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# ROLE OF CLINICAL PHARMACIST IN ASSESSMENT OF DRUG RELATED PROBLEMS OF CARDIO VASCULAR AGENTS IN DEPARTMENT OF CARDIOLOGY IN A TERTIARYCARE HOSPITAL – A PROSPECTIVE OBSERVATIONAL STUDY

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**ABSTRACT**

In total, of 173 prescriptions of the patient the total number of 329 drug interaction was found in which the 240 interaction was found in male and 89 in the female beraing the 72.90% and 27.10% respectively. Patient was of various age groups in which the maximum frequency was seen in the age group of 61- 70 years having 105 interaction bearing the percentage of 31.9% . According to the participation of different age group of the male and female with their corresponding age .The participation of male is high having frequency of 240 (72.9% )than female participation of frequency 89 (27.1%).The participation of male in the age group of 61-70 years is 83 and the female is 40 in the age group of 51-60 years. Potential drug interactions were categorized based on the gender. In that compared to 13 (40.6) females, males 19 (59.4%) were found to have more potential drug interactions. Our study more potential drug interactions in adult patients. Because, in adults lacking of nutrition's and in elderly patients multiple prescribers, multiple drugs and multiple diseases. The number of potential DDI increased with an increase in the number of drug prescribed. The numbers of drug prescribed increase with age .This drug interaction have a potential to increase or decrease the therapeutic effect or to increase the risk of ADR. An increased awareness of PDDIs ,rational co – prescription of drugs and a close monitoring of patients in whom these drugs are prescribed is recommended .The recommendation is based on the special monitoring and the perspiration of the clinical pharmacist .The Drug interaction observed in the geriatric patient are more severe and common in compared to the other group of study. The geriatric patient are physiological disability in correspond with the first pass metabolism and the presence of the other disease which also enables the multiple prescription causing poly pharmacy. The gender specification also the cause of the interaction , the female are more prone to the drug interaction due to the hormonal distribution in the body and inability of the physiological function to absorb and the distribution .The special training should be provided to the pharmacist for looking forward of the geriatric patient and female patient .The training regarding the prescription their adherence, use, toxicity, dosage regimen ,are being properly enabled in the training for the practical application. This study helps to know the different interaction related to the cardiovascular agent with own class of the drug and the other class of drugs used therapeutically to care the disease.

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## INTRODUCTION

All pharmacists working in a clinical settings, whether dispensing medicines or advice, require a well- grounded knowledge of drug interactions to prevent harm to patients from medicine combinations. This is an area in which a pharmacist's expertise a valued by other professionals and where a pharmacist's knowledge of pharmacology can be recognized and appreciated. On the ongoing diagnostics, prevention, treatment in the different department of the hospital in the various types of the patient grouping in correspondence of the age, poly pharmacy, gender, race and hereditary many drug interaction are been found. Those interactions are simple, usual or the life threatning which may effect the loss of pharmacological action of the body and other activities of the body. The interaction of the drug are more evenly found in the cardiac department in prevalence with the cardiac disease, patient are more commonly found with the Hypertension, Ischaemic Heart disease, myocardial Infraction etc.

A drug-drug interaction (DDI) may be defined as the pharmacological or clinical response to the administration of a drug combination which is different from that anticipated from the known effects of the two agents when given alone. The clinical result of a drug-drug interaction may manifest as antagonism, synergism, or idiosyn- cratic.

Drug- Drug interactions (DDIs) are changes in a drug's effects caused by another drug taken during the same time period. Potential drug interactions (PDIs) may include, drug contraindications, drug combinations that require monitoring and possible dosage adjustment when given concomitantly. It is important not only to identify PDIs that are clinically meaningful, but also to understand options to approaching the potential loss efficacy or toxicity that may result when combinations of drugs are administered together.

Potential drug interaction not only presents a danger to the patients but they can also greatly increase health care costs. The outcome can be harmful if the interaction causes an increase in the toxicity of the drugs.[1]

In epidemiology, it is difficult to have an accurate estimate of the incidence of drug interactions mainly because published studies have frequently used different criteria for defining a drug interaction, particularly in distinguishing between clinically significant and non-significant interactions. Some of the early studies uncritically compared prescribed drugs with list of possible drug interactions without taking into account their potential clinical significance. A review of nine studies of the epidemiology of drug-drug interactions (DDIs) in hospital admissions found that reported incidence ranged from 0% to 2.8%. Out of nine studies one study was like are drug interactions are important in clinical practice and have been estimated to account for 6-30% of all ADRs. One more in the Harvard Medical Practice study of adverse events, 20% in acute hospital in-patients settings were drug related. Of these, 8% were considered to be due to DDIs.[2]

Drug-Drug interactions (DDIs) are changes in a drug's effects caused by another drug taken during the same time period.[3]

Potential drug–drug interactions (PDIs) may include, drug contraindications, drug combinations that require monitoring and possible dosage adjustment when given concomitantly. It is important not only to identify PDIs that are clinically meaningful, but also to understand options to approaching the potential loss efficacy or toxicity that may result when combinations of drugs are administered together.[4]

In many cases, potentially interacting drugs can be given concurrently provided, the possibility of drug interactions is kept in mind and any necessary changes to dose or therapy is initiated promptly. However, concurrent use of potentially interacting drugs should be avoided altogether.[4]

The clinical management of PDIs generally implies monitoring of symptoms related to a possible side effect and laboratory parameters, such as serum-creatinine, inter nationalized ratio (INR) and blood- glucose, in order to prevent potentially serious adverse patients' outcomes.[5]

Potential drug interaction not only presents a danger to the patients, but they can also greatly increase health care costs. The outcome can be harmful if the interaction causes an increase in the toxicity of the drugs.[6]

The most important step in avoiding adverse clinical consequences is knowledge of the potential toxicity of drug combinations so that a rational prescription can be made. For example, the clinician may administer the antibiotic if the interaction is unlikely to be important or can choose an alternative antibiotic that does not have the potential for drug interaction. [14]

## OBJECTIVES

### General Objective:

Prospective Study on Potential Drug Interactions of Cardiovascular agents in the Department of Cardiology in a tertiary care teaching hospital

### Specific Objectives:

1. To assess the pattern of drug/drug class involved in these interactions
2. To assess the severity of drug interactions
3. To assess the onset of drug interaction
4. To Assess the outcome of the drug interactions
5. To evaluate and assess the individual drug interactions

## METHODOLOGY

**Study site:**

This study was conducted at Government General Hospital, Guntur.It is a 3000 bedded multi specialty /super specialty tertiary care teaching hospital. This hospital provides primary and specialized health care facilities to people in and around Guntur area. It is a major governmnent owned multi –specialty hospital in Guntur having the department like Cardiology, Neurology, Pediatrics, Obstetrics & Gynecology etc.. Approximately 1500-2000 patients are being treated every day.The patient is usually referred to this hospital by general practitioners.

**Study Design:**

This was Prospective and Observational study.

**Study period:**

The period of six month from October2015 to March 2016.

**Study criteria:**

**Inclusion Criteria:**

- Inpatients of department of cardiology with length of stay more than 24 hours.
- Patients on multiple drug therapy; with minimum of two drugs with at least one is an cardiovascular agent.

**Exclusion Criteria:**

- Patients not on any cardiovascular agent

Patients on single drug therapy with cardiovascular agent

- Outpatients of department of Cardiology

Patients whose length of stay in hospital is less than 24hrs

**Sources of data:**

All the necessary data were collected from the important of all the four unit of cardiology department. The main source of data collection included

- patient case studied
- treatment chart
- laboratory report
- Patient interview

**Study procedure:**

An approval from the institutional ethical committee of Government General hospital,Guntur was obtained prior to the study. All patients admitted to cardiology wards during the study period were screened for case of any anti –cardiology agent .Those who met the inclusion criteria were included for the study purpose enroll for the study. Follow was carried out till the day of discharge from the hospital .After the patient were included in the study , The data including , demographic data such as the age ,gender, past medical history,reason for admission, co–morbidities ,clinical data such as hematology ,bio chemistry ,and therapeutic data including dose, duration ,frequency ,route; time of administration and concomitmment medication were collected and documented in the suitably designed data collection form (Annexure –I) probable DIs were identified by using the software MICROMEDEX and the standard text books ( Martindate, Dipiro, Herdindal ,Kodakinalde ). The potential outcome of the interaction was accessed based on literature patient interview and discussion with clinician .Those interactions which were assumed to have happened in the patient were evaluated for various parameters. Nature of interaction were evaluated with regard to onset ,severity ,and documentation was evaluated .Data was accessed to evaluate the individual drugs and drug class involved in interactions. Data on interaction of the individual drugs were evaluated based on demographic (age and gender) and characteristics of interaction (onset and severity ).Data was evaluated using suitable statistical tools .

**Criteria for Evaluation Criteria for severity**

The potential severity of the interaction is important in assessing the risk versus benefits of therapeutic alternatives. With appropriate dosage adjustments or modification of the administration schedule. The negative effect of most interactions can be avoided.

i) Major interactions may be life –threatning ,or intoxication or permanent damage may be induced .Normally , these drugs should not be administered together .

ii) Moderate interactions frequently cause therapeutic difficulties, but the combination may be administered if the patient is carefully monitored (laboratory parameter ,for example quick value ,or clinical symptoms).

iii) minor interaction may cause increased or reduced effects or interactions only concerning a certain sub group (for example patient with renal or hepatic failure, slow acetylizers).

**Criteria for Onset**

How rapidly the clinical effects of an interactions can occur determines the urgency with which preventive measure should be instituted to avoid the consequences of the interaction.

**Two level of onset are used**

**Rapid**:

The effect will be evident within 24 hours of administration of the interacting drug. Immediate action is necessary to avoid the effects of interactions

**Delayed**:

The effect will not be evident until the interacting drug is administered for a period of days or weeks. Immediate action is not required.

**Criteria for Frequency**

Frequency of PDIs was calculated as the total number of potential drug -drug interactions per total number of patients.

**Statistical Analysis**

Descriptive statistical analysis has been carried out in the present study .Results on continuous measurement are presented on mean ± SD (min-max) & results on categorical measurements are presented in number, percentage etc. Confidence Interval (CI) has been computed to find the significant features. Confidence Interval with lower limit more than 50% is associated with statistical significance. Student T test has been used to find the continuous scale.

**Statistical Software**

The statistical software namely SPSS 20 Ver and Microsoft excel and diagrams advance analysis with chi-square test with 95% confidence interval.

**RESULTS**

**Tab: I. Drug Interaction Differentiated Based Age Group.**

| Age Group | Frequency | Percent |
|---|---|---|
| 25-30 | 4 | 1.2 |
| 31-40 | 20 | 6.1 |
| 41-50 | 37 | 11.2 |
| 51-60 | 102 | 31.0 |
| 61-70 | 105 | 31.9 |
| 71-80 | 55 | 16.7 |
| above 80 | 6 | 1.8 |
| Total | 329 | 100.0 |

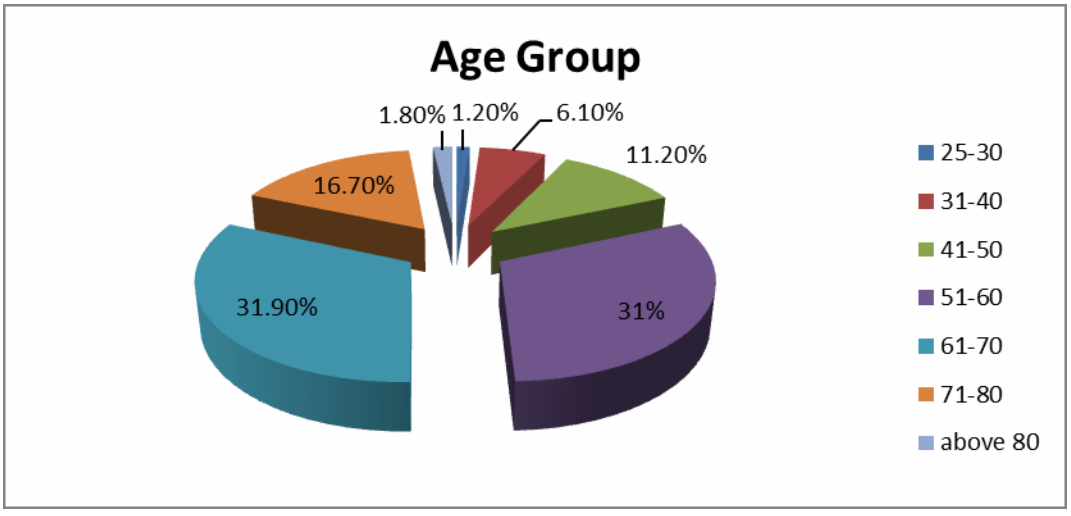



**Fig:I. Drug Interaction Differentiated Based Age Group.**

The Drug Drug interaction based on age group was found with ranging from age of 25 above .The highest frequency was in the age duration of the 61-70 age group with prevalence of the 105 frequency with the percentage of 31.9%.

**II. DI Differentiated based on Gender wise with Age.**

| Age Group | Gender | | Total |
|---|---|---|---|
| | Female | Male | |
| 25-30 | 0 | 4 | 4 |
| 31-40 | 9 | 11 | 20 |
| 41-50 | 3 | 34 | 37 |
| 51-60 | 40 | 62 | 102 |
| 61-70 | 22 | 83 | 105 |
| 71-80 | 10 | 45 | 55 |
| above 80 | 5 | 1 | 6 |
| Total | 89 | 240 | 329 |

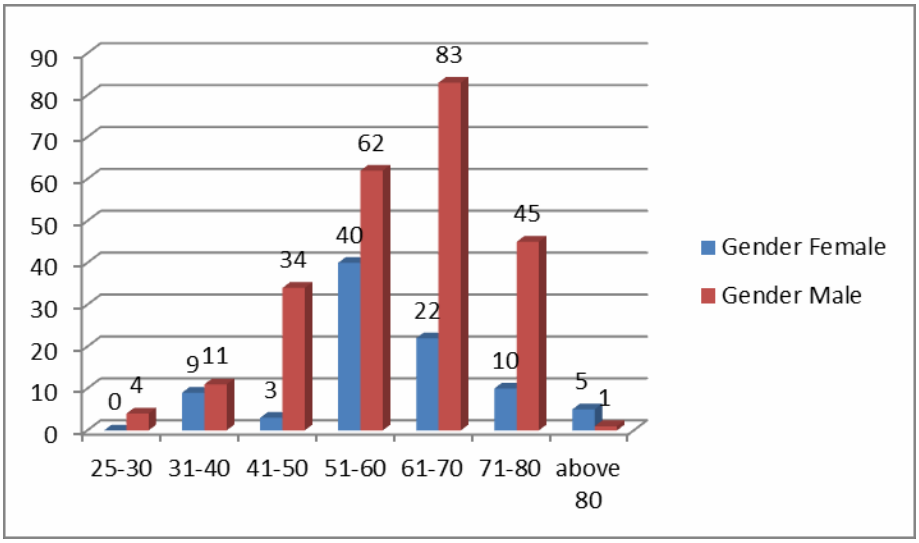



**Fig II. Drug Interaction Differentiated Based on Gender wise with Age.**

The gender based participation was studied well and the participation was differentiated based with the age group and their gender specific with male and female .Total 329 interaction was found in along with the 173 prescription in which the 89 drug interaction are found in male with high frequency in the age group of 51- 60 having frequency of drug drug interaction 40.The interaction on the male group is found to be 240 having high frequency in the age group of 61-70 years having frequency 83.

**Tab III.Drug Interaction Classified according to Gender wise.**

| Gender | Frequency | Percent |
|---|---|---|
| Female | 89 | 27.1 |
| Male | 240 | 72.9 |
| Total | 329 | 100.0 |

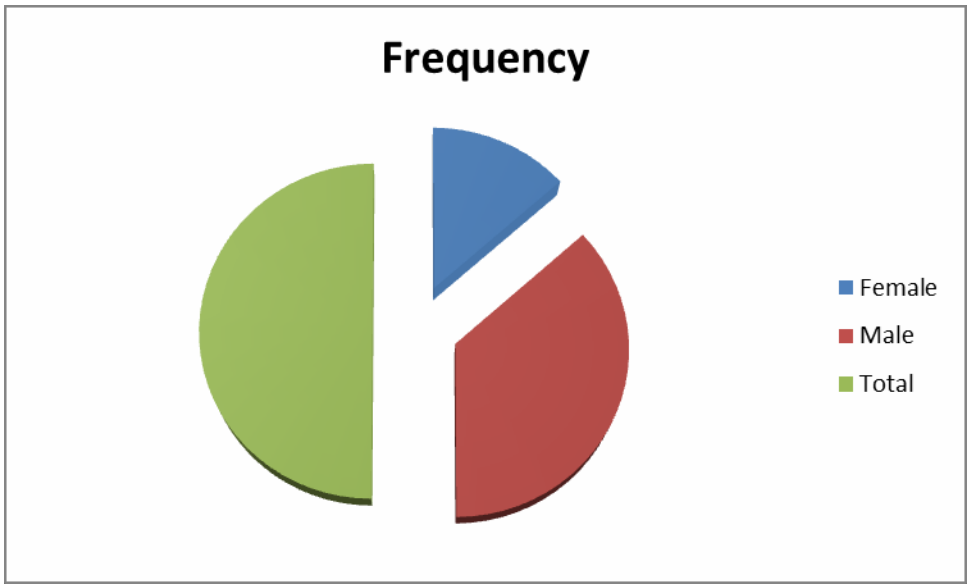



**Fig:III.DI Classified According to Gender.**

The participation of male and female with total expression with the percentage was statistically calculated and presented with the above tables and the graph .The maximum frequency in male and female is found to be 240 and 89 respectively with the Percentage 72.9% and 27.1%.

**Tab IV. Drug Interaction classified based on severity in the department of Cardiology.**

| Severity | Frequency | Percent |
|---|---|---|
| Major | 170 | 51.7 |
| Moderate | 158 | 48.0 |
| Minor | 1 | 0.3 |
| Total | 329 | 100.0 |

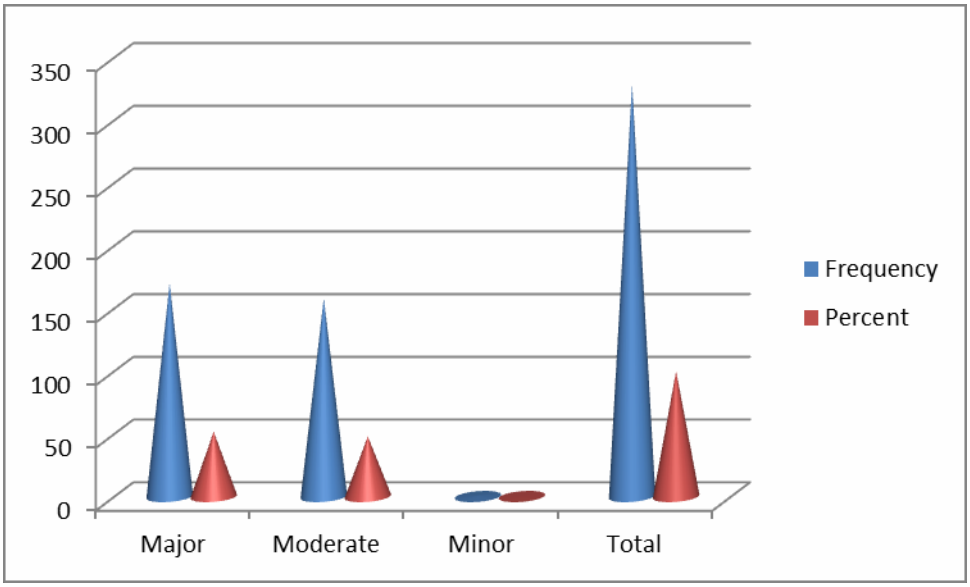



**Fig IV. Drug Interaction classified based on Severity in the Department of Cardiology.**

The main focus of the research is to determine the severity of interaction among the interactions. The major, moderate and minor was evaluated with the frequency 170,158,1 respectively having the percentage of 51.7%,48.0% and 0.03% respectively.

**Tab V. Drug Interaction classified based on Onset in the Department of Cardiology.**

| Onset | Frequency | Percent |
|---|---|---|
| Delayed | 95 | 28.9 |
| Not Specified | 215 | 65.3 |
| Rapid | 19 | 5.8 |
| Total | 329 | 100.0 |

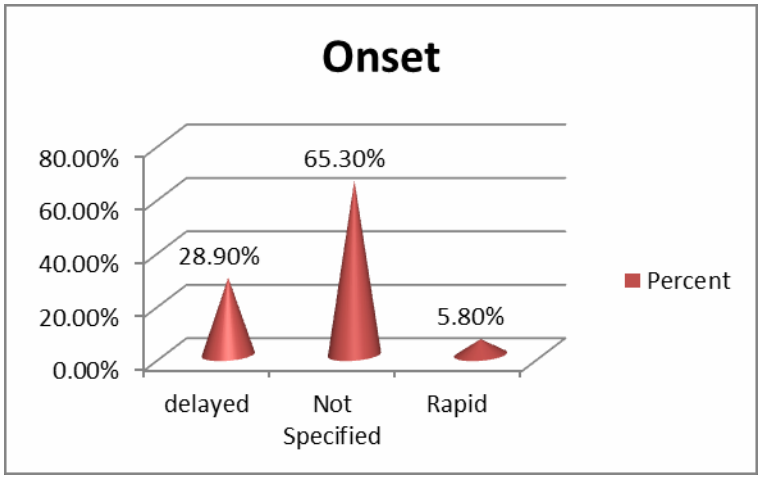



**Fig V. Drug Interaction classified based on Onset in the Department of Cardiology.**

The main focus of the research is to determine the onset of interaction among the interactions. The delayed ,not specified and rapid was evaluated with the frequency 95,215,19 respectively having the percentage of 28.9%, 65.3% and 5.8% respectively. This was evaluated with the corresponding excel sheet report and using the software MICROMEDIX.

**Tab VI A. Individual Drug –Drug Interactions.**

| Index drug | Interacting drug | Total |
|---|---|---|
| Atorvastatin calcium | Azithromycin | 3 |
| | Clopidogrel | 4 |
| | Digoxin | 1 |
| | Fentanyl | 3 |
| | Ranolazine | 4 |
| Tota | l | 15 |

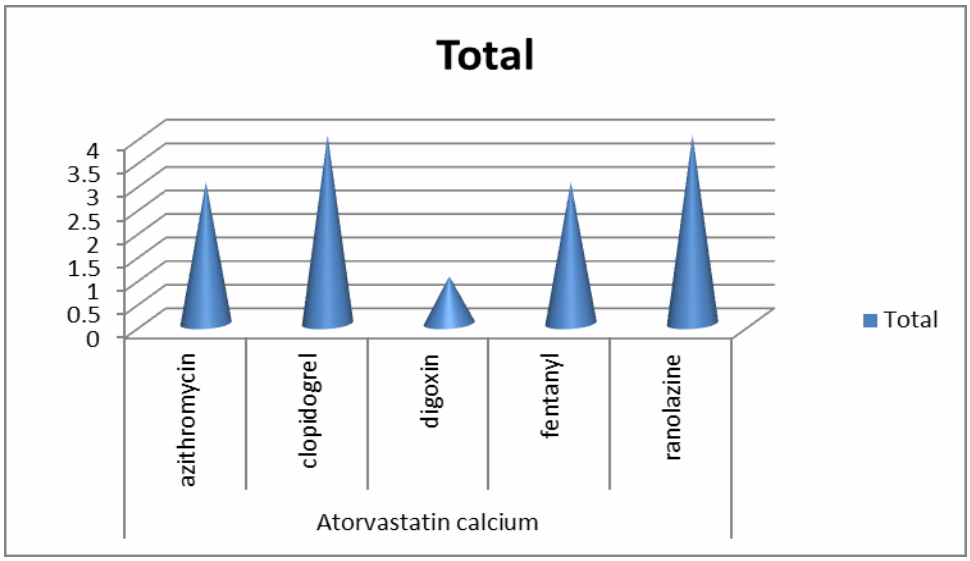



**Fig VI A. Individual Drug – Drug Interactions.**

The atorvastatin calcium react with the interacting Drugs Azithromycin, Clopidogrl, Digoxin, Fentanyl, Ranolazine with times of respectively 3,4,1,3,4 with total of 15 interaction were found in this study.

**Tab VI B. Individual Drug – Drug Interaction.**

| Index drug | Interacting drug | Total |
|---|---|---|
| Clopidogrel | Dabigatron etexilate mesylate | 1 |
| | Enoxaparin sodium | 4 |
| | Enoxaprioum sodium | 1 |
| | Fondaparinux sodium | 2 |
| | Heparin calcium | 7 |
| | Indomethacin | 1 |
| | Rivaroxaban | 1 |
| | Torsemide | 1 |
| | Total | 18 |

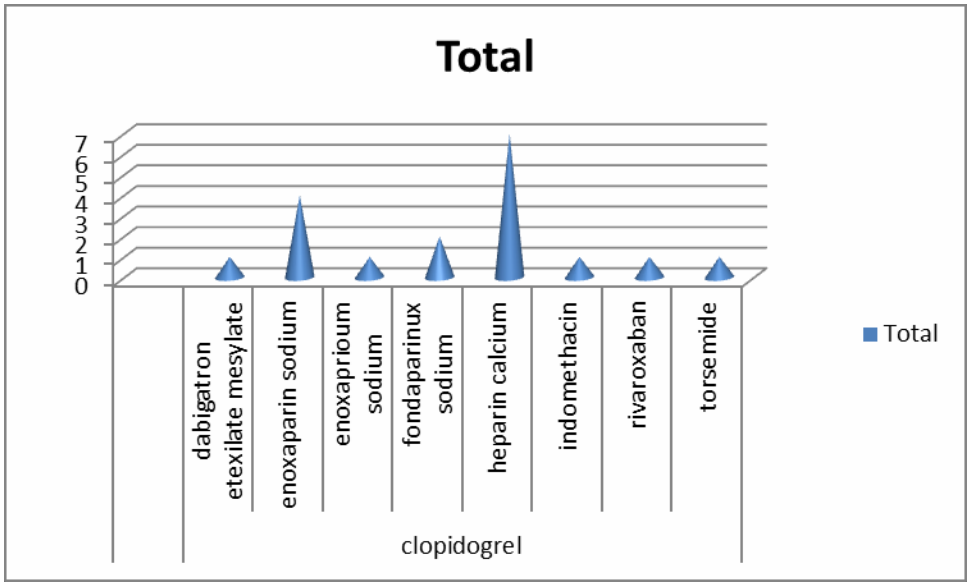
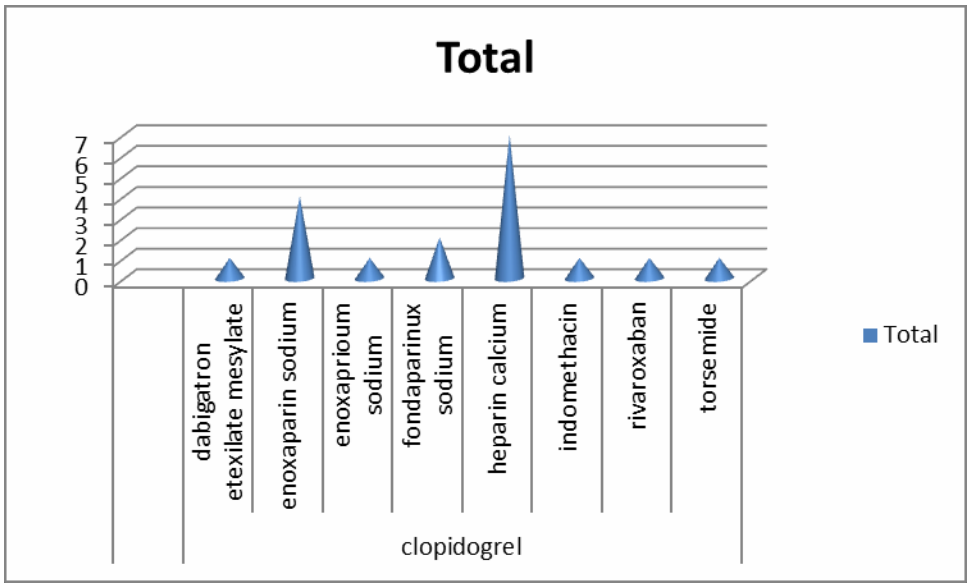



**Fig VI B. Individual drug –drug interaction.**

The Clopidogrel interact with the interacting drug Dabigatron Etexilate Mesylate, Enoxaparin Sodium, Fondaparinux,Heparin Calcium ,Indomethacin ,Rivaroaban , Torsemide with the number of respectively 1,5,2,7,1,1,1 with total of 18 interaction were found in this study.

**Tab VI C. Individual Drug – Drug Interactions.**

| Index drug | Interacting drug | Total |
|---|---|---|
| Clopidogrel | Dabigatron etexilate mesylate | 1 |
| | Enoxaparin sodium | 4 |
| | Enoxaprioum sodium | 1 |
| | Fondaparinux sodium | 2 |
| | Heparin calcium | 7 |
| | Indomethacin | 1 |
| | Rivaroxaban | 1 |
| | Torsemide | 1 |
| | Total | 18 |

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The Clopidogrel interact with the interacting drug Dabigatron Etexilate Mesylate, Enoxaparin Sodium, Fondaparinux,Heparin Calcium ,Indomethacin, Rivaroaban , Torsemide with the number of respectively 1,5,2,7,1,1,1 with total of 18 interaction were found in this study.

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| | Enoxaprioum sodium | 1 |
| | Fondaparinux sodium | 2 |
| | Heparin calcium | 7 |
| | Indomethacin | 1 |
| | Rivaroxaban | 1 |
| | Torsemide | 1 |
| | Total | 18 |

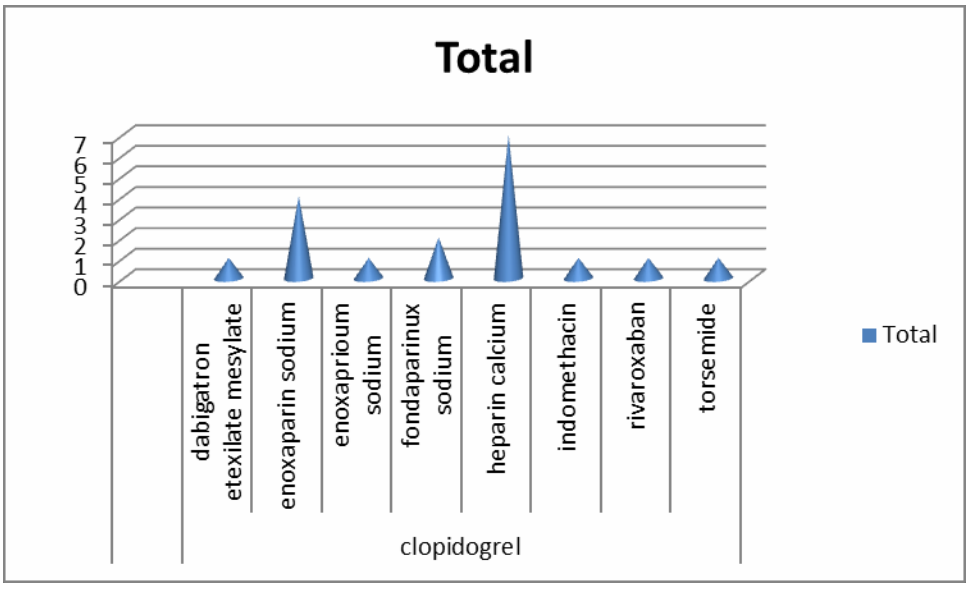


**Fig VI B. Individual drug –drug interaction.**

The Clopidogrel interact with the interacting drug Dabigatron Etexilate Mesylate, Enoxaparin Sodium, Fondaparinux,Heparin Calcium ,Indomethacin ,Rivaroaban , Torsemide with the number of respectively 1,5,2,7,1,1,1 with total of 18 interaction were found in this study.

**Tab VI C. Individual Drug – Drug Interactions.**

| Index drug | Interacting drug | Total |
|---|---|---|
| Insulin human Isophane | Dextrose | 1 |
| | Levofloxacin | 1 |
| | Metformin | 1 |
| | Metoprolol tartrate | 4 |
| | Ramipril | 2 |
| | Sitagliptin phosphate | 1 |
| | Total | 10 |

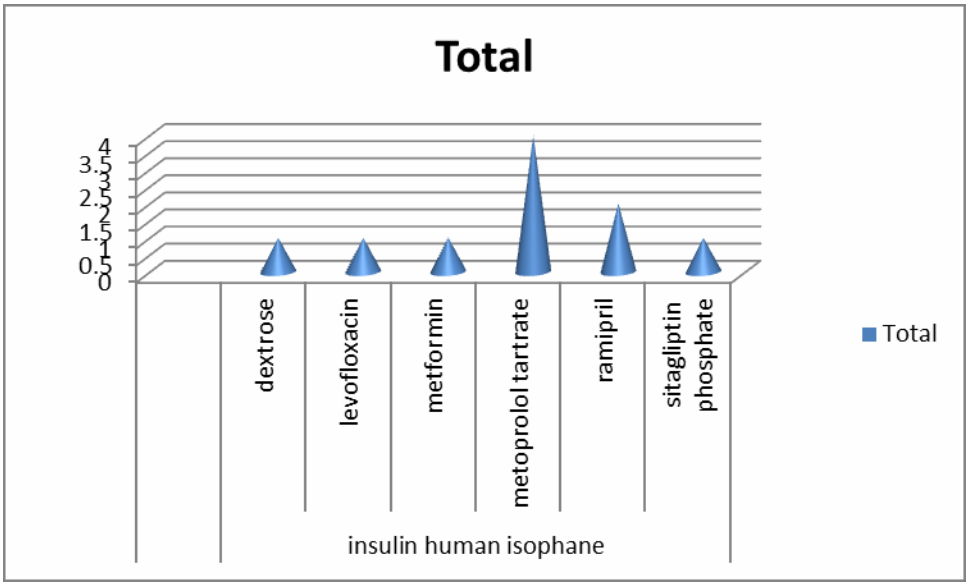


**Fig VI B. Individual Drug –Drug Interaction.**

The Insulin Human Isophane interact with the interacting drug Dextrose, Levofloxacin, Metformin, Metoprolol tartrate, Ramipril, sitagliptin phosphate with the number of respectively 1,1,1,4,2,1 with total of 10 interaction were found in this study.

**Tab VI D. Individual Drug –Drug Interactions.**

| Index drug | Interacting drug | Total |
|---|---|---|
| Aspirin | Atenolol | 3 |
| | Bisoprolol fumarate | 3 |
| | Carvedilol | 8 |
| | Cilostazol | 1 |
| | Clopidogrel | 23 |
| | Dabigatron etexilate mesylate | 1 |
| | Diclofenac | 1 |
| | Enoxaparin sodium | 11 |
| | Enoxaprin sodium | 1 |
| | Enoxaprioum sodium | 2 |
| | Fondaparinux sodium | 5 |
| | Furosemide | 11 |
| | Heparin | 1 |
| | Heparin calcium | 19 |
| | Heparin sodium | 2 |
| | Human insulin | 1 |
| | Insulin | 8 |
| | Insulin aspart | 2 |
| | Insulin human isophane | 6 |
| | Lisinopril | 1 |
| | Magnesium hydroxide | 9 |
| | Metoprolol tartrate | 29 |
| | Nebivolol | 1 |
| | Nph | 1 |
| | Perindopril erbumine | 1 |
| | Ramipril | 10 |
| | Sodium bicarbonate | 1 |
| | Spironolactone | 4 |
| | Ticagrelor | 30 |
| | Torsemide | 3 |
| | Total | 199 |

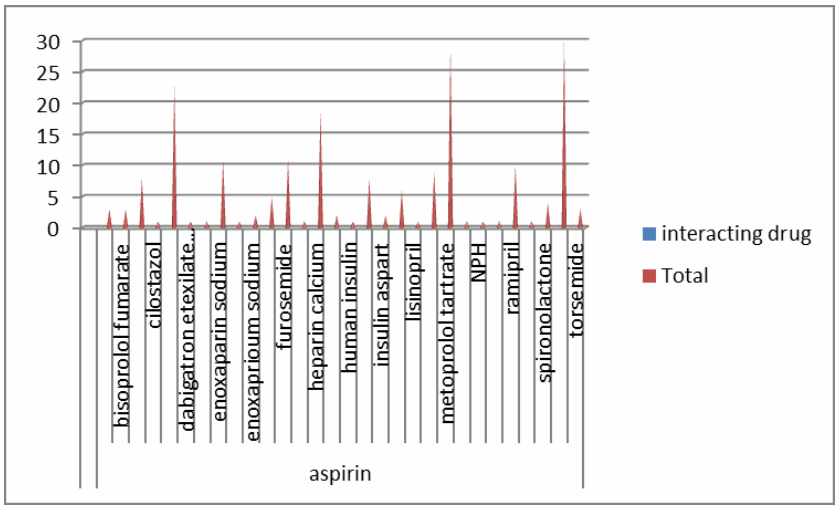


**Fig VI D. Individual Drug –Drug Interactions.**

The Aspirin interact with the interacting drug Atenolol, Bisoprolol Fumarate, Carvedilol, Cilostazol, Clopidogrel, Dabigatran Etexilate Mesylate, Diclofenac, Enoxaparin Sodium, Enoxaparium Sodium, Fondaparinux Sodium, Furosemide, Heparin, Heparin Calcium , Heparin Sodium, Human Insulin, Insulin, Insulin Aspart, Insulin Human Isophane, Lisinopril, Magnesium Hydroxide, Metoprolol Tartrate, Nebivolol, NPH, Perindopril Erbumine, Ramipril, Sodium Bicarbonate, Spironolactone, Ticagrelor, Torsemide with the number of respectively 3, 3, 8, 1, 23, 1, 1, 11, 1, 2, 5, 11, 1, 19, 2, 1, 8, 2, 6, 1, 9, 29, 1, 1, 1, 10, 1, 4, 30, 3 with total of 199 interaction were found in this study.

**Table No VII. Table below shows the Distribution of Gender among study sample. Chi-square value and p-value show there is no Statistically significant difference between the Age group in the Study sample**.

| Age Group | Frequ ency | Percent | Chi- square value | p-value | 95% confidence interval | |
|---|---|---|---|---|---|---|
| | | | | | Upper bond | Lower bond |
| ≤60 years | 163 | 49.55 | 0.027 | 0.912 | 0.917 | 0.906 |
| >60 years | 166 | 50.45 | | | | |
| Total | 329 | 100 | | | | |

The distribution of gender among the study sample were done and the value of frequency among the age group of below 60 years is 163 with total percentage bearing 49.55% having chi square value of 0.027 and p- value 0.192 .The 95% confidence interval of upper bond and lower bond is 0.197 and 0.906 respectively and the age group of above 60 years having the frequency of 166 bearing the 50.45%.

## DISCUSSION

Clinical pharmacists get an opportunity to work in a team and utilize the professional skills, knowledge and expertise for better patients care.

It is impossible to remember all drug interactions of potential clinically significance. Healthcare staff should be the continually alert to the possible of drug interactions and take appropriate steps to minimize their occurrence.

This is an area in which a pharmacist's expertise a valued by other professionals and where a pharmacist's knowledge of pharmacology can be recognized and appreciated. On the ongoing diagnostics, prevention ,treatment in the different department of the hospital in the various types of the patient grouping in correspondence of the age , poly pharmacy ,gender , race and hereditary many drug interaction are been found. Those interactions are simple , usual or the life threatning which may effect the loss of pharmacological action of the body and other activities of the body. The interaction of the drug are more evenly found in the cardiac department in prevalence with the cardiac disease , patient are more commonly found with the Hypertension, Ischaemic Heart disease ,myocardial Infraction etc.

It would be worth assessing the incidence and patterns of drug interactions for antimicrobials among these patients. Very few studies have been reported in literature to study the nature of drug interactions specifically among Cardiovascular agents. Such data can be helpful in understanding opportunities for improving drug use. Hence this study is taken to understand the incidence and pattern of drug interactions to cardiovascular agent in the cardiovascular department.

In total of 173 prescription of the patient the total number of 329 drug interaction was found in which the 240 interaction was found in male and 89 in the female beraing the 72.90% and 27.10% respectively.

## AGE

As shown in table No I in the current study the involvement of the patient was of various age group in which the maximum frequency was seen in the age group of 61- 70 years having 105 interaction bearing the percentage of 31.9% .as in the other age group less interaction was found which are as 25-30,31-40,51-60,71-80 are 4,20,37,102,55,6 bearing the percentage as respectively 1.2%,6.1%,11.2%,31%, 16.7%,1.8% .

In the reference study the adults are exposed to more single and multiple regimens than younger's. Majority 9 (28.1%) of patients with PDIs more in 51-60 years. More than one potential drug- laboratory interaction was present in majority 19(50%) of patients. Similar findings are found in a study conducted by Hovastadivs BO, Astrand B, Petresson G, which concluded multiple medications should be regarded as a risk in forms of PDIs and adverse drug reactions in all age groups**.**

Johnelli, Kristina, Klarin, Inga, which states that there seems to be a strong relationship between number of dispensed drugs and potential DIs, especially for potentially serious DDIs, which has implications for the importance of trying to minimize the number of drugs prescribed in the elderly, it was also found that the probability of potentially serious DDIs decreases with increasing age among the elderly and that elderly woman has a lower probability of potentially serious DDIs.

## GENDER

As per the table II and III and also the fig II and III represent the participation of different age group of the male and female with their corresponding age .The participation of male is high having frequency of 240 (72.9% )than female participation of frequency 89 (27.1%).The participation of male in the age group of 61-70 years is 83 and the female is 40 in the age group of 51-60 years.

In table No 3&4 and figure No 3&4 showed that, potential drug interactions were categorized based on the gender. In that compared to 13(40.6) females, males 19 (59.4%) were found to have more potential drug interactions. Our study more potential drug interactions in adult and patients. Because, in adults lacking of nutrition's and in elderly patients multiple prescribers, multiple drugs and multiple diseases. Study conducted by Hersh EV, states that particularly important that involvement of health care professional audit on these interactions would prevent potentially serious and life-threatening interactions of the antibiotics.

**WARDS**

In our study the various ward patient were studied in the Government General hospital, Guntur .The patient in the Intensive care unit was prescribed with the multiple drugs and the age was above 50 years .The male patient was found more as compared to the female with the age group of specification 61-70 years and 51-60 years respectively .The Intensive critical care unit was also found with the different aspect depending upon their their disease and the instability of conscious. The prescription of the drugs were followed up and the male patient was found to be 72.9% followed by female patient 27.1%.

**Potential drug interaction:**

A drug-drug interaction (DDI) may be defined as the pharmacological or clinical response to the administration of a drug combination which is different from that anticipated from the known effects of the two agents when given alone. The clinical result of a drug-drug interaction may manifest as antagonism, synergism, or idiosyn- cratic.

Drug- Drug interactions (DDIs) are changes in a drug's effects caused by another drug taken during the same time period. Potential drug interactions (PDIs) may include, drug contraindications, drug combinations that require monitoring and possible dosage adjustment when given concomitantly. It is important not only to identify PDIs that are clinically meaningful, but also to understand options to approaching the potential loss efficacy or toxicity that may result when combinations of drugs are administered together.

Potential drug interaction not only presents a danger to the patients but they can also greatly increase health care costs. The outcome can be harmful if the interaction causes an increase in the toxicity of the drugs.

The age bearing 61-70 years of male (geriatric patient )and the 51-60 years of female (geriatric patient) have more interaction due to their physiological and the kinetics of the body with the gastrointestinal and the other factors. Female are more contraindicated to the drugs as the results also shows the lees age of female are interacted with the drugs than the male .The multiple prescription also indicates the potential interaction due to their multiple interaction of therapy .Also the multiple diseases are observed in the patient having the age group above than the 50 years .

**Severity:**

The severity of interaction major ,moderate ,minor are indicated with the use of standard software MICROMEDIX. The prevalence of the study of interaction of severity is classified based on their priority of Interaction. As shown in the table no.IV and the fig no. IV the majority ,moderate ,minor was found with the frequency of 170,158,1 bearing the percentage of 51.7%,48%,0.3% in the total of 329 prescription..

**Onset:**

The Onset of interaction Delayed, Not specified and Rapid are indicated with the use of standard software MICROMEDIX. The prevalence of the study of interaction of Onset is classified based on their priority of Interaction .As shown in the table no.V and the fig no. V the Delayed, Not specified and Rapid was found with the frequency of 95,215,19 bearing the percentage of 28.9%, 65.3%,5.8% in the total of 329 prescription.

**Outcome of DIs:**

A total of 173 prescription were analyzed. A total of 329 potential DDIs were detected, which were graded according to severity as serious, significant, minor and contraindicated (Medscape ,2013 and Micro medics).

The prescriptions of every alternate patient was evaluated for potential DDIs using freely accessible web based drug interactions checkers of Medscape (Medscape , 2003) and current index of medical specialties (CIMS) (CIMS,2012), the average number of drugs prescribed, average number of potential DDIs per prescription and age wise distribution of potential DDIs.Nearly one third of potential DDIs were either serious or clinically significant . Polypharmacy was frequent in the present study with more than 50% prescription consisting of more than eight drugs and only 6.29 % with less than five drugs .The average number of drugs prescribed per prescription was 5.28.Polypharmacy was also observed in a study conducted in geriatric hospitalized patients at Nepal (Joshi et al., 1997).Poly pharmacy Increases risk of DDIs (Linn et al., 2011) and ADRs (satoskar et al., 2011) and hence should be avoided. An average of 7.3 potential DDIs were detected per prescription in the present study. The risk of DDIs increases with an increase in number of drugs prescribed (Tripathi KD, 2010). Accordingly, the average number of potential DDIs per prescription increased from in prescriptions with less than five drugs to 16.33 in prescriptions with more than seven drugs. In the study we came to know the age, poly pharmacy, presence of disease with gender specification plays the role of potential drug interaction.

**Individual drug interactions:**

The individual Drug interaction depend upon the age, gender and the concurrent use with the other medication. The different drugs has shown different number of interaction based on their class and their use with the refrence of the disease. As in this study, The atorvastatin calcium react with the interacting drugs azithromycin, clopidogrl, digoxin, fentanyl, ranolazine with times of respectively 3,4,1,3,4 with total of 15 interaction were found. Also The clopidogrel interact with the interacting drug dabigatron etexilate mesylate, enoxaparin sodium, fondaparinux,heparin calcium,indomethacin, rivaroaban, torsemide with the number of respectively 1,5,2,7,1,1,1 with total of 18 interaction were found in this study. The Insulin Human Isophane interact with the interacting drug Dextrose, Levofloxacin, Metformin, Metoprolol tartrate, Ramipril, sitagliptin phosphate with the number of respectively 1,1,1,4,2,1 with total of 10 interaction were found in this study.similarly The Aspirin interact with the interacting drug Atenolol, Bisoprolol Fumarate, Carvedilol, Cilostazol, Clopidogrel, Dabigatran Etexilate Mesylate, Diclofenac, Enoxaparin Sodium,

Enoxaparium Sodium, Fondaparinux Sodium, Furosemide, Heparin, Heparin Calcium , Heparin Sodium, Human Insulin , Insulin, Insulin Aspart, Insulin Human Isophane, Lisinopril, Magnesium Hydroxide, Metoprolol Tartrate, Nebivolol, NPH, Perindopril Erbumine, Ramipril, Sodium Bicarbonate, Spironolactone, Ticagrelor, Torsemide with the number of respectively 3,3,8,1,23,1,1,11,1,2,5, 11,1,19,2,1,8,2,6,1,9,29,1,1,1,10,1,4,30,3 with total of 199 interaction were found in this study. The severity of interaction among the interactions as major ,moderate and minor was evaluated with the frequency 170,158,1 respectively having the percentage of 51.7%,48.0% and 0.03% respectively .The onset of interaction among the interactions of delayed,not specified and rapid was evaluated with the frequency 95,215,19 respectively having the percentage of 28.9%, 65.3% and 5.8% respectively .This was evaluated with the corresponding excel sheet report and using the software MICROMEDIX.

## CONCLUSION

Drug interactions means two or more drugs given at the same time may exert their effects independently or may interact. Potential drug interactions (PDIs) may include, drug contraindications, drug combinations that require monitoring and possible dosage adjustment when given concomitantly. It is important not only to identify PDIs that are clinically meaningful, but also to understand options to approaching the potential loss efficacy or toxicity that may result when combinations of drugs are administered together.

The number of potential DDI increased with an increase in the number of drug prescribed. The numbers of drug prescribed increase with age. This drug interaction have a potential to increase or decrease the therapeutic effect or to increase the risk of ADR. An increased awareness of PDDIs ,rational co –prescription of drugs and a close monitoring of patients in whom these drugs are prescribed is recommended .The recommendation is based on the special monitoring and the perspiration of the clinical pharmacist. The Drug interaction observed in the geriatric patient are more severe and common in compared to the other group of study. The geriatric patient are physiological disability in correspond with the first pass metabolism and the presence of the other disease which also enables the multiple prescription causing poly pharmacy. The poly pharmacy shows the differential drug interaction based on the drug specification and their therapeutic action monitoring. The poly pharmacy increases the interaction so its should be minimized to certain extent and need to be prescribe only if necessary. The gender specification also the cause of the interaction, the female are more prone to the drug interaction due to the hormonal distribution in the body and inability of the physiological function to absorb and the distribution. The special training should be provided to the pharmacist for looking forward of the geriatric patient and female patient. The training regarding the prescription their adherence, use, toxicity, dosage regimen, are being properly enabled in the training for the practical application. During the prescription of the medication for the each patient, The history, background, the past medication, past allergies, interaction are being studied in correspond with the individual patient and the prescription is being followed up to decrease the drug interaction. Also the drugs are being evaluated with the various diagnostic data and the observation of the patient demographically and the correlation is done according to the requirement. The change of dosage route, dosage regimen, dose, duration of administration, combination therapy is being employed to minimize the interaction. This study helps to know the different interaction related to the cardiovascular agent with own class of the drug and the other class of drugs used therapeutically to care the disease.

**Conflicts of Interest**

Authors declare that there are no conflicts of interest

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