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Original Research Article

Influence of anticoagulant therapy in assessment of Fibrinolysis activity in post acute myocardial infarction patients

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Abstract: Acute myocardial infarction is a serious disease in which a patient can survive or die depending on his or her attitude towards life, myocardial infarction, commonly known as a heart attack, is the irreversible necrosis of heart muscle secondary to prolonged ischemia. Morbidity and mortality from myocardial infarction are significantly reduced if patients and bystanders recognize symptoms early, activate the emergency medical service (EMS) system, and thereby shorten the time to definitive treatment. The goal of antithrombotic therapy (the combination of anticoagulant and antiplatelet therapy) is to prevent clot extension and clot reformation in cases where the clot has undergone fibrinolysis either by intrinsic mechanisms, fibrinolytic treatment, or mechanical means .This is a descriptive analytical case control study aimed to evaluate the effect of anticoagulants therapy(heparin and warfarin) in D-dimer, PT, INR and PTT level among patients with acute myocardial infarction conducted in Sudan cardiac center hospital. Thirty patients after MI and twenty normal controls have been studied. Both male and female of different ages and different duration of disease from first day above to thirty day .The MI patients also include co-exist disease diabetes and hypertension, they received different Anticoagulants therapy. The results of PTT in patients in mean were (31.65 second) and the mean of PTT results in control were (32.71 seconds) demonstrated in table (2) the results of D-Dimer in patient in mean were (2264 ng/ml) and the mean of D-Dimer results in control (145.6ng/ml) demonstrated in table. In this study, we found a statistically significant superiority of warfarin in combination with aspirin (relative risk reduction, 29 percent) as well as of warfarin alone relative risk reduction, 19 percent) as compared with aspirin for the reduction in the composite end point.
Keywords: Post Myocardial infarction, Anticoagulant therapy, fibrinolysis activity.

INTRODUCTION

Acute myocardial infarction is a disease which affects the patient in an extremely stressful way. It is described as a threat that leads to a life crisis in one's whole life and it is also a high family stress especially for the couples [1]. One of the contributing mechanisms in the acute myocardial infarction (AMI) is plasma hypercoagulability state [2]. The goals of therapy in acute MI are the expedient restoration of normal coronary blood flow and the maximum salvage of functional myocardium. These goals can be met by a number of medical interventions and adjunctive therapies. The primary obstacles to achieving these goals are the patient's failure to recognize MI symptoms quickly and the delay in seeking medical attention [3]. The first use of thrombolytic therapy in patients with acute myocardial infarction was reported by Fletcher and colleagues in 1958. The primary goal of thrombolytic therapy is rapid, complete, and sustained restoration of infarct artery blood flow. The GUSTO-I angiographic sub study strongly correlated 90-minute patency of the infarct-related artery with the mortality reduction achieved with accelerated alteplase [4]. The goal of anticoagulant therapy with warfarin is to administer the lowest effective dose of the drug to maintain the target international normalized ratio (INR). Warfarin, a vitamin K antagonist, is an oral anticoagulant indicated for the prevention and treatment of venous thrombosis and its extension and the prevention and treatment of the thromboembolic

complications associated with atrial fibrillation. Warfarin has also been used to prevent recurrent transient is chemic attacks and to reduce the risk of recurrent myocardial infarction, but data supporting these indications are inconclusive at this time Antiplatelet medications work by decreasing platelet aggregation and inhibiting thrombus formation [5]. Antiplatelet therapy initiated during a hospitalization for UA/NSTEMI and continued for long-term management has been shown to reduce future cardiovascular events. Anticoagulant medications work by inhibiting blood clotting, either by antagonizing the effects of vitamin K or by blocking/inhibiting thrombin. The use of anticoagulants—traditionally heparin—is standard treatment for patients hospitalized with ACS, and newer anticoagulants have been developed that improve outcomes and reduce or have a bleeding risk similar to heparin [6]. Unfractionated heparin has been used in most fibrinolytic regimens, especially those that possess high fibrin specificity; uncertainty persists regarding the optimal timing, route of administration, and dose to be used. Recently, the role of heparin has been critically examined in the large phase 3 Intravenous lanoteplase for Infarcting Myocardium Early (InTIME)-2 studies, which compared lanoteplase to recombinant tissue plasminogen activator (rt-PA) [7].

MATERIALS AND METHODS

This study was carry out of thirty MI patients known case of myocardial infarction patient above 40 years (male and female) and twenty healthy people matched for age and gender were assigned to the healthy control group, admitted to Sudan Heart Center Al-shab teaching , Ahmed Gasim and Khartoum teaching hospital . After consent was obtained by patients then data collected using structure questionnaire and direct interview to collect information. Then three ml of venous blood has been collected, from each subject, in 3.8% trisodium citrate (9:1 vol/vol). D-dimer has been measured using i-CHROMA^{TM} system (Boditech – Korea) in rang of 50 – 10,000 ng/ml. The test used is the sandwich Immuno detection method. D-Dimer is bound with an antibody in buffer and the antigen-antibody complexes are captured by antibodies that have been immobilized on the test strip as sample mixture migrates through nitrocellulose matrix. Signal intensity of fluorescence on detection antibody reflects the amount of the antigen captured is processed by i-CHROMA^{TM} Reader to show D-Dimer concentration in the specimen. Also the blood coagulation markers, PT, INR and aPTT were measured by DiaPlastin and DiaClin kits (DiaMed GmbH, Switzerland). Data analysis was performed using statistical package for social science (SPSS) software. Evaluation of patient's data was performed using the t-test and Pearson correlation test. Results with p value < 0.05 were considered as statistically significant

RESULTS:

The Total numbers of the studied of MI patients on Cardiac centers were 30 .They were at different age groups whose frequencies are (<40 years), (40 – 50 years), (51 – 60 years) and (60 years), are demonstrated in Fig (1), they also were at different duration of disease that that distributed in groups (less than5 days), (5-15 days), (16-30 days) and (more than 30 days) that show in table (3).From all the patient they also were at different gender Male 77% affected and female 23% affected that show in figure (2), there were diseases associated to MI , there were 10 diabetic patients and 15 hypertensive patients show in table (1) from all patient there were 30% had history with MI, show in figure (3), and there were 63.3 % of all patient with family history show in figure (4),From all patients there were 40% smokers show in figure (5). The results of PT in patient in mean were (14.73 seconds) and the mean of PT result in control were (15.27 seconds) demonstrated in table (2), the mean of INR results in patients were 1.22 and the mean of INR results in control were 1.19 demonstrated in table (2) .The results of PTT in patients in mean were (31.65 second) and the mean of PTT results in control were (32.71 seconds) demonstrated in table (2) the results of D-Dimer in patient in mean were (2264 ng/ml) and the mean of D-Dimer results in control (145.6ng/ml) demonstrated in table (2).The peak mean of coagulation parameters were obtained in duration from 5-15 days demonstrated in table (3). The mean of PT results were (15.1 seconds) , the mean of INR were 1.14 , the mean of PTT (30.34 seconds) and the mean of D-Dimer were 3581.11ng/ml. demonstrated in table (2) . The maximum results of INR related to anticoagulants therapy were obtained in patients whose used Calaxin + Asprin together, were demonstrated in table (4).

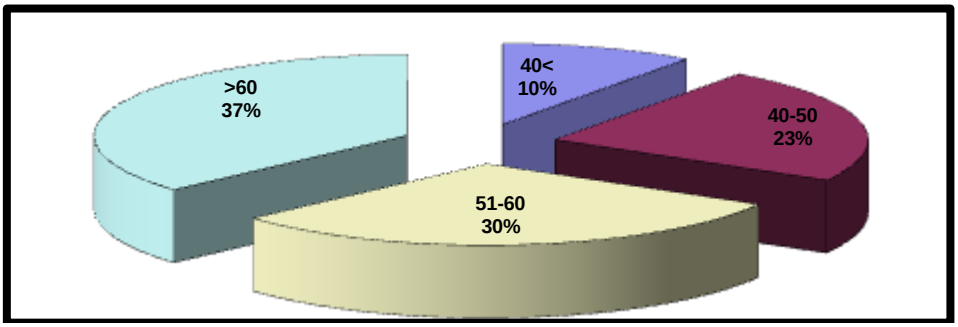

Fig-1: Age distribution on MI patients, n=30

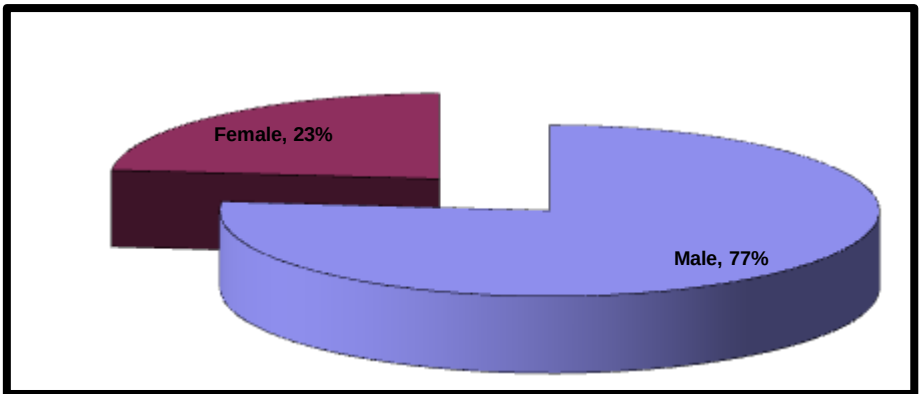

Fig-2: gender related incidence distribution among MI patients n=30

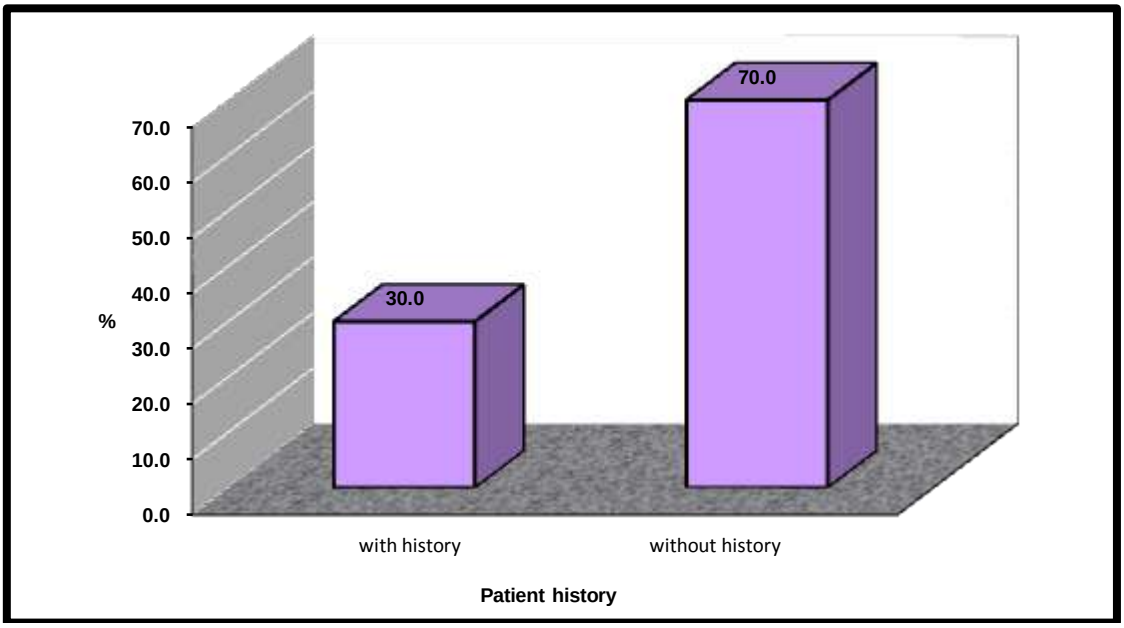

Fig-3: MI patients' history distribution, n=30

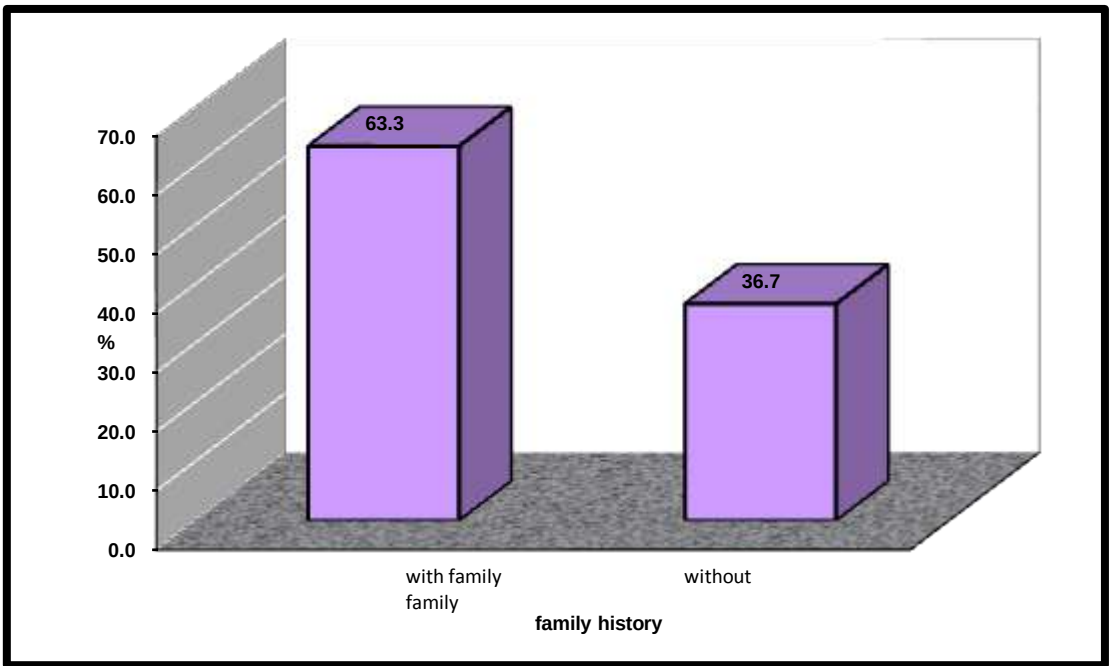

Fig-4: family history distribution among MI patients n=30

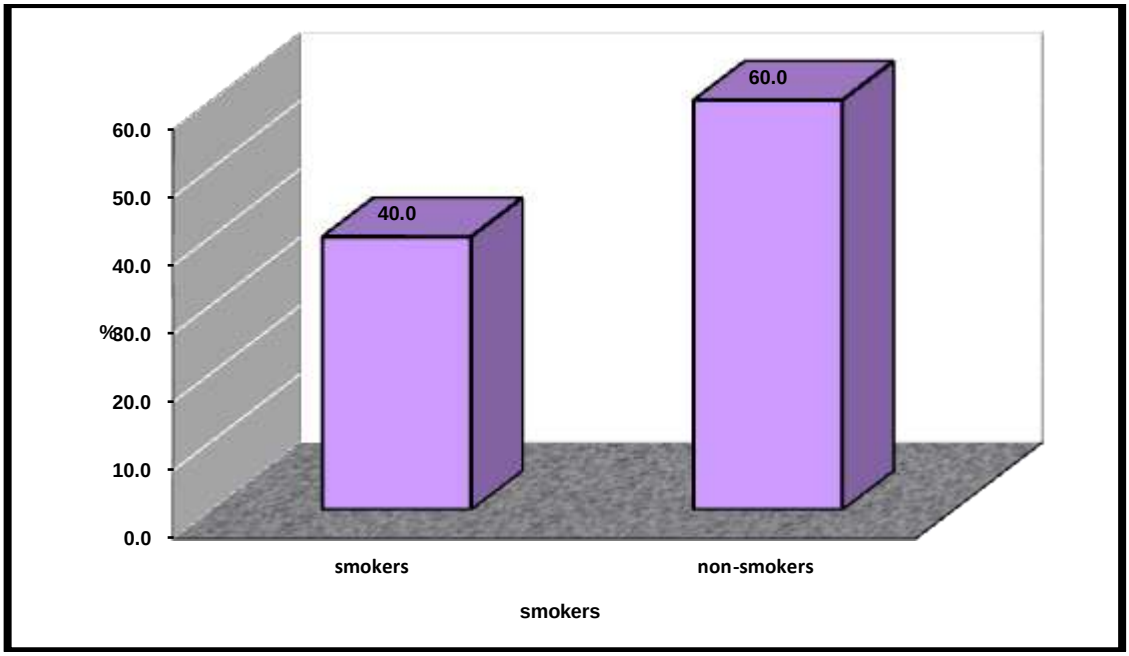

Fig- 5: the incidence of smokers and non-smokers among MI patients, n=30

Table 1: Diseases associated to MI frequency distribution among the study group.

Group	Diabetes		Hypertension	
	Frequency	Percent	Percent	Percent
Positive	10	33.3	15	50.0
Negative	20	66.7	15	50.0
Total	30	100.0	30	100.0

Table 2: the mean level of PT, INR, PTT and D-Dimer among MI patients, n=30 and control =20

sretemaraP	$Mean \pm SD$		P-value
	Patient	Control	
PT	14.73 ± 2.06	15.27 ± 1.99	0.393
INR	1.22 ± 0.25	1.19 ± 0.19	0.709
PTT	31.65 ± 7.96	32.71 ± 6.89	0.648
D-dimer	2264.17 ± 2855.33	145.59 ± 93.43	0.000

Table 3: the mean coagulation parameters related to the duration of MI, n=30

Duration	$Mean \pm SD$			
	PT	INR	PTT	D-dimer
<5 days	14.80 ± 2.04	1.21 ± 0.26	32.60 ± 9.23	1851.83 ± 2654.52
5-15 days	15.06 ± 2.19	1.14 ± 0.18	30.34 ± 6.05	3581.11 ± 3354.06
16-30 days	12.00 ± 0.00	1.2 ± 0.00	30.00 ± 0.00	300.00 ± 000.00
>30 days	14.00 ± 2.26	1.60 ± 0.00	29.80 ± 7.35	1031.00 ± 1038.03

Table 4: International Normalized Ratio related to the Anticoagulants therapy used in MI patients

	INR			
Anticoatgulants	<1	1-1.3	>1.3	Total
asprin	1	1	3	5
	3.3%	3.3%	10.0%	16.7%
calaxin+hepairn	2	0	1	3
	6.7%	.0%	3.3%	10.0%
calaxin	1	2	1	4
	3.3%	6.7%	3.3%	13.3%
calaxin+ asperin	2	8	2	12
	6.7%	26.7%	6.7%	40.0%
Heparin+asprin	1	1	1	3
	3.3%	3.3%	3.3%	10.0%
warfarin+asprin	0	1	1	2
	.0%	3.3%	3.3%	6.7%
Heparin	0	1	0	1
	.0%	3.3%	.0%	3.3%
Total	7	14	9	30
	23.3%	46.7%	30.0%	100.0%

DISCUSSION:

Acute myocardial infarction is a serious disease in which a patient can survive or die depending on his or her attitude towards life. This is because if one takes seriously doctors instructions there is a possibility of overcoming this condition. In this study of a large group of patients presenting with first myocardial infarctions who were eligible to receive thrombolytic therapy, we observed that in-hospital mortality increased from 2.8 percent among patients 60 years old or younger to 19.0 percent among those more than 70 years old, confirming the findings of previous study [8] . In this study, we found a statistically significant superiority of warfarin in combination with aspirin (relative risk reduction, 29 percent) as well as of warfarin alone (relative risk reduction, 19 percent) as compared with aspirin for the reduction in the composite end point. This also confirm by other study among patients with AMI [9]. In this study we found a significantly increase of D-dimmers was observed in patients under oral anticoagulant compared to normal control (p=0.00) .This finding agree with A cohort study with 70 patients conducted by Bitten court *et al.;* 2005 and concluded oral anticoagulant therapy did not influence circulating D-dimer levels. Also our finding agrees with study done by Ombandza, *et al.;* found that there was no correlation between INR and D-dimers levels in patients with oral anticoagulants [10]. The current study found there were different variations from first day to 15days in PT, INR and PTT among those patients, but after 15 days return to the normal value this variation due to sensitive of coagulation factor to anticoagulation drugs types and duration. These findings agree with many studies conducted among patients under oral anticoagulants [11, 12, 13, 14]. It has been seen equally occurring in both male and female. It has also been viewed as life threatening condition which needs a lot of attention to prevent, promote health and cure from the disease. Current medical and surgical treatments have reduced the mortality rate but still the prognosis of AMI patient is poor Several studies have provided data on sex differences in mortality after myocardial infarction [8]. Our studies show an increased mortality in women during the early phase after the infarction (hospitalization or first 4 to 6 weeks) in unadjusted analysis. In most studies, much of this early increase in female mortality is explained by the older age and higher prevalence of unfavorable baseline conditions of women. Also study that presented short-term mortality data adjusted for age alone or in combination with other factors reported a decrease in the magnitude of the female-to-male relative risk to <1.2 [15]. Several large cohort studies have reported an association between self-reported family histories of CHD with an RR for CHD that ranges from twice to 12 times that of the general population depending on the definition used. Age-Related Increase in Mortality among Patients with First Myocardial Infarctions Treated with thrombolysis [16]. In the last importantly, anticoagulation has been shown to reduce the incidence of stroke and mortality

after acute MI in randomized studies from the pre-thrombolytic era.

CONCLUSIONS:

In conclusion of our study indicated that anticoagulant therapy did not influence circulating D-dimer levels, despite adequate anticoagulation, but PT, INR and PTT were sensitive to anticoagulant therapy. Suggesting that this therapy does not completely protect against all coagulation abnormalities observed in this study. Also we suggesting all patients with myocardial infarction should be treated with anticoagulant therapy, which should be given as soon as possible after diagnosis. The choice of anticoagulant agent depends upon the treatment strategy for each patient.

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Conflicts of interest:

The authors had no conflicts of interest to declare in relation to this article.

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