International Journal of Advanced Research in Medicine

E-ISSN: 2706-9575
P-ISSN: 2706-9567
www.medicinepaper.net
IJARM 2023; 5(4): 45-49
Received: 09-09-2023
Accepted: 17-10-2023

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The study of serum lipoprotein (a) levels in patients with angiographically proved in CAD

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DOI: https://doi.org/10.22271/27069567.2023.v5.i4a.544

Abstract
Aim: To study the levels of serum Lipoprotein (a) in patients with angiographically proven coronary artery disease.
Methodology: This is a Cross-sectional, Hospital based study conducted at Medicover Hospital which is a tertiary care center situated in the capital of Telangana, Hyderabad. The study was conducted after obtaining approval from scientific and ethical committee of the hospital. Written and informed consent taken from all the patients and from the next of kin if the patient clinically not in a position to give consent. Study population includes patients admitted to Medicover Hospital MICU, ICCU, who are full filling the inclusion and exclusion criteria are included in our study.
Results: Lipoprotein (a) levels were higher in younger age group (≤ 55 years).Lipoprotein (a) levels were higher in patients with family history of coronary artery disease. Lipoprotein (a) levels were higher in patients with elevated LDL levels. Serum Lipoprotein (a) levels correlate directly with angiographic evidence of extent and severity of coronary artery disease. Lipoprotein (a) levels were higher in Triple vessel and Double vessel disease. Lipoprotein (a) is an emerging risk factor for coronary artery disease. There is no significant difference in Mean Lp (a) levels among Diabetics and Non Diabetics.
Conclusion: Lp (a) is associated with occurrence and extent of coronary stenosis we suggest that it should be screened in all young individuals with coronary artery disease without risk factors, familial hypercholesterolemia, family history of premature cardiovascular disease and/or elevated Lp (a), and individuals with recurrent cardiovascular disease. Lp (a) should be measured routinely in the coronary risk profile assessment of high-risk patients.

Keywords: Lp(a), Diabetics, Coronary Artery, Hypercholesteromia, Angiographic

1. Introduction
The 20th century saw unparalleled increases in life expectancy and a major shift in the cause of illness and death throughout the world. During this transition cardiovascular diseases became the most common cause of death worldwide. Driven by industrialization, urbanization and associated life style changes this ongoing transition is occurring around the world among all races, ethnic groups and cultures at an even faster rate than last century. Hypertension, high cholesterol, overweight and obesity, smoking, low fruit and vegetable intake, and physical inactivity were the leading contributors to ischemic heart disease and stroke burden worldwide [1]. Current predictions have estimated that cardiovascular diseases will be the leading global cause of total disease burden [2].
Atherogenesis occurs over a period of many decades. The growth of atherosclerotic plaques occurs discontinuously. Clinically atherosclerosis may be chronic, as in the development of stable, effort-induced angina pectoris. Alternatively, a dramatic acute clinical event, such as myocardial infarction or sudden cardiac death, may first herald the presence of atherosclerosis.
Accumulation of leukocytes characterizes the formation of early atherosclerotic lesions. Thus, from its very inception, atherogenesis involves elements of inflammation, a process that now provides a unifying theme in the pathogenesis of this disease. Once resident within the intima, the mononuclear phagocytes mature into macrophages and become lipid-laden foam cells, a conversion that requires the uptake of lipoprotein particles by receptor-mediated endocytosis. The arrival of smooth-muscle cells and their elaboration of extracellular matrix probably provides a critical transition, yielding a fibro fatty lesion in

place of a simple accumulation of macrophage-derived foam cells. As they advance, atherosclerotic plaques also accumulate calcium [3]. During the evolution of the atherosclerotic plaque, a complex balance between entry and egress of lipoproteins and leukocytes, cell proliferation and cell death, extracellular matrix production and remodeling as well as calcification and neovascularization contribute to the atherosclerotic lesion formation.

Lipoprotein (a) is a crucial risk factor for premature atherosclerosis [4]. It remains an important and multiplicative risk factor. The risk is markedly increased in patients with hypertension, diabetes, low HDL-C, high LDL-C and hyperhomocystinemia. In advanced atherosclerosis, Lp (a) is an independent risk factor not dependent on LDL. Also studies have shown positive correlation with the levels of Lipoprotein (a) and angiographic extent of coronary artery disease. So this study is undertaken to know the levels of serum lipoprotein (a) in patients presenting with a spectrum of angiographically proven coronary artery disease and correlate with the angiographic extent of lesion and compare with other known prognostic variables.

Aims and Objectives

1. To study the levels of serum Lipoprotein (a) in patients with angiographically proven coronary artery disease.
2. To compare the levels of serum Lipoprotein (a) in following groups of patients

a) Patients with single vessel, double vessel and triple vessel disease.
b) < 55 years age group and > 55 years age group.
c) Patients with and without family history of coronary artery disease.
d) Patients with normal and abnormal lipid profile.
e) Patients who are Diabetics and Non Diabetics.
f) Patients who are Smokers and Non Smokers.
g) Patients who are Hypertensives and Non Hypertensives.

Materials and Methods

Study Site: This is a Cross-sectional, Hospital based study conducted at Medicover Hospital which is a tertiary care center situated in the capital of Telengana, Hyderabad. The study was conducted after obtaining approval from scientific and ethical committee of the hospital. Written and informed consent taken from all the patients and from the next of kin if the patient clinically not in a position to give consent.

Study Population

Study population includes patients admitted to Medicover Hospital MICU, ICCU, who are full filling the inclusion and exclusion criteria are included in our study.

Inclusion criteria

1. Patients with angiographically proven coronary artery disease.
2. Patients who has given informed consent.

Exclusion criteria

1. Patients with insignificant coronary artery disease as defined by angiographic extent of the lesion.
2. (Significant stenosis: > 50% in Left main coronary artery and >70% in other vessels by Quantitative Coronary Analysis)
3. Patients with evidence of concomitant infection, neoplasm.
4. Patients with renal failure.
5. Patients on statins.
6. Patient who did not give informed consent.

Study Design: Cross-sectional, Hospital based study.

Sample size: The sample size is calculated depending on the previous study and the case load in the hospital with a power of 80% to detect a difference at the 95% confidence interval, considering a Type I error (α) of 5% and Type II error (β) of 20% Power of the study, the sample size is 100.

Study Duration: 18 months**,** May 1st 2018 to October 31st 2019.

Methodology

This study included 100 patients admitted in General Medicine and Cardiology Departments with a spectrum of coronary artery disease and undergoing coronary angiography. After admission, for all patients, complete clinical data (history of risk factors) was taken and physical examination was performed. Routine investigations including complete blood picture, complete urine examination, random blood sugar, lipid profile, ECG, Chest Radiograph, 2D Echo was done. Coronary angiography was performed in our cath lab. If the angiography is suggestive of significant lesion (Significant stenosis: > 50% in Left main coronary artery and >70% in other vessels by Quantitative Coronary Analysis) then Serum Lp (a) estimation was performed using quantitative latex-enhanced immunoturbidimetric test using Human Lp (a) kit.

Statistical Analysis

Data was entered in Microsoft excel and analysis was done using SPSS version 20. Descriptive statistical analysis was also done. Results on continuous measurements was presented as Mean & Standard Deviation. Results on categorical measurements was presented as Percentages. Significance was assessed at 5% level of significance.

Student t test (independent, two tailed) was used to find out the significance of study parameters on a continuous scale between two groups. ANOVA was used to find out the significance of study parameters on a continuous scale between three groups.

Observations and Results

The study entitled "The study of serum lipoprotein (a) levels in patients with angiographically Proven Coronary artery disease" is an institutional based cross sectional study and was conducted in the department of internal medicine and cardiology, Medicover hospitals, Hyderabad from 1st May 2018 to 31st October 2019.

Age Distribution

- Patients ≤ 55 years constituted 80 of the study group and 20 patients were >55 years.
- Of the 80 patients aged ≤ 55 years the mean Lipoprotein (a) level was 33±6.22 mg/d1.
- Of the 20 patients aged > 55 years was 29.20±4.37 mg/dl.
- The ≤ 55 years age group patients had a statistically significant rise in mean Lipoprotein(a) levels compared to patients aged >55 years (p = 0.012).

Table 2: Age distribution

Age	Number of patients	Mean lipoprotein (a) level (mg/dl)
≤ 55 yrs.	80	33±6.22
> 55 yrs.	20	29.20±4.37

Sex distribution of patients

In our study Males constituted 57 patients and Females constituted 43 patients.

The mean Lipoprotein (a) level among males was 33.68±6.61 mg/dl.

The mean Lipoprotein (a) level among females was 31.65±5.29 mg/dl.

There was no statistically significant difference among mean Lipoprotein (a) levels between males and female (P = 0.403).

Table 3: Sex distribution of patients

Sex	Number of patients	Mean of lipoprotein (a)
Male	57	33.68±6.61
Female	43	31.65±5.29

Mean LP (a) levels in hypertensives and non hypertensives

Of the 100 patients 35 patients were Hypertensives and 65 patients were Non Hypertensives.

The mean Lipoprotein (a) levels among Hypertensives was 33.60±5.75 mg/dl.

The mean Lipoprotein (a) levels among Non Hypertensives was 31.51±6.16 mg/dl.

There was no statistically significant difference in mean Lipoprotein (a) levels between Hypertensive and Non Hypertensive (p = 0.101).

Table 4: Mean LP (a) levels in hypertensives and non hypertensives

HTN vs Non-HTN	Number of patients	Mean lipoprotein (a) levels (mg/dl)
HTN	35	33.60±5.75
Non-HTN	65	31.51±6.16

Mean LP (a) Levels in Diabetics and Non Diabetic

- Of the 100 patients 19 were Diabetic and 81 patients Non Diabetic.
- The mean Lipoprotein (a) level among Diabetics was 34.16±6.09mg/ dl.
- The mean Lipoprotein (a) level among Non-Diabetics was 31.79±6.01mg/ dl.
- There was no statistically significant difference among mean Lipoprotein (a) levels between Diabetic and Non Diabetic patients (p = 0.127).

Table 5: Mean Lp (a) levels in diabetics and non-diabetics

Diabetes	Number of patients	Mean lipoprotein (a) levels (mg/dl)
Diabetic	19	3.16±6.09
Non-diabetic	81	31.79±6.01

Mean LP (a) levels in smokers and non-smokers

- Of the 100 patients 33 were Smokers and 67 were Non Smokers.
- The mean Lipoprotein (a) level among Smokers was 33.91±6.34 mg/ dl.
- The mean Lipoprotein (a) level among Non-Smokers was 31.42±5.80 mg/dl.
- There was no statistically significant difference among mean Lipoprotein (a) levels among Smokers and Non Smokers (p value = 0.053).

Table 6: Mean Lp (a) levels in smokers and non-smokers

Smoking	No. of patients	Mean lipoprotein (a) levels (mg/dl)
Smoker	33	33.91±6.34
Non-smoker	67	31.42±5.80

Mean LP (a) levels in patients with positive and negative family history of cad

- Of the 100 patients. 51 had Family history of CAD and 49 had no Family history of CAD.
- The mean Lipoprotein (a) level among patients who had Family history of CAD was 33.98±6.02 mg/dl.
- The mean Lipoprotein (a) level among patients without Family history of CAD was 30.43±5.63 mg/dl.
- There was statistically significant difference among mean Lipoprotein (a) level between patients with Family History of CAD and without Family history of CAD (p = 0.010).

Table 7: Mean Lp (a) levels in patients with positive and negative family history of CAD

Family history of CAD	No. of patients	Mean lipoprotein (a) levels (mg/dl)
Positive FH	51	33.98±6.02
Negative FH	49	30.43±5.63

Mean LP (a) levels in comparision with HDL levels

- Of the 100 patients 20 had HDL level ≤ 35 mg/dl and 80 had > 35 mg/dl.
- The mean Lipoprotein (a) level among patients with HDL ≤ 35 mg/dl was 34.35 ± 4.557mg/dl.
- The mean Lipoprotein (a) level among patients with HDL > 35 mg/dl was 31.71 ± 6.311 mg/dl.
- There is no statistically significant difference among mean Lipoprotein (a) levels between patients with HDL ≤35 mg/dl and patients with HDL > 35 mg/dl (p = 0.082).

Table 8: Mean Lp (a) levels in comparision with HDL levels

HDL (mg/dl)	No. of patients	Mean lipoprotein (a) levels (mg/dl)
≤35	20	34.35±4.557
>35	80	31.71±6.311

Mean levels of LP (a) in comparision with LDL levels

- Of the 100 patients 51 had LDL level ≤ 130 mg/dl and 49 had LDL level > 130 mg/dl.
- The mean Lipoprotein (a) level among patients with LDL level ≤ 130 mg/dL30.75±5.26 was mg/dl.
- The mean Lipoprotein (a) level among patients with LDL level > 130 mg/dl was 33.80±6.51 mg/dl.
- There was a statistically significant difference among Lipoprotein (a) level between patients with LDL level ≤ 130 mg/dl and with LDL level > 130 mg/dl (p = 0.011).

Table 9: Mean levels of Lp (a) in comparison with LDL levels

LDL (mg/dl)	No. of patients	Mean lipoprotein (a) levels (mg/dl)
≤130	51	30.75±5.26
>130	49	33.80±6.51

Mean lipoprotein (a) levels in comparision with extent of angiographic lesion

- Out of the 100 patients included in our study 62 of patients had evidence of Single vessel disease.
- The mean Lipoprotein (a) level among patients with Single vessel disease was 28.94±4.31 mg/dl.
- 29 of patients had evidence of Double vessel disease.
- The mean Lipoprotein (a) level among the patients with Double vessel disease was 36.24±3.75 mg/dl.
- 9 of the patients included in the study had evidence of Triple vessel disease.
- The mean Lipoprotein (a) level among the patients with Triple vessel was 42.11±3.55 mg/ dl.
- There was statistically significant association between the levels of Lipoprotein (a) and the angiographic extent of coronary artery disease (P <0.001).

Table 10: Mean lipoprotein (a) levels in comparison with extent of angiographic lesion

Extent of angiographic	Number of patients	Mean lipoprotein (a) levels (mg/dl)
Single vessel disease	62	28.94±4.31
Double vessel disease	29	36.24±3.75
Triple vessel disease	9	42.11±4.55

Discussion

Coronary artery disease is emerging as a global health problem assuming epidemic proportions worldwide, particularly in the Indian subcontinent. The age of onset in the Indian population is younger compared to the population in the west? The other aspect is the high incidence of Coronary artery disease in patients without conventional risk factors. Thus there is a need to investigate and identify the role of novel and emerging risk factors like Lipoprotein (a), which according to various studies has been proven to have an important role.

We conducted a study at our hospital to assess the levels of Lp (a) in patients with angiographically proven CAD. We initially included 150 patients in our study but 50 patients were excluded based on exclusion criteria and finally 100 patients were included in the study. After admission, for all patients, complete clinical data (history of risk factors) and physical examination was performed. Routine investigations including complete blood picture, complete urine examination, random blood sugar, lipid profile, ECG, Chest Radiograph, 2D Echo were done. Coronary angiography was performed in our cath lab and the angiography is suggestive of significant lesion i.e. Significant stenosis: > 50% in Left main coronary artery and >70% in other vessels by Quantitative Coronary Analysis, then Serum Lp(a) estimation was performed using quantitative latex-enhanced immune turbidimetric test using Human Lp(a) kit. The various risk factors and the mean lipoprotein (a) levels among these patients was assessed. The mean lipoprotein (a) levels and the angiographic extent of lesion was assessed.

We divided patients into two categories based on age i.e. ≤55 years and >55 years because risk, which appears to be limited to premature vascular disease, due to elevated lipoprotein (a) levels is strongest before age 45, declines after age 55, and often disappears after age 65. In our study patients ≤55years constituted 80 of the study group and >55years constituted 20 of the study group. The mean Lp(a) levels in patients aged ≤55 years is 33mg/dl and in patients aged >55 years is 29 mg/dl. Patients with age ≤55 years has a statistically significant rise in mean Lp (a) levels when compared to patients with age>55years (p= 0.012).

Isser HS, *et al*. conducted a study toassess lipoprotein (a) levels in 50 consecutive young North Indian patients (age less than 45 years) with myocardial infarctionand age and sex-matched controls (n=50, mean age 34+/-6.9 years). ELISA technique was used to estimate the Lipoprotein (a) levels using preformed antibodies. They found the mean lipoprotein (a) level was 22.28+5.4 mg/dl in patients and 9.28+22.59 mg/dl in controls. The Lp(a) levels were significantly higher in young patients with myocardial infarction when compared with control(p<0.001 for patients controls). They concluded that high lipoprotein (a) levels is an important risk factors for coronary artery disease in the younger population [5].

The findings in our study is in concordance with findings of other studies as mentioned above. Of the 100 patients included in our study, Males constituted 57 of the study group and females constituted 43 of the study group. The Mean Lp(a) levels in Males is 33mg/dl and in females is 31mg/dl. We found no statistically significant difference among Mean Lipoprotein a levels between males and females (p=0.403).

Of the 100 patients included in our study, 35 patients were Hypertensive and 65 patients were Non Hypertensive. The Mean Lp(a) Levels in Hypertensive is 33mg/dl and Non Hypertensive is 31mg/dl. We found no statistically significant difference among Mean Lipoprotein a levels between Hypertensives and Non Hypertensives (p=0.101).

Haffner *et al*. conducted a study in which they compared the plasma concentrations of Lp(a) in Type2 diabetic patients (n = 260) and non-diabetic subjects (n = 336) who participated in a population-based study (San Antonio Heart Study). Lp(a) was measured using a monoclonal anti-Lp(a) antibody. They found that Type 2 diabetic patients and non-diabetic subjects had similar Lp(a) concentrations for both men and women (P = 0.361). They found that there is no statistically significant difference in lipoprotein(a) level in diabetics [6]. Which is concordance with findings of our study.

Of the 100 patients included in our study, 51 had family history of CAD and 49 had no family history. The Mean Lp(a) levels among patients who had family history of CAD was 33mg/dl. The Mean Lp(a) levels among patients without family history of CAD was 30mg/dl. We found statistically significant difference in Mean Lp(a) levels between patients with family History of CAD and without family History of CAD (p=0.010).The findings in our study were concordance with the above conclusion.

Of the 100 patients included in our study, Smokers were 33 and Non-smokers were 67. The Mean Lp(a) Levels in smokers is 33mg/dl and Non-smokers is 31mg/dl. We found no statistically significant difference between Mean Lipoprotein a levels among Smokers and Non Smokers (p=0.053).

Of the 100 patients included in our study, 20 patients had HDL level ≤35 mg/dl and 80 had > 35 mg/dl.

The Mean Lp(a) level among patients with HDL ≤ 35 mg/dl was 34 mg/dl. The Mean Lp(a) level among patients with HDL > 35 mg/dl was 31 mg/dl. We found, there is no statistically significant difference among Mean Lp(a) level between patients with HDL ≤ 35 mg/dl and patients with HDL > 35 mg/dl (P value= 0.082).

Stephen *et al*. conducted a study to know the relationship between serum Lp(a) levels and both the extent of angiographic disease and 3-year incidence of major adverse cardiovascular events(MACE). They found a relationship between Lp(a) levels and cardiovascular outcome in patients with an LDL cholesterol (LDL) >100 mg/dl (P = 0.02), but not in LDL cholesterol levels <70 mg/dl (P = 0.77) [7].

Luc G *et al*. conducted PRIME study which is a prospective cohort study to known the association of an elevated level of lipoprotein (a) (Lp(a)) with the development of coronary heart disease (CHD). Lp(a) levels were analyzed. They found that Lp(a) was a significant risk factor (P<0.0006) among CHD patients. They alsofound a significant interaction between Lp(a) and LDL-cholesterol levels, high Lp(a) levels were in patients with high levels of LDL-cholesterol [8].

Habib *et al*. conducted a study in patients with angiographically defined coronary artery disease and to see lipoprotein (a) relationship with its severity and diffuseness. They conducted a cross sectional study in 147 patients with coronary artery disease and 49 healthy individuals matched for age and body mass index. They found thatcoronary artery disease patients had higher Lp(a) levels than controls (25.78 +/- 25.09 mg/dl versus 14.57 +/- 11.81 mg/dl, p=0.0030). Patients without stenosis and one vessel involvement had significantly lower levels of Lp(a) compared to double and triple vessel disease. They concluded that Lipoprotein (a) levels are significantly higher with CAD compared to healthy individuals, and are associated with more severe and diffuse blockage of the coronary vessels [9].

Conclusions

Lp(a) is associated with occurrence and extent of coronary stenosis we suggest that it should be screened in all young individuals with coronary artery disease without risk factors, familial hypercholesterolemia, family history of premature cardiovascular disease and/or elevated Lp(a), and individuals with recurrent cardiovascular disease. Lp(a) should be measured routinely in the coronary risk profile assessment of high-risk patients.

Limitations

1. Our study was conducted at a tertiary care center in south India hence results cannot be generalized to all population.
2. Our study was a single center study with a small sample of medical ICU and ICCU population therefore results may not be generalized.
3. We had enrolled only symptomatic patients of CAD referred for coronary angiography and had not included the entire spectrum of CAD patients. Hence the Lp(a) levels assessed in our study may not be representative of all patients with CAD.

Conflict of Interest

None.

Funding Support

Nil.

References

1. Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJ. Global Burden of Disease and Risk Factors. 2006.
2. Shivkar RR, Abhang SA. Ratio Of Serum Asymmetric Dimethyl Arginine (ADMA)/ Nitric Oxide in Coronary Artery Disease patients. J Clin Diagn Res. 2014;8(8):CC04–6.
3. Stocker R, Keaney JF. Role of oxidative modifications in atherosclerosis. Physiol Rev. 2004;84(4):1381–478.
4. Yusuf J, Yadav N, Mukhopadhyay S, Goyal A, Mehta V, Trehan V, *et al*. Relook at lipoprotein (A): independent risk factor of coronary artery disease in north Indian population. Indian Heart J. 2014;66(3):272–9.
5. Isser HS, Puri VK, Narain VS, Saran RK, Dwivedi SK, Singh S. Lipoprotein (a) and lipid levels in young patients with myocardial infarction and their first-degree relatives. Indian Heart J. 2001;53(4):463–6.
6. Haffner SM, Morales PA, Stern MP, Gruber MK. Lp(a) concentrations in NIDDM. Diabetes. 1992;41(10):1267–72.
7. Nicholls SJ, Tang WHW, Scoffone H, Brennan DM, Hartiala J, Allayee H, *et al*. Lipoprotein(a) levels and long-term cardiovascular risk in the contemporary era of statin therapy. J Lipid Res. 2010;51(10):3055–61.
8. Luc G, Bard J-M, Arveiler D, Ferrieres J, Evans A, Amouyel P, *et al*. Lipoprotein (a) as a predictor of coronary heart disease: the PRIME Study. Atherosclerosis. 2002;163(2):377-84.
9. Habib SS, Abdel-Gader AM, Kurdi MI, Al-Aseri Z, Soliman MM. Lipoproteina(a) is a feature of the presence, diffuseness, and severity of coronary artery disease in Saudi population. Saudi Med J. 2009;30(3):346–52.

How to Cite This Article

Khan MIGA, Aslam M, Koushik N. The study of serum lipoprotein (a) levels in patients with angiographically proved in CAD. International Journal of Advanced Research in Medicine. 2023;5(2):45-49.