https://doi.org/10.70844/jmhrp.2025.2.1.37

Journal of Medical Health Research and Psychiatry

Research Article

JMHRP-25-037

The Utility of High-Sensitive C-Reactive Protein and Cardiac Markers in the Prediction of Heart Diseases

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Received date: 11 February, 2025, **Accepted date:** 25 February, 2025, **Published date:** 04 March, 2025

Citation: Atween A, Fairooz A, Addin AS, Albadani A, Qaid S, et al. (2025) The Utility of High-Sensitive C-Reactive Protein and Cardiac Markers in the Prediction of Heart Diseases. J Med Health Psychiatry 2: 1.

Abstract

Background: Cardiovascular Diseases (CVDs) remain a leading cause of morbidity and mortality worldwide. Inflammation, as indicated by high-sensitivity C-reactive protein (hs-CRP), plays a significant role in CVD pathogenesis. This study aims to evaluate the correlation between hs-CRP levels and heart disease among patients in Ibb City, Yemen.

Methodology: A total of 205 participants were enrolled, including 153 heart disease patients and 52 healthy controls, selected randomly from Al-Noor General Hospital, Al-Manar Specialist Hospital, Al-Badr International Hospital, M. Alboni Cardiac Clinic and Ibb Cardiac Center. Data collection involved echocardiography, hs-CRP tests, CK-MB, Troponin I and ECG, along with symptom assessment (angina, nausea, dizziness and shortness of breath). Statistical analyses included t-tests, ANOVA and chi-square tests.

Results: Among the heart disease patients, the prevalence of symptoms was angina (84.31%), nausea (53.95%), dizziness (75.16%) and shortness of breath (67.32%). A significant correlation was found between heart disease and elevated hs-CRP levels ($p < 0.01$). Descriptive statistics revealed that 69.9% of heart disease patients had positive hs-CRP results, compared to 30.1% with negative results. The mean hs-CRP level was 48.37 mg/L (SD = 41.61) for positive cases and 1.22 mg/L (SD = 0.96) for negative cases. In the control group, 75% (n=39) had negative hs-CRP results, while 25% (n=13) tested positive ($p < 0.001$), demonstrating a significant difference from the patient group.

Conclusions: Patients with heart disease exhibit significantly higher hs-CRP levels than healthy individuals. Moreover, hs-CRP serves as an independent predictor of heart disease with statistical significance ($p < 0.01$). The moderate correlation (0.265) suggests that hs-CRP can be used as a biomarker for cardiovascular risk assessment, complementing traditional diagnostic tools.

Keywords: High sensitive CRP, MI, Troponin I, Cardiac markers, Heart disease, CK-MB.

Introduction

Cardiovascular Diseases (CVDs) remain the leading cause of morbidity and mortality worldwide, despite significant advancements in healthcare. Inflammation plays a crucial role in the development and progression of atherosclerosis, the primary underlying pathology of most CVDs. Studies have shown that inflammatory markers, such as high-sensitivity C-Reactive Protein (hs-CRP), are associated with increased cardiovascular risk and adverse clinical outcomes [1].

Inflammation-induced vascular changes are not easily detectable using standard cardiac imaging techniques. Therefore, identifying biomarkers that reflect these changes is essential for early diagnosis and risk stratification [2]. hs-CRP, a highly sensitive acute-phase protein, has emerged as a promising marker for assessing cardiovascular risk. Elevated hs-CRP levels have been linked to Coronary Artery Disease (CAD), Myocardial Infarction (MI) and stroke [3].

Literature Review

Cardiovascular diseases

CVD is a broad term encompassing various conditions affecting the heart and blood vessels. The most common types include:

Types of CVDs

Coronary Heart Disease (CHD): Coronary Heart Disease (CHD), also known as Coronary Artery Disease (CAD), is characterized by the accumulation of atheromatous plaques within the

https://doi.org/10.70844/jmhrp.2025.2.1.37

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coronary arteries. This process leads to narrowing and obstruction of blood flow, resulting in ischemia, angina and potential Myocardial Infarction (MI). CHD is the leading cause of sudden cardiac death worldwide [4].

Angina: Angina is a clinical manifestation of CHD, presenting as chest pain, pressure, or discomfort due to myocardial ischemia. It is typically triggered by physical exertion or emotional stress and relieved by rest or nitroglycerin. The severity and frequency of angina can indicate underlying coronary artery blockage [5].

Stroke: Stroke occurs due to interruption of blood supply to the brain, either by an arterial blockage (ischemic stroke) or rupture (hemorrhagic stroke). Ischemic strokes account for nearly 80% of all strokes, making them a significant public health concern [6].

Rheumatic heart disease: Rheumatic heart disease results from untreated streptococcal infections, leading to chronic inflammation and scarring of heart valves. It is a major cause of valvular heart disease in developing countries [7].

Congenital Heart Disease (CHD): Congenital heart disease refers to structural heart defects present at birth. These may include septal defects, valve abnormalities and complex malformations that require surgical intervention [8].

Peripheral Arterial Disease (PAD): PAD is characterized by the narrowing of peripheral arteries, primarily affecting the legs. It is associated with atherosclerosis and an increased risk of cardiovascular events, such as heart attacks and strokes [9].

Risk factors for CVD

CVD is influenced by a combination of modifiable and non-modifiable risk factors. Understanding these risk factors is crucial for prevention and early intervention.

Smoking: Smoking is a major independent risk factor for CVD, increasing the risk of CHD by 2-4 times. It promotes atherosclerosis, thrombosis and endothelial dysfunction, significantly raising the likelihood of myocardial infarction [10].

Obesity: Obesity, particularly central obesity, is associated with hypertension, dyslipidemia and insulin resistance, all of which contribute to CVD progression. The World Health Organization (WHO) estimates that obesity prevalence continues to rise globally [11].

Diabetes Mellitus (DM): Diabetes significantly increases the risk of atherosclerosis and cardiovascular complications. Hyperglycemia induces vascular inflammation and endothelial dysfunction, accelerating the progression of CHD [12].

Hypertension (HTN): Hypertension is a leading risk factor for stroke, heart failure and renal disease. Chronic high blood pressure causes arterial wall damage and left ventricular hypertrophy, increasing cardiovascular morbidity and mortality [13].

High LDL 0063holesterol: Elevated Low-Density Lipoprotein (LDL) cholesterol contributes to plaque formation and arterial blockage, increasing the risk of CHD. WHO estimates that 8% of global deaths are attributable to high cholesterol levels [14].

Other risk factors: Additional risk factors include physical inactivity, excessive alcohol consumption and genetic predisposition. Regular exercise and a heart-healthy diet are essential for mitigating cardiovascular risk [15].

High-sensitivity C-Reactive Protein (hs-CRP) test

Description: hs-CRP is a highly sensitive marker of systemic inflammation, synthesized by the liver in response to cytokine release. Elevated hs-CRP levels correlate with cardiovascular risk and adverse clinical outcomes [16].

Clinical use: The American Heart Association (AHA) recommends hs-CRP testing for individuals at intermediate risk (10-20%) of developing CVD. It aids in risk stratification and early intervention [7].

Clinical significance

- Elevated hs-CRP levels are associated with increased CHD risk.
- hs-CRP serves as a prognostic marker for MI, stroke and heart failure.
- Statin therapy has been shown to lower hs-CRP levels, reducing cardiovascular events [3].

Testing frequency: hs-CRP testing should be repeated after 2-3 weeks to confirm persistent elevation. Levels >10 mg/L may indicate acute infection or systemic inflammation, requiring further investigation [17].

Aims of the Study

General aim

To evaluate the association between high-sensitivity C-Reactive Protein (hs-CRP) levels and Myocardial Infarction (MI) in Ibb, Yemen.

Specific aim

- To assess the diagnostic value of hs-CRP in heart disease.
- To compare positive *vs*. negative hs-CRP cases in patients with heart disease.
- To analyze gender-based differences in hs-CRP, CK-MB and Troponin I levels.

Research problem

This study investigates the relationship between elevated hs-CRP levels and heart disease severity, assessing its role as a predictive biomarker for cardiovascular events.

Study hypothesis

- hs-CRP levels correlate with CVD severity and prognosis.
- Gender and age influence hs-CRP, CK-MB and Troponin I levels.

Materials and Methodology

Study sample

This study included 205 participants, divided into:

- 153 patients diagnosed with heart disease.
- 52 healthy control subjects.

https://doi.org/10.70844/jmhrp.2025.2.1.37

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Participants were randomly selected from the following medical institutions in Ibb, Yemen:

- Al-Noor General Hospital
- Al-Manar Specialist Hospital
- Al-Badr International Hospital
- M. Alboni Cardiac Clinic
- Ibb Cardiac Center

Chemicals and equipment

The study utilized the following laboratory instruments and reagents:

- Mindray BS-200 for hs-CRP measurement.
- Roche Cobas e411 Analyzer for cardiac biomarkers (CK-MB & Troponin I).
- 12-lead Electrocardiogram (ECG) machine to assess cardiac electrical activity.
- Echocardiography ultrasound system to evaluate heart structure and function.
- Standard reagents and kits for hs-CRP, CK-MB and Troponin I detection.

Study design

This study followed a case-control design, comparing hs-CRP levels between patients with heart disease (case group) and healthy individuals (control group). The research was conducted between January and June 2024 in Ibb, Yemen.

Data collection

Comprehensive clinical and laboratory data were collected, including:

- **Demographic information:** Age, gender, weight, smoking status, diabetes, hypertension and occupational status.
- **Clinical history:** Symptoms of cardiovascular disease (angina, nausea, dizziness, shortness of breath, etc.).
- **Laboratory tests:** hs-CRP, CK-MB and Troponin I levels.
- **Imaging studies:** Echocardiography and ECG results.

Blood Sample Collection and Analysis

Blood sample collection

- Venous blood samples were drawn from all participants after 8-12 hours of fasting.
- Samples were collected into EDTA tubes and processed within 2 hours of collection.

Laboratory analysis

- **hs-CRP measurement:** Conducted using the mindray BS-200 autoanalyzer.
- **Cardiac markers (CK-MB & Troponin I):** Assessed using the Roche Cobas e411 analyzer.
- **Electrocardiography (ECG):** Evaluated for ischemic changes, arrhythmias and infarction signs.
- **Echocardiography:** Used to assess left ventricular function and detect structural abnormalities.

Statistical analysis

Data were analyzed using SPSS (Version 26.0). The following statistical tests were performed:

- **Descriptive statistics:** Mean, standard deviation and percentages.
- **Chi-square test (χ^2):** Used to assess categorical variables.
- **Independent t-test:** Used to compare mean hs-CRP levels between groups.
- **ANOVA:** Applied to analyze differences between multiple subgroups.
- **Pearson correlation coefficient:** Used to determine the relationship between hs-CRP levels and cardiac biomarkers.

A p-value < 0.05 was considered statistically significant.

Study Strengths and Limitations

Strengths

- Randomized participant selection, reducing selection bias.
- Multicenter study, enhancing generalizability.
- Comprehensive biomarker assessment, including hs-CRP, CK-MB and Troponin I.

Limitations

- Small sample size, limiting statistical power.
- Potential confounding factors, such as undiagnosed infections affecting hs-CRP levels.
- Single-region study, reducing applicability to broader populations.

Results

Participant characteristics

A total of 205 participants were included in the study, with 153 heart disease patients (cases) and 52 healthy individuals (controls). Table 1 presents the demographic and clinical characteristics of the study population (Figure 1, 2).

Variable	Heart disease patients (n=153)	Controls (n=52)	p-value
Gender	Male: 86 (56.2%)	Male: 44 (84.6%)	0.002*
	Female: 67 (43.8%)	Female: 8 (15.4%)	
Age (years)	<30: 11 (7.2%)	<30: 32 (61.5%)	0.001*
	30-50: 95 (62.1%)	30-50: 20 (38.5%)	
	>60: 47 (30.7%)	>60: 0 (0.0%)	
Weight (kg)	<50: 18 (11.8%)	<50: 2 (3.8%)	0.021*
	51-65: 108 (70.6%)	51-65: 13 (25.0%)	

https://doi.org/10.70844/jmhrp.2025.2.1.37

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	>65: 21 (13.7%)	>65: 7 (13.5%)	
Diabetes mellitus	43 (28.1%)	0 (0.0%)	<0.001*
Hypertension	69 (45.1%)	0 (0.0%)	<0.001*
Smoking status	32 (20.9%)	0 (0.0%)	<0.001*
*Significant at $p < 0.05$			

Table 1: Demographic and clinical characteristics of participants.

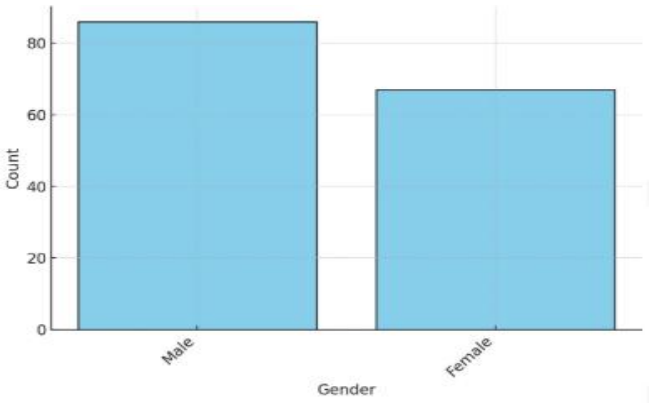

Figure 1: Gender distribution.

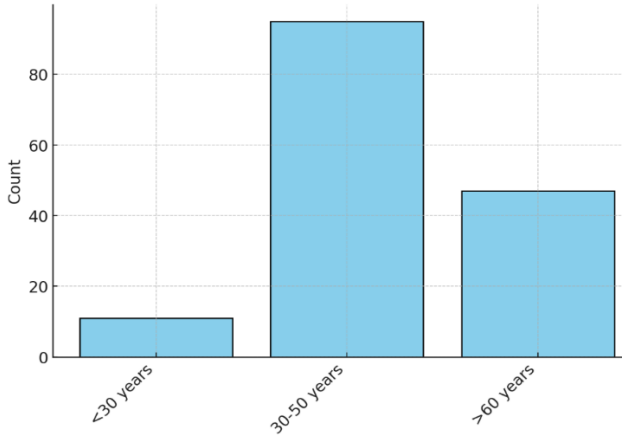

Figure 2: Age group distribution.

Clinical symptoms of heart disease

The most commonly reported symptoms among heart disease patients were angina (84.31%), dizziness (75.16%) and shortness of breath (67.32%) (Table 2) (Figure 3, 4).

Symptom	Frequency (n=153)	Percentage (%)
Angina	129	84.31%
Dizziness	115	75.16%
Shortness of breath	103	67.32%
Nausea	82	53.95%
Tiredness	118	77.12%
Limb coldness	68	44.44%

Table 2: Prevalence of symptoms in heart disease patients.

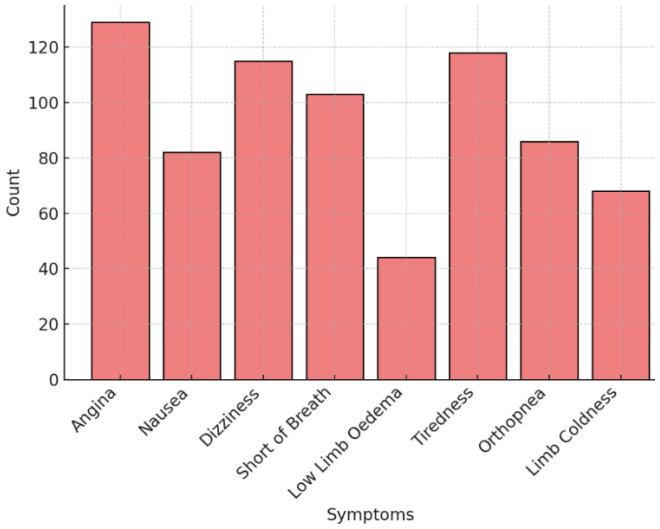

Figure 3: Prevalence of symptoms.

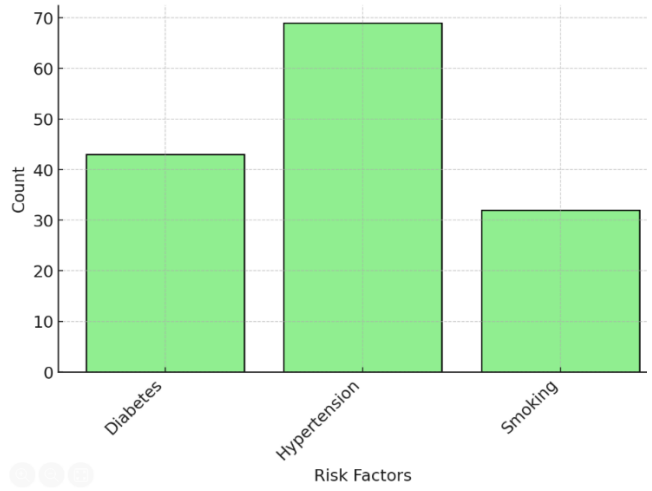

Figure 4: Risk factors in patients.

Correlation between hs-CRP and heart disease

A significant correlation was observed between hs-CRP levels and heart disease ($r = 0.265$, $p < 0.01$), confirming its potential role as a predictive biomarker (Table 3) (Figure 5).

- Heart disease patients had significantly higher hs-CRP levels than healthy controls ($p < 0.001$).
- 69.9% of heart disease patients had elevated hs-CRP levels (>2 mg/L), compared to only 25% of controls.

https://doi.org/10.70844/jmhrp.2025.2.1.37

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Group	Negative hs-CRP (≤2 mg/L)	Positive hs-CRP (>2 mg/L)	Mean hs-CRP (mg/L)	p-value
Heart disease patients (n=153)	46 (30.1%)	107 (69.9%)	48.37 ± 41.61	<0.001*
Controls (n=52)	39 (75.0%)	13 (25.0%)	5.26 ± 3.75	<0.001*
*Significant at $p < 0.05$				

Table 3: hs-CRP levels in cases and controls.

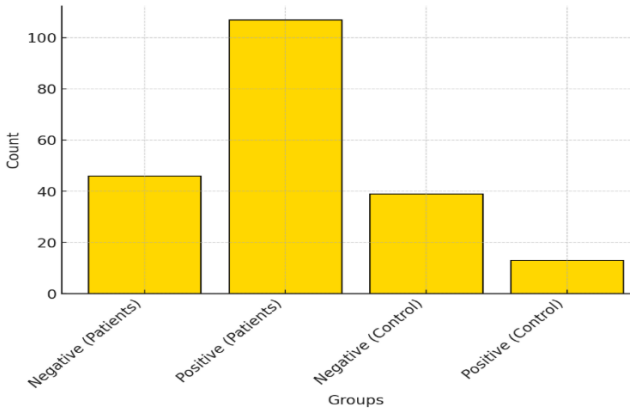

Figure 5: hs-CRP test result.

Discussion

hs-CRP as a biomarkser for heart disease

The findings of this study support the use of hs-CRP as a predictive biomarker for heart disease. Patients with elevated hs-CRP levels were significantly more likely to have heart disease compared to healthy individuals ($p < 0.01$). These results align with previous research:

- José et al. found that hs-CRP levels >3 mg/L were associated with a fourfold increase in cardiovascular risk [18].
- Pooya Koosha et al. demonstrated that hs-CRP predicts cardiovascular events even in patients with normal lipid levels [17].

The JUPITER trial also found that patients with elevated hs-CRP levels benefited from statin therapy, reducing their risk of major cardiovascular events.

Influence of risk factors on hs-CRP levels

Several risk factors were independently associated with higher hs-CRP levels:

- **Smoking:** Smokers had significantly higher hs-CRP levels ($p = 0.002$), consistent with studies by Lei Guo et al. [19].
- **Diabetes and hypertension:** Both conditions were linked to elevated hs-CRP levels ($p < 0.01$), supporting findings from Kramer CK et al. [12].

Gender and age differences

- No statistically significant differences in hs-CRP levels were found between males and females ($p = 0.177$).
- Age did not significantly impact hs-CRP levels, contradicting previous findings by Małgorzata et al. [2].

Key findings

- hs-CRP was significantly higher in heart disease patients than in controls ($p < 0.01$).
- Smoking, diabetes and hypertension were associated with higher hs-CRP levels.
- hs-CRP is a reliable marker for cardiovascular risk assessment [20-29].

Conclusion

This study demonstrates that high-sensitivity C-reactive protein (hs-CRP) is significantly elevated in patients with heart disease compared to healthy controls ($p < 0.01$). The findings suggest that hs-CRP is an independent predictor of cardiovascular disease and can serve as a valuable biomarker for risk assessment.

Key conclusions include:

- Patients with heart disease had significantly higher hs-CRP levels than the control group ($p < 0.001$).
- A moderate positive correlation ($r = 0.265$, $p < 0.01$) was found between hs-CRP levels and heart disease.
- Risk factors such as smoking, diabetes and hypertension were associated with elevated hs-CRP levels, further supporting its role as an inflammatory marker.
- The study findings align with global research demonstrating hs-CRP as a reliable predictor of cardiovascular risk.

While hs-CRP is not a standalone diagnostic tool, its use in combination with CK-MB, Troponin I and echocardiography enhances cardiovascular disease risk assessment.

Recommendations

Based on the study findings, the following recommendations are proposed:

Clinical recommendations

- Routine hs-CRP screening should be considered for individuals at moderate to high risk of heart disease, especially those with existing risk factors such as diabetes, hypertension and smoking.
- hs-CRP testing should be integrated with other diagnostic tools (e.g., Troponin I, CK-MB and ECG) for a comprehensive cardiovascular assessment.
- Physicians should consider anti-inflammatory strategies, such as statin therapy, for patients with persistently elevated hs-CRP levels, as supported by the JUPITER trial.

Research recommendations

- Further studies should explore the long-term predictive value of hs-CRP in cardiovascular disease progression.
- Future research should investigate the economic and lifestyle factors influencing hs-CRP levels in Yemen.
- Larger multicenter studies with a more diverse population should be conducted to confirm the generalizability of these findings.

Public health implications

- Public awareness campaigns should emphasize the role of inflammation in heart disease and promote early detection through hs-CRP screening.
- Preventive measures, such as smoking cessation programs, weight management and blood pressure control, should be prioritized to reduce cardiovascular disease burden.

Acknowledgments

We would like to thank Dr. Abeer Esmail, head of medical laboratory department at Aljazeera University for her help and effort she spent during our study period and her interest for better education and perfect skills associated with our specialist.

Special thanks to Dr. Hamood Almolaiki, Dr. Ahmed Ramadan, Dr. Anas Eiamer, Dr. Mohammed Molhem, Dr. Mohammed Alboni, Dr. Safana Abdullah and for their valuable helps and instructions provided to us during this scientific work.

Competing Interests

The authors report no conflicts of interest in this work.

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