INTRODUCTION

Hyper-lipidemia is one of the major determinant and a risk factor for cardiovascular disease. This is characterized by alterations in the lipid profile including high levels of low-density lipoprotein cholesterol (LDL-C), plasma triglyceride and low levels of high density lipoprotein cholesterol (HDL-C). LDL in its native form is not harmful; however, when it is oxidized, it becomes a real initiator of plaque formation. Oxidized LDL (ox-LDL) is crucial to cellular uptake to form macrophages derived foam cells in early development of atherosclerotic lesions. The association between serum LDL-C, ox LDL, triglycerides and cardiovascular diseases is very well recognized. However, considerable epidemiologic data showed that a low concentration of plasma HDL-C is also a major risk factor for coronary heart disease (CHD). In the United States, a low HDL-C concentration is the most prevalent lipid abnormality in men with known ischaemic heart disease (IHD). It is estimated that about 40% of patients with coronary disease have normal LDL-C levels, and most of these patients have low levels of HDL-C, with or without increased levels of triglycerides. Patients with angiographically proven IHD more often have low levels of HDL-C than high levels of LDL-C. HDL-C exerts its anti-atherogenic effects by reverse cholesterol transport mechanism in which the cholesterol from peripheral tissue like arterial wall is transported back to the liver, where it is eliminated in the bile. HDL also transports anti-oxidants to LDL-C making it less susceptible to oxidation. HDL-C also possesses anti-atherogenic effects, including anti-inflammatory, anti-thrombotic and endothelial-stabilizing properties. It is postulated that every unit-mg/dl decrease in HDL-C causes 3 – 4% increase in coronary artery disease (CAD). This study included only non-diabetic male individuals in the part of the world that has distinct dietary and smoking habits and generally has a sedentary life style.

The objective of the study was to find any difference in the fasting lipid profile in patients with history of ischaemic heart disease (IHD) and established atherosclerotic plaques on angiography and in subjects with no known history of IHD.

METHODOLOGY

The study population was based on a total of 200 male subjects between 40 and 60 years of age, divided into...
two groups. The patient group consisted of 99 male subjects with a diagnosis of ischaemic heart disease on angiography. Control group consisted of 101 subjects from same age and gender with no known history of ischaemic heart disease. All participants were asked to fill a questionnaire to obtain information on history of hypertension, diabetes mellitus, hyperlipidemia, ischaemic heart diseases and smoking. Subjects with diabetes mellitus and taking statins (lipid lowering drugs) were excluded from the study.

Five ml of venous blood was drawn from each fasting subject in a plain (red top) vacutainer tube (BD). Serum was separated by centrifugation at 1800 rpm for 10 minutes. All samples were stored at -80°C until the time they were tested.

Cholesterol and triglycerides were determined by enzymatic CHOD-PAP and GPO-PAP calorimetric method, HDL-C by accelerator selective detergent method and LDL-C by direct homogeneous enzymatic method using Architect c8000 system (Abbott Laboratories, Abbot Park, IL, USA). Serum ox-LDL content was determined by using quantitative sandwich enzyme immuno-assay kits (ox-LDL: DRG diagnostics, Marburg, Germany). Fasting blood glucose was measured on Architect c8000 system (Abbott Laboratories, Abbot Park, IL, USA) using Hexokinase method.

Statistical analysis was done using Statistical Package for Social Sciences (SPSS) version 12 (SPSS, Inc, Chicago, IL, U.S.A.). Categorical data is presented as percentages (frequencies), and quantitative data as medians and interquartile range values. For categorical data, Pearson chi-square test was used to determine any significant association between the groups for different variables. For quantitative data, Mann Whitney rank sum test was used to determine any significant differences between the study groups. Spearman's correlation coefficient test was used to determine any correlation between HDL-C and smoking and among ox-LDL and LDL-C, cholesterol, triglyceride and HDL-C. The p-value ≤ 0.05 was considered statistically significant.

RESULTS

The base line clinical characteristics of study subjects are summarized in Table I. Although the total cholesterol levels were within normal range in both study groups but surprisingly levels were significantly higher in the control group than in the test group (p = 0.002) with median values of 185.00 (inter-quartile range – IQR 43.00) and 165.00 (IQR 58.50) respectively. No significant difference (p = 0.101) was present in serum triglyceride levels between the control and patient groups and was within normal range with median values of 156.00 (IQR 100.00) and 124.00 (IQR 107.00) respectively. With no significant difference (p = 0.073) serum LDL-C levels were also within the normal range in the control and patient groups having median values of 106.00 (IQR 44.50) and 100.00 (IQR 50.50). The serum ox-LDL levels were higher in patient group as compared to the control group but the difference was not statistically significant (p = 0.114). The median values were 106.12 (IQR 79.30) and 112.63 (IQR 66.26) for control and patient groups respectively. The total serum HDL-C levels were significantly higher in the control group compared to the patient group (p = 0.001). The median values of control vs. patients groups were 40.00 (IQR 8.50) vs. 36.00 (IQR 6.50) [Table II].

A positive correlation was observed by Spearman's correlation coefficient test among ox-LDL and chole-

Table I: Baseline clinical characteristics in the study groups.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Control</th>
<th>Patient</th>
<th></th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>101</td>
<td>99</td>
<td>Frequency</td>
<td>24</td>
</tr>
<tr>
<td>Percentage</td>
<td>12</td>
<td>10</td>
<td>Frequency</td>
<td>31</td>
</tr>
<tr>
<td>%Smoking</td>
<td>101</td>
<td>99</td>
<td>Percentage</td>
<td>15.5</td>
</tr>
<tr>
<td>%Family H/O IHD</td>
<td>101</td>
<td>99</td>
<td>Percentage</td>
<td>14.5</td>
</tr>
<tr>
<td>%Fasting Blood Sugar</td>
<td>101</td>
<td>99</td>
<td>Median</td>
<td>89.00</td>
</tr>
<tr>
<td>%IQR</td>
<td>16.50</td>
<td>16.00</td>
<td>IQR</td>
<td>15.5</td>
</tr>
</tbody>
</table>

*p-value was determined by Pearson+ chi-square test; bSmoking = considered as smoker if the individual is currently smoking or has quitted smoking within the last six months; cFamily H/O IHD = It is positive if first degree relatives have ischaemic heart disease; dIQR = Inter-quartile range value; eFasting Blood Sugar = reference values by Expert Committee on the Diagnosis and Classification of Diabetes Mellitus eFasting Blood Sugar = p-value was determined by Mann Whitney rank sum test.

Table II: Comparison of fasting lipid profile and oxidized LDL between ischaemic heart disease patients and control group.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Control</th>
<th>Patient</th>
<th></th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>100</td>
<td>99</td>
<td>Median</td>
<td>156.00</td>
</tr>
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<td>%IQR</td>
<td>43.00</td>
<td>44.50</td>
<td>IQR</td>
<td>156.00</td>
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<tr>
<td>Cholesterol</td>
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<td>99</td>
<td>%IQR</td>
<td>100.00</td>
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<tr>
<td>Triglyceride</td>
<td>100</td>
<td>99</td>
<td>%IQR</td>
<td>106.00</td>
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<td>%LDL-C</td>
<td>100</td>
<td>99</td>
<td>%IQR</td>
<td>44.50</td>
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<tr>
<td>%Ox-LDL</td>
<td>101</td>
<td>95</td>
<td>%IQR</td>
<td>106.12</td>
</tr>
<tr>
<td>%HDL-C</td>
<td>100</td>
<td>99</td>
<td>%IQR</td>
<td>40.00</td>
</tr>
</tbody>
</table>

*p-value = determined by Mann Whitney rank sum test; aLDL-C = Low density lipoprotein-cholesterol; cOx-LDL = oxidized low density lipoprotein; dHDL-C = High density lipoprotein-cholesterol; eIQR = Inter-quartile range value.
terol, triglycerides, LDL with r-values of ox-LDL 1.00, cholesterol 0.23, triglycerides 0.10 and LDL 0.20 respectively whereas HDL-C has a negative correlation with r-values of -0.003. Correlation between ox-LDL and cholesterol, ox-LDL and LDL was significant (p = 0.001 and 0.005 respectively) whereas for triglycerides and HDL-C it was not significant.

The number of individuals with the history of smoking was higher among the test group (27%) than the control group (15.5%). A significant difference in the frequency of smoking between control and test groups was observed (p = 0.003, Table I).

Fasting blood glucose levels were significantly higher in the test group as compared to the control group (p = 0.001, z-value = -5.164), although they still remain within the expected normal range.

A significant difference (p = 0.001) for HDL-C levels was observed between smokers and non-smokers with the median values of 36.00 (IQR 8.00) and 40.00 (IQR 9.00) respectively (Table III).

DISCUSSION

The relation of serum LDL-C and triglycerides with the development and progression of atherosclerosis and IHD is well established by numerous clinical and epidemiological trials. However, a number of studies have concluded that low HDL-C was associated with a substantial increase in the risk of IHD. In this study, it was sought to determine the lipid abnormalities present in non-diabetic IHD patients and their healthy counterparts. Serum total cholesterol, LDL-C and triglyceride levels were within normal reference values in both groups. Serum HDL-C levels were significantly lower in the patient group as compared to the control group having normal HDL-C levels. This data is consistent with the results of BIP trial in which IHD patients were screened for dyslipidemia and among 1/3 of participants with normal total cholesterol, 50% had HDL-C levels < 35 mg/dl and 50% had HDL-C levels < 30 mg/dl. Similarly, in a study by Skoczynska et al. patients with normal plasma cholesterol levels suffering from atherosclerosis of coronary arteries had lower HDL-C levels.

Various studies have found a direct relationship between LDL-C and IHD. However, in VA-HIT the reduction in non-fatal myocardial infarction and IHD, death was strongly correlated with treatment concentrations of HDL-C but not triglycerides or LDL-C. Indeed, a substantial proportion of patients who developed IHD had plasma LDL-C concentrations below the average of men who remained IHD-free. ARBITER 2 trial included patients with low LDL-C levels with statins and targets their HDL-C by giving Niacin, and the progression of carotid artery intima media thickness was markedly slowed down in these patients. In the ARIC study Astor et al. concluded that there is a strong graded association between HDL-C and intima media thickness, which remained after adjustment of other risk factors such as LDL-C.

Many prospective studies have reported a positive relationship between serum triglyceride levels and incidence of IHD. However, early multivariate analyses generally did not identify serum triglycerides as an independent risk factor for IHD. The association of hypertriglyceridemia with an increased risk of CHD is not as strong as it is for LDL-C. Serum triglycerides up to 450 mg/dl predict the risk of IHD but this data showed triglyceride levels within normal range in both the study groups. Consistent with the present finding, Austin observed that there is no residual association between triglyceride levels and CHD risk and low HDL-C concentrations are associated with increased risk of IHD.

Oxidative modification of LDL has been widely accepted as one of the crucial steps in the development of atherosclerosis. A study by Tsimikas et al. showed an association of ox-LDL with a graded increase in the extent of CAD. Fredrickson et al. reported an association between plasma levels of oxidized LDL and the risk for acute myocardial infarction and / or death by CHD. In the present study although overall oxidized-LDL was higher in the patient group albeit not significantly compared to the control group. It may be assumed that some of these control individuals may have sub-clinical atherosclerosis. Their inclusion in the control group may have contributed to a lack of significant correlation between oxidized-LDL and atherosclerosis. This is consistent with and supported by Hulthe et al. who reported that subjects with no plaques had significantly lower levels of ox-LDL compared with subjects having sub-clinical atherosclerotic plaques. Moreover, in this study both patients and controls had normal fasting lipid profile and this may be the reason not to obtain a significant difference of ox-LDL between the two groups. Perhaps a larger study population may establish this relationship with statistical significance. Ox-LDL has a significant positive correlation with total cholesterol and LDL cholesterol. This finding is consistent with the previous study by Itabe et al, who...
also noted a correlation of ox-LDL to LDL cholesterol and suggested that one ox-LDL particle is present in every 10000 LDL particles. So, higher the concentration of LDL, more is the serum level of ox-LDL.

There are several acquired and genetic factors that contribute to low HDL-C cholesterol levels. About 50% of the variability of serum HDL-C levels derives from genetic factors. In the population acquired factors responsible for low HDL-C levels most probably are sedentary life style, cigarette smoking and dietary habits (increased intake of carbohydrate). Cigarette smoking has been identified as an independent and strong risk factor for CHD. Cigarette smoke produces its effect on atherosclerosis by various mechanisms. It causes the anti-oxidant depletion, production of oxidants, lipid abnormalities and activation of inflammatory and pro-coagulant system. Among lipid abnormalities, most important is LDL oxidation and HDL-C depletion. The meta-analysis of 54 published studies by Craig et al. showed 5.7% reduction in the concentrations of HDL-C among smokers. This study also shows a significant correlation between smoking and lower HDL levels. Overall HDL levels were significantly lower in smokers than non-smokers in patient as well as in the control group. This greater impact on HDL-C levels suggests that abnormalities in HDL-C metabolism could constitute a major metabolic effect of the smoking habit. Thus, even in normolipidemic subjects, smoking may possibly confer atherogeneity by preventing the intravascular remodeling of HDL-C.

A low HDL-C could be seen as a more stable marker for the risk of IHD than fasting triglycerides or LDL-C because low HDL-C level better distinguishes population with CHD than does a high level of LDL-C. Despres et al. in the Quebec study pointed out that there is a considerable overlap in the distribution of plasma LDL-C levels between IHD patients and healthy individuals and relative reduction in the number of CHD events achieved with hypolipidemic agents has been approximately 30%. Thus, there is a need to go beyond LDL-C measurement and determine the importance of other lipid abnormalities for the proper evaluation and optimal management of CHD risk. Thus, our ability to identify high-risk patients solely on the basis of LDL-C, triglycerides and cholesterol may be limited.

**CONCLUSION**

The significantly lower HDL levels in patient population with normal LDL and triglyceride levels may depict a different pattern of dyslipidemia in our society. It may be due to sedentary life style, smoking, dietary habits and perhaps genetic factors. There is a need for further trials to establish the fact that low HDL level has a greater role in pathogenesis of IHD in native population. Raising plasma HDL-cholesterol through weight loss, healthy diet, by an increased physical activity and if required, by proper pharmacotherapy is, therefore, a legitimate therapeutic target for the optimal prevention of CHD in a large proportion of high risk patients.

**REFERENCES**


