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The Relationship Between Serum Apolipoprotein B Levels and Severity of Coronary Lesions Using The Syntax Score in Non-St Segment Elevation Acute Myocardial Infarction Patients at Haji Adam Malik General Hospital Medan

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ABSTRACT

Introduction: Acute coronary syndrome mainly occurs as a result of plaque rupture of atherosclerosis. Apolipoprotein B (apoB) is a large glycoprotein, playing a role in lipoprotein metabolism and human lipid transport reflecting the number of circulating atherogenic particles. The purpose of this study was to assess the relationship of serum apoB levels with coronary lesion severity.

Method: This is a cross-sectional study involving patients who was diagnosed with Non-ST Elevation Myocardial Infarction (NSTEMI) who underwent coronary angiography in November 2021 to July 2022. The NSTEMI criteria follow the Universal Definition of Myocardial Infarction and coronary severity is assessed using a SYNTAX score. Bivariate analysis was conducted looking for the relationship between apoB with SYNTAX scores with $p<0.05$ considered statistically significant.

Results: The subjects of the study is 70 people, dominated by male 50 patients (71.4%). The median age of the subjects was 56 (38-77) years. Median levels of apoB was 107 (32-150) mg/dL. The average SYNTAX score was 25.66 ± 10.83. Using the Pearson correlation test, it was shown that there is a significant correlation between apoB and coronary lesion severity obtained $r=0.442$ ($p<0.001$).

Conclusion: There is a significant correlation between apoB and coronary lesion severity using SYNTAX scores in NSTEMI patients.

Keywords

Apolipoprotein B, NSTEMI, SYNTAX score, Acute Coronary Syndrome

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INTRODUCTION

Cardiovascular disease ranks first as the cause of death in the world.[1] Data from the Global Burden of Cardiovascular Disease and Risk Collaboration released in December 2022 revealed that Coronary Artery Disease (CAD) is the main cause of death from cardiovascular causes, namely 9.44 million people in 2021 and the number 185 million people with disabilities.[2] Indonesian data was consistent with the prevalence in the global population, namely the ratio of deaths due to CAD is almost close to 150 per 100,000 population.[2] Riskesdas data in 2018 shows the prevalence of CAD sufferers in North Sumatra is around 1.3% of the total population.[3]

Coronary artery disease is a pathological process characterized by accumulation of atherosclerotic plaque in epicardial arteries, both obstructive and non-obstructive. This process can occur over a long period of time, in stable periods but can suddenly change to become unstable, usually due to an acute atherothrombotic event due to plaque rupture or erosion. The dynamic course of this disease process can appear in a variety of

clinical presentations, which are categorized into Acute Coronary Syndrome (ACS) and Chronic Coronary Syndrome (CCS). ST (IMANEST), and Acute Myocardial Infarction with ST Segment Elevation (IMAEST).[5] Partial thrombus occlusion occurs in IMANEST and APTS, while total thrombus occlusion occurs in IMAEST.[6]

Various risk factors affect the development of CAD, including Low-density Lipoprotein Cholesterol (LDL-C), Apolipoprotein (Apo) B, ApoA1, total cholesterol, triglycerides, high-density lipoprotein (HDL-C), and lipoprotein (a) (Lp[a]) so that it is used as a therapeutic target based on current clinical practice guidelines. 7 It is recommended that patients with high risk undergo a second layer of examination, including non-HDL cholesterol, apoprotein B (apoB), apoprotein A (apoA), lipoprotein (a), small- dense LDL, and oxidized-LDL.[7,8]

Apolipoprotein B is a structural protein that is the main component of very low density lipoprotein (VLDL), medium density lipoprotein (IDL), and low density lipoprotein (LDL). Each of these lipoprotein particles carries one apoB molecule.[9] Knowledge of apoB levels can describe the number of potentially atherogenic lipoprotein particles.[7] Apolipoproteins also play an important role in structural bonding, lipid transport and stable lipoproteins, but also play a role in regulating enzyme activity in metabolism. lipoprotein and recognition of lipoprotein receptors.[10] Apolipoprotein B also plays a role in stimulating smooth muscle proliferation in the arteries and into the subendothelium. Because of this role, it is suspected that apoB is the most likely component to cause atherosclerosis.

Currently, there are various scoring systems used to assess the severity of coronary artery stenosis. The SYNergy score between percutaneous coronary intervention (PCI) with TAXus and cardiac surgey (SYNTAX) (SS) is a scoring system that has been widely and routinely used in clinical practice to determine the complexity of coronary lesions based on anatomical characteristics such as lesion location, severity, bifurcation, and calcification.[11,12] In a study conducted by Boyraz B (2022) comparing the SYNTAX score and the Gensini score in the severity of coronary lesions and the selection of Coronary Artery Bypass Surgery (CABG) decisions in multivessel CAD patients at Diyarbakir Gazi Yaşargil Education and Research Hospital Turkey showed the SYNTAX score was superior to the score Gensini (AUC 0.759 vs 0.680; $p<0.001$).[13] In its development, the SYNTAX score began to be applied in risk stratification of coronary lesions, identification of individual risk profiles, which allows its application as a predictor of coronary lesion severity in general.[14]

In a study that tested the relationship between serum LDL-C and ApoB on the severity of coronary lesions as assessed by the SYNTAX score by Taiwu Lin, et al (2018) concluded that ApoB and LDL-C had a positive correlation with the SYNTAX score ($r=0.632$ and 0.599; $p< 0.1$), but this study excluded ACS patients, patients with a history of myocardial infarction and CABG.[7] Another study conducted by Nurulita, et al (2011) at Dr. Wahidin Sudirohusodo Makassar concluded that ApoB could be used as a predictor of ACS ($r>0.4$; $p<0.01$) but did not correlate it with the severity of the lesion.[15] Until now, no studies had been conducted linking apoB levels and severity of coronary lesions using the SYNTAX score specifically in the IMANEST population.

METHOD

The research was an analytic study with cross-sectional study design. Researchers took blood samples to check apolipoprotein B levels for all research subjects diagnosed with IMANEST who underwent coronary angiography at Haji Adam Malik General Hospital, and the severity of coronary lesions was assessed from the SYNTAX score.

The study was conducted at the Department of Cardiovascular Disease, Faculty of Medicine, Universitas Sumatera Utara, Medan, in collaboration with the Department of Clinical Pathology Haji Adam Malik General Hospital from November 2021 to July 2022. Sampling was carried out by consecutive sampling of all populations that met the research criteria.

The inclusion criteria were patients diagnosed with non-ST segment elevation acute myocardial infarction based on clinical, EKG and cardiac biomarkers, patients undergoing coronary angiography

procedures during treatment at H. Adam Malik General Hospital Medan. Patients with routine use of lipid lowering drugs for more than 6 weeks, Patients with a history of previous heart attacks and undergoing Percutaneous Coronary Intervention (PCI), Patients who have undergone Coronary Artery Bypass Surgery (BPAK), Patients with malignancies obtained through anamnesis, Patients with liver disease, blood disorder, infection (sepsis), abnormal kidney function, and incomplete medical data, and patients who did not agree to participate in the study were included as exclusion criteria.

Apolipoprotein B examination is an immunoturbidimetric procedure with the principle that Human apolipoprotein B forms a precipitate with specific antiserum determined turbidimetrically at a wavelength of 604 nm. Strengthening quality is important to prevent errors in inspection. Strengthening the quality of the apolipoprotein B examination follows the recommendations of Abbot Laboratories for quality control. with the Architect tool with an automatic system, namely REF 5P56-01 Lipid Constituent Calibrator.

The calculation of the SYNTAX score is assessed using the SYNTAX score by using the application on *http://www.syntaxscore.com/calculator/start.htm*. The SYNTAX score will be assessed by two different observers.

Bivariate analysis using the Chi-square test for categorical data. Bivariate analysis for numerical data with independent t-test. The correlation between the two variables was calculated by statistical analysis of Pearson's correlation. Variables are considered significant if the p value <0.05 To analysis the predictor value of Apolipoprotein B in the severity of coronary lesions, a Receiving Operator Curve (ROC) was performed which produced the AUC (Area Under Curve) cut off point, sensitivity, and specificity.

RESULT

Demographic Characteristics of Research Subjects

This study was followed by 70 IMANEST patients who underwent coronary angiography at Haji Adam Malik General Hospital Medan. All patients who met the inclusion and exclusion criteria were then included in the study. All subjects recorded data in the form of anthropometric indices, risk factors, basic ECG rhythms, laboratory results, and coronary angiography results. Laboratory results include complete blood count, kidney function, glucose level, lipid profile, Apolipoprotein B, blood glucose profile, and cardiac enzymes. The full characteristics of the research subjects are shown in table 1.

Of the 70 research subjects, the average age of the subjects was 56 years and 50 people (71.4%) were dominated by males. Risk factors such as hypertension, smoking and diabetes mellitus were sequentially found in 51 people (72.9%), 34 people (48.6%), 40 people (57.1%). There were 20 people (28.6%) diagnosed with either acute or chronic heart failure.

On physical examination, the average body mass index (BMI) was 24.1 (20.2-31.2) kg/m ^{2}. The basic ECG rhythm was dominated by sinus rhythm in 65 people (92.9%), followed by Atrial Fibrillation in 3 people (4.3%) and AV Block in 2 people (2.8%).

Based on laboratory tests, the median hemoglobin value was 13.5 g/dL (7.8-16.3), the median leukocyte value was 10.145 (5.15-21.77) thousand/ µL and the median platelet value was 266 (148-461) thousand/ µL. On renal function examination, the median urea was 29 (9-65) mg/dL and creatinine 0.93 (0.4-1.53) mg/dL. Electrolyte examination obtained a median sodium level of 135 (123-155) mEq/L, a median potassium level of 3.95 (3.1-5.7) mEq/L, and a median chloride level of 103.5 (86-110) mEq/L. Median value of fasting blood sugar (GDP) 118.5 (58-415) mg/dL, median value of 2 hours post prandial blood sugar (GD2JPP) 149 (68-473) mg/dL, median value of HbA1c 7 (5.1-13.5) %, mean total cholesterol value 180.74 ± 41.58 mg/dL, median triglyceride value 145 (75-445) mg/dL, mean HDL-C value 36.64 ± 10.48 mg/dL, mean LDL-C value 129.84 ± 32.80 mg/dL. The median Troponin I value was 2.8 (0.05-15) µ/mL and the median Apolipoprotein B value was 107 (32-150) mg/dL.

On angiography examination, it was found that 61 people (87.2%) had *multivessel disease*. Based on the SYNTAX score, the average was 25.66 ± 10.83. The measurement results of the SYNTAX score from the

results of the angiography are numerical data, measured 2 times by 2 experienced observers (interventional cardiologists).

Table 1. Characteristics of research subject data

Demographic Characteristics	n = 70
Gender, n (%)	
Man	50 (71.4)
Woman	20(28,6)
Age (years)	56 (38-77)
History of Hypertension, n (%)	
Yes	51(72,9)
No	19(27,1)
Smoking, n (%)	
Yes	34 (48.6)
No	36 (52.4)
DM Type 2, n (%)	
Yes	40 (57.1)
No	30 (42.9)
ECG, n (%)	
Rhythm sinus	65 (92.9)
Atrial Fibrillation	3 (4,3)
AV Block	2(2,8)
Angiography, n (%)	
Single vessel disease	9 (12,8)
Multivessel disease	61 (87.2)
Heart failure, n (%)	
Yes	20 (28.6)
No	50 (71.4)
BMI (kg/m ^{2})	24.1 (20.2-31.2)
Laboratory	
Apolipoprotein B (mg/dL)	107 (32-150)
Triglycerides (mg/dL)	145 (75-445)
HDL-C (mg/dL)	36.64 ± 10.48
LDL-C (mg/dL)	129.84 ± 32.80
Total cholesterol (mg/dL)	180.74 ± 41.58
HbA1C (%)	7 (5.1-13.4)
Fasting GD (mg/dL)	118.5 (58 - 415)
GD2PP (mg/dL)	149 (68 - 473)
Current GD (mg/dL)	140.5 (53 – 463)
Hemoglobin (g/dL)	13.5 (7.8 – 16.3)
Leukocytes (thousand/ μL)	10,145 (5,150 – 21,770)
Platelets (thousand/ μL)	266 (148 – 461)
Urea (mg/dL)	29 (9 - 65)
Creatinine (mg/dL)	0.93 (0.4 – 1.53)
Sodium (mg/dL)	135 (123 – 155)
Potassium (mg/dL)	3.95 (3.1 – 5.7)
Chloride (mg/dL)	103.5 (86 – 110)
Troponins (μ/mL)	2.8 (0.05 – 15)
SYNTAX score	25.66 ± 10.83

The interobserver reliability was assessed using the Bland-Altman test, and the difference in measurements between the two observers did not exceed 5, so the results obtained were quite reliable for the SYNTAX score (Figure 1).

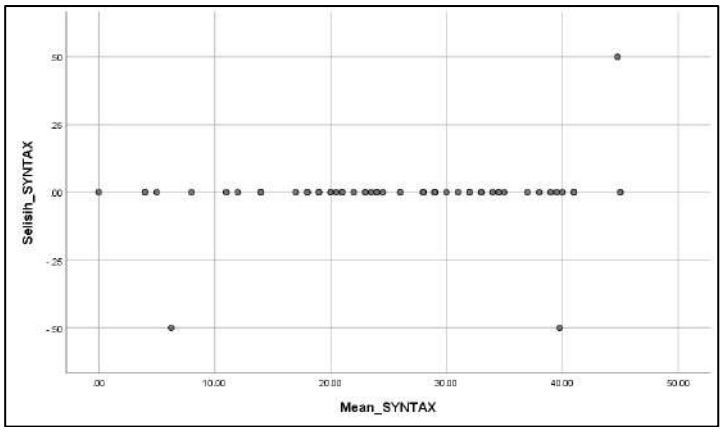

Figure 1. Graph of Bland-Altman SYNTAX scores on the intraobserver reliability test

Apolipoprotein B serum levels were validated through calibration with Lot No. 29006CH according to the recommendations of Abbott Laboratories. During the study, quality control of Apolipoprotein B examination was carried out 3 times with *quality control results* of ± 2 SD so that the study sample was considered controlled (Figure 2).

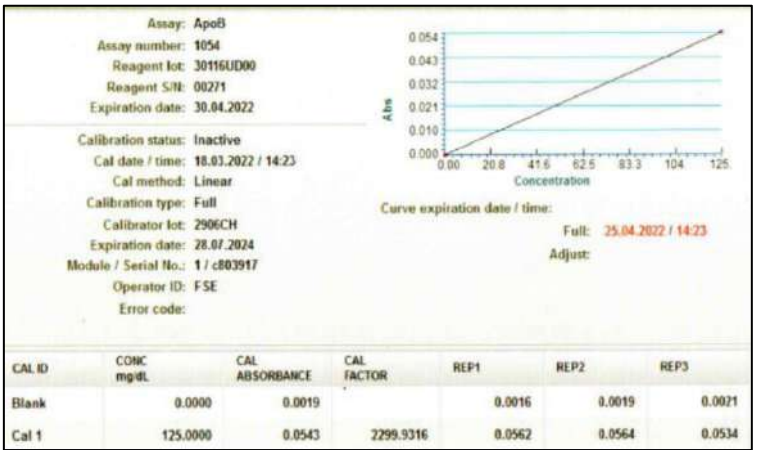

Figure 2. Calibration results on the Apolipoprotein B *assay*

Characteristics of Research Subjects Based on Coronary Lesion Severity

Group of patients with score SYNTAX ≥ 23 significantly had risk factors for Type 2 DM (p=0.046), with coronary angiography results of *multivessel disease* (p<0.001). The group of patients with a SYNTAX score ≥ 23 tended to have higher LDL-C values (p=0.029), higher HbA1C (p=0.013), higher fasting blood sugar levels (p=0.009), higher transient blood sugar levels (0.029), as well as higher levels of Apolipoprotein B (p<0.001) than the group of patients with a SYNTAX score <23. The data on the characteristics of the study subjects based on the severity of the coronary lesions are presented in table 2.

Relationship of Apolipoprotein B to coronary lesion severity

The results of the correlation analysis using the Spearman correlation test showed that there was a significant correlation between Apolipoprotein B and the SYNTAX score (p<0.001). The correlation value obtained is 0.442. Based on this correlation value, it can be concluded that there is a positive correlation between Apolipoprotein B levels and the SYNTAX score with a moderate strength level (r value> 0.6 – 0.8). The higher levels of Apolipoprotein B will be followed by an increase in the SYNTAX score (table 3 and figure 3).

Table 2. Characteristics research subject based on severity lesion coronary artery

Variable	SYNTAX score		p value
	< 23 (n=30)	≥23 (n=40)	
Gender, n (%)			
Man	24 (46)	26 (54)	0.338
Woman	6 (30)	14 (70)	
Age (years)	56 (42 – 77)	62 (38 -76)	0.026
History of Hypertension, n (%)	21 (41.2)	30(58.8)	0.358
Smoking, n (%)	17 (50)	17 (50)	0.541
DM Type 2, n (%)	12 (30)	28 (70)	0.046
ECG, n (%)			
Rhythm sinus	28 (41.5)	37 (58.5)	0.531
Atrial Fibrillation	1 (33.3)	2 (66.7)	
AV Block	1 (50)	1 (50)	
Angiography, n (%)			
Single vessel disease	9 (100)	0 (0)	<0.001
Multivessel disease	21 (34.4)	40 (65.6)	
Heart failure, n (%)			
Yes	6 (30)	13 (70)	0.214
No	24 (46)	27 (54)	
BMI (kg/m ^{2})	22.9 (20 – 30.4)	25.7 (20.7 – 31.2)	0.050
Laboratory			
Apolipoprotein B (mg/dL)	100 (32 – 123)	110 (67 – 150)	0.002
Triglycerides (mg/dL)	122 (75 – 259)	155 (78 – 445)	0.067
HDL-C (mg/dL)	35.38 ± 10.63	37.54 ± 10.42	0.400
LDL-C (mg/dL)	119.69 ± 38.27	137.02 ± 26.52	0.029
Total cholesterol (mg/dL)	171.79 ± 40.95	187.07 ± 41.35	0.131
HbA1C (%)	6.3 (5.3 – 10)	7.3 (5.1 – 13.4)	0.013
Fasting GD (mg/dL)	108 (58 – 216	126 (78 - 415)	0.009
GD2PP (mg/dL)	135 (86 – 473)	160 (68 – 328)	0.435
Current GD (mg/dL)	113 (75 – 463)	160 (53 -389)	0.029
Hemoglobin (g/dL)	13.4 (9 – 16.2)	13.8 (7.8 – 16.3)	0.995
Leukocytes (thousand/ μL)	10.15 (5.15 – 21.77)	10.14 (5.94 – 21.49)	0.770
Platelets (thousand/ μL)	245 (165 – 398)	276 (148 – 461)	0.147
Urea (mg/dL)	21 (13-30)	30 (18-65)	0.023
Creatinine (mg/dL)	0.9 (0.55 – 1.32)	0.97 (0.4 – 1.53)	0.520
Sodium (mg/dL)	135 (123 – 143)	135 (123 – 155)	0.986
Potassium (mg/dL)	3.8 (3.2 – 5.1)	4 (3.1 – 5.7)	0.607
Chloride (mg/dL)	105 (94 – 110)	103 (86 – 110)	0.266
Troponins (μ/mL)	2.59 (0.19 – 15)	4.15 (0.05 – 15)	0.434

Table 3. Correlation test of Apolipoprotein B levels with SYNTAX Score

	SYNTAX score
Apolipoprotein B	r = 0.442 p* < 0.001 n = 70

* Significant : p <0.05; Pearson correlation test

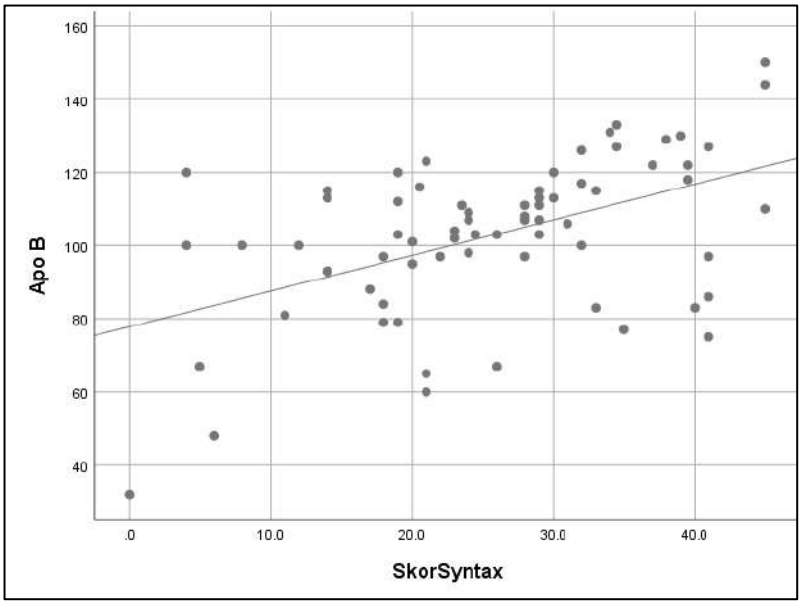

Figure 3. Scatterplot graph of the correlation of apolipoprotein B with the severity of coronary lesions based on the SYNTAX score

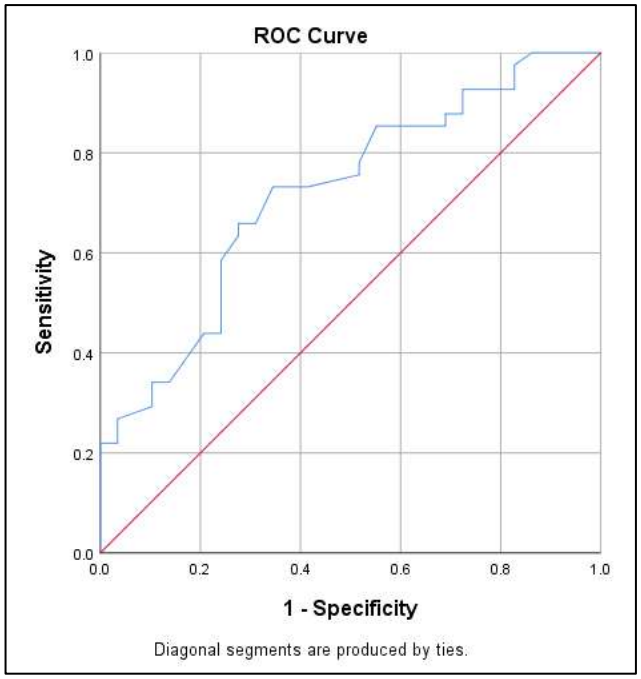

Figure 4. ROC curve for apolipoprotein B levels against the SYNTAX score

Accuracy of Apolipoprotein B in Predicting SYNTAX Scores

The results of the analysis using the ROC curve (Figure 4) showed that the AUC area of Apolipoprotein B levels in predicting the complexity of severe and intermediate degrees of angiography in IMANEST patients was 72%

with a p=0.002 with 95% CI 60% - 84%. It can be concluded that Apolipoprotein B levels can be used to predict the complexity of coronary angiography in IMANEST patients with a moderate level of ability (AUC > 70%).

Cut-off value of Apolipoprotein B levels for predicting angiographic complexity in IMANEST patients is 102.5 mg/dL with a sensitivity of 73.2% and a specificity of 65.5% (Table 4).

Table 4. *Cut-off* ROC analysis of ApoB on coronary lesion severity

Parameter	AUC	p value	*cut off*	Sensitivity	specificity
ApoB	72.0%	0.002	102.5	73.2%	65.5%

DISCUSSION

Disease cardiovascular still become reason main death in the world [1]. Disease heart coroner is marked pathological process with accumulation plaque atherosclerosis of the arteries epicardial , fine obstructive or non-obstructive, where one the subset is IMANEST [4]. A atherosclerosis is known is an inflammatory process initiated by lipids, which is one its components is apolipoprotein B.

Troponin I levels tend to more increase in the group with high SYNTAX scores (≥ 23) were compared group low SYNTAX score (<23) i.e. 4.15 (0.05 – 15) μ/mL vs 2.59 (0.19 – 15) μ/mL although no significant difference statistics (p=0.434). This study was in line with study conducted by Burak et al (2018) on 287 connecting AMI patients complexity lesion coroner with High-sensitivity Troponin T (Hs- TnT) where HsTnT correlated with SYNTAX score (r = 0.327, p<0.001). Multiple linear regression analysis on the study it also shows hs-TnT was an independent predictor of SYNTAX score in IMANEST patients (β = 0.317, p < 0.001) [16]. Atherosclerosis considered as an inflammatory process initiated by lipids. Height LDL-C and triglyceride levels and low low HDL-C levels considered is factor CAD risk [17].

Findings study similar with subject IMA research conducted by Hua et al, 2021. Researcher do studies in a manner cross sectional of 6956 CAD patients who will done PCI, then all subject study done Apo B examination and score Gensini. Study results they show there is significant relationship _ between Apo B and CAD and there is also significant relationship with score Gensini (p<0.001). Study Khadem Ansari et al (2009) in the Iranian population with CAD and non CAD patients performed screening angiography mention ApoB as factor independent risk for incidence of atherosclerosis in Iranian population (p<0.05) [18].

On the subject of IMA based a study conducted by Yaseen et al (2021) on 90 AMI patients was concluded apolipoprotein B levels correlated significant with severity lesion measured coronary with score Gensini (r = 0.32, p value <0.001) [19]. this study show consistency significant relationship and positive correlation between Apolipoprotein B levels with severity lesion assessed coroner with various modality score and a subset of the CAD population.

Studies composition plaque with modality virtual histology intravascular ultrasound VH-IVUS) in the population stable CAD study by Takayuki, et al identified connection meaning enhancement rate apoB to percentage necrotic core in the target coronary lesion (r=0.2353, p<0.0114). this support study advanced possibility apoB as a biomarker in unstable CAD populations [20].

Studies about Apolipoprotein B levels in CAD patients This is not the first time this has been done in Indonesia. Aswin Nurulita, et al have researching connection rate apolipoprotein B in the ACS population concluded enhancement ApoB in a manner meaning present in the IMA population (p<0.05) [15]. In the studies conducted with population population of Medan, Indonesia by Siallagan et al correlation significant between Apolipoprotein B and wide lesion coronary r = 0.288 (p=0.012). On study cut latitude the Siallagan et al included subject study whole good CAD patients stable CAD spectrum as well as IMA as well do calculation severity lesion use score Gensini . Findings more correlation strong on studies This suspected Because election subject more research specific to the CAD subset of the IMANEST type. Besides That use assessed SYNTAX score superior in comparison with score Gensini in evaluate severity coronary lesion [14].

More analysis deep in research This show ApoB show strength mark predictive currently For predict severity lesion kononer in IMANEST patients with (AUC 72% p=0.002; 95% CI 60-82%). Same result found in studies Lin et al (2018), obtained AUC = 0.741 ± 0.025; 95% CI: 0.694-0.783) [7].

Apolipoproteins are component important from lipoprotein particles, and measurement various apolipoprotein form increase predictor severity disease cardiovascular. Amount overall Apo B describes amount influential particles strong atherogenic in a manner independent related with PJK. Apo B works For stabilize and transport cholesterol and triglycerides, VLDL, IDL, LDL and sd -LDL in plasma. Excess particles containing Apo B constitute originator main atherogenic process. The plasma Apo B concentration is related strong with rate cholesterol non-HDL (non-HDL-C), given limitation as amount whole cholesterol minus HDL-C [17]. European Society of Cardiology/ European Atherosclerosis Society 2019 issued the guide says apoB more accurate in evaluate risk cardiovascular and can become guide in determine adequacy lipid therapy versus LDL-C or HDL-C [21,22].

Besides it , implies that monitoring ApoB related with pathology inflammation in CAD. A studies previously show that ApoB can predict vulnerability CAD plaque. ApoB also predicts level CAD severity, giving more Lots information prognostic than routine lipid profile. However, some study has answer that ApoB related with level severity disease coroner use complex and systemic approach score, that is, score Gensini or SYNTAX score. ApoB can too used For predict arterial stenosis severity coroner more accurate. The study by Yaseen et al, 2021 states high levels of apolipoprotein B have also been associated with risk of STEMI with OR 2.17 95% CI 38.2% -75.3% [23]. Use ApoB also has a number of advantage in CAD patients, eg non-invasive, is more simple, and more cheap compared to with angiography coroner. in the future inspection This can considered For a number of patient with contraindicated For angiography coroner nor CT Scan coronary artery [17].

CONCLUSION

There is a significant correlation between apoB and coronary lesion severity using SYNTAX scores in NSTEMI patients.

DECLARATIONS

Ethics approval and consent to participate. Permission for this study was obtained from the Ethics Committee of Universitas Sumatera Utara and H. Adam Malik General Hospital.

CONSENT FOR PUBLICATION

The Authors agree to publication in Journal of Society Medicine.

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COMPETING INTERESTS

None.

AUTHORS' CONTRIBUTIONS

All authors significantly contribute to the work reported, whether in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas. Contribute to drafting, revising, or critically reviewing the article. Approved the final version to be published, agreed on the journal to be submitted, and agreed to be accountable for all aspects of the work.

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