Association Of Lipoprotein [A] In Genders, Age And Lifestyle Related To Coronary Heart Disease In The Dehradun Population.

A Sharma, V Mehrotra, G Awasthi, M Rawat

Citation

Abstract
Background: The study of increase Lipoprotein (a) [Lp[a]] is an important risk factor for coronary heart disease (CHD). Lp[a] levels in different populations can help in identifying the high risk group requiring aggressive medical treatment. Many studies have been conducted in India and abroad for screening population for higher Lp[a] levels related to CHD. However no study has yet been done on Uttarakhand population in particular Dehradun for screening of Lp[a] on CHD.

Methods: A total of 600 serum samples including 200 rural, 200 urban and 200 suburban populations Dehradun district with various age groups and sex were evaluated. 50% among above patients were identified with myocardial Infarction. The estimation of serum Lp[a] was done and data obtained was statistically analyzed.

Results: The analysis of Lp[a]values showed that it differed significantly between the genders and among age-groups, but no significant variation was observed among localities (strata).

INTRODUCTION
Coronary Heart Disease (CHD) is progressively increasing in Indian population and projected to be the number one killer in the next decade (1). Traditional risk factors like smoking, hyper-tension, diabetes are reported to account for only 50% of prevalence and severity of this disease (2). This led to studies on newer risk factors like fibrinogen, Lipoprotein [a](Lp[a]), homocysteine, tissue plasminogen activator, etc. Studies on overseas Indians have shown that Lp[a] is an important risk factor for CHD (3). Studies on evidence of relationship between Lp[a] and CHD have shown discordant results but majority of the studies show higher levels of Lp[a] in patients than in controls (4-7). Lp[a] levels correlate with both early and advanced atherosclerosis, severity, extent and progression of atherosclerosis and all complications of CHD. Lp[a] excess increases the risk of premature CHD 3 to 100 fold depending on the absence or presence of concomitant risk factors (8).

The Indian population is undergoing epidemic transition as a result of affluence, urbanization and mechanization. Study of Lp[a] will help in the process of identifying the risk factors associated with the malignant nature of CHD in Indian population. Additionally, measurement of Lp[a] levels in different populations can help in identifying the high risk group requiring aggressive medical treatment (9-10).

Hence the present study was undertaken to find out the trends in the variation of Lp[a] in different segments of Dehradun population for screening of CHD.

MATERIAL AND METHODS
The present study was done at Biochemistry Departments of Himalayan Institute of Medical Sciences, Jolly Grant and Dolphin (P.G.) Institute of Biomedical and Natural Sciences, Dehradun, India.

A total of 600 serum samples including 200 rural, 200 urban and 200 suburban populations Dehradun district with various age groups and sex were evaluated. 50% among above patients were identified with myocardial Infarction. All the subjects gave their informed consent which includes information regarding occupation, medical history, smoking, drinking habits and use of medication. This was used for the discrimination of CHD patients with control.

The CHD was diagnosed if there is documented history of chest pain suggestive of Angina or Infarction and/or
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previously diagnosed as coronary artery disease. The Electrocardiograph studies were done. Dietary intake was assessed as per information provided by subjects. Blood samples were collected and all samples were analyzed within 6 hours of collection for Lp[a].

QUALITY CONTROL
External and internal quality controls were used for each test. External quality was from Christian Medical College Vellore, having our lab ranking within first 500 in India. Internal quality controls was run by Bayer, run every day to ensure that values of different level were in range.

STATISTICAL ANALYSIS
The statistical analysis was performed using Genststat 32 for factorial experiments. The three main factors were –gender, strata (localities) and age groups. It was the case of 2x3x4 factorial analysis.

RESULTS
The results of statistical analysis of Lp[a] data in whole population is given in Table 1. The analysis of Lp[a]values showed that it differed significantly between the genders and among age-groups, but no significant variation was observed among localities (strata) i.e. average values of LP[a] of different localities irrespective of age and gender are statistically same or say whatever difference is seen in average values, is due to chance factor i.e. shall not remain consistent.

Figure 1

Figure 2

Table 1: ANOVA of whole population

<table>
<thead>
<tr>
<th>Sources of variation</th>
<th>Average level of Lp[a] (mg/dl)</th>
<th>Level of significance</th>
<th>CD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>12.92</td>
<td></td>
<td>***</td>
</tr>
<tr>
<td>Male</td>
<td>13.54</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strata</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>13.91</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sub-urban</td>
<td>15.15</td>
<td></td>
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<tr>
<td>Urban</td>
<td>14.70</td>
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<tr>
<td>Age-Groups</td>
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</tr>
<tr>
<td>20-30yrs</td>
<td>15.15</td>
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<tr>
<td>30-40yrs</td>
<td>14.57</td>
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<td>40-50yrs</td>
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<tr>
<td>50-60yrs</td>
<td>18.11</td>
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</tbody>
</table>

*** indicates significance at0.1% level of probability

The variation among the localities was not significant, more or less they were statistically same i.e., people of rural (13.91mg/dl) or urban (14.78mg/dl) or sub-urban (15.15mg/dl) had insignificant difference in their Lp[a]values.

From the results of Lp[a] for age-groups, it is found that Lp[a] levels rises significantly with the age.

It was observed that the Lp[a] levels in myocardial Infarction patients in our study of Dehradun region was found to be 20.26 mg/dl. The values were significantly high (p<0.001) as compared to normal population of Dehradun region (14.61mg/dl).

The female and male data were compared in different localities and in different age groups as shown in Table 2 and 3. The Lp[a] level in female suburban population was insignificantly highest and rural population was insignificantly lowest. Among the age groups Lp[a] value in youngest age group (20-30 year) was lowest and highest in oldest age group. The values in 30-40 year age group and 40-50 year age groups are almost same.

Figure 3

Table2: ANOVA of Female Data

<table>
<thead>
<tr>
<th>Sources of variation</th>
<th>Average level of Lp[a] (mg/dl)</th>
<th>Average level of Lp[a] (mg/dl)</th>
<th>CD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strata</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>13.91</td>
<td></td>
<td></td>
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<tr>
<td>Sub-urban</td>
<td>15.15</td>
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<td></td>
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<tr>
<td>Urban</td>
<td>14.70</td>
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<tr>
<td>Age Group</td>
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<td>30-40yrs</td>
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<td>40-50yrs</td>
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<tr>
<td>50-60yrs</td>
<td>18.11</td>
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</tbody>
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The variation among the localities was not significant, more or less they were statistically same i.e., people of rural (13.91mg/dl) or urban (14.78mg/dl) or sub-urban (15.15mg/dl) had insignificant difference in their Lp[a]values.

The male data analysis show almost identical result as that of females. The strata differs insignificantly with each other the rural population being the lowest and urban population being the highest. The concentration of Lp[a] rises significantly from lowest age group to highest age group.

The different strata in similar age groups in both the genders were compared as shown in Table 4 and 5. The different strata in similar age group and similar genders demonstrate insignificant difference between Lp[a] values.

Figure 4

Table3: ANOVA of male Data

<table>
<thead>
<tr>
<th>Sources of variation</th>
<th>Average level of Lp[a] (mg/dl)</th>
<th>Average level of Lp[a] (mg/dl)</th>
<th>CD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strata</td>
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<td></td>
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</tr>
<tr>
<td>Rural</td>
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<td>Sub-urban</td>
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<td>Urban</td>
<td>13.81</td>
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<td>Age Group</td>
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<tr>
<td>20-30yrs</td>
<td>14.57</td>
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<td>30-40yrs</td>
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<td>18.11</td>
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The variation among the localities was not significant, more or less they were statistically same i.e., people of rural (13.91mg/dl) or urban (14.78mg/dl) or sub-urban (15.15mg/dl) had insignificant difference in their Lp[a]values.

The different strata in similar age groups in both the genders were compared as shown in Table 4 and 5. The different strata in similar age group and similar genders demonstrate insignificant difference between Lp[a] values.
DISCUSSION

It was noticed that females had significantly higher LP[a] than males. Similar observations were recorded in other reports (11-15). Higher level in males as compared to females may be due to lowering effect of Testosterone and presence of menopausal status in women. However some studies reported no gender differences (16-18).

Considering LP[a] as an independent risk factor urban, suburban and rural population are at equal risk for Myocardial infarction. These findings appear to be true as level of LP[a] is mostly governed at the genetic level and lifestyle variation has very little effect. The rate of secretion by liver determines the LP[a] levels. Ninety percent of the variation in plasma levels is accounted by the apo(a) gene and 70% by the size of apo(a) isoforms (19). Previous studies have shown significantly higher values of LP[a] in off springs of parents with past history of premature Myocardial Infarction as compared to controls (20-22). A study conducted in Iranian population observed the higher value of LP[a] children of patients with premature Myocardial Infarction (23).

Mechanism of pathogenecity of LP[a] excess include enhanced thrombogenesis and impaired fibrinolysis by competing with plasminogen, inhibition of transforming growth factor, destabilization of plaque, increased smooth muscle cell proliferation and migration, formation of occlusive thrombus, impaired formation of collateral vessels, enhanced oxidation uptake and retention of LDL-C and upregulation of expression of the plasminogen activator inhibitor (PAI-I) (24-26).

Higher mean LP[a] levels were observed in patients than controls and difference was statistically significant (P<0.01). This is in agreement with earlier studies conducted in India and abroad (27-28).

The distribution of LP[a] levels showed skewed distribution in Chinese, Asian Indians, whites, blacks and Indians (29-31). In the present study also distribution of LP[a] levels showed skewness.

Among Asian Indians world wide the mean level of LP[a] is 18-20 mg/dl. The median level is 16mg/dl in Asian Indians, 22mg/dl in blacks, 6mg/dl in Whites and 3mg/dl in American Indians (32-34). A study conducted on Tirupati population observed the mean of 16.04 mg/dl and suggested the cut off level of 25mg/dl for LP[a] to determine the risk of CHD (12). Enans et al 2002, suggested LP[a] 20mg/dl as upper limit of the normal. As per these guide lines all the population of our study are safe. However LP[a] in conjugation with other risk factors which are due to unhealthy lifestyle increase cardiovascular risk in urban population (35-37).

From the result of LP[a]for age-groups, it is found that LP[a] varied significantly among the age-groups. LP[a] was lowest in the lower age group of 20-30 yrs and higher in higher age-groups of 50-60 yrs. It is worth noting that LP[a] remained same from the age-group of 30-40 yrs to 40-50 yrs, as the difference between their averages. LP[a] is less than the least significant difference (LSD). This observation may be due to lowering effect of testosterone in males and presence of menopausal status in women as reported previously.

From the joint effect of gender and strata it may be observed, that though females LP[a] remains higher than that of males but the values from one locality to another were nearly same.

The gender and age-group inter action show that value of LP[a]for females exceeded the values of males in all age groups. It was also observed that LP[a]show a rising trend from lower age to higher age. From the interaction of strata and age-groups it was found that LP[a] increases with age in all the localities but locality to locality value of LP[a] showed no significant difference.

When the data for different genders was analyzed separately similar trend in the variation of LP[a] levels among the
localities and age groups were observed as for whole population. The data for different genders was subdivided into different age groups and the different localities were compared. The insignificant variation in the Lp[a] values among the localities was observed. The sex hormones which primarily govern the Lp[a] levels may not vary among the different localities in similar age groups and similar genders. These observations suggest that in addition to conventional lipid profile, estimation of Lp[a] can prove to be a valuable tool in risk assessment of population in general and management of disease in particular and should be routinely screened. Our findings suggest a cut-off level of 20 mg/dl for Lp[a] to determine the risk of CHD. This value is much less than cut off value of 25 mg/dl reported in south Indian population (12). Studies from different areas involving larger sample size are needed to confirm the findings of the present study.

CONCLUSIONS

The analysis of Lp[a]values showed that it differed significantly between the genders and among age-groups, but no significant variation was observed among localities in CHD cases. Lp[a] values are valuable tool in risk assessment of population in general and management of disease in particular and should be routinely screened for heart diseases patients.

References

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