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TO STUDY THE DRUG UTILIZATION EVALUATION OF ANTIPLATELET AGENTS IN CARDIOVASCULAR DISEASE IN A TERTIARY CARE TEACHING HOSPITAL

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ABSTRACT

Background: Cardiovascular diseases (CVDs) are a leading cause of morbidity and mortality. Antiplatelet agents help prevent thrombotic events by inhibiting platelet aggregation and are central to CVD management. Drug Utilization Evaluation (DUE) ensures appropriate prescribing practices and optimises therapeutic outcomes. **Objective:** To identify and evaluate the utilisation of antiplatelet agents in hospitalised CVD patients. **Methodology:** A prospective observational study was conducted over six months in a tertiary care teaching hospital. Ethical clearance was obtained from the Institutional Ethical Committee of SCS College of Pharmacy, Harapanahalli. Data from 207 inpatients from the Medicine and CICU departments were analysed using MS Office, Micromedex, and Medscape interaction checker. **Results:** Of 207 patients, 54.11% were male and 45.89% female. STEMI (32.85%) and NSTEMI (21.74%) were the most common indications for antiplatelet therapy. Hypertension was the most frequent comorbidity (35.27%). Aspirin was the most prescribed antiplatelet (97.58%), followed by clopidogrel and ticagrelor. Dual antiplatelet therapy (DAPT) was more common (79.23%) than monotherapy (19.80%) or triple therapy (0.97%). Most drug interactions were moderate (61.35%), followed by major (17.29%) and minor (21.36%). Antiplatelet prescriptions were rational in 99.19% of cases, in line with the WHO Model List of Essential Medicines (2023). **Conclusion:** The study emphasises rational use of antiplatelet agents in CVD management. Aspirin was most commonly prescribed, and DAPT was favoured due to its clinical benefits. Despite potential

interactions, aspirin-clopidogrel combinations remain widely used due to their favourable benefit-to-risk ratio.

KEYWORDS: *Cardiovascular Disease; Drug Utilization Evaluation; Antiplatelet Agents; WHO Model List of Essential Medicines 2023.*

INTRODUCTION

Cardiovascular diseases are a group of disorders affecting the heart and blood vessels, and some of they include Hypertension, Atherosclerosis, Angina Pectoris, Myocardial Infarction, Coronary heart disease, Cerebrovascular disease, etc.[1] Cardiovascular diseases are the leading condition to cause high mortality and morbidity.[2] According to the Global Burden of Disease study, it is estimated that nearly one-fourth of all the deaths in India occurred because of CVDs.[3]

Among all the CVDs, ischemic heart disease like angina pectoris and myocardial infarction, is the world's major health problem.[4] Platelets have a major role in arterial thrombosis, which is the final event complicating cardiovascular diseases. Antiplatelet agents are drugs that reduce the ability of platelets to engage in thrombus formation.[5] Antiplatelet treatment is a cornerstone of managing patients with cardiovascular disease.[6]

Aspirin, clopidogrel, Ticagrelor, dipyridamole, and the glycoprotein IIb/ IIIa receptor antagonists (abciximab and tirofiban) are antiplatelet drugs commonly used in India.

Aspirin

Aspirin (acetylsalicylic acid) reduces cardiovascular patients' risk of serious vascular events by about a quarter and is recommended as the first-line antiplatelet drug.

Mechanism of action: Aspirin irreversibly inhibits prostaglandin H synthase (cyclooxygenase-1) in platelets and megakaryocytes and thereby blocks the formation of thromboxane A2 (a potent vasoconstrictor and platelet aggregator).

Dose and Administration: Formulations of aspirin currently available in India include a 75mg and 150mg enteric-coated form as well as 300 mg and 325mg tablets. Aspirin is rapidly absorbed from the gastrointestinal tract and reaches peak plasma concentrations in 30–40 minutes.

Clopidogrel

Clopidogrel reduces the risk of serious vascular events among high-risk patients by about 10% compared with aspirin.

Mechanism of action: Clopidogrel is metabolised in the liver to active compounds that covalently bind to the adenosine diphosphate (ADP) receptor on platelets and dramatically reduce platelet activation.

Dose and administration: An oral loading dose of 300– 600 mg clopidogrel produces detectable inhibition of adenosine phosphate-induced platelet aggregation after 2 hours, which becomes maximal after 6 hours. If a loading dose of clopidogrel is not used, repeated daily oral doses of 75 mg of clopidogrel are required to achieve a steady-state maximal platelet inhibition.

Ticagrelor

Ticagrelor is an antiplatelet medication used in managing CVDs.

Mechanism of action: Ticagrelor is a direct-acting P2Y12 receptor antagonist; it works by reversibly binding to the P2Y12 receptor on the platelet membrane, preventing the binding of adenosine diphosphate, thereby inhibiting platelet activation and aggregation.

Dose and administration: An oral dose of 180mg should be administered as soon as possible after diagnosis, followed by a maintenance dose of 90mg orally twice daily after 12h from the administration of the loading dose. Ticagrelor is usually given in combination with low-dose aspirin.

Cardiovascular diseases are severe conditions in which multiple antiplatelet and other drugs are used among cardiac patients with co-morbidities, which leads to polypharmacy and other drug-related problems like drug-drug interactions.[7]

DUE plays an important role in modernized clinical settings. Drug utilization evaluation, according to the WHO, is an ongoing, systematic, criterion-based program of medicine evaluation that aids in applicability. DUE improves medication use by 1. Promoting optimal medication therapy. 2. Preventing medication-related problems. 3. Rational use of drugs and management of cardiovascular risk factors.[8] The current study was undertaken to evaluate the drug use pattern of antiplatelet agents and to study the prescribing pattern, observe co-

morbid conditions, social habits [alcohol/smoking], and drug-drug interactions associated with antiplatelet agents.[9]

MATERIALS AND METHODS

STUDY SITE

Chigateri District Hospital (tertiary care teaching hospital), Davangere.

STUDY DESIGN

Prospective observational study.

STUDY DURATION

The study was conducted for six months.

PROPOSED SAMPLE SIZE

The study was conducted on 207 patients admitted to the medicine and cardiac intensive care department of the tertiary care teaching hospital.

SOURCE OF DATA

- Data was collected from case sheets of patients admitted to the medicine and cardiac intensive care departments of the tertiary care teaching hospital.
- The data collection form is designed as per the project.

STUDY CRITERIA

The study was carried out by considering the following inclusion and exclusion criteria.

INCLUSION CRITERIA

- Patients of either gender.
- Cases with comorbid conditions.
- Patients admitted for more than 2 days.
- In-patients admitted to the medicine and cardiac intensive care department.
- Newly detected and known cases of cardiovascular diseases.

EXCLUSION CRITERIA

- Pregnant and lactating women.
- Pediatric patients.
- Out-patient department.

- Patients with insufficient data

ETHICAL CONSIDERATION

The ethical approval for the study was obtained from the Institutional Ethical Committee of S.C.S College of Pharmacy. The IEC approval is attached with the thesis copy as Annexure - 1.

MATERIALS USED

- Patient's case sheets
- Journal article.
- Data collection form
- Laboratory investigation report.
- MS Office.
- Micromedex and Medscape interaction checker.

RESULTS

1. GENDER-WISE DISTRIBUTION OF THE STUDY POPULATION

Out of 207 patients involved in the study population, the percentage of males was 54.11% (112) compared to females 45.89% (95).

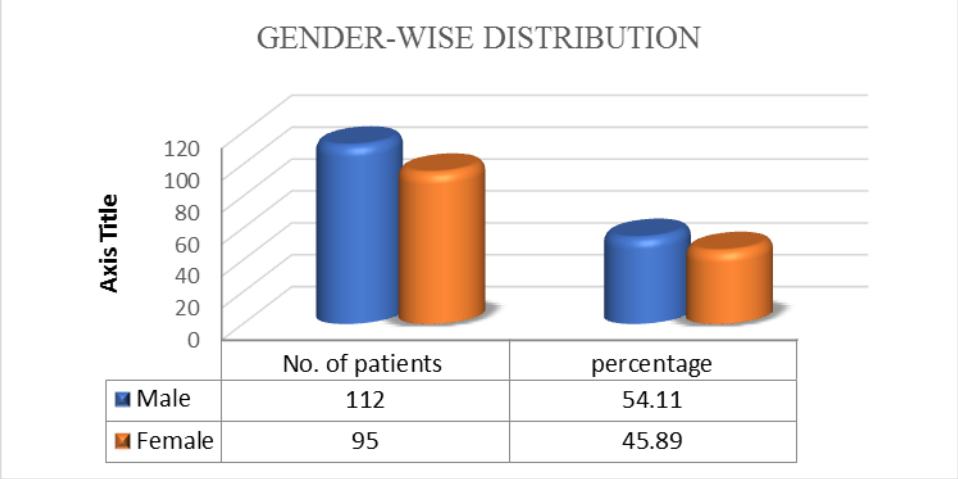

Figure 1: gender-wise distribution of the study population.

2. AGE-WISE DISTRIBUTION OF THE STUDY POPULATION

Out of 207 cases, the patients are divided into seven categories according to their age. Patients who are aged between 61-70 have a higher incidence of cardiovascular diseases. A

total of 177 patients were above 50 years of age in that 95 were males and 82 were females, while 30 were below 50 years of age in that 17 were males and 13 were females.

Table 1: Age-wise distribution of the study population.

AGE GROUPS	NO. of PATIENTS	MALE	FEMALE	PERCENTAGE%
21-30	3	0	3	1.45
31-40	5	1	4	2.41
41-50	22	16	6	10.63
51-60	48	26	22	23.19
61-70	74	46	28	35.75
71-80	44	21	23	21.26
81-90	11	2	9	5.31

3. INDICATION BASED SEGREGATION

In the study population, the most common CVD treated with antiplatelet therapy was STEMI in 68 patients (32.85%) followed by NSTEMI in 45 (21.74%), IHD in 38(18.36%), LVF in 13(6.28%), A-fib in 11(5.31%), DCM in 11(5.31%), CVA in 7 (3.38%), CCF in 6 (2.90%), LBBB in 3(1.45%), SVT in 2(0.97%), TVD in 2(0.97%) and RBBB in 1 patient (0.48%).

Table 2: Indication based segregation.

SL NO.	INDICATION	NO. of PATIENTS	PERCENTAGE %
1	ST elevation MI	68	32.85
2	Non-ST elevation MI	45	21.74
3	Ischemic heart disease	38	18.36
4	Left Ventricular Failure	13	6.28
5	Atrial fibrillation	11	5.31
6	Dilated cardiomyopathy	11	5.31
7	Cerebro vascular accident	7	3.38
8	Congestive cardiac failure	6	2.90
9	Left bundle branch block	3	1.45
10	Supraventricular tachycardia	2	0.97
11	Triple vessel disease	2	0.97
12	Right bundle branch block	1	0.48

4. CO-MORBIDITIES

Among the study population, 73 patients had hypertension, 45 patients had both hypertension and TYPEII DM, 39 patients had TYPEII DM, 27 had LRTI, 8 had kidney diseases, 5 had hypothyroidism, 4 had epilepsy, and 3 had asthma and liver diseases.

Table 3: Co-morbidities.

SL. NO	COMORBIDITIES	NO. OF PATIENTS	PERCENTAGE %
1	Hypertension	73	35.27
2	Hypertension +TYPE II DM	45	21.74
3	TYPEII DM	39	18.84
4	LRTI	27	13.04
5	Kidney diseases	8	3.86
6	Hypothyroidism	5	2.42
7	Epilepsy	4	1.93
8	Asthma	3	1.45
9	Liver Diseases	3	1.45

5. SOCIAL HABITS

Out of 207 patient participants, 28 were found to be alcoholics, 28 were smokers, 26 were tobacco chewers, 14 were both smokers and alcoholics, and 1 was found to be both an alcoholic and tobacco chewer. Table 5.5 and Figure 5.5 represent the data distribution of social habits of the study population.

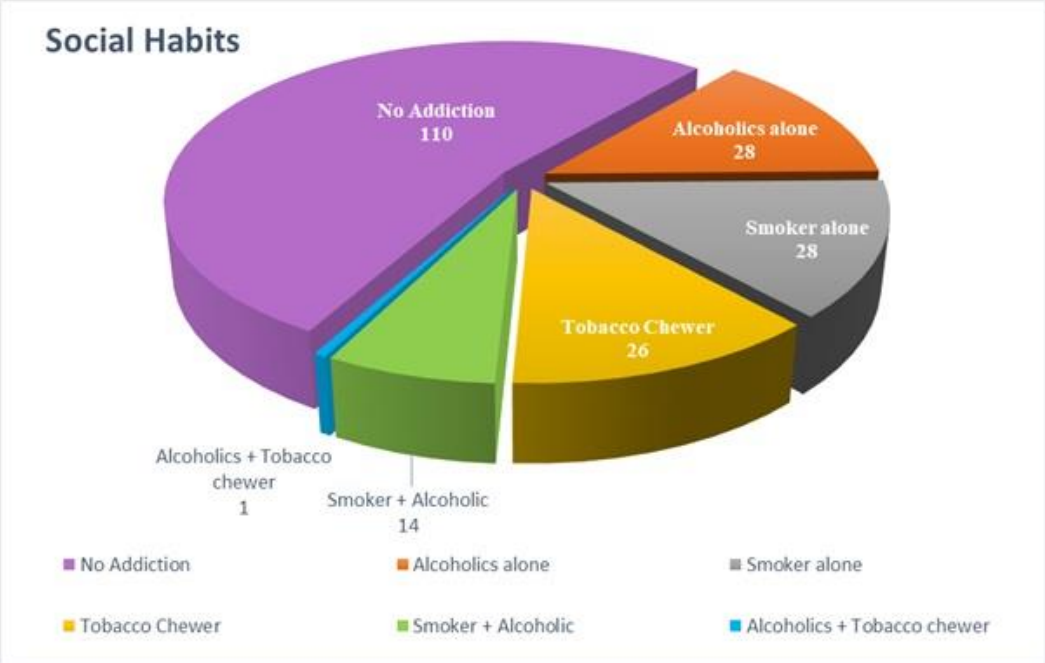

Figure 2: Social habits.

6. MOST PRESCRIBED ANTIPLATELET AGENTS

Among 207 patient participants in the study, aspirin frequency was found to be 202 [97.58%] which was the most used antiplatelet agent followed by clopidogrel in 165 [79.71%] and ticagrelor 3 [1.45%].

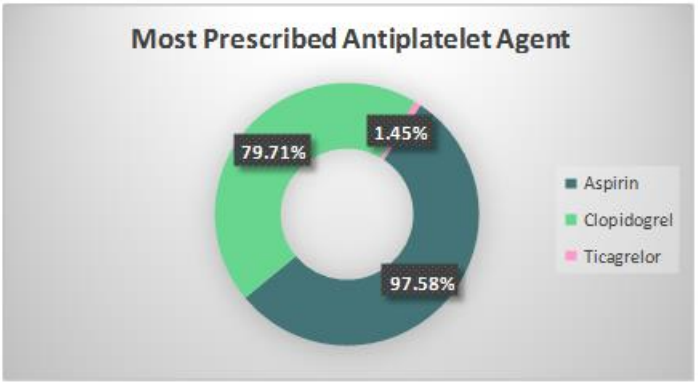

Figure 3: Most prescribed antiplatelet agent.

7. UTILIZATION PATTERN OF ANTIPLATELET AGENTS

In this study, the dual antiplatelet therapy was highest at 79.23% compared to single antiplatelet therapy at 19.80% and triple therapy at 0.97%. Data distribution of utilization of antiplatelet agents based on age group: 1 participant in the age group between 21-30 was using single antiplatelet therapy and 2 were using dual antiplatelet therapy 1 participant in the age group between 31-40 was using single antiplatelet therapy and 4 were using dual antiplatelet therapy, 5 participants in the age group between 41-50 were on single antiplatelet therapy and 17 were using dual antiplatelet therapy, 6 participants in the age group between 51-60 were under single antiplatelet therapy and 42 were under dual antiplatelet therapy, 16 participants in the age group between 61-70 were on single antiplatelet therapy, 56 were under dual antiplatelet therapy and 2 were on triple antiplatelet therapy, 9 participants in the age group between 71-80 years were found to be using single antiplatelet therapy and 35 were using dual antiplatelet therapy, 3 participants in the age group between 81-90 were on single antiplatelet therapy and 8 were using dual antiplatelet therapy.

Table 4: Utilization pattern of antiplatelet agents.

Age Group	No. of Patients	Single Antiplatelet Therapy	Dual Antiplatelet Therapy	Triple Antiplatelet Therapy
21-30	3	1	2	0
31-40	5	1	4	0
41-50	22	5	17	0
51-60	48	6	42	0
61-70	74	16	56	2
71-80	44	9	35	0
81-90	11	3	8	0
Total no. of patients (%)	207	41(19.80%)	164(79.23%)	2(0.97%)

8. PRESCRIBING PATTERNS OF DRUGS OTHER THAN ANTIPLATELET AGENTS

Many other drugs were prescribed with antiplatelet agents. They were also further classified into the basic classes: antibiotics, proton pump inhibitors, antihypertensives, Anti-diabetics, Anti-hyperlipidemics, etc. The highest number of drugs prescribed was from antibiotics (14.99%), followed by proton pump inhibitors (12.53%), Anti-hyperlipidemic (11.59%), etc.

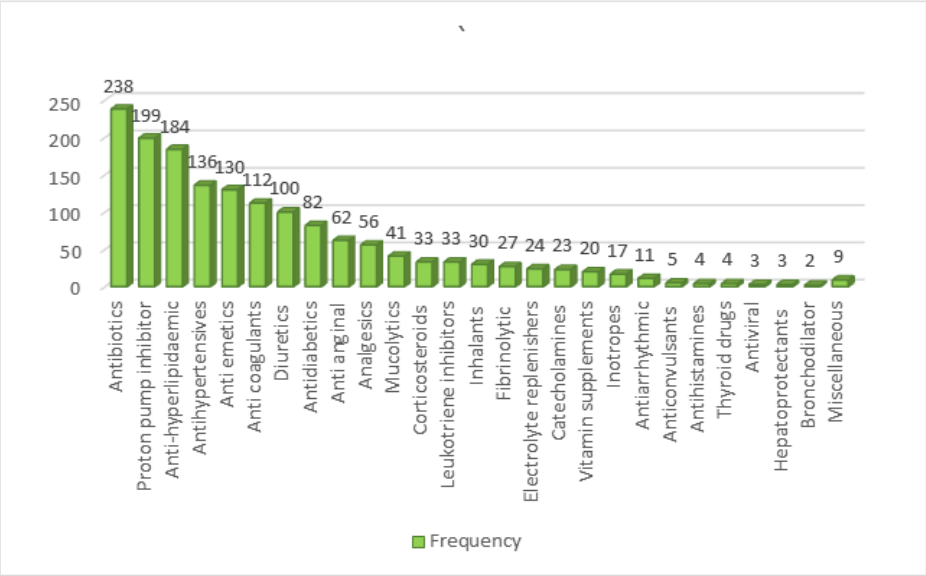

Figure 4: Prescribing patterns of drugs other than antiplatelet agents.

9.1 DRUG-DRUG INTERACTIONS ASSOCIATED WITH ANTIPLATELET AGENTS

In this study, based on severity probable drug-drug interactions were observed, out of which 17.29% were major followed by 61.35% were moderate and 21.36% were minor interactions

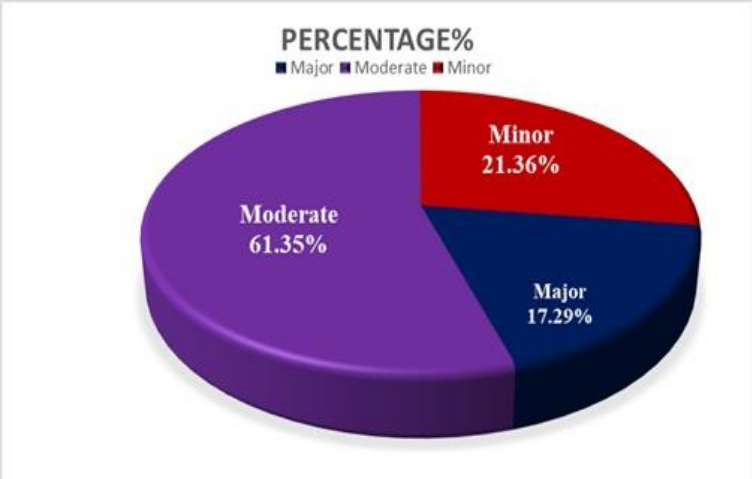

Figure 5.9.1: Frequency distribution for severity of drug-drug interaction.

9.2 FREQUENCY DISTRIBUTION OF DRUG-DRUG INTERACTION ASSOCIATED WITH ANTIPLATELET AGENTS

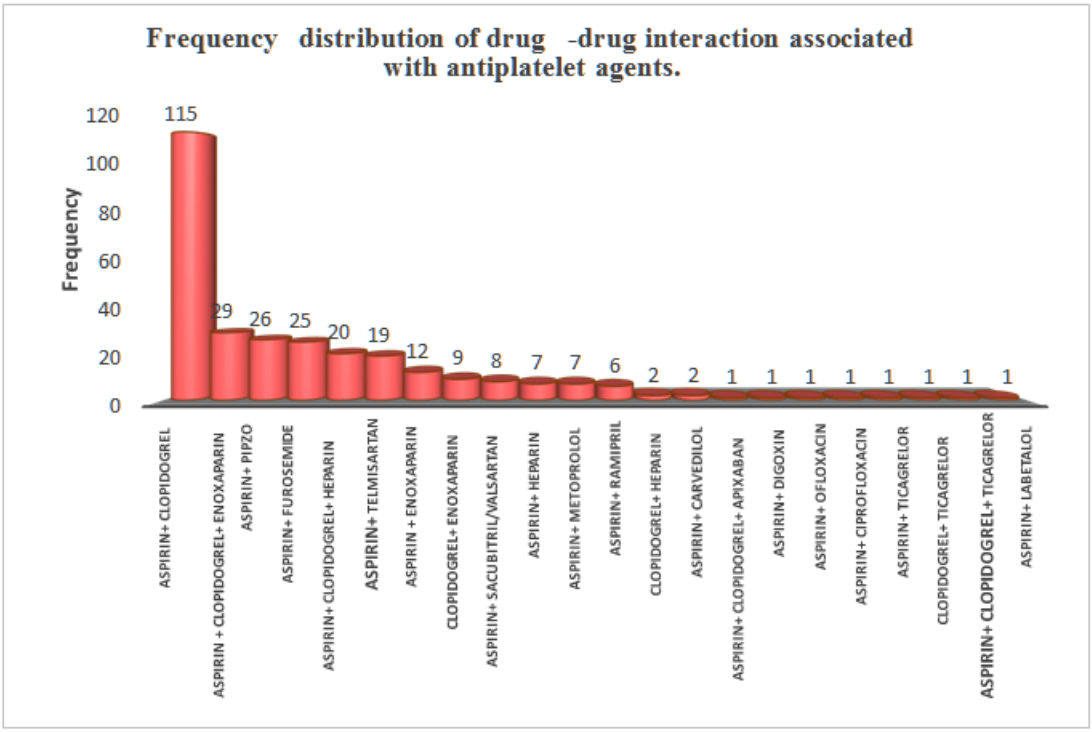

Figure 5.9.2: Frequency distribution of drug-drug interaction associated with antiplatelet agents.

10. ASSESSMENT OF WHO PRESCRIBING INDICATORS.

Table 5: Assessment of WHO prescribing indicators.

PARAMETERS ASSESSED	RESULT
Average no. of drugs per prescription	9.45
Percentage of antiplatelet agents prescribed by generic name	32.70%
Percentage of encounters with an antiplatelet agent	100%
Percentage of encounters with an antiplatelet injection	0%
Percentage of Antiplatelet agents prescribed from the WHO model list of essential medicines 2023	99.19%

DISCUSSION

Cardiovascular diseases are the leading cause of morbidity and mortality worldwide. By, 2030 almost a 23.6million people are estimated to die from CVDs. Evaluating the drug utilisation of antiplatelet drugs in cardiovascular patients helps us to understand the drug use pattern and rational use of the drug. It also helps to ensure the effectiveness of therapy given to patients. The current study was conducted to identify and evaluate the utilisation of antiplatelet agents in patients with cardiovascular diseases. In our study we analysed 207 patients diagnosed with CVDs who were prescribed antiplatelet agents during the study

period of 6 months, it has been observed that aspirin, clopidogrel, and ticagrelor were the three antiplatelet drugs prescribed in our study population. Among the study population, the frequency of antiplatelet agent prescription in males (54.11%) was higher than in females (45.89%) in concordance with a study conducted by Pramod B et al.2 In the current study, the participants were categorised into seven groups based on their age groups being kept at an interval of 10 years, most of the patients prescribed with antiplatelet agents were in the age groups 51-60 years (23.19%) and 61-70 years (35.75%). Similarly, in a study conducted by Rishitha et al., 21 the risk of cardiovascular disease increases with age, as age is an independent risk factor for developing cardiovascular diseases. It is observed in our study population, that myocardial infarction has the highest incidence, in that STEMI has the highest incidence rate of 32.85% followed by NSTEMI at 21.74% followed by others (fig:6.3) in concordance with Hadia R et al.4 On the distribution of participants' data based on co-morbidities, it was found that hypertension was the most frequent co-morbidity associated with CVDs with a percentage of occurrence of about 35.27% of the study population, followed by participants having both hypertension and type-II DM (21.74%), type-II DM (18.84%), LRTI (13.04%), kidney diseases, hypothyroidism, epilepsy, asthma, and liver diseases. A higher incidence of hypertension in CVD patients was noted in a similar study conducted by Rishitha et al.21 The social history review of the study population revealed that the majority of the participants (53.14%) did not have any social habits, 13.53% of patients were "To study the drug utilization evaluation of antiplatelet agents in Cardiovascular Disease in a Tertiary Care Teaching Hospital" 48 Discussion smokers and alcoholics, and 12.56% of patients were tobacco chewers. A similar study was done by Emil G Rajesh et al., 15 where most of their study population was people without any social habits. Among our study population of 207 patients, the most prescribed antiplatelet agent was aspirin (97.58%) followed by clopidogrel (79.71%) and ticagrelor (1.45%), which was consistent with the study conducted by P. Divya Jyothi et al.3 Aspirin was the most prescribed antiplatelet agent because of its cost-effectiveness and wide availability (Doses-75mg and 150mg). The utilization of antiplatelets in our study shows that the patients prescribed dual antiplatelet therapy with aspirin and clopidogrel (79.23%) were more and has shown to be more beneficial compared to single antiplatelet therapy (19.80%) and triple antiplatelet therapy (0.97%). This result was similar to the study conducted by Hadia et al.4 In our study, the highest number of drugs prescribed other than antiplatelet agents were antibiotics (14.99%), followed by proton pump inhibitors (12.53%), Anti hyperlipidemic (11.59%), (Table 6.8). This result was in contrast to the study conducted by Dr. Dilipkumar A

A et al.20 Out of 207 prescriptions analysed, based on severity probable drug-drug interactions were observed, in that 17.29% were major, 61.35% were moderate and 21.36% were minor interactions. The majority of drug-drug interaction occurred due to dual antiplatelet therapy with aspirin and clopidogrel, this combination is prescribed as the benefits outweigh its risks in concordance with a study conducted by Pramod B et al.2 Among 207 prescriptions average number of drugs per prescription was found to be 9.45, despite exceeding WHO standards, it was justifiable as most of the drugs were prescribed for cardiovascular emergencies. Out of 370 antiplatelet drugs, the percentage of antiplatelet drugs prescribed by generic name was 32.70%. WHO highly recommends healthcare professionals to prescribe drugs in generic names, as branded drugs are costlier than generic drugs. However, in our study, antiplatelet agents (99.19%) were found to be prescribed rationally as of the drugs were prescribed from the WHO model list of essential medicines 2023.

CONCLUSION

This study focuses on the drug utilisation evaluation of antiplatelet agents in patients presenting with cardiovascular diseases in a tertiary care teaching hospital. Total 207 patients prescribed with various antiplatelet agents were enrolled in the study based on inclusion criteria. It was found that aspirin is the most prescribed antiplatelet agent in the study population followed by clopidogrel and the least prescribed drug was ticagrelor. The current study concludes that dual antiplatelet therapy is more beneficial than monotherapy or triple therapy, even though it presents with the risk of bleeding complications. It also came to our notice that in our study population, geriatric patients (61-70) were prescribed single, double, and triple antiplatelet therapies at similar rates, which highlights the significance of personalized treatment regimens for this category of patients, and we recommend healthcare professionals to take utmost care while prescribing. Out of the probable drug-drug interactions observed during the study, the most prevalent interacting pair was found to be aspirin and clopidogrel but this combination is being continued to be prescribed as the benefits outweigh its risk. This shows that a clinical pharmacist must play an important role in detecting, understanding, and preventing possible drug-drug interactions. This study shows that antiplatelet drugs are prescribed rationally in compliance with WHO prescribing standards, and most of them are prescribed from the WHO model list of essential medicines 2023.

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AUTHOR'S CONTRIBUTION

All the authors have contributed equally.

CONFLICT OF INTEREST

All authors declare that there are no conflicts of interest.

ETHICS DECLARATION

The Institutional Ethics Committee at SCS College of Pharmacy approved the protocol. All residents in the hospital provided informed consent.

CONSENT FOR PUBLICATION

All authors have consented to the publication of their work.

COMPETING INTERESTS

The authors hereby declare that they did not obtain any financial support from any source for the writing or publication of this article.

AUTHORS FUNDING

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