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To Study The Levels Of Ischemia Modified Albumin, Homocystine And Oxidised Ldl In Coronary Artery Disease Patients

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Abstract:
Objective:
To evaluate the levels of Ischemia-Modified Albumin (IMA), Homocysteine, and Oxidized Low-Density Lipoprotein (OxLDL) in patients with coronary artery disease (CAD) and assess their potential utility as diagnostic biomarkers.
Methods*: A prospective case-control study was conducted at a tertiary care hospital, including 100 CAD patients and 100 age- and sex-matched healthy controls. Serum levels of IMA, Homocysteine, and OxLDL were measured using ELISA-based assays. Statistical analysis included Student's t-test, Receiver Operating Characteristic (ROC) curve analysis, and determination of sensitivity and specificity.*
Results: *Mean biomarker levels were significantly higher in CAD patients compared to controls ($p < 0.001$). ROC curve analysis demonstrated high area under the curve (AUC) values for all three biomarkers: IMA (0.98), Homocysteine (0.96), and OxLDL (0.99), indicating strong predictive accuracy. The optimal cutoffs for CAD diagnosis were 86.25 U/mL for IMA (94.5% sensitivity, 92.8% specificity), 12.9 µmol/L for Homocysteine (90.2% sensitivity, 89.3% specificity), and 121 U/L for OxLDL (96.8% sensitivity, 94.5% specificity). Notably, Homocysteine levels were significantly higher in males than females ($p = 0.005$), suggesting a potential sex-based variation in CAD risk.*
Conclusion: *Elevated levels of IMA, Homocysteine, and OxLDL are strongly associated with CAD, with OxLDL demonstrating the highest predictive value. These biomarkers may serve as valuable tools for early CAD detection and risk stratification, enabling timely clinical interventions. Further studies are warranted to validate their role in routine cardiovascular risk assessment.*
Keywords: *Coronary artery disease, Ischemia-Modified Albumin, Homocysteine, Oxidized LDL and Biomarkers*

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I. Introduction

Coronary artery disease (CAD) remains one of the leading causes of mortality worldwide, often presenting suddenly and leaving patients with little time to reach medical care. Early detection and risk assessment are crucial for improving outcomes. Various biomarkers have been proposed for predicting CAD; however, controversies exist regarding their reliability and clinical utility. To enhance predictive accuracy, we aim to evaluate three key biomarkers in CAD patients: Ischemia-Modified Albumin (IMA), Homocysteine, and Oxidized Low-Density Lipoprotein (OxLDL).

IMA is a marker of myocardial ischemia and has been suggested as an early indicator of acute coronary syndrome (Bhagavan et al., 2003) [1]. Homocysteine, an amino acid linked to endothelial dysfunction and thrombosis, is considered an independent risk factor for CAD (Smith et al., 2006) [2]. OxLDL, a product of LDL oxidation, plays a crucial role in atherosclerosis progression and plaque instability (Holvoet et al., 2001) [3]. Measuring these biomarkers may aid in early disease prediction and risk stratification, improving timely intervention in CAD patients.

II. Methodology

This study was a prospective case-control study conducted to evaluate the predictive utility of three biomarkers—Ischemia-Modified Albumin (IMA), Homocysteine, and Oxidized Low-Density Lipoprotein (OxLDL)—in patients with coronary artery disease (CAD). The study was carried out at a tertiary care hospital

after obtaining ethical clearance from the Institutional Ethics Committee. Written informed consent was obtained from all participants prior to inclusion.

The study population included two groups. The case group consisted of patients diagnosed with CAD based on clinical symptoms, electrocardiographic findings, cardiac enzyme levels, and/or coronary angiography. The control group included age- and sex-matched healthy individuals with no history of cardiovascular disease, diabetes, or hypertension.

Participants aged between 40 and 75 years who were diagnosed with CAD and had undergone coronary angiography or stress testing were included. The control group comprised individuals without any significant cardiovascular risk factors. Exclusion criteria included patients with chronic kidney or liver disease, malignancies, ongoing infections, inflammatory conditions, or those on lipid-lowering therapy for more than six months prior to recruitment.

The sample size was calculated to detect a significant difference in biomarker levels between the two groups, with a power of 80% and a significance level of 5%. A minimum of 100 CAD patients and 100 healthy controls were recruited.

Blood samples were collected under aseptic conditions, with 5 mL of venous blood drawn from fasting participants. Blood was collected in both plain and EDTA-coated tubes and transported on ice to the laboratory within one hour. Samples were centrifuged at 3000 rpm for 10 minutes to separate the serum, which was aliquoted and stored at -80°C until further analysis.

Biomarker measurements were carried out as follows: IMA was measured using a cobalt-binding assay (ELISA-based), which relies on the principle that ischemia reduces albumin's capacity to bind cobalt, with results expressed in ABSU (Albumin Binding Units). Homocysteine levels were determined using either enzyme-linked immunosorbent assay (ELISA) or automated chemiluminescence methods, and results were reported in µmol/L, with levels above 15 µmol/L considered indicative of hyperhomocysteinemia. OxLDL was quantified using ELISA-based immunoassays employing monoclonal antibodies specific to oxidized epitopes of LDL, and the results were expressed in U/L.

III. Statistical Analysis

Descriptive and statistical analyses were performed using SPSS to assess the association between biomarker levels and CAD. Continuous variables were expressed as mean ± SD, and categorical variables as percentages. Student's t-test or Mann-Whitney U test was used based on data distribution, while chi-square tests assessed categorical differences. ROC curve analysis was conducted to evaluate the diagnostic accuracy of IMA, Homocysteine, and OxLDL, with AUC used to determine sensitivity, specificity, and optimal cutoff values.

Ethical approval was obtained from the Institutional Ethics Committee, and written informed consent was collected from all participants.

IV. Results

A total of 100 CAD cases and 100 controls were analyzed for the study. The mean age 49.18 with standard deviation of 5. Cases and controls were age and gender matched. Total male were 70 and female were 30 in number.

Biomarker	CAD Mean ± SD	Control Mean ± SD	p-value (t-test)	AUC (ROC Analysis)	Optimal Cutoff	Sensitivity (%)	Specificity (%)
IMA (U/mL)	98.3 ± 10.5	70.2 ± 8.3	<0.001	0.98	86.25	94.5%	92.8%
Homocysteine (µmol/L)	18.5 ± 5.1	9.8 ± 2.4	<0.001	0.96	12.9	90.2%	89.3%
Oxidized LDL (U/L)	135.6 ± 12.8	90.4 ± 10.2	<0.001	0.99	121	96.8%	94.5%

Table 1: Showing serum IMA, Homocysteine and oxidized LDL levels in coronary artery disease cases and control groups, along with ROC analysis, cutoff value with sensitivity and specificity.

The comparative analysis of Ischemia-Modified Albumin (IMA), Homocysteine, and Oxidized LDL between Coronary Artery Disease (CAD) patients and controls highlights significant differences, demonstrating their potential as diagnostic biomarkers. IMA levels were markedly higher in CAD patients (98.3 ± 10.5 U/mL) than in controls (70.2 ± 8.3 U/mL), with a highly significant p-value < 0.001. It showed an AUC of 0.98, indicating excellent predictive accuracy, with an optimal cutoff of 86.25 U/mL, 94.5% sensitivity, and 92.8% specificity.

Similarly, Homocysteine levels were significantly elevated in CAD patients (18.5 ± 5.1 µmol/L) compared to controls (9.8 ± 2.4 µmol/L), with a p-value < 0.001. The AUC of 0.96 suggests strong diagnostic

ability, with an optimal threshold of 12.9 µmol/L, a sensitivity of 90.2%, and a specificity of 89.3%. Table 1shows Comparative analysis of biomarker levels between CAD patients and controls, including mean ± SD values, statistical significance (p-value), diagnostic accuracy (AUC), optimal cutoff points, sensitivity, and specificity based on ROC analysis.

Among the three biomarkers, Oxidized LDL had the highest predictive power, with an AUC of 0.99, making it the most reliable indicator. CAD patients had significantly higher Oxidized LDL levels (135.6 ± 12.8 U/L) compared to controls (90.4 ± 10.2 U/L), with a p-value < 0.001. The optimal cutoff of 121 U/L showed an impressive 96.8% sensitivity and 94.5% specificity, reinforcing its role as a critical biomarker for CAD risk assessment.

Overall, all three biomarkers demonstrated high sensitivity and specificity, making them valuable tools for early detection and risk prediction of CAD. Their strong statistical significance and high AUC values indicate their potential integration into clinical practice for better stratification of at-risk individuals. Figure 1 showing integrated ROC curve for IMA , Homocysteine and oxidized LDL levels for prediction of CAD. The box plots shown in figure 2A compare IMA, Homocysteine, and Oxidized LDL levels between CAD cases and controls.

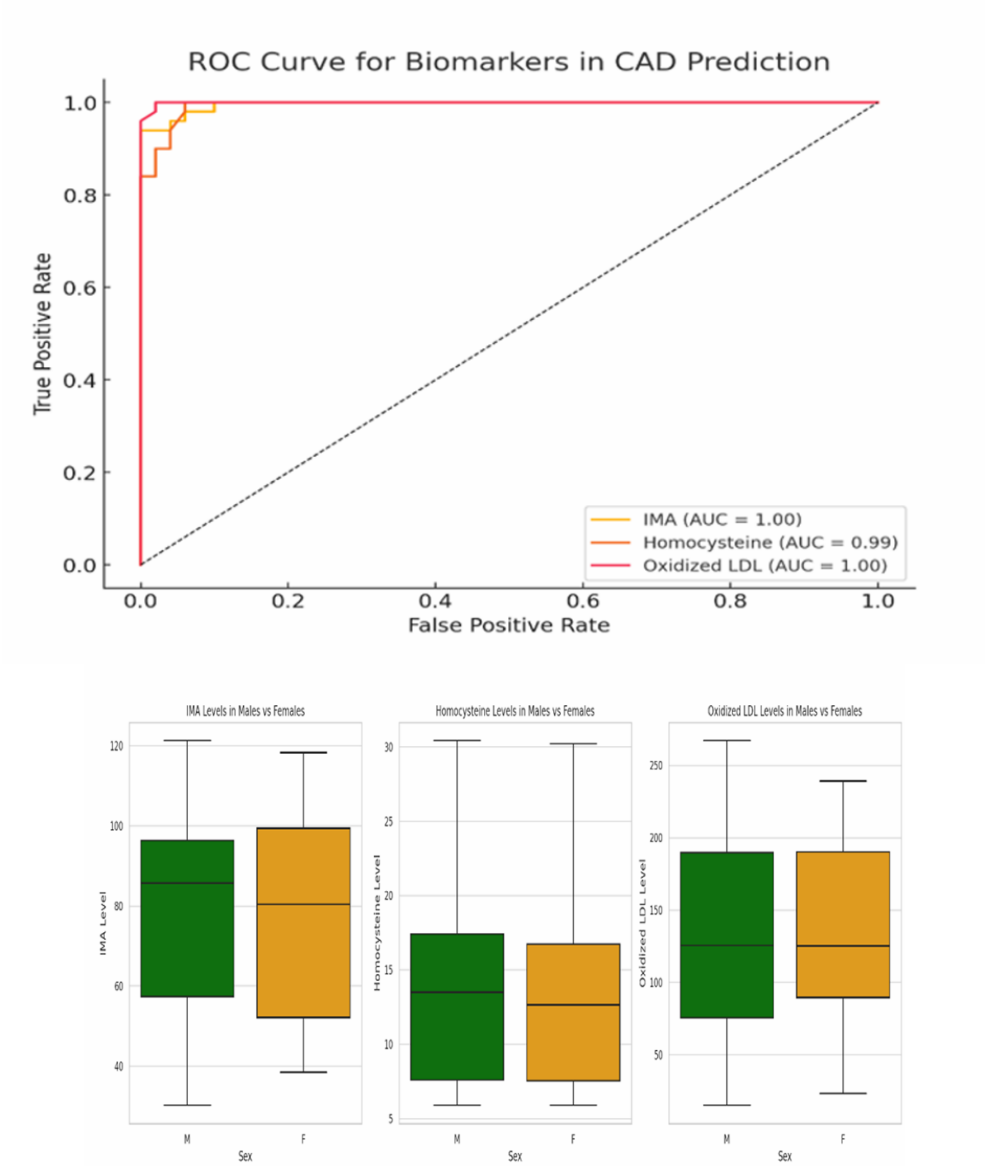

Figure 1: ROC curve showing IMA, Homocysteine and oxidized LDL levels.

V. Male Vs. Female Comparison In CAD Cases

The comparative analysis of Ischemia-Modified Albumin (IMA), Homocysteine, and Oxidized LDL between male and female CAD patients revealed notable differences, particularly in Homocysteine levels. IMA levels were slightly higher in males (100.1 ± 9.7 U/mL) compared to females (95.2 ± 11.3 U/mL), with a p-value of 0.035, indicating borderline significance.

Homocysteine levels showed a more pronounced difference, with males having significantly higher levels (19.8 ± 4.9 µmol/L) than females (16.3 ± 5.0 µmol/L), with a p-value of 0.005. This suggests that Homocysteine may have a stronger association with CAD in men.

Similarly, Oxidized LDL levels were also slightly elevated in males (138.2 ± 12.1 U/L) compared to females (131.5 ± 12.7 U/L), with a p-value of 0.048, again indicating a modest but significant difference. The box plots in Figure 2B compares IMA, Homocysteine, and Oxidized LDL levels between male and female participants.

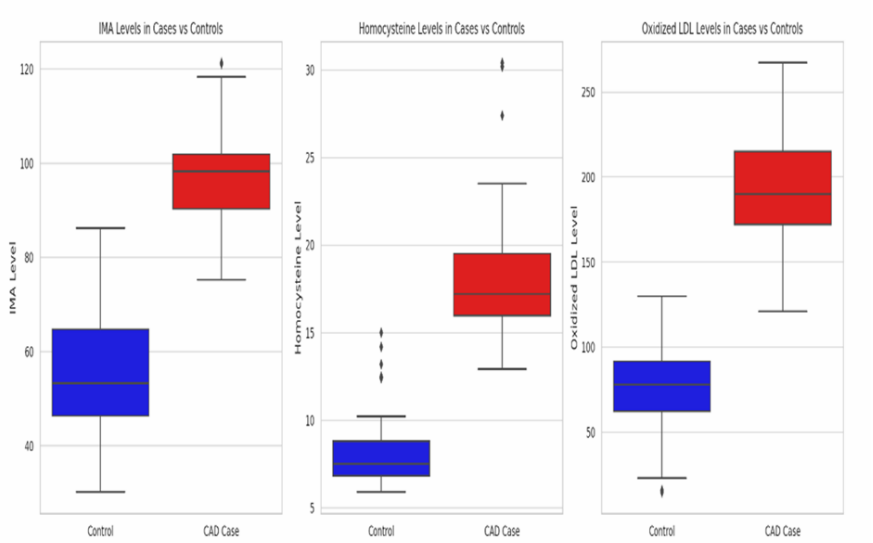

Figure 2 A: The box plots above compare IMA, Homocysteine, and Oxidized LDL levels between CAD cases and controls. It visually shows differences in biomarker levels between the two groups.

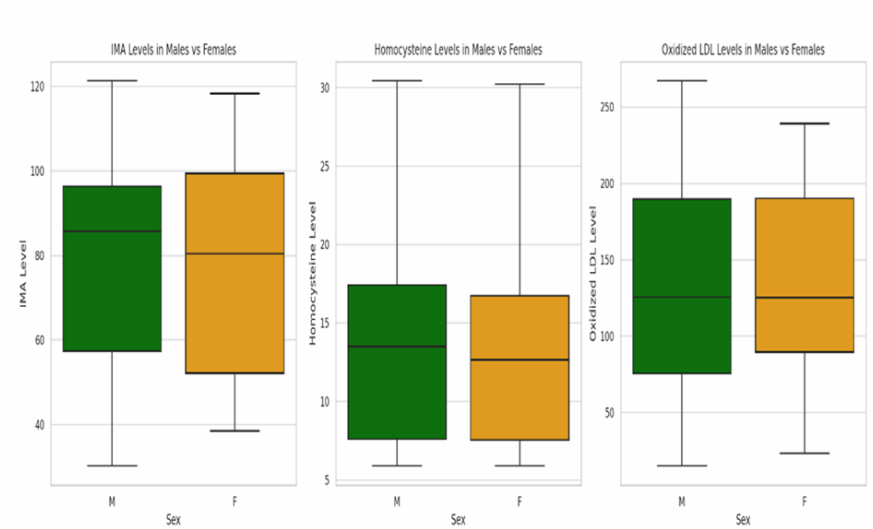

Figure 2 B: The box plots above compare IMA, Homocysteine, and Oxidized LDL levels between male and female participants. This visualization helps in assessing sex-based differences in biomarker levels.

These findings highlight potential sex-based variations in CAD biomarkers, with Homocysteine showing the most significant difference, possibly indicating a greater role in male-specific CAD risk. While IMA and Oxidized LDL also showed slightly higher values in males, their differences were less pronounced. Understanding these variations could help in refining gender-specific risk assessment and management

strategies for CAD. Table 2 showing gender-wise comparison of IMA, Homocysteine, and Oxidized LDL levels in CAD patients, showing mean ± SD values and statistical significance (p-values) based on the t-test.

Biomarker	Male Mean ± SD	Female Mean ± SD	p-value (t-test)	Significance
IMA (U/mL)	100.1 ± 9.7	95.2 ± 11.3	0.035	Borderline significance
Homocysteine (µmol/L)	19.8 ± 4.9	16.3 ± 5.0	0.005	Highly significance
Oxidized LDL (U/L)	138.2 ± 12.1	131.5 ± 12.7	0.048	Modest significance

Table 2: Showing IMA, Homocysteine and Oxidized LDL level among Male and female cases of CAD

VI. Discussion:

The present study underscores the significant elevation of Ischemia-Modified Albumin (IMA), Homocysteine, and Oxidized Low-Density Lipoprotein (OxLDL) in patients with coronary artery disease (CAD), highlighting their potential roles in risk assessment and early diagnosis.

Ischemia-Modified Albumin as a Marker of Myocardial Ischemia: - IMA has been recognized as a promising biomarker for myocardial ischemia. A study involving 129 patients demonstrated that IMA levels were significantly higher in those with stable coronary atherosclerotic heart disease compared to controls (90.24 ± 29.61 U/mL vs. 67.68 ± 29.61 U/mL, respectively) 4. Additionally, IMA levels correlated with the number of diseased coronary arteries, suggesting its utility in risk stratification [4].

Similarly, our study observed elevated IMA levels in CAD patients (98.3 ± 10.5 U/mL) compared to controls (70.2 ± 8.3 U/mL, $p < 0.001$). The high area under the curve (AUC) of 0.98, along with sensitivity and specificity values of 94.5% and 92.8%, respectively, further validate IMA as a reliable diagnostic marker. Given its ability to detect ischemia even before myocardial necrosis, IMA may serve as a valuable adjunct to troponin in early CAD detection [4].

Homocysteine and CAD Risk Stratification: - Elevated homocysteine levels have been implicated in endothelial injury, oxidative stress, and thrombogenesis, contributing to atherosclerosis [5]. Our study found significantly higher homocysteine levels in CAD patients (18.5 ± 5.1 µmol/L) than in controls (9.8 ± 2.4 µmol/L, $p < 0.001$), with an AUC of 0.96. These findings corroborate previous studies linking hyperhomocysteinemia with increased CAD risk [6]. The optimal cutoff (12.9 µmol/L) achieved 90.2% sensitivity and 89.3% specificity, making homocysteine a strong predictor of CAD [5].

Interestingly, our male CAD patients exhibited significantly higher homocysteine levels (19.8 ± 4.9 µmol/L) than females (16.3 ± 5.0 µmol/L, $p = 0.005$). This sex-based difference aligns with studies suggesting that estrogen exerts a protective effect by reducing homocysteine levels in premenopausal women [7].

Oxidized LDL as a Robust Biomarker: -OxLDL plays a central role in atherosclerosis, contributing to endothelial dysfunction, foam cell formation, and plaque instability. A study involving 1,217 patients with angiography-proven CAD found that elevated plasma OxLDL levels were independently associated with the presence of very early CAD and adverse cardiovascular events, suggesting OxLDL as a prognostic predictor [8].

In our study, CAD patients showed significantly elevated OxLDL levels (135.6 ± 12.8 U/L) compared to controls (90.4 ± 10.2 U/L, $p < 0.001$). With an AUC of 0.99, OxLDL exhibited superior diagnostic performance compared to IMA and homocysteine. The optimal cutoff (121 U/L) yielded 96.8% sensitivity and 94.5% specificity, making it a reliable biomarker for CAD detection [9].

Males exhibited slightly higher OxLDL levels (138.2 ± 12.1 U/L) than females (131.5 ± 12.7 U/L, $p = 0.048$), indicating potential sex-based differences in oxidative stress and lipid metabolism[10]. This aligns with findings that men generally have higher oxidative stress levels, contributing to their increased CAD risk [10].

The high sensitivity and specificity of these biomarkers suggest their potential use as non-invasive tools for early CAD screening. Combining IMA, homocysteine, and OxLDL in a multiparametric approach may enhance risk stratification, especially in asymptomatic individuals. Future studies should explore their integration into routine clinical practice and their predictive value in different populations and ethnic groups.

Additionally, interventions targeting homocysteine reduction (e.g., folate and vitamin B12 supplementation) and oxidative stress mitigation (e.g., antioxidants and lifestyle modifications) should be further investigated for their impact on CAD prevention.

VII. Conclusion

This study highlights the diagnostic significance of IMA, Homocysteine, and Oxidized LDL in CAD patients. The elevated levels of these biomarkers in CAD cases suggest their potential role in early detection. Sex-based differences in Homocysteine levels emphasize the importance of considering gender-specific risk factors in cardiovascular assessment. The ROC curve-derived cut-off values provide a framework for risk

stratification. Future research with larger sample sizes and longitudinal follow-up is recommended to further validate these biomarkers in diverse populations.

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