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Pharmacosurveillance on Antiplatelet Drugs Usage at Various Hospitals in Narasaraopeta – A Prospective Observational Study

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ABSTRACT

BACKGROUND: Pharmacosurveillance on antiplatelet drugs usage at tertiary care hospitals, antiplatelet therapies are essential to reduce the risk of developing cardiovascular, cerebrovascular and peripheral artery diseases.

METHOD: A prospective observational study was conducted to monitor the usage of antiplatelet drugs in tertiary care hospitals. This study was carried out for a period of six months at Narasaraopeta tertiary care hospitals.

RESULTS: Total of 160 patients was enrolled in this study. People at the age group of 60 – 69 (n= 46) were more susceptible for risk of getting cardiovascular and neurovascular diseases. Males (n= 108) are more prone to diseases when compared to females. In the study 84 were prescribed with monotherapy treatment whereas 30 patients were prescribed with combinational therapy accounting 52.5% and 18.7% respectively indicating monotherapy as a primary choice of medication. The most commonly prescribed antiplatelets of all the antiplatelets are Aspirin (n= 82), followed by clopidogrel (n= 80).

DISCUSSION: In our prospective observational study we intended to monitor the antiplatelet therapy usage in various tertiary care hospitals

CONCLUSION: Antiplatelet usage varies with individuals according to their disease conditions to minimize the adverse drug reaction, drug-drug interaction, cost of the treatment and other medication errors. The mostly prescribed antiplatelet drug was aspirin and monotherapy was highly preferred then the combinational therapy.

KEY WORDS: Antiplatelets, coronary artery disease, stroke, monotherapy, combinational therapy.

I. INTRODUCTION

Platelets are called as thrombocytes. They are derived from the cytoplasm of megakaryocytes in bone marrow or lungs with a diameter of 3 to 5 micrometer. The normal platelet count ranges from 150,000 to 450,000 cells per micro liter. The life span of platelets is between 8 to 11 days. The kidney release a substance called thrombopoietin which stimulate platelet synthesis. (1) Platelets are minute flattened colorless non nucleated disc shaped bodies which are present in the mammalian blood that helps in blood clotting by attaching to other platelets and to injured epithelium.(1)

Functions of Platelets:

- They internalize and destroy the bacteria
- They secrete vasoconstrictors, chemicals that stimulate spasmodic constriction of injured vessels and help to reduce blood loss
- Platelets stick together and form a temporary platelet plug which help to seal the injured blood vessels
- They secrete growth factors that stimulate mitosis in fibroblast and smooth muscle and thereby help to maintain and repair the blood vessels
- They secrete chemicals that attract neutrophils and monocytes to sites of inflammation.
- They secrete procoagulants or clotting factors which promote blood clotting
- They initiate the formation of clot dissolving enzyme that dissolve blood clots and outlasted their usefulness.(1)

Anti-platelets are drugs which interfere with platelet function and are useful in the prophylaxis of thromboembolic disorders. (2)

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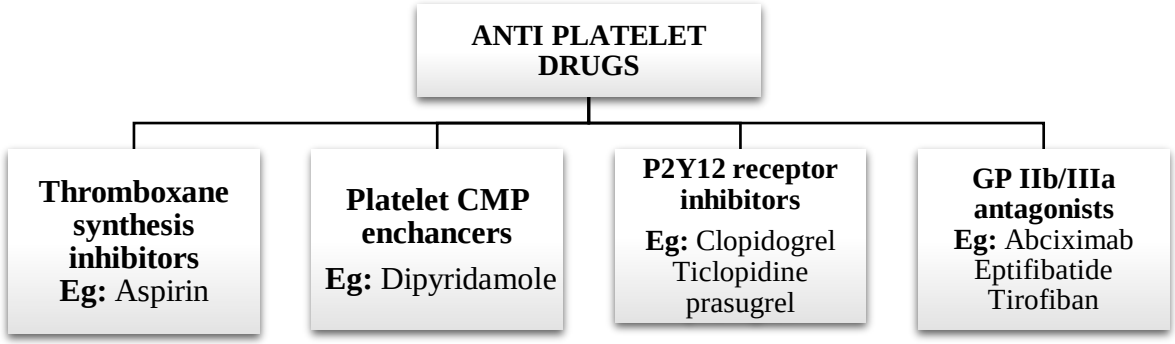

Whenever there is a damage in the blood vessel our body takes immediate action by forming a clot this is called as haemostasis.(3)

Generally/ normally the blood vessel containing endothelial cells releases vasoactive hormones called nitric oxide and prostacyclin. These hormones works synergistically to inhibit platelet aggregation and activation there by it prevent the unnecessary thrombosis in healthy blood vessel.(3)

Damage to these endothelial cells may unable to releases the vasoactive hormones and leads to platelet activation and vasoconstriction.(3)

Endothelium also release a chemical peptide called endothelin which is a potent vasoconstrictor.(3)

Platelets first adhere to macromolecules in the sub endothelial region of the injured blood vessel. They then aggregate to form the primary haemostatic plug (3)

Primary haemostatic plug involves 3 steps

- Platelet adhesion
- Platelet activation
- Platelet aggregation

When blood vessel endothelium damaged

⇩

Leads to Exposure of sub endothelial collagen

⇩

A glycoprotein called von willebrand factor (VWF) is released in respond to damage

⇩

Collagen tightly bound to VWF

⇩

Circulating platelets in blood vessel having a receptors called glycoprotein Ib (GP Ib)

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⇩

GP Ib binds to VWF that bound to collagen

⇩

This is called platelet adhesion

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After platelet adhesion it leads to activation of platelets. During platelets activation it undergoes different changes.(3)

- Degranulation
- Expression of surface glycoprotein i.e. GPIIB/GPIIIA they are called as fibrinogen receptors
- Alteration in platelets morphology

Activated platelets secrete a variety of compounds i.e.

- Alpha granules – It release VWF for further platelets adhesion and activation and also release platelet derived growth factors (PDGF) it helps for wound healing
- Dense granule – It release ADP that binds to P2Y12 & also release thromboxane A2 that binds to thromboxane receptor it facilitate further platelet activation.(3)

The fibrinogen receptors i.e. GP IIB/IIA which are produced by liver binds to activated platelet and allows to adhere one platelet to another platelet. This fibrinogen receptors act as a linking molecule between one to another platelet. This results in platelet aggregation.(3)

DOSES:

- Aspirin: 75 to 150mg/day.
- Dipyridamole: 150 to 300mg/day.
- Ticlopidine: 250mg BID with meals.
- Clopidogrel: 75mg OD.
- Abciximab: 0.25mg/kg IV 10-60min before PCI followed by

10microgram/min for 12hr.

- Eptifibatide: Unstable angina – 180microgram/kg IV bolus followed by 2microgram/kg /min infusion upto72hr.
- Tirofiban: 0.4microgram/kg/min for 30min followed by 0.1microgram/kg/min upto 48hrs.(2)

USES:

The aim of using antiplatelets drugs is to prevent intravascular thrombosis and embolization with minimal risk of hemorrhage

CAD: The recommended dose of aspirin is 75 to 150mg per day

ACS:

I. Unstable angina – Aspirin reduce the risk of progression to MI and sudden death. Clopidogrel is generally combine with aspirin or may be used as a alternative.

II. NSTEMI – it is managed without thrombolysis are generally put on a combination of aspirin along

III. With clopidogrel continued upto 1yr.

IV. STEMI – STEMI as well as high risk of NSTEMI patients who present within 12hrs prasugrel along

V. With aspirin used as most common regimen.

Cerebrovascular disease –

I. Aspirin has reduced the incidents of TIA's

II. Aspirin/clopidogrel is recommended in patients with persistent atrial fibrillation

III. Combination of dipyridamole with low doses aspirin

Venous thromboembolism – trails have shown antiplatelets drug also to have prophylactic effect

Peripheral vascular disease – aspirin/clopidogrel may produce some improvement and reduce the incidence of thromboembolism. (2)

II. METHODOLOGY

Study site:

This study was conducted at various tertiary care hospitals in Narasaraopeta.

Study design:

Prospective observational study.

Study size:

A total of 160 patients from the in-patient department who fulfilled the inclusion and exclusion criteria were enrolled.

Study period:

This study was conducted for a period of 6 months.

Study criteria:

Inclusion criteria:

1) The study population may be either male or female.
2) The patients must stay in the hospital for more than 24hours.
3) Any kind of disease or disorder that is experienced by the study population is taken into account.

Exclusion criteria:

1) Uncooperative and non-responding patients must be excluded.
2) Immune compromised patients cannot be taken as study subjects.
3) Irrelevant categories in respective to our aim is excluded.

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Source of data:

The patient's demographic data, reason for admission, past medical history, past medication history, medications prescribed, their dose and frequency of admission were collected from patient medical records and noted in designed data collection form.

Parameters measured:

The parameters that are measured in this study are age, gender, body weight, complete blood count, Prothrombin time, APTT (if present in patient's record).

III. RESULTS

AGE CATEGORIZATION IN STUDY POPULATION:

S.No	AGE GROUPS(YEARS)	NUMBER OFCASES	PERCENTAGE(%)
1	30-39	8	5
2	40-49	35	21.8
3	50-59	36	22.5
4	60-69	51	31.8
5	70-79	22	13.7
6	80-89	8	5

Table 1: Age Categorization in Study Population

Table 1: The Age Categorization in Study Population shows that 60-69 (n=51, 31.8%) followed by 50-59 were more susceptible for risk of getting a disease when compared to other age groups.

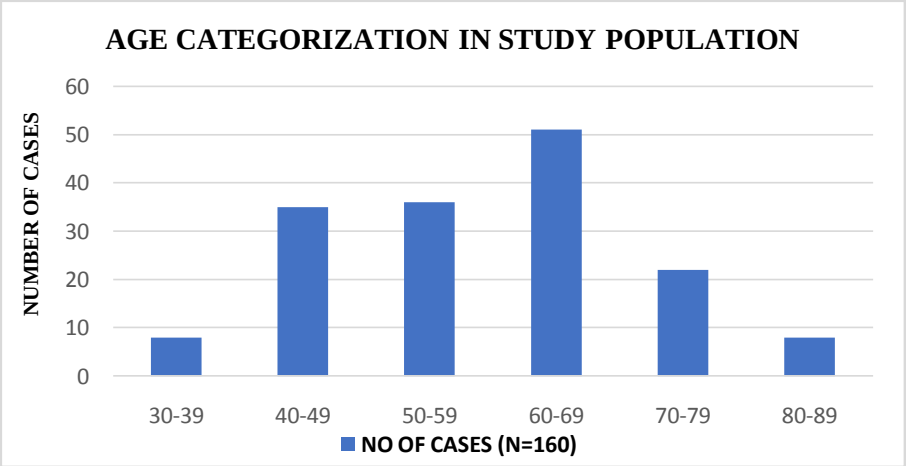

Figure: Age Categorization in Study Population

DISTRIBUTION OF ANTIPLATELET THERAPY:

ANTIPLATELET THERAPY	NO OF PATIENTS (N=160)	PERCENTAGE(%)
Single Antiplatelet therapy	77	48.12%
Dual Antiplatelet therapy	57	35.62%

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Triple Antiplatelet therapy	2	1.25%
Combination Antiplatelet therapy	74	46.25%

Table 2: Distribution of Antiplatelet therapy

Table 2: Out of all the antiplatelet therapies given in the patients, single antiplatelet therapy i.e., Aspirin/clopidogrel is prescribed the most (n= 77), followed by combination antiplatelet therapy i.e.,(n=74), followed by Dual Antiplatelet therapy and triple antiplatelet therapy.

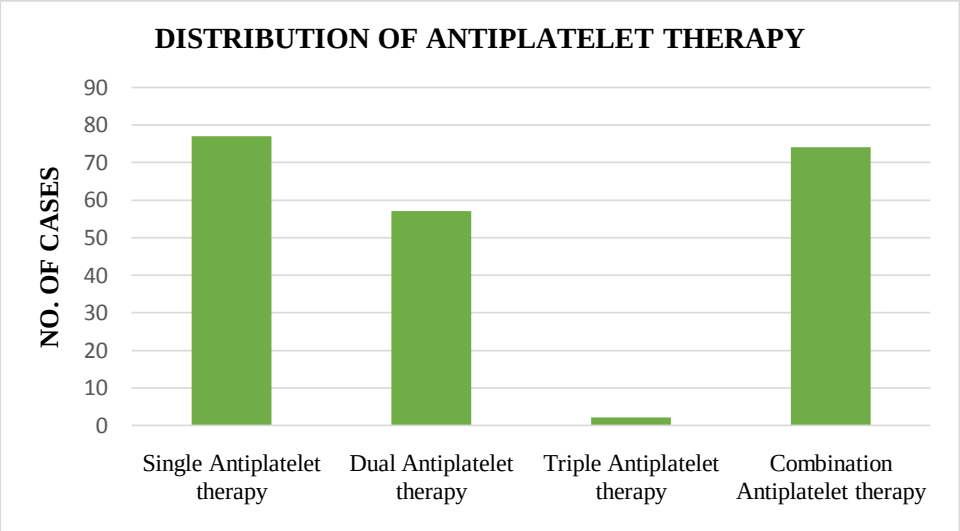

Figure: Distribution of antiplatelet therapy

MOST COMMONLY PRESCRIBED ANTIPLATELET:

S.NO	NAME OF THE ANTIPLATELET PRESCRIBED	NO.OF CASES (N=160)	PERCENTAGE (%)
1.	Aspirin	84	52.5%
2.	Clopidogrel	78	48.3%
3.	Ticagrelor	7	4.37%
4.	Aspirin + Clopidogrel	66	41.2%
5.	Atorvastatin + Clopidogrel	1	0.625%
6.	Aspirin + Clopidogrel + Atorvastatin	2	125%

Table 3: Most commonly prescribed Antiplatelets

Table 3: The most commonly prescribed antiplatelets of all the antiplatelets are Aspirin (n= 84), followed by clopidogrel (n= 78) and combination drugs were also prescribed out of which aspirin and clopidogrel were most commonly prescribed (n= 66).

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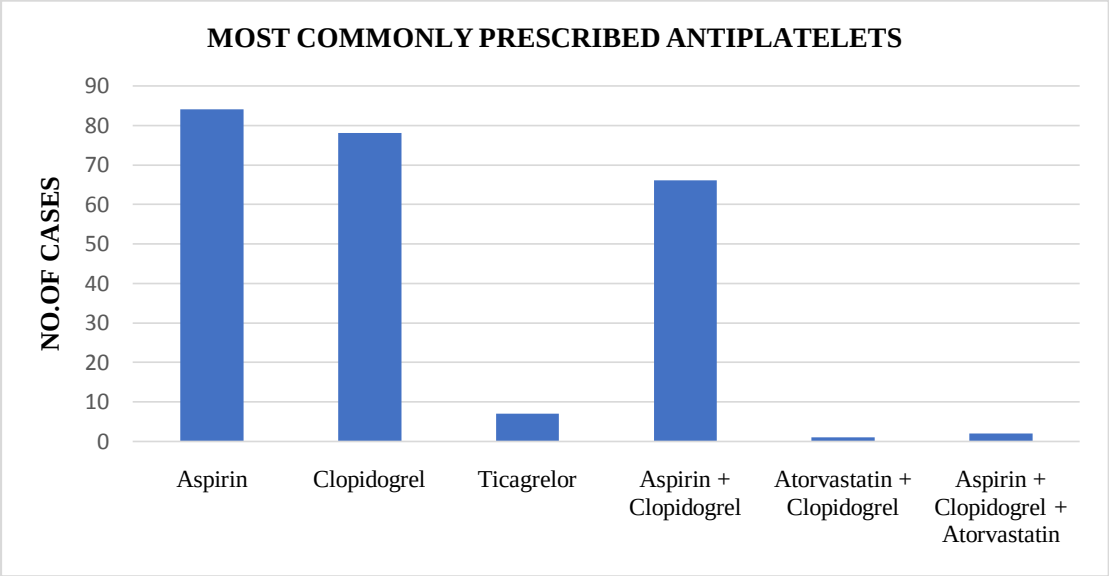

Figure: Most commonly prescribed Antiplatelets

MOST COMMONLY PRESCRIBED BRANDS:

S.NO	BRAND NAME	NO. OF CASES (N=160)	PERCENTAGE(%)
1	ECOSPRIN	57	35.6%
2	ASPIRIN	11	9.16%
3	DISPRIN	9	7.5%
4	CLOPITAB	27	22.5%
5	CLOPITAB-A	24	15%
6	CLOPILET	14	8.75%
6	DEPLATT	14	8.75%
7	DEPLATT-A	17	20.4%
8	CLAVIX	15	9.37%

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9	CLOPIVAS	2	1.25%
10	BRILLINTA	2	1.25%
11	AXCER	5	3.12%
12	AZOLET-10	2	1.25%
13	ANTIPLAR PLUS	1	0.83%
14	ROSULIFE GOLD	2	1.25%
15	CLOPRIDE A	2	1.25%

Table 4: Most commonly prescribed brands

Table 4: Out of all the brands prescribed in antiplatelets, the most commonly prescribed brand is ECOSPRIN (n=47), followed by CLOPITAB (n= 27), CLOPITAB-A (n=24), DEPLATT-A (n=17) and so on.

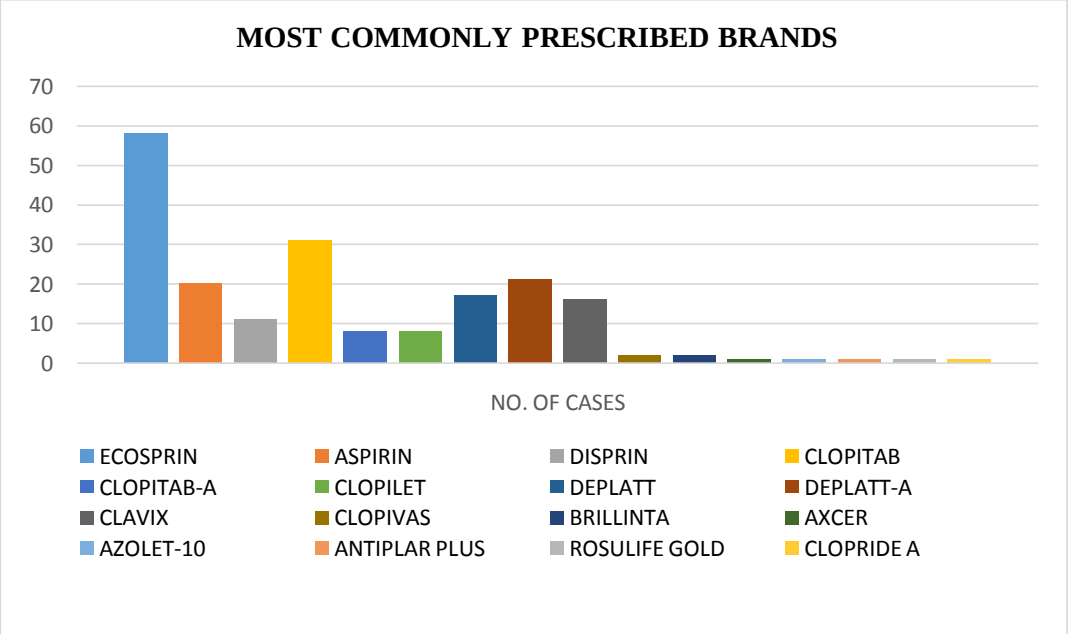

Figure: Most commonly prescribed brands

COST vs DRUG COMBINATION:

BRAND NAME	INDIVIDUALCOST (single unit)
CLOPITAB-A-75-75/150mg	□ 11.9
CLOPITAB-A75-75/75mg	□ 6.52
CLOPITAB-75/75mg	□ 6.52

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DEPLATT-A75-75/75mg	□ 5.39
CLOPRIDE-A-75/75mg	□ 3.68
ANTIPLAR PLUS-75/75mg	□ 3.27
AZOLET10-20/75mg	□ 3.85
ROSULIFEGOLD-75/75/10mg	□ 11

Table 5: Cost Vs Drug combination

Table 5: shows the combination drug cost of the antiplatelet in the study. CLOPITAB A bares the highest cost and ANTIPLAR PLUS bares the least cost respectively.

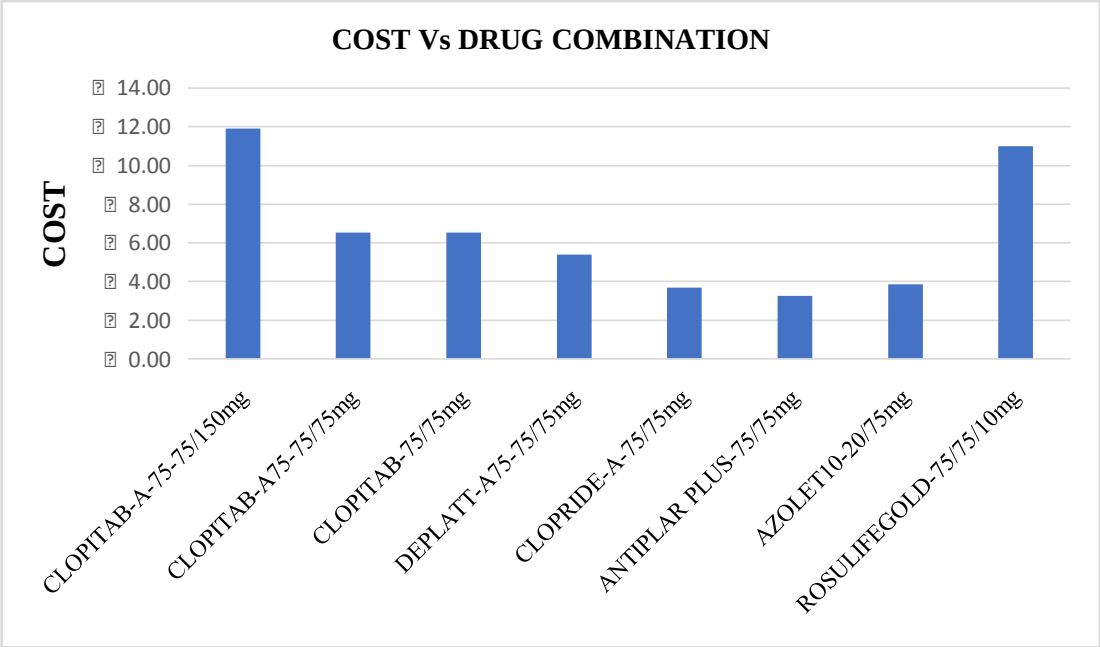

Figure: Cost Vs Drug combination

PRESCRIPTION ANALYSYS:

S.No	PRESCRIPTION CATALOGUE	RESULTS	PERCENTAGE(%)
1	Average drugs per prescription	2	1.25%
2	Total number of CVS patients	118	73.75%
3	Total number of CVA patients	36	22.5%
4	Total number of single drugsPrescribed	77	48.12%
5	Total number of dual drugs Prescribed	57	35.62%
6	Total number of combinational Drugs prescribed	74	46.25%
7	Antiplatelets prescribed in Generic names	1	0.62%

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8	Antiplatelets prescribed in Brand names	15	9.37%

Table 6:Prescription analysis

Table 6: In prescription analysis a total number of 160 case sheets were analyzed,in this at least on average of two antiplatelets were prescribed to the patients. The total number of CVS and CVA patients were found to be 118 (73.75%) and 36 (22.5%). Single antiplatelet therapy is mostly prescribed 7 (48.12%) followed by combinational therapy 74 (46.25%) and dual therapy 57 (35.62%). Drugs are mostly prescribed in brand names 15 (9.37%) when compared to generic names 1

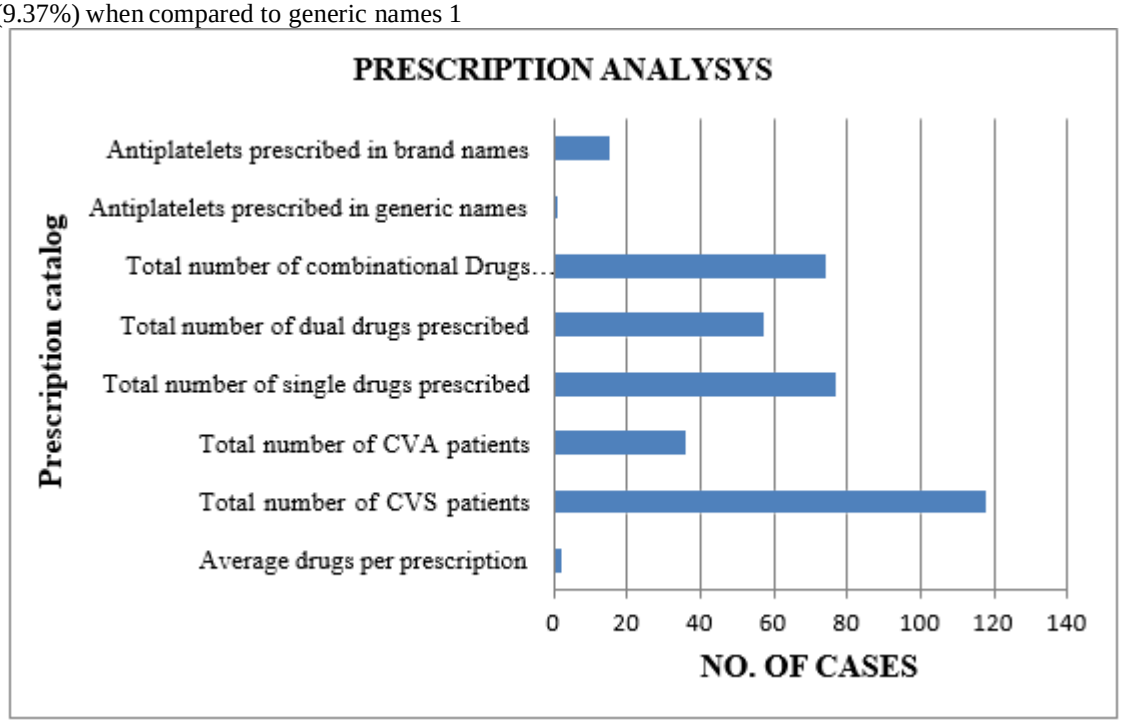

Figure: prescription analysis

TYPE OF INTERACTION:

S.No	DRUG INTERACTION	NUMBER OFCASES	PERCENTAGE(%)
1	Major	13	8.125
2	Moderate	66	41.25
3	Minor	7	4.37
4	Total	86	53.75

Table 7: Type of interaction

Table 7: The below mentioned table and figure shows that in a total of 160 prescriptions,we have found that 86 drug interactions out of which 66 were moderate, assessed that 13 were major and 7 were minor interaction.

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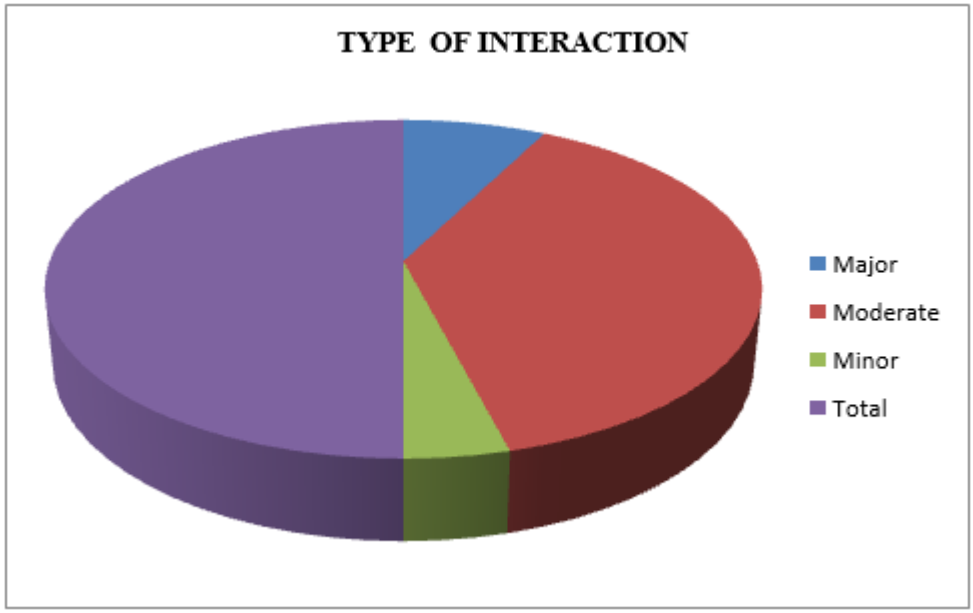

Figure: type of interaction

DRUG INTERACTIONS:

S.No	DRUG COMBINATIONS	INTERACTION TYPE	MECHANISM OF INTERACTION	NUMBER OF CASES(n=160)	PERCENTAGE (%)
1	ENOXAPARIN+ ASPIRIN	Major	May increase risk of bleeding and sometimes fatal hemorrhage.	6	3.75
2	CLOPIDOGREL+ TIROFIBAN	Major	This combination may cause increase Bleeding.	2	1.25
3	ESMOPRAZOLE+ CLOPIDOGREL	Major	This combination may reduce the effect of Clopidogrel	2	1.25
4	APIXIBAN+ ASPIRIN	Major	This combination may increase risk of Bleeding.	2	1.25

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5	OMEPRAZOLE+ CLOPIDOGREL	Major	This combination may reduce the effect of Clopidogrel.	1	0.625
6	CLOPIDOGREL+ ATORVASTATIN	Moderate	This combination decreases the effect of Clopidogrel.	16	10
7	PANTOPRAZOLE+ CLOPIDOGREL	Moderate	This combination may reduce the effect of Clopidogrel	10	6.25
8	ASPIRIN+INSULIN	Moderate	This combination may cause increase the risk of Hypoglycaemia.	8	5
9	TICAGRELOR+ ASPIRIN	Moderate	High doses of aspirin may reduce the effect of Ticagrelor	7	4.375
10	ASPIRIN+ HEPARIN	Moderate	This combination increases the Bleeding.	5	3.125
11	STREPTOKINASE + ASPIRIN	Moderate	This combination may increase the risk of Bleeding.	4	2.5
12	BUDESONIDE+ ASPIRIN	Moderate	This combination may cause increase risk of side effects in theGIT.	4	2.5

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13	CLOPIDOGREL+ ASPIRIN	Moderate	This combination may cause unusual Bleeding	3	1.875
14	CLOPIDOGREL+ TRAMADOL	Moderate	This combination may reduce the blood levels and effect of Clopidogrel.	3	1.875
15	DILTIAZEM+ ASPIRIN	Moderate	This combination may cause unusual Bleeding.	2	1.25
16	AMLODIPINE+ ASPIRIN	Moderate	This combination may cause increase Blood pressure.	1	0.625
17	CLOPIDOGREL+ RIFAMPICIN	Moderate	This combination may cause increase effect ofClopidogrel	1	0.625
18	DEXAMETHASONE +ASPIRIN	Moderate	This combination may cause increase risk of side effects in theGIT.	1	0.625
19	NEFIDIPINE+ ASPIRIN	Moderate	This combination may cause increases Bleeding.	1	0.625

Table 8: Drug interactions

Table 8: The above table shows about the drug interactions in the prescriptions observed. Major interactions are found to be 6 between Enoxaparin and Aspirin with 3.75% and Moderate interactions are found to be 16 between Clopidogrel and Atorvastatin comprising 10%.

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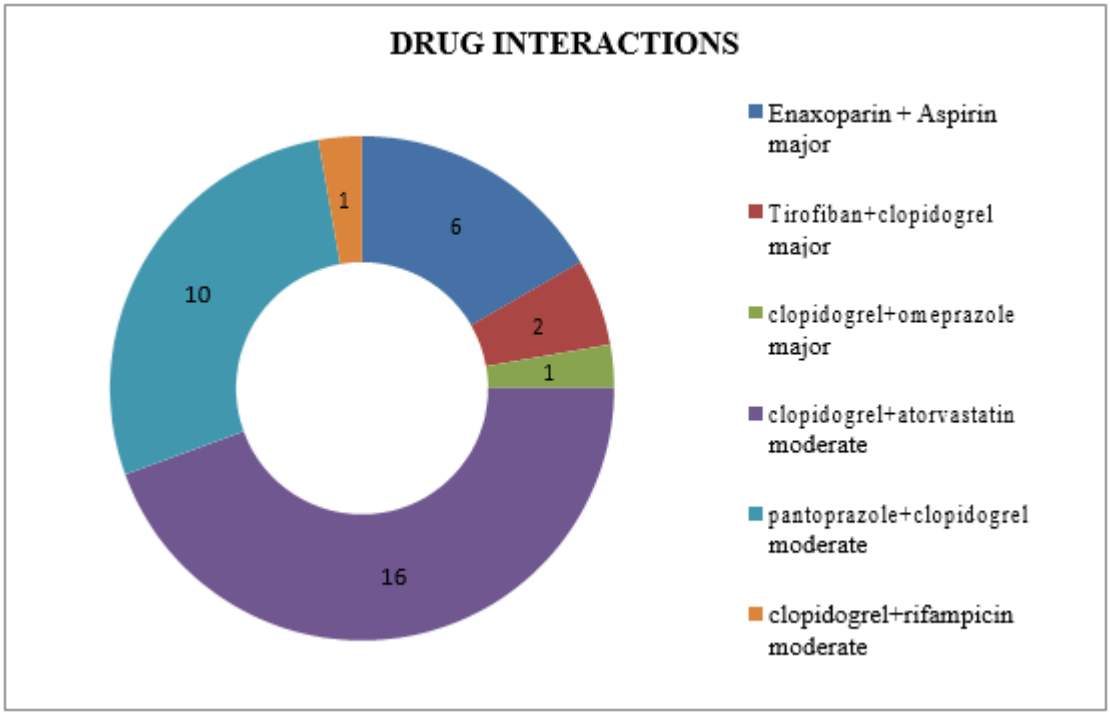

MEDICATION ERRORS:

S.No	TYPE OF ERROR	NUMBER OFCASES	PERCENTAGE(%)
1	Improper dose error	19	11.87
2	Compliance error	3	1.87
3	Drug duplication	4	2.5
4	Prescription error	2	1.25

Table 9: Medication errors

Table 9: Out of all prescriptions observed, a total of 28 medication errors were found out of which 19 were improper dose errors bearing 11.87%, 3 were compliance errors with 1.87%, 4 were drug duplication errors with 2.5% and 2 were prescription errors bearing 1.25%.

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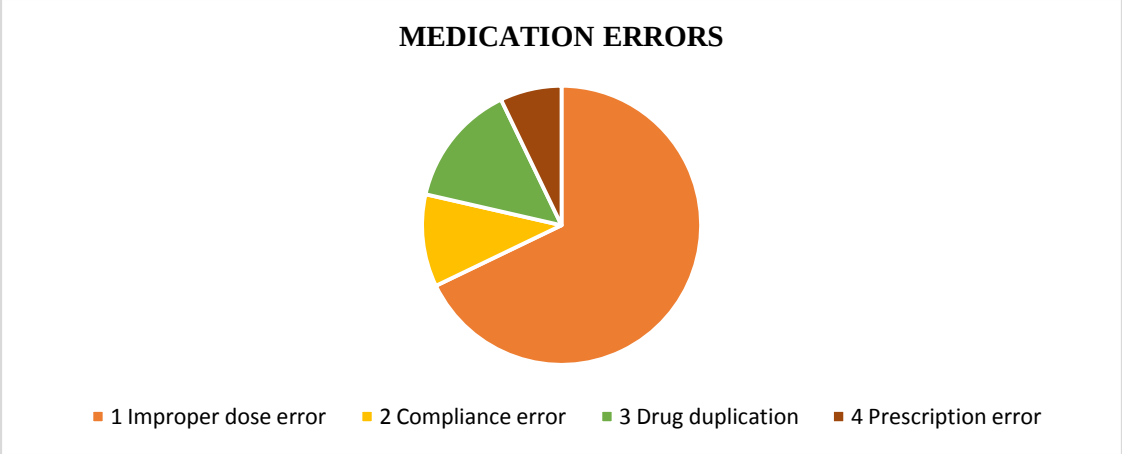

IV. DISCUSSION:

In our study, we educated patients regarding medications, Dietary and Lifestyle modifications. A total of 160 study population were reviewed and quantified the proportion of usage of antiplatelets in different age groups. Regarding the age categorization in the study population of 160 subjects 60-69 age group (n=51, 31.8%) were found to be more susceptible for risk of getting a disease followed by 50-59(n=36, 22.5%), 40-49(n=35, 21.8%), 70-79(n=22, 13.7%), 30-39(n=8, 5%) and 80-89(n=8, 5%).

Regarding the type of antiplatelet therapy given to the patients, single antiplatelettherapy i.e., Aspirin is prescribed the most (n=77, 48.1%), followed by dual antiplatelet therapy i.e., both aspirin and clopidogrel (n=66, 41.2%), followed by combination antiplatelet therapy (n=40, 25%) and triple antiplatelet therapy (n=2, 1.25%).

Out of all the antiplatelets given, the most commonly prescribed antiplatelets are Aspirin (n= 84, 52.5%),followed by clopidogrel (n= 78, 48.3%) and combination drugs were also prescribed out of which aspirin and clopidogrel were mostcommonly prescribed (n= 66, 41.2%) followed by aspirin and atorvastatin (n=5, 3.12%).

Regarding mostly prescribed brands Out of all the brands prescribed in antiplatelets, the most commonly prescribed brand is ECOSPRIN (n=57, 35.6%)), followed by CLOPITAB (n= 27, 22.5%), CLOPITAB-A(n=24, 15%), DEPLATT-A(n=17, 20.4%), CLAVIX(N=15, 9.37%), CLOPILET and DEPLATT (n=14, 8.75%) and so on.

Regarding the cost of drugs based on the brands prescribed shows the combination drug cost of the antiplatelet in the study. CLOPITAB A bares the highest cost and ANTIPLAR PLUS bares the least cost respectively.

In prescription analysis a total number of 160 case sheets were analyzed, in this at least on average of two antiplatelets were prescribed to the patients. The total number of CVS and CVA patients were found to be 118 (73.75%) and 36 (22.5%). Single antiplatelet therapy is mostly prescribed 77 (48.12%) followed by combinational therapy 74 (46.25%) and dual therapy 57 (35.62%). Drugs are mostly prescribed in brand names 15 (9.37%) when compared to generic names 1 (0.62%).

In severity of drug interactions, we have found that 86 drug interactions of which 66 were moderate (n=66, 76.74%) followed by 13 major(n=13,15.1%) and 7 minor (n=7, 8.13%).

The drug interactions in the prescriptions observed. Major interactions are found to be 6 between Enoxaparin and Aspirin with 3.75% and Moderate interactions are found to be 16 between Clopidogrel andAtorvastatin comprising 10%.

Out of all prescriptions observed, a total of 28 medication errors were found out of which 19 were improper dose errors bearing 11.87%, 3 were compliance errors with 1.87%, 4 were drug duplication errors with 2.5% and 2 were prescription errors bearing 1.25%.

V. CONCLUSION:

Antiplatelet usage varies with individuals according to their disease conditions to minimize the adverse drug reaction, drug-drug interaction, cost of the treatment and other medication errors. The mostly prescribed antiplatelet drug was aspirin and monotherapy was highly preferred followed by the combinational therapy. The dose was prescribed as per the severity of the patient's condition. Mostly prescribed antiplatelet drugs

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were Aspirin and Clopidogrel and they have shown desired efficacy in patients who were prescribed with both monotherapy and dual antiplatelet therapy.

In our study, it was observed the incidence of CAD was more common in male compared to female and the risk for coronary artery disease increased with increase in the age. The maximum number of patients was male; it may be due to smoking and alcoholic habits. Few drugs were prescribed by generic name. By prescribing the generics patients can be able to economize the expenses spent on the health-related problems.

Though the utilization of antiplatelets were appropriate concerning their indications, their associated risks should also be considered according to the individual basis. Rationalization of therapy should have to be promoted by the clinical pharmacist through individualized therapy based on the patient's age, comorbidities and other relevant risk factors. The clinical pharmacist should have to aid in modifying the risk factors especially hypertension, alcoholism, smoking, blood sugar, blood cholesterol and poor compliance which were most common causes of CVDs as well as responsible for poor prognosis of the diseases. It is prudent to monitor the parameters especially platelet count for antiplatelet therapy and PT, INR for antiplatelets before as well as after initiation of therapy in order to prevent bleeding risk.

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