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Dual Antiplatelet Therapy (DAPT) Induced Gastrointestinal (GI) Bleeding Among Patients with Acute Coronary Syndrome (ACS) in A Tertiary Care Hospital



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**Anjali.R^{1*}, Sidhi Sunil², Haritha Rajmohan³,
Praveen Chacko⁴, Sherin Alexander⁵, Philip Jacob⁶**

*1-6th Year Pharm D student, Nazareth College Of
Pharmacy, Othara P.O, Thiruvalla, Kerala, India*

*2-6th Year Pharm D student, Nazareth College Of
Pharmacy, Nazareth College Of Pharmacy, Othara P.O,
Thiruvalla, Kerala, India*

*3-6th Year Pharm D student, Nazareth College Of
Pharmacy, Nazareth College Of Pharmacy, Othara P.O,
Thiruvalla, Kerala, India*

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Keywords: Dual Antiplatelet Therapy (DAPT); Gastrointestinal (GI) Bleeding; coronary artery disease (CAD); aspirin; clopidogrel.

ABSTRACT

Background: Dual antiplatelet therapy (DAPT) is the cornerstone of the treatment of acute coronary syndrome (CAD), ischemic stroke, and peripheral arterial disease (PAD). While preventing ischemic recurrences, inhibition of platelet function is related to an increased bleeding risk. However, they are associated with bleeding complications mainly gastrointestinal (GI) bleeding. The proportion of GI bleeding was estimated among acute coronary syndrome patients on dual antiplatelet therapy (DAPT). Methodology: This was a retrospective study of 6 months that analyzed 508 patients of a tertiary care hospital in Thiruvalla, who were under the cardiology department between January 2015 and December 2018, and those receiving dual antiplatelet therapy. Data were collected from medical records and analyzed using Microsoft Excel-2010. Results: Among the 508 cases, 9 cases of GI bleeding were observed during the follow-up period. Most of the bleeding was observed in the 70-89 age groups, 67% had GI bleeding. GI bleeding was found more in females (67%) than males (33%). The rate of GI bleeding was 1.8%. In this study, we found that 56% showed hematuria, 33% showed melena and 11% showed hematemesis. Conclusions: Age is a risk factor for DAPT induced GI bleeding. The high proportion of GI bleeding was among the older age group. Considering the gender, the proportion of gastrointestinal bleeding was found more among females. In this study, it was found that 1.8% of gastrointestinal bleeding in patients was due to DAPT. The prevalence of upper GI bleeding and lower GI bleeding are approximately similar.



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INTRODUCTION

Acute coronary syndrome (ACS) is a medical term that is used in patients in whom there is a suspect or confirmation of acute myocardial infarction or ischemia. Types of ACS include Non-ST-elevation myocardial infarction (NSTEMI), ST-elevation MI (STEMI), and unstable angina.^[1] Cardiovascular diseases (CVDs) are the number 1 cause of death globally, taking an estimated 17.9 million lives each year,^[2] accounting for one-third of all deaths worldwide. More than one-third of these deaths occur in middle-aged adults.^[3] The prevalence of CHD in rural India was estimated to be 3%–4% and 8%–10% in urban areas.^[4]

The platelet has a major role in the formation of atherothrombosis, involved in both the development and encroachment of atherosclerotic heart disease and the attendant acute thrombotic complications. Antiplatelet drugs interfere with platelet function and are useful in the prophylaxis of thromboembolic disorders.^[5] Dual antiplatelet therapy (DAPT) with aspirin and a potent P2Y₁₂ inhibitor is the cornerstone of therapy for patients with acute coronary syndromes (ACS) treated invasively with percutaneous coronary intervention (PCI).^[6] Antiplatelet therapy is effective in preventing vascular events both during short- and long-term treatment in patients with vascular disease, including after percutaneous coronary intervention (PCI) with or without stenting.^[7,8]

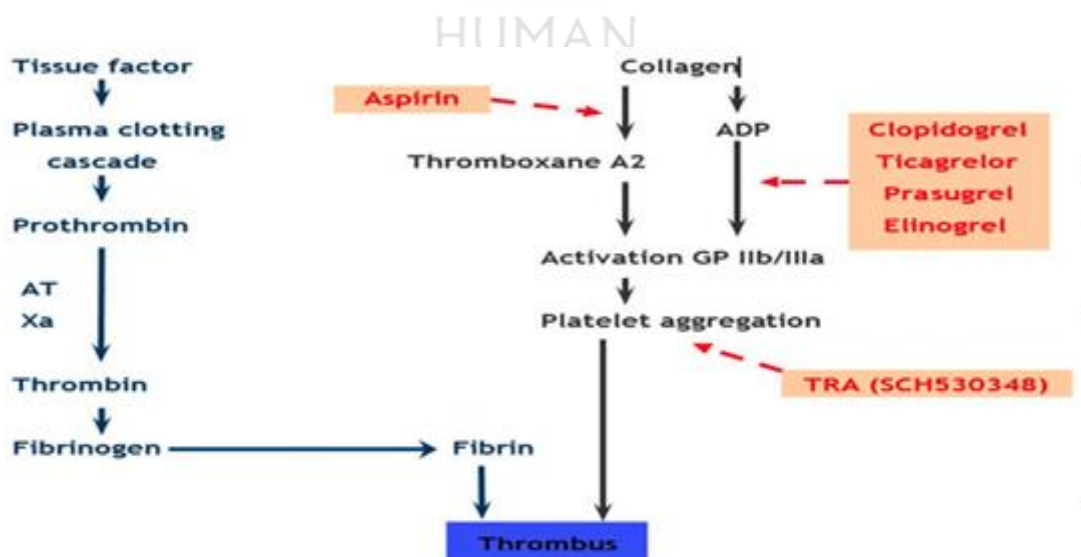


Figure No.1: Mechanism of dual antiplatelet drugs ^[9]

TRA: Thrombin receptor antagonist, GP: Glycoprotein, Xa: Xa factor, ADP: Adenosine diphosphate.

Treatment with both aspirin and clopidogrel

Clopidogrel administration was associated with a 20% relative risk reduction of a composite endpoint of cardiovascular death, nonfatal MI, or stroke compared with placebo. There was more major GI bleeds in the clopidogrel plus aspirin compared with aspirin alone (75–325 mg/day). In patients who are high-risk ACS, 1 year of therapy with aspirin plus clopidogrel results in considerably more life expectancy than aspirin alone. Patients treated with combined therapy experienced a non-significant trend toward an increase in major bleeding. In contrast, when aspirin is added in patients taking clopidogrel, the larger increase in UGI bleeds can be attributed to the deleterious effects of aspirin on the GI mucosa in addition to dual platelet inhibition.^[7]

The benefits of DAPT are counterbalanced by the increased incidence of GI complications. The risk of overt GI bleeding with DAPT can be as high as 1.3% within the first 30 days of treatment. The mechanisms of the ability of aspirin to induce GI bleeding involve the inhibition of gastroduodenal prostaglandin synthesis and it is raised with increasing doses of aspirin. The mechanism behind the action of clopidogrel in the GI endothelium is unclear.^[10]

However, antiplatelet therapy is associated with gastrointestinal bleeding has been reported as one of the most common causes of life-threatening complications.^[11] In this study, the objective was to estimate the proportion of gastrointestinal bleeding among acute coronary syndrome patients on dual antiplatelet therapy (DAPT).

METHODOLOGY

Study design:

The retrospective observational study was carried out for 6 months (November 2019 to April 2020) in the cardiology department of Believers Church Medical College Hospital (BCMCH), Thiruvalla. According to the standard statistical formula the sample size was calculated as 500. The sample size has been calculated by the formula:

$$n=4PQ/d^2$$

(n = Sample size, P = Prevalence, Q = 100- P, d = Effective size).

Ethics approval and consent to participate:

This study was approved by the Institutional Human Ethics Committee (IEC STUDY NO. IEC/2020/04/135). The written consent was taken from the participants.

Inclusion criteria:

1. Age above 18yrs.
2. Patients under Dual-anti platelet therapy.
3. Patients who were on regular follow-up.

Exclusion criteria:

1. Patients previously diagnosed with GI disorder.
2. Patients with anticoagulant therapy.
3. Patients who have any hepatic dysfunction.

Study variables:

- Demographic profile: Name, Age, Gender, Date of prescription
- All details regarding diagnosis, comorbidities.
- Details of Prescription: Brand/Generic name, Dosage, Route, Frequency, and Duration.

Data collection tool:

A pre-designed validated data collection form was used.

Data collection procedure:

All patients who satisfied the study criteria were enrolled in the study. The required data were retrieved and entered into the pre-designed data collection proforma. Patients were assessed for any symptoms of GI bleeding, or any gastroenterology consultations and endoscopy.

Data analysis:

The data collected were entered in the Microsoft Excel-2010 version and statistically analyzed. Results were presented in tabular form as well as frequency and percentages.

RESULTS

1. AGE DISTRIBUTION

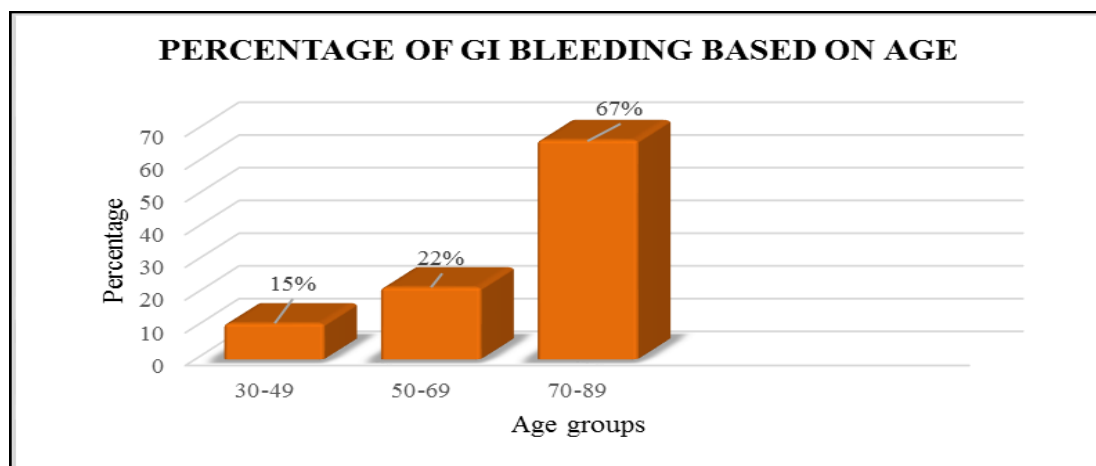


Figure No.2: Percentage of GI bleeding based on age group

Among the 508 study population, the 30-49 age group was around 15% subjects, 40% subjects were supposed to be in the 50-69 age group, and 45% belonged to the 70-89 age group. In the 30-49 age group 11% had GI bleeding, in the 50-69 age group 22% had GI bleeding and in the 70-89 age group 67% was found to have GI bleeding. It was noticeably higher than other groups.

2. GENDER DISTRIBUTION

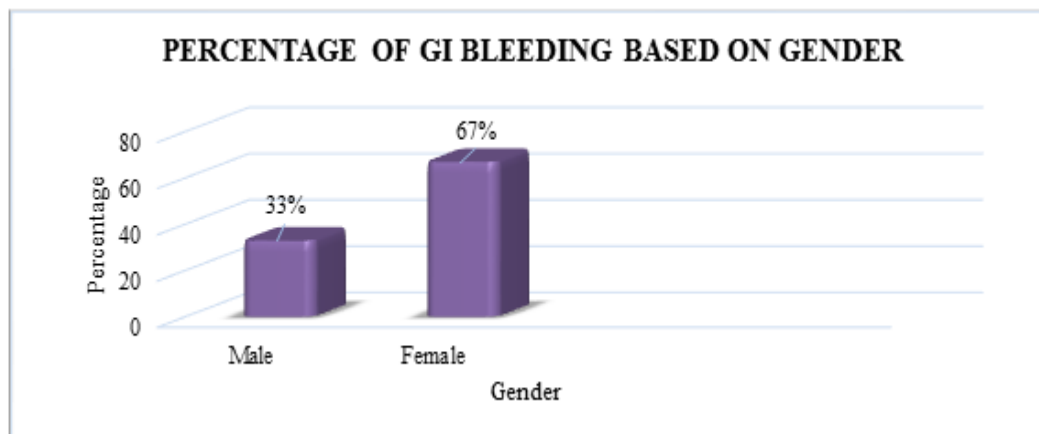


Figure No.3: Percentage of GI bleeding based on gender

Depicts the distribution of patients based on gender. 74% of subjects were males as well as 26% were females. GI bleeding was found more in females (67%) rather than males (33%).

3. PERCENTAGE OF DAPT INDUCED GI BLEEDING

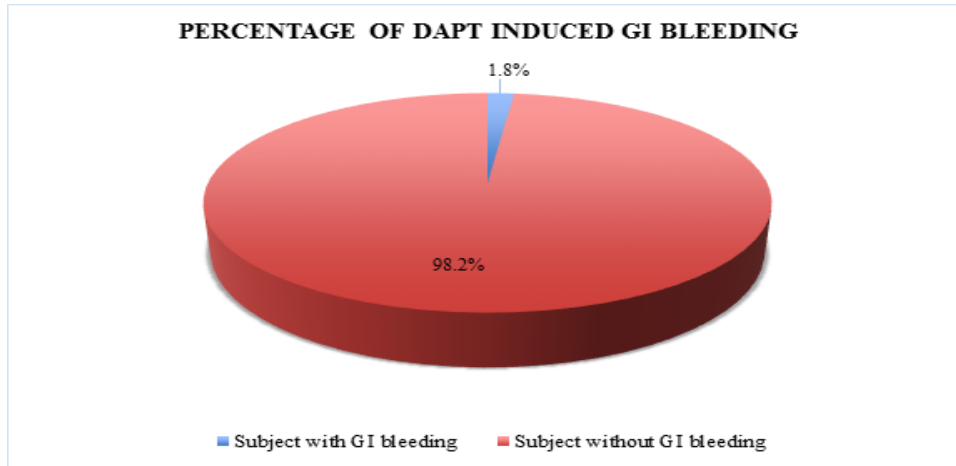


Figure No.4: Percentage of DAPT induced GI bleeding

9 cases of GI bleeding were observed and no GI bleeding was observed among 499 patients. 1.8% of subjects had GI bleeding and 98.2% couldn't have GI bleeding.

4. PERCENTAGE OF SYMPTOMS OF GI BLEEDING

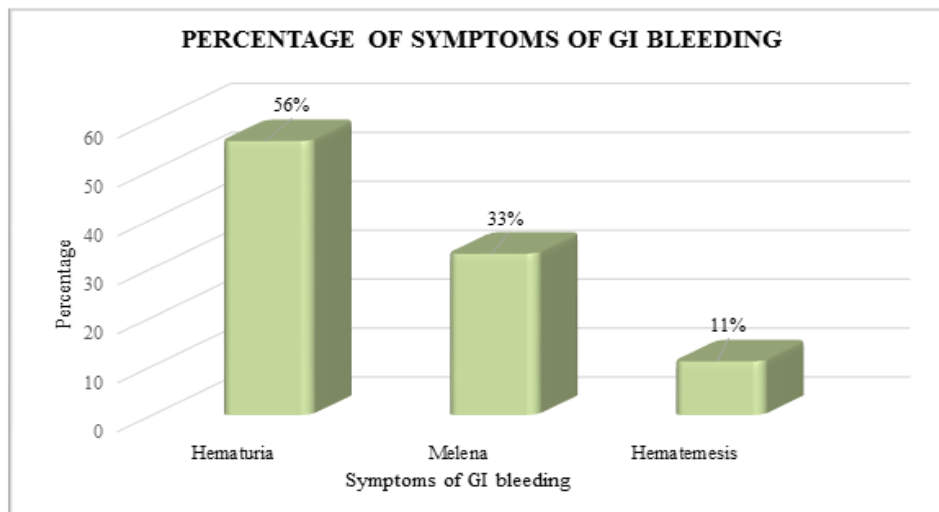


Figure No.5: Percentage of symptoms of GI bleeding

In this graph, 56% showed hematuria, 33% showed melena and 11% showed hematemesis.

DISCUSSION

The objective of the study was to assess the proportion of dual antiplatelet therapy (DAPT) induced gastrointestinal bleeding. The study population consisted of 508 samples. The study was a hospital-based retrospective observational study. The data of patients were collected from November 2019 to April 2020 in the department of cardiology of BCMCH and then the data was entered into a predesigned data collection proforma.

Age-wise distribution among 508 total patients based on the DAPT use, DAPT induced GI bleeding cases were analyzed and found that the majority of the subjects were among 70- 89 years (227 subjects) where 6 subjects had GI bleeding. A study conducted by **L C.Joyce et.al.**, show that patients ≥ 75 years of age had an increased risk for major adverse cardiac events and bleeding compared with younger patients.

The GI bleeding was more in females (6 subjects out of 9) than males (3 subjects out of 9). Females are exposed to a greater risk of bleeding compared to men due to gender-related differences in anatomy and physiology.^[12] A study by **K. Grodecki et.al.** focuses on long-term bleeding events after hospital discharge. In their study, 13,727 ACS patients treated with PCI and discharged on DAPT were included in their sub-analysis of the BleeMACS database. Post-discharge bleeding was reported more commonly in females as compared with males (3.7% vs. 2.7%) Bleeding events occur more frequently in women, but the female sex itself was not an independent predictor of post-discharge major bleedings. The administration of newer antiplatelet agents was identified as an independent risk factor of bleeding after hospital discharge in females, but not in male patients. They suggest that females are more prone to suffer from bleeding complications rather due to less favorable baseline characteristics than true differences in physiology related to gender. Moreover, a significant increase in bleeding rates among women legitimizes further research on differences among specific groups of patients to determine potential targets for future tailored antiplatelet therapies.^[13]

In this study, 9 subjects among 508 patients had GI bleeding which was 1.8%. In a similar study By **H. Yasuda et.al.**, 8 cases of GI bleeding were observed among 243 patients which was 3%.^[14] In another study by **N.V. Deshpande et.al.**, Overall GI bleeding is estimated to occur in 1.2–2.4% of patients undergoing coronary interventions.^[15]

In this study, we found that 56% shows hematuria, 33% shows melena and 11% shows hematemesis. The prevalence of upper GI bleeding and lower GI bleeding are approximately similar. In a similar study conducted by **Shaukat A et.al.**, patients presenting with GIB while on DAPT, the prevalence of UGIB and LGIB is similar to those who are not on DAPT and the overall prevalence of UGIB is not significantly higher than that of LGIB. Patients on DAPT have a significantly higher likelihood of bleeding from upper GI inflammation.^[16]

CONCLUSION

Gastrointestinal bleeding remains a concern while prescribing dual antiplatelet drugs. From our study, it was found that the percentage of gastrointestinal bleeding in patients due to DAPT was 1.8%. While considering the age distribution, the high proportion of GI bleeding was among older age groups. Considering the gender, the proportion of gastrointestinal bleeding was found more among females. Legitimize further research on gender-specific distribution is required to determine the possible targets for future tailored dual antiplatelet therapies. The prevalence of upper GI bleeding and lower GI bleeding are approximately similar.

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