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### Correlation of High Sensitive Troponin I (hsTnI) with Platelet Distribution Width (PDW) in Acute Myocardial Infarction Patients

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#### ABSTRACT

**Background:** Acute myocardial infarction (AMI) occurs due to rupture of atherosclerotic plaque which triggers platelet activation and aggregation to form a thrombus. Several studies have examined the relationship between PDW and AMI, but there is no specific correlation with hsTnI as the most sensitive and specific cardiac biomarker for AMI. This study aims to analyze the correlation between hsTnI levels and PDW values in AMI patients. **Methods:** Cross-sectional study of 60 AMI patients in the emergency room of Dr. M. Djamil General Hospital Padang from April to August 2022. Research subjects who met the inclusion and exclusion criteria underwent hsTnI and PDW examinations. The correlation of hsTnI with PDW was analyzed using the Spearman correlation test. Correlation is declared significant if the p-value is <0.05. **Results:** The research sample consisted of 48 men (80%) and 12 women (20%). The average age is 60.67 (10.73) years with an age range of 33-82 years. The mean hsTnI level was 2,606.10 (2,404.79) ng/L and the mean PDW value was 10.97 (2.26) fL. There was a strong and significant positive correlation between hsTnI and PDW in AMI patients ( $r = 0.618$ ,  $p = 0.000$ ). **Conclusion:** There is a correlation between hsTnI levels and PDW values at AMI.

#### 1. Introduction

The prevalence of heart disease in Indonesia based on Basic Health Research by the Ministry of Health of the Republic of Indonesia in 2018 is 1.5%. The prevalence of heart disease in West Sumatra province reaches 1.6%. Acute myocardial infarction (AMI) is a frequent emergency. Increased mortality due to AMI occurs in Indonesia every year, 70% of fatal events are caused by atherosclerotic plaque occlusion.<sup>1</sup> The European Society of Cardiology (ESC) recommends checking troponin one to three hours after an attack using a probe highly sensitive troponin compared to conventional troponin. Inspection high sensitive troponin I (hsTnI) can significantly diagnose early

acute coronary syndrome (ACS).<sup>2</sup> Platelets play an important role in the pathogenesis of AMI. Platelet reactions appear after atherosclerotic plaque ruptures in the form of increased platelet activation and aggregation. The activation and aggregation of large numbers of platelets causes the release of young platelets from the bone marrow, resulting in heterogeneity in the size of platelets circulating in the circulation.<sup>3</sup> Platelet distribution width (PDW) shows the different sizes of platelets (anisocytosis), indicating platelet activation.<sup>3,4</sup> PDW values increase in AMI patients due to increased bone marrow activity during thrombopoiesis.

Research by Alvitigala et al. in Sri Lanka, in 52 STEMI patients and 52 control groups, it was found that STEMI patients experienced a significant increase in mean PDW compared to the control group ( $15.81 \pm 0.41$  fL vs  $15.62 \pm 0.33$  fL,  $p = 0.007$ ). There was a significant positive correlation between PDW in STEMI patients ( $r = 0.556$ ,  $p = 0.000$ ).<sup>3</sup> Reddy et al. examining the relationship between platelet index in STEMI patients, it was found that the PDW value was significantly higher in STEMI patients compared to the control group ( $p < 0.05$ ). This study found that increasing PDW is an independent risk factor for STEMI and correlates with the severity of STEMI.<sup>5</sup> Mailoa and Adhipireno studied the relationship between platelet index (platelet count, mean platelet volume (MPV), PDW, platelet large cell ratio (PLCR)) with creatinine kinase myocardial band (CKMB) and troponin in ACS. This study found a significant relationship between PDW and CKMB ( $r=0.849$ ,  $p=0.000$ ) and troponin ( $r=0.610$ ,  $p=0.000$ ). Platelet size variability is considered to be a marker for assessing the risk of cardiovascular disease.<sup>6</sup> Platelet distribution width is a simple routine hematology examination, and indicates platelet activity. The results of several studies regarding increasing PDW are considered to have a role in assessing the risk of AMI, but there is no specific correlation with hsTnI as the most sensitive and specific cardiac biomarker for AMI. This study aims to analyze the correlation between hsTnI levels and PDW values in AMI patients at Dr. M. Djamil General Hospital Padang, Indonesia.

## 2. Methods

This research is an analytical study with a cross-sectional design carried out at the central laboratory installation, emergency room installation, and medical records installation at Dr. M. Djamil General Hospital Padang from April to August 2022. The research population is all patients who have been diagnosed with AMI (STEMI and NSTEMI) by a heart and blood vessel specialist, who carried out laboratory examinations at the Central Laboratory Installation of

Dr. M. Djamil General Hospital Padang. The research sample is part of the population that meets the inclusion and exclusion criteria. Inclusion criteria were adult patients over 18 years old. Exclusion criteria include patients with heart disease other than AMI, autoimmune and infectious diseases, essential thrombocytosis, bleeding/blood clotting disorders, malignancy, blood transfusion within 3 months before the study, kidney failure, and liver disease.

Data collected from research samples were the results of hsTnI and PDW examinations. hsTnI examination using an automatic immunoassay tool enzyme-linked fluorescent assay (ELFA) method. The PDW value is obtained by calculation from an automatic hematology tool using the impedance method. Research data was analyzed using a computer program. Data distribution was assessed using the Kolmogorov-Smirnov normality test ( $n>50$ ), data distribution is normal if the  $p$ -value $>0.05$ . The Pearson correlation test is used if the data is normally distributed and the Spearman correlation test is used if the data is not normally distributed. Research results are considered significant if the  $p$ -value is  $<0.05$ . The positive correlation direction shows that the higher the hsTnI, the higher the PDW, while the negative correlation direction shows that the higher the hsTnI, the lower the PDW.

## 3. Results

The results of research on 60 patients who had been diagnosed with AMI (STEMI and NSTEMI) by heart and blood vessel specialists, who carried out laboratory examinations at the Central Laboratory Installation of Dr. M. Djamil General Hospital Padang found that most of the research subjects (80%) were men. The mean age was 60.67 (10.73) years with an age range of 33-82 years. Smoking was the most common risk factor in this study, followed by hypertension and diabetes mellitus. The diagnosis of STEMI was present in 78.3% of the sample and NSTEMI in 21.7% of the sample (Table 1).

Table 1 Characteristics of research subjects.

Variable	f (%)	Mean (SD)
Gender		
Male	48 (80 %)	
Female	12 (20 %)	
Age (years)		60,67 (10,73)
AMI risk factors		
Hypertension	31 (51,7 %)	
Diabetes mellitus	28 (46,7 %)	
Smoking	33 (55%)	
Dyslipidemia	22 (36,7%)	
Family history	9 (15%)	
Diagnosis classification		
STEMI	47 (78,3%)	
NSTEMI	13 (21,7%)	

Table 2. Levels of hsTnI and PDW.

Variable	f (%)	Mean (SD)	Median (minimum-maximum)
HsTnI (ng/L)		2.606,10 (2.404,798)	1.498 (114 - 9.122)
PDW (fL)		10,976 (2,2671)	
Normal (9-13 fL)	44 (73,3 %)		
Above normal (>13 fL)	16 (26,7 %)		

The results of hsTnI and PDW levels for all subjects are shown in Table 2. The mean hsTnI level of the research sample was 2,606.10 (2,402,798) ng/L. The median hsTnI level was 1,498 ng/L with a minimum level of 114 ng/L and a maximum level of 9,122 ng/L. The mean PDW value for the research sample was 10.976 (2.2671) fL, with a minimum value of 6.8 fL and a maximum value of 16.5 fL. Normal PDW values were found in 44 (73.3%) research samples, while PDW

values above normal were found in 16 (26.7%) research samples. The correlation test between hsTnI levels and PDW values was carried out using the Spearman correlation test using a computer program. The research showed that there was a strong positive and statistically significant correlation between hsTnI levels and PDW values ( $r = 0.618$ ,  $p = 0.000$ ), as shown in Figure 1.

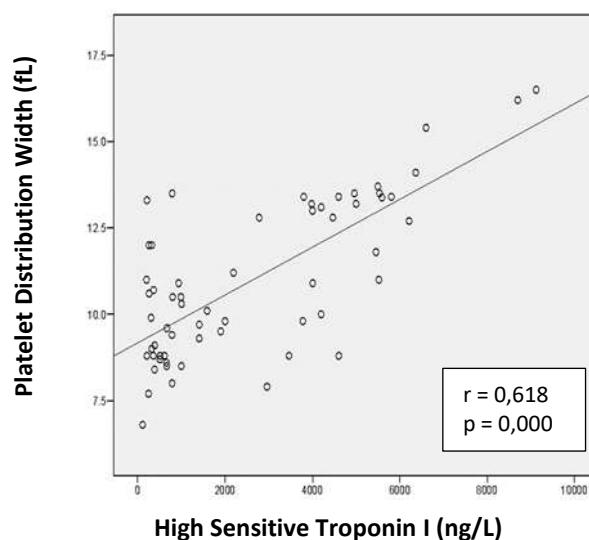


Figure 1. Linear curve of hsTnI levels and PDW values.

#### 4. Discussion

The subjects of this research were 60 subjects. The majority of subjects were 48 men (80%), while 12 were women (20%). These results are almost the same as Maiola and Adhipireno's research, in 68 ACS patients consisting of 44 (64.71%) men and 24 (35.29%) women.<sup>6</sup> Research by Putri et al. in 64 AMI patients consisting of 57 (89.1%) men and 7 (10.9%) women.<sup>4</sup> Research by Alvitigala et al. in 52 STEMI patients consisting of 43 (83%) men and 9 (17%) women.<sup>3</sup> Research by Reddy et al. in 173 STEMI patients consisting of 129 (74.6%) men and 44 (25.4%) women.<sup>5</sup> This is because estrogen in women has a protective effect on the vascular endothelium. The effect of estrogen on the vascular system is increased excretion of nitric oxide which can cause vasodilation of blood vessels, regulate prostaglandin production, and inhibit smooth muscle proliferation.<sup>7,8</sup>

The mean age of AMI patients in this study was 60.67 (10.73) years with an age range of 33-82 years. The results of this research are almost the same as the results of Maiola and Adhipireno's research. get the average age of the research subjects was 59 years.<sup>6</sup> Research by Reddy et al. obtained a mean age of research subjects of 59.4 (11.9) years.<sup>5</sup> The incidence of AMI increases with age. Older AMI patients are more likely to develop various clinical symptoms and lesions in multiple myocardial branches, whereas younger AMI patients have relatively fewer symptoms, and tissue lesions are more limited.<sup>8,9,11-13</sup>

Based on risk factors, it was found that smoking was the highest risk factor (55%) followed by hypertension (51.7%) and diabetes mellitus (46.7%). Results are similar to research by Putri et al. Smoking was also the most common risk factor for AMI in the study sample (84.4%), followed by diabetes mellitus (59.4%) and hypertension (56.3%).<sup>4</sup> Research by Reddy et al. smoking was also found to be the highest risk factor for AMI in the study sample (69.9%), followed by diabetes mellitus (36.1%) and hypertension (51.4%).<sup>5</sup> Smoking was the first most common risk factor in this study. Cigarettes contain oxidant particles that can trigger blood vessel

inflammation which results in the narrowing of the blood vessels, reducing blood flow and oxygen supply to organs including the heart, which can cause myocardial infarction. Nicotine in cigarettes too stimulates the sympathetic nerves so it will increase heart rate, blood pressure, and myocardial contractility which aggravates myocardial ischemia.<sup>10,14</sup>

Hypertension was the second most common risk factor in this study. Increased blood pressure is a heavy burden on the heart, causing left ventricular hypertrophy. High and persistent blood pressure will also cause direct trauma to the coronary artery walls, making it easier for atherosclerosis to occur. The more severe the hypertension condition, the greater the risk of developing AMI.<sup>4</sup> This study obtained research samples with a diagnosis of STEMI (78.3%) and NSTEMI (21.7%). The results of this study are similar to other studies in that STEMI diagnoses were more frequently found in the study sample.<sup>15-17</sup>

This study found that the mean hsTnI level of research subjects was 2,606.10 (2,404.798) ng/L. The entire sample of this study complied rule in criteria myocardial infarction is >100 ng/L. The average PDW value was 10.976 (2.2671) fL, with a minimum value of 6.8 fL and a maximum value of 16.5 fL. Platelet distribution width reflects variation or heterogeneity in the size of platelets circulating in the circulation. High PDW values reflect varying platelet sizes (anisocytosis), an indication that there is platelet activation.<sup>3-5</sup> This study found that there was a significant relationship between hsTnI and PDW in AMI patients (0.618,  $p=0.000$ ). This shows that the higher the hsTnI level, the higher the PDW value in AMI patients. The results of this study are similar to research conducted by Maiola and Adhipireno. which found a significant relationship between PDW and troponin ( $r=0.610$ ,  $p=0.000$ ). Platelet size variability is considered to be a marker for assessing the risk of cardiovascular disease.<sup>6</sup> Similar research results were also obtained in the research of Putri et al. who examined the correlation of PDW and troponin I (TnI), which obtained a strong correlation between PDW and TnI ( $r=0.72$ ,  $p<0.001$ ).<sup>4</sup>

Acute myocardial infarction begins with atherosclerotic plaque rupture, followed by platelet activation and aggregation. This activation process will stimulate platelets to change size and shape so that they become more active in secreting thromboxane A2 (TxA2) and adenosine diphosphate (ADP) into the circulation. The release of TxA2 and ADP will stimulate surrounding platelets to become more active and also secrete more TxA2 and ADP. Activated platelets also directly bind to circulating coagulation proteins, namely fibrinogen, via the platelet integrin, glycoprotein (GPIIb/IIIa). Activation and aggregation of platelets causes stimulation of thrombopoiesis with increased release of young platelets from the bone marrow resulting in heterogeneity in platelet size in the circulation, causing the PDW value to increase.<sup>3,18-20</sup>

Thrombus formation will cause occlusion in the coronary area, resulting in disruption of blood flow which results in an imbalance between oxygen availability and oxygen demand. Severe obstruction due to thrombus will cause ischemia and necrosis. Myocardial necrosis causes the release of enzymes that mark myocardial damage. High-sensitive troponin I is a cardiac marker that is often used because it is rapidly released after the onset of ischemia persists for a long time in the blood, and is specific for heart damage.<sup>2</sup> The limitation of this study is that it did not group the research samples based on AMI risk factors. This study only examined the risk factors of hypertension, smoking, dyslipidemia, and family history, while other risk factors such as lifestyle and body mass index were not studied. It is recommended that further research be carried out with a wider range of risk factors and research with a larger number of samples to evaluate the diagnostic value of this parameter.

## 5. Conclusion

This research shows that there is a correlation between hsTnI levels and PDW values in AMI patients at Dr. M. Djamil General Hospital Padang.

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