Original Article

# Confounding Factors Responsible for Elevated Lp(a) Levels in Patients with Coronary Artery Disease

Navaneeth Amin, Tom Devasia, Shobha Ullas Kamath[1], Ganesh Paramasivam, Prasad Narayana Shetty, Ajit Singh[2], Ganesha N. S. Prakash

Departments of Cardiology, [1]Biochemistry, and [2]Medicine, Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Manipal, Karnataka, India

## ABSTRACT

**Background:** Cardiovascular diseases (CVDs) are a leading cause of global mortality, motivating research into novel approaches for their management. Lipoprotein(a) (Lp(a)), a unique lipoprotein particle, has been implicated in atherosclerosis and thrombosis, suggesting its potential as a therapeutic target for CVDs.

**Aim:** This study aimed to investigate the association of Lp(a) levels with various cardiovascular parameters and events among patients with confirmed cardiovascular disease.

**Methodology:** A prospective study was conducted, enrolling 600 participants, predominantly comprising males (79%), with a mean age of 52.78 ± 0.412 years diagnosed with cardiovascular disease. The follow-up was done for 18 months. Patient demographics, blood investigations, and occurrence of major adverse cardiac events (MACE) were collected. SPSS version 21 was used to statistically analyze the relationships between elevated Lp(a) levels and factors such as age, glycated hemoglobin, mortality, MACE, cardiac death, target vessel revascularization, and stroke.

**Results:** The study revealed significant ($P < 0.05$) associations between elevated Lp(a) levels and advanced age, increased glycated hemoglobin levels, as well as occurrences of all-cause mortality, MACE, cardiac death, target vessel revascularization, and stroke. Notably, a significant ($P < 0.05$), association between high Lp(a) levels and acute coronary syndrome (ACS) emerged, suggesting Lp(a)'s role in advanced cardiac events.

**Conclusion:** The findings highlight the potential significance of Lp(a) as a notable risk factor in cardiovascular health. The observed associations between elevated Lp(a) and adverse cardiovascular events, including ACS, underscore its pathogenic role. Consequently, this study supports the rationale for further research into Lp(a)-specific therapeutic interventions, offering substantial promise in refining the management strategies for cardiovascular diseases.

**Keywords:** Cardiovascular, coronary artery disease, lipoprotein(a), MACE

**Address for correspondence:** Dr. Tom Devasia, Department of Cardiology, Kasturba Medical College, Manipal Academy of Higher Education, Manipal, Karnataka, India.
E-mail: gt.cardiology@gmail.com

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## INTRODUCTION

Cardiovascular diseases (CVDs) remain to be the key contributor to global mortality and several kinds of disability. According to the World Health Organization, CVD-related deaths were estimated to be above 17.7 million in 2015, and the burden exceeds several billion dollars. The prevalence of CVD increased drastically over a decade.[1,2] There are currently no statistics available on the prevalence of CVD and the secular trends of CVD mortality in India. Three extensive prospective studies roughly predict that CVDs are responsible for a quarter of all deaths in India.[3]

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CVD has numerous underlying causes, some of which can be altered. Dyslipidaemia is a modifiable risk factor, defined as a lipid metabolic disorder marked up by an alteration in the plasma lipid fraction.[4] The elevated lipid profile is the major risk factor of atherosclerosis damaging both large and medium-sized arteries.[5] The deposition of plasma lipids within the blood vessel membrane induces a neighborhood inflammatory response and intensive vascular remodeling leading to the formation of plaques. Rupture or erosion of plaque causes infarction or stroke.[6,7] Public health organizations worldwide have been engrossed in reducing modifiable CVD risk factors to control its rising prevalence.[5]

The primary course for managing CVD includes lifestyle and diet modification, prescription drugs, and surgical procedures.[8] Several treatment methods have ascended to compensate for the current problems in managing CVD[9] Lipoprotein a (Lp(a)) (reported in 1963) is the novel target molecule to reduce cholesterol risk and is the novel approach in CVD management. It is a polymorphic Lp consisting of apoprotein B-100 binding with apolipoprotein(a) by a single disulfide bond.[9-11] Lp(a) is accompanied by inflammation and endothelial dysfunction of blood vessels.[12] Numerous investigations revealed Lp(a) as a sovereign predictor of atherosclerotic vascular disorders. Lp(a) serum levels are genetically determined and are unaffected by a person's lifestyle or use of statins. Due to this significant genetic significance, age, sex, and environmental factors have a negligible impact on Lp(a) levels. Hence Lp(a) can be used as the potential therapeutic target in the treatment of CVDs.[13-15] Despite these developments, it is still unknown which patient populations might most benefit from Lp(a) decrease and what level of Lp(a) lowering would be necessary to establish incremental clinical benefit despite background-established medicinal therapy. In the present, we assessed the prevalence and distribution of Lp(a) levels among patients with established CVD.

## METHODS

### Study population

We assessed 600 consecutive patients admitted under the Department of Cardiology, Kasturba Medical College, Manipal, Karnataka, India, after obtaining permission from the institutional ethics committee (IEC772/2019), Manipal Academy of Higher education, Manipal. The population selection was based on both inclusion and exclusion criteria. Patients above the age of 18 years with coronary artery disease are recruited and subjects already in clinical studies with investigational drugs, or psychiatric illnesses on medications, suffering from chronic liver disease, pregnant women, and terminal malignancy patients are excluded from the study.

### Demographic and laboratory parameters

The basic demographic parameters were noted: weight, BMI, height, waist and hip circumference, and waist-to-hip ratio. The essential clinical and biochemical variables like lipid profile, total protein, creatinine, HbA1c, TSH, NT-proBNP, and hemoglobin were evaluated.

### Major adverse cardiac events (MACE)

The subjects were keenly monitored to observe following cardiac events like cardiac death, non-fatal MI by ECG, ECHO, and Trop T, clinically driven target lesion revascularization, and target vessel revascularization by repeat coronary angiogram and repeat angioplasty report, stroke by clinical evaluation and CT-brain and lastly Stents thrombosis.

### Biomarker analysis

After signing informed consent, blood samples (2 ml) were obtained from the subjects. The lipoprotein(a) analysis is measured employing a particle-enhanced immunoturbidimetric technique (Roche Diagnostics) using cobas c 501 analyzers by Tina—quant lipoprotein(a) Gen. 2. Human Lp(a) agglutinates with latex particles layered with anti-Lp(a) antibodies. Turbidimetric analysis at 659 nm is utilized to show the precipitate level. Regarding Lp(a) values, recent studies have suggested a potential cutoff point, indicating that Lp(a) values exceeding 30 mg/dL might be associated with coronary artery disease.[16-18] Based on this insight, our study stratified participants into two groups: those with Lp(a) levels exceeding 30 mg/dL and those with levels below this threshold.

### Follow-up and assessment of compliance with medication

A total of 18 months of follow-up was carried out among the subjects. Simultaneously, all patients underwent telephonic follow-ups (typically every 6 months) for MACE, including death, evaluation of BMI, and other basic parameters. Correlation between Lp(a) and MACE rate on 18 months follow-up of patients with documented ASCVD on standard medical therapy, including statins, was recorded.

### Statistical analysis

Microsoft Excel and SPSS version 21 were used for data cleaning and statistical analysis. Categorical and continuous variables were reported in proportions and mean ± standard deviation (SD) for the socio-demographical parameters. Chi-square or $\chi 2$ test and *t*-test methods were used for

continuous and categorical variables, respectively. The statistical significance was determined at $P < 0.05$.

## RESULTS

### Demographic characteristics

A total of 600 patients were enrolled in this study. All patients were completely followed up. The mean SD age of patients is 52.78 ± 0.412, the male being the majority of the participants (79%). High LP(a) [≥30] appeared to be significantly increased among the subjects with tobacco users. Dyslipidaemia, thyroid dysfunction, diabetes, and CKD were non-significantly high in Lp(a) group with a concentration ≥30 mg/dL. Table 1 shows the frequency of demographic variables in the study subjects concerning the Lp(a) levels.

**Table 1: Demographic characteristics**

| Demographic variables | Lp(a) ≤30 | Lp(a) ≥30 | *P* |
|---|---|---|---|
| Sex, [Frequency *n* (%)] | | | |
| Male | 190 (31.7%) | 284 (47.3%) | 0.688 |
| Female | 53 (21.8%) | 73 (20.4%) | |
| BMI | | | |
| 1-underweight-BELOW 18.5 | 13 (2.2%) | 21 (3.5%) | 0.186 |
| 2-normal-18.5–24.9 | 123 (20.6%) | 205 (34.3%) | |
| 3-overweight-25–29.9 | 106 (17.8%) | 129 (21.6%) | |
| Family history of CVD | 69 (11.5%) | 127 (21.2%) | 0.066 |
| Smoking | 63 (10.5%) | 73 (12.2%) | 0.116 |
| Tobacco | 42 (9.3%) | 77 (11.2%) | 0.011* |
| Alcohol | 97 (16.2%) | 125 (20.8%) | 0.222 |
| Hypertension treated | 113 (18.9%) | 163 (27.2%) | 0.469 |
| DM diagnosed | 89 (14.8%) | 141 (23.5%) | 0.188 |
| Dyslipidaemia, | 144 (24.0%) | 206 (34.4%) | 0.272 |
| Thyroid dysfunction | 37 (6.2%) | 47 (7.9%) | 0.498 |
| CKD | 31 (5.2%) | 41 (6.8%) | 0.625 |

BMI=Body Mass index, CKD=Chronic kidney disease, CVD=Cardiovascular disease, DM=Diabetes mellitus, *=Significant

### Baseline characteristics, anthropometric, and laboratory measurements

Patients with older age have significantly high Lp(a). Similarly, the high Glycated hemoglobin (Gly Hb) level was significantly increased in Lp(a) [≥30] level. Table 2 represents the following characteristics below.

**Table 2: Baseline characteristics, anthropometric, laboratory measurements across different Lp(a) levels**

| Variables | Lp(a) ≤30 | Lp(a) ≥30 | *P* |
|---|---|---|---|
| Age | 54.29±8.687 | 51.75±10.843 | 0.002* |
| BMI | 24.269 3.7308 | 24.228±4.4819 | 0.905 |
| WC | 34.666±8.3641 | 34.436±8.1585 | 0.738 |
| HC | 37.018±11.8657 | 36.592±8.0131 | 0.600 |
| SBP | 128.523±20.7755 | 128.375±20.2967 | 0.931 |
| DBP | 80.108±11.6407 | 79.445±11.5738 | 0.494 |
| w H _ratio | 0.9520±0.0587 | 0.943±0.0741 | 0.148 |
| FBS (mg/dL) | 140.106±54.1989 | 146.362±59.7978 | 0.200 |
| Glyco_HB(%) | 6.674±1.5971 | 6.993±1.9418 | 0.035* |
| TC (mg/dL) | 186.773±54.6660 | 191.106±51.6029 | 0.325 |
| LDL (mg/dL) | 124.818±48.7507 | 128.381±46.0891 | 0.365 |
| HDL (mg/dL) | 39.872±10.4320 | 39.378±10.4701 | 0.571 |
| TG (mg/dL) | 155.302±80.6819 | 159.661±91.6145 | 0.549 |
| TC: HDL_ratio | 4.961±1.7558 | 5.082±1.5957 | 0.383 |
| VLDL (mg/dL) | 30.779±15.5477 | 31.469±16.7395 | 0.610 |
| Total protein (g/dL) | 7.133±0.777 | 7.5433±0.8632 | 0.062 |
| Creatinine (mg/dL) | 0.987±0.3061 | 0.995±0.6504 | 0.863 |
| TSH (mg/dL) | 2.968±3.3069 | 3.868±9.2393 | 0.146 |
| Hb (g/dL) | 13.983±2.0005 | 13.976±1.9719 | 0.963 |
| NT_proBNP (pg/dL) | 423 (129,1049) | 319 (66,828) | 0.109 |

*=Significant, BMI=Body mass index, WC=Waist Circumference, HC=Hip circumference, SBP=Systolic blood pressure, DBP=Diastolic blood pressure, w_H_ratio=Waist and Hip ratio, FBS=Fasting blood sugar, Gly_Hb=Glycated hemoglobin, TG=Triglycerides, LDL=Low density lipoprotein, HDL=High density lipoprotein=TC=Total cholesterol, VLDL=Very-low-density lipoprotein, TSH=Thyroid stimulating hormone, Hb=Hemoglobin, NT_proBNP=N-terminal pro b-type natriuretic peptide

### Correlation between Lp(a) levels and cardiac outcomes

The connection between Lp(a) levels and the occurrence of MACE in patients with the acute coronary syndrome was assessed. Upon analysis, we found that all-cause mortality, MACE, and Cardiac death were significantly high among patients with Lp(a) levels ≥30mg/dL. Similarly, target vessel revascularization and stroke were statistically significant among the high Lp(a) (≥30mg/dL) group. The table below shows the relation between cardiac outcome and Lp(a) levels Table 3.

## DISCUSSION

Lp(a) emerges as a fundamental factor in the initiation of coronary artery disease (CAD), actively contributing to its development. This investigation encompassed a cohort of 600 post-ACS patients, scrutinizing plasma Lp(a) levels primarily for their correlation with cardiovascular outcomes and all-cause mortality. Demographic analysis unveiled that plasma Lp(a) levels displayed no significant variance concerning gender, diverse BMI categories, or patients with prior CVD history. However, a noteworthy finding was that non-tobacco users exhibited significantly elevated Lp(a) levels. Correspondingly, Simony *et al.*'s study[19] also documented escalated Lp(a) levels in both genders, reinforcing this observation. Interestingly, their research established an age-related increase in Lp(a) levels, a finding that contrasts with the present study's outcomes. In our study, patients with an average age of 51.75 years exhibited a notably higher Lp(a) level, indicating a distinctive demographic pattern.

Generally, excessive alcohol consumption and smoking exert adverse impacts on lipid and lipoprotein profiles,[20] potentially fostering atherosclerosis and contributing to cardiovascular disease (CVD). In our investigation, Lp(a) levels were elevated, but not significant among individuals engaging in smoking and alcohol consumption. Multiple studies in the context of primary CAD prevention among

**Table 3: Lp(a) level and cardiac outcome**

| Variables | Lp(a) ≤30 | Lp(a) ≥30 | *P* |
|---|---|---|---|
| Cardiac death | 0 (0.0%) | 15 (2.5%) | 0.001* |
| Non-fatal MI | 10 (1.7%) | 21 (3.5%) | 0.279 |
| TLR | 1 (0.2%) | 6 (1.0%) | 0.140 |
| TVR | 3 (0.5%) | 18 (3.0%) | 0.010* |
| Stroke | 1 (0.2%) | 11 (1.8%) | 0.018* |
| All-cause mortality | 3 (0.5%) | 25 (4.2%) | 0.001* |
| MACE, | | | 0.000* |
| No MACE | 232 (38.6%) | 255 (42.4%) | |
| SCD | 18 (3.0%) | 96 (16.0%) | |

*=Significant, TVR=Tricuspid valve repair, TLR=Target Lesion Revascularization, MACE=Major adverse cardiac events, SCD=Sudden cardiac death, Non-Fatal MI=Non- fatal myocardial infarction

patients with chronic kidney disease (CKD) have indicated a correlation between high serum Lp(a) levels and augmented CVD risk.[21] Interestingly, our study also revealed elevated Lp(a) levels among most CKD patients. However, other research has produced conflicting outcomes, leaving the precise role of Lp(a) in heightened CVD risk within the CKD population uncertain.[22] While a predominant genetic influence suggests a possible slight impact of hypothyroidism on Lp(a) levels, the study by Lee *et al.*[23] did not unveil any notable distinction in Lp(a) levels concerning thyroid functions.

As lipid profiles are concerned, the results of our study showed a trend, though not significant, toward higher levels of Lp(a) in patients for TC, LDL, TG, TC, and HDL ratios. In the present study, a high level of Glycated Hb was present among patients with high Lp(a) levels. A contradictory result was observed in a study conducted that there was no correlation between Lp(a) level and glycated Hb ($P = 0.075$).[24]

In the present study, Lp(a) plasma levels were associated with cardiovascular and all-cause mortality, respectively. Patients with cardiac death, tricuspid valve repair, stroke, all-cause mortality, and MACE (Sudden cardiac death) were significantly high in the higher Lp(a) group. This was in accordance with the large pooled analysis conducted by Erqou *et al.*,[25] combining data from 126,634 study subjects from 32 prospective studies. The study analysis showed a significant association of Lp(a) with cardiovascular events, like cardiovascular death, myocardial infarction (MI), and stroke. The study also stated elevated Lp(a) levels of cardiovascular events. However, the statistical analysis conducted by Roth *et al.* on 1,245 subjects with CAD from observed no major significant association between Lp(a) and the jeopardy of cardiovascular events like MACE, which was defined as the composite of CV death, MI, or stroke.[26] Another investigation by Konishi *et al.* observed the frequency of cardiac death and ACS was significantly higher in the higher Lp(a) levels than in the lower Lp(a) group ($P = 0.03$).[27]

The study's key takeaway is that heightened Lp(a) values may correlate with increased occurrence of advanced cardiac events in ACS patients, thereby designating it as a notable risk factor for ACS. Promisingly, the realm of Lp(a)-specific therapeutic interventions, which notably target apolipoprotein(a) synthesis, has exhibited potential in reducing Lp(a) levels by a substantial 90%.[28] This underscores a fertile avenue for subsequent research, nurturing optimism for the management of ACS and other adverse cardiac events. In the event that a strategy centered around lowering Lp(a) is validated as effective, it will be of great interest to ascertain whether the benefits extend across varying baseline Lp(a) concentrations or if they are particularly pronounced with targeted reductions in Lp(a).

The major confines of this study are its a single-center study, and therefore the results have been confined to a single center. Additionally, because Lp(a) level fluctuates among different races, findings could not be generalized to other races or regions. It is well established that apo(a) size influences Lp(a) levels, with smaller sizes being linked to greater Lp(a) levels. In this investigation, there are no data on apo(a) size that could be the shortcoming of our findings.

## CONCLUSIONS

The present study interprets that there is an association of cardiovascular diseases with Lp(a) level; hence, a high level of Lp a is observed in advanced cardiac events among the patients. On this basis, high Lp(a) can be considered one of the significant risk factors for CVD. The study also sheds light on the scope for further research, which is mainly focusing on Lp(a)-specific lowering drugs. This could be a game changer in the treatment of CVD, as a reduction in Lp(a) could indirectly help in the management of coronary artery disease and other adverse cardiac events.

### Abbreviations

- ACS = Acute coronary syndrome.
- ASCVD = Atherosclerotic cardiovascular disease.
- BMI = Body mass index.
- CVD = Cardio vascular disease.
- CKD = Chronic kidney disease.
- HDL = High density lipoprotein.
- LDL = Low density lipoprotein.
- Lp(a) = Lipoprotein(a).
- MACE = Major adverse cardiac events.
- TC = Total cholesterol.
- TG = Triglycerides.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

## REFERENCES


1. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, *et al*. Global burden of cardiovascular diseases and risk factors, 1990-2019: Update from the GBD 2019 study. J Am Coll Cardiol 2020;76:2982-3021.
2. Dunbar SB, Khavjou OA, Bakas T, Hunt G, Kirch RA, Leib AR, *et al*. Projected costs of informal caregiving for cardiovascular disease: 2015 to 2035: A policy statement from the American heart association. Circulation 2018;137:e558-77.
3. Prabhakaran D, Jeemon P, Roy A. Cardiovascular diseases in India: Current epidemiology and future directions. Circulation 2016;133:1605-20.
4. Ariyanti R, Besral B. Dyslipidemia associated with hypertension increases the risks for coronary heart disease: A case-control study in Harapan Kita Hospital, National cardiovascular center, Jakarta. J Lipids 2019;2019:2517013.
5. Hedayatnia M, Asadi Z, Zare-Feyzabadi R, Yaghooti-Khorasani M, Ghazizadeh H, Ghaffarian-Zirak R, *et al*. Dyslipidemia and cardiovascular disease risk among the MASHAD study population. Lipids Health Dis 2020;19:42.
6. Spagnoli LG, Bonanno E, Sangiorgi G, Mauriello A. Role of inflammation in atherosclerosis. J Nucl Med 2007;48:1800-15.
7. Luo X, Lv Y, Bai X, Qi J, Weng X, Liu S, *et al*. Plaque erosion: A distinctive pathological mechanism of acute coronary syndrome. Front Cardiovasc Med 2021;8:711453.
8. Chandra KS, Sarat Chandra K, Bansal M, Nair T, Iyengar SS, Gupta R, *et al*. Consensus statement on management of dyslipidemia in Indian subjects. Indian Heart J 2014;66(Suppl 4):S1-51.
9. Jang AY, Lim S, Jo S-H, Han SH, Koh KK. New trends in dyslipidemia treatment. Circ J 2021;85:759-68.
10. Berg K. A new serum type system in man-the LP system. Acta Pathol Microbiol Scand 1963;59:369-82.
11. Lamon-Fava S, Diffenderfer MR, Marcovina SM. Lipoprotein(a) metabolism. Curr Opin Lipidol 2014;25:189-93.
12. Ference BA, Ginsberg HN, Graham I, Ray KK, Packard CJ, Bruckert E, *et al*. Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel. Eur Heart J 2017;38:2459-72.
13. Puri R, Nissen SE, Arsenault BJ, St John J, Riesmeyer JS, Ruotolo G, *et al*. Effect of C-reactive protein on Lipoprotein(a)-associated cardiovascular risk in optimally treated patients with high-risk vascular disease: A prespecified secondary analysis of the ACCELERATE trial. JAMA Cardiol 2020;5:1136-43.
14. Gurdasani D, Sjouke B, Tsimikas S, Kees Hovingh G, Luben RN, Wainwright NWJ, *et al*. Lipoprotein(a) and risk of coronary, cerebrovascular, and peripheral artery disease. Arterioscler Thromb Vasc Biol 2012;32:3058-65.
15. Khera AV, Everett BM, Caulfield MP, Hantash FM, Wohlgemuth J, Ridker PM, *et al*. Response to letter regarding article, "Lipoprotein(a) concentrations, rosuvastatin therapy, and residual vascular risk: An analysis from the JUPITER trial (justification for the use of statins in prevention: An intervention trial evaluating rosuvastatin)". Circulation 2014;129:635-42.
16. Adults I. Chinese guideline for the management of dyslipidemia in adults. Zhonghua Xin Xue Guan Bing Za Zhi 2016;44:833-53.
17. Zhu L, Zheng J, Gao B, Jin X, He Y, Zhou L, *et al*. The correlation between lipoprotein(a) elevations and the risk of recurrent cardiovascular events in CAD patients with different LDL-C levels. BMC Cardiovasc Disord 2022;22:171.
18. Cui K, Yin D, Zhu C, Yuan S, Wu S, Feng L, Dou K. Impact of Lipoprotein(a) concentrations on long-term cardiovascular outcomes in patients undergoing percutaneous coronary intervention: A large cohort study. Nutr Metab Cardiovasc Dis 2022;32:1670-80.
19. Simony SB, Mortensen MB, Langsted A, Afzal S, Kamstrup PR, Nordestgaard BG. Sex differences of lipoprotein(a) levels and associated risk of morbidity and mortality by age: The Copenhagen general population study. Atherosclerosis 2022;355:76-82.
20. Wu DM, Pai L, Sun PK, Hsu LL, Sun CA. Joint effects of alcohol consumption and cigarette smoking on atherogenic lipid and lipoprotein profiles: Results from a study of Chinese male population in Taiwan. Eur J Epidemiol 2001;17:629-35.
21. Kovesdy CP, Astor BC, Longenecker JC, Coresh J. Association of kidney function with serum lipoprotein(a) level: The third national health and nutrition examination survey (1991-1994). Am J Kidney Dis 2002;40:899-908.
22. Shlipak MG, Fried LF, Cushman M, Manolio TA, Peterson D, Stehman-Breen C, *et al*. Cardiovascular mortality risk in chronic kidney disease: Comparison of traditional and novel risk factors. JAMA 2005;293:1737-45.
23. Lee W-Y, Suh J-Y, Rhee E-J, Park J-S, Sung K-C, Kim S-W. Plasma CRP, apolipoprotein A-1, apolipoprotein B and Lp(a) levels according to thyroid function status. Arch Med Res 2004;35:540-5.
24. Xuejin C, Chunmei Q, Lele W, Mei SH, Yu WJ, Dan FX, *et al*. The relationship between Lipoprotein a and glycosylated hemoglobin and the degree of coronary artery stenosis in non-diabetic coronary heart disease patients. Biomed J Sci Techn Res 2019; 21:15992-7.
25. Emerging Risk Factors Collaboration; Erqou S, Kaptoge S, Perry PL, Di Angelantonio E, Thompson A, *et al*. Lipoprotein(a) concentration and the risk of coronary heart disease, stroke, and nonvascular mortality. JAMA 2009;302:412-23.
26. Roth C, Krychtiuk K, Gangl C, Schrutka L, Distelmaier K, Wojta J, *et al*. Lipoprotein(a) plasma levels are not associated with survival after acute coronary syndromes: An observational cohort study. PLoS ONE, 2020. doi: 10.1371/journal.pone.0227054.
27. Konishi H, Miyauchi K, Shitara J, Endo H, Wada H, Doi S, *et al*. Impact of Lipoprotein(a) on long-term outcomes in patients with diabetes mellitus who underwent percutaneous coronary intervention. Am J Cardiol 2016;118:1781-5.
28. Vavuranakis MA, Jones SR, Cardoso R, Gerstenblith G, Leucker TM. The role of Lipoprotein(a) in cardiovascular disease: Current concepts and future perspectives. Hellenic J Cardiol 2020;61:398-403.