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# Lp(a) as a Cardiovascular Risk Predictor: Current Status In North Indian Population

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***Abstract***
***Background:*** *Coronary Artery Disease (CAD) is the leading cause of death in India, its contribution to mortality is rising. Conventional risk factors do not entirely account for the severity and prevalence of this disease thus, necessitating the need to search for newer risk factors.*
***Aims:*** *To find out the relevance of Lp(a), Ratio Lp(a)/HDL-C & Ratio Lp(a)/apoA-1 as a predictor of CAD in the north Indian population.*
***Methods:*** *CAD patients of either sex with a history of acute chest pain with the diagnosis of STEMI, NSTEMI, unstable and stable angina, examined and treated at advanced cardiac centre, PGIMER, Chandigarh were enrolled in the present study. Fifty age and sex matched healthy controls were selected. Patients with diabetes mellitus, nephrotic syndrome, acute or chronic renal failure, thyroid disorders, acute infection or any other systemic illness and on lipid lowering drugs for the past 3 months were excluded from the present study. Blood samples were analyzed for serum total Cholesterol, triglycerides, HDL-C, LDL-C, Lp(a) and serum apolipoprotein A-1. Ratios of Lp(a)/HDL-C and Lp(a)/apoA-1 were calculated.*
***Statistical Analysis:*** *Independent samples t-test was used to calculate difference between the two means. Areas under receiver operating characteristic curve (ROC) were evaluated as a measure of diagnostic accuracy.*
***Results:*** *The CAD patients had significantly higher levels of Lp(a), Lp(a)/HDL-C and Lp(a)/apoA-1 as compared to control group.*
***Conclusion:*** *They may serve as valuable predictive markers for assessing cardiovascular risk in north Indian population.*
***Keywords****: Coronary Artery Disease, Lp(a), North Indian Population, Ratio Lp(a)/apo A-1, Ratio Lp(a)/HDL-C,*

## I. Introduction

Coronary Artery Disease (CAD) is one of the most common causes of mortality and morbidity in both developed and developing countries and proposed to be the number one killer in the next decade [1]. It is the foremost cause of death in India, its contribution to mortality is rising, the number of deaths due to CAD in 1985 is expected to have doubled by 2015 [2]. Classic risk factors for predicting cardiovascular risk show wide variations across the globe. These however have failed to validate the surge of increased risk of CAD in more than 60% of Asian and Indian population, hence paving the way for efforts endeavouring to identify newer risk factors like lipoprotein (a), apolipoproteins and homocysteine etc. [3]. Various studies on overseas Indians have revealed that Lp(a) is an imperative risk factor for CAD [4]. Studies substantiating relationship between Lp(a) and CAD have shown incongruous results but majority of them observed higher levels of Lp(a) in cases than in controls [5-8]. Lipoprotein (a) levels have found to correlate with early as well as advanced atherosclerosis and also with the progression and severity of the disease. It further increases the risk of premature CAD many fold depending on the presence or absence of allied risk factors [9]. Globalization and automation are leading to epidemic transition of the Indian population. Study of Lp(a) will help in the recognising the risk factors associated with the malevolent nature of CAD in Indian population. Moreover, estimating Lp(a) levels in different populations can help in recognition of the high risk group requiring intensive treatment [10-11]. Hence the present study was undertaken to find out the relevance of Lp(a), Ratio Lp(a)/HDL-C & Ratio Lp(a)/apoA-1 as a predictor of CAD in the population of North India.

## II. Methods

Subjects, from November 2010 to August 2013, a total of 110 patients (aged 20-60 years, mean age 41.01± 9.20) of coronary heart disease of either sex with a history of acute chest pain with the diagnosis of STEMI, NSTEMI, unstable and stable angina, examined and treated at advanced cardiac centre, PGIMER,

Chandigarh were enrolled in the present study. Fifty age and sex matched healthy controls (mean age 33±10.32 years) were selected. Patients with diabetes mellitus, nephrotic syndrome, acute or chronic renal failure, thyroid disorders, acute infection or any other systemic illness and on lipid lowering drugs for the past 3 months were excluded from the present study. Regular tobacco, alcohol abusers and smokers were also excluded. The institutional Ethical Committee approved the study and informed consent was taken from all the participants. The patient's demographic profile, socioeconomic status, behavioural and disease risk factor histories were recorded. Fasting venous blood samples were collected and analyzed by using enzymatic procedures with Johnson & Johnson's Vitros 250 auto analyzer for serum total Cholesterol, triglycerides, HDL-C and LDL-C by direct assay. Serum apolipoprotein A-1 estimation was carried out in NEPHSTAR (PROTEIN ANALYSIS SYSTEM) and Lp(a) was determined by latex enhanced immunoturbidimetric method. Ratios of Lp(a)/HDL-C and Lp(a)/Apo A-1 were calculated.

**Statistical analysis*:*** Results were presented as mean ± standard deviation. The unpaired't' test was used to compare the levels of the test and control group. P value <0.05 was taken as significant. Area under receiver operating characteristic curve (ROC) was calculated. The area under the ROC curve was considered a global performance indicator for a prognostic factor [12]. Greater AUC of the ROC curve indicated better markers of the study. Sensitivity and specificity were calculated at a particular cut off point to predict the usefulness of each marker in CAD patients. All statistical analysis was performed using SPSS version 20.

## III. Results

The study population included 110 patients of CAD in the age group of 20-60 years, of which (41%) were in age group of 30-40 years and 33% were in the 40-50years of age group. This shows early occurrence of CAD in younger age. Majority of the CAD patients (65%) were found to have sedentary life style. The demographic characteristics of the study population are shown in **[Table 1]**.

Table 1: Demographic Characteristics of CAD patients and Controls

| | | **CAD (n=110) No. (%)** | **Controls (n=50) No. (%)** | **P Value** |
|---|---|---|---|---|
| Age (years) | **< 40** | **54(49.1)** | **40(80)** | **P<0.001** |
| | **≥ 40** | **56(50.9)** | **10(20)** | |
| Sex | **Male** | **81(73.6)** | **26(52.0)** | **P=0.007** |
| | **Female** | **29(26.4)** | **24(48.0)** | |
| BMI | **< 25** | **44(40.0)** | **32(64.0)** | **P=0.005** |
| | **≥ 25** | **66(66.0)** | **18(36.0)** | |
| Sedentary life Style | **Yes** | **72(65.5)** | **11(22.0)** | **P<0.001** |
| | **No** | **38(34.5)** | **39(78.0)** | |
| Diet | **Veg** | **45(40.9)** | **23(46.0)** | **P=0.55** |
| | **Non-Veg** | **65(59.1)** | **27(54.0)** | |
| Drinker | **Yes** | **21(19.1)** | **1(2.0)** | **P=0.002** |
| | **No** | **89(80.9)** | **49(98.0)** | |
| F/H DM | **Yes** | **49(44.5)** | **28(56.0)** | **P=0.18** |
| | **No** | **61(55.5)** | **22(44.0)** | |
| F/H CHD | **Yes** | **52(47.3)** | **21(42.0)** | **P=0.53** |
| | **No** | **58(52.7)** | **29(58.0)** | |

A significant difference was observed between the Lp(a), Ratio Lp(a)/HDL-C and Ratio Lp(a)/apo-A1 levels of CAD patients and control (p<0.001) as shown in **[Table 2]** **and** **[Figure 1,2 & 3 respectively].** The CAD patients had significantly higher levels Lp(a), Lp(a)/HDL-C & Lp(a)/apoA-1 as compared to control group.

Table 2: Biochemical Characteristics of CAD Patients and Controls

| | **CAD** | **Controls** | **p value** |
|---|---|---|---|
| | **Mean ± SD** | **Mean ± SD** | |
| TC | 199.49±54.14 | 152.54±29.62 | <0.001 |
| LDL-C | 132.4±48.88 | 91±25.3 | <0.001 |
| HDL-C | 40.28±8.43 | 45.3±6.37 | <0.001 |
| TG | 189.89±87.25 | 97.78±30.05 | <0.001 |
| apoA-1 | 1.29±0.29 | 1.41±0.34 | <0.05 |
| Lp(a) | 24.07±7.84 | 15.29±4.93 | <0.001 |
| Lp(a)/HDL-C | 0.62±0.24 | 0.35±0.13 | <0.001 |
| Lp(a)/apoA-1 | 19.55±8 | 11.18±3.86 | <0.001 |

TC; total cholesterol, LDL-C; low density lipoprotein cholesterol; HDL-C; high density lipoprotein cholesterol; TG; Serum Triglycerides, apoA-1; apolipoprotein A1, Lp(a); lipoprotein (a).

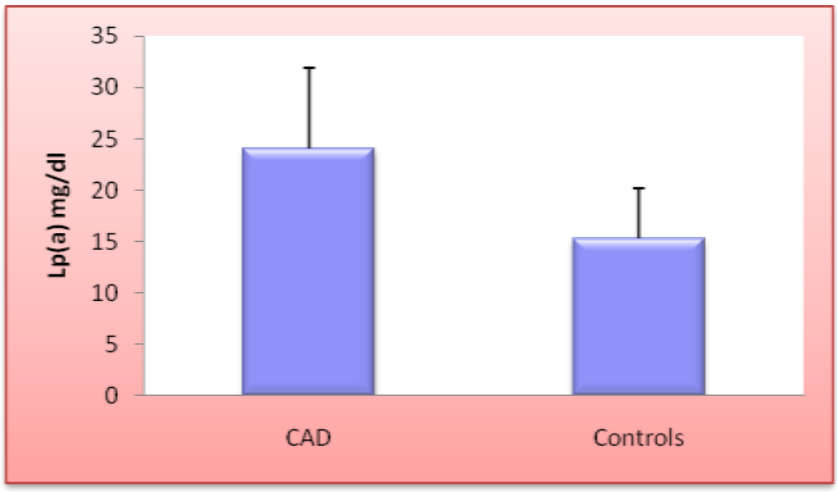


**Figure1: Lp(a) levels in CAD and Control group**

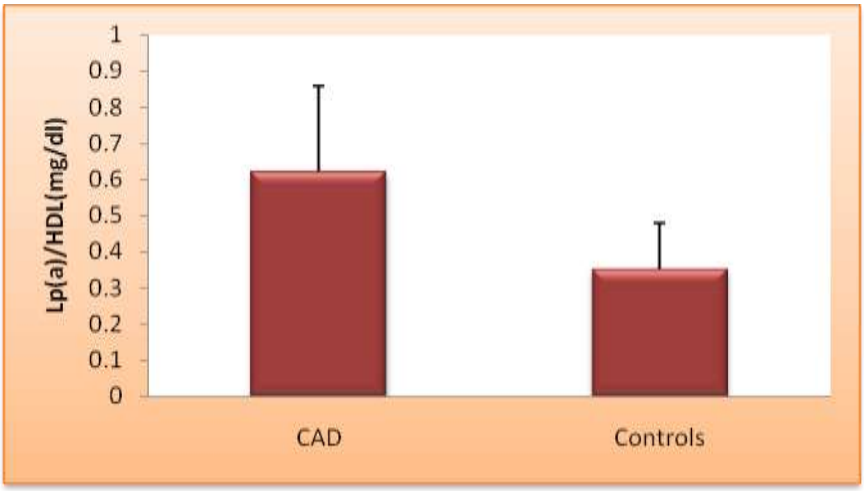


**Figure 2: Ratio Lp(a)/HDL-C in CAD and control group**

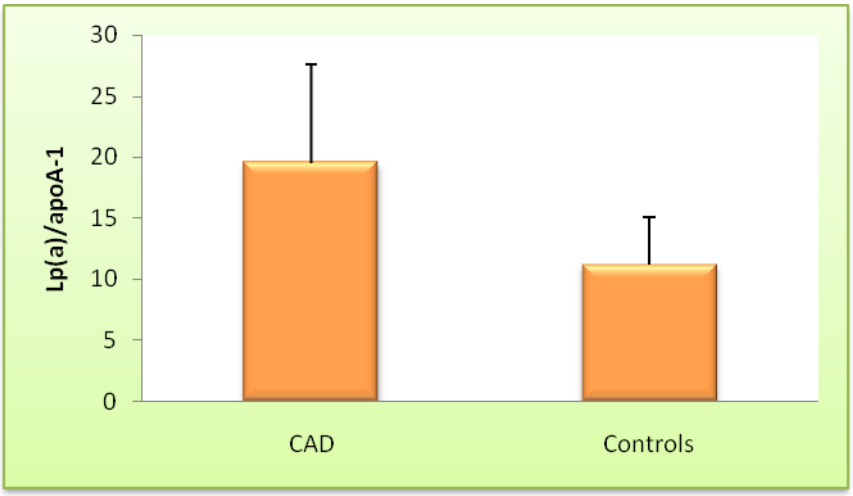


**Figure 3: Ratio Lp(a)/apoA-1 levels in CAD and control group**

AUROC was > 0.7 for all the three parameters, thus suggesting that these parameters can be used to evaluate risk of CAD in Indian population **[Figure 4]**. Sensitivity and specificity of each parameter at a particular cut off point has been shown **[Table 3]**.

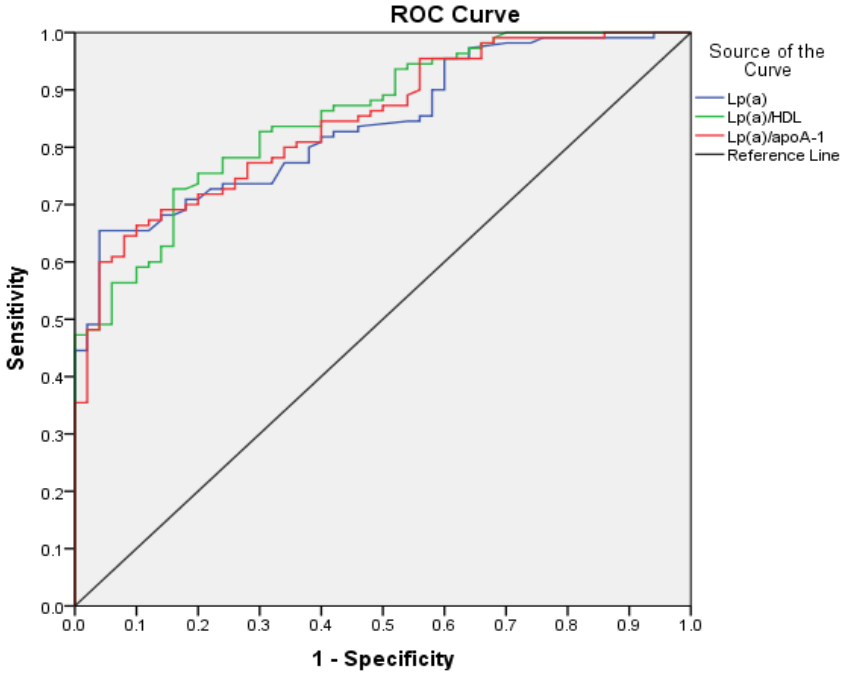


**Figure 4:** Receiver Operating Characteristic Curve for Lp(a), Ratio Lp(a)/HDL-C & RatioLp(a)/apoA-1

**Table 3:** Lp(a), Ratio Lp(a)/HDL & RatioLp(a)/apoA-1 as a screening tests in CAD patients

| Variable(s) | Area | Sensitivity | Specificity | Cut off value | p-value |
|---|---|---|---|---|---|
| **Lp(a)** | 0.839 | 0.736 | 0.740 | 19.15 | p< 0.001 |
| **Lp(a)/HDL** | 0.856 | 0.764 | 0.760 | 0.450 | p< 0.001 |
| **Lp(a)/apoA-1** | 0.847 | 0.745 | 0.740 | 13.66 | p< 0.001 |

## IV. Discussion

The present study evaluated the significance of Lp(a), Ratio Lp(a)/HDL-C & Ratio Lp(a)/apoA-1 in CAD patients. The levels of these biomarkers were found to be significantly higher in the CAD patients as compared to the controls. Conventional risk factors for cardiovascular disease have been ineffective in completely predicting the progression of atherosclerosis. In the present study 65% of the patients were found to have sedentary life style. There is evidence for an association between greater sedentary behaviour and an increased cardiovascular risk [13, 14]. Significantly higher mean levels of Lp(a) were observed in patients than in controls (P<0.01) which is in agreement with earlier studies conducted in India and abroad [15-16]. Vashisht et al [17] in 1992 were the first to demonstrate the presence of elevated Lp(a) in patients of CAD from North India. Since then, only few small studies have been conducted from North India which have shown the association of Lp(a) with CAD [4-5,7,18-20].

The median level observed in our study is 23 mg/dl where as blacks and Asian Indians showed the median levels of 22mg/dl and 16mg/dl respectively [21,22]. The cut off value observed in our study is 19mg/dl with the specificity and sensitivity of 74% and 73.6% respectively, which is consistent with the studies conducted by Rajashekhar et al [23] and Enans et al [6] who suggested the cut off level of 25mg/dl and 20mg/dl respectively to determine the risk of CAD. Hoogeveen RC et al [24] had proposed a cut off value of Lp(a) of >19 mg/dl on a study in 103 North Indian subjects (57 cases and 46 controls). Similar findings have been also observed by Vandana et al [25], who observed 82% specificity and 70% sensitivity. Based on our observations we suggests that in addition to conventional lipid profile, estimation of Lp(a) can prove to be a valuable tool in cardiovascular risk assessment of subjects with multiple risk factors for CAD as has been recommended by The European Atherosclerosis Society [26] and The National Lipid Association [27].

We also calculated the Ratios of Lp(a)/HDL and Lp(a)/apoA-1 and the results were found to be highly significant. The cut off value for Ratio Lp(a)/HDL was found to be 0.45 with 76% specificity and 76% sensitivity, and for Ratio Lp(a)/apo A-1 cut off value was 13.66 with 74% specificity and 74.5% sensitivity. So far, to best of our knowledge, no study has reported the predictive value of these ratios in CAD patients. More studies from different areas with larger sample size are required to confirm the present findings.

## V. Conclusion

The levels of Lp(a), Ratio Lp(a)/HDL-C and Ratio Lp(a)/apoA-1 are significantly elevated in CAD patients as compared to controls. Thus, they may serve as valuable predictive markers for assessing cardiovascular risk in Indian population.

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## References

[1]. Reddy KS. Cardiovascular disease in India. Wld. Hlth. Stat. Q. 1993; 46:101-107.
[2]. Misra A, Nigam P, Hills AP et al. Consensus physical activity guidelines for Asian Indians. Diabetes Technol Ther 2012; 14:83-98.
[3]. Sekhri T, Kanwar RS, Wilfred R, et al. Prevalence of risk factors for coronary artery disease in an urban Indian population. BMJ Open 2014; 4:e005346.
[4]. Gambhir JK, Harsimrut K, Gambhir DS and Prabhu KM. Lipoprotein (a) as an independent risk factor for Coronary artery disease in patients below 40 years of age. Ind. Heart. J 2000; 52: 411-415.
[5]. Gupta R, Vasisht S, Bahl VK, and Wasir HS. Correlation of lipoprotein[a] to angiographically defined coronary artery disease in Indians. Int. J. Cardiol.1996; 57: 265-270.
[6]. Enas EA, and Senthilkumar A. Role of Lipoprotein (a): Reality and Relevance. In:Gambhir, D. (ed.) Cardiology Update. CSI, New Delhi 2002; 8-25.
[7]. Geethanjali FS, Jose VJ and Kanagasabapathy. Lipoprotein (a) phenotypes in South Indian patients with coronary artery disease. Ind. Heart. J 2002; 54:50-53.
[8]. Mohan V, Deepa R, Harnath, SP et al. Lipoprotein(a) is an independent risk factor for Coronary artery disease in NIDDM patients in South India. Diab. Care1998; 2: 1819-1823.
[9]. Hopkins PN, Wu LL, Hunt SC, James BC, Vincent GM and Williams RR. Lipoprotein (a) interactions with lipid and nonlipid risk factors in early familial coronary artery disease. Arterioscler. Thromb. Vasc. Biol 1997; 17: 2783-2792.
[10]. Dahlen, GH, Srinivasan SR, Stenlund H, Wattingney WA, Wall S and Berenson GS. The importance of serum lipoprotein(a) as an independent risk factor for premature coronary artery disease in middle-aged black and white women from the United States. J. Intern. Med 1998; 244: 417-424.
[11]. Wang XL, Cranney G and Wilcken DE. Lp[a] and conventional risk profiles predict the severity of coronary stenosis in high-risk hospital-based patients. Aust. N Z. J. Med. 2000; 30: 333-338. 1655-1658.
[12]. Greiner, M.,D.Pfeiffer, and R.D. Smith.Principles and practical application of the receiver-operating characteristic analysis for diagnostic tests. Prev. Vet. Med.45: 23-41.
[13]. Proper KI, Singh AS, VAN Mechelen W, et al. Sedentary behaviours and health outcomes among adults: a systematic review of prospective studies. American journal of preventive medicine 2011; 40(2):174-82.
[14]. Henson J, Yates T, Biddle SJ et al. Associations of objectively measured sedentary behaviours and physical activity with markers of cardiometabolic health. Diabetologia 2013; 56(5):1012-20.
[15]. Bolibar T, Thompson SG, Von Eckardstein A, Sandkamp M. and Assmann G. Dose response relationship of serum lipid measurement with the extent of coronary stenosis, strong, independent and comprehensive, ECAT Angina pectoris study Group. Arterioscler. Thromb. Vas. Biol 1995; 15, 1035-1042.
[16]. Miwa K. and Nakagawa K. Risk factors that discriminate high risk from low risk.Jap. Cir. J 2000; 64: 825-830.
[17]. Vashisht S, Wasir HS, Srivastava LM. Association between incidence of lipoprotein positivity and coronary heart disease. Ind Heart J. 1992; 44:223e226.
[18]. Gupta R, Kastia S, Rastogi S, et al. Lipoprotein (a) in Coronary heart disease: a case - control study. Ind Heart J. 2000; 52:407e410.
[19]. Vashisht S, Gulati R, Srivastava LM, et al. Apolipoprotein (a) polymorphism and its association with plasma lipoprotein (a): a North Indian study. Ind Heart J. 2000; 52:165e170.
[20]. Ashfaq F, Goel PK, Sethi R, et al. Lipoprotein (a) levels in relation to severity of coronary artery disease in North Indian patients. Heart Views. 2013; 14:12e16.
[21]. Anand, S., Enas, E.A., Pogue, J., Haffner, S., Pearson, T. and Yousuf, S. Elevated lipoprotein (a) levels in South Asians in North America. Metabolism. 1998; 47: 182-184.
[22]. Bhatnagar D, Anand IS, Durrington PN and Patel DJ. Coronary risk factors in people from the Indian subcontinent living in west London and their siblings in India. Lancet 1995; 345: 405-409.
[23]. Rajashekhar D, Saibaba KSS,.Srinivasa Rao et al. Lipoprotein(a): Better assessor of coronary heart disease risk in south Indian population. Indian Journal of Clinical Biochemistry, 2004;19(2):53-59.
[24]. Hoogeveen RC, Ghambir JK, Gambhir D, et al. Evaluation of Lp(a) and other independent risk factors for CHD in Asian Indians and their USA counterparts. J Lipid Res. 2001; 42:631e638.
[25]. Vandana Saini, M K Bhatnagar, Jayashree Bhattacharjee. Evaluation of Homocysteine, Lipoprotein(a) and Endothelin as diagnostic markers of Coronary Artery Disease in Indian population. Internet Journal of Medical Update, 2013 January; 8(1):17-23.
[26]. Nordestgaard BG, Chapman MJ, Ray K, et al. Lipoprotein (a) as a cardiovascular risk factor: current status. Eur Heart J. 2010; 31:2844e2853.
[27]. Davidson MH, Ballantyne CM, Jacobson TA, et al. Clinical utility of inflammatory markers and advance lipoprotein testing: advice from an expert panel of lipid specialists. J Clinl Lipidol. 2011; 5:338e367.