## **RESEARCH ARTICLE**

# Importance of lipid-lipoprotein ratios as a diagnostic tool in metabolic syndrome population

## Bhagyashree N<sup>1</sup>, Ramaswamy C<sup>2</sup>, Ganesh M<sup>1</sup>

<sup>1</sup>Department of Physiology, ACS Medical College and Hospital, Chennai, Tamil Nadu, India, <sup>2</sup>Department of Physiology, Saveetha Medical College and Hospital, Thandalam, Chennai, Tamil Nadu, India

Correspondence to: Bhagyashree N, E - mail: bhagyashivanugraha@gmail.com

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#### ABSTRACT

**Background:** Metabolic syndrome (MS) is a constellation of diseases caused by several interconnected cardiometabolic risk factors such as obesity, hypertension, hyperglycemia, and dyslipidemia. Lipid-lipoprotein ratios can be considered as an alternative for identifying individuals with MS. **Objectives:** The objectives of this study were to compare the lipid profile and lipid-lipoprotein ratios of different groups formed based on the progression of the severity of MS. **Materials and Methods:** A total of 195 participants who volunteered with the signs of MS were divided into three groups based on the presence of metabolic abnormalities as Group I (with <3 components of MS - control group), Group II (with any three components of MS group), and Group III (with >3 components of MS - severe MS group). **Results:** Results showed that triglycerides (TG), ratio of TG-to-high-density lipoprotein, and total cholesterol (TC)-to-high-density lipoprotein ratio showed significant difference (P < 0.001) between the groups, whereas the results of high-density lipoprotein and low-density lipoprotein-to-high-density lipoprotein ratio were significantly more (P < 0.001) in severe MS in comparison with control and MS. TC showed significant difference (P = 0.004) in MS and severe MS when compared with that of control. **Conclusion:** Early identification and treatment of individuals with MS is very important to prevent debilitating effects associated with its development.

KEY WORDS: Lipoprotein Ratios; Metabolic Syndrome; Severity; Cardiovascular Disease

### INTRODUCTION

Metabolic syndrome (MS) is a complicated, constellation of diseases caused by several interconnected cardiometabolic risk factors such as obesity, hypertension, hyperglycemia, and dyslipidemia.<sup>[1]</sup> MS not only associated with increased cardiovascular disease (CVD) risk but also produced a prothrombotic and pro-inflammatory state.<sup>[2]</sup> Subjects with

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MS showed risk for coronary heart disease and stroke which was 3 times greater than that of controls.<sup>[3]</sup> CVD is the most important cause of death worldwide, and majority of deaths take place in low- and middle-income countries are related to CVD.<sup>[4]</sup> Dyslipidemia is a component of MS, as well as a major risk factor for CVD. Triglycerides (TG) and HDL-C are not only the components of MS but also act as independent risk factors of CVD.<sup>[5]</sup> Evidence shows that lipid ratios perform better than individual lipids in predicting cardiovascular risk.<sup>[6]</sup> Hence, it has been suggested that ratios of lipid-lipoproteins can be considered as an alternative for identifying individuals with MS.

Although atherosclerosis is a multifactorial process, abnormalities in lipid metabolism constitute one of the important factors for developing CVD risk, which represents

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about 50% of the population. It has been said that CVD risk begins with the presence of one component of MS itself and MS predicts the future CVD mortality.<sup>[6]</sup> Yet, the study on clinical importance of lipid-lipoprotein ratios in MS population to identify individuals at greater cardiometabolic risk is rarely available. Hence, this study was aimed to explore the magnitude of lipid-lipoprotein ratios with the severity of MS.

## Objective

The objective of this study was to compare the lipid profile and lipid-lipoprotein ratios of different groups formed based on the progression of the severity of MS.

## MATERIALS AND METHODS

This cross-sectional study consisting of 195 participants between the age of 30 and 60 years and was divided into three groups based on the presence of metabolic abnormalities as Group I or control (with <3 components of MS), Group II/ MS group (with any three components of MS), and Group III/ severe MS (with >3 components of MS). The study commenced after obtaining the Institutional Ethical Committee clearance with number 005/12/2014/IEC/SU, dated December 18, 2014, and the participants written informed consent. National Cholesterol Education Program Adult Treatment Panel III criteria were used to diagnose MS and grading the severity. According to this criterion, patients with any three of five components as mentioned below can be considered as MS. Participants with waist circumference  $\geq 102$  cm in men and ≥88 cm in women, systolic and diastolic blood pressure  $\geq 130/85$  mm Hg, low-high-density lipoprotein (HDL) cholesterol, HDL  $\leq 40 \text{ mg/dL}$  in men and  $\leq 50 \text{ mg/}$ dL in women, TG  $\geq$ 150 mg/dL, and fasting blood glucose  $\geq$ 100 mg/dL were included for the present study. To analyze the lipid profile, 3 ml of venous blood sample was collected from all participants after overnight fast. With the collected blood, total cholesterol (TC) (mg/dL), TG (mg/dL), highdensity lipoprotein (HDL), and low-density lipoprotein (LDL) cholesterol were measured, and then, the ratios TC/ HDL, TG/HDL, and LDL/HDL were calculated.

## **Statistical Analysis**

Statistical analyses were carried out by SigmaPlot 13.0 (Systat software, USA). Data were expressed as mean  $\pm$  standard error. The means were analyzed by one-way analysis of variance with multiple comparison test of Student–Newman–Keuls test.

## RESULTS

The values of the serum lipid profile, TC, TG, HDL cholesterol, and LDL cholesterol were depicted in Table 1. The statistical analysis showed that the value of TC was significantly varied among the study groups (F = 5.739; P < 0.004) which was lower in control (150.7 mg/dL) than the other two groups (MS 161.8 mg/dL and severe MS 164.2 mg/dL). Similarly, the values of serum TG also showed statistically significant difference between all the groups (F = 21.339, P < 0.001) in which control was 132.858 mg/dL which was less when compared with the TG values of the MS (145.9 mg/dL) and severe MS (174.3 mg/dL). The serum HDL is considered as good cholesterol, showed significant difference among the groups (F = 40.676, P < 0.001) with the lower value in severe MS (41.6 mg/dL) when compared with both MS (47.4 mg/dL) and control (49.0 mg/dL). Another lipid parameter called LDL, which did not show significant variations (F = 1.162, P = 0.315) among the groups; control (74.4 mg/dL), MS (78.3 mg/dL), and severe MS (79.7 mg/dL).

In the present study [Table 2], the ratio of TG/HDL (TC to HDL), TC/HDL (TC to HDL), and LDL/HDL was compared in control, MS, and severe MS groups. The values of TG/HDL ratio in control were 2.7, in MS 3.1, and in severe MS 4.3. It was found that there was significant difference of TG/HDL among all the groups (F = 38.378, P < 0.001). Similarly, the values of TC/HDL showed increasing tendency with the severity of MS which showed statistically significant difference among all the groups (F = 26.538, P < 0.001). Here, the values were 3.1 in control, 3.5 in MS, and 4.0 in severe MS groups. The significant difference (F = 11.401, P < 0.001) attributed when analyzed the values of LDL/HDL

Table 1: Comparison of lipid parameters in different study groups							
Variable	<b>Control Group I</b>	MS Group II	Severe MS Group III	<b>F-value</b>	<i>P</i> -value		
TC (mg/dl)	150.7±2.9	161.8±2.6	164.2±3.3	5.739	0.004 Group I and III, Group I and II		
TG (mg/dl)	132.8±2.5	145.9±4.5	174.3±5.9	21.339	<0.001 Group I and II Group I and III Group II and III		
HDL (mg/dl)	49.1±0.5	47.4±0.6	41.5±0.6	40.676	<0.001 Group I and III, Group II and III		
LDL (mg/dl)	74.4±2.8	78.3±2.1	79.7±2.7	1.162	0.315 NS		

<b>Table 2:</b> Comparison of lipid-lipoprotein ratios indifferent study groups								
TG/HDL	2.7±0.1	3.1±0.1	4.2±0.1	38.378	<0.001 Group I and II Group I and III Group II and III			
TC/HDL	3.1±0.1	3.4±0.1	4.0±0.1	26.538	<0.001 Group I and II Group I and III Group II and III			
LDL/HDL	1.5±0.1	1.6±0.05	1.9±0.08	11.401	<0.001 Group I and III Group II and III			

among the groups was due to higher ratio in severe MS (1.9) compared with both control (1.5) and MS (1.6), as there was no significant difference in the LDL/HDL values between MS and control.

## DISCUSSION

In this study, dyslipidemia, one of the components of MS, was targeted to identify the severity of the MS conditions with possible intention to utilize the knowledge for the better understanding of MS. The result of the present study [Table 1] showed that TC increased as the number of components of MS increase in an individual. Further, it showed that this increase was proportionate to the severity of MS. Among the other lipid profile parameters, the TG level recorded in this study showed that the level of it in MS and severe MS was more than the control. On the other hand, the HDL cholesterol level in severe MS group was less which about 10% was lower than that of the control level. However, LDL which was considered as bad cholesterol did not show a significant difference between the groups.

The recent report of Ying et al. (2017) stated that TG and LDL cholesterol were increased with the decrease in HDL cholesterol in MS group in comparison with that of non-MS group was in parallel with the result of the present study except the LDL cholesterol level which was not significant in the present study.<sup>[7]</sup> Furthermore, the importance of lipid profile in the development of MS was well documented. Abnormalities of serum lipid profile are an important risk factor for coronary artery disease and responsible for fatal myocardial infarction, mortality from CVD and cerebral stroke.<sup>[8]</sup> Hyperinsulinemia is known to enhance hepatic very low-density lipoprotein synthesis and thus may directly contribute to the increased plasma triglyceride and LDL cholesterol levels.<sup>[9]</sup> The other major lipoprotein disturbance in the MS is a reduction in HDL cholesterol, which is due to changes in HDL composition and metabolism.<sup>[10]</sup> HDL cholesterol has antiatherosclerotic and anti-inflammatory properties. Reduced HDL cholesterol in plasma has been related to a greater risk of CHD and stroke.<sup>[11]</sup> Abdominal obesity forms another important factor responsible for lipid abnormalities.<sup>[8]</sup> It has been reported that reducing the serum cholesterol in patients with increased rates of cardiac disease is an important, safe, and an effective method by which rates of heart disease can be reduced.<sup>[12]</sup> Thus, the notion that the dyslipidemia as one of the important causative factors for MS was supported by this study also.

It has been reported in literature that TG/HDL, TC/HDL, and LDL/HDL ratio are the important biomarkers due to its CVD predictability.<sup>[8]</sup> TG/HDL ratio was high in severe MS group which was in accordance with the literature stated that TG/HDL ratio more than 3.5 seems to be related with high CVD risk<sup>[8]</sup> and that the lipid and lipoprotein ratio is considered as an alternative method for identifying MS patients.<sup>[13]</sup> Furthermore, the result of the present study about the TC/HDL and LDL/HDL ratio which was increased in MS and severe MS group was in agreement with the report that showed higher TC/HDL and TG/HDL ratios in males compared with that of non-MS group.<sup>[13]</sup> Thus, the result of the study confirmed that lipid profile played a major role in the progression of MS. It has been observed that the treatment of MS risk factors at the earliest decreases morbidity and mortality.<sup>[14]</sup>

Major strength of the study is the sample size of 195, divided into three groups, each with 65 participants. Since abnormalities in lipid profile contribute as a major risk factor for CVD, knowledge of lipid profile may to great extent help in diagnosing and treating the patients at the earliest. Limitation of the study is that molecular mechanism of increased lipid-lipoprotein ratio in causing CVD was not able to do in the present study.

#### CONCLUSION

In spite of advanced treatment, incidence and prevalence of CVD increase every year. Hence, importance should be given to each component of MS and by detecting the disease in the early stage itself, the burden of MS as well as CVD can be reduced. Early identification and management of individuals with MS is very important to prevent debilitating effects associated with its development.

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