Hyperlipoproteinemias may actually be acute phase reactants in the plasma

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Abstract

Background: We tried to understand the significance of hyperlipoproteinemias, clinically.

Methods: We studied consecutive patients, applying for check up procedure, below the age of 70 years, to avoid debility induced weight loss in elders.

Results: The study included 252 cases (156 females), totally. The female ratio was significantly higher in the obesity (78.0%) than the overweight (51.7%, p<0.001) and normal weight groups (56.6%, p<0.001). The mean age increased from the normal weight (32.9 years) towards the overweight (45.0 years, p= 0.000), and obesity groups, significantly (51.0 years, p= 0.006). Parallel to the mean body mass index (BMI), the mean body weight increased from the normal weight (62.0 kg) towards the overweight (75.5 kg, p= 0.000), and obesity groups, again (87.2 kg, p= 0.000). Fasting plasma glucose (FPG), systolic and diastolic blood pressure (BP), total cholesterol (TC), low density lipoproteins (LDL), high density lipoproteins (HDL), and triglycerides all increased nearly in all steps from the normal weight towards the overweight and obesity groups parallel to the increased mean age, BMI and body weight, significantly.

Conclusion: The accelerated atherosclerotic process all over the body may be the major consequence of the metabolic syndrome. FPG, systolic and diastolic BP, TC, LDL, HDL, and triglycerides all increased parallel to the increased age, BMI, and body weight, significantly. Hyperlipoproteinemias may actually be acute phase reactants indicating the disseminated endothelial damage, inflammation, fibrosis, and eventual atherosclerosis by aging all over the body.

Key words: Hyperlipoproteinemia, acute phase reactant, metabolic syndrome, accelerated atherosclerosis

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Introduction

Due to the prolonged survival of human beings, systemic atherosclerotic sequelae may be the major health problems in this century, and their associations with excess weight, some metabolic disorders, smoking, and alcohol are collected under the title of metabolic syndrome (1, 2). The syndrome is characterized by a low-grade chronic inflammatory process on vascular endothelium all over the body (3). The inflammatory process is accelerated by some factors including excess weight, smoking, alcohol, chronic infection and inflammations, and cancers (4, 5). The syndrome can be slowed down with appropriate nonpharmaceutical approaches including lifestyle changes, diet, and exercise (6). The syndrome contains indicators including overweight, white coat hypertension (WCH), impaired fasting glucose (IFG), impaired glucose tolerance (IGT), hyperlipidemia, alcohol, and smoking for the development of irreversible consequences including obesity, hypertension (HT), type 2 diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), cirrhosis, chronic renal disease (CRD), peripheral artery disease (PAD), coronary artery disease (CAD), and stroke (7). In another perspective, the metabolic syndrome may be the most important disease of the human lifespan decreasing its quality and duration at the moment. The syndrome has become increasingly common all over the world, for instance 50 million people in the United States are affected (8). The syndrome induced accelerated atherosclerotic process all over the body may be the leading cause of early aging and premature death for both genders. For example, CAD is the leading cause of death in developed countries. On the other hand, plasma lipoproteins are under active metabolic control, and they may be influenced from several factors including body mass, physical inactivity, elevated blood pressure (BP), increased plasma glucose, smoking, alcohol, prolonged infection and inflammations, and cancers. We tried to understand significance of plasma lipoprotein levels, clinically.

Material and methods

The study was performed in the Internal Medicine Polyclinic of the Mustafa Kemal University between March 2007 and April 2009. We studied consecutive patients applying for check up procedure between the ages of 15 and 70 years. Cases above the age of 70 years were excluded to prevent debility induced weight loss in elders. Their medical histories were learnt, and a routine check up procedure including body mass index (BMI), impaired fasting glucose (IFG, FPG), total cholesterol (TC), low density lipoproteins (LDL), high density lipoproteins (HDL), impaired glucose tolerance (IGT), hyperlipidemia, alcohol, and smoking for the development of irreversible consequences including obesity, hypertension (HT), type 2 diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), cirrhosis, chronic renal disease (CRD), peripheral artery disease (PAD), coronary artery disease (CAD), and stroke (7). In another perspective, the metabolic syndrome may be the most important disease of the human lifespan decreasing its quality and duration at the moment. The syndrome has become increasingly common all over the world, for instance 50 million people in the United States are affected (8). The syndrome induced accelerated atherosclerotic process all over the body may be the leading cause of early aging and premature death for both genders. For example, CAD is the leading cause of death in developed countries. On the other hand, plasma lipoproteins are under active metabolic control, and they may be influenced from several factors including body mass, physical inactivity, elevated blood pressure (BP), increased plasma glucose, smoking, alcohol, prolonged infection and inflammations, and cancers. We tried to understand significance of plasma lipoprotein levels, clinically.

Results

The study included 252 cases (156 females and 96 males), totally. There were 83 cases in the normal weight, 87 cases in the overweight, and 82 cases in the obesity groups. The mean BMI values were 22.4, 27.2, and 34.3 kg/m², respectively. The female ratio was significantly higher in the obesity (78.0%) than the overweight (51.7%, p<0.001) and normal weight groups (56.6%, p<0.001). The mean age increased from the normal weight (32.9 years) towards the overweight (45.0 years, p=0.000), and obesity groups, significantly (51.0 years, p=0.006). Parallel to the mean BMI, the mean body weight increased from the normal weight (62.0 kg) towards the overweight (75.5 kg, p=0.000), and obesity groups, again (87.2 kg, p=0.000). On the other hand, the mean body heights remained stable in the normal weight and overweight groups (165.8 cm in both), whereas it decreased in the obesity groups, significantly (158.8 cm, p=0.000), probably due to the female predominance of the obesity group. As the most significant result of the study, FPG, systolic and diastolic BP, TC, LDL, HDL, and triglycerides were detected in each group, and compared by some metabolic risk factors for the development of systemic atherosclerotic endpoints, those probably are the leading cause of early aging and premature death for both genders in human beings. Physical inactivity, excess weight, smoking and alcohol are probably the most common causes of the systemic endothelial damage and inflammation (10). Definition of the metabolic syndrome or aging syndrome or accelerated endothelial damage syndrome includes metabolic indicators including physical inactivity, overweight, smoking, alcohol, WCH, IFG, IGT, and hyperlipidemia for the development of irreversible endpoints including obesity, HT, DM, COPD, cirrhosis, CRD, PAD, CAD, stroke, early aging, and premature death (11, 12). In a previous study (13), prevalences of hypertriglyceridemia, hyperbetalipoproteinemia, dyslipidemia, IGT, and WCH had parallel fashion to excess weight by increasing until the seventh decade of life and decreasing afterwards, significantly (p<0.05 nearly in all steps). On the other hand, prevalences of HT, DM, and CAD always continued...
to increase by aging without any decrease (p<0.05 nearly in all steps) indicating their irreversible properties. After development of one of the irreversible consequences, the non-pharmaceutical approaches will provide little benefit to prevent development of the others probably due to cumulative effects of the risk factors on the endothelial system for a long period of time (11, 12).

Obesity is probably found among one of the irreversible endpoints of the metabolic syndrome, since after development of obesity, nonpharmaceutical approaches provide limited success either to heal obesity or to prevent its complications. Overweight and obesity probably lead to a chronic and low-grade inflammation on vascular endothelium, and risk of death from all causes including cardiovascular diseases and cancers increases parallel to the range of weight excess in all age groups (14). The low-grade chronic inflammation may cause genetic changes on the epithelial cells, and the systemic atherosclerotic process may decrease clearance of malignant cells by the immune system, effectively (15). The effects of excess weight on BP were shown in a previous study (16) that the prevalence of sustained normotension (NT) was significantly higher in the underweight (80.3%) than the normal weight (64.0%) and overweight groups (31.5%, p<0.05 for both), and 52.8% of cases with HT had obesity against 14.5% of cases with NT (p<0.001) in another study (17). So the dominant underlying factor of the metabolic syndrome appears as weight gain, which is probably the major cause of insulin resistance, hyperlipidemia, IGT, and WCH via a chronic inflammatory process (6). Even prevention of the accelerating trend of weight gain with diet or exercise, even in the absence of a prominent weight loss, will probably result with resolution of many adverse parameters of the syndrome (18, 19). But according to our opinion, limitation of excess weight as an excessive fat tissue around abdomen under the heading of abdominal obesity is meaningless, instead it should be defined as overweight and obesity by means of BMI since adipocytes function as an endocrine organ and they produce a variety of cytokines and hormones anywhere in the body (6). The resulting hyperactivities of sympathetic nervous system and renin-angiotensin-aldosterone system are probably associated with chronic endothelial inflammation, insulin resistance, and an elevated BP. Similarly, the Adult Treatment Panel III reported that although some people classified as overweight with a large muscular mass, most of them also have excess fat tissue, and excess weight does not only predispose to CAD, stroke, and other endpoints, it also has a high burden of other CAD risk factors including hyperlipidemia, HT, and DM (9).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Normal weight</th>
<th>p-value</th>
<th>Overweight</th>
<th>p-value</th>
<th>Obesity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>83</td>
<td>Ns*</td>
<td>87</td>
<td>&lt;0.001</td>
<td>82</td>
</tr>
<tr>
<td>Female ratio</td>
<td>56.6%</td>
<td>51.7%</td>
<td>78.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age (year)</td>
<td>32.9 ± 13.0</td>
<td>0.000</td>
<td>45.0 ± 13.2</td>
<td>0.006</td>
<td>51.0 ± 9.9</td>
</tr>
<tr>
<td>Mean BMI† (kg/m²)</td>
<td>22.4 ± 1.5</td>
<td>0.000</td>
<td>27.2 ± 1.3</td>
<td>0.000</td>
<td>34.3 ± 4.2</td>
</tr>
<tr>
<td>Mean weight (kg)</td>
<td>62.0 ± 7.6</td>
<td>0.000</td>
<td>75.5 ± 8.5</td>
<td>0.000</td>
<td>87.2 ± 10.6</td>
</tr>
<tr>
<td>Mean height (cm)</td>
<td>165.8 ± 8.4</td>
<td>Ns</td>
<td>165.8 ± 9.5</td>
<td>0.000</td>
<td>158.8 ± 8.3</td>
</tr>
<tr>
<td>Mean FPG‡ (mg/dL)</td>
<td>95.2 ± 11.7</td>
<td>0.012</td>
<td>102.2 ± 22.1</td>
<td>0.018</td>
<td>109.2 ± 28.8</td>
</tr>
<tr>
<td>Mean systolic BP$ (mmHg)</td>
<td>115.3 ± 16.9</td>
<td>0.000</td>
<td>133.6 ± 23.6</td>
<td>0.000</td>
<td>147.3 ± 26.8</td>
</tr>
<tr>
<td>Mean diastolic BP (mmHg)</td>
<td>82.7 ± 8.5</td>
<td>0.000</td>
<td>90.1 ± 11.1</td>
<td>0.000</td>
<td>96.8 ± 11.9</td>
</tr>
<tr>
<td>Mean TC‖ (mg/dL)</td>
<td>180.5 ± 40.9</td>
<td>0.050</td>
<td>197.1 ± 39.6</td>
<td>0.016</td>
<td>211.3 ± 44.7</td>
</tr>
<tr>
<td>Mean LDL† (mg/dL)</td>
<td>109.1 ± 29.3</td>
<td>0.000</td>
<td>130.4 ± 30.9</td>
<td>Ns</td>
<td>131.9 ± 37.0</td>
</tr>
<tr>
<td>Mean HDL** (mg/dL)</td>
<td>40.9 ± 8.9</td>
<td>0.025</td>
<td>46.0 ± 10.7</td>
<td>0.050</td>
<td>50.1 ± 10.4</td>
</tr>
<tr>
<td>Mean triglycerides*** (mg/dL)</td>
<td>113.6 ± 73.1</td>
<td>0.003</td>
<td>136.3 ± 73.7</td>
<td>0.004</td>
<td>150.0 ± 85.2</td>
</tr>
</tbody>
</table>

*Nonsignificant (p>0.05) †Body mass index ‡Fasting plasma glucose §Blood pressure ||Total cholesterol ‖Low density lipoproteins **High density lipoproteins
Plasma lipoprotein levels probably are under dynamic control, and they may act as acute phase reactants indicating disseminated inflammation anywhere in the body. Physical inactivity, increased BMI, smoking, alcohol, elevated BP, increased plasma glucose, prolonged infection and inflammations, and cancers may cause overproduction of very low density lipoproteins (VLDL) in liver. VLDL carry endogenous triglycerides from liver to peripheral tissues either to use or to store. In capillaries of adipocytes and muscle tissue, 90% of triglycerides is removed by a specific group of lipases. These lipases degrade VLDL into intermediate density lipoproteins (IDL), and IDL and are then degraded into LDL by removal of more triglycerides. The fate of LDL is uncertain, and liver removes about 70%. A small amount of LDL in circulation is uptaken by scavenger receptors on macrophages that may migrate into arterial walls, where they become the foam cells of atherosclerotic plaques. Hyperlipoproteinemia can result either from overproduction or defective clearance of VLDL or increased conversion of VLDL into LDL. The increased lipoprotein levels by aging may actually be a result of physical inactivity, excess weight, elevated BP, and increased plasma glucose induced disseminated endothelial damage, inflammation, fibrosis, and eventual atherosclerosis all over the body. Eventually, high TC and LDL levels are independently associated with CAD. Familial hypobeta- and alphalipoproteinemia are associated with decreased prevalences of CAD and other atherosclerotic sequelae, and they have been referred as the Longevity syndromes. Similarly, low HDL levels often occur in vegetarian populations, in whom LDL levels and CAD rates are low, too.

As a conclusion, the accelerated atherosclerotic process all over the body may be the major consequence of the metabolic syndrome. FPG, systolic and diastolic BP, TC, LDL, HDL, and triglycerides all increased parallel to the increased age, BMI, and body weight, significantly. Hyperlipoproteinemia may actually be acute phase reactants indicating the disseminated endothelial damage, inflammation, fibrosis, and eventual atherosclerosis by aging all over the body.

References
