ASSOCIATION OF INCREASED FIBRINOLYSIS WITH FIBRINOGEN LEVELS AND PLATELET COUNT AFTER CORONARY ARTERY BYPASS GRAFTING

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ABSTRACT

Objective: To determine the association of increased fibrinolysis with fibrinogen levels and platelet count after coronary artery bypass grafting.

Study design: Descriptive study.

Settings and duration: One year duration conducted in the department of Pathology, Army Medical College in collaboration with Armed Forces Institute of Cardiology from December 2013 to November 2014.

Subjects and Methods: A total of sixty patients were included in the study which were admitted in AFIC for CABG surgery. 1.8 ml venous samples were collected from the patients when they were shifted to post op ITC immediately after surgery.

Results: Out of 60 patients which were included in the study fifty (83.3%) were males and 10 (16.7%) were females. Average fibrinogen level was 123mg/dl (SD=8.21) with minimum fibrinogen level of 14mg/dl and maximum fibrinogen level of 56mg/dl. Average platelet count was 111.90 (SD=49.141) with minimum platelet count of 22 and maximum platelet count of 278.

Conclusion: Increased fibrinolysis was seen in patients with lower platelet count than in patients with normal platelets count that is 78.4% vs 0. Patients with fibrinogen level<150mg/dl % had higher frequency of fibrinolysis as compared to fibrinogen level of >150mg/dl that is 88.9% vs 0%

Key Words: Fibrinolysis, Coronary Artery Bypass Grafting, Fibrinogen, Platelets.

INTRODUCTION

Coronary diseases along with its complications are a major cause of mortality and morbidity across the world[1]. The common procedure done for Coronary Artery Diseases is Coronary Artery Bypass Grafting (CABG) and 800,000 cases are done per year in USA[2]. The important cause of postoperative mortality/ morbidity is excessive postoperative bleeding and transfusion related complications after surgery[3].

Fibrinolysis is a physiological process and is a hemostatic response of our body to any vascular trauma. It causes dissolution of fibrin clot within the circulation. Plasminogen a pro enzyme present in the circulation is activated by tissue plasminogen activator (tPA) and is converted into plasmin. This plasmin breaks down the fibrin meshwork and releases fibrin degradation products (FDPs). FDPs interfere with the coagulation system and inhibits the platelet function. It also interfere with the thrombin which decreases the clot formation by preventing conversion of fibrinogen to fibrin[4]. Fibrinolysis is a major cause of post CABG bleeding in twenty five to forty five percent of cases[5].

CABG is usually associated with activation of hemostatic mechanisms which causes release of tissue factors, resulting in excess thrombin generation and formation of fibrin, platelet activation and fibrinolysis even after full heparinization[6-12]. CABG results in increased thrombin generation and active fibrinolysis, despite adequate heparinization.[6]

Excessive fibrinolysis, dilutional coagulopathy, platelet function defects, decreased platelet count and heparinization during surgery are the major cause of post CABG bleeding[13]. Fibrinogen is a large plasma protein which has several functions such as fibrin clot formation, aggregation of platelets, an acute phase reactant in inflammation and infections[14]. Several mechanisms are responsible for hemostatic failures after CABG such as decreased platelet count or function, decreased levels of coagulation factors, decreased neutralization of heparin, presence of fibrinolysis inhibitors in circulation, increased fibrinolysis, decreased body temperature and DIC[15].

The aim of the study is to determine the asso-

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ciation of post-operative increased fibrinolysis with fibrinogen levels, platelet count, age, gender, duration of surgery and number of vessels involved.

MATERIAL AND METHODS

STUDY DESIGN

Descriptive study.

SETTING

The study is conducted in the Haematology Department, Army Medical College, National University of Sciences and Technology (NUST) in collaboration with Armed forces institute of cardiology, Military Hospital, Rawalpindi.

DURATION OF STUDY

One year, from October 2013-September2014.

SAMPLE SIZE

A total of 60 samples are included in this study.

SAMPLE TECHNIQUE

Non probability purposive sampling.

SAMPLE SELECTION

Inclusion Criteria

Patients undergoing CABG irrespective of age and sex.

Exclusion Criteria

Patients with history of any coagulation or bleeding disorder.

SAMPLE COLLECTION AND PROCESSING

Total of 5 ml venous sample of each patient was taken when the patient was shifted to post operation ITC after CABG surgery.

Approximately 2 ml sample was drawn in a test tube containing 0.2 ml trisodium citrate anticoagulant and was used to measure D-dimer, fibrinogen levels, prothrombin time, activated partial thromboplastin time. 2 ml sample was drawn in EDTA tube for estimating CBC to assess the platelet count. CBC was done on Sysmex KX 21, Fibrinogen levels were done on Hemostat Fibrinogen Kit (Human). D- dimers were done by Sekisui Diagnostica DIMER TEST Latex method. Pt and APTT were done by the manual method using Soluplastin kits.

Data analysis

Data was analyzed using SPSS Version 20. Descriptive statistics were used to describe the data. Frequency and percentages for qualitative variables, mean and standard deviation for quantitative variables.

RESULTS

A total of sixty patients were included in the study. Out of those fifty (83.3%) were males and ten (16.7%) were females. Patient having D dimer more than 200ng/ml were considered positive for increased fibrinolysis. Average fibrinogen level was 123mg/dl (SD=8.21) with minimum fibrinogen level of 14mg/dl and maximum fibrinogen level of 56mg/dl. Average platelet count was 111.90 (SD=49.141) with minimum platelet count of 22 and maximum platelet count of 278.

Patients with lower platelet count had higher frequency of increased fibrinolysis than patients with normal platelets count that is 78.4% vs 0%.Fibrinolysis was significantly associated with platelet count ($p<0.001$). Frequency of fibrinolysis was higher in patients with

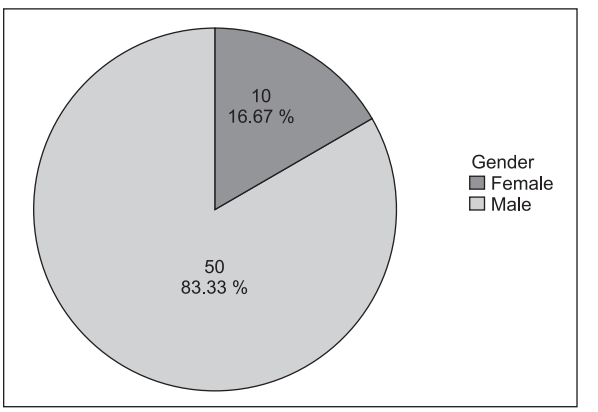

Fig 1: Gender description of the patients (n=60)

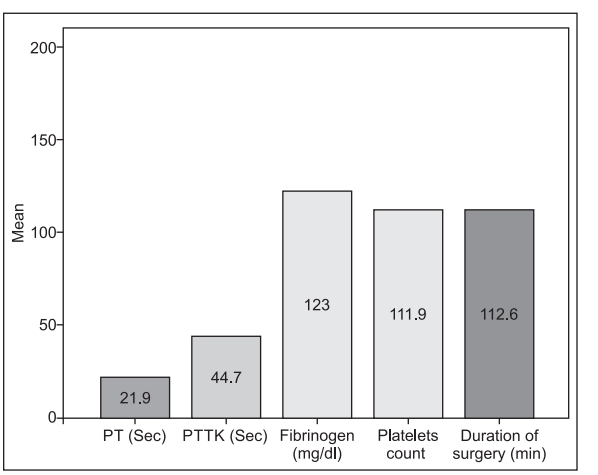

Fig 2: Description of PT, PTTK, Fibrinogen level, Platelets count and Duration of surgery among patients (n=60)

Table 1: Association of fibrinolysis with platelet count and fibrinogen levels.

	Normal (n = 20)	Fibrinolysis (n = 40)	p-value
Platelets count			
< 150	11 (21.6%)	40 (78.4%)	< 0.001
> 150	9 (100%)	0 (0%)	
Fibrinogen level			
< 48	5 (11.1%)	40 (88.9%)	< 0.001

fibrinogen level<150mg/dl as compared to fibrinogen level of >150mg/dl that is 88.9% vs 0%. Association of fibrinolysis and fibrinogen level is significant

DISCUSSION

Cardiac surgeries usually results in coagulopathies. As a result of contact of large surface area of CPB circuit and blood there is activation of contact phase of coagulation. Intrinsic pathway of coagulation is activated by the contact of CPB circuit and factor XII. There is also generation of plasmin due to activation of fibrinolytic system which causes consumption of clotting factors, dissolution of fibrin clot and the patient develops the tendency to bleed. Synder-Ramos in their study demonstrated that there is consumption of clotting factors and platelets along with platelet dysfunction in a patient undergoing cardiac surgery with CPB circuit, and this results in severe bleeding [16]. Hemostatic activation after CABG is usually due to decreased protein c, protein s, fibrinogen and increased t-PA production[17].

Despite of administration of large doses of heparin to a patient undergoing CABG there is increased thrombin production during the bypass. This results in hemostatic dysfunction causing consumption of platelets and clotting factors, platelet dysfunction and leading to increased fibrinolysis [9,18].

Heart surgery is associated with hemorrhagic perioperative and postoperative syndromes, due to this reason the variables of fibrinolysis and coagulation are extensively investigated. In present study sixty patients were included and D dimers were increased in forty patients (66.7%) and were not raised in twenty patients (33.3%). A study performed by Ray et al showed that D dimers are raised in the post bypass period, which supports the present study [19]. Another study demonstrated that CABG surgery with CPB results in activation of hemostatic system as compared to CABG performed off-pump [20]. Casati et al also demonstrated that there is increased production of D dimers in the post bypass period in surgeries performed on pump [12]. In the present study D dimers were significantly raised postoperatively and the frequency of increased fibrinolysis is 66.7%.

In present study the frequency of increased fibrinolysis was higher in patients with fibrinogen levels <150mg/dl as compared to fibrinogen levels of >150 mg/dl which is 88.9% vs 0%. Association of fibrinolysis with fibrinogen levels is significant (P<0.001). Casati et al also demonstrated in his study that fibrinogen levels are significantly decreased after CABG with p value of 0.0001[12]. Another study also showed that fibrinogen levels are decreased in cardiac surgeries performed on pump [21]. These studies supports the present study and describes that fibrinogen levels are significantly decreased after on pump CABG.

In the present study we also demonstrated that fibrinolysis was significantly associated with decreased platelet count (P<0.001). A study performed by Bernard Lo et al demonstrated that there was 60% decrease in platelet count in cardiopulmonary bypass group [20]. Holloway DS in his study showed that there is a decrease in platelet count after CABG performed on pump and he also demonstrated that the chest tube drainage of blood was associated with thrombocytopenia and platelet aggregability [22]. Casati et al in another study also demonstrated that the platelet count was reduced after CABG with a p value of 0.0001 [12]. Heparin induced thrombocytopenia should also be considered while investigating for thrombocytopenia after CABG [23]. These studies supports the present study and CABG results in consumption of platelets which contributes to post bypass bleeding.

CONCLUSION

It is concluded that after coronary artery bypass surgery there is increase in D dimers with consumption of platelets and fibrinogen due to which the patient can develop severe bleeding. With the help of these parameters surgeons can differentiate between surgical and nonsurgical bleeding and will help to reduce mortality and morbidity associated with CABG.

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