Applicability of Lipoprotein (a) as a Risk Predictor for Cerebrovascular Disease
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Abstract: Lipoprotein (a) is independently associated with Atherosclerotic Cardiovascular Disease (ASCVD) and is referred to as the most atherogenic lipoprotein. It is synergistic with the effects of low density lipoprotein cholesterol (LDL-C). Unlike other major classes of lipoproteins that have a normal distribution in the population, plasma levels of Lipoprotein (a) / Lp (a) have a skewed distribution towards the lower end with 85% population having concentration <30 mg/dL. The aim of present study is to estimate the level of serum Lp(a) in cerebrovascular diseases or Strokes. The study was conducted in the Department of Medicine, Department of Biochemistry, Sushila Tiwari Memorial Hospital, the teaching hospital of Uttaranchal Forest Hospital Trust (UFHT) Medical College, Haldwani (Nainital), Uttarakhand, on patients of cerebrovascular disease (CVD) which included estimation of Lp(a) and lipid profile (TC, TG, HDLc, LDLc, VLDLc) test. Out of the 17 women and 36 men in whom Lp (a) was measured, 2 women (mean age63.5 years) and 21 men (59years) had CVD (CVD(+), while 15 women (50.13 years) and 15 men (52.33 years) had no CVD [CVD(-)]. As shown in Table 1, there were no significant differences between women with or without CVD in age and concentration of total plasma cholesterol. The study was based on a small sized cohort of 23 cases suffering from (CVD) out of which 21 were males and 2 were females. Thirty (30) healthy subjects were taken as controls, who were not suffering from any disease, which may affect serum lipid levels and without any history of cerebrovascular disease. Total-C, LDLc, VLDLc, Triglyceride, HDLc, LDL/HDLc, Cholesterol/HDL and Lp(a) were estimated in all the cases.

Keywords: Cerebrovascular disease (CVD), Lp(a) lipoprotein, chylomicron

INTRODUCTION
Lipoprotein(a) is found in lower concentrations than other lipoproteins, yet it carries a unique and significant risk for cerebrovascular disease. Because of its similarity to LDL, test methods often don’t measure it separately, but include it within the LDL class. Testing specifically for this class may uncover why a person is not responding to standard cholesterol-lowering treatment. High lipoprotein(a) levels may not respond to treatment aimed at high LDL[1].

Lipoprotein (a) was discovered by chance by Berg in 1963; after twenty years of research, the chemical, physical and metabolic characteristics of Lp (a) are now known. This lipoprotein forms the missing link between the lipid metabolism and the coagulation-fibrinolysis process. The A. describe its similarity to plasminogen, its capacity to delay coagulum or embolus destruction and highlight its structural and functional similarity to lipid metabolism. Today, a total of 6 Lp (a) isoforms have been identified with different molecular weights: in addition, the inverse proportion between the isoforms’ molecular weight and Lp(a) plasma concentration has been demonstrated. Lp(a) is not the product of the metabolism of other lipoproteins nor is it a catabolite of LDL; it is produced ex-novo and does not apparently exchange its proteic fraction with other lipoproteins. The paper also examines the question of whether Lp(a) is a plasma marker which increases during the formation of atherosclerotic plaque or whether it should not be considered an atherogenetic factor[2]. To this end the possible mechanisms by which Lp(a) is deposited in plaque are examined. Lastly, the paper reviews all studies concerning the relationship between Lp(a) and cerebrovascular disease.

High Lp(a) concentration is associated with a higher incidence of ischemic stroke in blacks and white women, but not in white men.
Lipoproteins: Lipoproteins are the "packages" in which cholesterol and triglycerides travel throughout the body. Measuring the amount of cholesterol carried by each type of lipoprotein helps determine a person's risk for cerebrovascular disease (disease that affects the brain and blood vessels, also called CVD).

Clinically important lipids are Cholesterol and triglycerides. Cholesterol is used to build cell membranes and hormones[5]. The body makes cholesterol and gets it from food. Triglycerides provide a major source of energy to the body tissues. Both cholesterol and triglycerides are vital to body function, but an excess of either one, especially cholesterol, puts a person at risk of cardiovascular disease.

Because cholesterol and triglycerides can't dissolve in watery liquid, they must be transported by something that can dissolve them in blood serum. Lipoproteins contain cholesterol and triglycerides at the core and an outer layer of protein, called apolipoprotein.

There are four major classes of lipoproteins: chylomicrons, very low-density lipoproteins (VLDL), low-density lipoproteins (LDL), and high-density lipoproteins (HDL). There also are less commonly measured classes such as lipoprotein(a) and subtypes of the main classes.

Each lipoprotein has characteristics that make the cholesterol it carries a greater or lesser risk. Measuring each type of lipoprotein helps determine a person's risk for cerebrovascular disease (CVD) more accurately than cholesterol measurement alone. When a person is discovered to be at risk, treatment by diet or medication can be started and his or her response to treatment monitored by repeated testing[6].

**Aims and objective:** To estimate the level of serum Lp(a) in cerebrovascular diseases or Strokes.

**MATERIALS & METHODS**

**Study design:** An observational analytical study.

**Ethical approval:** This study was approved by Institutional Ethical committee (IEC) of UFHT Medical College and Sushila Tiwari Hospital, Haldwani, along with informed consent.

**Study setting:** The present study was carried out on patients of CVD attending “Department of Medicine”, Sushila Tiwari Memorial Hospital, the teaching hospital of Uttranchal Forest Hospital Trust Medical College, Haldwani (Nainital),UK. All the patients were asked for history of vascular disease, family history and presence of major risk factors for CVD.

**Study duration:** Duration of this study was Jan 2005 to July 2007.

**Sample size:** Sample size was n= 30 taken as controls and n=53 taken as CVD patients.

**Inclusion criteria:** Men/Women 18-70 years of age and clinically stabilized CVD patients. In this study fifty three clinically, pathologically proven fresh cases of CVD (age: 21-45 years), only minimal and moderately advanced patients of CVD were included. For comparison 30 clinically healthy volunteers of either sex (age: 17-40 years) were included as control group.

**Exclusion criteria:** CAD patients, Psychiatric patients, pregnant, lactating womenand patients with Diabetes and hypertension.

**Grouping:** Group 1: Control n= 30, Group 2: CVD n=53

**Sample collection:** Six milliliters of blood was collected from each subject in plain and sterile vials containing heparin as anticoagulant.

**METHODOLOGY**

- Lipoprotein (a): Measurement of Lipoprotein (a) by Lp(a)-Turbitlatex method
- Photometric determination of serum total Cholesterol: CHOD-PAP method.
- Photometric Estimation of Triglycerides: Enzymatic method.
- Enzymatic determination of HDL-Cholesterol In serum or plasma: HDL-Direct Method.
• LDLc estimation without the need of any centrifugation steps: Calculated method.

Statistical analysis:
Statistical analysis of data was done by using the statistical package for social sciences (SPSS 12) for windows software, Microso excel 2007 and Scientific Calculator. Result were expressed as Mean±S.D.

RESULTS
Of the 17 women and 36 men in whom Lp(a) was measured, 2 women (mean age 63.5 years) and 21 men (59 years) had CVD (CVD(+), while 15 women (50.13 years) and 15 men (52.33 years) had no CVD [CVD(−)], there were no significant differences between women with or without CVD in age and concentration of total plasma cholesterol. Women with CVD(+) had slightly higher triglycerides, LDL-cholesterol and lower HDL-cholesterol levels compared to CVD(−), while the two groups of men differed in age only. There were several significant differences between men and women. Women were older than men in both CVD groups; plasma cholesterol, HDL- and LDL-cholesterol were higher in women compared to men with CVD(+), while in those with aCVD(−) the only difference was in higher concentration of HDL-C in women.

Table-1: CVD(+) vs CVD(-) men

<table>
<thead>
<tr>
<th></th>
<th>MEN</th>
<th>p value</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>59±12</td>
<td>52.33±7.02</td>
<td>63.5±1.5</td>
</tr>
<tr>
<td>HDL-C (mg/dl)</td>
<td>38.9±10.7</td>
<td>41.33±4.92</td>
<td>35±2</td>
</tr>
<tr>
<td>Total-C(mg/dl)</td>
<td>168±36.4</td>
<td>161.66±8.85</td>
<td>159.5±24.5</td>
</tr>
<tr>
<td>LDL-C(mg/dl)</td>
<td>105±26.9</td>
<td>119±14.44</td>
<td>104.5±25.5</td>
</tr>
<tr>
<td>VLDL-C(mg/dl)</td>
<td>30±31</td>
<td>17.73±4.50</td>
<td>20±1</td>
</tr>
<tr>
<td>Triglyceride(mg/dl)</td>
<td>124±62.89</td>
<td>106.13±34.94</td>
<td>10.5±5.5</td>
</tr>
<tr>
<td>LDL/HDL</td>
<td>3.04±1.17</td>
<td>2.94±0.58</td>
<td>3±0.9</td>
</tr>
<tr>
<td>Cholesterol/HDL</td>
<td>4.69±1.61</td>
<td>3.94±0.34</td>
<td>4.6±1</td>
</tr>
<tr>
<td>Lp(a) (mg/dl)</td>
<td>29.2±1.96</td>
<td>13.4±2.24</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

DISCUSSION AND CONCLUSION
The study was based on a small sized cohort of 23 cases suffering from Cerebrovascular disease(CVD) out of which 21 were males and 2 were females.

Thirty (30) healthy subjects were taken as controls, who were not suffering from any disease, which may affect serum lipid levels and without any history of Cerebrovascular disease. Total-C, LDLc, VLDLc, Triglyceride, HDLc, LDL/HDL, Cholesterol/HDL and Lp(a) were estimated in all the cases. After careful analysis of the results following conclusions were drawn-

Abnormal level of Total-C (>200 mg/dL) was seen in 21.74% cases of the CVD this proves a poor correlation between serum cholesterol level and Cerebrovascular disease.

Level of HDLc below 35 mg/dL (<35 mg/dL) has been taken as abnormal, was seen in 30.43% cases of CVD this degree of abnormality is again the same as that of serum cholesterol therefore there is no use of measuring serum HDLc alone over Total-C to predict the risk of CVD.

Serum LDLc was abnormally high (that is >130 mg/dL) in 26.09% cases of CVD again there is no use of measuring serum HDLc alone over Total-C to predict the risk of CVD.

Levels above 30 mg/dL which was the abnormal level of serum VLDLc was seen in 30.43% cases of CVD this was too low a value to predict the risk of CVD.

Hypertriglyceridemia (>170 mg/dL) was seen in 30.43% cases of the CVD this again was too low a value to predict risk of CVD.

Cholesterol/HDL ratio was abnormal in 73.91% cases of CVD the correlation of this ratio with CVD was seemed to be more related to CVD then Total-C, HDLc, LDLc, triglyceride and VLDLc.


