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RESEARCH ARTICLE

EVALUATION OF REMNANT LIPOPROTEIN CHOLESTEROL AND OXIDIZED LDL IN RELATION TO LOW-GRADE INFLAMMATION IN YOUNG INDIAN CORONARY HEART DISEASE PATIENTS

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Abstract

Introduction: Coronary heart disease (CHD) remains a leading cause of global mortality, particularly in younger populations. Emerging evidence highlights the role of remnant lipoprotein cholesterol (RLP-C) and oxidized low-density lipoprotein (ox-LDL) in contributing to low-grade inflammation, a significant factor in the progression of atherosclerosis. This study aimed to assess the levels of remnant lipoprotein cholesterol, ox-LDL, and low-grade inflammation in young Indian CHD patients.

Methods: This cross-sectional study included 180 participants aged ≤ 45 years, divided into three groups: non-diabetic CHD patients, diabetic CHD patients, and healthy controls. After overnight fasting, blood samples were collected and analyzed for lipid profiles, ox-LDL, and hs-CRP. Lipid profiles were measured using the Auto Analyzer AU480, while ox-LDL and hs-CRP were determined using enzyme-linked immunosorbent assay (ELISA). Statistical analysis involved Student's t-test and Pearson's correlation to assess relationships between variables.

Results: CHD patients (both diabetic and non-diabetic) had significantly higher total cholesterol, LDL cholesterol, triglycerides, ox-LDL, and hs-CRP levels compared to healthy controls ($p < 0.001$). Diabetic CHD patients showed the highest levels of ox-LDL and hs-CRP. Pearson's correlation revealed a strong positive correlation between ox-LDL, hs-CRP, and lipid abnormalities, particularly LDL cholesterol and triglycerides ($r = 0.52$, $p < 0.001$). These findings suggest that both oxidative stress and low-grade inflammation are crucial contributors to CHD in young adults.

Conclusion: Young CHD patients exhibit elevated levels of ox-LDL and hs-CRP, highlighting the interplay between oxidative stress, inflammation, and lipid abnormalities in the disease's progression. Diabetic CHD patients are at a particularly high risk, indicating the need for early detection and targeted intervention.

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Keywords: Coronary Heart Disease, Remnant Lipoprotein Cholesterol, Oxidized LDL, Hs-CRP, Low-Grade Inflammation, Young Adults

BACKGROUND/INTRODUCTION

Due to intricate interactions between lipid abnormalities, oxidative stress, and inflammation, coronary heart disease (CHD) is a leading cause of death globally, especially in younger people. Emerging research shows that remnant lipoprotein cholesterol (RLP-C) and oxidised low-density lipoprotein (ox-LDL) are crucial to atherosclerosis, a major cause of CHD. Residual cholesterol, including triglyceride-rich lipoproteins, contributes to cardiovascular risk even in patients with ideal LDL-C levels after lipid-lowering treatments [1-3].

RLP-C causes low-grade inflammation, which worsens atherosclerosis. LDL-C drives plaque accumulation, while residual cholesterol is becoming recognised as a pro-inflammatory chemical that activates macrophages and forms foam cells, which accelerate atherogenesis [4]. In coronary artery disease patients, residual cholesterol and elevated high-sensitivity C-reactive protein (hs-CRP) are linked to ischaemic events, cardiac death, and all-cause mortality [5, 6].

Oxidized LDL (ox-LDL) plays a pivotal role in the oxidative modification of lipids within arterial walls, further driving inflammation and plaque instability. Oxidation of LDL promotes the recruitment of macrophages to vascular lesions, stimulating the release of pro-inflammatory cytokines and enhancing the formation of foam cells, which are precursors to atherosclerotic plaques [7]. Additionally, increased levels of ox-LDL have been consistently correlated with elevated hs-CRP, an inflammatory marker often elevated in patients with CHD, linking oxidative stress with systemic inflammation [8,9].

In younger populations, particularly in those with metabolic disorders like diabetes, the interplay between dyslipidemia, remnant cholesterol, ox-LDL, and inflammation is particularly pronounced. Diabetic patients with CHD exhibit significantly higher levels of both RLP-C and ox-LDL, which are strongly associated with heightened inflammatory responses and accelerated atherosclerosis

Given this evidence, assessing remnant lipoprotein cholesterol and ox-LDL levels in conjunction with inflammatory markers such as hs-CRP offers valuable insight into the underlying mechanisms of CHD, particularly in younger, high-risk populations. Early identification and management of these risk factors may lead to improved cardiovascular outcomes by targeting both lipid abnormalities and the associated inflammatory pathways [10].

The study aimed to evaluate the association between remnant lipoprotein cholesterol, ox-LDL, and low-

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grade inflammation in coronary heart disease individuals within a young Indian population.

MATERIALS AND METHODS

Study Design

A cross-sectional study.

Study Setting

The study was conducted at a tertiary care hospital in India, spanning a period of one year with participants recruited from individuals appearing for routine master health check-ups and consultations at the Medicine Department.

Participants

A total of 180 age- and sex-matched participants were enrolled in the study, all aged ≤ 45 years. Participants were grouped into three categories:

- Group 1: Non-diabetic subjects with confirmed CHD.
- Group 2: Diabetic subjects with confirmed CHD.
- Group 3: Healthy control subjects without CHD or diabetes.

Inclusion Criteria

- Individuals aged ≤ 45 years.
- CHD confirmed through clinical diagnosis and diagnostic tests.
- Willing to provide informed consent for participation.
- For the control group: healthy individuals without any history of CHD, diabetes, or other major comorbidities.

Exclusion Criteria

- Participants with severe comorbid conditions such as renal failure, liver dysfunction, or any systemic inflammatory disease.
- Individuals on lipid-lowering or anti-inflammatory medications.
- Pregnant or breastfeeding women.

Bias

To minimize bias, the study employed age- and sex-matched groups to ensure comparability between cases and controls. The recruitment process was done consecutively to avoid selection bias. Additionally, all laboratory assessments were performed under standardized conditions, and the personnel conducting biochemical analyses were blinded to the participant's group.

Variables

Variables included ox-LDL, hs-CRP, lipid profile, presence of coronary heart disease, diabetic status, age, sex, body mass index (BMI), and lifestyle factors.

Data Collection

After obtaining informed consent, participants underwent an overnight fasting period of 8–12 hours. Following this, body fluid samples (blood) were collected under aseptic conditions. The lipid profile was measured using an automated clinical chemistry analyzer (Auto Analyser AU480). Oxidized LDL and hs-CRP were measured using the enzyme-linked immunosorbent assay (ELISA) technique.

Procedure

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Eligible participants were recruited from master health check-up and medicine departments after confirming their CHD status, diabetic status, and health status for control participants. After overnight fasting, venous blood samples were collected from each participant. The samples were processed immediately for lipid profile, ox-LDL, and hs-CRP analysis. Fasting lipid profile (including total cholesterol, triglycerides, HDL, LDL, and VLDL) was measured using the Auto Analyser AU480. Ox-LDL and hs-CRP levels were assessed using a validated enzyme-linked immunosorbent assay (ELISA) method. All data were recorded systematically, and double-entry procedures were followed to ensure data integrity.

Statistical Analysis

Data was analysed using SPSS 21.0. To summarise baseline characteristics, descriptive statistics were used (percentages for categorical categories, mean ± SD for continuous variables). Student's t-test was used to compare continuous variables (CHD vs. control, diabetic CHD vs. non-diabetic CHD). Using Pearson's correlation analysis, ox-LDL, hs-CRP, and lipid profile components were examined. P-values under 0.05 were statistically significant for all tests. Diabetes subgroup analysis was also performed to compare CHD patients with and without diabetes. Results were provided with 95% confidence intervals and odds ratios when suitable.

Ethical considerations

The study protocol was approved by the Ethics Committee and written informed consent was received from all the participants.

RESULTS

The study included 180 participants divided into three groups: 60 non-diabetic CHD patients, 60 diabetic CHD patients, and 60 healthy controls. The mean age of the participants across all groups was approximately 41.2 ± 3.8 years, and the groups were balanced in terms of gender distribution (male-to-female ratio: 1.2:1). Table 1 presents the demographic and clinical characteristics of the study participants.

Table 1: Baseline Characteristics

Characteristics	Non-Diabetic CHD	Diabetic CHD	Healthy Controls	p-value (CHD vs Control)
Age (years)	40.7 ± 3.5	41.5 ± 3.9	41.3 ± 4.0	0.68
Male, n (%)	34 (56.7%)	36 (60%)	33 (55%)	0.81
BMI (kg/m²)	26.4 ± 2.7	27.2 ± 3.1	24.9 ± 2.3	<0.05
Systolic BP (mmHg)	136.5 ± 14.2	145.7 ± 12.8	122.1 ± 10.5	<0.001
Diastolic BP (mmHg)	85.9 ± 8.7	89.3 ± 9.1	79.5 ± 7.9	<0.01
Fasting Blood Glucose (mg/dL)	98.7 ± 10.5	152.8 ± 32.1	92.5 ± 8.9	<0.001

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The lipid profile of the participants is summarized in Table 2. Total cholesterol, LDL, and triglycerides were significantly elevated in both non-diabetic and diabetic CHD patients compared to healthy controls. HDL levels were lower in both CHD groups compared to controls.

Table 2: Lipid Profile of Study Participants

Lipid Parameter	Non-Diabetic CHD	Diabetic CHD	Healthy Controls	p-value
Total Cholesterol (mg/dL)	213.5 ± 35.4	225.2 ± 40.1	180.7 ± 28.3	<0.001
Triglycerides (mg/dL)	170.4 ± 45.6	182.9 ± 48.2	134.8 ± 36.7	<0.01
LDL (mg/dL)	139.3 ± 31.2	150.7 ± 33.4	108.4 ± 26.5	<0.001
HDL (mg/dL)	38.7 ± 6.2	36.5 ± 5.8	48.6 ± 7.1	<0.001
VLDL (mg/dL)	33.5 ± 10.2	36.4 ± 9.9	27.2 ± 7.1	<0.05

Both ox-LDL and hs-CRP levels were significantly raised in CHD patients (both diabetic and non-diabetic) compared to healthy controls. Diabetic CHD patients had higher ox-LDL and hs-CRP levels compared to non-diabetic CHD patients, suggesting a stronger association of oxidative stress and inflammation with diabetes in CHD.

Table 3: Oxidized LDL and hs-CRP Levels

Biomarker	Non-Diabetic CHD	Diabetic CHD	Healthy Controls	p-value
Ox-LDL (U/L)	86.3 ± 15.7	95.6 ± 18.2	52.4 ± 12.3	<0.001
hs-CRP (mg/L)	4.6 ± 1.2	5.9 ± 1.7	2.1 ± 0.9	<0.001

Pearson's correlation analysis was conducted to assess the relationship between ox-LDL, hs-CRP, and lipid profile variables. Significant positive correlations were observed between ox-LDL and LDL cholesterol ($r = 0.52$, $p < 0.001$), as well as between hs-CRP and triglycerides ($r = 0.48$, $p < 0.001$). hs-CRP was also positively correlated with ox-LDL ($r = 0.58$, $p < 0.001$), suggesting an association between oxidative stress and inflammation.

Table 4: Pearson's Correlation Coefficients between Key Variables

Variable	LDL (mg/dL)	Triglycerides (mg/dL)	HDL (mg/dL)	hs-CRP (mg/L)	Ox-LDL (U/L)
Ox-LDL (U/L)	r = 0.52**	r = 0.36*	r = -0.22*	r = 0.58**	-

hs-CRP (mg/L)	r = 0.41**	r = 0.48**	r = -0.29**	-	r = 0.58**

*Statistical significance: *p < 0.05; **p < 0.001

When comparing the CHD patients (both diabetic and non-diabetic) with healthy controls, significant differences were found in lipid profile parameters, ox-LDL, and hs-CRP levels. Both diabetic and non-diabetic CHD patients exhibited significantly higher ox-LDL and hs-CRP levels, with diabetic CHD patients showing the highest values across all variables.

Table 5: Comparison of CHD Patients and Controls (Mean ± SD)

Parameter	CHD Patients (n=120)	Healthy Controls (n=60)	p-value
Total Cholesterol (mg/dL)	219.3 ± 38.9	180.7 ± 28.3	<0.001
Triglycerides (mg/dL)	176.6 ± 47.2	134.8 ± 36.7	<0.01
LDL (mg/dL)	145.0 ± 32.5	108.4 ± 26.5	<0.001
HDL (mg/dL)	37.6 ± 6.1	48.6 ± 7.1	<0.001
Ox-LDL (U/L)	91.0 ± 17.5	52.4 ± 12.3	<0.001
hs-CRP (mg/L)	5.3 ± 1.5	2.1 ± 0.9	<0.001

DISCUSSION

In this study involving 180 participants, we investigated the association between remnant lipoprotein cholesterol, ox-LDL, and low-grade inflammation, as measured by hs-CRP, in young South Indian CHD patients. The study population consisted of three groups: non-diabetic CHD patients, diabetic CHD patients, and healthy controls, all aged ≤ 45 years. Significant differences in lipid profiles, ox-LDL, and hs-CRP levels were observed between the CHD patients (both diabetic and non-diabetic) and healthy controls, with diabetic CHD patients showing the highest values.

Both non-diabetic and diabetic CHD patients had significantly higher total cholesterol, LDL cholesterol, triglycerides, and lower HDL cholesterol compared to healthy controls. This dyslipidemic pattern is well-known to contribute to atherosclerosis and CHD development, particularly in the context of young individuals. The results indicated a stronger lipid abnormality in diabetic CHD patients, emphasizing the increased cardiovascular risk associated with diabetes.

The levels of ox-LDL and hs-CRP were significantly elevated in CHD patients, particularly in those with diabetes. Ox-LDL levels were 95.6 ± 18.2 U/L in diabetic CHD patients, compared to 86.3 ± 15.7 U/L in non-diabetic CHD patients and 52.4 ± 12.3 U/L in healthy controls. Similarly, hs-CRP levels were 5.9 ±

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1.7 mg/L in diabetic CHD patients, 4.6 ± 1.2 mg/L in non-diabetic CHD patients, and 2.1 ± 0.9 mg/L in healthy controls. The elevated ox-LDL and hs-CRP in CHD patients suggest increased oxidative stress and systemic inflammation, both of which are critical in the pathogenesis of atherosclerosis and CHD.

Pearson's correlation analysis revealed significant positive correlations between ox-LDL and LDL cholesterol, as well as between hs-CRP and triglycerides, highlighting the interconnected roles of lipid abnormalities, oxidative stress, and inflammation in CHD progression. The strong correlation between ox-LDL and hs-CRP ($r = 0.58$, $p < 0.001$) supports the notion that oxidative stress and inflammation are closely linked in CHD pathophysiology.

The findings of this study suggest that both dyslipidemia and elevated ox-LDL are strongly associated with CHD, particularly in younger individuals with diabetes. Elevated hs-CRP levels indicate the presence of chronic low-grade inflammation in CHD patients, which may exacerbate atherosclerotic processes. The more pronounced lipid and biomarker abnormalities in diabetic CHD patients further emphasize the additional cardiovascular risk posed by diabetes. This highlights the need for early intervention and aggressive management of both lipid levels and inflammatory processes in high-risk populations to prevent the progression of coronary heart disease.

Young South Indian CHD patients were tested for RLP-C, ox-LDL, and hs-CRP in a cross-sectional investigation. RLP-C, ox-LDL, and hs-CRP levels were considerably higher in CHD patients than healthy controls. A positive connection between these indicators suggests that their combined action may accelerate atherosclerosis and increase CHD risk in younger populations [11].

Similarly, a study measured circulating ox-LDL, RLP-C, and hs-CRP levels in CHD patients and found that all three biomarkers were significantly elevated in the CHD group compared to healthy controls. The researchers noted that ox-LDL and RLP-C levels were particularly elevated in diabetic CHD patients, indicating a stronger association between oxidative stress, inflammation, and lipid abnormalities in these individuals. This study further highlighted the potential role of these biomarkers in early risk assessment for cardiovascular events [12].

The Miami Heart Study examined the role of remnant cholesterol (RC) in coronary plaque characteristics. The study showed that elevated RC levels were independently associated with non-calcified coronary plaques, even in individuals with low LDL-C. This finding is crucial as non-calcified plaques are more vulnerable to rupture, which can lead to acute coronary events. The study suggests that RC is a significant risk factor for atherosclerosis progression, independent of traditional lipid markers [13].

Additionally, a study looked at the levels of circulating ox-LDL in individuals who had acute myocardial

infarction (AMI), unstable angina pectoris (UAP), and stable angina pectoris (SAP). According to the study, CHD patients' ox-LDL levels were noticeably higher than those of controls. It's interesting to note that patients with UAP and AMI had lower ox-LDL levels than SAP patients, suggesting that ox-LDL may be more important in the early stages of CHD. Additionally, the study showed a negative correlation between ox-LDL and hs-CRP, indicating a possible role for inflammation and oxidative stress in the development of CHD [14].

Research focused on the residual inflammatory risk in CHD patients by measuring hs-CRP levels. The study revealed that over 30% of CHD patients with optimal LDL-C levels still had elevated hs-CRP levels, indicating residual inflammation. These findings suggest that traditional lipid-lowering therapies may not fully address the inflammatory component of atherosclerosis, emphasizing the need for targeted anti-inflammatory treatments in managing CHD [15].

CONCLUSION

The study highlight the elevated levels of oxidized LDL and hs-CRP in young South Indian CHD patients, particularly among those with diabetes. The significant correlations observed between ox-LDL, hs-CRP, and lipid parameters suggest that oxidative stress and low-grade inflammation play a crucial role in the pathophysiology of CHD in this population. Elevated LDL cholesterol and triglycerides in CHD patients, along with reduced HDL levels, further emphasize the role of dyslipidemia in the development and progression of coronary heart disease.

LIMITATION

The limitations of this study include a small sample population who were included in this study. Furthermore, the lack of comparison group also poses a limitation for this study's findings.

RECOMMENDATION

Early screening for remnant cholesterol and ox-LDL, especially in diabetic individuals, along with aggressive lipid-lowering and anti-inflammatory treatments, may help reduce the burden of CHD in younger populations.

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CONFLICT OF INTEREST

The authors have no conflicting interests to declare.

LIST OF ABBREVIATION

MDA - Malondialdehyde

CHD - Coronary Heart Disease

RLP-C - Remnant Lipoprotein Cholesterol

ox-LDL - Oxidized Low-Density Lipoprotein

LDL-C - Low-Density Lipoprotein Cholesterol

hs-CRP - High-Sensitivity C-Reactive Protein

HDL - High-Density Lipoprotein

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LDL - Low-Density Lipoprotein

VLDL - Very Low-Density Lipoprotein

BMI - Body Mass Index

BP - Blood Pressure

ELISA - Enzyme-Linked Immunosorbent Assay

SPSS - Statistical Package for the Social Sciences

AMI - Acute Myocardial Infarction

UAP - Unstable Angina Pectoris

SAP - Stable Angina Pectoris

RC - Remnant Cholesterol

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