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Research Article

Association of Remnant Lipoprotein Cholesterol with Cardiovascular Risk Markers in Patients with Metabolic Syndrome

Dr. Abha[1], Dr. Garima Sehgal[2], Dr. Aman Thathai[3], Dr. Jaswant Kaur[4*]
[1]Associate Professor, Department of Pathology, Dr. S.S. Tantia Medical College Hospital & Research Centre, Sri Ganganagar.
[2]Assistant Professor, Department of Biochemistry, Pesuimsr, Bangalore.
[3]Assistant Professor, Department of General Medicine, Dr. S.S. Tantia Medical College Hospital & Research Centre, Sri Ganganagar.
[4*]Associate Professor, Department of Biochemistry, Dr. S.S. Tantia Medical College Hospital & Research Centre, Sri Ganganagar.
Corresponding Author: Dr. Jaswant Kaur
Associate Professor, Department of Biochemistry, Dr. S.S. Tantia Medical College Hospital & Research Centre, Sri Ganganagar
Corresponding Email: jaswantkaur_2006@yahoo.co.in
Email: [1]abha1884@gmail.com, [2]sehgalgarima4@gmail.com, [3]thathaiaman@gmail.com, [4*]jaswantkaur_2006@yahoo.co.in
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ABSTRACT
Background: Metabolic syndrome is a multifactorial condition associated with increased cardiovascular risk due to insulin resistance, central obesity, hypertension, and atherogenic dyslipidemia. Conventional lipid parameters may not fully reflect residual cardiovascular risk. Remnant lipoprotein cholesterol (RLP-C), a component of triglyceride-rich lipoprotein remnants, has emerged as a potential atherogenic biomarker. This study aimed to evaluate the association of RLP-C with established cardiovascular risk markers and its diagnostic utility in patients with metabolic syndrome.
Methods: This case–control pilot study included 100 participants, comprising 50 patients with metabolic syndrome and 50 age and sex-matched healthy controls. Anthropometric measurements (body mass index and waist circumference) and biochemical parameters, including fasting blood glucose and comprehensive lipid profile, were analyzed using standardized laboratory techniques. RLP-C levels were calculated and correlated with conventional cardiovascular risk markers.
Results: RLP-C levels were significantly elevated in patients with metabolic syndrome compared with controls ($p<0.05$). Significant positive correlations were observed between RLP-C and total cholesterol, triglycerides, LDL cholesterol, and VLDL cholesterol, indicating its association with atherogenic lipid patterns.
Conclusion: Patients with CAD and metabolic syndrome show significant alterations in anthropometric, hemodynamic, and biochemical parameters, including elevated remnant lipoprotein cholesterol (RLP-C). These findings suggest that RLP-C may serve as a potential biomarker for identifying increased cardiovascular risk in metabolic syndrome.

Keywords: Metabolic Syndrome, Remnant Lipoprotein Cholesterol, Cardiovascular Risk, Dyslipidemia, Lipid Profile.

INTRODUCTION

Cardiovascular diseases (CVDs) remain the leading cause of mortality worldwide. According to the latest World Health Organization (WHO) estimates, approximately 19.8 million deaths were attributed to CVDs globally in 2022, accounting for nearly 32% of all deaths, with myocardial infarction and stroke contributing to nearly 85% of these fatalities. The burden of cardiovascular disease disproportionately affects low- and middle-income countries, underscoring the urgent need for improved risk stratification, preventive strategies, and early therapeutic interventions (1).

Metabolic syndrome (MetS) is characterized by a cluster of interrelated cardiometabolic abnormalities, including central obesity, hypertension, dyslipidemia, insulin resistance, and impaired glucose metabolism. These components synergistically increase the risk of cardiovascular disease (CVD), type 2 diabetes mellitus, and overall mortality, making MetS an

important clinical target for early identification and management (2).

Remnant cholesterol (RC) refers to the cholesterol content within triglyceride-rich lipoproteins, primarily consisting of very-low-density lipoproteins (VLDL) and intermediate-density lipoproteins (IDL) in the fasting state, and chylomicron remnants in the postprandial state (3). Recent studies have supported that RC plays a pivotal role in the pathogenesis of CVD through pro-atherogenic, pro-inflammatory, and endothelial dysfunction–mediated mechanisms. Importantly, even in individuals with well-controlled low-density lipoprotein cholesterol (LDL-C), elevated RC has been identified as a major contributor to residual cardiovascular risk despite standard lipid-lowering therapy (4,5). Beyond cardiovascular outcomes, emerging data suggest that increased RC levels are independently associated with metabolic disturbances, including an elevated risk of type 2 diabetes mellitus, particularly among younger individuals and those with fewer traditional cardiometabolic risk factors (6). In this context, remnant lipoprotein cholesterol has emerged as a potentially important contributor to residual cardiovascular risk, particularly in individuals with metabolic syndrome. However, its relationship with established cardiovascular risk markers remains inadequately explored. Therefore, the present study aimed to evaluate the association of remnant lipoprotein cholesterol with cardiovascular risk markers in patients with metabolic syndrome to improve risk stratification and clinical understanding in this high-risk population.

MATERIAL AND METHODS

A case-control study was conducted at the Departments of Biochemistry, Dr. S.S. Tantia Medical College, Hospital and Research Centre, Sri Ganganagar. Institutional ethical approval was obtained, and written informed consent was secured from all participants.

Participants

100 individuals were enrolled, comprising 50 CAD patients with Metabolic syndrome and 50 clinically healthy controls. Patients who were suffering from CAD with MetS were considered cases, and normal healthy individuals served as controls. A history of alcohol consumption, smoking, pregnancy, drug abuse, and liver diseases was excluded from the study.

Clinical and Biochemical Assessment

All participants underwent a detailed medical history and physical examination. Anthropometric parameters (BMI and waist circumference) and blood pressure (SBP and DBP measured in sitting position using a sphygmomanometer) were recorded. BMI was calculated as weight (kg) divided by height squared (m^2); a BMI ≥25 kg/m^2 was classified as obese based on Indian guidelines.

Venous blood samples (3 mL) were collected after 8–12 hours of fasting. Fasting glucose was collected in sodium fluoride vials, while other parameters were drawn into serum separator tubes. Biochemical parameters- lipid profile and fasting glucose were analyzed using a fully automated clinical chemistry analyzer (EM 360). Remnant Lipoprotein Cholesterol (RLP-C) was calculated using the formula:

RLP-C = Total Cholesterol – (HDL-C + LDL-C).

Statistical Analysis

Statistical analysis was performed using SPSS version 28.0. Data were expressed as mean ± SD for normally distributed variables and median (IQR) for non-parametric data. Group comparisons were performed using the Student's t-test or Mann–Whitney U test, while the chi-square test was used for categorical variables. Spearman's correlation assessed the association between RLP-C and other variables. A p-value < 0.05 was considered statistically significant.

RESULTS

The study comprised 50 CAD patients with Metabolic syndrome and 50 healthy control subjects. The age and sex distribution of participants is summarized in Table 1 and Fig. 1. Among the healthy controls, 48% were male, and 52% were female; in the CAD with Mets group, 41% were male, and 59% were female. The mean age of CAD patients was 50.1 ± 10.16 years, compared with 48.52 ± 9.3 years in the control group; however, the difference was not statistically significant.

Table 1. Age and Sex Distribution of the Study Population.

	CAD with MetS (n=50)	Control (n=50)	p-value
Age (years) (Mean ± SD)	50.1±10.16	48.52±9.3	0.42

The anthropometric parameters and blood pressure of the study participants are presented in Table 2. The body mass index (BMI) of patients with coronary artery disease (CAD) and metabolic syndrome (MetS) was significantly higher than that of the control group ($p = 0.01$). A statistically significant difference was also observed in systolic blood pressure (SBP) between the case and control groups ($p = 0.001$). However, no significant difference was noted in waist circumference (WC) and diastolic blood pressure (DBP) between the CAD with MetS group and the control group ($p > 0.05$).

Table 2. Anthropometric and Blood Pressure Characteristics of the Study Population.

Variable	CAD with MetS	Control	p-value
	(Mean ± SD)	(Mean ± SD)	
Weight (kg)	77.4 ± 5.6	65.16±8.2	0.034
Height (m)	1.70±0.77	1.65±0.67	<0.001
BMI (kg/m^2)	27.6±4.25	24.0±1.33	0.001
WC (cm)	95.1±1.40	91.3±0.87	0.087
SBP (mmHg)	129.48±14.9	120.28±7.85	0.001
DBP (mmHg)	82.6±10.7	83.9±16.30	0.928

BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; $p < 0.05$ considered as a statistically significant difference.

Table 3 shows the comparison of biochemical parameters between patients with coronary artery disease (CAD) associated with metabolic syndrome (MetS) and healthy controls. The mean total cholesterol level was significantly higher in the CAD with MetS group (224.65 ± 38.40 mg/dL) compared to the control group (178.32 ± 30.15 mg/dL) ($p < 0.001$). Similarly, serum triglyceride levels were markedly elevated in CAD with MetS patients (198.45 ± 35.62 mg/dL) compared to healthy controls (132.18 ± 28.47 mg/dL), indicating a significant difference ($p < 0.001$). VLDL levels also showed a significant increase in the CAD with MetS group (39.69 ± 7.12 mg/dL) compared with controls (26.44 ± 5.69 mg/dL) ($p < 0.001$). In contrast, HDL-C levels were significantly lower in CAD with MetS patients (36.52 ± 6.14 mg/dL) than in healthy individuals (45.83 ± 7.02 mg/dL) ($p = 0.004$). Fasting blood glucose levels were significantly higher in the CAD with MetS group (126.78 ± 24.55 mg/dL) compared to the control group (92.46 ± 12.38 mg/dL) ($p < 0.001$). Additionally, RLP-C levels were significantly elevated in CAD with MetS patients (26.47 ± 2.08 mg/dL) compared to healthy controls (18.20 ± 1.40 mg/dL), with a p-value of 0.005. Overall, these findings indicate that patients with CAD and metabolic syndrome exhibit significant dyslipidemia, elevated remnant lipoprotein cholesterol, and impaired glucose metabolism compared to healthy individuals.

Table 3: Comparison of Biochemical Parameters between CAD with Mets Patients and Healthy Controls

Parameter	CAD with MetS (Mean ± SD) (mg/dL)	Healthy Controls (Mean ± SD) (mg/dL)	p-value
Total Cholesterol (TC)	224.65 ± 38.40	178.32 ± 30.15	<0.001
Triglycerides (TG)	198.45 ± 35.62	132.18 ± 28.47	<0.001
VLDL-C	39.69 ± 7.12	26.44 ± 5.69	<0.001
LDL -C	98.8±38.38	99.5±29.7	0.681
HDL-C	36.52 ± 6.14	45.83 ± 7.02	<0.001
Fasting Blood Glucose	126.78 ± 24.55	92.46 ± 12.38	<0.001
RLP-C	26.40 ± 1.98	18.02 ± 1.50	<0.001

DISCUSSION

The present study evaluated the biochemical and anthropometric characteristics of patients with coronary artery disease associated with metabolic syndrome and compared them with those of healthy controls.

The findings indicate that patients with CAD and MetS exhibit significant dyslipidemia, elevated RLP-C levels, and impaired glucose metabolism, which may contribute to increased cardiovascular risk.

In the present study, the mean age of the CAD with MetS group was comparable to that of the

control group, and no statistically significant difference was observed. Anthropometric analysis revealed that body mass index was significantly higher among CAD patients with MetS compared to healthy controls. Increased BMI reflects excess adiposity and is strongly associated with metabolic abnormalities such as insulin resistance, dyslipidemia, and systemic inflammation. These factors play a crucial role in the development and progression of atherosclerosis (7). However, waist circumference did not show a statistically significant difference between the groups. Blood pressure analysis demonstrated a significant increase in systolic blood pressure in the CAD with MetS group compared to controls, while diastolic blood pressure did not differ significantly. Elevated SBP is a well-recognized independent risk factor for cardiovascular disease and contributes to endothelial dysfunction and arterial stiffness (8). These findings are consistent with previous reports highlighting the association between hypertension and metabolic syndrome. The biochemical profile of CAD patients with MetS in this study revealed significant abnormalities in lipid metabolism. Total cholesterol and triglyceride levels were significantly higher in the CAD with MetS group compared to controls. Hypertriglyceridemia is a characteristic feature of metabolic syndrome and is associated with increased production of triglyceride-rich lipoproteins such as very low-density lipoprotein (VLDL) (9). Elevated VLDL levels observed in the present study further support the presence of altered lipid metabolism in CAD patients. In contrast, HDL-C levels were significantly lower in CAD patients with MetS compared to healthy controls. HDL-C plays a protective role in cardiovascular health through reverse cholesterol transport and anti-inflammatory effects. Reduced HDL-C levels therefore contribute to increased cardiovascular risk and promote the progression of atherosclerosis (10). Fasting blood glucose levels were also significantly higher in CAD patients with MetS compared to controls, as shown in Table 3, indicating impaired glucose metabolism and insulin resistance. Hyperglycemia is known to induce oxidative stress, endothelial dysfunction, and vascular inflammation, all of which contribute to the pathogenesis of atherosclerosis and cardiovascular disease (11).

An important finding of the present study was the significantly elevated level of remnant lipoprotein cholesterol (RLP-C) in CAD patients with MetS. Remnant lipoproteins are triglyceride-rich lipoprotein particles derived from chylomicrons and VLDL remnants. These particles are highly atherogenic because they can penetrate the arterial wall and contribute to foam cell formation and plaque development (12). Several studies have suggested that elevated RLP-C levels may represent an independent cardiovascular risk factor and may contribute to residual cardiovascular risk even when conventional lipid parameters are controlled (13). The results of the present study are consistent with previous research demonstrating the role of remnant lipoproteins in the development of atherosclerosis and cardiovascular disease. Elevated RLP-C levels in patients with CAD and metabolic syndrome highlight the potential importance of remnant lipoproteins as a biomarker for cardiovascular risk assessment. However, certain limitations should be considered. The sample size was relatively small, and the study was conducted at a single center, which may limit the generalizability of the findings.

CONCLUSION

In conclusion, the present study demonstrates that patients with CAD and metabolic syndrome exhibit significant alterations in anthropometric and biochemical parameters, including elevated remnant lipoprotein cholesterol levels. These findings suggest that RLP-C may serve as a useful biomarker for identifying individuals at increased risk of cardiovascular disease and may provide additional insight into the pathophysiology of atherosclerosis in metabolic syndrome.

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Conflict of Interest: None

Author Contribution: Dr. Abha contributed to the conceptualization and participated in drafting the initial manuscript. Dr. Garima and Dr. Aman Thathai assisted in data collection and interpretation of the results. Dr. Jaswant Kaur contributed to data analysis and manuscript drafting. All authors read and approved the final version of the manuscript.

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