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Diagnostic Utility of Inflammatory and Cardiac Biomarkers (IL-1, IL-6, TNF-α, CRP, ProBNP, BNP) in Obstructive Hypertrophic Cardiomyopathy (OHCM): Study Protocol

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ABSTRACT

Background: Obstructive hypertrophic cardiomyopathy (OHCM) is a genetic cardiac disorder characterized by asymmetric left ventricular hypertrophy and dynamic obstruction of the left ventricular outflow tract. The disease manifests with dyspnea, chest pain, and syncope, but diagnosis can be challenging when imaging findings are equivocal. Biomarkers reflecting myocardial stress, inflammation, and fibrosis may enhance diagnostic accuracy and prognostication.

Objective: This study aims to evaluate the diagnostic utility of inflammatory biomarkers (IL-1, IL-6, TNF-α, CRP) and cardiac biomarkers (BNP, NT-proBNP) in patients with OHCM, and to explore their role in differentiating obstructive from non-obstructive hypertrophic cardiomyopathy.

Material and Methods: This cross-sectional observational study will be conducted in the Department of Biochemistry and Cardiology, Jawaharlal Nehru Medical College, Wardha. Adults aged 18–75 years with confirmed HCM will be recruited and stratified into obstructive and non-obstructive groups, alongside healthy controls. Serum IL-1, IL-6, TNF-α, CRP, BNP, and NT-proBNP levels will be measured and correlated with echocardiographic parameters and clinical severity (NYHA functional class). Exclusion criteria include ischemic heart disease, valvular disease, chronic kidney disease, active inflammatory conditions, or use of biomarker-modifying drugs. Statistical analyses will assess diagnostic accuracy and associations with clinical outcomes.

Expected Result: It is anticipated that OHCM patients will show significantly elevated biomarker levels compared to non-obstructive and control groups. Combined biomarker panels may improve sensitivity and specificity for diagnosing OHCM and provide prognostic insights.

Conclusion: Biochemical markers hold promise as adjunctive tools for early detection, differential diagnosis, and monitoring of therapy response in OHCM, potentially reducing reliance on invasive or costly tests.

KEYWORDS: Obstructive hypertrophic cardiomyopathy, IL-1, IL-6, TNF-α, CRP, BNP and NT-proBNP

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INTRODUCTION

Obstructive hypertrophic cardiomyopathy (OHCM) is a genetic heart condition characterized by abnormal and asymmetrical thickening of the left ventricular (LV) wall. This hypertrophy, particularly in the interventricular septum, can lead to a dynamic obstruction of blood flow from the left ventricle into the aorta during systole, resulting in symptoms such as dyspnea on exertion, chest pain, and syncope. [1]

The utility of biomarkers in OHCM is grounded in their ability to reflect key pathological processes that underpin the disease's clinical expression and progression. The sustained mechanical stress on the hypertrophied and stiff LV myocardium triggers a cascade of cellular and molecular responses, including myocyte stretch, microvascular ischemia, cellular injury, and the activation of fibrotic pathways. The release of specific proteins and peptides into the bloodstream provides a quantifiable measure of these processes. Thus, the analysis of these biomarkers can be useful for early diagnosis of the disease. [2]

IL-1 is a potent regulator of inflammatory signaling and has been implicated in adverse cardiac remodeling, fibrosis, and arrhythmogenesis [3].

IL-6 is one of the most consistently elevated cytokines in HCM, correlating with myocardial fibrosis, hypertrophy severity, and adverse clinical outcomes [4].

TNF-α contributes to myocardial hypertrophy, apoptosis, and interstitial fibrosis, and its expression has been documented in myocardial tissue of obstructive HCM patients [5].

C-reactive protein (CRP) is an acute-phase protein synthesized in the liver in response to interleukin-6 (IL-6) and other pro-inflammatory cytokines. High-sensitivity CRP (hs-CRP) has been extensively studied in atherosclerotic cardiovascular disease as a marker of systemic inflammation and risk predictor [6]. In the context of hypertrophic cardiomyopathy, elevated CRP levels have been associated with myocardial fibrosis, diastolic dysfunction, and worse symptomatic status [7].

Although none of these cytokines is sufficiently specific to serve as a standalone diagnostic marker, their elevation in OHCM reflects underlying disease activity and may complement imaging in identifying patients at higher risk of progression. Investigating IL-1, IL-6, TNF-α, **C-reactive protein,** B-type natriuretic peptide (BNP), N-terminal pro-B-type natriuretic peptide (NT-proBNP) in obstructive cardiomyopathy may therefore provide insights into disease mechanisms and open avenues for biomarker-based diagnosis and therapeutic targeting.

Need for the Study

1. Improve early detection of obstruction, including latent obstruction [8].
2. Assist in distinguishing obstructive vs non-obstructive phenotypes where imaging is equivocal [9].
3. Reduce reliance on more invasive or expensive tests.
4. Potentially help in monitoring response to therapies (which reduce obstruction) via biochemical markers.[10]

RESEARCH QUESTION

Can inflammatory (IL-1, IL-6, TNF-α, CRP) and cardiac (BNP, NT-proBNP) biomarkers be utilized for the diagnosis, risk stratification, and prediction of clinical severity and adverse outcomes in patients with obstructive hypertrophic cardiomyopathy (OHCM) compared with non-obstructive HCM and healthy controls?

AIM AND OBJECTIVES

Aim

To Study the Diagnostic Utility of Inflammatory and Cardiac Biomarkers (IL-1, IL-6, TNF-α, CRP, ProBNP, BNP) in Obstructive Hypertrophic Cardiomyopathy (OHCM)

Objectives

1. To measure and compare serum levels of IL-1, IL-6, TNF-α, CRP, BNP, and NT-proBNP in patients with OHCM, non-obstructive HCM, and healthy controls.
2. To explore whether combining inflammatory markers (IL-1, IL-6, TNF-α, CRP) with cardiac stress markers (BNP, NT-proBNP) improves diagnostic accuracy and risk stratification in OHCM.
3. To assess the relationship between biomarker levels and clinical severity (NYHA functional class, symptom burden).

MATERIAL AND METHODOLOGY

Study Design

Cross-sectional observational study.

Methodology

Place of Study:

The study will be conducted in the Department of Biochemistry along with Cardiology, at Jawaharlal Nehru Medical College, Datta Meghe Institute of Higher Education and Research Sawangi Meghe Wardha.

Study Population: The study will be done among diagnosed OHCM patients (18-75 years) admitted in cardiology department.

Inclusion Criteria:

- Adults aged 18–75 years

- Confirmed diagnosis of OHCM via imaging (LV wall thickness ≥15 mm and LVOT gradient ≥30 mmHg at rest or provocation)
- Confirmed diagnosis of Hypertrophic Cardiomyopathy (HCM) via imaging left ventricular wall thickness ≥15 mm in the absence of other causes of hypertrophy.
- Willingness to provide informed consent

Exclusion criteria:

- History of ischemic heart disease or valvular heart disease
- Chronic kidney disease (eGFR <60 ml/min/1.73 m²)
- Active infection or inflammatory disease
- Use of medications affecting cardiac biomarkers (e.g., statins, corticosteroids)

Statistical Analysis

The collected data will be analyzed using appropriate statistical software. Continuous variables will be expressed as mean ± standard deviation (SD) and compared using Student's *t*-test or ANOVA, while categorical variables will be presented as frequencies/percentages and analyzed using Chi-square test. Correlations between biomarker levels and clinical/echocardiographic parameters will be assessed using Pearson's or Spearman's correlation coefficients. Diagnostic accuracy will be evaluated by receiver operating characteristic (ROC) curve analysis. A *p*-value <0.05 will be considered statistically significant.

Ethical Considerations

Institutional ethics committee approval obtained.

Confidentiality and informed consent maintained.

5. Scope of the Study

Evaluation of Inflammatory Biomarkers

- To assess the levels of IL-1, IL-6, TNF-α, and CRP in patients with OHCM.
- To determine their role as indicators of myocardial inflammation, fibrosis, and systemic inflammatory response.
- To explore their utility in differentiating obstructive HCM from non-obstructive HCM and other causes of ventricular hypertrophy.

Assessment of Cardiac Biomarkers

- To evaluate BNP and NT-proBNP as markers of ventricular wall stress and hemodynamic burden in OHCM.
- To establish correlation between biomarker levels and echocardiographic parameters such as LVOT gradient, diastolic dysfunction, and left atrial size.
- To analyze their role in reflecting **symptom severity and functional status** (NYHA classification).

Comparative and Combined Utility

- To compare the diagnostic performance of inflammatory and cardiac biomarkers individually.
- To investigate whether **combined biomarker panels** improve sensitivity and specificity for diagnosis compared to single markers.

Expected Outcomes:

The present study is expected to demonstrate that biochemical parameters, including inflammatory markers (IL-1, IL-6, TNF-α, CRP) and cardiac biomarkers (BNP, NT-proBNP), have significant diagnostic utility in obstructive hypertrophic cardiomyopathy (OHCM). It is anticipated that these biomarkers will be elevated in patients with OHCM compared to controls and may help in the early detection of obstruction, including latent or subclinical forms where imaging findings are inconclusive. The study is also expected to show that biomarker profiles can aid in differentiating obstructive from non-obstructive HCM.

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