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(RESEARCH ARTICLE)

A study on association of serum bilirubin, c-reactive Protein and lipid profile in coronary artery disease

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Abstract

Background: Coronary artery disease (CAD) remains one of the leading causes of death worldwide, primarily due to atherosclerosis, a chronic inflammatory condition affecting the vascular endothelium. Among the key mechanisms contributing to CAD progression are lipid abnormalities, oxidative stress, and systemic inflammation. Biomarkers such as C-reactive protein (CRP) and bilirubin have gained attention for their potential roles in risk assessment. While CRP is a known pro-inflammatory marker associated with acute coronary syndromes, bilirubin, traditionally seen as a waste product, is now recognized for its antioxidant and anti-inflammatory properties. The interplay between lipid profile, CRP, and bilirubin may provide a better understanding of CAD risk and prognosis.

Objective: To evaluate the relationship of serum bilirubin and C-reactive protein levels with coronary artery disease, and assess their association with lipid profile parameters in CAD patients compared to non-coronary controls.

Methods: A cross-sectional prospective study was conducted over 18 months (July 2023 to December 2024) at Al-Ameen Medical College Hospital, Vijayapura, Karnataka. The study enrolled patients aged 26 to 75 years admitted to the medicine department with confirmed diagnoses of CAD, ischemic heart disease, or myocardial infarction based on electrocardiogram, echocardiography, angiographic findings, and cardiac history. Age and sex-matched controls without CAD were also included. Patients with liver, renal, inflammatory, autoimmune, or infectious diseases were excluded. Serum CRP was measured using a CRP-Latex slide agglutination test and categorized into low, average, and high-risk groups. Serum bilirubin and lipid profiles were measured using standard laboratory methods.

Results: The majority of CAD patients exhibited elevated CRP levels, particularly in the high-risk range (>3 mg/L), whereas controls showed lower levels. Serum bilirubin levels were significantly lower in CAD patients compared to controls, supporting its proposed protective role. Lipid analysis revealed elevated total cholesterol, triglycerides, and LDL cholesterol in CAD patients, while HDL levels were reduced. A significant inverse correlation was observed between bilirubin levels and CRP, indicating the potential of bilirubin to counteract inflammation. Patients with both high CRP and low bilirubin demonstrated greater severity of CAD. Lipid abnormalities, especially raised LDL and low HDL, showed strong associations with CRP levels and adverse cardiovascular risk stratification.

Conclusion: Low bilirubin and high C-reactive protein levels are independently associated with an increased risk of coronary artery disease. Their combination, along with deranged lipid parameters, significantly contributes to cardiovascular risk. These findings support the integration of bilirubin and CRP in risk prediction models for CAD. Early detection and targeted intervention based on inflammatory and oxidative biomarkers may improve outcomes in at-risk populations

Keywords: Coronary Artery Disease; C-Reactive Protein; Serum Bilirubin; Lipid Profile; Inflammation; Oxidative Stress; Atherosclerosis; Cardiovascular Risk; Myocardial Infarction

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1. Introduction

Atherosclerosis, the basis of CAD, is now recognized as a chronic inflammatory process. Inflammation promotes plaque formation, instability, and rupture, leading to acute events[2]. Inflammatory biomarkers, especially C-reactive protein (CRP), are widely used for risk assessment[3]. CRP is valued for its predictive stability and affordability[4], and contributes to atherosclerosis by impairing vascular dilation, binding LDL-C to foster foam cell formation, and increasing monocyte infiltration into plaques[5]. Elevated CRP correlates with greater risk of myocardial infarction (MI), stroke, and adverse outcomes in ACS, though its direct causal role is debated[6].

Bilirubin, once viewed only as a waste product[7], is now understood to have antioxidant, vasodilatory, anti-inflammatory, and lipid-lowering properties[8,9]. Produced during heme degradation, bilirubin at physiological levels scavenges free radicals and inhibits LDL oxidation—a key atherogenic step[10,11]. Higher bilirubin levels are linked to lower cardiovascular risk[12], as seen in Gilbert's syndrome, although paradoxically, high bilirubin during acute MI may indicate worse outcomes due to its role as a stress marker.

Dyslipidemia remains central to atherosclerosis, with LDL-C promoting, and HDL-C counteracting, plaque development and inflammation[13,14]. Higher LDL-C and lower HDL-C increase CAD risk, and other lipid measures—such as triglycerides, Lp(a), and cholesterol-to-HDL ratios—further improve prediction[15,16].

Interactions among bilirubin, CRP, and lipid profiles provide insights into CAD pathogenesis. Bilirubin's antioxidant effects may reduce CRP-mediated inflammation and LDL oxidation[17]. Individuals with low bilirubin and high CRP face higher cardiovascular risk[18], while elevated LDL-C heightens inflammation, increasing CRP and exacerbating endothelial dysfunction[19]. The primary aim of this study is to investigate the relationship between serum bilirubin levels and coronary artery disease (CAD) by comparing CAD patients with non-coronary controls. Additionally, the study seeks to correlate C-reactive protein (CRP) levels with the presence of CAD and to evaluate lipid profile parameters for risk estimation, thereby assessing the overall risk level of CAD among hospitalized patients.

2. Materials and Methods

This cross-sectional prospective study was conducted over 18 months (July 2023 to December 2024) at Al-Ameen Medical College Hospital, Vijayapur, Karnataka. The study population included patients admitted to the wards and intensive care unit who were diagnosed with coronary artery disease (CAD), ischemic heart disease (IHD), or myocardial infarction in the Medicine Department. Cases included both male and female patients aged 26–75 years who were willing to participate and had evidence of myocardial infarction based on electrocardiogram (ECG) abnormalities, enzyme changes, significant stenosis on coronary angiogram, unequivocally positive stress ECG, or a diagnosis of CAD within the previous five years confirmed by ECG, echocardiography, and prior cardiac records. Controls comprised age- and sex-matched patients without CAD, also aged 26–75 years and willing to participate. Exclusion criteria were a history of liver or renal disease, joint pain, thyroid disorders, neurological or psychiatric illness, anemia, chronic obstructive pulmonary disease, unwillingness to participate, alcoholism, cerebrovascular accident, hemoglobin <10 g/dL or >20 g/dL, malignancy, CAD with heart failure, hepatotoxic drug intake, hemodynamic instability, autoimmune disease, chronic or current infections, and recent use of anti-inflammatory drugs (within the past 30 days).

Data collection was performed using a structured proforma (Appendix IIG), and all patients underwent a thorough history, detailed clinical examination, and standard twelve-lead ECG. Informed consent was obtained prior to study inclusion. Patient demographics (age, gender, body mass index), clinical parameters (blood pressure, heart rate), medication history, and laboratory values (serum cholesterol, triglycerides, LDL, HDL, glucose, creatinine, total serum bilirubin) were recorded using standard laboratory procedures. C-reactive protein (CRP) was measured by the CRP-Latex slide agglutination test, and patients were categorized into three risk groups according to CRP levels: low (<1 mg/L), average (1–3 mg/L), and high risk (>3 mg/L). Cardiac assessment included measurement of left ventricular (LV) end diastolic and systolic dimensions and LV ejection fraction by 2D echocardiography.

All data were compiled in Microsoft Excel and analyzed using SPSS version 26.0. Descriptive statistics were used to summarize the data. Qualitative variables were expressed as frequency and percentage, while quantitative variables were presented as mean and standard deviation. The chi-square test was used to compare proportions, while Student's t-test and ANOVA were employed to compare mean values, with the significance level set at 5% ($\alpha = 0.05$).

3. Results

The age distribution shows a significantly higher proportion of older individuals in the CAD group, with 73.5% aged 55 and above, compared to a more youthful control group. Gender distribution was identical in both groups, confirming well-matched sampling. Smoking, diabetes, and hypertension were all significantly more prevalent among CAD patients, as indicated by p-values less than 0.05. Specifically, 73.5% of CAD patients were smokers (vs. 18.1% of controls), 53% were diabetic (vs. 12%), and 68.7% were hypertensive (vs. 16.9%). These findings highlight advancing age, smoking, diabetes, and hypertension as strong, statistically significant risk factors for coronary artery disease in this study population.

Interestingly, bilirubin levels were lower in CAD patients across all categories. Direct bilirubin averaged 0.22 mg/dL in CAD patients versus 0.32 mg/dL in controls, indirect bilirubin was 0.51 vs. 0.72 mg/dL, and total bilirubin was 0.73 vs. 1.03 mg/dL. All differences were statistically significant, suggesting that lower bilirubin levels might be associated with increased oxidative stress and CAD risk.

Table 1 Distribution of Demographic and Clinical Risk Factors in CAD and Control Groups

Variable	Category	CAD (n=83)	Control (n=83)	P Value
Age Group	25–34	0 (0%)	20 (24.1%)	
	35–44	0 (0%)	17 (20.5%)	
	45–54	22 (26.5%)	19 (22.9%)	
	55–64	25 (30.1%)	16 (19.3%)	
	65–75	36 (43.4%)	11 (13.3%)	<0.05
Gender	Female	41 (49.4%)	41 (49.4%)	
	Male	42 (50.6%)	42 (50.6%)	1.00
Smoking	Yes	61 (73.5%)	15 (18.1%)	
	No	22 (26.5%)	68 (81.9%)	<0.05
Diabetes	Yes	44 (53.0%)	10 (12.0%)	
	No	39 (47.0%)	73 (88.0%)	<0.05
Hypertension	Yes	57 (68.7%)	14 (16.9%)	
	No	26 (31.3%)	69 (83.1%)	<0.05

Table 2 Inflammatory Marker and Lipid Profile in CAD and Control Groups (Mean ± SD)

Parameter	CAD (n=83)	Control (n=83)	P Value
CRP (mg/L)	4.88 ± 1.95	2.07 ± 0.91	<0.05
Total Cholesterol (mg/dL)	211.15 ± 31.40	185.69 ± 25.22	<0.05
Triglycerides (mg/dL)	177.18 ± 40.15	142.84 ± 31.87	<0.05
HDL (mg/dL)	35.71 ± 4.47	54.52 ± 6.81	<0.05
LDL (mg/dL)	130.06 ± 23.47	101.97 ± 20.76	<0.05

The findings demonstrate that CAD patients have significantly higher mean CRP, total cholesterol, triglycerides, and LDL levels, and markedly lower HDL levels compared to controls, with all differences reaching statistical significance. Elevated CRP in CAD patients underscores the central role of inflammation in atherosclerosis and its value as a risk marker. The lipid profile of higher total cholesterol, LDL, and triglycerides, combined with lower HDL, represents the classic atherogenic pattern seen in CAD. This combination of systemic inflammation and adverse lipid profile

substantially increases the risk of coronary artery disease, reinforcing the need for comprehensive cardiovascular risk assessment and targeted interventions in clinical practice.

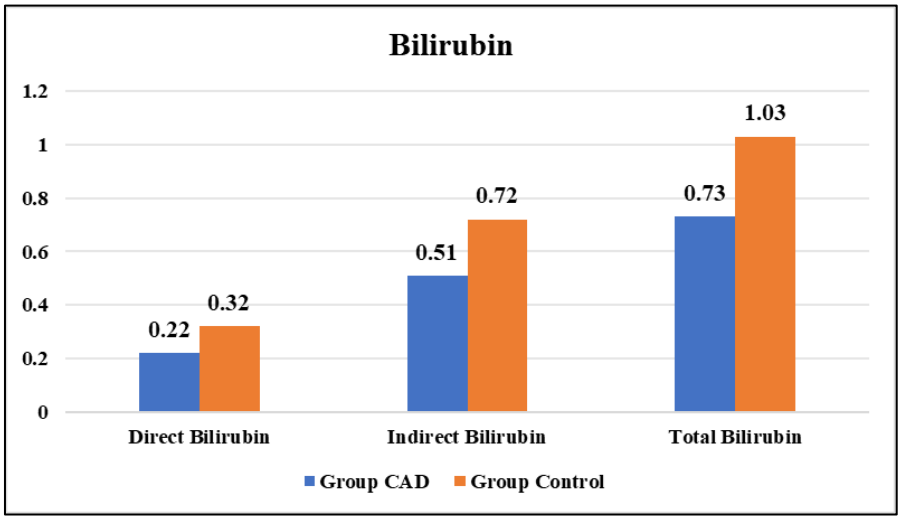

Figure 1 Bilirubin levels comparison between cad group and control group

4. Discussion

Coronary artery disease (CAD) remains a major cause of morbidity and mortality worldwide, shaped by a combination of demographic, metabolic, lifestyle, and inflammatory factors. This study compared CAD patients to age- and gender-matched controls to clarify the significance of these risk factors.

4.1. Demographic Characteristics

Our results show that CAD patients were predominantly older, with 73.5% aged 55 or above, while the control group was generally younger ($p < 0.05$). Both groups had identical gender distributions, indicating effective matching. These trends are consistent with studies by Adepu C et al.[21], Kumar R et al.[20], and Yatoo BA et al.[22], which also reported no significant differences in age and gender between cases and controls.

4.2. Risk Factors

Smoking, diabetes, hypertension, and obesity were all significantly more common in the CAD group. Specifically, 73.5% of CAD patients smoked, 53% were diabetic, and 68.7% were hypertensive, each with strong statistical significance ($p < 0.05$). The mean BMI was also higher in CAD patients. These findings reinforce the well-established roles of these modifiable risk factors in CAD pathogenesis, aligning with prior studies[20],[21],[18], even where some did not achieve statistical significance.

4.3. Clinical Parameters

CRP levels were significantly elevated in CAD patients (4.88 mg/L vs. 2.07 mg/L in controls), emphasizing the inflammatory nature of atherosclerosis. This is in agreement with Yatoo BA et al.[22], Patil VC et al.[23], and Sara JDS et al.[24], who all found higher CRP or hs-CRP associated with greater CAD severity and multi-vessel involvement.

4.4. Bilirubin Levels

Mean total bilirubin was lower in CAD patients (0.73 mg/dL) compared to controls (1.03 mg/dL; $p < 0.05$), supporting its possible protective, antioxidant role. This mirrors findings by Kumar R et al.[20] and Jayanthi N et al.[18], but contrasts with Adepu C et al.[21], who found no significant association.

4.5. Lipid Profile

CAD patients had higher mean total cholesterol, triglycerides, and LDL, and lower HDL than controls (all $p < 0.05$), confirming the central role of dyslipidaemia in CAD. Similar patterns were observed by Kumar R et al.[20], Jayanthi N et al.[18], Adepu C et al.[21], and Yatoo BA et al.[22], all of whom reported that lipid abnormalities are strongly linked with CAD.

5. Conclusion

In conclusion, our study highlights a significant association between coronary artery disease and multiple risk factors including older age, smoking, diabetes, hypertension, higher BMI, dyslipidaemia, elevated CRP, and lower bilirubin levels. These parameters were markedly different in CAD patients compared to the control group, reinforcing their role in the pathogenesis of coronary artery disease. The findings underscore the need for comprehensive risk assessment and early intervention strategies to mitigate cardiovascular morbidity and mortality. Enhanced public awareness, lifestyle modification, and clinical vigilance remain essential pillars in combating the growing prevalence of CAD.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

Approved by the Institutional Ethical Committee of Al-Ameen Medical College & Hospital (Ref No: IEC/AMC/2023/105).

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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