we found that moderate drug-drug interactions are more prevalent in all age groups, when compared to minor and severe, especially 55years or more age group has higher DDIs in 13-18years age group has lower DDIs. In age group of 36-55 years patients are more prone moderate drug-drug interactions with 66.03% followed by minor DDIs found in age group of 13-18 years with 36.84% and followed severe DDIs found high with age group of 55 years or more with 20.90%. This study has the similar results when compared with Raman sripada, Sv. suresh kumar. et al study. The age group 36-55 years in the present study is at more risk for drug-drug interactions when compared with other age groups.

We also studied DDIs according to departments,of which cardiology department has more moderate DDIS (444), neurology department has the lowest severe DDI and highest mild DDI found (32.09%) in general surgery department, followed by moderate DDI are high (71.39%) in neurology and also severe DDI are high (22.02%) in cardiology. The present study reveals cardiology department is more prone to DDI.

Based on the type of interactions 55 years or more age group are highest to be effected with with pharmacokinetic(318) and pharmacodynamic(315) DDIs and the lowest is the 13-18 years age group with pharmacokinetic (14) and pharmacodynamic(2) DDIs. Cardiology has the highest number of pharmacokinetic(260) and pharmacodynamic(217) DDIs and pediatrics

has the lowest pharmacodynamic (38) and neurology has the lowest pharmacokinetic(39) DDIs.

For the patient, diagnosis of a disease is a confounding factor which is related to the treatment and DDI occurrence. The single diagnosis patient requires fewer medications when compared to co-morbid patient and reduces chance of DDIs occurrence. In this study highest no. of DDIs found in age group of 55 years or more in both conditions of without co-morbidity(single diagnosis) (32.32%) and co-morbidity (32.21%). The lowest no. of DDIs found in without co-morbidities (single diagnosis) with age group of 13-18years (4.54%) and incase of co-morbidity condition with age group of 13-18 years (2.96%). The reason for higher number of DDIs with age group of 55 or more is age related changes in physiological conditions.

In the case of department it was found that the cardiology has the most number of DDIs without co-morbidities (single diagnosis) with 31.72% when compared to other departments hence acquiring highest position in DDIs. The lowest DDIs without co-morbidities patient was found in the pediatrics with 14.09% followed by general surgery (22.62%), general medicine (16.17%) and neurology (15.37%). In the cardiology the drug of choice for many cardiac diseases is digoxin which has long half life and interacts with other drugs given after its administration and hydrochlorothiazide (antihypertensive drug) with 8 hours of activity. This can be managed by choosing antihypertensive drugs with short half life.

Patients with co-morbidity conditions have high number of DDIs due to increase in the number of medications for multiple diseases. In this study the high percentage with 32.21% found in the age group of 55 years or more and the low DDIs found in age group of 13-18 years with percentage of 2.96% followed by age group of 35-54 with 28.91%, age group of 19-34 with 23.88% and the age group of 0-12 with percentage of 12.02%. the reason for more DDIs in age group 55 or more patients is their age factor with reduced functional capacity along with polypharmacy due to co-morbidities.

In accordance with department the DDIs in co-morbidities found mostly in cardiology with 30.89% percentage when compared to other departments and the lowest is pediatrics with 10.55% followed by neurology with 25.81%, general medicine with 17.05% and general surgery with 15.62%.

In this study we found more frequent fixed dose combinations involving in DDIs in each department. In the total 266 prescriptions of inpatients in general medicine the doxycycline+ceftriaxone is the most frequent drug combination involved in DDI with 32%, followed by furosemide+spironolactone (23%), metronidazole+paracetamol (19%), ceftriaxone+furosemide (15%), digoxin+furosemide (11%). In the cardiology in the total of 175 cases the combination of enalapril+furosemide is the most frequent DDI with 28% followed by furosemide+digoxin (27%), enalapril+digoxin (21%), digoxin+pantoprazole (16%), aspirin+clopidogrel (8%). In the general surgery in the total of 124 cases the combination of diclofenac+gentamicin mostly involved in DDI with 34% followed by metronidazole+diclofenac (31%), diclofenac+amikacin (17%), ranitidine+diclofenac (10%), metronidazole+amlodipine (8%). In the neurology in the total of 66 cases the combination of most frequent DDI is telmisartan+atorvastatin with (29%), followed by phenytoin+ clopidogrel (22%), ranitidine+ vitamin B12 (21%), phenytoin+amlodipine (14%), Phenytoin+ ranitidine (14%). In the pediatrics department in the total of 239 cases the most repeated combination with DDI is ampicillin+amikacin with (48%) followed by phenytoin+ paracetamol (20%), ceftriaxone+amikacin (16%), phenobarbotone+ paracetamol (10%), chlorpheniramine+salbutamol (6%).

In the Ramam sripada, Sv.Suresh kumar. et al., study, poly pharmacy can be observed in the prescriptions as a reason for possible drug-drug interactions with 131(57.7%) were observed with major poly pharmacy, 65(28.6%) were observed with moderate poly pharmacy and 31(13.7%) were observed with minor polypharmacy11.

In the study we collected 816 prescriptions with 1261 drug-drug interactions, of which we observed 17 cases having 16 DDIs in prescription contains major polypharmacy (prescriptions contain more than 15 drugs), followed by 99 drug interactions in 114 moderate polypharmacy (prescription contains drug nos.11 to 15) cases and followed by 321 drug interactions in 722 minor polypharmacy (prescription contains 4 to 10 drugs) cases. This study has the similar results compared with a study done by Raman sripada and Sv. suresh kumar et al.; we observed that major poly pharmacy is more prone to drug-drug interactions when compared with moderate and minor.

Drug interactions are frequent among inpatient that were on multiple medications, the prevalence rate cannot be directly compare with those reported previously by other reports

from different countries, because of the differences in the study design and severity rating of drug interactions.

Neurology department had mostly moderate DDIs in severity. Based on the diagnosis of a patient the (55 years or more) age co-morbid, single diagnosis patients are more prone to DDIs specifically in the department of cardiology. In the total prescriptions minor polypharmacy (4-10 drugs contained prescriptions) is observed which involved in majority of DDIs. Highest fixed drug combination is ampicillin+amikacin involved in DDIs when compared with other fixed drug combinations.

In this study we found single DDI prescriptions are more in 55 years or more age group when compared to other age groups. In accordance with department general medicine is more prone to single DDI prescriptions when compared with other departments.

CONCLUSION

In the present study we have worked on drug-drug interactions in the inpatient prescriptions and we observed that most of the DDIs are present in the age group of (36-54 years) with majority of moderate DDIs. Elderly people were more prone to drug-drug interactions due to physiological changes, multiple diseases, polypharmacy and immunosupression. Hence special care must be taken while prescribing drugs to elderly patients specifically in co-morbid conditions. The drug activity is influenced mainly due to fixed drug combinations which is one of the main reason for the DDIs.

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