

**DIFFERENCES OF FIBRINOGEN LEVELS WITH THE NUMBER OF CORONARY ARTERIAL LESIONS IN PATIENTS OF ACUTE CORONARY SYNDROME****Aprilia Jati\*<sup>1</sup>, Rahmad Isnanta<sup>2</sup> & Zainal Safri<sup>3</sup>**<sup>\*1</sup>Department of Internal Medicine, Faculty of Medicine Universitas Sumatera Utara<sup>2,3</sup>Division of Cardiology, Department of Internal Medicine, Faculty of Medicine Universitas Sumatera UtaraDOI: 10.5281/zenodo.3612048

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**Abstract**

**Introduction:** Coronary heart disease (CHD) is a disease caused by plaque that builds up in the coronary arteries that supplies oxygen to the heart muscle. The main clinical manifestations of CHD and most often causing death is acute coronary syndrome (ACS). The process of atherosclerosis is the most common cause of CHD. Coronary atherosclerosis is a pathological condition of the coronary arteries that results in changes in the structure and function of the arteries as well as a decrease in the volume of blood flow to the heart. Several studies have prospectively reported that fibrinogen is a risk factor for ACS.

**Aim:** The aim in this study is to know the difference fibrinogen levels between multiple lesion compared with a single lesion group in ACS patients.

**Methods:** This study is analytic observational with cross sectional design was using secondary data within medical records of ACS patients who underwent coronary angiography and were treated at Haji Adam Malik (HAM) General Hospital from July 2017-July 2019. Data analysis using SPSS 20nd.

**Result:** Based on bivariate analysis, hypertension and NLR (Neutrophyl Lymphocyte Ratio) were a significant factors for groups of simple and multiple arterial lesions ( $p = 0.002$ ). This study found that there were differences in mean and standard deviation levels of fibrinogen between simple lesion and the multiple lesion group ( $178.2 + 34.01$  vs.  $333.6 \pm 117.81$ ,  $p = 0.000$ ).

**Conclusion:** There was a significant difference in fibrinogen levels correlate with the number of coronary artery lesions, which is the more higher levels of fibrinogen, the more coronary artery lesions was found in ACS.

**Keywords:** Fibrinogen, Coronary Arterial Lesion, Angiography.

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**Introduction**

Cardiovascular disease contributes the highest mortality rate in the group of non-communicable diseases. The mortality rate of cardiovascular disease in the world in 2008 was 17 million deaths. This figure is also expected to increase from year to year to reach 25 million deaths by 2030. Coronary heart disease (CHD) is a disease caused by plaque that builds up in the coronary arteries that supplies oxygen to the heart muscle<sup>2</sup>.

CHD is defined as the presence of stenosis of more than 50% at least in one coronary artery as evidenced by angiographic examination<sup>3</sup>. Coronary angiography can provide information about the location of the lesion or blockage in the coronary, the degree of obstruction, the presence of collateral circulation, the extent of tissue disturbance in the distal area of the coronary blockage and the type of lesion morphology<sup>4</sup>.

Several studies prospectively report that fibrinogen is a risk factor for CHD and they prove that increased levels of fibrinogen are associated with heart disease. Increased fibrinogen is a marker of systemic inflammation that is easily measured and is an acute phase reactant, which is a response to acute exacerbations of chronic infarction<sup>5</sup>.



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**Method**

This cross-sectional study was carried out on patients with Acute Coronary Syndrome who underwent angiography in Division Cardiology at General Hospital of Haji Adam Malik, Medan, North Sumatera from July 2017 to July 2019. A total 66 adult subjects (both male and females) of aged  $\geq 18$ , years were for in this study.

The study population was drawn from consecutive acute coronysindrome patients who presented to Haji Adam Malik General Hospital who underwent angiography coroner which in line with inclusion criteria are inclusion criteria: patients with acute coronary syndrome that are established based on history taking, physical examination, ECG, and cardiac enzyme examination, aged  $\geq 18$  years and a coronary angiography has been performed also exclusion criteria : patients stable angina pectoris, chronic liver disease, chronic kidney failure, malignancy, systemic collagen disease, infectious diseases; patients with Percutaneous Transluminal Coronary Angioplasty (PTCA), Coronary Artery Bypass Grafting (CABG) and patients with previous history of trauma, surgery and burns.

The study subjects were taken within medical record after Ethical Clearance approved by the Ethics Commission, which patients were taken who included the inclusion and exclusion criteria until the minimum sample size obtained. Data collected included: characteristics of the study sample such as age, sex, recent education, ethnicity, dyslipidemia, hypertension, diabetes mellitus, Neutrophyl Lymphocyte Ratio (ACS) and the type of ACS diagnosis. The value of fibrinogen levels obtained before the patient underwent coronary angiography examination. The results of coronary angiography examination are divided into; simple lesions consisting of involvement of 0 and 1 vessel disease and multiple lesions consisting of involvement of 2 and 3 vessel disease.

Data was analyzed using SPSS version 20 (SPSS Inc., Chicago, IL). Student's t-test was used to ascertain the significance of differences between mean values of two continuous variables and confirmed by nonparametric Mann-Whitney test. Chi-square and Fisher exact tests were performed to test for differences in proportions of categorical variables between two or more groups were simple lesion and multiple lesion group. The level  $P < 0.05$  was considered as significance.

**Result**

Distribution frequency of demographic characteristics of research subjects (Table 1). The mean age of respondents was ( $53.0 \pm 11.04$ ) years with the most sex were male (65.2%). The majority of respondents have self-employed jobs (50.0%) with the most educational background are high schools (59.1%) and come from the Batak Ethnic (59.1%). Most respondents had a diagnosis of STEMI (53.0%) followed by UAP (27.3%) and NSTEMI (19.7%).

The risk factors found in most respondents were dyslipidemia (40.9%) and diabetes mellitus (50.0%), followed by hypertension (28.8%). Based on coronary artery lesions, the most common category of lesions is multiple lesions [3-VD (53.0%) and 2-VD(19.7%)] and followed by simple coronary artery lesions [1 -VD (21.2%) and 0-VD (6.1%)] The results of NLR and fibrinogen levels have a median value as well as minimum and maximum values of NLR 4.09 (1.45-46, 00) and fibrinogen 253.5 (113-754) mg / dL.

*Table 1. The characteristics of research subjects.*

Variable	n = 66
Age (Years), Mea $\pm$ SD	53,0 $\pm$ 11,04
Sex	
Male	43 (65,2%)
Female	23 (34,8%)
Employee	
Wiraswasta	33 (50,0 %)
Civil servants	12 (18,2%)
Farmer	4 (6,1%)
Housewife	14 (21,2%)



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Retired	3 (4,5%)
Education Levels	
Primary school	5 (7,6%)
Junior high school	5 (7,6%)
Senior high school	39 (59,1%)
College	17 (25,8%)
Ethnics	
Batak	39 (59,1%)
Jawa	27 (40,9%)
Diagnosis	
UAP	18 (27,3%)
NSTEMI	13 (19,7%)
STEMI	35 (53,0%)
Diabetes mellitus	
Yes	33 (50,0%)
No	33 (50,0%)
Hypertension	
Yes	19 (28,8%)
No	47 (71,2%)
Dyslipidemia	
Yes	27 (40,9%)
No	39 (59,1%)
Vessel Disease	
0	4 (6,1%)
1	14 (21,2%)
2	13 (19,7%)
3	35 (53,0%)
Fibrinogen Levels (mg/dL)	
Median (Min-Maks)	253,5 (113-754)
NLR	4,09 (1,45-46,00)

Records the distribution of patient characteristics based on simple lesion and multiple coronary artery lesions (Table 2). Respondents had a higher mean age in the multiple lesion group than respondents in simple lesions ( $54.2 \pm 7.91$ ;  $p = 0.387$  vs.  $52.2 \pm 7.79$ ), but did not show a statistically significant relationship.

Based on sex in the group of simple lesions the majority were female (34.8% vs. 23.3%) in contrast to the group of multiple lesions getting more with the percentage of men (76.7% vs. 65.2%), however this difference does not have a significant relationship ( $p = 0.316$ ).

Based on several types of work, all ACS patients had more multiple lesions compared to simple lesions including self-employed (75.8% vs. 24.2%), civil servants (75.0% vs. 25.0%), farmers (75, 0% vs. 25.0%), IRT (57.1% vs. 42.9%) and retirees (100.0% vs. 0%) but this difference did not have a significant relationship ( $p = 0.552$ ). Respondents came from several educational backgrounds, all ACS patients had more multiple lesions compared to simple lesions including PS (100% vs. 0%), JHC (60.0% vs. 40.0%), SHS (71.8% vs 28.2%) and college (70.6% vs. 29.4%), but this difference did not have a significant relationship ( $p = 0.552$ ).

Based on ethnicity, in the group of multiple lesions the majority of respondents were from the Javanese ethnic group compared to the Batak Ethnic (81.5% vs. 66.7%), different from the group of simple lesions which came from the Batak ethnic group compared to the Javanese Ethnic (33.3% vs. 18.5%), but this difference did not have a significant relationship ( $p = 0.184$ ).

The diagnosis respondents found that all had multiple lesions compared to simple coronary artery lesions including UAP (77.8% vs. 22.2%), NSTEMI (38.5% vs. 61.5%) and STEMI (74, 3% vs. 25.7%), but this difference did not have a significant relationship ( $p = 0.578$ ).



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**Table 2. Characteristics subjects based on simple lesion and multiple coronary artery lesions in ACS**

Variable	Vessel Score		P-Value
	Simple Lesion (0-1 VD)	Multipel Lesion (2-3 VD)	
Age (Years),	52.2 ± 7,79	54,2 ± 7,91	0,387
Sex			0,316
Male	10 (23,3%)	33 (76,7%)	
Female	8 (34,8%)	15 (65,2%)	
Employee			0,552
Wiraswasta	8 (24,2%)	25 (75,8%)	
Civil servants	3 (25,0%)	9 (75,0%)	
Farmer	1 (25,0%)	3 (75,0%)	
Housewife	6 (42,9%)	8 (57,1%)	
Retired	0 (0%)	3 (100,0%)	
Education Levels			0,505
Primary school	0 (0%)	5 (100 %)	
Junior high school	2 (40,0%)	3 (60,0%)	
Senior high school	11 (28,2%)	28 (71,8%)	
College	5 (29,4%)	12 (70,6%)	
Ethnics			0,184
Batak	13 (33,3%)	26 (66,7%)	
Jawa	5 (18,5%)	22 (81,5%)	
Diagnosis			0,578
UAP	4 (22,2%)	14 (77,8%)	
NSTEMI	5 (38,5%)	8 (61,5%)	
STEMI	9 (25,7%)	26 (74,3%)	
Diabetes mellitus			0,269
Yes	7 (21,2%)	26 (78,8%)	
No	11 (33,3%)	22 (66,7%)	
Hypertension			0,002*
Yes	0 (0%)	19 (100,0%)	
No	18 (38,3%)	29 (61,7%)	
Dyslipidemia			0,443
Yes	6 (22,2%)	21 (77,8%)	
No	12 (30,9%)	27 (69,2%)	
NLR	2,26 (1,45-4,22)	4,87 (2,03-46,00)	0,000*

Based on bivariat analysis showed the value of Fibrinogen levels is based on a simple lesion and multiple coronary artery lesions of ACS patients (Table 3).

**Table 3. Fibrinogen levels based on a simple lesion and multiple coronary artery lesions of ACS**

Fibrinogen Levels (mg/dL)	Vessel Score		P-Value
	Simple Lesion (0-1 VD)	Multipel Lesion (2-3 VD)	
Median	175	332	0,000*
Minimum - Maximum	113-233	158-754	

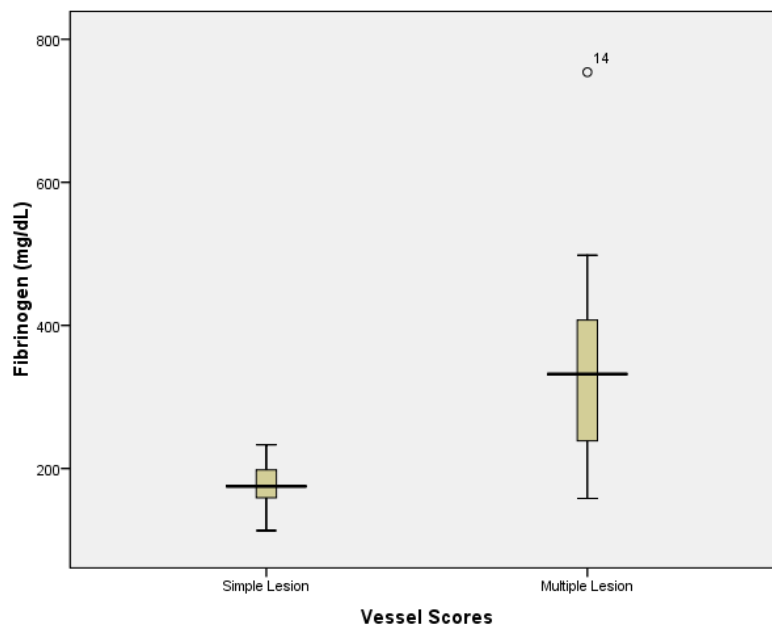


Figure 1.Box plots of fibrinogen to Vessel Scores

These findings showed that the median, minimum and maximum levels of fibrinogen levels in the multiple lesion group are higher than those in the coronary artery simple lesion group [332 (158-754) vs. 175 (113-233)] mg / dL. Based on the bivariate analysis above, it can be explained that fibrinogen levels have a significant relationship to vessel scores in ACS patients ( $p = 0,000$ ).

## Discussion

Coronary heart disease (CHD) is the most common of heart disease which is the most important cause of early death in the world so that it experiences many many major breakthroughs in its management. According to WHO, CHD was responsible for 8.1 million deaths worldwide in 2013 (IK: 95%, 7.3–8.8 million) and there has been a 42% increase in the number of CHD deaths since 1990<sup>5</sup>. In general, the prevalence of ACS in Indonesia increases with age groups 45-54 years, 55-64 years and 65-74 years, although there are quite a lot of symptoms of ACS in the population aged 15-24 years<sup>6</sup>. In line with studies in China with all male patients <35 years old getting an average age of  $31.58 \pm 3.35$  years, where "early" deaths caused by heart disease occur in the range of 4% in high-income countries up to 42% occur in low-income countries<sup>7</sup>.

Almost the same as studies in Sweden which are found in the 50-70 years age group, studies in Britain aged 31-70 years<sup>8</sup>. The Tabakci et al study<sup>9</sup>, with an average age of 60.8 years, a study by Sudrajat et al<sup>10</sup>, with the most age groups being 50-60 years, the Sihombing et al<sup>11</sup>, study, 50-59 years, Kurtul et al<sup>12</sup>, (61,6 + 12.8) years and study of Ralapanawa et al<sup>6</sup>, (61.3 + 12.6) years.

This is in line with this study which found that the average age was 53 years from the age range 31-68 years. Respondents in this study were dominant male (65.2%). In line with the study of Sudrajat et al<sup>10</sup>, The number of men (76.3%), the Sihombing et al<sup>12</sup>, study, men (75%), the Ralapanawa et al<sup>5</sup>. Study, men (66.3%), studies Kurtul et al<sup>12</sup>, Male (67.3%) and Ahmed et al. Study, male (85.23%)<sup>13</sup>. Based on this data ACS was found more in men where in previous studies it was associated with (80%) smoking habits<sup>13</sup>. Although on the contrary the Pusdatin data shows that sufferers of coronary heart disease based on doctor's diagnosis or diagnosis / symptoms are estimated to occur more frequently in women compared to men<sup>6</sup>. In this study, most ACS respondents were diagnosed with STEMI (53.0%) followed by UAP (27.3%) and NSTEMI (19.7%). In line with studies by ACCESS reporting 46% of ACS in developing countries is STEMI. Rajapakse et al. (2010) reported 33.6% ACS in Sri Lanka became STEMI, while Medagama et al. (2012) reported 32.8% of ACS to be STEMI<sup>5</sup>. While other



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studies in Sri Lanka in 2019 showed steam (37.7%), NSTEMI (36.7%), STEMI (25.7%). 11-year follow-up cohort study in New Zealand with NSTEMI (54.5%), UAP (25.7%), STEMI (16.0%), MI Unspecified (MIU) (3.8%) where all ACS will fall at STEMI at a rate of 3.4 %/year<sup>14</sup>. Study of Sudrajat et al, with a diagnosis of UAP (42.1%), STEMI (36.8%) and NSTEMI (21.1%)<sup>10</sup>.

Differences in epidemiology can occur because of the heterogeneity of variety subjects such as age, education, ethnicity and occupation. In this study the majority of respondents had self-employed jobs (50.0%) with high school education (59.1%) and came from the Batak ethnic (59.1%). Analysis of risk factors including DM, Ht and dyslipidemia, the most commonly found in this study is DM. Previous studies have shown that type 2 diabetes is an important factor for coronary atherosclerosis plaque rupture in ACS. Diabetic patients have more macrophage infiltration and large necrotic cores compared to patients without diabetes who increase the attack of ACS<sup>14</sup>. Although DM was associated with a group of multiple lesions and simple coronary artery lesions did not show statistically significant results. This could be due to the proportion between the groups of multiple lesions and simple lesions having almost the same percentage of respondents with DM or no DM.

The INTERHEART study found nine risk factors that cause > 95% ACS such as dyslipidemia, smoking, Ht, DM, abdominal obesity, psychosocial factors, rarely eating fruits, vegetables and rarely physical activity showed statistically significant results ( $p < 0.0001$ ) ( $p < 0.0001$ )<sup>5</sup>. The study by Sudrajat et al. found that the most risk factors in patients with ACS were Ht (60.5%) followed by smoking (57.9%), obesity (36.8%), dyslipidemia (26.3%), previous history of ACS (23.7%) and DM (15.8%) which had the smallest proportion. Risk factor data from RSCM also showed the same results, Ht (60.96%), DM (30.45%), smoking (53.96%), obesity (33.58%) dyslipidemia (23.45%) and previous history of ACS (27.16%)<sup>10</sup>. The Anget al<sup>15</sup>, study found that the greatest risk was the proportion of Ht (90.6%) followed by hyperlipidemia (87.2%) and DM (42.9%). Other studies that analyze risk factors for the severity of coronary artery lesions include the study of Gao et al. Study multivariate analysis that risk factors associated with increased fibrinogen in the severity of coronary artery lesions are age, BMI, smoking, Ht, previous history of ACS, hs-CRP, glucose and HbA1C<sup>7</sup>. The Karahan et al. Study found that the proportion of Ht increased with increasing severity of coronary artery lesions ie SYNTAX Score (SS) > 22 compared to SS < 22 (17% vs. 14%,  $p = 0.663$ )<sup>17</sup>. The Karahan et al<sup>16</sup>, study found more DM percentages than Ht in the group SS < 22 compared to SS > 22 (19% vs. 17%,  $p = 0.832$ ) as well as the mean total cholesterol and LDL although the value was higher in lesions with SS > 22 but did not show a meaningful relationship. Study of Tabakci et al, proportion of DM (52% vs. 30%,  $p = 0.461$ )<sup>9</sup>. Study Kurtul et al<sup>12</sup>, that the proportion of Ht and DM SS > 23 is higher than SS < 23 proportion Ht (44.9% vs. 44.1%,  $p = 0.848$ ) and DM (43.9% vs. 27.2%,  $p = < 0.001$ ).

The study of Shi et al<sup>17</sup>, DM analysis of fibrinogen found that DM had more proportion in fibrinogen levels > 350 mg/dL compared with fibrinogen levels < 350 mg/dL (15% vs. 8%,  $p = 0.1$ ), the proportion of dyslipidemia (20% vs. 18%,  $p = 0.6$ ) but different from the higher proportion of hypertension in fibrinogen < 350 mg/dL (31% vs. 30%,  $p = 0.8$ ). A novel study of risk factors for mortality shows that risky Ht (57%) increases mortality and DM (30.8%) increases mortality of ACS patients<sup>18</sup>. In this study Ht risk factors have a significant relationship where the proportion is 100% in the group of multiple lesions compared to a simple coronary artery lesion<sup>5</sup>.

A large proportion of Ht was also in the Sihombing et al study<sup>11</sup> (70%). Hypertension causes sympathetic hyperactivity which contributes to sudden death, coronary spasm and the incidence of thrombosis<sup>11</sup>. Based on coronary artery lesions, the most common category of lesions is multiple lesions vessel stenosis scores with the most with 3-VD (53.0%) followed by 2-VD (19.7%), 1-VD (21.2%) and 0-VD (6.1%). The results of fibrinogen levels have mean and SD ( $291.2 \pm 123.29$ ) with minimal and maximum values of fibrinogen levels (113-754). In line with the study of Zhang et al<sup>19</sup>, with the percentage of vessel scores in the ACS is 3-VD (34.4%), 2-VD (24.5%), 1-VD (25.7%) and 0-VD (15.4%) where with the average levels greater fibrinogen is  $3.23 \pm 0.77$  gr/L. While other studies found more often with a vessel score of 0-VD (47%), 1-VD (42%), 2-VD (8%) and 3-VD (3%)<sup>20</sup>. Respondent characteristics were related to lesions, based on age in the multiple lesion group getting an average age older than simple lesions. This is in line with other studies although using a different method, study in Turkey using the SYNTAX Score (SS), the group with SS > 22 had an average age older than SS < 22 ( $65.6 \pm 14.2$  vs.  $57.0 \pm 16.4$ )<sup>16</sup>. Studies in China with a Gensini Score (GS) found a population



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increased in average age by increasing the GS scores <16 ( $57.7 \pm 9.9$ ), scores 16-39 ( $58.1 \pm 9.7$ ) and scores > 39 ( $59.0 \pm 10.0$ )<sup>19</sup>.

Based on occupation, all of them are related to the large percentage with multiple lesions, retirees (100%), other occupations (75%) with multiple lesions include wiaswasta, civil servants and farmers, while housewife just (57.1%) related to multiple lesions. The educational background also influences where in this study the lower the greater the percentage related to multiple lesions PS (100%) and related to simple lesions is JHC (40%). All rates are greater percentage associated with multiple lesions where the Javanese ethnic is greater risk than the Batak (81.5% vs. 18.5%). Diagnosis based on vessel scores, UAP obtained the highest percentage with multiple lesion groups (77.8%), then STEMI (74.3%) and NSTEMI (61.5%). This is in line with a cohort study in Sri Lanka where the ACS with the most rapid growth rates was UAP (8.5%/year) then NSTEMI (9%/year) and STEMI (3.4%/year)<sup>14</sup>.

Significant differences were found both NLR and Fibrinogen between groups of simple lesions and multiple coronary artery lesions. In line with the study of Chen et al<sup>21</sup>, which found that NLR was an independent risk factor for CHD both at low GS <41 or at high GS > 41 (OR = 1.18, 95% CI: 1.09-1.27, p = 0.009 vs. OR = 1.10, 95% CI: 1.01-1.16, p = 0.032). Other studies also found that NLR was the strongest prediction for CHD with (OR: 1.495; 95% CI: 0.942-2.371; p<0.048). NLR is a simple indicator that can be used effectively for CAD diagnosis with a cut-off of 2.13 AUC-0.823; p<0.001; sensitivity: 83.64%; specificity: 63.46%) in the West Indian population<sup>22</sup>. Multivariate studies also found that NLR was higher in those with moderate-severe stenosis compared with mild stenosis (OR: 1.34, 95% CI: 0.77-1.92; n = 6) and moderate stenosis (OR: 0, 52, 95% CI: 0.36-0.68; n = 6). High NLR levels are recognized as independent predictors for severe stenosis in CAD (OR: 1.50, 95% CI: 1.32-1.72; n = 11) with a cut-off: 1.95-3.97, AUC: 0.66, 95% CI: 0.64-0.68; n = 8)<sup>23</sup>. Fibrinogen is a coagulation factor, which also plays an important role in proinflammatory cytokines in acute inflammatory reactions. Many studies have found that fibrinogen levels are associated with increasing the incidence of atherosclerosis and cardiovascular disease.

Study Peng et al<sup>18</sup> showed fibrinogen levels were associated with cases of death in respondents with ACS with high fibrinogen level ( $3.51 \pm 1.05$ ) gr / L. In this study showed a significant difference in fibrinogen levels between simple lesions and multiple lesions with mean fibrinogen levels ( $178.2 \pm 34.01$  vs.  $333.6 \pm 117.81$ , p = 0.000) with many respondents diagnosed with STEMI. In line with previous studies where the mean and standard standards of fibrinogen levels increased with the amount of vessel score were 0-VD ( $3.00 \pm 0.62$ ) g/L, 1-VD ( $3.10 \pm 0.71$ ) g/L, 2-VD ( $3.22 \pm 0.76$ ) g/L and 3-VD ( $3.33 \pm 0.81$ ) g/L<sup>19</sup>. In line with previous studies showed high fibrinogen levels as a predictor of increased SS scores with fibrinogen in the group with SS <22 was higher than in the control group ( $391.9 \pm 79.7$  vs  $321.0 \pm 72.1$ , P <.001); and high fibrinogen levels in the SS group > 22 compared with SS <22 ( $472.3 \pm 79.7$  vs  $391.9 \pm 79.7$ , P <.001) and in multivariate analysis found that fibrinogen could be a predictor factor were significantly related for increased SS (OR, 1.01; 95 % CI, 1.01-1.02; P <.001)<sup>9</sup>. In line with other studies with higher fibrinogen levels the SS scores were higher in the SS group > 22 compared with SS <22 ( $354.51 \pm 148.30$  vs  $247.46 \pm 82.50$ , P <.001) and fibrinogen levels became predictors of improvement in SS scores (OR, 3.331; 95% CI, 0.016-0.062; P = 0.001)<sup>17</sup>. Studies in Turkey show the same thing that higher fibrinogen levels in the SS group > 23 compared with SS <23 [492 (428-581) vs. 370 (209-428), P <.001] and fibrinogen levels were predictors of increased SS scores (OR: 1.008, P = 0.041) and showed a cut-off value of fibrinogen > 417 mg/dL (sensitivity: 80%; specificity: 71.3%)<sup>12</sup>.

Another study with a different score was Gensini Score to determine the severity of stenosis also found that fibrinogen levels were significantly related to the increased severity of stenosis associated with higher fibrinogen levels in the group with stenosis compared to the group without stenosis ( $3.10 \pm 0.58$  vs  $3, 53 \pm 1.10$ , P <.001) g / L and high fibrinogen levels in the high GS group ( $3.84 \pm 1.18$ ) compared to moderate GS ( $3.49 \pm 1.08$ ) and low GS ( $3, 23 \pm 0.94$ , P <.01) and the cut-off value analysis found that fibrinogen levels > 3.75 g/L were related to the severity of stenosis (AUC: 0.656 2 P <.001, sensitivity: 64%, specificity: 70%)<sup>7</sup>.

The same thing also in other studies using GS scores obtained higher fibrinogen levels in the group with stenosis compared to the group without stenosis ( $3.23 \pm 0.77$  vs.  $3.00 \pm 0.62$ , P <.01) g/L and high fibrinogen levels in



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the high GS group ( $3.33 \pm 0.81$ ) compared to moderate GS ( $3.24 \pm 0.77$ ) and low GS ( $3.10 \pm 0.71$ ,  $P < 0, 01$ )<sup>19</sup>. This is of concern because elevated fibrinogen levels often persist in patients with recurrent angina and patients with myocardial infarction after stenting, in the Kavitha et al study<sup>24</sup>, ( $288.64 \pm 59.43$  vs.  $393.75 \pm 32.97$ ) mg/dL where fibrinogen levels are still increasing by serial examination. The Sudrajat et al<sup>10</sup> study, which analyzed fibrinogen in the acute and post-acute phases found that (52.6%) settled as hyperfibrinogenemia. The Ang et al study found an increase in fibrinogen levels  $> 280$  mg/L associated with major adverse cardiovascular events (MACE) in the 2 years after Percutaneous Intervention (PCI)<sup>15</sup>. Fibrinogen can increase endothelial cell migration and extracellular accumulation of low density lipoproteins. Fibrinogen can increase platelet aggregation by interacting with GP IIb / IIIa receptors on the platelet membrane. In addition, increased plasma fibrinogen levels increase blood viscosity, which causes disruption of microcirculatory flow, damage to endothelial shear stress, and predisposition to thrombosis and can be considered a risk factor for restenosis in MI patients after stenting<sup>24</sup>. Limitations in this study were carried out in the with a cross-sectional study design.

### Conclusion

There was a significant difference in fibrinogen levels correlate with the number of coronary artery lesions, which is the more higher levels of fibrinogen, the more coronary artery lesions was found in ACS.

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