Research Article

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Drug utilisation evaluation of antiplatelet agents in a tertiary care teaching hospital-a prospective observational study

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Abstract

Background: Cardiovascular and cerebrovascular diseases were becoming predominant cause of morbidity and mortality in India. Antiplatelet agents remain as the cornerstone therapy for acute thrombotic coronary syndromes, IHD, STROKE, CHD and PCI and are essential for thromboprophylaxis. The current study was undertaken to evaluate the drug use pattern of antiplateletagents and to study the prescribing pattern, observe co-morbid conditions, social habits [alcohol/smoking], adverse events and drug-drug interactions associated with antiplatelet agents.

Methods: A prospective observational study was conducted at MIMS hospital, study population of 160 inpatients from cardiology, general-medicine and neurology departments. Data was analyzed in Microsoft excel.

Results: Data records obtained from 160 patients in which 51.87% were females followed by males 48.125%. Most patients with IHD and stroke were found in age group 50-70 years. Hypertension was most found co-morbidity among the patients [61.88%] followed by diabetes [34.38%], hypothyroidism [5%], epilepsy[3.75%]. Utilisation pattern of antiplatelet agents aspirin, clopidogrel were found to be[97.5%] [82.5%] respectively. Patients on DAPT[81%] were highest compared to monotherapy [19%]. Patients found with social habits were 38.75% smokers, 31.25% alcoholics and 22% both alcohol and smoking.

Conclusion: The present study concludes that DAPT [aspirin+clopidogrel] was found to be superior to monotherapy, and incidence of IHD which is more common in males compared to females. Patients in the group 51-70 were most affected with stroke, IHD and with female predominance over male. Antiplatelet therapy which is clearly efficacious in reducing the incidence of ischemic events/ thromboembolic events DAPT[aspirin+ clopidogrel] was most effective and reduced ischemic events, yet have the risk of bleeding or resistance. Newer anti platelet agents such a Prasugrel and Ticagrelor can be utilised considering the bleeding risk.

Keywords: Antiplatelet agents, aspirin, clopidogrel , dual antiplatelet therapy [DAPT], monotherapy, utilisation pattern and adverse event.

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Introduction

A drug utilisation evaluation(DUE) program is often defined as an authorised, structured, ongoing system for improving the standard of drug use within a healthcare Organisation [1]. Drug use is evaluated by using pre-determined standards and efforts are initiated to correct patterns of use which aren't according to these standards. This terminology DUE is similar to the drug use review (DUR) and medication use review (MUR) [2].

DUE might be applied to a drug, therapeutic category, disease state or condition, a drug use method or specific outcomes [3]. It may be applied in various practice settings, as well as hospitals, other health facilities, and community practice environments [4]. Cardiovascular

diseases (CVDs) have currently become the leading reason for mortality in India. 1/4 of all mortality is due to CVD. Ischemic heart condition and stroke are the predominant causes and are liable for >80% of CVD deaths. Developing countries like India face a double burden of transmissible and non-transmissible diseases. Stroke is one among the leading causes of death and disability in India. As per the recent population based studies, the incident rate of stroke was found to be 119-145/100,000 3. Coronary artery disease (CAD) represents about 610,000 deaths yearly (estimated 1 in 4 deaths) and is the major cause of mortality in the United States. It is the third leading reason behind mortality worldwide and is accompanied with 17.8 million deaths yearly [5]. Antiplatelet drug therapy is one of the major strategies used for preventing recurrent stroke in patients who have previously experienced ischaemic stroke or transient ischaemic attack TIA of non-cardio embolic aetiology. Aspirin is nowadays the most widely tested antiplatelet agent and, hence, it has the most immense evidence regarding its benefits in patients with prior ischaemic stroke and TIA [6]. Platelet inhibition plays a significant role for treatment and prevention of atherothrombotic events in patients with CAD. Oral antiplatelet agents for secondary prevention of patients with CAD comprise the COX-1 inhibitor aspirin, and the platelet ADP P2Y12 receptor inhibitors clopidogrel, prasugrel and ticagrelor. Aspirin and clopidogrel have been studied across the entire spectrum of CAD, whereas the more recent potent adenosine diphosphate P2Y12 platelet receptor inhibitors prasugrel and ticagrelor have been evaluated in patients with ACS [7].

Recent studies, including randomized trials and a large observational study, have found that dual antiplatelet therapy with clopidogrel-aspirin is more effective at preventing early vascular events than aspirin monotherapy in patients with acute stroke or a high risk transient ischemic attack [8]. Antiplatelet therapy decreases the incidence of cardiovascular events by about 20-25% in patients with established cardiovascular disease or at high risk of CVD [9]. The current study focuses on utilisation pattern of antiplatelet agents in a tertiary care teaching hospital.

Methods And Methodology

Study Design: This study is a prospective and observational study involving drug utilisation evaluation of antiplatelet agents.

Study Site: This study was conducted in various departments of MAHARAJA INSTITUTE OF MEDICAL SCIENCES (MIMS hospital) a tertiary care teaching hospital which provides all facilities and health care services to all the people in and around Vizianagaram.

Study Population: 160 inpatients in departments (cardiology [83], general medicine [65] and neurology[12]) were included in the study and were assessed.

Selection Of Study Subjects

1.Inclusion Criteria: Patients of either sex admitted in MIMS hospital, receiving antiplatelet drugs in any form. Patients aged above 30 years.

2.Exclusion Criteria: Pregnant women, lactating mothers, prescription without antiplatelet agents and patients below 30 years and out patients were not involved in this study and patients who are not willing to participate in the study.

Duration Of Study: November 2020 to April 2021.

Data Collection: The data is collected in a pre-designed case report form through direct interview with patients or from patient medical records, without interfering with their treatment. Patient demographic data, including age, sex, habits (smoking or alcoholic), socioeconomic details(based on Kuppuswamys socioeconomic status scale 2020) , current diagnosis, co-morbid conditions, details of antiplatelet therapy (whether monotherapy – either aspirin or clopidogrel or any other antiplatelet agent or dualtherapy – combination of two antiplatelet drugs). Adverse drug reactions reported by the patients were assessed based on Naranjo scale. Based on the details of therapy, drugs interacting with antiplatelet agents were identified. (Drug interaction checker- epocrates and Medscape.)

Data Analysis: Data was analysed in MS Excel, Descriptive statistics expressed in terms of actual numbers and percentage was used for data analysis and statistical interpretation was drawn by using SPSS software.

Ethical Considerations: Ethics Committees of MIMS hospital have reviewed and verified all documents related to Research proposal, Informed Consent, budget and granted approvals in the Ethics Committee and given proposal numbers.

Results

Data was retrived from 160 medical records from patients who were admitted as inpatients cardiology, general medicine and neurology departments in MIMS hospital

Age

In this study 160 patient participants were involved within the age range 30 – 90years. From the analysed data 18 study participants were between the age group 31 – 40 years, 32 participants were found between 41-50 years, 55 participants were in the age group between 51-60 years, 34 participants were found between 61-70years, 20 participants were found between 71-80years, 1 study subject was in between 81-90 years. Most of the patients admitted were in the age group between 50 -70 year.

Table1: represents age distribution of the patients.

Age Group	No Of Patients	Percentage
31 – 40	18	11.25
41 – 50	32	20
51 – 60	55	34.375
61 – 70	34	21.25
71 – 80	20	12.5
81 – 90	1	0.625

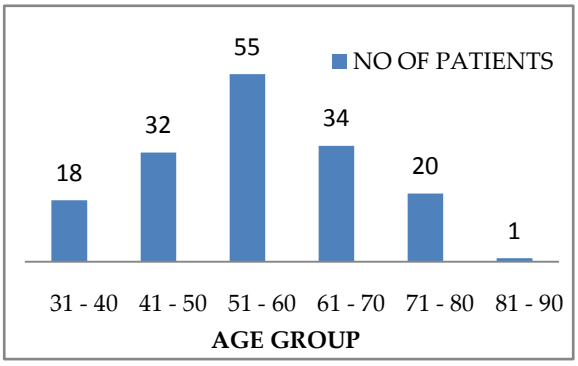

Fig1: represents the age distribution of 160 patients.

Gender

out of 160 patient participants 77 were male (48.125) and 83 were female paricipants (51.875).

Table 2: gender wise distribution.

Gender	No Of Patients	Percentage
Male	77	48.125
Female	83	51.875

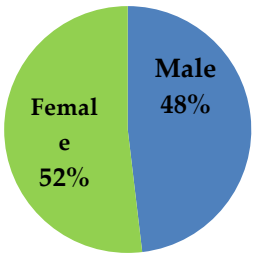

Fig 2 : gender wise representation of 160 patients

Socio – economic status

In this study socio economic class of most of the patients was found to UPPER LOWER[55%], LOWER MIDDLE[23.125%] followed by LOWER [14.375%] and 6.25% from UPPER MIDDLE and 1.25% from upper socio economic class.

Table 3: Socio-economic status

Score	Socioeconomic Class	No Of Patients	Percentage
26 TO 29	UPPER (I)	2	1.25
16 TO 25	UPPER MIDDLE (II)	10	6.25
11 TO 15	LOWER MIDDLE (III)	37	23.125
5 TO 10	UPPER LOWER (IV)	88	55
<5	LOWER (V)	23	14.375

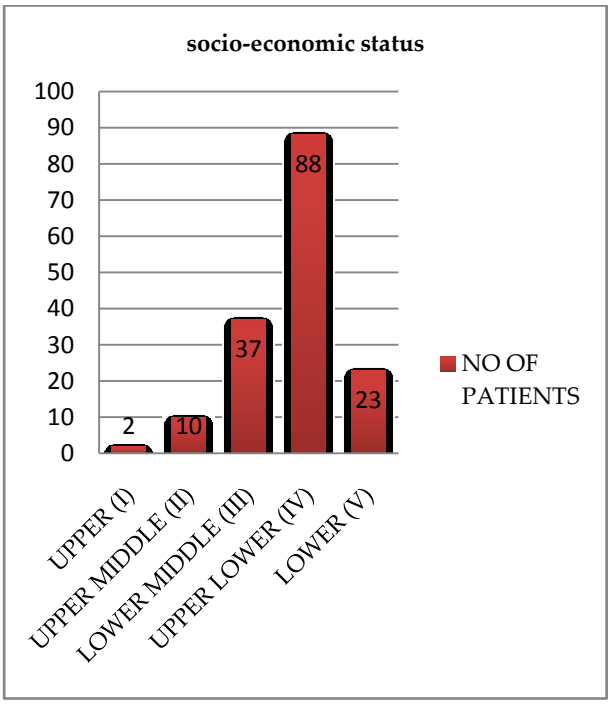

Fig 3: Social-economic status representation

Social habits

(*p value: 0.1789; non-significant)

Smokers

In this study out of 160 patient participants 62 participants were found to be smokers and 98 were non-smokers.

Alcoholics

Out of 160 patient participants 50 participants were found to be alcoholics and 110 were non-alcoholics. Percentage of smokers, non-smokers and alcoholics and

non- alcoholics is represented in table 4, fig 4 represents the data distribution of smoker–non-alcoholics, alcoholic–non-smokers, both smokers and alcoholics and neither of the social habits.

Table 4: represents social habits of patient participants.

Social Habit	No Of Patients	Percentage
Smokers	62	38.75
Non-Smokers	98	61.25
Alcoholic	50	31.25
Non-Alcoholic	110	68.75

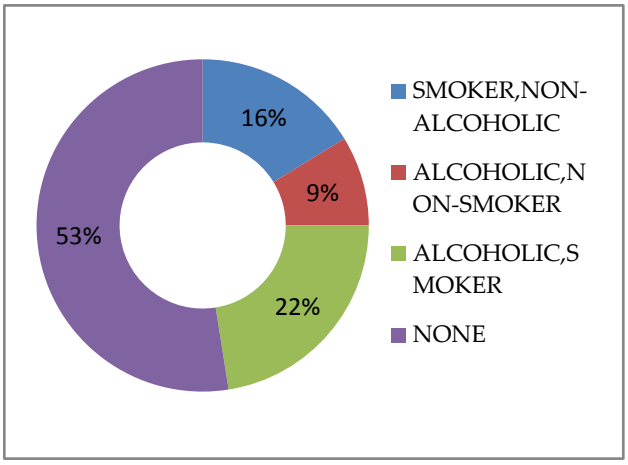

Fig 4: represents percentage distribution of social habits.

Prevalent diseases among patient participants

Ischemic heart disease [63.125%] is found to be most prevalent disease among patients prescribed with antiplatelet agents followed by stroke[28.1%] and congestive heart failure [6.875%]. Peripheral arterial disease[1], post mitral valve replacement[1] and deep vein thrombosis(DVT)[1] were the other conditions for which antiplatelet agents were prescribed . (represented in fig 5).

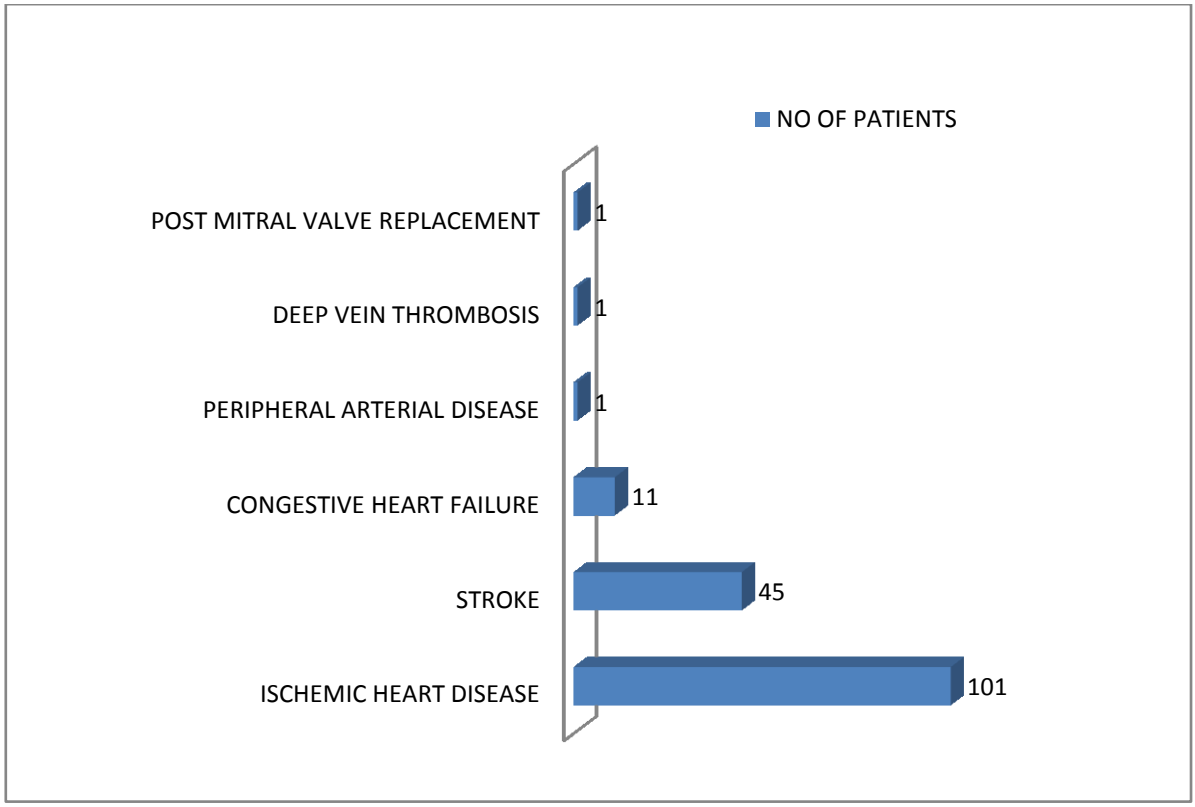

Fig 5: represents prevelant diseases among patient participants.

Gender wise and age wise distribution of prevalent diseases among patient participants

Most of the patients with IHD were in the age group 51-60 (in years) , followed by age group (61-70) and (41-50). Similar pattern was observed in CHF and stroke. Among 101 patients with IHD, 53 were male, 48 were female patients. Among 45 patients with stroke, 27 were female and 18 were male patients. Among 11 patients with CHF, 10 were female.

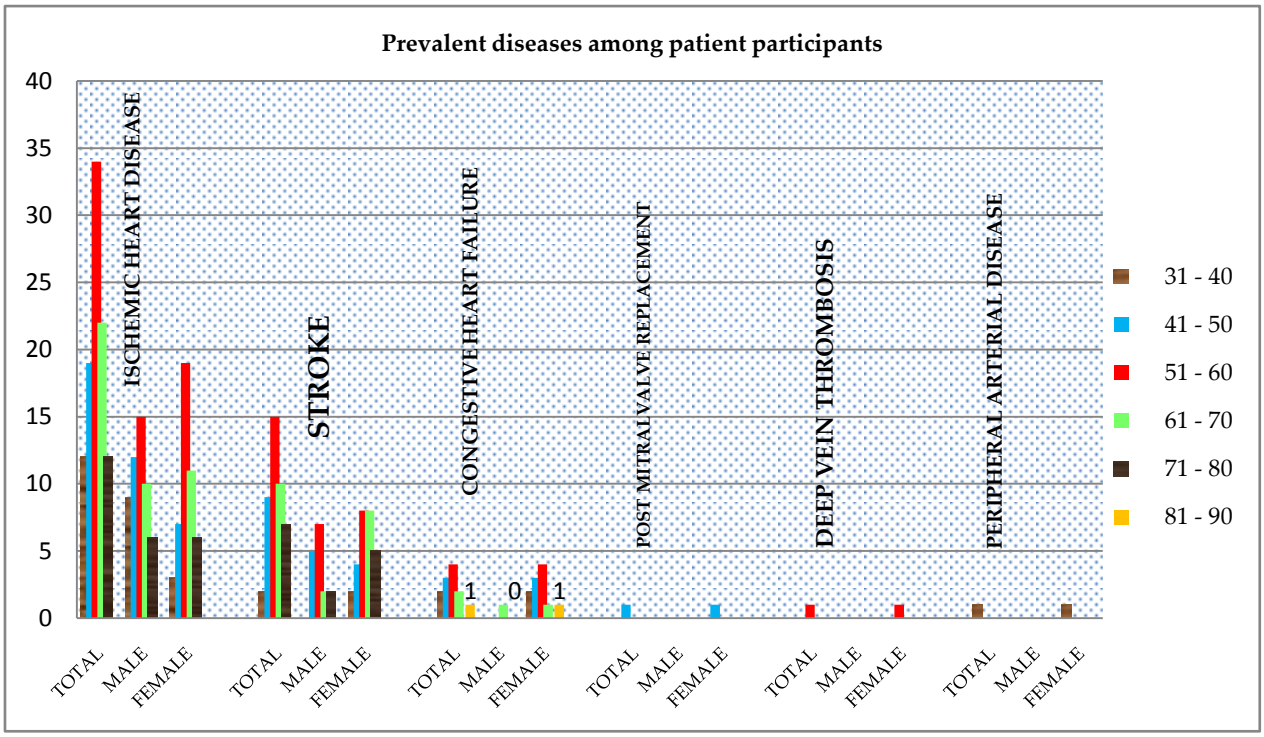

Fig 6: represents prevalent diseases among patient participants gender and age group wise.

Comorbidities

Participant's data was distributed based on co-morbid conditions in the study. Hypertension was found to be the comorbidity with highest frequency i.e., 99[61.875%] followed by diabetes[34.375%] out of which 43 study participants were both diabetic and hypertensive [27%], 56 patients were hypertensive non-diabetic[35%] and 12 patients were diabetic and non-hypertensive [7%]. Both non-diabetic and non-hypertensive participants were 49 [31%] and 5% of patients have hypothyroidism followed by 3.75% with epilepsy, 1.875% with anemia, 1.25% with LRTI and bronchitis, 0.625% with CKD, COPD, psoriasis, dengue and depression. Comorbidities frequency and percentage are represented in table , graph and pie chart. (*p value: 0.0070; significant)

Table 5: represents comorbidities of participants.

Comorbidities	Frequency	Percentage
Hypertension	99	61.875
Diabetes Mellitus	55	34.375
Hypothyroidism	8	5
Epilepsy	6	3.75
Anaemia	3	1.875
Lrti	2	1.25
Bronchitis	2	1.25
Ckd	1	0.625
Depression	1	0.625
Dengue	1	0.625
Copd	1	0.625
Psoriasis	1	0.625

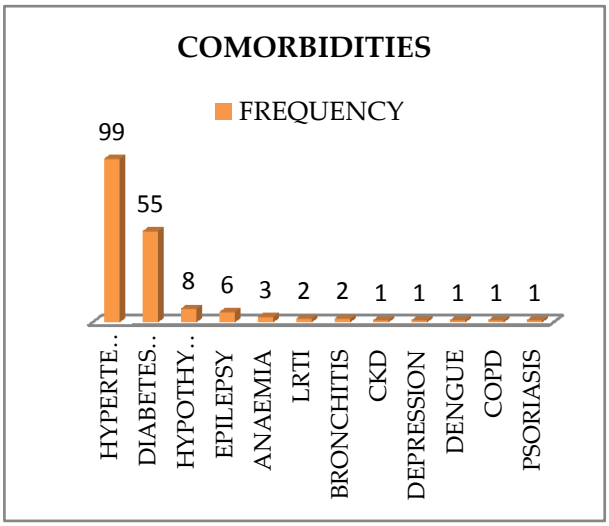

Fig 7: represents frequency of comorbidities in a graph

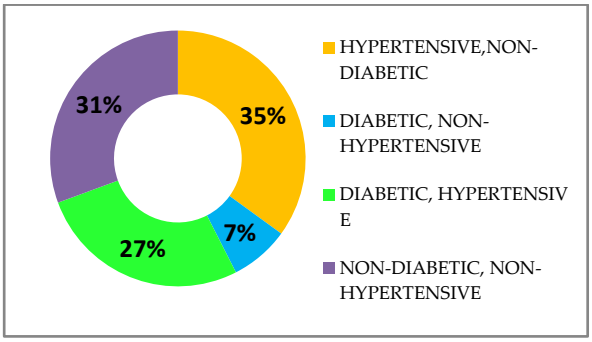

Fig 8 : represents percentage distribution of comorbidities.

Utilisation pattern of antiplatelet agents

(*p value: 0.2675; non-significant)

Among 160 patient participants in the study aspirin frequency was found to be 156 [97.5%] which was the most used antiplatelet agent followed by clopidogrel in 132 [82.5%] participants and cilostazol frequency 1 [0.625]. In this study dual antiplatelet regimen was highest 81.25% compared to patient participants who were on monotherapy 18.75%.

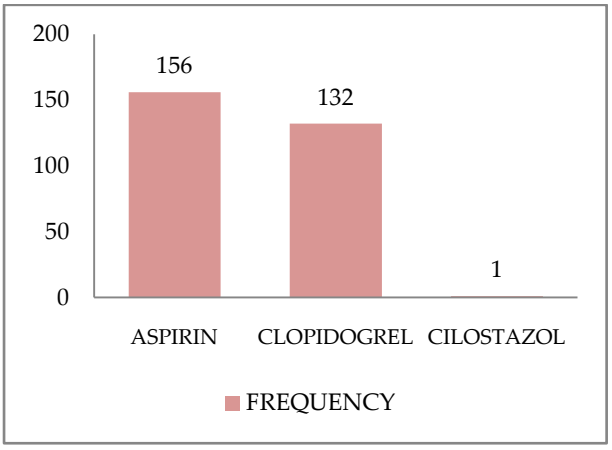

Fig 9: represents frequency of antiplatelet agents used.

Data distribution of utilisation of antiplatelet agents based on age and gender: 5 female participants in age group between 31-40 were using monotherapy, 3 males and 3 females between 41-50 were on single antiplatelet treatment, 2 males and 8 female participants between 51-60 under monotherapy,1male and 1 female between 61-70 , 3 males and 5 females between 71-80 years were found to be using monotherapy.

9 male and 4 female participants between 31-40 were on dual antiplatelet treatment, 4 males 12 females between 41-60 years using DAPT , 20 males and 25 males between the age group 51-60 were found to be highest DAPT compared to other age groups, 12 males and 20 females between age group 61-70 years on DAPT, 5 male and 8 female participants between 71-80 years on DAPT and 1 female between age group 80-90 years on DAPT.

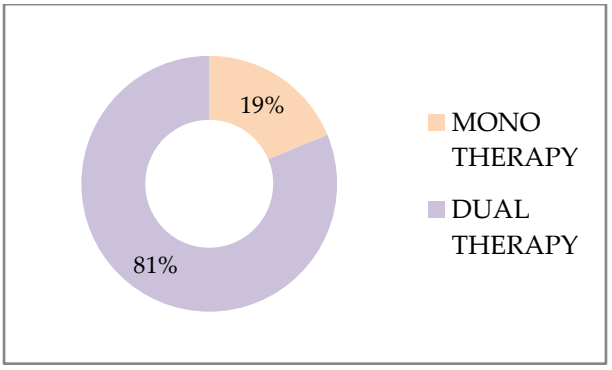

Fig 10: represents percentage of monotherapy and dual antiplatelet therapy in pie chart.

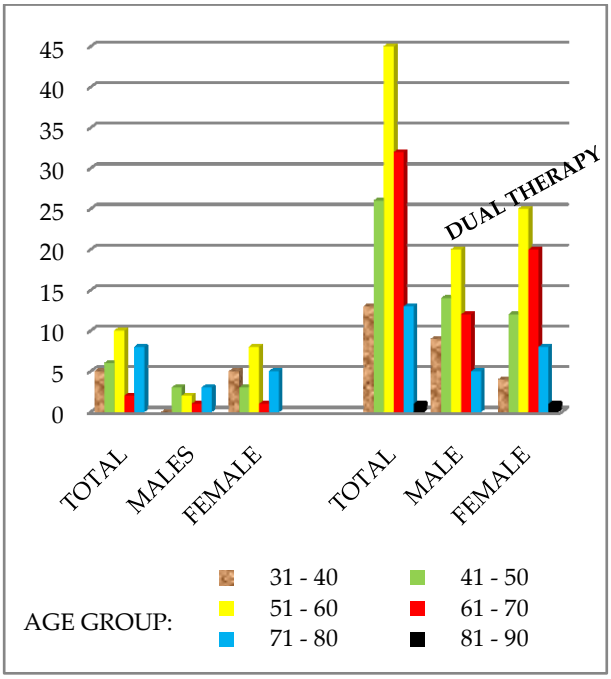

Fig 11: graph representation based age wise and gender wise utilisation of monotherapy and dual antiplatelet therapy

Drug-drug interactions associated with antiplatelet agents

(*p value: 0.0021; significant)

Table6: represents severity of drug-drug interactions

Severity	No Of Interactions
Minor	4
Moderate	27
Major	4

DRUGS INVOLVED	SEVERITY	INTERACTIONS
Aspirin + Furosemide	MILD	Aspirin decreases effects of furosemide by pharmacodynamic antagonism.
Aspirin + Folic acid	MILD	Aspirin decreases levels of folic acid by inhibition of GI absorption.
Aspirin + Metolazone	MILD	Metolazone will increase the level or effect of aspirin by acidic (anionic) drug competition for renal tubular clearance.
Aspirin + Metoprolol	MODERATE	Aspirin decreases effects of metoprolol by pharmacodynamic antagonism. metoprolol and aspirin both increase serum potassium
Aspirin + Enoxaparin	MODERATE	Either increases toxicity of the other by pharmacodynamic synergism.
Aspirin + Atenolol	MODERATE	Aspirin decreases effects of atenolol by pharmacodynamic antagonism.

Aspirin + Cilostazol	MODERATE	Either increases toxicity of the other by pharmacodynamic synergism.
Aspirin + Clopidogrel	MODERATE	Either increases toxicity of the other by pharmacodynamic synergism
Aspirin + Spironolactone	MODERATE	Aspirin decreases effects of spironolactone by unspecified interaction mechanism.
Aspirin + Heparin	MODERATE	Heparin and aspirin both increase anticoagulation.
Clopidogrel + Enoxaparin	MODERATE	Either increases effects of the other by pharmacodynamic synergism.
Clopidogrel + Heparin	MODERATE	Either increases effects of the other by pharmacodynamic synergism.
Clopidogrel + Pantoprazole	MODERATE	Pantoprazole decreases effects of clopidogrel by affecting hepatic enzyme CYP2C19 metabolism.
Aspirin + Enalapril	MAJOR	Pharmacodynamic antagonism. Coadministration may result in a significant decrease in renal function.
Aspirin + Ramipril	MAJOR	Pharmacodynamic antagonism. Coadministration may result in a significant decrease in renal function.

In this study , 35 probable drug interactions were observed , out of which 27 were moderate followed by 4 minor and 4 major interactions. Out of interventions made in 35 drug-drug interactions, 18 were accepted by the physicians. Physician's acceptance ratio for the pharmacist's intervention in the DDI was 51.4%. After accepting the interventions, change in dose intervals, optimization of administration. Most of the DDI were observed in elderly patients and patients on polypharmacy the changes made in the prescription by the prescriber were as follows: change in drug choice, dose adjustments, change in dose intervals, optimization of administration. Most of the DDI were observed in elderly patients and patients on polypharmacy.

Adverse drug reactions

(*p value: 0.0112; significant)

In this study 5 adverse drug reactions were assesed which were observed and reported by patient participants. Out of 5 ADR, 3 were probable and 2 were possible.Three adverse drug reactions occurred due to aspirin and two adverse drug reactions due to clopidogrel.

Table7: represents drug which is causing ADR based on Naranjo algorithm probability scale

Adverse Effect	Score	Probability
Aspirin induced bronchospasm	3	Possible
Aspirin induced dyspepsia	7	Probable
Aspirin induced gastrointestinal ulcer	5	Probable
Clopidogrel induced diarrhoea	6	Probable
Clopidogrel induced rash/pruritis	4	Possible

Patient drug compliance

All the participants involved in this study were found to be medication adherent. The reasons may include:

- Patients were under continuous medical supervision
- All the participants in this study were inpatients
- Patient drug charts were regularly monitored by the medical staff.
- Patients were counseled about the beneficial effects of the drugs. So they were more adherent.

Sometimes non adherence may occur due to improper monitoring of patients by the medical staff, recklessness of patients to administer drugs, duty nurses' forgetfulness to administer the drugs to the patients.

Overdose

In this study, out of 160 participants, one patient was observed to be overdosed with aspirin (loading dose 300mg and maintenance dose 150mg). This is because the patient is a known CKD patient. Aspirin is primarily hepatically metabolized, with some dose and urine pH dependent renal excretion. Moreover, aspirin has been shown to increase risk of either developing CKD or enhancing progression of underlying CKD, particularly in subjects with more than 500 g of aspirin intake per year and also in the elderly.

Assessment of WHO Prescribing Indicators

Table 8 : represents WHO prescribing indicators in our study.

Parameters Assessed	Results
Average no. of drugs per prescription	7.725
Percentage of drugs prescribed by generic name	33%
Percentage of encounters with an antiplatelet drug prescribed	23.38%
Percentage of encounters with an antiplatelet injection	0
Is the drugs prescribed are from the hospital formulary	Yes

Discussion

The indications for the utilisation of antiplatelet drugs in management of thrombotic diseases include stroke, acute myocardial infraction (AMI), acute coronary syndrome (ACS), angina, percutaneous coronary intervention (PCI), cardiac surgery, primary and secondary CVD prevention, PVD, and thrombotic disorders such as atrial fibrillation [10].

Ischemic heart disease(IHD) includes stable coronary syndrome and acute coronary syndrome(ACS). Myocardial infarction and no obstructive coronary artery disease (MINOCA), NSTEMI, STEMI and unstable angina comes under ACS. Obstructive CAD and ischemia and no obstructive coronary artery disease (INOCA) comes under stable coronary syndrome [11].

In the current study, the participants were categorised into 6 groups based on their age groups being kept at an interval of 10 years (fig.1) and most of the patients prescribed with antiplatelet agents were in the age groups [51-60]years (34.375%) and [61-70]years (21.25%). Similarly in a study conducted by Pramod.B et.al, most of the patients were in the age groups [51-60] years (50%) and [61-70]years (31%) [12].

In a study conducted by K.Jyothi, most of the patients with IHD were in the [60-80] years age group [13], whereas in the present study most patients with IHD were in the [51-70] years age group (fig 6). Males [53] were slightly more affected with IHD in comparision with females [48]. In a study conducted by Pramod.B et.al, percentage 7% of patients were affected with stroke [12], whereas in the present study it was found to be 28.1%.

Hypertension was observed to be the comorbidity with highest frequency(61.88%), followed by diabetes mellitus(34.38). 5% of patients had hypothyroidism as a comorbidity (fig 7). Comorbidity is a major public health concern that poses a barrier to disease-centered health care. Despite using proper doses of oral antiplatelet medications, recurring occurrences of acute coronary events are still common [14]. This could be attributed to anti-platelet resistance or the existence of co-morbid illnesses such as diabetes, high blood pressure, and hyperlipidemia. Coronary heart disease patients with type 2 diabetes mellitus have elevated platelet reactivity and reduced in vitro responsiveness to anti-platelet agents, which include P2Y12 receptor antagonists, compared with nondiabetic patients [15].

In the present study, utilization of antiplatelet agents was observed in patients(males- 48.13% and females– 51.88%) with IHD, stroke, CHF, DVT, PAD and post-mitral valve replacement. Patients were either on monotherapy either apirin(300mg loading dose or 150mg maintainance dose) or clopidogrel(150mg loading dose or 75mg maintainance dose) or dual therapy mostly aspirin with clopidogrel. 19% of patients were on monotherapy (fig10). The percentage of patients on dual antiplatelet therapy(DAPT) was higher (81%). Out of 160 cases included in the study, only one patient was with PAD, and was on DAPT involving aspirin(150mg) and cilostazol(100mg). Utilisation of antiplatelet agents (fig 9) was found to be as – aspirin(97.5%), clopidogrel(82.5), and cilostazol(0.625%). In a study conducted by Pramod.B et al, utilization of aspirin and clopidogrel was 100% and 89% respectively and patients on monotherapy and DAPT was 11% and 89% respectively [12]. In a study conducted by Muneeshwar et.al, utilization of aspirin, clopidogrel, cilostazol was observed as 61.86%, 32.64%, and 5.5% respectively [16]. DAPT with apirin and a P2Y12 receptor inhibitor can reduce the risk of ischemia events. Clopidogrel treatment lowered the incidence of myocardial infarction and recurrent ischemia, with a tendency toward lower stroke and cardiovascular death rates. Due to the patients' advanced age and various comorbidities, DAPT was postponed or discontinued [17,18]. In this study antiplatelet agents were prescribed in post-mitral valve replacement[MVR] case to reduce the risk of clots that may form on new valve.

Cigarette smoking is the major preventable risk factor for cardiovascular disease (such as sudden death,

coronary artery disease and stroke) [19]. Increased cardiovascular risks of heavy alcohol drinking has been associated with cardiomyopathy, systemic hypertension, supraventricular arrhythmias, hemorrhagic stroke and heart failure that is not associated with coronary artery disease (CAD). Light and moderate alcohol consumption is unlikely to be associated with an increased risk of any cardiovascular condition and is associated with lower risks of CAD, ischemic stroke and CAD-related heart failure [20]. In the present study, out of 160 patients 53% of patients have no social habits. 38.75% of patients were smokers and 31.25% were alcoholics. 22% of patients were having both smoking and alcohol as social habits(fig4). In a study conducted by G Rajesh et al, 15% and 4% of patients were smokers and alcoholics respectively and 23% of patients were having both smoking and alcohol as social habits [21].

Smoking and/or alcohol addiction led to sympathetic activation and parasympathetic inhibition. Reduced vagal activity also predisposes to cardiac arrhythmias; this means an increased risk of cardiovascular mortality, including sudden cardiac death.When alcohol is consumed together with smoking, the adverse effects of smoking on the heart are further increased [22]. Chronic alcohol abuse is the most common cause of secondary dilated cardiomyopathy. The most important indicators of the effects of long-term alcohol use have high blood pressure, cardiac arrhythymia, cardiomyopathy, and congestive heart failure. Abstinence from alcohol can lead to better outcomes for established hypertension, arrhythmia and cardiomyopathy, but may not be a feasible or acceptable goal for many patients [23].

Aspirin can induce adverse gastrointestinal effects ranging from dyspepsia with endoscopically normal gastric mucosa, asymptomatic and symptomatic lesions such as erosions and ulcers, and complications of ulcers including bleeding and perforation. Despite the fact that these gastrointestinal side effects are dosage dependent, even low doses of aspirin are increasingly being recognised as a cause of gastrointestinal haemorrhage [24].

In the present study, out of 160 cases, 5 ADRs (table 7) were reported out of which 3 were associated with aspirin, 2 were associated with clopidogrel. Two probable(dyspepsia and GI ulcer) and 1 possible(bronchospasm) adverse reactions due to aspirin were observed. Aspirin induced bronchospasm was observed in a diabetic patient with alcohol abuse. Aspirin induced dyspepsia was observed in a 63 years old female patient with history of smoking. Aspirin induced GI ulcer was also observed in patient with contributing factor found to be its interaction with ramipril. Clopidogrel induced diarrhoea was assesed to be probable adverse reaction with contributing factors(age, hypertensive, alcoholic). Clopidogrel induced rash was assesed to be possible adverse reaction with no contributing factors. In a previous study by Muneeshwar et.al, 4 adverse reactions associated with aspirin were observed i.e; aspirin induced nephrotoxicity, GI irritation and epistatis(probable) and aspirin induced epigastric pain(possible) [16].

The Naranjo method was modified in this study to use the drug combination as the suspect drug. The system calculates a score based on the answers to ten objective questions. Finally, a classification is assigned based on the score attained, in which less than or equal to zero means that the event is doubtful; from 1 to 4, possible; from 5 to 8, the adverse event is categorized as probable; and, if equal to or greater than 9, as defined [25].

In this study 35 probable drug –drug interactions were found 27, 4, 4 moderate, minor, serious interactions respectively. In this study most frequent interacting pair were identified as aspirin–clopidogrel followed by clopidogrel–pantoprazole. Aspirin and clopidogrel DAPT has benefit over its risk, which is a pharmacodynamic interaction. The most often interacting pair in this analysis was aspirin and clopidogrel, which was linked to an increased risk of bleeding; however, they may be taken together in some individuals to avoid thromboembolism. It can create an extensive health risk to the patients when the risk – benefit ratio of combining interacting drugs isn't always correctly anticipated [26]. Proton pump inhibitors inhibit CYP2C19 enzyme that might cause therapeutic impotency of clopidogrel as enzyme is needed for its bio-activation. However, proton pump inhibitors are suggested in patients at high risk for gastrointestinal bleed, such as those taking dual antiplatelet regimen with aspirin and clopidogrel [27].

Asprin+enalapril serious drug-drug interaction found in the study pharmacodynamic antagonism as aspirin decreases prostaglandin synthesis and co-administration may result in decrease in renal function. Aspirin+furosemide may decrease serum potassium, [aspirin+enoxaparin] and [heparin+ aspirin] both may increase anticoagulation. [aspirin+spironolactone], [aspirin+metoprolol], [aspirin+glimepride], [clopidogrel+enoxaparin], [clopidogrel+heparin] were other moderate interactions found in the study.

This interaction at the level of renal tubular secretion can also diminish the excretion of glimepiride, leading to hypoglycemia. As a result, if an interaction is suspected, glimepiride dosage may need to be adjusted. The signs and symptoms of hypoglycemia should be explained to patients.

Drug-drug interactions are predictable and preventable. whereas the consequences of moderate interactions ought to be noted, these rarely cause grievous complications. However, in case of severe interactions necessary measures are required to prevent harm [28].

Patients with Chronic Kidney Disease (CKD) are at increased risk of major cardiovascular diseases (CVD) such as myocardial infarction, stroke, and PVD. Patients with CKD tend to have an atherothrombotic predisposition yet are also prone to bleeding complications. In this study, out of 160 participants one patient with known CKD and CAD was observed to be overdosed with aspirin. Low dose of aspirin or other antiplatelet agents such as clopidogrel, prasugrel can be utilized.

Conclusion

The current study concludes that dual anti platelet therapy[Aspirin + Clopidogrel] was observed to be superior to single antiplatelet treatment monotherapy, and incidence of IHD which is more common in males compared to females. Patients in the age group 51-70 were most affected with stroke, IHD, and with female pre-dominance.

Antiplatelet therapy which is clearly efficacious in reducing the incidence of ischemic events/ thromboembolic events. DAPT therapy [aspirin & clopidogrel] was most commonly prescribed therapies in cardiovascular medicine because Dual antiplatelet therapy (DAPT) was found to be superior when compared with antiplatelet monotherapy. DAPT was most effective in reducing ischemic events, yet have the risk of bleeding complications or resistance. Thus DAPT should be reassessed for the patients with recurrent bleeding risk. The newer P2Y12 inhibitors such as Prasugrel,Ticagrelor,etc can be utilised with necessary precautions. Further additional studies are required for the balance of ischemic and bleeding risks associated with antiplatelet therapy. Till then physicians should follow a evidence based approach with an ongoing risk–benefit assessment or standardized approach. In this study the probable drug - drug interactions are associated with old age and number of medications given, clinical pharmacist a must play a role in understanding possible drug-drug interactions, detection and prevention of associated morbidity.

Abbreviations

DUE: Drug utilisation evaluation.
CAD: Coronary artery disease.
CVD: Cardiovascular disease.
TIA: Transient ischaemic attack.
ACS: Acute coronary syndromes.
IHD: Ischemic heart disease.
CHF: Congestive heart failure.
PAD: Peripheral arterial disease.
DVT: Deep vein thrombosis.
LRTI: Lower respiratory tract infections.
CKD: Chronic kidney disease.
COPD: Chronic obstructive pulmonary disease.
PCI: Percutaneous coronary intervention
AMI: Acute myocardial infraction.
STEMI: ST-segment-elevation myocardial infarction
NSTEMI:Non-ST-segment-elevation myocardial infarction
DAPT: Dual antiplatelet therapy.
MINOCA: myocardial infarction with no obstructive coronary arteries.
INOCA: ischemia and no obstructive coronary artery disease.
MVR: mitral valve replacement.
DVT: deep vein thrombosis.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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