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RESEARCH

THE DIFFERENCE OF PLASMA D-DIMER LEVELS IN ACUTE MYOCARDIAL INFARCTION WITH AND WITHOUT ST ELEVATION

(Perbedaan Kadar D-dimer Plasma di Infark Miokard Akut dengan ST Elevasi dan Tanpa ST Elevasi)

Desi Kharina Tri Murni[1], Adi Koesoema Aman[1], Andre Pasha Ketaren[2]

ABSTRAK

D-dimer terlibat di tahap awal patofisiologi proses Infark Miokard Akut (IMA). Kenaikan Kadar D-dimer di IMA mencerminkan adanya trombosis. Penelitian ini bertujuan untuk mengetahui perbedaan kadar D-dimer plasma di IMA dengan ST elevasi dan tanpa ST elevasi. Penelitian ini berupa analitik observasional dilakukan secara potong lintang di Instalasi Gawat Darurat RSUP. Adam Malik Medan, masa waktu bulan April–September 2015. Sampel dikelompokkan menjadi 2 kelompok yaitu sampel dengan diagnosa NSTEMI berjumlah 18 sampel dan sampel dengan diagnosa STEMI berjumlah 18 orang. Semua sampel diperiksa Kadar D-dimer plasma. Penelitian ini menunjukkan ada perbedaan kadar D-dimer plasma di IMA dengan ST elevasi (STEMI) dan tanpa ST elevasi (NSTEMI) yaitu kadar D-dimer di kelompok NSTEMI adalah 440,39±209,33 dan kelompok STEMI adalah 654,89±229,88 (nilai p<0,05). Kadar rerata D-dimer di kelompok STEMI lebih tinggi daripada kadar D-dimer di kelompok NSTEMI.

***Kata kunci**: Infark miokard akut, D-dimer, trombosis*

ABSTRACT

D-dimer is involved in the early stage of Acute Myocardial Infarction (AMI) pathophysiological process. The increase of D-dimer level in AMI reflects the existence of a thrombosis. This study aimed to know the difference of plasma D-dimer level in AMI with and without ST elevation. This study was a cross-sectional observational analytical approach that was performed in the Adam Malik Hospital Emergency Room in Medan, from April-September 2015. Samples were separated into 2 groups: NSTEMI and STEMI each with 18 samples. All samples' were examined for plasma D-dimer levels. This study suggested that there was a difference in plasma D-dimer level in AMI with ST elevation (STEMI) and without ST elevation (NSTEMI) in which the level of D-dimer in NSTEMI group was 440.39±209.33 and in STEMI group 654.89±229.88 ($p<0.05$). The mean levels of D-dimer in the STEMI group were higher than the levels of D-dimer in NSTEMI group.

Key words: Acute myocardial infarction, D-dimer, thrombosis

INTRODUCTION

Acute Myocardial Infarction (AMI) is a barrier of blood flow to the heart that can cause death of heart muscle. AMI is part of coronary heart disease with a high mortality rate.[1]

Acute Myocardial Infarction is divided into two types, ST elevation myocardial infarction (STEMI) and Non-ST elevation myocardial infarction (NSTEMI). In STEMI, total obstruction of the coronary arteries leads to myocardial infarction at all levels, characterized by the presence of a ST segment elevation on electrocardiography. Meanwhile, in NSTEMI blockage occurs in only a portion of the coronary arteries without involving all levels of myocardial infarction, so there is no ST segment elevation on electrocardiography.[2]

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Acute Myocardial Infarction, moreover, can also be triggered by a sudden occlusion in coronary arteries and plaque rupture activating the coagulation system. Atheroma and clot will fill the lumen of the artery, which finally occludes the lumen of the coronary arteries that have undergone an atherosclerosis. Ischemia then will occur, eventually causing myocardial necrosis.[3]

Furthermore, artery coronary thrombus formed can cause total and subtotal occlusion. When the occlusion lasts longer and causes myocardial cell death, it still can be overcome by collateral or lysis of thrombus quickly. As a result, there will be AMI without ST elevation or known as NSTEMI (not all levels of myocardial damage). Thrombus can be more persistent and lasts for more than one hour because it is not compensated by collateral or lysis. In such circumstances, the entire layers will undergo myocardial necrosis (transmural necrosis), clinically known as AMI with ST elevation or STEMI, also accompanied by the emergence of a pathological Q.[4]

Next, D-dimer is the final result of degeneration of cross-linked fibrin by plasmin in fibrinolytic system. Fibrinolysis is a process of destruction of fibrin deposits by the fibrinolytic system so that blood flow will be open again. An increase in D-dimer can indicate the presence of a thrombus, however, it still has a disadvantage because it can not show the location of abnormalities and can not get rid of other causes.[5]

In addition, thrombus can actually freeze and melt. Consequently, intermittent coronary obstruction can be triggered. Melting of thrombus is affected by plasmin with a stable fibrin as the final result, known as D-dimer.[6]

Thus, an increase in D-dimer can be considered as an indicator of thrombotic complications in patients with myocardial infarction, D-dimer indicators, are a useful marker for early diagnosis, as well as a risk factor for the development of complications of Myocardial Infarction.[7] Therefore, this research aimed to determine the differences of D-dimer plasma levels in Acute Myocardial Infarction with and without ST elevation.

METHODS

This research was an observational analytical research with a cross sectional design. The population of this research comprised patients with the diagnosis of Acute Myocardial Infarction, who came to the Emergency Room of the Adam Malik Hospital from April to September 2015.

Next, sampling was conducted by consecutive sampling technique in the population that met the criteria. Inclusion criteria were patients with a diagnosis of Acute Myocardial Infarction less than 24 hours after the onset of symptoms as well as at the age of ≥18 years old. Meanwhile, exclusion criteria were patients with a history of trauma and surgical operations within four weeks earlier, anticoagulant medication 1 week prior to the sampling and history of Coronary Artery Bypass Grafting (CABG) and Percutaneous Coronary Intervention (PCI).

Next, measurement of D-dimer levels was conducted in several phases after a number of samples collected. First, the measurement was performed using Coatron A4 instrument (Automated Coagulation Analyzer). Second, frozen samples were melted at room temperature, and then their temperatures were equated to the room temperature. Temperatures of solutions of calibrators and controls were also equated to the room temperature (20–25°C). In other words, this measurement method was carried out using an immuno turbidimetric assay technique with material samples in the form of plasma.

Afterwards, principles of material examination conducted also consisted of several phases. First, reagent R1 (buffer) and R2 (latex D-dimer antibody) were added. Second, D-dimer antibody binding to latex microparticles reacted with the antigen in the samples to form the Ag-Ab complex. Agglutination of the Ag-Ab complex then was measured turbidimetrically with a wavelength of 400 nm. Cutoff value of D-dimer was 500 ng/mL.

And the last, to reveal the differences of D-dimer plasma levels in patients with Acute Myocardial Infarction, unpaired T-test was performed. Thus, if the statistical P value obtained was less than 0.05, it would mean that there was a significant difference. SPSS version 22 was also used to support statistical analysis.

RESULTS AND DISCUSSION

Most of the research subjects in the NSTEMI group were males as many as 14 (77.8%) compared to females as many as 4 (22.2%). Similarly, in the STEMI group, most of the research subjects were males as many as 11 (61.11%) compared to females as many as 7 (38.89%).

The mean age of the research subjects in the NSTEMI group was 54.11 years with the youngest aged 38 years and the oldest one 82 years. On the other hand, the mean age of the research subjects in the

Table 1. General characteristics of research variables

Variables	Group	
	NSTEMI n (%)	STEMI n (%)
Sex		
• Males	14 (77.8)	11 (61.11)
• Females	4 (22.2)	7 (38.89)
Age		
• 35–58 years	11 (61.11)	10 (55.56)
• 59–82 years	7 (38.89)	8 (44.44)
Risk Factors		
• Hypertension	16 (88.89)	13 (72.22)
Non-Hypertension	2 (11.11)	5 (27.78)
• DM	11 (61.11)	12 (66.67)
Non-DM	7 (38.89)	6 (33.33)
• Dyslipidemia	6 (33.33)	7 (38.89)
Non-dyslipidemia	12 (66.67)	11 (61.11)
• Smoking	5 (27.78)	9 (50)
Non-smoking	13 (72.22)	9 (50)

Note: NSTEMI (Non-ST Elevation Myocardial Infarction); STEMI (ST Elevation Myocardial Infarction)

STEMI group was 54.72 years with the youngest aged 35 years and the oldest one 74 years. In the distribution of age, the number of the research subjects in the NSTEMI group at an age range of 35–58 years was 11 subjects (61.11%), while at an age range of 59–82 years was 7 subjects (38.89%). On the other hand, the number of the research subjects in the STEMI group at an age range of 35–58 years was 10 subjects (55.55%) and at an age range of 59–82 years was 8 subjects (44.44%).

Moreover, hypertension was the largest risk factor found in both, the NSTEMI group and the STEMI group. There were 16 subjects (88.89%) in the NSTEMI group and 13 subjects (77.22%) in the STEMI group. The second largest risk factor found in both of the groups was diabetes mellitus. There were 11 subjects (61.11%) in the NSTEMI group and 12 subjects (66.67%) in the STEMI group.

Table 2 showed that D-dimer levels in all of the research subjects in both NSTEMI and STEMI groups were more than 500 ng/mL as many as 18 subjects (50%). There were 5 subjects (27.78%) in NSTEMI group and 13 subjects (72.22%) in the STEMI group.

Table 3 showed that there were differences of D-dimer plasma levels in Acute Myocardial Infarction between with ST elevation (STEMI) and without ST elevation (NSTEMI). The mean levels of D-dimer were 440.39±209.33 in the NSTEMI group, while 654.89±229.88 in the STEMI group (p value<0.05).

Table 2. Examination results of D-dimer in the research subjects

D-Dimer Levels (ng/mL)	Group		Total n (%)
	NSTEMI n (%)	STEMI n (%)	
<500	13 (77.22)	5 (27.78)	18 (50)
>500	5 (27.78)	13 (72.22)	18 (50)
Total	18 (100)	18 (100)	36 (100)

Note: NSTEMI (Non-ST Elevation Myocardial Infarction); STEMI (ST Elevation Myocardial Infarction)

The number of male research subjects in both of the NSTEMI and STEMI groups, furthermore, was higher than the females, about 77.78% and 22.22%. Similarly, previous researches conducted by Derhasching *et al.*[8] and McCann *et al.*[9] showed that the prevalence of myocardial infarction in male patients was higher than in females.[8,9] It may be due to a fact that males are more prone to atherosclerosis process than females since estrogen in women allegedly can give protective effect.[10] Besides, it may also be due to smoking dominated by males, which can cause endothelial dysfunction and then trigger atherosclerosis.[11]

Table 3. Differences of D-dimer levels in the research subjects

Group (n)	Mean±SD of D-dimer levels (ng/mL)	P-value
NSTEMI (18)	440.39±209.33	
STEMI (18)	654.89±229.88	0.006*

Note: P=Probability, with unpaired t-test. * Significant P<0.05

In addition, the mean age of the research subjects in the NSTEMI group was 54.11 years, while the mean age of the research subjects in the STEMI group was 54.72 years. In the distribution of age, the number of the research subjects in the NSTEMI group with an age range of 35–58 years was 11 (61.11%), while in the STEMI group was 10 (55.55%). These findings were supported by the results of a research conducted by Ting *et al.*[12] showing an increase in the number of patients aged above 50 years treated in the Intensive Cardiac Care Unit (ICCU) because of Acute Myocardial Infarction.[12]

According to the Framingham Heart Study, moreover, risk factors have multiple effects on myocardial infarction. Thus, if there are two risk factors found, the incidence of Acute Myocardial Infarction will increase four times. The risk factors mostly found in this research were hypertension and diabetes mellitus. The risk factors of hypertension and diabetes mellitus found in the NSTEMI group were 88.89% and 61.11%, while in the STEMI group 77.22% and 66.67%. Similarly, previous researches conducted by Bayes *et al.*[13] and Zheng *et al.*[14] also showed that patients with Acute Myocardial Infarction were mostly triggered by hypertension and diabetes mellitus as the dominant risk factors.[13,14]

High blood pressure can trigger trauma directly on the walls of coronary arteries, so coronary atherosclerosis easily happens. However, the incidence of myocardial infarction in patients with diabetes mellitus is two times higher than non-diabetic ones. This may be due to endothelial damage and increased levels of oxidized LDL. Besides, blood coagulability will increase in diabetic patients due to an increase in plasminogen activator inhibitor 1 (PAI-1) and an increase in platelet aggregation.[15]

Another risk factor, smoking, in the STEMI group was approximately about 50%. Smoking can increase the load of the heart due to catecholamine stimulation and decrease oxygenation consumption. Smoking also can cause endothelial dysfunction leading to atherosclerosis, as well as can stimulate adhesion and aggregation of platelets and artery spasm.[10,16]

Based on the results of this research, the number of the research subjects with D-dimer levels above 500ng/mL were 27.78% in the NSTEMI group and 72.22% in the STEMI group. In contrast, a research conducted by Yaputra[17] and Orak *et al.*[18] showed a significant increase in D-dimer levels above 500 ng/mL in both NSTEMI and STEMI groups.[17,18]

This may occur because in the research conducted by Orak *et al.*[18], sampling was conducted more than 12 hours of the onset of chest pain symptom arisen, whereas in this research more than 24 hours of the onset of chest pain symptom. Therefore, it may be related to the length of time for breaking fibrinogen and fibrin to produce an FDP (Fibrin Degradation Product) as the final result of D-dimer.

In addition, subtotal obstruction accompanied by vasoconstriction can also cause ischemia and necrosis of heart muscle tissue. Coronary artery narrowing occurred partly as a result of thrombus in the atherosclerotic plaque that is torn, but not to clogged. Microemboli of platelets and its aggregation component then cause small infarcts.

CONCLUSION AND SUGGESTION

Based on the results of this research, it can be concluded that the mean levels of D-dimer in the STEMI group were higher than in the NSTEMI group. D-dimer is a breakdown of fibrin triggered by plasmin. D-dimer examination, therefore, is useful to determine the indirect thrombus formation and direct thrombus breakdown.

For these reasons, D-dimer determination can be used as an additional examination in patients treated in the Emergency Room with chest pain complaint alleged as an Acute Myocardial Infarction with NSTEMI and STEMI as a consideration for clinicians in conducting therapy.

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