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Prevalence of elevated Lipoprotein (a) among young and middle-aged patients with acute coronary syndrome and its correlation with angiographic findings at Sulaimani Cardiac Hospital

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Abstract

Background and objectives: The relation of elevated lipoprotein (a) to severity of coronary artery disease is still debatable. This study was conducted to show the correlation between high levels of Lipoprotein (a) and severity of coronary artery disease.

Methods: This was a prospective longitudinal study, conducted at Sulaimani Cardiac Hospital in Sulaimani-Iraq, from March/2024 to June/2024. The sample consisted of 150 cases of acute coronary syndrome. The blood was sent for lipid profile, and patients were taken to the catheterization lab for further management. SYNTAX score was calculated to determine the correlation between coronary artery disease severity and SYNTAX score.

Results: Out of 150 participants, 115(76.7%) were males and 35(23.3%) were females. The mean age was 51.6±7.193, ranging from 25 to 59 years. There was a significant positive correlation between Lp (a) ≥ 126 nmol/L and SYNTAX score (p < o.oo1).Overall,30.6% of the cases (n= 46, 38 males and 8 females) had abnormal Lp (a) results (more than 75 nmol/L).Patients with highest lipoprotein(a) were more likely to be older (mean age = 56,27±5.22 , p = 0.03).There was a positive correlation between cases with positive family history and elevated lipoprotein(a)(p = 0.012).No statistically significant correlation was established among other risk factors(Diabetes, hypertension, smoking , lifestyle , previous angiography, ethnicity , and body mass index) and lipoprotein(a) level.

Conclusion: There was a statistically significant positive correlation between elevated Lp (a) and severity of coronary lesions assessed by SYNTAX score.

Keywords: Acute coronary syndrome, Coronary angiography, Lipoprotein (a), SYNTAX score

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Introduction

Coronary Artery Disease (CAD) is a chronic progressive disease characterized by the accumulation of atherogenic lipoproteins, inflammatory cells and fibrillary collagens in focal areas of arteries which results in formation and progression of atherosclerotic plaques. As plaques build up, the cause partial or complete obstruction to blood flow, which may lead to clinical manifestations like stable/ unstable angina or myocardial infarction.[1] It is proven that low density lipoprotein cholesterol (LDL-C) is one of the main factors which has role in progression of atherosclerosis, but evidence for new atherogenic lipoproteins is present. Lipoprotein (a) {Lp (a)} is a genetically determined lipoprotein which has an LDL-like structure linked to apolipoprotein (a) and apolipoprotein B-100.[2] The American Association of Clinical Endocrinologists/American College of Endocrinology specifically recommend that Lp(a) be measured in individuals of South Asian or African descent. The European Atherosclerosis Society/European Society of Cardiology and Canadian Cardiovascular Society recommend all adults be tested for elevated Lp(a) at least once in their lifetime.[3] Elevated Lp(a) level has been shown to cause increased cardiovascular risks in some studies during the last decade.[4] A recent study from China shows that elevated Lp(a) is associated with presence and elevated risk of CAD , especially in patients with familial hypercholesterolemia.[5] Plasma Lp(a) levels vary remarkably between individuals, with Lp(a) levels less than 30 mg/dl (less 65 nmol/L) is generally considered to be normal.[6] Approximately one in five individuals globally has levels more than 100 nmol/L.[2] One of the most widely used methods to assess severity and complexity of CAD, which was a significant issue cardiologists had in the past, is SYNTAX score. The SYNergy between the percutaneous coronary intervention (PCI) with Taxus and cardiac surgery (SYNTAX) score calculates the complexity of CAD based on invasive coronary angiography (ICA).[7] SYNTAX score is the sum of the points assigned to each individual lesion identified in the coronary tree with >50% narrowing in the diameter of the vessels that measure greater than 1.5 mm.[8] Coronary artery bypass grafting(CABG) remains the treatment of choice in patients with high (≥33) or intermediate (23-32) SYNTAX scores, whereas PCI is an acceptable option in patients with low SYNTAX score (≤22).[7] Our goals were to find out the relation between elevated lipoprotein (a) and complexity of coronary angiography lesions in patients with acute coronary syndrome using SYNTAX score.

Patients and methods

This prospective longitudinal study was conducted at Sulaimani Cardiac Hospital/Sulaimani city-Kurdistan region of Iraq/Iraq. It tried to find the correlation between high SYNTAX score and severity of coronary artery disease. Patient enrollment started after getting ethical approval letters/ research protocol approval from Ethical Committee/Directorate of Sulaimani and Kurdistan Higher Council of Medical Specialties with code 1362, dated 10-5-2024. Verbal consent was obtained from the patients. The total of 150 patients with acute coronary syndrome were enrolled. Direct

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interview was done by the investigator. Questions included age, gender, weight, height, diabetes mellitus, hypertension, history of cerebrovascular events, lifestyle, ethnicity, positive family history of premature coronary artery disease, previous coronary artery intervention, and drug history. After stabilizing the patients, blood was taken and sent to the lab to obtain the results of lipid profile (low density lipoprotein-LDL-, high density lipoprotein-HDL-, triglycerides-TG-, and cholesterol) and Lp(a). The study population was divided into three groups based on Lp(a): ≤ 75 nmol/L, 76-125 nmol/L, and ≥126 nmol/L. All the tests were carried out by the same lab so as to avoid inter-laboratory bias. Coronary angiogram was performed either emergently or within 24 hours after admission, by either radial or femoral approach. SYNTAX score was determined using the online calculator (http://www.syntaxscore.org) by two cardiologists, without being aware of Lp(a) results to keep the blindness of the procedure and the score. The population was divided into two groups based on results of SYNTAX score: SYNTAX ≤ 22 and SYNTAX ≥ 23.[9] Lastly, the correlation between SYNTAX score and severity of CAD was looked for (to see whether higher SYNTAX score meant more severe CAD on coronary angiography, or not).Data were analyzed using Statistical Package for Social Sciences (SPSS), version 26.Continuous variables were expressed as means± standard deviation and categorical variables were expressed as numbers. Categorical variables were compared using Chi-square test, and continuous variables were compared using Student t-test. Pearson's correlation was used to analyze the correlation between SYNTAX score and Lp(a). A p value of less than 0.05 was considered statistically significant.

Results

The study enrolled 150 cases of acute coronary syndrome; the age range of the participants was 25 to 59 years. The mean age was 51.6±7. 193.Males comprised 115 (76.7%) patients, and females comprised 35 (23.3%) patients of the study population. Majority of the patients belonged to age group 40-59 years (88%). The baseline demographic, biochemical and clinical characteristics of the study population stratified by SYNTAX score and Lp(a) are shown in tables (1) and (2) respectively. Patients with SYNTAX score ≥ 23 were more likely to: be older (mean 53.33±5.12), have higher BMI (mean 28.76±2.9), be smoker (n=66, 78% of all smokers), be diabetic (n=35, 76% of all diabetics), and have higher LDL-cholesterol (mean 123±36.1) (P = 0.05). NSTEMI comprised the most common presentation (38.7%) (P=0.002), followed by anterior STEMI (32.7%), (P=0.012), while unstable angina, lateral and inferior STEMI were not statistically significant. On the other hand, hypertension, positive family history, previous PCI, stroke and other lipid parameters were not significantly correlated with increased SYNTAX score. The mean Lp(a) was 61.3±74.85. Patients with Lp(a) ≥ 126 nmol/L were more likely to be older (mean age = 56.27±5.220, P value = 0.038). Out of the 150 cases, 30.6% of them (n= 46, 38 males and 8 females) had abnormal Lp(a) results (more than 75 nmol/L).There was a strong correlation between positive family history and Lp(a) ≥ 126nmol/L(50% of all cases with positive family history, n=18)(P

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value = 0.012),table(2).Regarding the correlation between lipid profiles and Lp(a), LDL was found to be more elevated(mean 129.1±40.2) among patients with Lp(a) ≥ 126 nmol/L (P value = 0.001).

Table (1): Clinical, demographic and biochemical risk factors related to SYNTAX score

Risk factors (n or mean)	Syntax ≤ 22	Syntax ≥23	p value
Age (years)	51.09±7.62	53.33±5.12	0.05
Gender			
Male	86	29	0.082
Female	31	4	0.05
BMI (kg/m2)	25.55±3.53	28.76±2.9	0.001
Smoking (current and past), n	18	66	0.031
Diabetes Mellitus	11	35	0.001
Hypertension	52	11	0.256
Stroke, n	9	1	0.346
Active life style	8	0	0.124
Positive family history	26	5	0.379
Previous PCI	23	3	0.159
Presentation			
Anterior STEMI	41	8	0.012
Inferior STEMI	23	9	0.156
Lateral STEMI	4	0	0.564
NSTEMI	44	14	0.002
Unstable angina	5	2	0.011
Drugs			
None	79	24	0.045
Aspirin	2	3	0.430
Statin	11	0	0.012
Clopidogrel	2	0	0.231
HDL (mg/dl)	43±10.52	39.9±8.84	0.234
LDL (mg/dl)	112±41.68	123±36.1	0.012
TG (mg/dl)	135±72.8	140±55	0.332
Cholesterol(mg/dl)	165±44.9	175±42.3	0.421

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Table (2): Clinical, demographic and biochemical data related to Lp(a)

Risk factors	Lipoprotein (a) nmol/L			p value
	≤75	76-125	≥126	
Age(years), mean	50.65±7.79	54.25±4.919	56.27±5.220	0.038
Gender				
Male	77	15	23	
Female	27	5	3	
BMI (kg/m2), mean	25.73±3.529	24.95±3.734	26.54±2.533	0.626
Smoking				
Current	46	9	13	
Ex-smokers	14	1	4	
Nonsmokers	44	10	9	
DM	37	0	9	0.353
HTN	42	10	11	0.708
Stroke	5	2	3	0.177
Active lifestyle	6	2	0	0.390
Ethnicity				0.195
Kurd	90	20	24	
Arab	13	0	2	
Others	1	0	0	
Positive family history	12	5	18	0.012
Previous PCI	19	4	3	0.205
Presentation				0.890
Anterior STEMI	34	10	5	
Inferior STEMI	21	2	9	
Lateral STEMI	3	0	1	
NSTEMI	41	8	9	
U/A	5	0	2	

It was found that majority of the patients had low SYNTAX score (n=117, 78%). The mean SYNTAX score of patients with Lp(a) ≥126 nmol/L was higher (22.5±6.725) compared to Lp (a) ≤ 125 nmol/L. Out of the 26 patients with Lp(a) ≥ 126 nmol/L, 16(61%) of them had SYNTAX score ≥ 23(P= 0.012), Table (3).

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Table (3): Correlation between Lp (a) and Syntax score

LP(a) Nmol/L (%)	Syntax ≤22 N, (%)	Syntax ≥23 N, (%)	p value
1-75(69)	94 (80.3)	10(30.3)	0.001
76-125(13)	13(11.1)	7(21.2)	0.002
≥126(18)	10(8.5)	16(48.5)	0.012

Univariate logistic regression analyses of Lp(a) ≥ 126 nmol/L showed an increase in the odds ratio for SYNTAX score ≥ 23(Odds Ratio = 1.8, 95% Confidence Interval 1.345-2.43), Figure (1).

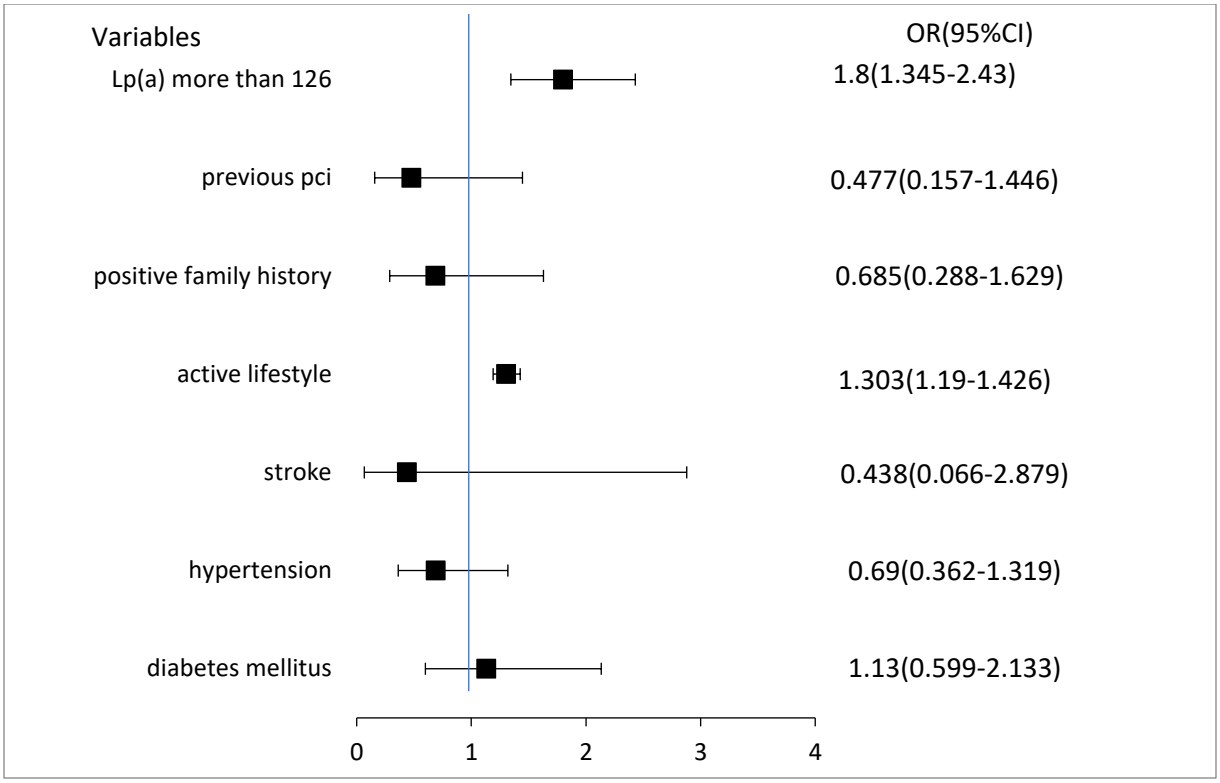

Figure (1): Univariate analysis showing effect of risk factors on SYNTAX score ≥ 23

Discussion

This study was conducted to determine the prevalence of Lp(a) among patients with ACS, and to see the relationship between elevated Lp(a) and severity of coronary lesions determined by SYNTAX score. Our study showed that the prevalence of elevated lipoprotein (a), (more than 75nmol/L), was 30.7% among hospitalized ACS patients , which is in alignment with other previous reports.[3-7] But in another study which was conducted in China, 20% of participants had elevated Lp(a).[10] While another study found Lp(a) was increased in the majority of participant (73.5%).[11] This could be explained by difference in sample size and ethnicity related normal variations. The current study revealed a correlation between Lp(a) and severity of CAD using SYNTAX score. Those patients with Lp(a) ≥ 126

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nmol/L showed more severe CAD (48.5% of patients with SYNTAX ≥ 23, n=16), as compared to those with Lp(a)≤ 126 nmol/L, this is consistent with the study done by Leistner, Bhandari And Xu, which showed patients with higher Lp(a) were more likely to have more severe CAD lesions.[2,4,12] On the other hand, another study found that elevated Lp(a) had no association to CAD severity.[13] These conflicting results might be due to different factors, for example, different population characteristics (age, sex, treatment), study design (cross sectional or not, follow up duration and sample size), assay method of Lp(a),and the fact that some of the patients were on statin therapy at the time of enrolment, although statins have inconclusive effect on Lp(a).[14] The current study showed that ACS patients with Lp(a) ≥ 126 nmol/L were older (mean age 56 years) than those with less Lp(a),which is similar to the results from another study done by Simony that revealed Lp(a) increased around the age of 50.[15] While another study done by Shah showed different results of elevated Lp(a) in favor of younger age groups (less than 50 years).[16] This difference can be due to larger sample size in their study (almost 70,000 cases) and the fact that they enrolled random individuals from the community, not hospital admissions like in our study. According to our study, there was no association between active lifestyle and Lp(a) level. This is in agreement with the previous study done by Mackinnon which did not show any impact on Lp(a) by daily physical activity.[17] The current study showed significantly higher Lp(a) in the group with highest LDL (mean 129.1 mg/dl), which is similar to the results of the study done by Xu that showed LDL more than 100 mg/dl were highly likely to be associated with elevated Lp(a).[10] Positive family history of premature CVD was significantly associated with elevated Lp(a), this goes with the results revealed by the study of Gulayin which concluded that one out of ten individuals with ACS and positive family history had elevated Lp(a).[18] Our study did not show any difference in the mean Lp(a) between diabetic and non-diabetic patients, and between those with hypertension and without hypertension. This was true for other previous studies, like the one which was conducted by Nasri, who found no statistically significant relation between those two and elevated Lp(a).[19] The current study showed higher mean age among patients with higher SYNTAX score (53.33± 5.12), this has been confirmed before by other studies.[20] In our study, diabetic patients and smokers were more likely to have higher syntax score Table (1), this is in agreement with the study done by Tofaha.[21] Although in our study the patients with SYNTAX score ≥ 23 were more likely to be overweight or obese Table (1), another study done by Nabati showed the opposite of this.[22] This diversity could be explained by the fact that while we only used BMI, they calculated waist circumference, waist to hip ratio and waist to height ratio in addition to BMI ,which could give more precise measures on body build.

Conclusion

This study revealed that Lp(a) is an independent predictor of CAD severity and that high Lp(a) level is associated with high SYNTAX score in young and middle-aged patients with ACS. Our study suggests that measuring Lp(a) may be particularly important as a screening biomarker to identify high risk patients susceptible for developing CAD.

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Conflict of interest

The authors recorded no conflict of interest.

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