STUDY OF LIPID ABNORMALITIES IN POST MENOPAUSAL WOMEN WITH SPECIAL REFERENCE TO LIPOPROTEIN (a)

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ABSTRACT

BACKGROUND
Hyperlipidemia is one of the important risk factor the development of coronary heart disease. The prevalence of the coronary heart disease is more in postmenopausal women when compared to menstruating women. This is in part due to the lipid abnormalities associated with cessation of menstruation. The present study is therefore undertaken to evaluate lipid profile and serum lipoprotein (a) levels in postmenopausal women.

METHODS
In this study total 120 subjects were included, who were equally divided into two groups, premenopausal and postmenopausal. Females with aged above 50 years with the history of amenorrhea of more than one year. Obese or overweight women with body mass index more than 25, to minimize the confounding effect on lipid and lipoprotein concentration. Those who have undergone premature menopause before 45 years. Patients on anti-inflammatory drugs, antidepressants thyroid hormone. Patients with history of liver disease, alcohol consumption, smoking, hypertension and diabetes mellitus
Those who are on medication known to influence lipid metabolism (e.g. Sex steroids).

RESULTS
In our study all the lipid profiles (total cholesterol, triglycerides, LDL, VLDL & Lp (a)) are significantly higher in postmenopausal compared to premenopausal women and HDL is significantly lower in postmenopausal women although all the lipid parameters were within the normal range.

CONCLUSIONS
We can conclude that the significant increase in the total cholesterol, triglycerides, LDL, VLDL and Lp (a); and decrease in the HDL in postmenopausal women are probably because of the effect of estrogen deficiency associated with menopause.

KEYWORDS
Hyperlipidemia; Low-density Lipoprotein (LDL); Very Low-density Lipoprotein (VLDL); High-density Lipoprotein (HDL); Lipoprotein (a).


BACKGROUND
Menopause is a Greek word, "men" meaning menses and "pauo" meaning to stop.
Menopause is defined as permanent cessation of menses for 1 year following loss of ovarian activity.
Postmenopausal stage is an estrogen deficient state. Postmenopausal women are more prone to atherosclerosis related disorders. This is mainly because they lose their relative protection against atherosclerosis after menopause due to the change in the lipid profile resulting from estrogen deficiency.
Lipoprotein (a) is also an independent risk factor for atherosclerosis. Several studies have shown that serum LDL & VLDL cholesterol levels, triglycerides and lipoprotein (a) are significantly higher and HDL cholesterol levels are lower in postmenopausal women when compared to age matched premenopausal women. Hence, this study was undertaken to study the lipid changes in postmenopausal women and to counsel them regarding prevention of cardiac complications.

Aims and Objectives of the Study
To study the levels of serum lipids and lipoprotein (a) in postmenopausal women who are free from obesity, hypertension, diabetes and cardiac disorders and to compare it from premenopausal women. History -Virchow first suggested lipid infiltration theory of atherosclerosis in 1862.

Lipids
Lipids are a heterogenous group of compounds that are insoluble in water and soluble in non-polar solvents. The biologically important lipids are the fatty acids and their derivatives, the neutral fats (Triglycerides), the phospholipids and related compounds and the sterols.
Lipoproteins
Lipoproteins are combinations of fat and protein. They are macromolecular complexes that carry hydrophobic lipids, particularly cholesterol and triglyceride in the plasma and are important cellular constituents, occurring both in the cell membrane and in the mitochondria.

Lipoproteins are spherical particles made up of hundreds of lipid and protein molecules. They are smaller than red blood cells. The major lipids of lipoproteins are cholesterol, triglycerides and phospholipids.

Table Major Classes of plasma lipoproteins (Havel et al., Lipoprotein (a) or Lp (a) was detected by Kare Berg in 1963 in Norway.1 The clinical interest in Lp (a) arose when Dahlen and co-workers recognized a higher frequency of Lp (a) positive subjects among men with coronary artery disease as compared with the controls.2

Lp (a) and Atherosclerosis Vascular Disease
Numerous epidemiological studies have shown that primary genetic risk factor for coronary artery disease and stroke.3,4 The Framingham study reported that Lp (a) levels above 30 mg/dl are similar in risk to total cholesterol greater that 240 mg/dl or HDL cholesterol lesser that 35 mg/dl. The mechanisms responsible for the increased risk are largely speculative.

One is the modulation of the balance between clotting and fibrinolysis at the endothelial layer of blood vessel wall, which results in a prothrombotic state. The in vitro studies also suggests that a forming fibrin thrombus at a damaged vessel wall has the capacity to bind Lp(a) this may not only inhibit thrombus degradation but may also result in trapping of Lp (a) particle by cross linking with fibrinogen. Incorporation of the thrombus into the vessel wall would then result in accumulation of Lp (a). Atherosclerosis lesions develop in mice that are transgenic for the human apo (a) gene on fat feeding, providing the most direct evidence for the role of apo (a) / Lp (a) in atherosclerotic vascular disease.6 Lp (a) inhibits fibrinolysis by competing with plasminogen for its binding site on cell surface or on target molecules. It is believed that this may inhibit cell surface associated plasmin generation and fibrinolysis. Besides its function in clot lysis, Plasmin also has other functions. One is the plasma dependent activation of TGF-Î±, TGF-Î², is able to block the migration of smooth muscle cells. Thus, high Lp (a) plasma concentration by inhibiting plasmin generation might enhance smooth muscle cell migration. Lp (a) may also bind to fibrinogen or fibrin in a clot. Lp (a) also Inhibits tissue plasminogen activator binding to fibrin. Lp (a) has thus been described as an interloper into the fibrinolytic system.

Secondary Causes of Lipoprotein Abnormalities6
Hypercholesterolaemia

<table>
<thead>
<tr>
<th>Lipoproteins</th>
<th>LDL</th>
<th>HDL</th>
<th>TRIGLYCERIDES</th>
</tr>
</thead>
<tbody>
<tr>
<td>With Cardiovascular Disease (mg/dl)</td>
<td>&lt;130</td>
<td>&lt;130</td>
<td>&lt;150</td>
</tr>
<tr>
<td>With Cardiovascular Disease (mg/dl)</td>
<td>&lt;100</td>
<td>&lt;100</td>
<td>&lt;150</td>
</tr>
</tbody>
</table>

According to recent 2005, American Diabetes Association guidelines, for people with diabetes and overt cardiovascular disease at very high-risk for further events should be treated with statins. A lower LDL cholesterol goal of <70 mg/dl using high-dose of statins is an option in these high-risk patients.

Relation to Atherosclerosis
In individuals with elevated plasma cholesterol levels, there is an increased incidence of atherosclerosis and its complications.
It is now clear that lowering plasma cholesterol by diet and drugs slows and may even reverse the progression of atherosclerotic lesions and the complications they cause.

M There is evidence that reducing plasma cholesterol may also inhibit the rupture of atherosclerotic plaques?

Atherogenesis
The importance of atherosclerosis as a principal cause of myocardial and cerebral infarction and thrombosis has been appreciated for many years. Nevertheless, it’s cause and pathogenesis remains unsolved. A major problem is that the disease progresses insidiously for many years before symptoms develop, making it difficult to follow the early development of the disease in individual patients, and to relate casually, the several types of lesion that have been described. For the same reason, identification of risk factors for the disease has depended upon the relation of these factors to the clinical symptoms rather than on the extent and severity of the primary arterial lesions. Not surprisingly, much research in the area of atherosclerosis has involved these risk factors, especially hyperlipidemia and hypertension.7

Menopause
Cardiovascular Disease
Cardiovascular disease, especially atherosclerosis is a consequence of multiple metabolic changes that interacts with each other.8,9

Adverse Changes in Circulating Lipid-lipoprotein Profile
• Oxidation of LDL producing a modified LDL is characteristic for circulating monocytes, that inhibits macrophages motility (thus trapping macrophages in the intima), and that causes cell injury and death in endothelium.
• Endothelial injury and dysfunction affects nitric oxide and prostacyclin production.
• Macrophage migration and functions influenced by growth factors and cytokines.
• Proliferation and migration of smooth muscle cells also influenced by growth factors and cytokines; these cells become the dominant cell type and source of connective tissue matrix in atherosclerotic lesion, the fibrous plaque.10
• Vasoconstriction and thrombogenic events.
• Remodeling of coronary arteries. An artery is able to respond to a developing atherosclerotic plaque by increasing its overall diameter in an attempt to maintain flow. The mechanism of this adaptive remodeling is not known, but the extent of this process must affect the risk of occlusion and infarction.

Serum Lipids and Cardio-vascular Disease in Postmenopausal State
Fatty streak in arterial vessel is the precursor to clinically significant atherosclerotic lesions. The fatty streak lesion, therefore, antedates the fibrous plaque, developing under the endothelial surface and dominated by fat laden macrophages (the foam cells). The process is initiated by the aggregation and adherence of circulating monocytes to a site on the arterial endothelium. When the monocytes penetrate through the endothelium and even the intima, they become loaded with lipids and converted to foam cells. Modification of LDL, especially oxidation, is crucial in this conversion and monocytes to foam cells. The initial step adherence of monocytes to endothelium can be induced by elevated cholesterol and LDL cholesterol in circulation.

During the reproductive year, women are protected from the CHD (Coronary Heart Disease). For this reason women lag behind in incidence of CHD by 10 years, and for myocardial infarction and sudden death, women had a 20 years advantage. The reasons for this are complex, but significant contribution to this protection can be assigned to the higher high-density lipoprotein (HDL) levels in younger women, an effect of estrogen. Through the adulthood, the blood HDL-cholesterol level is about 10 mg/dl higher in women, and this difference continues through the postmenopausal years. Total and low-density (LDL) cholesterol levels are lower in premenopausal women than in men. Although the levels gradually increase with aging and after menopause they raise rapidly. 56 After menopause the risk of CHD doubles for women as the atherogenic lipids above the age 60 years reach the levels greater than those in men. The changes are favorably reduced by dietary changes.

Of course, these lipid changes at menopause (whether natural or surgical) can be reversed with estrogen treatment7 At all the ages, however, HDL cholesterol in women is 10 mg/dl higher than in men. Coronary heart disease risk appears greater at higher total cholesterol levels for women than men. Women with total cholesterol concentrations greater than 265 mg/dl have rates of CHD three times that of women with low levels. Strongest predictor of CHD in women is low HDL cholesterol. A decrease in HDL-cholesterol. 10 mg/dl increases CHD by 40-50%.

It is appropriate to be concerned when HDL cholesterol levels are lower than 150 mg/dl.

The optimal cholesterol/ lipoprotein profile
Total cholesterol - <200 mg/ dl
HDL cholesterol - >50 mg/ dl
LDL cholesterol - <130 mg/ dl
Triglycerides - <150 mg/ dl

If triglycerides level is greater than 400 mg/dl and HDL cholesterol is less than 50 mg/dl, the risk of heart disease is substantially increased. Patients with elevated triglyceride level and positive family history of heart disease most likely to have an autosomal dominant disorder classified as familial combined hyperlipidemia. This disorder accounts for most of the myocardial infarctions in women less than 40 years old. Triglyceride level 200–400 mg/dl are considered as borderline elevated. Triglyceride levels can be elevated because of obesity, smoking and lack of exercise.
An important contribution to the gender difference in cardiovascular disease prevalence and age of onset is the favorable effect of estrogen on important endothelial events. Vasodilatory and antithrombotic activities can be attributed to endothelial production of nitric oxides and Prostacyclin, a process favorably influenced by estrogen. Hypercholesterolaemia adversely affects this important endothelial process, and estrogen protects this important endothelial function in the presence of hypercholesterolemia. Estrogen inhibits oxidation of LDL, also protects against toxic effects of oxidized LDL on endothelium.

Lp (a) lipoprotein is an LDL like lipoprotein particle that is distinguished by the presence of apolipoprotein (a) covalently bound to apolipoprotein B.

Apolipoprotein (a) confers thrombogenic properties to Lp (a) lipoprotein presumably by its structural homology to plasminogen. Lp (a) lipoprotein concentration is associated with coronary atherosclerosis. Endogenous estrogen appears to lower levels of Lp (a) lipoprotein and it is found that postmenopausal women have higher Lp (a) lipoprotein levels than premenopausal women. Hormone replacement lowered Lp (a) lipoprotein levels by 40% to 50%.11,12,13

**Stroke**

The epidemiological evaluation of the association between postmenopausal HRT and stroke is consistent with the possibility that hormone use decreases the severity of strokes, and thus reduces the incidence of fatal strokes.

**Effects of Estrogen on Lipid Profile**

Estrogen has a favourable effect on lipid profile. It increases triglyceride levels and increases LDL catabolism as well as lipoprotein receptor numbers and activity, resulting in decreasing LDL levels. The increase in HDL levels, particularly the HDL2 sub fraction, is due to the consequence of the inhibition of hepatic lipase activity, which converts HDL2 to HDL1.

Estrogen decreases the apoprotein B levels and increases apoprotein A-I. LDL particles size gets smaller (potentially a more atherogenic adverse effect), a change that is associated with an increase in the triglyceride content of LDL, however, it is not certain to what degree this change is related to dose nor is the clinical significance. Therefore, estrogen induces a change in LDL towards a smaller more dense particle, but it is in a form with a more rapid turnover in the circulation, allowing less time for oxidation and acquisition of cholesterol.

Estrogen is also an antioxidant. It directly inhibits LDL oxidation in response to copper and decreases the overall formation of lipid oxides. In addition estrogen may regenerate circulating antioxidants (tocopherols and f3-carotene) and preserve these antioxidants within LDL particles. This antioxidant action of estrogen preserves endothelial-dependent vasodilator function by preventing the deleterious effect that oxidized LDL has on endothelial production of vasoactive agents.

Estrogen replacement therapy (ERT) is associated with about 30-50% decrease in CVD risk in postmenopausal women and about 50% decrease in atherosclerosis in animal model. The foregoing findings suggest beneficial effect of estrogen on cardiovascular system. Surprisingly, randomized trials in postmenopausal women with preexisting CVD have found no benefits of combined hormonal replacement therapy.14

**Cardiovascular disease and Progestins**

Conclusions regarding the impact of progestational agents on cardiovascular disease are very much influenced by dose and duration of administration of the progestational agents involved. While short-term studies suggest a negative impact of progestin (i.e., subtracting from the beneficial effect of estrogen), long-term studies indicate that this short-term effect disappears. This was shown in the Heart and Estrogen Progestin Replacement Study (HERS trial) and in The Women's Health Initiative (WHI) Study

**METHODS**

The present study was carried out in the Meenakshi medical college Kanchipuram, from March 2013 to February 2014. The ethical committee clearance obtained from the appropriate authority appointed by the institution. In this study total 120 subjects were included, who were divided into two groups, 60 premenopausal and 60 postmenopausal groups.

**Inclusion Criteria**

- Females aged above 50 years with amenorrhoea of more than 1 year.
- No pre-existing medical disease (diabetes mellitus, hypertension, hypothyroidism, chronic illness).
- No history of premature menopause or surgical menopause.
- No history of steroid hormone intake.

**Exclusion Criteria**

- Obese women with body mass index more than 25, to minimize the confounding effect on lipid and lipoprotein concentration.
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- Those who are on medication known to influence lipid metabolism (e.g. Sex steroids).

<table>
<thead>
<tr>
<th>Lower risk</th>
<th>&lt;2.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Below average risk</td>
<td>2.5 - 3.7</td>
</tr>
<tr>
<td>Average risk</td>
<td>3.8 - 5.6</td>
</tr>
<tr>
<td>High risk</td>
<td>5.7 - 8.3</td>
</tr>
<tr>
<td>Dangerous</td>
<td>&gt;8.3</td>
</tr>
</tbody>
</table>

**Table 2. Heart Disease Based on Cholesterol / HDL Ratio**

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Methods of Collection of Data
- The study consists of both clinical and biochemical assay.
- Detailed history taken and clinical examination was done.

All the Patients were Investigated as per Requirement:
Lipid Profile Procedure
- Blood samples were drawn from all subjects after a minimum of 12 hours of complete fasting.
- The subjects were asked to have a light fat free diet on the day prior to the sampling.
- Venipuncture was done in the cubital fossa.
- About 10 ml of blood was drawn using perfectly dry and sterile syringes and blood was transferred to dried glass vessel.
- Serum was separated within 2 hours of collection to prevent artifactual changes in the concentration of HDL cholesterol.
- The serum was transferred to centrifuge and centrifuged at 5000 rpm for 10 minutes.
- The supernatant clear serum was then pipetted out using dry pipettes and stored at 4°C.
- The samples were analyzed the same day or within 48 hours.

i. Serum total cholesterol estimation
This was done by the method based on CHaD-PAP, enzymatic colorimetric method.

Test Principle:
Cholesterol ester <Cholesterol Esterase>-Cholesterol + Free Fatty acids
Cholesterol + O2 ->Oxidase> Cholesterol-3-one + H2O2
2H2O2 + Phenol + 4 Amino Antipyrine--------> Peroxidase---> Quinonimine + 4H2O (Pink)
The intensity of Pink / Red color IS proportional to the cholesterol concentration.

ii. Serum Triglyceride Estimation
Triglyceride concentration is determined by glycerol phosphate oxidase/ peroxidase enzymatic method.

iii. HDL cholesterol estimation
This involves two steps- precipitations and cholesterol estimation of HDL fraction by modification described by Burstein et al.

Test Principle
Chylomicrons, VLDL and LDL are precipitated by adding phosphotungstic acid and magnesium ions to the sample, centrifugation leaves HDL in the supernatant. Their cholesterol content is determined enzymatically.

iv. LDL Cholesterol Estimation
LDL cholesterol is calculated by using a standard WHO approved formula based on total cholesterol, HDL cholesterol and triglyceride values.

\[ \text{LDL cholesterol} = \text{Total cholesterol} - \text{HDL cholesterol} - \text{Triglyceride}/5 \]

v. VLDL Cholesterol Estimation
Dividing the amount of plasma triglyceride by 5 can approximate VLDL concentration.
\[ \text{VLDL} = \text{Triglyceride} / 5 \]

RESULTS
The mean levels of various lipid fractions were correlated with those of values for normal individuals.

Statistical Methods
Student t test of significance has been carried out find the significance of lipid profiles between the premenopausal and postmenopausal women. The Chi square and Fisher Exact test has been used to find the significance of proportions between the premenopausal and postmenopausal women. The odds ratio has been computed to find the relationship between the abnormal levels of lipid profiles between the premenopausal and postmenopausal women.

Statistical Software
The statistical software namely SPSS 1.0 and Systat 8.0 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

Study Design
A comparative study consisting of 60 each premenopausal and postmenopausal women is taken for investigating the pattern and association of lipid profiles.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Pre-Menopausal</th>
<th>Post-Menopausal</th>
<th>Significance (Student t and p Value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>31.80 ± 5.18</td>
<td>55.42 ± 5.41</td>
<td>t=24.46, p=0.000</td>
</tr>
<tr>
<td>BMI</td>
<td>20.50 ± 3.12</td>
<td>20.93 ± 3.19</td>
<td>t=0.671, p=0.504</td>
</tr>
<tr>
<td>FBS</td>
<td>86.57 ± 9.56</td>
<td>86.02 ± 9.32</td>
<td>t=0.319, p=0.750</td>
</tr>
<tr>
<td>PPBS</td>
<td>108.53 ± 13.93</td>
<td>108.19 ± 13.96</td>
<td>t=0.132, p=0.895</td>
</tr>
</tbody>
</table>

BMI is also statistically similar (P>0.05). The samples are matched with respect to FBS, PPBS and BMI.

Table 3. Background Characteristics

Lipid Profiles Table

<table>
<thead>
<tr>
<th>Lipid Profiles (mg/dl)</th>
<th>Pre-menopausal (Mean ± SD)</th>
<th>Post-menopausal (Mean ± SD)</th>
<th>Significance (Student t and p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Cholesterol</td>
<td>186.00 ± 19.76</td>
<td>198.57 ± 46.92</td>
<td>t=1.912, p=0.058</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>108.83 ± 29.18</td>
<td>131.82 ± 51.41</td>
<td>t=3.053, p=0.003</td>
</tr>
<tr>
<td>HDL</td>
<td>55.13 ± 5.52</td>
<td>49.35 ± 13.92</td>
<td>t=2.999, p=0.004</td>
</tr>
<tr>
<td>LDL</td>
<td>113.43 ± 21.53</td>
<td>129.37 ± 49.06</td>
<td>t=2.304, p=0.023</td>
</tr>
<tr>
<td>VLDL</td>
<td>20.95 ± 4.83</td>
<td>27.70 ± 16.33</td>
<td>t=3.071, p=0.003</td>
</tr>
<tr>
<td>LP(a)</td>
<td>11.03 ± 4.33</td>
<td>17.39 ± 8.84</td>
<td>t=5.019, p=0.000</td>
</tr>
</tbody>
</table>

Table 4. Lipid Profile Analysis

* Statistical significance at 5% 
** Statistical significance at 1% a: near statistical significance at 5%


### Table 5. Association of Total Cholesterol with Two Groups

<table>
<thead>
<tr>
<th>Total Cholesterol (mg/dL)</th>
<th>Premenopausal (n=60)</th>
<th>Post-menopausal (n=60)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 140</td>
<td>2 (3.3)</td>
<td>7 (11.7)</td>
<td>p=0.163</td>
</tr>
<tr>
<td>141-170</td>
<td>12 (20.0)</td>
<td>13 (21.7)</td>
<td>X²=0.935</td>
</tr>
<tr>
<td>171-200</td>
<td>37 (61.7)</td>
<td>11 (18.3)</td>
<td>X²=23.472</td>
</tr>
<tr>
<td>&gt;200</td>
<td>9 (15.0)</td>
<td>29 (48.3)</td>
<td>X²=15.404</td>
</tr>
</tbody>
</table>

**Inference**

Significantly increased proportion of total cholesterol >200 mg/dL postmenopausal women with odds ratio 5.30 indicating the abnormal TC in postmenopausal women is 5.30 times more likely compared to premenopausal women.

### Table 6. Association of Triglycerides with Two Groups of Women

<table>
<thead>
<tr>
<th>Triglycerides (mg/dL)</th>
<th>Premenopausal (n=60)</th>
<th>Post-menopausal (n=60)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;100</td>
<td>29 (48.3)</td>
<td>15 (25.0)</td>
<td>X²=7.033</td>
</tr>
<tr>
<td>101-150</td>
<td>26 (43.3)</td>
<td>27 (45.0)</td>
<td>X²=0.034</td>
</tr>
<tr>
<td>151-200</td>
<td>5 (8.3)</td>
<td>10 (16.7)</td>
<td>X²=1.905</td>
</tr>
<tr>
<td>&gt;200</td>
<td>0 (0.0)</td>
<td>8 (13.3)</td>
<td>X²=8.571</td>
</tr>
</tbody>
</table>

**Inference**

Premenopausal women have significantly increased triglycerides level >150 mg/dL compared to premenopausal women. The odds ratio for postmenopausal in abnormal triglycerides is 4.71, indicating the abnormal triglycerides in postmenopausal women is 4.71 times more likely compared to premenopausal women.

### Table 7. Association of LDL with Two Groups of Women

<table>
<thead>
<tr>
<th>LDL (mg/dL)</th>
<th>Premenopausal (n=60)</th>
<th>Post-menopausal (n=60)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤100</td>
<td>13 (21.7)</td>
<td>14 (23.3)</td>
<td>X²=0.086</td>
</tr>
<tr>
<td>101-130</td>
<td>41 (68.3)</td>
<td>23 (38.3)</td>
<td>X²=10.848</td>
</tr>
<tr>
<td>&gt;130</td>
<td>6 (10.0)</td>
<td>23 (38.3)</td>
<td>X²=13.141</td>
</tr>
</tbody>
</table>

**Inference**

Significantly increased proportion of abnormal LDL (>130 mg/dL) in postmenopausal women compared to premenopausal women with odds ratio 5.59 indicating the abnormal level of LDL in postmenopausal women is 5.59 times more likely compared to premenopausal women.

### Table 8. Association of HDL with Two Groups of Women

<table>
<thead>
<tr>
<th>HDL (mg/dL)</th>
<th>Premenopausal (n=60)</th>
<th>Post-menopausal (n=60)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;45</td>
<td>0 (0.0)</td>
<td>29 (48.3)</td>
<td>X²=38.242</td>
</tr>
<tr>
<td>46-55</td>
<td>37 (61.7)</td>
<td>8 (13.3)</td>
<td>X²=29.902</td>
</tr>
<tr>
<td>&gt;55</td>
<td>23 (38.3)</td>
<td>23 (38.3)</td>
<td>p&lt;0.05</td>
</tr>
</tbody>
</table>

**Inference**

The proportion of abnormal HDL (<45 mg/dL) is significantly higher in postmenopausal women compared to premenopausal women (p<0.001).

### Table 9. Association of Lp (a) with Two Groups of Women

<table>
<thead>
<tr>
<th>Lp (a) (mg/dL)</th>
<th>Premenopausal (n=60)</th>
<th>Post-menopausal (n=60)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10</td>
<td>25 (41.7)</td>
<td>16 (26.7)</td>
<td>X²=3.001</td>
</tr>
<tr>
<td>11-30</td>
<td>35 (58.3)</td>
<td>36 (60.0)</td>
<td>X²=0.034</td>
</tr>
<tr>
<td>&gt;30</td>
<td>0 (0.0)</td>
<td>8 (13.3)</td>
<td>X²=8.571</td>
</tr>
</tbody>
</table>

**Inference**

The proportion of abnormal Lp (a) >30 mg/dL is also significantly increased in postmenopausal women compared to premenopausal women. About 13.3% postmenopausal women had abnormal Lp (a) levels while none of the women in premenopausal group had. The inverse relationship between HDL level and the incidence of coronary artery disease has been demonstrated by Castelli et al., 1977.19

His study also shows that the ratio of total cholesterol / HDL of >4.5 is associated with greater incidence of coronary artery disease. In this study, total cholesterol / HDL ratio >4.5 was seen 44% of women.

### DISCUSSION

Our study group consisted of 60 pre- menopausal and 60 post- menopausal women with the average age of 3 1 years in premenopausal group and 55 years in postmenopausal groups. In our study, most of the cases have the normal body mass index in the range of 17-23kg/m² and they are free from hypertension, diabetes mellitus, heart and kidney disease. In comparing pre- and post- menopausal females, there is elevation of total cholesterol, triglycerides, LDL and Lp (a) levels and decrease in HDL levels in the postmenopausal age group, p-value is less than 0.05 in all the six lipid levels. Thus, the results of this study demonstrate that menopause has profound effect on lipid and lipoprotein concentrations independent of any effect of the ageing processes and body mass index changes.

The mean values of total cholesterol, LDL and triglyceride levels in the postmenopausal females are significantly higher than those in the premenopausal females. The fall in HDL cholesterol level is significant (p<0.05) as compared to the control group.

These data correlate well with other studies on serum lipids in pre- and post- menopausal females by Ushiroyama et al 1993,16 Framingham study on lipid profile.17 ICMR study at Maulana Azad Medical College, New Delhi, 2000, Jensen et al., 1990 etc.

In the study conducted by Ushiroyama et al 1993,16 percentage of postmenopausal women with: Total cholesterol> 220 mg/dL -- 31%

HDL <45 mg/dL --75%

LDL >140 mg/dL --27.2%

Triglyceride> 140 mg/dL --22%

In the ICMR study at Maulana Azad Medical College, New Delhi 2000, the percentage of post-menopausal women with:

Total cholesterol >220 mg/dL - 18%

HDL <45 mg/dL -75.6%

LDL>140 mg/dL - 24.5%

Triglyceride> 140 mg/dL - 52%

In our study, the percentage of post-menopausal women with:

Total cholesterol >220 mg/dL - 38%

HDL <45 mg/dL - 53%

LDL>140 mg/dL - 38%

Triglycerides> 140 mg/dL - 35%

The proportion of abnormal Lp (a)>30 mg/dL is also significantly increased in postmenopausal women compared to premenopausal women. About 13.3% postmenopausal women had abnormal Lp (a) levels while none of the women in premenopausal group had. The inverse relationship between HDL level and the incidence of coronary artery disease has been demonstrated by Castelli et al., 1977.19

His study also shows that the ratio of total cholesterol / HDL of >4.5 is associated with greater incidence of coronary artery disease. In this study, total cholesterol / HDL ratio >4.5 was seen 44% of women.
In the Framingham Heart Study, plasma triglyceride level is found to be an independent predictor of coronary artery disease. This study presented with triglyceride levels >140 mg/dL in the postmenopausal age group in 35% of cases.

The effect of endogenous and exogenous hormones in females is potentially a major factor in determining cardiovascular risk. Premenopausal females have a considerably lower incidence of cardiovascular disease than postmenopausal females of the same age. Moreover, oestrogen replacement has been shown in cohort epidemiological studies to be remarkably effective in providing protection against cardiovascular morbidity and mortality.

Estrogen appears to increase triglyceride levels and increases LDL catabolism as well as lipoprotein receptors numbers and activity, resulting in decreasing LDL levels. The increase in HDL levels particularly the HD~ subtraction, is due to the consequence of the inhibition of hepatic lipase activity, which converts HDL2 to HDL3. Postmenopausal estrogen therapy with or without added progestin also produces a beneficial reduction in the circulating levels of lipoprotein (a).

Estrogen is also an antioxidant. Estradiol directly inhibits LDL oxidation in response to copper, and decreases the overall formation of lipid oxides. In addition estrogen may generate circulating antioxidants (tocopherols and J3-carotene) and preserve these antioxidants within LDL particles. This will prevent the lipid peroxidation and accumulation of LDL cholesterol inside the macrophages and the smooth muscle cells.

Several aspects of coronary risk in females include the stronger role of diabetes mellitus, hypertriglyceridemia and HDL compared to men. Hence, careful attention to these issues holds the promise of reduction of cardiovascular morbidity in adult women.

CONCLUSIONS
Serum dyslipidemia is one important risk factor for the coronary heart disease and Lp (a) is also one of the emerging lipid risk factor. Serum dyslipidemia is much more common in postmenopausal age group compared to premenopausal group. This may be the reason for increased prevalence of coronary heart disease in postmenopausal women. In our study there was significant difference in all the six lipid parameters between the two groups. Total cholesterol, triglycerides, LDL, VLDL and Lp (a) were higher in postmenopausal women compared to premenopausal women as HDL was lower in postmenopausal.

We can opine that the significant increase in the total cholesterol, triglycerides, LDL, VLDL and Lp (a); and decrease in the HDL in postmenopausal women are probably because of the effect of estrogen deficiency associated with menopause.

Summary
The study group consisted of 120 cases, 60 in postmenopausal group and 60 in premenopausal group. Average age in premenopausal group was 32 years and in postmenopausal group was 55 years. They were match for BMI and had no incidence of diabetes, renal or cardiac disorders. Serum lipid profile of 60 postmenopausal women was studied and compared with those of the premenopausal women. The mean values of lipid fractions like serum cholesterol, triglycerides, LDL, VLDL and Lp (a) were significantly higher in postmenopausal women when compared to premenopausal controls. HDL also showed significant difference and was lower in postmenopausal women when compared to premenopausal women.

REFERENCES