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Study on Heparin-Induced Thrombocytopenia and Blood Group among Individuals Suffering from Acute Coronary Syndrome

Dr. Mugni Sunny[1*], Dr. Kamrunnahar[2]

[1]Associate Professor (Current Charge), Department of Cardiology, Northeast Medical College, Sylhet
[2]Consultant Microbiology and Virology, Sheikh Fazilatunnessa Mujib Memorial KPJ Specialized Hospital and Nursing College, Gazipur

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***Corresponding author:** Dr. Mugni Sunny
Associate Professor (Current Charge), Department of Cardiology, Northeast Medical College, Sylhet

Abstract

Background: Clinicians confront heparin-induced thrombocytopenia (HIT) as the most pertinent pathological relationship. Antibodies directed against complexes of heparin molecules and platelet factor 4 (PF4) are the cause of this immune-mediated phenomena. HIT is a significant adverse event that affects individuals with acute coronary syndromes (ACS). ***Objective:*** To assess the frequency of HIT in patients presenting with ACS. ***Materials and Methods:*** This study was carried out the Northeast Medical College's Department of Cardiology in Sylhet from June 2021 to December 2022. A total of 234 individuals aged 40 to 70 years old presented with ACS within 24 hours of symptom onset. This study excluded patients with idiopathic thrombocytopenic purpura (ITP), aplastic anemia, myeloproliferative diseases, or pre-existing thrombocytopenia. Thrombocytopenia was evaluated using medical records and a full blood count (CBC), with isolated thrombocytopenia (platelets <150 x109/L) prior to heparin administration. ***Results:*** Diabetes mellitus, hypertension, a history of ACS, and obesity were the most frequent comorbidities, accounting for 41.03%, 33.76%, 43.16%, and 14.96%, respectively. The incidence of HIT in NSTEMI and STEMI was higher than in unstable angina, although still comparable. The delayed presentation of ACS > 12 hours was also strongly correlated with the occurrence of HIT ($p<0.05$). Unstable angina and middle age (50–60 years) were found to have a significant relationship with HIT ($p<0.05$). ***Conclusion:*** HIT is more common in patients who have had a myocardial infarction or who have had symptoms for more than 12 hours at the time of hospitalization. Cardiologists and internal medicine experts must take extra precautions when administering heparin to high-risk patients to prevent problems.

Keyword: Myocardial infarction, Acute coronary syndrome, heparin-induced thrombocytopenia (HIT).

INTRODUCTION

Acute coronary syndrome (ACS), by definition, is the pathological rupture of an atherosclerotic plaque within the coronary artery endothelium, resulting in partial or complete thrombosis of the artery and subsequent infarction of the cardiac muscle. On electrocardiography (ECG), it may present as ST-segment elevation (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI), or unstable angina (UA) [1].

Heparin-induced thrombocytopenia (HIT) is a prothrombotic condition produced by antibodies that detect PF4-heparin complexes. HIT is widely used in the differential diagnosis of thrombocytopenia in individuals on heparin treatment [2].

Its use can cause a life-threatening prothrombotic reaction, leading to amputations or fatal consequences annually [3]. HIT has been estimated to occur in approximately 1%–5% of patients receiving therapeutic doses of heparin. Additionally, it has been observed that up to 1 in 1,500 hospitalized patients may suffer from HIT [4, 5].

HIT caused by UFH is approximately 10-fold higher than that caused by LMWHs. HIT is an immune-mediated reaction caused by the formation of antibodies against the complex of platelet factor 4 (PF4) and heparin. These antibodies can activate platelets to a hypercoagulable state, which resulted in thrombocytopenia and increased the risk of venous and arterial thrombosis [6].

Heparin is an anticoagulant that has been used extensively in a variety of clinical contexts, including thromboprophylaxis and thromboembolism therapy.[7]Heparin-induced thrombocytopenia (HIT) is an uncommon medical disorder that bears a high risk of mortality and serious consequences if left undiagnosed. Low molecular weight heparin has a comparatively lower incidence of HIT. Multi-vessel coronary artery thrombosis caused by HIT is uncommon, and HIT is more common in the venous system than the arterial circulatory system [7].

This study aims to evaluate the prevalence of HIT in individuals who arrive with ACS. In HIT, thrombosis that already exists worsens or develops in previously unaffected vascular areas. Sometimes the real goal of treatment is to quit using heparin, but in order to counteract these thrombotic episodes; heparin is continued or dosed up. Because of this unusual characteristic, the cardiologist must exercise extreme caution while giving heparin to a patient who has ACS.

MATERIALS AND METHODS

This study was conducted at the Department of Cardiology, Northeast Medical College, Sylhet, from June 2021-December'2022. Total 234 patients aged between ≥40 and ≤70 years presenting with ACS within 24 hours of onset of symptoms. Patients with idiopathic thrombocytopenic purpura (ITP), aplastic anemia, myeloproliferative disorders, and pre-existing thrombocytopenia were excluded in this study. Thrombocytopenia was assessed through medical records and by complete blood count (CBC), having isolated thrombocytopenia (platelet <150 x109/L) before heparin therapy. Patients who were lost to follow-up - either transferred to another hospital or died during the hospital stay - were also excluded. During the study period, firstly we included 385 patients with ACS were admitted in the cardiology unit. Forty-nine patients already had a duration of symptoms more than 24 hours when presenting (either delayed presentation or referred from another hospital). Another 67 patients were excluded due to either of the above-mentioned comorbidities. Out of the remaining 269 patients, 23 died during the hospital stay and 12 either left against medical advice or were transferred to another hospital by the family. Hence, 234 patients completed this study. The baseline platelet count before the initiation of heparin therapy was recorded. Low molecular weight heparin 5000 units stat and then 12 units/ kg/ hr, for 72 hours, intravenous were initiated. On Day 5, blood samples were repeated for platelet count. Thrombocytopenia was labeled as platelet <150x109/L, as recommended by ACC [7]. Data were analyzed using SPSS for Windows version 25.0 (IBM Corp, Armonk, NY, USA). Quantitative variables like age and platelet count were presented with mean and standard deviation (±SD). Gender and heparin-induced thrombocytopenia were presented with frequency and percentage. Data were stratified for gender (male/female), age (≥40 to ≤70 years), type of ACS, time of presentation of the ACS, and platelet count at presentation. Stratified groups were compared by using the chi-square test, taking p-value<0.05 as significant.

RESULTS

Table 1 shows, the majority of ACS patients were between the ages of 60 and 70, with 147 (62.82%), followed by 20.94% between the ages of 51 and 60, and 38 (16.24%) between 40 and 50. Female were predominant 133(57%) and male were found 101(43%) (Figure I). Table shows diabetes mellitus, hypertension, a history of ACS, and obesity were the most frequent comorbidities, accounting for 41.03%, 33.76%, 43.16%, and 14.96%, respectively (Table-2). The figure illustrates the types of patients with ACS: non-ST elevation MI 44 (19%), unstable angina 103 (44%), and ST elevation MI 87 (37%) (Figure II). The incidence of heparin-induced thrombocytopenia was found 31(13%) (Figure III). The incidence of HIT in NSTEMI and STEMI was higher than in unstable angina, although still comparable. The delayed presentation of ACS > 12 hours was also strongly correlated with the occurrence of HIT, with 20 (64.52%) in the HIT group and 85 (41.87%) in the non-HIT group (p<0.05). Unstable angina and middle age (50–60 years) were found to have a significant relationship with HIT (p<0.05). Gender and other types of ACS were not shown to be significantly correlated (Table-3).

Table 1: Distribution of patients ACS according to age in years (n=234)

Age in years	Number	Percentage
40-50 yr	38	16.24
51-60 yr	49	20.94
60-70 yr	147	62.82
Total	**234**	**100.00**

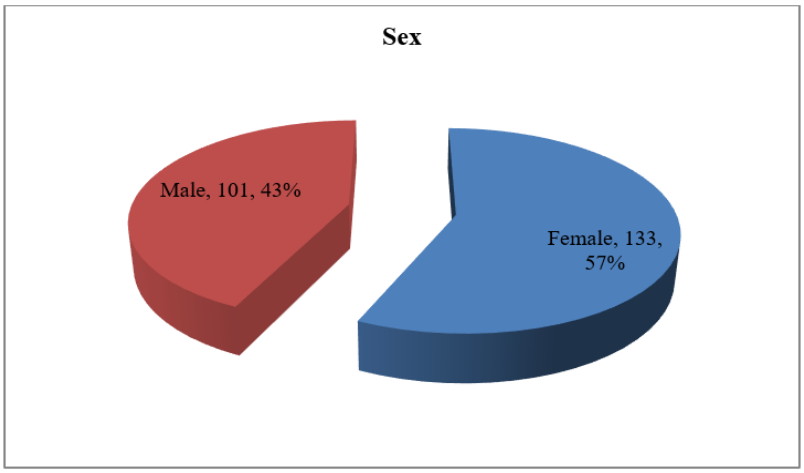

Figure I: Sex distribution of the ACS patients (n=234)

Table 2: Distribution of ACS patients according to Co-morbidities (N=234)

Co-morbidity	Number	Percentage
Diabetes mellitus	96	41.03
Hypertension	79	33.76
Previous history of ACS	101	43.16
Obesity	35	14.96
Chronic renal insufficiency	19	8.12

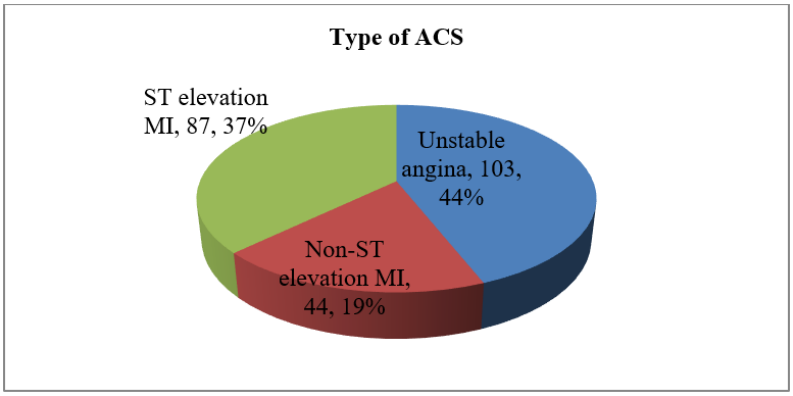

Figure II: Type of ACS of the study population (n=234)

Table 3: Comparison of demographic characteristics with ACS patients between Heparin-Induced Thrombocytopenia (n=234)

	Heparin-Induced Thrombocytopenia		Total	P value
	Yes=31	No=203		
Age in years				
40-50 yr	3 (9.68)	35 (17.24)	38	0.28
51-60 yr	12 (38.71)	37 (18.23)	49	0.009
60-70 yr	16 (51.61)	131 (64.53)	147	0.16
Sex				
Male	15 (48.39)	87 (42.86)	101	0.56
Female	17 (54.84)	116 (57.14)	133	0.81
Type of ACS				
Unstable angina	7 (22.58)	96 (47.29)	103	0.01
Non-ST elevation MI	12 (38.71)	32 (15.76)	44	0.47
ST elevation MI	12 (38.71)	75 (36.95)	87	0.85
Time of presentation of ACS				
1-12 hrs	11 (35.48)	118 (58.13)	131	0.01
>12 hr	20 (64.52)	85 (41.87)	103	0.01

DISCUSSION

Heparin-induced thrombocytopenia (HIT) is by far the most common pathological associated of heparin therapy seen by doctors. It is an immune-mediated phenomenon generated by antibodies that target heparin-platelet factor 4 (PF4) complexes. HIT is a major side effect of heparin therapy in ACS patients. If the diagnosis is missed, cardiologists may continue or even raise the dose of heparin to prevent thrombotic episodes, despite the fact that the proper care involves discontinuing heparin and replacing non-heparin anticoagulation medication.

In this study showed that the majority of ACS patients were between the ages of 60 and 70, with 147 (62.82%), followed by 20.94% between the ages of 51 and 60, and 38 (16.24%) between 40 and 50. Female were predominant 133(57%) and male were found 101(43%). Liu *et al.*, [8] reported that the median age of 43 patients (12 men and 31 women) with HIT in our study was 67 years, with an age range of 11–87 years. Kumar *et al.*, [1] also reported there were 134 (49.3%) men and 138 (50.7%) women. Their mean age was 58.49 ± 5.87 years.

Table shows diabetes mellitus, hypertension, a history of ACS, and obesity were the most frequent comorbidities, accounting for 41.03%, 33.76%, 43.16%, and 14.96%, respectively. Kumar *et al.*, [1] also reported common comorbidities were diabetes mellitus 38.9%, Hypertension (32.7%) and Previous history of ACS 41.9%. Liu *et al.*, [8] also reported that the common medical history in the patients with HIT was diabetes (10/43), obesity (6/43), hypertension (6/43).

The incidence of heparin-induced thrombocytopenia was found 31(13%). Kumar *et al.*, [1] reported there was a 9.5% incidence of HIT in this study, which was correlated with the type and delayed presentation of ACS. Varying incidence of HIT in ACS patients. Where some studies have reported HIT to be as low as only 0.3%, the incidence of HIT has also been reported to be as high as 13% [9, 10].

The incidence of HIT in NSTEMI and STEMI was higher than in unstable angina, although still comparable. The delayed presentation of ACS > 12 hours was also strongly correlated with the occurrence of HIT, with 20 (64.52%) in the HIT group and 85 (41.87%) in the non-HIT group ($p<0.05$). Unstable angina and middle age (50–60 years) were found to have a significant relationship with HIT ($p<0.05$). Gender and other types of ACS were not shown to be significantly correlated. Kumar *et al.*, [1]. The HIT incidence in STEMI and NSTEMI were equal but higher than that in unstable angina ($p<0.05$). The incidence of HIT was also significantly associated with the delayed presentation of ACS ($p<0.05$). Hypotension in these patients may also inhibit platelet production from bone marrow [11]. As evidenced by the CRUSADE trial (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the American Cardiology Council/American Heart Association Guidelines), 13% of NSTEMI patients experienced thrombocytopenia. Reduced platelet count in patients with ACS has been reported on a number of occasions. Thrombocytopenia was observed in 6.8% of ACS patients in the Acute Catheterization and Urgent Intervention Triage approach study (ACUITY trial) and 1.6% of STEMI/NSTEMI patients in the Global Registry of Acute Coronary Events (GRACE) experiment [9]. While bleeding is uncommon in these patients, [12] thromboembolic consequences such deep vein thrombosis (DVT) and pulmonary embolism (PE) are highly associated with HIT after it has started. These complications can be lethal for these patients. Postoperative patients are more likely to experience both DVT and PE, and having a central venous catheter increases the risk of upper-extremity venous thrombosis, an HIT consequence [13]. Arterial thrombosis is more common in ACS patients receiving heparin as compared to venous thrombosis. Thrombosis in patients with HIT has a 20%-30% mortality risk [14].

CONCLUSIONS

In patients with acute coronary syndrome, HIT is an important side effect of heparin therapy that should not be ignored. Patients experiencing myocardial infarction and those whose symptoms have persisted for longer than 12 hours at the time of hospital arrival are more likely to get HIT. To prevent complications when administering heparin therapy to high-risk patients, cardiologists and internal medicine specialists must take safeguards such as serial platelet count monitoring.

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