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Original Article

Comparative Assessment of Mannose-Binding Lectin And C-Reactive Protein as Inflammatory Biomarkers for Coronary Artery Disease in Hypertensive Patients

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ABSTRACT

Background: Cardiovascular disease (CVD) is a primary cause of global mortality, with hypertension identified as a powerful, independent risk factor (Mahmood et al., 2014). Inflammation is critical in all phases of atherogenesis. While C-Reactive Protein (CRP) is a recognized inflammatory marker, Mannose-Binding Lectin (MBL) is increasingly scrutinized for its role in the complement-mediated vascular damage that characterizes coronary artery disease (CAD) (Smith, J.,2020).

Aim & Objectives: This study evaluated serum levels of MBL and CRP in hypertensive patients with and without recent myocardial infarction (MI). The objective was to assess whether MBL offers superior or complementary diagnostic value compared to CRP in identifying the presence of CAD in hypertensive patients.

Materials & Methods: A cross-sectional case-control study was conducted with 180 subjects divided into three groups: Group A (Hypertension, n=60), Group B (Hypertension with recent MI, n=60), and Group C (Healthy controls, n=60). Serum MBL was quantified via ELISA (Enzyme-Linked Immunosorbent Assay) and CRP was measured using particle-enhanced immunoturbidimetry.

Results: MBL and CRP levels were significantly higher in hypertensive patients and peaked in those with recent MI compared to controls ($p < 0.001$). A significant positive correlation ($r = 0.66$, $p = 0.01$) was observed between MBL and CRP specifically in the MI group. Furthermore, Random Forest modeling identified MBL as a powerful non-linear predictor of MI, demonstrating a sharp threshold effect at 800–1000 ng/mL.

Conclusion: Both MBL and CRP are elevated in hypertensive patients. However, MBL serves as a more specific marker for advanced subclinical atherosclerosis and MI risk due to its unique non-linear threshold behavior.

Keywords: Hypertension, C-Reactive Protein (CRP), Mannose-Binding Lectin (MBL), Atherosclerosis / Atherogenesis, Cardiovascular Risk Stratification.

INTRODUCTION

Hypertension is a major independent risk factor for ischemic coronary disease and stroke. Recent cardiovascular research has pivoted from a purely hemodynamic model to an inflammatory one, recognizing atherogenesis as a chronic, low-grade inflammatory response within the arterial intima (Ross, 1993 ; Brown & Lee, 2019).

C-Reactive Protein (CRP) is a well-documented acute-phase reactant used to predict future coronary events, its elevation is often non-specific (Ridker et al., 2000; Voudris, K. V., et al.,2023). Mannose-Binding Lectin (MBL), a key component of innate immunity, activates the complement system via the lectin pathway and has been implicated in the biochemical cascade leading to plaque instability (Guo et al., 2024).

Previous studies have largely focused on either chronic hypertension or acute MI in isolation, often ignoring the comparative diagnostic weight of MBL versus CRP in a hypertensive cohort. Furthermore, traditional linear statistical methods often fail to identify specific biological thresholds where risk escalates. This study was undertaken to bridge this gap by using both comparative biochemical analysis and advanced predictive modeling to improve risk stratification in hypertensive individuals (Ogunpola et al., 2024).

MATERIALS AND METHODS:

Study Design: Cross sectional Case Control study

The study protocol was approved by the Institutional Ethics Committee of Madras Medical College, Chennai.180 subjects were selected for the study. They were divided into three groups as follows

- Group A - 60 Recently diagnosed hypertensive patients of 6 months duration from the outpatients attending hypertension clinic in Rajiv Gandhi Government General Hospital, Chennai
- Group B - 60 Hypertensive patients who had myocardial infarction recently. (< 7 days duration) from the Inpatients admitted in the cardiology department in Rajiv Gandhi Government General Hospital, Chennai.
- Group C – 60 Age and sex matched apparently healthy subjects who were staffs of Madras Medical College, their relatives and friends.

Exclusion criteria :

- Patients with Diabetes mellitus
- Patients with renal disorders.
- Patients with Liver diseases.
- Patient with acute illness / infection.
- Chronic Smokers and alcoholics.
- Other endocrinological disorders

Venous blood samples were collected. Serum MBL was estimated using a non-competitive sandwich ELISA (measurable range: 10–3000 ng/mL). BT LAB ELISA Kit (Lot No: E0335Hu) was used. The measurable range for the kit ranges from 10ng / mL – 3000 ng / mL with sensitivity of 5.16 ng/mL, inter assay CV < 10% & intra assay CV < 5%. CRP was measured via particle-enhanced immunoturbidimetry. Cobas C packs by Roche Hitachi systems was used for CRP estimation. Statistical analysis was performed using Python-based tools (version 3.9) with scikit-learn and statmodels libraries. Continuous variables are expressed as Mean ± SD. Comparative analysis across groups was performed using ANOVA, and categorical variables were assessed via chi-square test. To evaluate the diagnostic accuracy and feature importance, a Random Forest algorithm was utilized to identify non-linear relationships and thresholds for MI prediction (Kiran et al., 2022: Mansoori et al., 2025).

RESULTS:

Table 1: Demographic and Anthropometric Characteristics of the Study Population

Variable	Group A (HTN)	Group B (HTN+MI)	Group C (Control)	P-value
Age (years)	52.37 ± 8.15	54.17 ± 9.67	54.03 ± 8.39	0.68 (NS)
Gender (M/F)	13/17	16/14	16/14	0.68 (NS)
BMI (kg/m²)	24.51 ± 3.37	25.15 ± 3.40	24.43 ± 2.87	0.46 (NS)

***NS = Not Significant, HTN – Hypertension, MI* – Myocardial Infarction**

Data indicates groups were well-balanced for age, gender, and BMI.

Table 2: Inflammatory Markers among study groups

Biomarkers	Group A (HTN) Mean ± SD	Group B (HTN+MI) Mean ± SD	Group C (Control) Mean ± SD	P-value
CRP (mg/L)	5.34 ± 1.92	7.79 ± 2.74	1.41 ± 0.73	**< 0.001** (Highly significant)
MBL (ng/mL)	823.45 ± 51.72	1163.39 ± 218.24	607.15 ± 94.18	**< 0.001** (Highly significant)

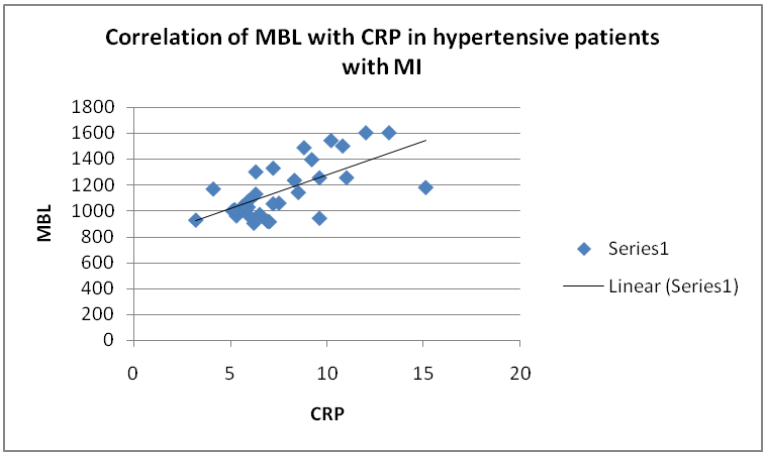
Table 3: Correlation between MBL and CRP

	HYPERTENSION	HYPERTENSION WITH MI	CONTROL

	R	P-value	R	P-value	R	P-value
CRP	0.15	0.64	0.66*	0.01	0.002	0.99

* Significant at 0.05 Level

Correlation analysis showed a strong positive correlation between MBL and CRP (r = 0.66, p = 0.01) only in the hypertension with MI group, suggesting a synergistic inflammatory response during acute events.



CRP and MBL for MI Prediction

Fig 1: Predictive Modeling

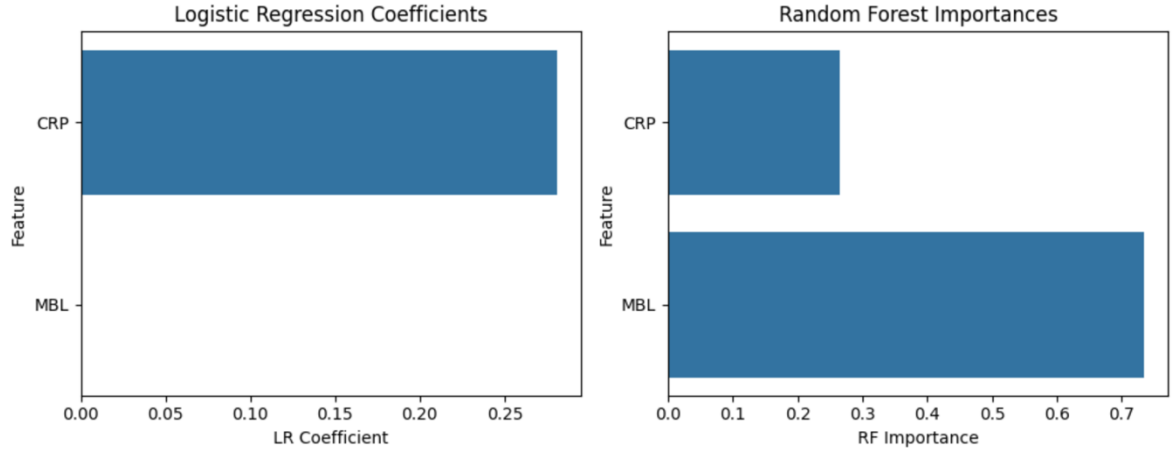


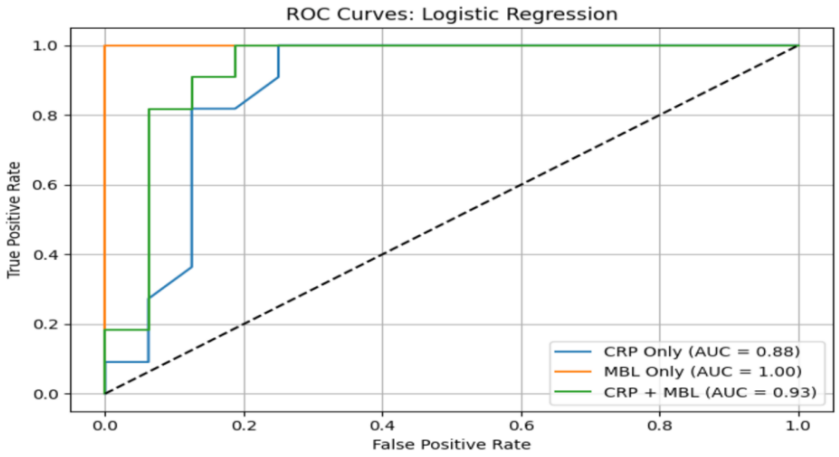
Table 4: Logistic Regression Coefficients

Markers	Coefficient
CRP	0.28
MBL	0.001

Table 5: Feature Importance for MI Prediction (Random Forest Model)

Marker	Importance Score	Interpretation
MBL	0.73	Most dominant predictor; non-linear threshold effect.
CRP	0.27	Meaningful linear predictor, but less dominant.

Fig 2 : ROC Curve – Logistic Regression

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Comparison of Linear and Nonlinear Importance:
  Feature  LR Coefficient  RF Importance
0     CRP        0.280658       0.265362
1     MBL        0.000929       0.734638
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Table 6: ROC Curve – Logistic Regression Model Performance

Biomarkers	AUC Score
CRP only	0.88
MBL only	1.00
CRP + MBL	0.93

Fig 3: Partial Dependence plot

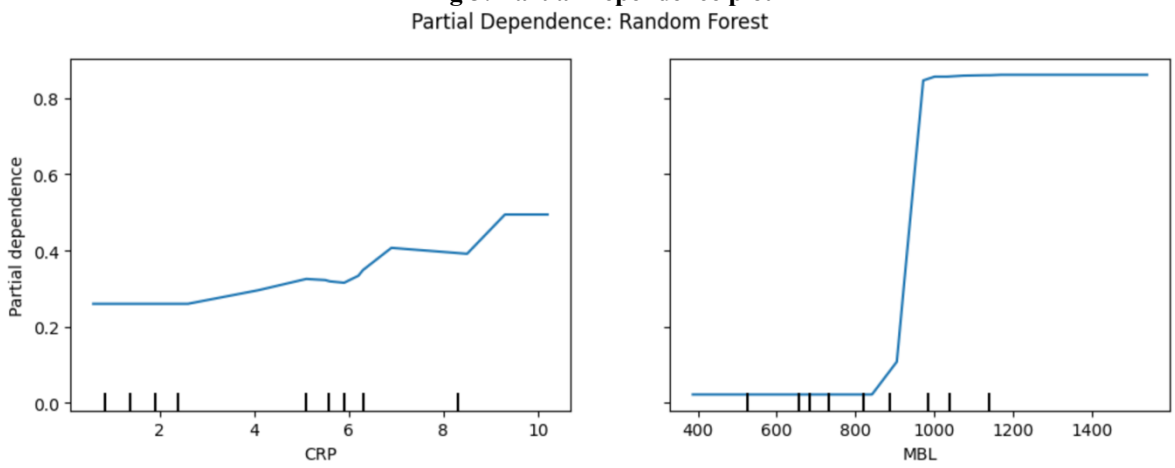

Table 7: Partial Dependence Plot (PDP) – Random Forest

Feature	Pattern Observed	Interpretation
CRP	Gradual increase in MI probability with rising CRP	CRP has a positive but gradual effect on MI risk
MBL	Sharp rise at 800–1000 units	MBL shows a threshold effect — MI risk spikes sharply after a point

DISCUSSION:

Hypertension is a pro-inflammatory state that promotes vascular remodeling and atherosclerosis. The elevation of MBL in hypertensive patients compared to healthy controls suggests that the lectin pathway is activated during the early, subclinical phases of vascular remodeling (Smith, 2020; Sumida et al., 2015). While hypertension provides the mechanical stress, MBL-mediated complement activation likely facilitates the progression of atherosclerotic plaques.

The most important finding of this study is the non-linear threshold behavior of MBL(Fig 1). While CRP levels rise steadily with systemic inflammation, Random Forest modeling indicates that MI risk spikes sharply once MBL reaches the 800–1000 ng/mL range (Fig 3). This threshold effect suggests that MBL may serve as a "trigger" marker for plaque rupture or acute ischemia rather than just a general indicator of inflammation.

The findings align with research by Keller et al. and Pesonen et al., which identified elevated MBL as a risk factor for future coronary events (Pesonen et al., 2009; Keller et al., 2006). The superior specificity of MBL (95.30%) compared to CRP in predicting Myocardial Infarction (MI) among hypertensive patients can be attributed to its unique role in the Lectin Complement Pathway (Ridker et al., 2000; Voudris et al., 2023). While CRP is a sensitive but non-specific marker of the general systemic inflammatory burden, MBL acts as a targeted initiator of vascular-specific immune responses.

In hypertensive individuals, chronic shear stress leads to endothelial dysfunction, exposing mannose-rich carbohydrate patterns on the damaged basement membrane (Dorflinger, G. H., et al.,2022). MBL binds specifically to these patterns, initiating a complement cascade that directly contributes to plaque instability. Unlike the linear increase observed with CRP (Table 4), the Random Forest modeling in this study revealed a sharp non-linear threshold effect at approximately 800–1000 ng/mL(Shishehbori & Awan, 2024).

This suggests that while low-level MBL elevation may be present in stable hypertension, crossing this specific concentration threshold acts as a "biological tripwire," triggering the acute complement-mediated tissue damage and plaque rupture that characterizes an MI. Consequently, MBL serves not just as a marker of inflammation, but as a specific indicator of imminent or active coronary events, offering a more precise tool for risk stratification than traditional biomarkers.

Limitations:
Longitudinal studies are required to establish a temporal causal relationship. Larger, multi-ethnic datasets are needed to account for genetic polymorphisms and ensure global applicability of the identified diagnostic thresholds.

CONCLUSION:

Serum MBL is a novel and significant marker of myocardial infarction and subclinical atherosclerosis in hypertensive individuals. Its novelty lies in its non-linear threshold behaviour, which offers higher diagnostic specificity than CRP. Monitoring MBL alongside CRP can enhance early identification of high-risk patients, allowing for timely interventions to prevent the progression of cardiovascular disease.

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