BIOCHEMICAL EVALUATION OF LIPID PROFILE IN METABOLIC SYNDROME

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Abstract:

The metabolic syndrome consists of a constellation of metabolic abnormalities including central obesity, hypertriglyceridemia, low high-density lipoprotein (HDL) cholesterol, hyperglycemia and hypertension. The traditional factors associated with the syndrome are obesity, insulin resistance, hyperglycemia, dyslipemia, hypertension and microalbuminuria. One of the major risk factors in metabolic syndrome is dyslipidemia which can be related to a changed lipoprotein spectrum and to modified lipoproteins.

Aim: The aim of the study was to evaluation of lipid profile in metabolic syndrome patients.

Materials and methods: The Present study was carried out in the department of Biochemistry, SLIMS (Sri Lakshmi Narayana Institute of Medical Sciences), Puducherry. The present study was conducted on 100 patients with metabolic syndrome, and 100 patients with controls as per IDF criteria and waist circumference.

Results: Serum Cholesterol, TGL, LDL levels were significantly increased in metabolic syndrome patients when compared with controls. Serum HDL levels were significantly decreased in metabolic syndrome (MetS) patients when compared with controls.

Discussion: There is significant correlation observed between dyslipidaemia and hyperglycaemia and also found positive correlation between dyslipidaemia and hypertension and waist circumference of metabolic syndrome patients.

Conclusion: The lipid profile, Serum cholesterol, LDL as well as TG and HDL-C were consistently associated with
MetS. Lipid profile may be used as a reliable markers. Further prospective studies are needed to investigate the changes in lipid metabolism by lifestyle interventions in metabolic syndrome patients.

**Key Words:** Metabolic syndrome, Dyslipidaemia, HDL-cholesterol, Lipid profile.

**Introduction:**

Metabolic syndrome is a growing epidemic throughout the world. Approximately 1 adult in every 4 or 5, depending on the country, has metabolic syndrome. The incidence increases with age; Currently around one-third of the population in India are living with metabolic syndrome, the majority of them being women. Increasing inactivity and Westernization of the Indian diet are partly to blame. Multinational fast food companies with huge advertising budgets have radically changed the way in which Indian adults and children eat, and the rush to copy the Western model has led to even easier access to unhealthy food choices [1].

According to the Third National Health and Nutrition Examination Survey (NHANES III) criteria, about 47 million people have metabolic syndrome[2], including 44% of those in the ≥ 50-year age group.[3] Metabolic syndrome is present in 10% of women and 15% of men with normal glucose tolerance, 42% and 64% of those with impaired fasting glucose levels, and 78% and 84% of those with type 2 diabetes mellitus.[4] Most patients (> 80%) with type 2 diabetes have metabolic syndrome, but the converse is not necessarily true. In a developing country like India, increasing urbanization and lifestyle changes have led to an increased incidence of Metabolic syndrome. Though a limited amount of data exists on the prevalence of metabolic syndrome in India, prevalence data from the diabetic population is lacking.

Nowadays Human lifestyle is gradually shifting towards an increase in the consumption of high energy diet (over-nutrition) and decrease in physical activity (sedentary lifestyle) [5]. This shift can lead to metabolic disorders and associated abnormalities often characterized by central obesity, hypertension, dyslipidemia and hyperglycemia, and other conditions such as non-alcoholic fatty liver disease [6,7]. These conditions are collectively termed metabolic syndrome (Figure 1). Metabolic syndrome indicators are also the known major risk factors of CVD disease, a leading cause of death with estimated contribution to almost half of global mortality due to non-communicable diseases [7]. The molecular processes that occur in metabolic syndrome can lead to cardiovascular disease pathogenesis and involve risk factors such as oxidative stress and inflammation [7, 8]. To date, changes in lifestyle (e.g., weight loss, physical activity and consumption of energy-restricted diet) have been recommended as primary strategies for controlling metabolic syndrome.
and related health problems. Moreover, therapeutic agents that target metabolic processes associated with the controllable risk factors have also been explored for the management of these health conditions [9]. Nutritional and secondary metabolites in food (e.g., dietary fibers, phytosterols, polyphenols, polyunsaturated fatty acids, carotenoids and proteins) have demonstrated biological activities that can be applied in ameliorating abnormal metabolic processes related to metabolic syndrome [10]. Lipids synthesized in the liver and intestines are transported in the plasma in macromolecular complexes known as lipoproteins. Lipoproteins have been categorized based on difference in their hydrated densities, as determined by ultracentrifugation. These categories include chylomicrons, Very Low Density Lipoproteins, Intermediate Density Lipoproteins, Low Density Lipoproteins, High Density Lipoproteins, Lipoproteins(a).

Lipid profile refers to a group of blood tests done to evaluate the risk of atherosclerosis in an individual. Alterations in the levels of several blood lipids are known to be the independent such as hypercholesterolemia, hypertriglyceridemia, increased LDL-cholesterol, decreased HDL-Cholesterol, increased lipoproteins, etc. Evaluation of cholesterol content of HDL and LDL is particularly important, they are actively involved in cholesterol transport.[11]

Figure 1. Dyslipidemia, abnormal endogenous lipid metabolism (including hyperlipidemia), is associated with metabolic syndrome.

National Cholesterol Education Program Adult Treatment Panel III recommended that metabolic syndrome is diagnosed when an individual manifests three or more of the risk determinants [11].
White adipose tissue, the fat is mostly stored and this tissue metabolically very less active, and storage form of energy is contains TAGs (triacylglycerols), produced mainly by FAs (fatty acids) derived from chylomicrons and circulating VLDLs [very-LDL (low density lipoproteins)], released through the action of LPL (lipoproteinlipase), is an insulin-stimulated enzyme. Glucose provides the glycerol backbone for TAG. In humans, FAs can also be synthesized from glucose, although the rate of synthesis is lower than in rodents. Adipose tissue is also able to release NEFAs [non-esterified FAs (‘free FAs’)]; during lipolysis, TAGs are hydrolysed in a reaction catalysed by HSL (hormone-sensitive lipase), which is, in turn, regulated by numerous factors and hormones. Catecholamines, by binding to β-adrenergic receptors, stimulate lipolysis, whereas insulin inhibits this process [12].

The metabolic syndrome is associated with an increased risk of coronary heart disease (CHD), myocardial infarction, stroke and cancers in both sexes. This substantially increased risk of CV morbidity and mortality associated with the presence of metabolic syndrome appears independent of other significant, factors such as smoking, plasma LDL cholesterol levels or alcohol consumption. Dyslipidaemia is an integral part of metabolic syndrome since both definitions include hypertriglyceridemia (defined as serum triglycerides ≥ 150 mg/dL) and a low HDL cholesterol concentration as components. Individuals with metabolic syndrome, particularly those with abdominal obesity, exhibit a highly atherogenic lipid profile which may account for their high risk of CVD [13]. Central fat accumulation and the presence of insulin resistance have both been associated with a cluster of dyslipidemic features, i.e., elevated plasma triglyceride level, an increase in very-low-density lipoprotein (VLDL) and intermediate-density lipoprotein (IDL), the presence of small dense LDL particles, and a decrease in HDL-cholesterol. These abnormalities of lipoprotein metabolism are more likely to occur together than separately and constitute the key component traits of the metabolic syndrome[13-16].

Figure 2: Relationship between lipid metabolism and Metabolic syndrome.
Materials & Methods:

The Present study was carried out in the Central Laboratory, SLIMS (Sri Lakshmi Narayana Institute of Medical Sciences), Puducherry. In this study total number of patients divided in to 2 different groups.

The distributions of subjects in the study were as follows

Study group:
1. Metabolic syndrome - 200 subjects
2. Control group – 200 subjects

All the data were collected in a prescribed preform. The 200 patient was diagnosed as having metabolic syndrome based on the history, clinical examination. The control groups were 200, they were collected from medical staff members and relatives who were free from signs and symptoms of metabolic syndrome, like lipid disorders, diabetes mellitus and hypertension.

All the patients were asked to fast overnight for a period of minimum 12 hours. 5ml of the blood samples which were taken for analysis were obtained from the antecubital vein.

5 ml of venous blood samples were collected from patients and controls. Same up to criteria .The analysis of plasma glucose was done by the glucose oxidase method, while the serum Total Cholesterol, HDL-Cholesterol, TG triglycerides were done by using enzymatic kits on Siemens TM autoanalzyer.

The serum Total Cholesterol, HDL-Cholesterol, TG were estimated by conventional kits by using with Siemens TM fully autoanalzyer [17]. The LDL-C was calculated by the following equation: LDL-C = TC – HDL-C – (TG × 0.2).

Results

Serum Cholesterol levels were significantly increased in metabolic syndrome patients when compared with controls. The p-value <0.001 is comparatively highly significant. Serum LDL, TG levels were significantly increased in metabolic syndrome patients when compared with controls. The p-value <0.001 is comparatively highly significant. Serum HDL levels were significantly decreased in metabolic syndrome patients when compared with controls. The p-value <0.001 is comparatively highly significant. Serum FBS levels were significantly increased in metabolic syndrome patients when compared with controls. The p-value <0.001 is comparatively highly significant. (Table No.1). The statistical analysis was done by the unpaired two tailed ‘t’ test and the Pearson’s correlation coefficient by using online calculator. The data were
presented as mean with SE. The statistical significance was kept of P value <0.001 is comparatively highly significant.

Graph of all the investigations of this study were plotted by using the 100 individual values of all investigations done in metabolic syndrome and 100 individual values of all investigations done in control subjects.

### Table-1: Mean ± SEM levels in metabolic syndrome and controls.

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Parameters (mg/dl)</th>
<th>Metabolic Syndrome(200) Mean ± SE</th>
<th>Control(200) Mean ± SE</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cholesterol</td>
<td>245 ±30.51</td>
<td>188.5±27.3</td>
<td>P &lt;0.001</td>
</tr>
<tr>
<td>2</td>
<td>TGL</td>
<td>243± 28.62</td>
<td>169.2 ±28.4</td>
<td>P &lt;0.001</td>
</tr>
<tr>
<td>3</td>
<td>HDL</td>
<td>30± 5.52</td>
<td>50±8.25</td>
<td>P &lt;0.001</td>
</tr>
<tr>
<td>4</td>
<td>LDL</td>
<td>123.8± 31.4</td>
<td>68.3±13.2</td>
<td>P &lt;0.002</td>
</tr>
<tr>
<td>5</td>
<td>FBS</td>
<td>156.55± 4.82</td>
<td>106.12±1.68</td>
<td>P &lt;0.001</td>
</tr>
</tbody>
</table>

Graph 1: Shows the values of the Serum cholesterol, TGL, HDL, LDL, and FBS in Metabolic syndrome.

Graph 2: Shows the values of the Serum cholesterol, TGL, HDL, LDL, and FBS in controls.
Discussion:

Metabolic syndrome (MetS) as a clustering of cardiovascular risk factors associated with insulin resistance, hypertriglyceridemia, hypertension, glucose intolerance, [18,20], and low levels of high-density lipoprotein cholesterol (HDL-C), is a major worldwide public health problem. Metabolic syndrome is also associated with an increased risk of some common cancers [21]. One of the major risk factors in metabolic syndrome is dyslipidemia which can be related to a changed lipoprotein spectrum and to modified lipoproteins. Abnormalities in serum lipid profile (predominantly hypercholesterolaemia and hypertriglycerydaemia), arterial hypertension, diabetes and obesity are often associated with the same individual [22]. The association of these factors in the same individual greatly increases cardiovascular risk.

In the present study the results of lipid profile status of case group have shown that there is significantly increase in TG, LDL, total cholesterol and decrease in HDL levels which is positively correlated with FBS. There is significant correlation observed between dyslipidaemia and hyperglycaemia and also found positive correlation between dyslipidaemia and hypertension and waist circumference of metabolic syndrome patients.

Abdominal adipose tissue releases excess Influx of nonesterified fatty acids (NEFA) s and adipokines into the circulation. Increased blood NEFAs inhibit the uptake of glucose by muscle. Even though excess insulin is produced by pancreas, it is not enough to control the hyper- glycaemia, thus explaining the paradox of fasting hyperglycaemia despite increased plasma insulin levels, which is known as Insulin Resistance[23]. Hyperglycaemia and increased circulating NEFAs leads to increased production of Triacylglycerols (TAGs) by the liver. Release of NEFAs by adipocytes is greater in central obesity with no concomitant increase in oxidation by peripheral tissues, which is related to Insulin Resistance (IR) and the lack of inhibition of hormone sensitive lipase (HSL). The failure of insulin to suppress HSL stimulates the release of NEFAs from lipolytically active visceral fat. In addition, an increased rate of hepatic NEFA uptake stimulates the secretion of apoB-100, leading to increased numbers of apo B-containing particles and, indeed, the secretion of VLDL is enhanced. Increased plasma VLDL and TAG is usually associated with decreased HDL levels [24]. Cholesteryl ester transfer protein (CETP) mediates the transfer of cholesterol from HDL to the apoB-containing lipoproteins, and HSL and endothelial lipase are up-regulated in the MetS, thus promoting hypercatabolism of HDL and leading to the generation of small-dense LDL (Sd-LDL) particles and a decrease in HDL2-C. Elevated NEFA levels increase hepatic gluconeogenesis and lower peripheral tissue glucose uptake, prompting a further increase in the hyperinsulinaemia typically found in the
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Elevated NEFA concentrations are toxic to pancreatic β-cells, inducing their apoptosis, accelerating pancreas failure and favouring progression to diabetes. Low plasma levels of adiponectin decreases the activities of FATP-1 (FA transporter protein-1) and AMP-activated protein kinase (AMPK), leading to lower FA oxidation. Likewise, insulin signalling mediated though IRS-1 (insulin receptor substrate-1) is altered and glucose uptake is impaired. In addition, low levels of adiponectin activate phosphoenolpyruvate carboxykinase, a key enzyme of glyconeogenesis, resulting in hyperglycaemia[26]. Central obesity is the main cause of the MS, which in turn related to hormonal changes, including increased insulin synthesis and peripheral IR, increased leptin synthesis and decreased adiponectin synthesis by adipose tissue, lead to diminished FA oxidation [27].

Our study correlated with other studies, Kimm et al. [28] demonstrated that the lipid ratios of TC/HDL-C, LDL-C/HDL-C and TG/HDL-C, as well as TG and HDL-C, were each consistently associated with the number of metabolic syndrome components, insulin resistance quartiles (based on homeostatic model assessment), and log-transformed adiponectin quartiles. The lipids ratios that include information on at least two measures might have a more integrated explanation than single lipid measures such as TG or HDL-C [29]. Ryuichi Kawamoto study [30], both TG/HDL-C and TC/HDL-C ratios as well as TG were useful makers of MetS associated variables in both men and women, especially TG/HDL-C ratio in men.

Conclusion:
The present study demonstrated that altered lipid profile is associated with MetS-associated variables in a general population. The results of our study shows that, there is significant correlation in between dyslipidemia and hyperglycaemia and also found positive correlation between dyslipidaemia and hypertention and waist circumference of metabolic syndrome patients. The ability to identify who have MetS could help health care professionals in bringing about lifestyle interventions. Findings emerging from other studies about the behaviour of lipid metabolism and adipose tissue could modify the future evolution and treatment in MetS. Further prospective studies are needed to investigate the changes in lipid metabolism by lifestyle interventions in metabolic syndrome patients.

References:
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