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Alterations in D-Dimer, Prothrombin Time and Activated Partial Thromboplastin Time as Thrombogenesis Activity Markers in Patients with Acute Myocardial Infarction

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Abstract

Cardiovascular disease remains the leading cause of mortality and morbidity despite the identification of major risk factors and risk reduction strategies. Myocardial infarction (MI) is a relevant cardiovascular worldwide event for morbidity and mortality. In most cases, sudden cardiac death is triggered by ischemia-related ventricular tachyarrhythmia and accounts for 50% of deaths from cardiovascular disease in developed countries. This is a descriptive analytical case control study aimed to determine D-dimer, PT and PTT level and among patients with acute myocardial infarction conducted in Sudan cardiac center hospital. Thirty patients after MI and twenty normal controls have been studied. The MI patients also include co-exist disease diabetes and hypertension, they receive different anticoagulants therapy. The result demonstrates a significant increase post MI in the mean level of D-dimer (p = 0.00) whereas none significantly compares to control group. There are no differences between INR (0.393), PTT (0.648) and PT (0.393), parameters between cases and controls. In conclusion, our study reveals higher D-dimer level among patients than the control. In conclusion, serum D-dimer levels appear to be useful for diagnosing MI and may assist in the prediction of mortality among those patients which are presented with acute chest pain or

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known diagnosed with MI and should be done as indicator for thrombosis risk during therapy in post MI.

Keywords

Myocardial Infarction, D-Dimer Level, PT, PTT

1. Introduction

Myocardial infarction (MI) is the result of occlusive coronary thrombosis; as a result of exposure of blood to atherosclerotic plaque contents [1]. In the pathogenesis of acute myocardial infarction (MI), common risk factors for atherosclerosis as well as hemostatic factors are important determinants. The development of a first MI is attributed to a large number of contributing factors and is influenced by multiple genetic, environmental and lifestyle factors. Thrombosis is generally accepted as a common pathogenic pathway for the risk of MI and is itself also influenced by several risk factors [2]. Myocardial infarction occurs when myocardial ischemia, a diminished blood supply to the heart, exceeds a critical threshold and overwhelms myocardial cellular repair mechanisms designed to maintain normal operating function and homeostasis [3]. Significant elevation in fibrin peptide A in the early phase of myocardial infarction identifies patients with increased risk for subsequent cardiac death [4]. Besides platelets and other cellular constituents, the plasma compartment supports the formation of a fibrin thrombus. During AMI, but also afterwards, hypercoagulable state is detectable by several methods assessing ongoing thrombin and fibrin formation and cleavage in plasma. D-dimer, the final product of plasma in-mediated degradation of fibrin-rich thrombi, has emerged as a simple blood test that can be used in diagnostic algorithms for the exclusion of venous thromboembolism. D-dimer levels have certain advantages over other measures of thrombin generation, because it is resistant to *ex vivo* activation, relatively stable, and has a long half-life [5]. Both PT and APTT are significantly increased in AMI patients on anticoagulation therapy. The elevations in PT values are more than 2.5-fold greater than aPTT suggesting a high potential of PT for predicting blood clotting tendency in patients receiving anticoagulation therapy [6]. There are many markers including D-dimer (reflecting fibrin degradation), tissue-type plasminogen activator (t-PA), activation peptides of FIX and FXI and fibrinogen, which have been shown to be independent risk factors for (recurrent) cardiovascular disease [7] [8]. According to our country (Sudan), there has been little research on the associations between plasma D-dimer level, PT and PTT among Sudanese patients with MI. Thus, the purpose of this study is to investigate the association between plasma D-dimer levels, PT and PTT among those patients.

2. Materials and Methods

This study was conducted on thirty MI patients (case) 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™ 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™ 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.

3. Results

The studied of total MI patients on Cardiac centers were 30. They have been categorized into different ages

whose frequencies are (<40 years), (40 - 50 years), (51 - 60 years) and (60 years), the most affected categories were above 60 years which was 37% and the lowest categories were below 40 years shown in **Figure 1**. From all the patient they also have been divided into different gender Male and Female, the affected Male with MI were 77% while affected female were 23% as show in **Figure 2**, The results of D-dimer in MI in all patient in mean were (2264 ng/ml), the D-dimer level was significantly higher among MI patients (*p* value 0.00) compared to control group. While the mean of D-dimer results in control (145.6 ng/ml) as show in **Table 1**. The results of PT in patient in mean were (14.73 seconds) and the mean of PT result in control were (15.27 seconds), the mean of INR results in patients were 1.22 and the mean of INR results in control were 1.19. The results of PTT in patients in mean were (31.65 second) and the mean of PTT results in control were (32.71 seconds) **Table 1**.

4. Discussion

Myocardial infarction is still an important cause of morbidity and mortality. One of the contributing mechanisms in the acute myocardial infarction (AMI) is plasma hypercoagulability. Sudan has been classified as one of the countries with the highest death rates attributed to ischaemic heart disease. Numerous studies conducted in the world to determine the effects of coagulation in MI patients, but there are no enough studies conducted in Sudan in open literature, to our knowledge. In this study we found high levels of plasma D-dimer ($p = 0.00$) were found among patients with MI, while normal levels of PT and PTT were found among those patients. This finding was consistent with several studies showed that D-dimer levels are associated with severity of atherosclerosis and the peak in plasma levels occurring after the acute myocardial infarction event also suggests that it is not a simple marker of hypercoagulability in blood, but may reflect an unstable atherosclerotic process. The fact that, even in this relatively small patient sample and this finding was in agreement to our results obtained [9]-[11]. In contrast, Gurfinkel *et al.* 22 found normal D-dimer concentrations in patients with MI compared with healthy volunteers [12]. Also Wen *et al.* had shown that plasma D-dimer levels increased with increasing severity of stroke as defined by the NIHSS score and infarct volume. These associations were independent other possible variables. In addition, cardio embolic strokes can be distinguished from other stroke etiologies by measuring plasma D-dimer

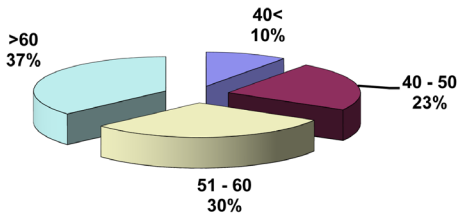

Figure 1. Age distribution on MI patients.

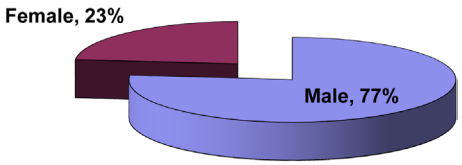

Figure 2. Gender related incidence distribution among MI patients n = 30.

Table 1. The mean level of PT, INR, PTT and D-dimer among MI patients and control.

Parameters	Mean ± 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

levels very early (0 - 48 hours from stroke symptom onset) [13]. Lee *et al.* 21 showed that marked increases in circulating D-dimer were indicative of thrombotic complications in patients with MI, suggesting that D-dimer, besides being a useful marker for early diagnosis, is also a risk factor for the development of MI complications [14]. There are several plausible mechanisms through which D-dimer levels could be closely related to stroke. Firstly, increased D-dimer levels may reflect ongoing thrombus formation within cerebral vessels or may be a marker of systemic hypercoagulability [15]. Present study reported that there were no differences between, PT, INR, and APTT parameters between cases and controls. This finding me be supported by that Age, gender and smoking were found to be the major confounders of plasma fibrinogen levels and the main effect among patients with myocardial infarction is anticoagulant treatment. The plasma composition may be influenced in a direction of impaired thrombin potential during and after MI and this may explain the sometimes extremely low values observed in patients at the time of MI, as well as during follow-up. Must be take care to exclude the influence of anticoagulants in these plasma analyzes. But also in contrast differ with several studies concluded both PT and aPTT are significantly increased in AMI patients on anticoagulation therapy [6] [16] [17]. There were a number of limitations to our study. The major of this the study was undertaken in a small patient population. Thus, the association between myocardial infarction and the mechanism of coagulation must be in a larger patient population. The second limitation in this study not included advance technique to ass the mechanism of the alteration in coagulation during MI like thrombin generation curve test, measuring the main effective coagulation factor (intrinsic and extrinsic path way) by factor assy.

5. Conclusion

In conclusion, our study revealed higher D-dimer levels among patient with MI and appeared to be useful for diagnosing MI and might assist in the prediction of mortality, in patients presenting with any symptoms of MI or any cardiac problem. In addition, prothrombin time and activated partial thromboplastin time didn't show any significance as among those patients due to effect with numerous factors like, anticoagulant therapy, sex, age and duration of MI.

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