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Revisit lipoprotein(a): An independent risk factor for coronary artery disease severity in Indian population and its correlation with Gensini score

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ABSTRACT

Aims: Lipoprotein(a) [Lp(a)] levels have shown wide ethnic variations. Further studies are needed, as there are sparse data in Indian population on mean Lp(a) levels and its link with clinical variables and severity of coronary artery disease (CAD).
Methods: In present study total 516 patients of suspected CAD undergoing coronary angiography were included after applying inclusion and exclusion criteria on the target population. Serum Lp(a) estimation was performed by immunoturbidimetric method.
Results: Among patients with normal coronaries, 67.3% patients had lipoprotein(a) levels <25 and 32.7% patients had lipoprotein(a) levels ≥25. In patients where 1 vessel was involved, 66.7% patients had lipoprotein(a) levels <25 and 33.3% patients had lipoprotein(a) levels ≥25. In patients where 2 vessels were involved 56% patients had lipoprotein(a) levels <25 and 44% patients had lipoprotein(a) levels ≥25. In patients where 3 vessels were involved 27.6% patients had lipoprotein(a) levels <25 and 72.6% patients had lipoprotein(a) levels ≥25. These results were significant and the *p*-value <0.001. The Gensini score was 29, when patients had lipoprotein(a) levels <25, while the Gensini score was 61, when patients had lipoprotein(a) levels ≥25 (*p*-value <0.001). Mean number of diseased vessels, when lipoprotein(a) levels were <25 was 1, while the mean number of vessels were 3 when the lipoprotein(a) levels were ≥25 (*p*-value of <0.001).
Conclusion: Lipoprotein(a) was found to be an important independent risk factor for CAD in Indian population and raised Lp(a) levels were also associated with increasing severity of the coronary vessel disease and multivessel CAD.

1. Introduction

It is widely acknowledged that cardiovascular diseases (CVDs) are the leading causes of death and disability in high per capita income countries (HIC).[1] What is less appreciated is that this holds true for the low- and middle-income countries (LMIC) as well.[1] Indians are in the midst of a true global cardiovascular disease (CVD) epidemic.[2] CVD is responsible for about 30% of all deaths worldwide each year.[3] Of note, nearly 80% of these deaths occur in LMIC, and half occur in women. Indeed, CVD is the leading cause of mortality in every region of the world with the sole exception of sub-Saharan Africa, where infectious diseases are still the leading cause.

Conventional risk factors have failed to explain the increasing burden of CAD, thus necessitating the need to search for newer risk factors like insulin resistance, thrombogenic factors, infection, inflammation and Lipoprotein A (Lpa). Lipoprotein A (Lpa) excess increases the risk of premature CAD 3–100 fold depending on the absence or presence of concomitant risk factors.[4,5] Uninfluenced by age, sex, diet or environmental factors, the Lp(a) values are genetically determined by Lp(a) gene located on chromosome 6q26-27 and stable lifelong levels are attained by age of two.[5,6] Though earlier studies on relationship between Lp(a) and CAD had shown negative results, recently multiple studies have shown that elevated Lp(a) is independently and linearly predictive of future adverse coronary events.[7,8] Lp(a) levels have shown worldwide ethnic variation with different levels associated with CAD in different populations.

Data on levels of Lp(a) associated with risk of CAD from large Indian population are still lacking, though there are few small

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studies to suggest its association with CAD. Thus this study was carried out to find out the level of Lp(a) independently associated with risk of CAD in the Indian population.

2. Material and methods

This study was conducted at Sir Sunder Lal Hospital, IMS, BHU, Varanasi, U.P., India. It included 516 patients of suspected CAD undergoing coronary angiography admitted in cardiology department during March 2015–October 2015.

Study population was derived using inclusion and exclusion criteria on the target population. Signed written informed consent was taken from each of the patient for participation in the study. All patients in this study underwent routine investigations before angiography. Statistical analysis was done after obtaining the data using SPSS-16.

Initial evaluation

1. CBC
2. Renal function test
3. Lipid profile
4. Lipoprotein A level
5. Fasting blood sugar
6. 2D echocardiography

Inclusion criteria:

1) Age >18 year
2) Patient undergoing coronary angiography
3) Competency to give consent

Exclusion criteria:

1) Previous PTCA/CABG
2) Presence of Acute heart failure
3) Acute ischemic stroke or transient ischemic attack (TIA)
4) Pregnancy
5) Marked anemia (Hb < 8 g/dl)

CAG was performed using the Judkins technique. Significant CAD was diagnosed, if there was 50% diameter stenosis in at least 1 major epicardial coronary artery. The severity of CAD was determined by the number of significantly diseased coronary arteries. Vessel disease was defined as the presence of 50% luminal diameter stenosis in at least 1 major coronary artery. Multivessel coronary disease was defined as the presence of 50% luminal diameter stenosis involving at least 2 major epicardial coronary arteries. Left main coronary artery narrowing of 50% was considered as 2-vessel disease. The stenosis less than 50% was considered mild coronary arteries disease. The Gensini score was calculated for each patient from the coronary angiogram by assigning a severity score to each coronary stenosis as 1 for 1–25% narrowing, 2 for 26–50%, 4 for 51–75%, 8 for 76–90%, 16 for 91–99%, and 32 for a completely occluded artery. The score is then multiplied by a factor according to the importance of the coronary artery. The multiplication factor is 5 for a left main coronary artery, 2.5 for proximal left anterior descending artery and proximal circumflex artery, 1.5 for a mid left anterior descending artery, and 1 for distal left anterior descending artery, mid or distal circumflex artery, and right coronary artery.

Serum Lp(a) estimation was performed using quantitative Latex-enhanced Immunoturbidimetric test using human Lp(a) kit (Human Gesselschaft, Weisbaden, Germany). Strict external quality control using sera with known values was performed to validate the results.

2.1. Statistical analysis

Continuous data are presented as mean ± SD and/or median (minimum–maximum). One-way analysis of variance or Kruskal–Wallis tests was used to compare the 3 groups. Differences in continuous variables between 2 groups were determined by *t* test or Mann–Whitney *U* test. Correlation analysis was performed using Pearson or Spearmen tests. Categorical variables are summarized as percentages and compared with the chi-square or Fisher's exact test. Statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS 16) for Windows (SPSS Inc., Chicago, IL).

3. Results

The study population consisted of 516 patients (Table 1). The mean age of patients with normal coronaries, SVD, DVD, and TVD groups were 54.19, 53.45, 58.03 and 56.33 years respectively. This difference is not significant and the study population had a more or less equal distribution of age in all the four groups thus eliminating any age-based bias.

In present study, mean systolic B.P. in patients with normal coronaries, SVD, DVD, and TVD groups were 119.48, 140.71, 143.97 and 135.45 mmHg respectively. This difference between the groups was statistically highly significant (<0.001). A similar association is seen with mean diastolic B.P. in patients with normal coronaries, SVD, DVD, and TVD groups were 76.52, 86.42, 85.17 and 82 mmHg respectively. This difference between the groups was statistically highly significant ($p < 0.001$).

In present study, mean total cholesterol values in patients with normal coronaries, SVD, DVD, and TVD groups were 143.06, 152.54, 179.04 and 182.52 mg/dl respectively. This difference between the groups was statistically highly significant (*p*-value <0.001) and mean HDL values in patients with normal coronaries, SVD, DVD, and TVD groups were 36.13, 41.7, 39.25 and 39.96 mg/dl respectively. This difference between the groups was not statistically significant (*p*-value >0.05). Although HDL cholesterol has emerged as a negative risk factor for coronary artery disease but our results did not show significant correlation. The probable reason may be that HDL is not an isolated factor affecting risk of coronary disease and other factors are also involved which act as confounding factors. In present study mean LDL values in patients with normal coronaries, SVD, DVD, and TVD groups were 81.52,

Table 1
Comparison of mean and median values of demographic and laboratory parameters with severity of CAD.

Variables	Normal coronories	SVD	DVD	TVD	*p*-Value
Age (years)	54.19 ± 5.275	53.45 ± 11.660	58.03 ± 6.788	56.33 ± 10.780	0.06
SBP (mmHg)	119.48 ± 11.673	140.71 ± 19.558	143.97 ± 21.637	135.45 ± 20.207	<0.001
DBP (mmHg)	76.52 ± 6.966	86.42 ± 10.963	85.17 ± 12.743	82.00 ± 8.670	<0.001
Total cholesterol (mg/dl)	143.06 ± 39.952	152.54 ± 31.236	179.04 ± 46.310	182.52 ± 55.483	<0.001
HDL (mg/dl)	36.13 ± 8.747	41.70 ± 7.193	39.25 ± 5.698	39.96 ± 11.241	0.016
LDL (mg/dl)	81.52 ± 38.129	90.73 ± 25.056	117.79 ± 29.188	112.75 ± 45.082	<0.001
Creatinine (mg/dl)	1.0258 ± .35774	1.2272 ± .32405	0.9480 ± .13692	1.0538 ± .22729	<0.001
Lipoprotein(a) (mg/dl)	17.9 (10.5–37)	16.90 (12.4–29.0)	21.3 (12–58)	33.5 (24–42)	<0.001

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