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An observational study on pharmacokinetic drug interaction profiles of cardiac medication in a tertiary care corporate hospital.

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ABSTRACT

In this study with sample size 250, it was observed that the ratio of male: female (inpatients) is males 148 and 102 females. The male patients percentage (59.2%) and females (40.8%) in cardiac departments. Maximum number of patients belonged to the age group of 51-60 years were 67 (26.8 %) and 41-50 years were 66(26.4%). A total of 2799 drugs were prescribed. The different types of Interactions observed In Patients Drug-Drug interaction in 147 (58.8%) and drug food interaction in 103 patients (42.2%). Majority of them had cigarette smoker's 93 patients (36%) and alcohol consumption habit 75 patients (29 %) followed by cigarette smoking and alcohol consumption were 61 (24.4%). BMI Was observed normal 61 Patients (24%) Over Weight 48 Patients (19.2%) Under Weight 3 Patients (1.2%). False 9 Patients (3.6%). The Pharmacokinetics interactions observed in patient's absorption.In 72 Patients (30%).Distribution in 26 Patients (10%).Metabolism in 129 Patients (51%) and Elimination in 23 Patients (10%). The P Value Was Found To Be0.21245.In a sample of 250 patients the types of severity of interactions were observed in patients were Mild 52 patients (21%), Moderate 150 patients (60%) and severe were 58 patients (59%) the value was found to be0.202255.

Keywords: Cardiac medication, Drug interaction, ceritinib, beta- blockers

INTRODUCTION

Drug interactions are one of the important factors that modify the response to a drug. A drug interaction is said to occur when the effects of a drug is altered by another drugs, food, drink or an environmental chemical. Drug interactions are defined as the modifications of the effects of one drug by the prior or concomitant use of another drug. The main cases of hospital admission and mortalities are related to drug interactions and their corresponding adverse events. It has been estimated that 10 -20% of hospital admissions are caused by drug related events, and about 1% are caused by drug interactions.

Drug interactions can occur both in vivo and in vitro. Drug interactions outside the body can occur when different drugs are mixed in an intravenous infusion. Drug interactions inside the body can be pharmacodynamics or pharmacokinetics in nature. Basically, drug interaction cause altered pharmacological response leading to toxicity or therapeutic failure.

These processes are considered preventable and need intervention by improvement in diagnosing and prescribing skills. Currently, data regarding the

incidence of potential DDIs in Indian settings is limited. The present study was therefore carried out to evaluate the potential DDIs and their clinical significance in inpatients of the medicine department of a tertiary care hospital. We hope to identify potentially serious and significant DDIs along with the common drug groups involved. The information could prove useful to suggest modifications in the prescribing patterns and to optimize drug therapy in these patients.

Alterations of pharmacological or clinical responses that occur during polytherapy are defined as drug interactions. Drug interaction may lead to life-threatening adverse reactions or therapeutic failure by influencing the therapeutic efficacy of drugs. Five to twenty percent of serious adverse drug reactions due to drug interaction have been reported to result in hospitalization or death. Many factors such as age, multiple diseases, and sex have been found to be risk factors for potential drug interaction. Occurrence of drug interaction is correlated with the number of prescriptions.

The incidence of DDIs increases by 10%–20% in patients using 10–20 drugs. In the elderly, drug interaction may be diagnosed as adverse outcomes associated with drug therapy. The impact of drug interactions on the mortality rate of elderly patients was determined in a retrospective research. Consideration of DDIs for patients in the intensive care unit (ICU) is critical for the quality of the patient's life. Clinically important DDIs are more likely for ICU patients with many medications, co morbid diseases, and altered organ functions [1-5].

The risk of DDIs can increase the length of hospital stay because new drugs are often added to an existing drug therapy.Therefore, it is essential to identify possible drug interactions in clinical settings and approach towards the management of potential loss of effectiveness and appearance of toxicity because of the use of certain drug combination. Clinical pharmacist occupies an important position in healthcare settings as it gets an opportunity to work in a team and utilize the professional skills, knowledge and expertise for better patientcare.

Among the various professional services provided by the pharmacists, monitoring drug interactions is the most important one as it helps in improving patient safety in hospital settings. Since drug interaction is an important cause for increase in morbidity and mortality rates in hospitalized patients, it is imperative to assess the insight of drug interaction in hospitalized patients.

Drug therapy is growing more complex, thus making appropriate decision on drug therapy increasingly challenging. Drug interactions are most important in this context and proper handling of drug–drug interactions (DDIs) may prevent harmful events. DDI in patients receiving multidrug therapy is a major concern. Such interactions may lead to an increased risk of hospitalization and higher health care costs. Some studies have found that up to 11% of patients experience symptoms associated with DDIs and that DDIs are responsible for up to 2.8% of hospitaladmissions.

Accordingtorecentlypublishedstudy,1%ofallhospitaladmissionsarecausedbyDDIs,and 0.05% emergency department visits, 0.6% of the hospital admissions and 0.1% of hospitalizations are caused by adverse drug reactions (ADRs) due to DDIs.

MATERIALS AND METHOD

Study site

The study was conducted in Sunshine hospital, behind paradise hotel, Secunderabad.

Study period

The study was conducted for a period of 6 months.

Study design

The study is prospective and observational.

INCLUSION CRITERIA

- Patients above 18 years of age
- Both males and females
- In-patients

EXCLUSION CRITERIA

- Pediatrics
- Pregnant and lactating women
- Psychiatric patients
- Patients who are not willing to give consent.

SOURCE OF DATA COLLECTION
Study materials

- Patient consent form
- Patients data collection orm
- Drug interactions documentation forms

Patient consent form

It contains the demographic details of the patient, title of the study, details of the study and signature of the participant and researcher. The patient consent form is the document that participants must sign voluntarily to ensure their willingness to participate in a clinical research study.

Patient data collection form

It contains patient demographic details like age, sex, weight, date of admission, date of discharge, complains on admission, medical history, medication history, social history, family history, previous allergies and it includes physical examination, provisional diagnosis, routine biochemical investigations, final diagnosis, drug treatment chart, progress chart and discharge medications. It contains patient demographic details like name, age, sex, weight, date of admission, final diagnosis, drug interaction table (interaction drugs , dose , route , frequency), objective drug, Precipitant drug, no of interaction, type of interaction, classification of drug interaction (Pharmacokinetic drug interactions, pharmacodynamics drug interactions), pharmaceutical interaction, pharmacokinetic interactions (onset of action, severity, documentations, effects), Mechanism of drug interaction, management of drug interaction, Description of drug mechanism, References, notified to action taken, Name and Sign of the attending Pharmacist and the staff [6-9].

STUDY PROCEDURE

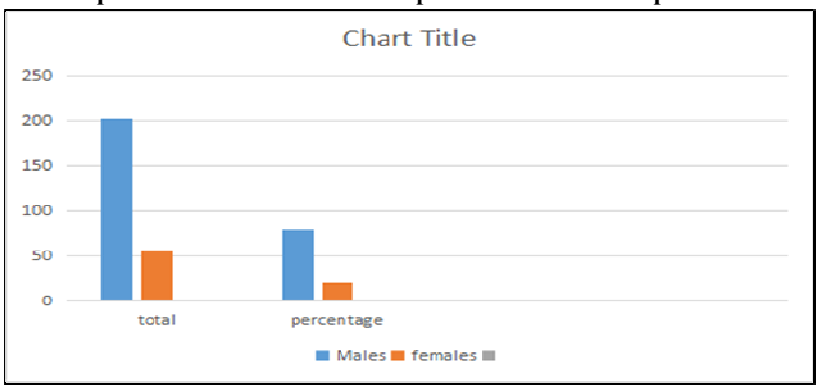
This is an observational study where patients are willing for enrollment into the study after obtaining the consent. The study didn't require any investigation or intervention on patients. The Ethical Committee of Sunshine hospital has given approval for the conduct of the study. We have enrolled 250 patients of both the gender in our study. All the data required for our study was collected through patient data collection forms. During the six months study period, initial two months were utilized for data collection. In the process of data collection, we have approached patients who satisfied our study inclusive criteria and we have explained the details of our study to them clearly and obtained consent after they understood the study well. A Cardiology, department is considered. We have also asked them about their past medical history and social habits. After data collection, we utilized the next two months for data analysis. All statistical analysis was done using the software - Microsoft Office Excel has been used to generate the graphs, tables etc. Study was conducted in Sunshine hospital. The latter two months of the study period were utilized in preparing the thesis.

RESULTS

Table 1: Gender distribution of patients in cardiac departments

S.no	Gender	No of Patient	Percentage	P.Value
1	Males	148	59.2	0.093967632
2	Females	102	40.8	

Graph 1: Gender distribution of patients in cardiac departments

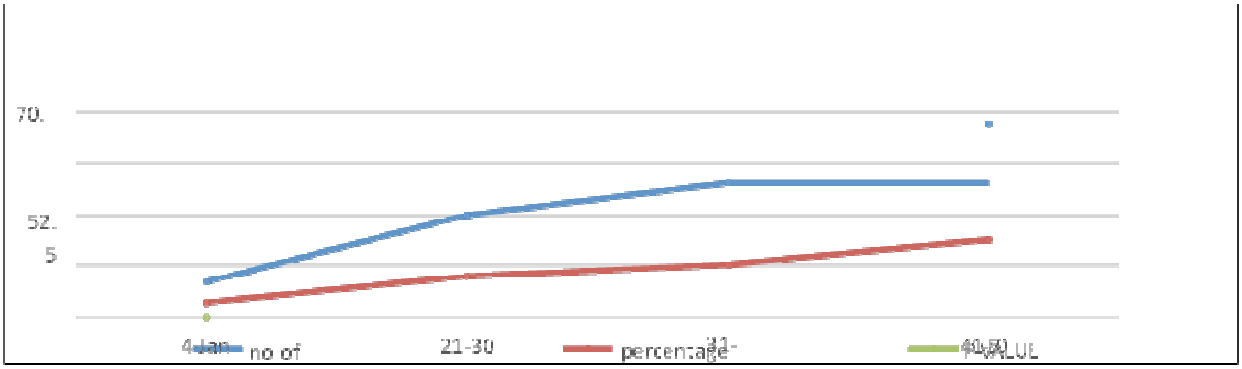


A total of 250 prescriptions were analyzed for various parameters during the tenure of this study in various departments of Sunshine Hospitals, Secunderabad. We took either gender into consideration and patients above the age 18 years. Among 250 inpatients, 148 were males and102 were females. The male patient's percentage (59.2%) and females (40.8%) in cardiac departments. The P Value is found 0.093967632.

Table 2: Age wise distribution of patients in cardiac departments

Age	No of patients	percentage	P VALUE
10-20	12	4.8	0.056085667
21-30	35	14	
31-40	46	18	
41-50	66	26.4	
51-60	67	26.8	
61-70	21	8	
71-80	4	1.6	

Graph 2: Age wise distribution of patients in cardiac departments

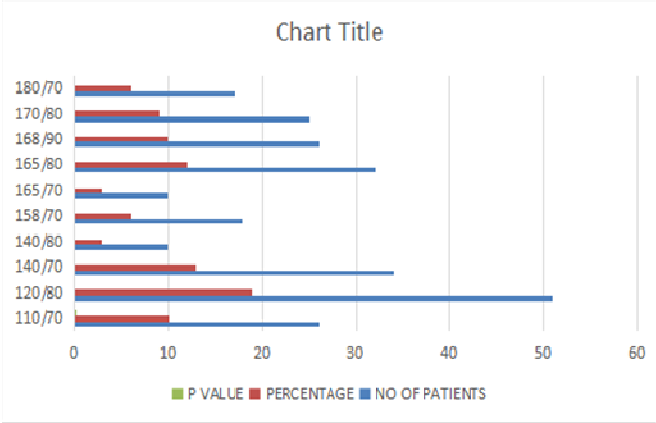


In a sample of 250 patients The majority of the patients were taken in age of 51-60 years were 67 (26.8 %) and 41-50 years were 66 (26.4 %) followed by the age group 31-40 years were 46 (18 %) and 21-30 years were 35 (14%) and 61-70 years were (8%) . The age group with least number of patients is 10- 20 were 12 (4.8%) and 71-80 years were 4 (1.6 %). The P value is0.056085667.

Table 3: Blood pressure of patients in cardiac departments

B.P	NO OF PATIENTS	PERCENTAGE	P VALUE
110/70	26	10.07	0.002570188
120/80	51	19	
140/70	34	13	
140/80	10	3	
158/70	18	6	
165/70	10	3	
165/80	32	12	
168/90	26	10	
170/80	25	9	
180/70	17	6	

Graph 3: Blood pressure of patients in cardiac departments



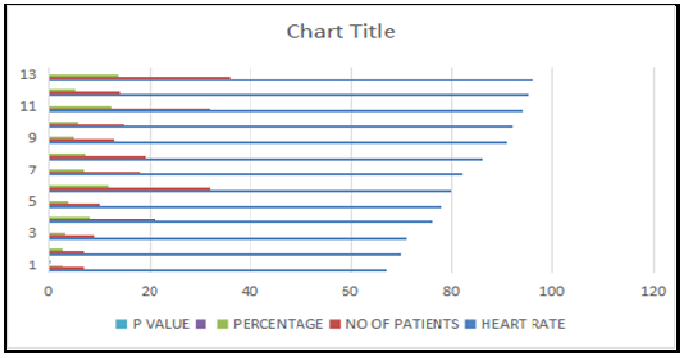
In a sample of 250 patients the Blood Pressure of the patients were reordered as Normal 110/70 mm hg in 26 patients (10.07 %) , 120/80 mm hg in 51 patients (19 %) and high blood Pressure (Hypertension) Stage 1 140/ 70 mm hg were 34 (13 %), followed by 140/80 mm hg were 10 (3 %) and High Blood Pressure (Hypertension) Stage2 158/70 were 18 (6 %) ,165/ 70 mm hg were10(3%)followedby165/89were32(12%),168/90mmhg26(10%),70/80mmhg 25 (9 %) high blood Pressure (Hypertension) Stage 3 were 17 (6 %). The P value is 0.002570188 [10-14].

Table 4: Heart rate of patients in cardiac departments

HEART RATE	NO OF PATIENTS	PERCENTAGE	P VALUE
67	7	2.7	0.000917967
70	7	2.7	
71	9	3.4	
76	21	8.1	
78	10	3.8	
80	32	12	
82	18	6.9	
86	19	7.2	

91	13	5.03
92	15	5.8
94	32	12.4
95	14	5.4
96	36	13.9

Graph 4: Heart rate of patients in cardiac departments

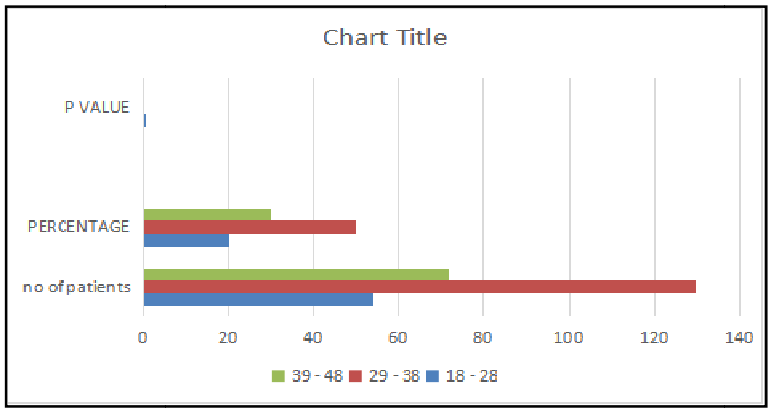


In a sample of 250 patients the heart rate of the patients were recordered as the range of bradycardia 7 b/min in 7 patients (2.7 %) , 70 b/min in 7 patients (2.7 %) , 71 b/min in 9 patients (3.4 %). The P value was found to be 0.000917967.

Table 5: Respiratory rate of patients in cardiac departments

Respiratory range rate	No of patients	PERCENTAGE	P VALUE
18 – 28	130	50	0.101727605
29 – 38	72	30	
39 – 48	54	20	

Graph 5 : Respiratory rate of patients in cardiac departments

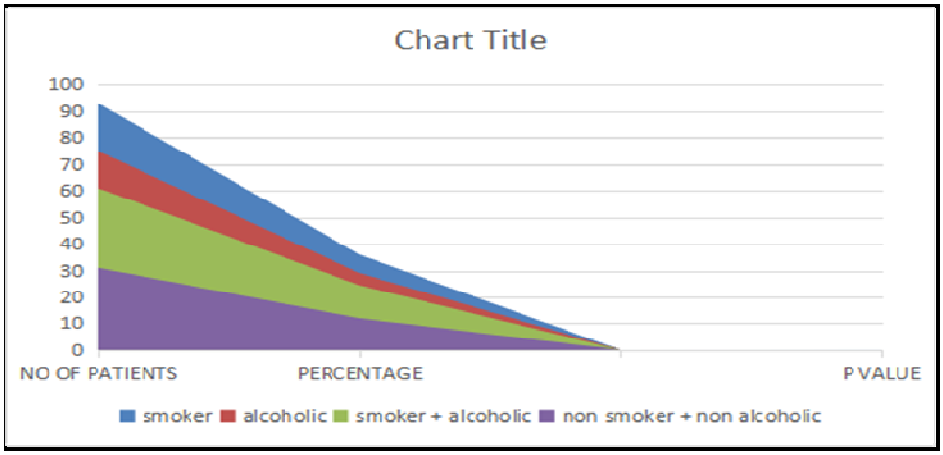


In a sample of 250 patients the RESPIRATORY RATE of the patients were reordered as the range of normal 18 -28 b/min in 130 patients (50 %) , 29 - 38 b/min in 72 patients in (30 %) ,Tachypnea 39 - 48 patients were found to be 54 (20 %). The P VALUE was found to be 0.101727605.

Table 6: Social habits observed in patients

Social history	No of patients	Percentage	P value
Smoker	93	36	0.030106982
Alcoholic	75	29	
smoker + alcoholic	61	24.4	
Nonsmoker + non alcoholic	31	12	

Graph 6:Social habits observed in patients

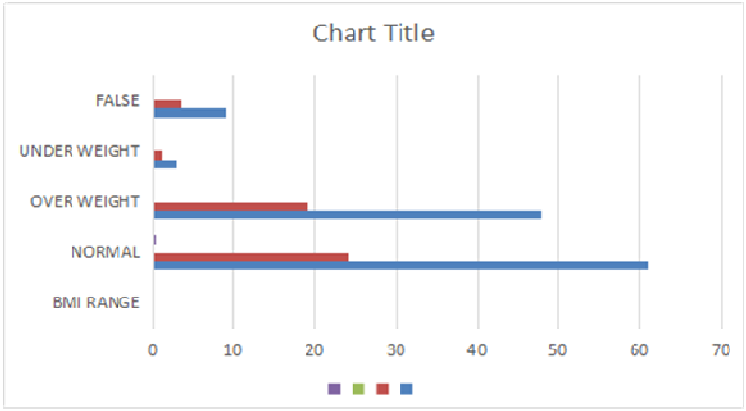


A total of 250 as sample patients were found to be associated with social habits. Majority of them had cigarette smokers 93 patients (36 %) and alcohol consumption habit 75 patients (29 %) followed by cigarette smoking and alcohol consumption were61 (24.4%). The non-cigarette smokers and non-alcoholics were 31 patients (12%).

Table 7: Bmi observed in patients

Bmi range	No of Patients	Percentage	P value
Normal	61	24	0.280175982
Over weight	48	19.2	
Under weight	3	1.2	
False	9	3.6	

Graph 8: Bmi observed in patients

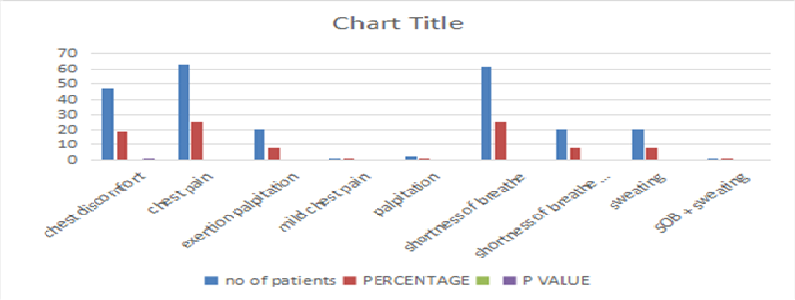


A Total No. of 250 Patients were Taken. Bmi was observed normal 61 Patients (24%) OverWeight48Patients (19.2%) Underweight3Patients(1.2%)false9Patients(3.6%). The P Value found as 0.280175982.

Table 8: Complains observed in patients

Complaints	No of patients	PERCENTAGE	P VALUE
Chest discomfort	47	18.8	0.099966598
Chest pain	63	25.2	
Exertion palpitation	20	8	
Mild chest pain	1	0.4	
Palpitation	2	0.8	
Shortness of breathe	62	24.8	
Shortness of breath grade 3	20	8	
Sweating	20	8	
SOB + sweating	1	0.4	

Graph 8: Complaints observed in patients



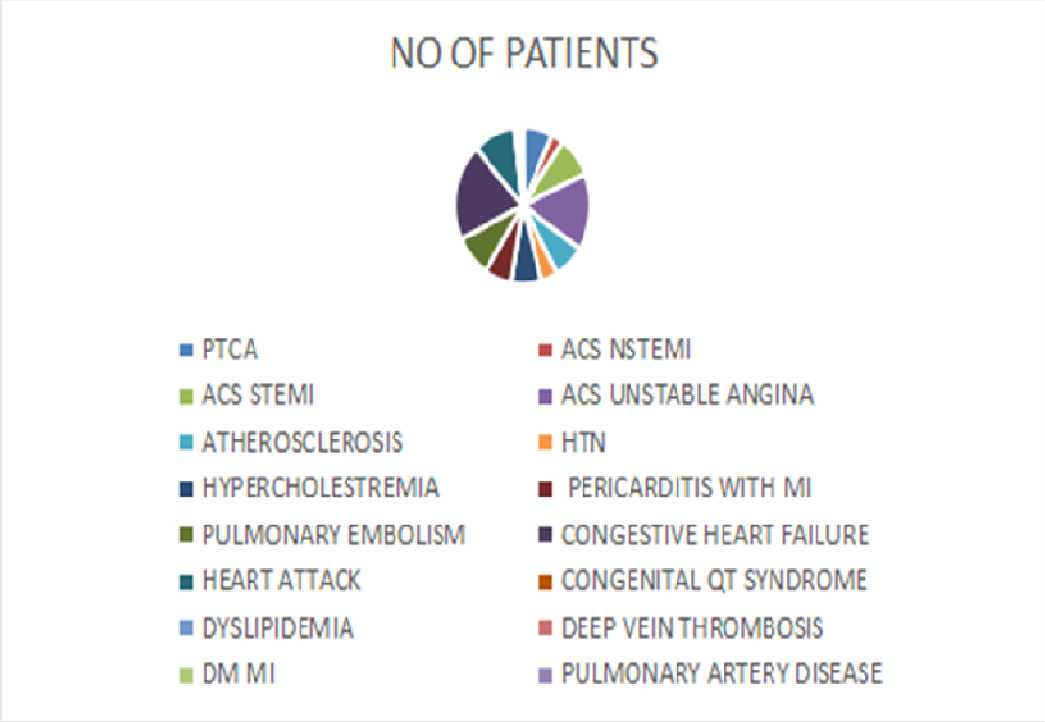
A total no.of 250 patients were taken with complains of chest pain,palpitation,sweating, cheat discomfort , exertion palpitation , mild chest pain , shortness of breath , shortness of breath with sweating and shortness of breath with grade 3. The majority patients complained of chest pain were 63 (25.5 %), followed by shortness of breathe (24.8), chest discomfort ere 47 (18.8%), followed by exertion palpitation and shortness of breathe grade 3, sweating were 20 (8%)theleastpalpitationwere2(0.8%),andsob+sweating,mildchestpainwere1(0.4%). The P.Value is0.099966598.

Table 9: Diagnosis observed in patients

DIAGNOSIS	NO OF PATIENTS	%	P VALUE
PTCA	18	7.2	0.021924309
ACS NSTEMI	7	2.8	
ACS STEMI	21	8.4	
ACS UNSTABLE ANGINA	40	16	
Atherosclerosis	18	7.2	
HTN	10	4	
Hypercholestremia	18	7.2	
Pericarditis with mi	16	6.4	
Pulmonary embolism	22	8.5	
Congestive heart failure	50	20	
Heart attack	25	10	
Congenital qt syndrome	1	0.4	

Dyslipidemia	1	0.4
Deep vein thrombosis	1	0.4
DM MI	1	0.4
Pulmonary-artery disease	1	0.4

Graph 9: Diagnosis observed in patients

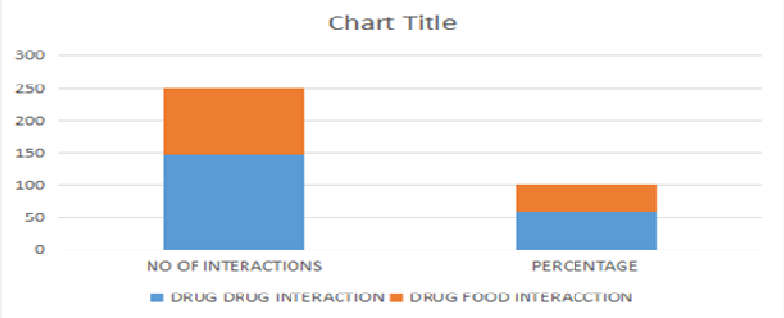


In A Sample of 250 Patients. The types of DIAGNOSIS Observed in Patients. The P Value Was Found To Be 0.086836304.

Table 10: Types of interactions observed in patients

	NO OF INTERACTIONS	**PERCENTAGE**	**P.Value**
DRUG DRUG INTERACTION	147	58.8	0.086836304
DRUG FOOD INTERACCTION	103	42.2	

Graph 10: Types of interactions observed in patients



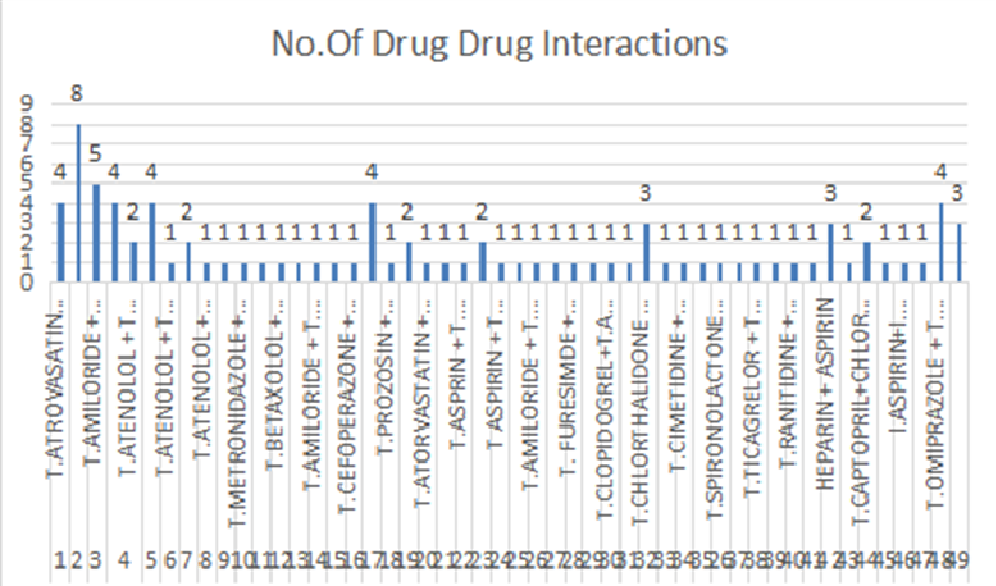
In A Sample Of 250 Patients the types of Interactions Observed In Patients DRUG INTERACTION in 147 (58.8 %) and DRUG FOOD INTERACTION in 103 patients (42.2 %) The P Value was found to be 0.086836304 [15-20].

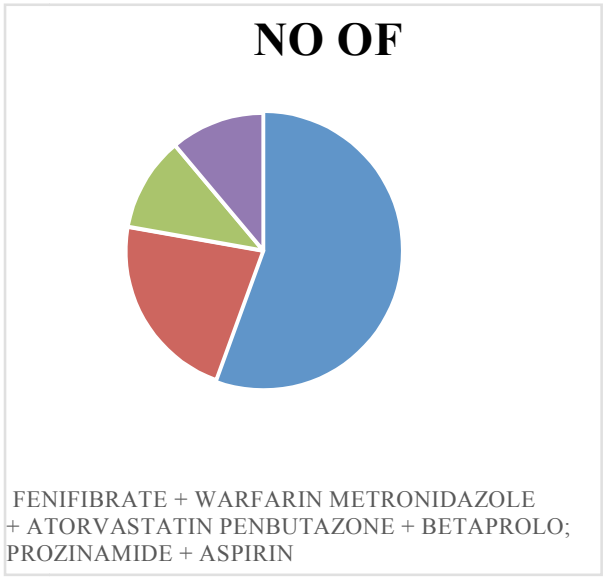
Table 11: Types of drug - drug interactions observed in patients

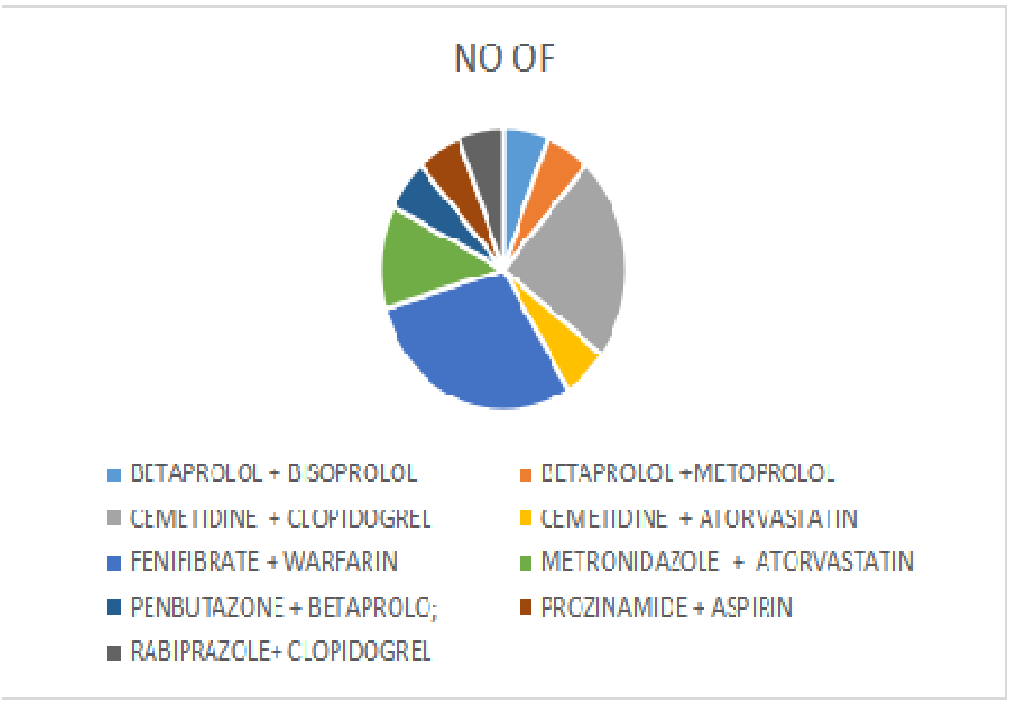
S.NO	DRUG DRUG INTERACTIONS	No. of Drug Drug Interactions
1	T.ATROVASATIN +PIOGLITAZONE	4
2	FENOFIBRATE + INSULINE DETEMIR	8
3	T.AMILORIDE + T.EPLERENONE	5
4	T.SPRINOLACTONE + T.EPLERENONE	4
5	T.ATENOLOL + T BETAXOLOL	2
6	T.ATENOLOL + T.BISOPROLOL	4
7	T.ATENOLOL + T METOPROLOL	1
8	T.ATENOLOL + T.PINDOLOL	2
9	T.ATENOLOL + T.PROPRANOLOL	1
10	T.BETAXOLOL + T.BISOPROLOL	1
11	T.METRONIDAZOLE + T. ATOVASTATIN	1
12	I.FEROUS SULPHATE + I. PAN	1
13	T.BETAXOLOL + T.METAPROLOL	1
14	T.PENBUTOLOL +T.BETAXOLOL	1
15	T.AMILORIDE + T. FURESIMDE	1
16	T.CIMETIDINE + T.ATROVASTATIN	1
17	T.CEFOPERAZONE + HEPARIN	1
18	T.ASPIRIN + T.AMLODIPINE	4
19	T.PROZOSIN + T.ASPIRIN	1
20	T.BETAXOLOL + T HYDROCHLOROTHIAZIDE	2
21	T.ATORVASTATIN + T.PAN	1
22	T.BETAXOLOL + INDAPAMIDE	1
23	T.ASPRIN + T. METOPROLOL	1
24	T ASPIRIN + T AMLODIPINE	2
25	T ASPIRIN + T TIGAGRELOR	1
26	T. ASPIRIN+ T. ACEBUTOLOL	1

27	T.AMILORIDE + T. FURESIMDE	1
28	T.WARAFIN + T. SPRINOLACTONE	1
29	T. FURESIMDE + T .INDAPAMIDE	1
30	T.MAGNESIUMHYDROXIDE + T.ASPIRIN	1
31	T.CLOPIDOGREL+T.ATORVAS	1
32	T.CHLORTHALIDONE + T.HYDROCHOLITHIAZUIDE	1
33	T.CHLORTHALIDONE + T.INDAPAMIDE	3
34	I.PANTOPRAZOLE + I.CYANOCOBALAMINE	1
35	T.CIMETIDINE + T.METOPROLOL	1
36	T.CEMITIDINE + T. WARFARIN	1
37	T.SPIRONOLACTONES + T. ATROVASTATIN	1
38	T.SPIRONOLACTONES + T. WARFARIN	1
39	T.TICAGRELOR + T PRASOGREL	1
40	T. CLOPITAB+ T. OXCARBAZEPINE	1
41	T.RANITIDINE + T.PRASUGREL	1
42	T.ASPRIN + T.AMIKACIN	1
43	HEPARIN + ASPIRIN	3
44	T.BENAZEPRIL+CHLORTHALIDONE	1
45	T.CAPTOPRIL+CHLORTHALIDONE	2
46	T.ASPRIN + T.AMIKACIN	1
47	I.ASPIRIN+I. HYROCARTISONE	1
48	T.FUROSEMIDE + SYP.CODEIN	1
49	T.OMIPRAZOLE + T. CLOPIDOGREL	4
50	T.ASPIRIN+ T. FOLIC ACID	3

Graph 11: Types of drug - drug interactions observed in patients







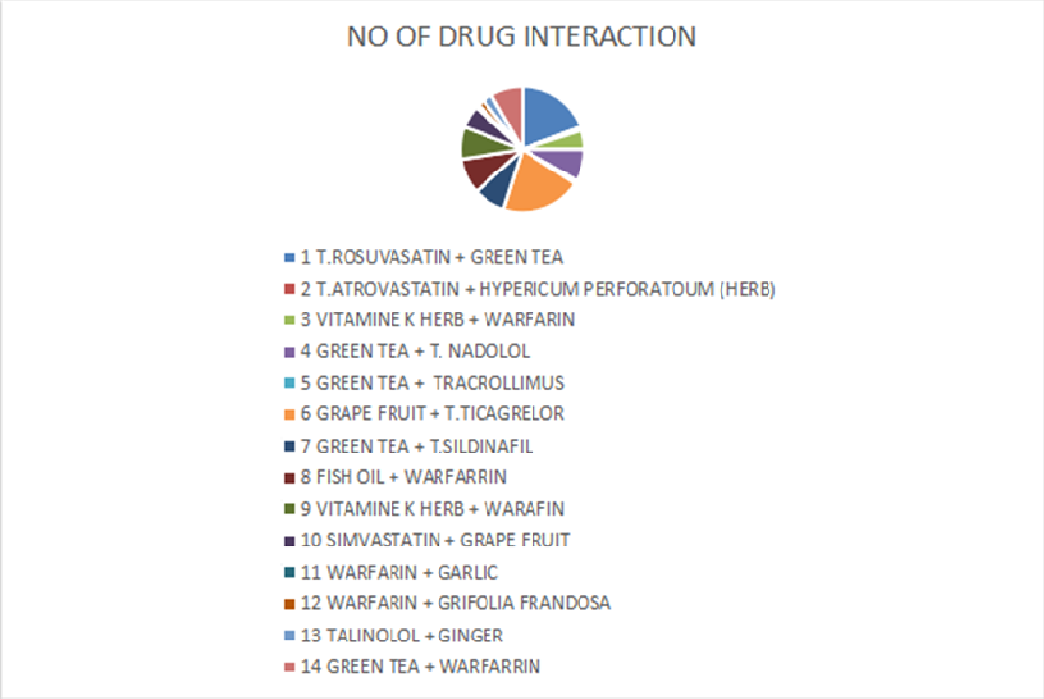
In a sample Of 250Patients. The types of Drug-Drug Interactions Observed In Patients.

Table 12: Types of drug - food interactions observed in patients

S.NO	DRUG FOOD INTERACTIONS	NO OF DRUG INTERACTION
1	T.ROSUVASATIN + GREEN TEA	23
2	T.ATROVASTATIN + HYPERICUM PERFORATOUM (HERB)	1
3	VITAMINE K HERB + WARFARIN	6
4	GREEN TEA + T. NADOLOL	10

5	GREEN TEA +TRACROLLIMUS	1
6	GRAPE FRUIT + T.TICAGRELOR	25
7	GREEN TEA + T.SILDINAFIL	10
8	FISH OIL + WARFARRIN	11
9	VITAMINE K HERB + WARAFIN	10
10	SIMVASTATIN + GRAPE FRUIT	7
11	WARFARIN + GARLIC	1
12	WARFARIN + GRIFOLIA FRANDOSA	2
13	TALINOLOL + GINGER	3
14	GREEN TEA + WARFARRIN	10

Graph 12: Types of drug - food interactions observed in patients

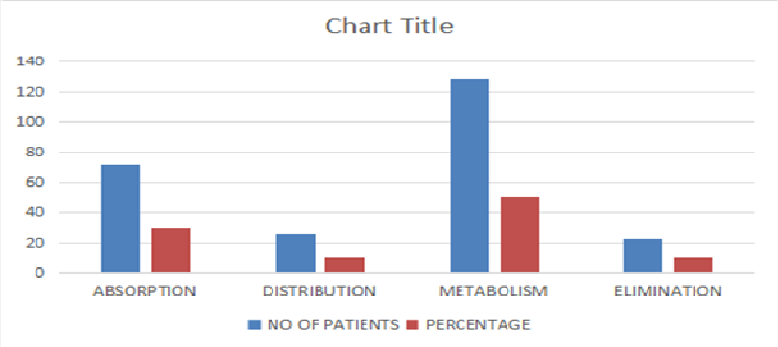


In A Sample Of 250 Patients the types Of Drug - food Interactions Observed in Patients.

Table 13: Pharmacokinetics interactions observed in patients

PHARMACOKINETICS	NO OF PATIENTS	PERCENTAGE	P VALUE
Absorption	72	30	0.21245
Distribution	26	10	
Metabolism	129	51	
Elimination	23	10	

Graph 13: Pharmacokinetics interactions observed in patients

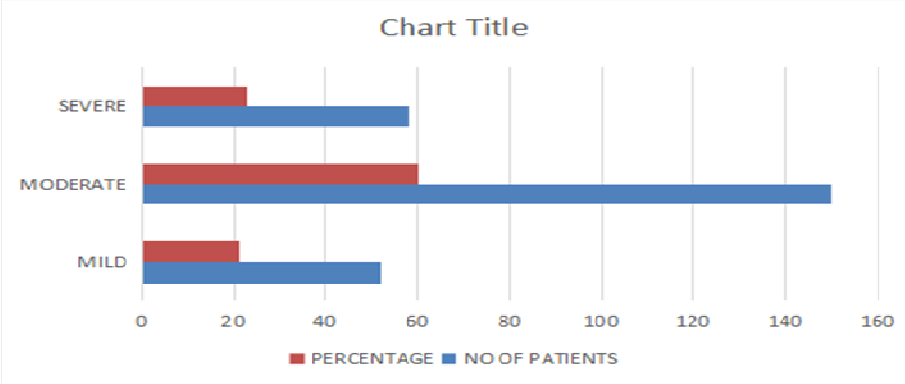


In A Sample Of 250 Patients The Pharmacokinetics Interactions Observed In Patients Absorption In 72 Patients (30 %) , Distribution in 26 Patients (10 %) Metabolism in 129 Patients (51 %) and Elimination in 23 Patients (10%) . The P Value was found to be 0.21245.

Table 14: Types of severity interactions observed in patients

Types of severity	No Of Patients	Percentage	P value
Mild	52	21	0.202255
Moderate	150	60	
Severe	58	23	

Graph 14: Types of severity interactions observed in patients



In a sample of 250 patients the types of severity of interactions were observed in patients were Mild 52 patients (21 %), Moderate 150 patients (60 %) and severe were 58 patients (59 %). The value was found to be 0.202255.

DISCUSSION

The use of drugs is a complex practice. With the enormous growth of pharmaceutical industry, thousands of drugs have made their way into the market. This has further complicated the clinical practice. The intricacy of drug use means that the optimal benefits of drug therapy in patient care may not be achieved because of underuse, overuse or misuse of drugs. Irrational or inappropriate drug use may lead to increased cost of medical care, anti-microbial resistance, adverse effects, drug interactions and patient mortality.

The latest guidelines from the American College of Cardiology and the American College of Gastroenterology recommend that PPIs should be prescribed when there is a clinical indication for them. The use of multiple medications was associated with significantly increased risk of being prescribed potentially harmful drug–drug combinations; in fact, the odds of being prescribed potentially interacting drug more than doubled for

each additional medication prescribed, after controlling for other factors.

Monitor blood pressure and heart rate regularly. Dose reduction or discontinuation of one of the agents may be necessary if clinically significant bradycardia occurs.Monitor for evidence of increased adverse effects or Amlodipine dose reduction may be necessary.

Monitor blood pressure and heart rate closely if concomitant therapy is necessary. Dose reduction or discontinuation of carvedilol may be necessary if clinically significant bradycardia or hypotension occurs.

Monitor blood pressure and heart rate regularly. Dose reduction or discontinuation of one of the agents may be necessary if clinically significant bradycardia occurs.

The evidence that one PPI might be safer than another for patients also taking clopidogrel is evolving and controversial. The increased risk of cardiovascular events was similar among all PPIs studied (omeprazole, esomeprazole, pantoprazole, and lansoprazole), with the highest rate of cardio-vascular events occurring among patients taking pantoprazole. Thus, there are conflicting data about whether one particular PPI is safe for use by patients taking clopidogrel

Avoid using the combination of ceritinib with beta- blockers. If concomitant use is necessary and symptomatic bradycardia occurs, hold ceritinib, adjust or discontinue the beta-blocker, and upon recovery resume ceritinib at a reduced dose with frequent monitoring of heart rate.

Drugs Like

Amiodarone Dofetilide Dronedarone Flecainide Sotalol leads to Moderate risk QTc prolongers Recommend ECG and electrolyte monitoring. Frequency to be determined by patient-specific factors and QT- prolonging drug risk. Avoid combination of high-risk QT- prolonging chemotherapy and cardiac drugs (i.e., arsenic and dofetilide).

All beta- blockers when taken with Ceritinib or Crizotinib effects Additive bradycardia so manage with Avoid using the combination of ceritinib with beta- blockers. If concomitant use is necessary and symptomatic bradycardia occurs, hold ceritinib, adjust or discontinue the beta- blocker, and upon recovery resume ceritinib at a reduced dose with frequent monitoring of heart rate. Monitor blood pressure and heart rate regularly. Dose reduction or discontinuation of one of the agents may be necessary if clinically significant bradycardiaoccurs.

Digoxin with Ceritinib cause Additive bradycardia Monitor levels and signs/symptoms of digoxin toxicity closely. Decreased digoxin doses may be required. Avoid co-administration if possible. If concomitant use cannot be avoided, consider digoxin dose reduction and monitor levels and signs/symptoms of digoxin toxicity closely. Monitor for increased adverse effects or toxicity due to flecainide. Avoid using the combination of ceritinib with digoxin. If concomitant use is necessary and symptomatic bradycardia occurs, hold ceritinib, adjust or discontinue digoxin, and upon recovery resume ceritinib at a reduced.

Consider alternative antiarrhythmic agent if possible.Avoid co-administration if possible.

Consider alternative antiarrhythmic agent during chemotherapy that does not inhibit P-gp. If concomitant therapy is necessary and drug-drug interaction involves QT- prolonging chemotherapy drug, ensure appropriate ECG and electrolyte monitoring. Monitor for increased adverse effects or toxicity due to amiodarone or dronedarone. Dose reduction may be necessary.

Lapatinib Neratinib Sunitinib Vandetanib Vemurafeni P-gp inhibition if taken with Edoxaban Rivaroxaban may cause edoxaban exposure; consider alternative anticoagulant, Rivaroxaban exposure. No action needed because not clinically significant unless significant renal impairment. Avoid combination with strong CYP3A4 inhibitor.

CrizotinibImatinib Nilotinib Ribocicli CYP3A4 inhibition (moderate) taken with rivaroxabanticagrelor may cause rivaroxaban exposure. No action needed because not clinically significant unless significant renal impairment. Avoid combination with P-gp inhibitor. ticagrelor exposure. Monitor for increased adverse effects (i.e., bleeding). No dose adjustment recommended.

Doxorubicin CYP3A4 inhibition taken with ticagrelor cause ↑ doxorubicin exposure. Consider alternative antiplatelet agent during chemotherapy. If concomitant therapy is necessary, monitor for toxicities.

DabrafenibIvosidenib CYP3A4 induction taken with ticagrelor and rivaroxaban can cause ↓ rivaroxaban concentration. Consider alternative anticoagulant during chemotherapy. ↓ ticagrelor

concentration. Consider alternative antiplatelet agent during chemotherapy.

Enzalutamide, Paclitaxel taken with may cause ↓rivaroxaban concentration (significant). Avoid concomitant use alternative anticoagulant. ↓ ticagrelor concentration (significant). Avoid concomitant use use alternative antiplatelet agent. ↑ paclitaxel exposure. If concomitant therapy is necessary, monitor for toxicities (i.e., severe neuropathy,neutropenia) [21-25].

Additive clinical effect EdoxabanRivaroxabanticagrelorincrease antithrombotic effects and increased risk of bleeding. Consider the benefit to risk ratio of antithrombotic therapy. If concomitant therapy is necessary, use caution and frequently monitor platelet counts and evidence of bleeding or hemorrhagic events.

In patients on chronic Phenprocoumon, the increased risk of bleeding of patients co-medicated with verapamil and the increased risk of thrombosis of patients co-medicated with carbamazepine suggest changes in Phenprocoumon bioavailability as well as specific effects on CYP450 enzymes playing a major role in the metabolism of this VKA. Interactions between Phenprocoumon and Ambrisentan, esomeprazole and metformin were also reported. In addition, interactions with older macrolide antibiotics erythromycin and clarithromycin, which inhibit CYP3A4, can trigger life-threatening hemorrhage and contribute to the incidence of medical drug-related hospitalizations .Likewise, inhibition of CYP3A4-catalyzed metabolism of Phenprocoumon by clarithromycin may result in an increase of both bioavailability and risk of bleeding Avoidance of concomitant use of co-trimoxazole with Phenprocoumon (or Acenocoumarol) is a safer approach for the prevention of these potential interactions.

Multiple pharmacokinetic and pharmacodynamic interactions with food, herbs, over-the-counter and other drugs can influence efficacy and safety of both vitamin K antagonists (VKAs) and direct oral anti- coagulants (DOACs).

Bleeding disorders associated to VKAs-interactions have been often described as severe, life- threatening and even fatal, whereas those associated to DOACs-interactions appear to be less relevant.

VKAs interactions have been widely investigated; those involving DOACs were much less studied.

Regarding drug-herb interaction, the interaction between some types of herbs and statins that are commonly used for improving hyperlipidemia has been considered. As previously shown, the herbal reaction towards different types of statins is varied so that grapefruit or pomegranatewere interacted with only some types of statins, but not with all statin types. In this context, administration of herbal materials can lead to decreased absorption of statins or decreasedthe plasma concentration of these drugs. Simvastatin, pravastatin, and lovastatin are inhibitors of HMG-CoA reductase, the rate-limiting step in cholesterol synthesis.9 Thus, any herbs involved in activation or inhibition of this enzymatic pathway can induce changes in drug absorption orcatalysis

Medications are a valuable part of preventing and treating many chronic conditions, including cardiovascular diseases.

Medications can help keep your blood pressure and cholesterol where they need to be. They can help steady an uneven heart rhythm, prevent your blood from clotting together if you are at risk for stroke, and guard against plaque build-up in the blood vessels that supply your heart. But medications only work if you take them correctly. An important part of taking your medications is knowing whether any of the medications you take will interact with one another. That's because taking certain medications or supplements together can be dangerous.

CONCLUSION

In this study with sample size 250, it was observed that the ratio of male: female (inpatients) is males 148 and 102 females. The male patients percentage (59.2%) and females (40.8%) in cardiac departments. Maximum number of patients belonged to the age group of 51-60 years were 67 (26.8 %) and 41-50 years were 66(26.4%). A total of 2799 drugs were prescribed. Among them the average number of drugs per encounter was 9.3±4.18.This indicates a certain degree of poly-pharmacy. Which refers to prescription of too many medications for an individual patient. It is associated with higher risk of adverse drug reactions and interactions. Poly-pharmacy is a

problem of substantial importance in terms of both direct medication costs and indirect medication costs resulting from drug-related morbidity.

The different types of Interactions observed In Patients Drug-Drug interaction in 147 (58.8%) and drug food interaction in 103 patients (42.2%). Majority of them had cigarette smoker's 93 patients (36%) and alcohol consumption habit 75 patients (29 %) followed by cigarette smoking and alcohol consumption were 61 (24.4%). BMI Was observed normal 61 Patients (24%) Over Weight 48 Patients (19.2%) Under Weight 3 Patients (1.2%). False 9 Patients (3.6%).The Pharmacokinetics interactions observed in patient's absorption.In 72 Patients (30%).Distribution in 26 Patients (10%).Metabolism in 129 Patients (51%) and Elimination in 23 Patients (10%). The P Value Was Found To Be0.21245.In a sample of 250 patients the types of severity of interactions were observed in patients were Mild 52 patients (21%), Moderate 150 patients (60%) and severe were 58 patients (59%) the value was found to be0.202255.

Evidence is emerging of an association between concurrent use of clopidogrel and PPIs and adverse cardiac outcomes, which supports the mechanistic hypothesis that PPI inhibits the bio activation of clopidogrel. However, the data are conflicting, and it is not clear if there is one PPI that is safer than the others. On the basis of the data available, use of PPIs should be avoided by patients who are already taking clopidogrel. Histamine2 receptor antagonists should be considered, if appropriate, in lieu of a PPI. If a PPI is absolutely necessary, Omeprazole should be avoided, given laboratory and clinical studies that have consistently demonstrated an interaction. Pantoprazole is preferred if a PPI is strongly indicated, based solely on laboratory and mechanistic data. The benefit of spacing the administration of clopidogrel and PPI over time, to minimize the impact of this potential drug interaction is unclear. This study reports the incidence of DDIs in the cardiology department in a hospital from Indian setting. This study also examined patient, drug characteristics, causality and severity of DDIs. This study shows that DDIs are frequent among hospitalized cardiac patients. The factors influencing DDIs are age, gender, number of prescribed drugs and length of hospital stay and cost. Thus, development and implementation of cautionary guidelines and computer-based screening might help to prevent potentially harmful drug interactions.

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