LINKING IMMUNE ACTIVATION TO ACUTE EVENTS IN CHRONIC HEART FAILURE PATIENTS

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Abstract: This study investigates the role of inflammatory cytokines in the acute decompensation of chronic heart failure (CHF). A total of 56 patients were observed over three years at the Bukhara Branch of the Republican Scientific Center for Emergency Medical Care. Cytokine profiling showed significantly elevated levels of TNF-α, IL-6, and IL-1β in acutely decompensated CHF patients compared to stable ones. These levels correlated with worsened clinical status, including higher NYHA class and NT-proBNP. The results suggest that cytokine activation is closely associated with myocardial stress and can serve as a marker for early decompensation. Targeted anti-inflammatory therapies, particularly IL-1 inhibitors, may improve outcomes. Cytokine profiling, therefore, holds promise as both a diagnostic and therapeutic tool in CHF management.

Keywords: cytokines, heart failure, inflammation, IL-6, TNF-α

Introduction

Inflammatory biomarkers play a crucial role in predicting acute decompensation in chronic heart failure (CHF) patients, offering significant implications for personalized treatment strategies. These biomarkers, including high-sensitivity C-reactive protein (hsCRP), soluble ST2 (sST2), galectin-3, interleukin-6 (IL-6), and growth differentiation factor-15 (GDF-15), are associated with the pathogenesis and progression of heart failure (HF) and have been linked to adverse outcomes in both chronic and acute settings[1] [6]. In particular, sST2 and galectin-3 are recommended for clinical use due to their ability to track treatment responses and predict mortality in HF patients[1]. The pan-immune inflammation value (PIV), a composite score based on blood counts, has emerged as a potent predictor of in-hospital mortality in acute heart failure (AHF) patients, outperforming other inflammatory markers[7] [10]. This suggests that PIV could be integrated into clinical models to enhance prognostic accuracy and guide therapeutic decisions. Furthermore, the CRP/albumin ratio has been shown to predict hospitalization risk for HF decompensation, highlighting the potential of inflammatory markers in risk stratification[5]. The integration of these biomarkers into clinical practice could facilitate the development of personalized treatment strategies, allowing for targeted anti-inflammatory therapies that address specific pathophysiological defects in HF patients[2] [3]. Despite the promising role of inflammatory biomarkers, further research is needed to fully understand their causal associations with HF and to optimize their use in routine clinical practice[1] [9]. Overall, the use of inflammatory biomarkers in predicting acute decompensation in CHF patients underscores the potential for personalized treatment approaches that could improve patient outcomes and quality of life.

Relevance of the Topic: Understanding the immune-inflammatory mechanisms involved in acute decompensation of CHF is critical for developing novel biomarkers and anti-inflammatory treatment strategies. Identifying cytokine patterns may offer clinicians predictive tools and therapeutic targets to reduce hospitalizations and improve survival in heart failure patients.

Purpose of the Study: To evaluate laboratory cytokine profiles in patients with CHF during stable and acutely decompensated phases and assess their association with clinical severity and comorbidities.

Materials and Methods: This retrospective cohort study was conducted at the Bukhara Branch of the Republican Scientific Center for Emergency Medical Care over a three-year period (2022–2025). Fifty-six patients with diagnosed CHF were divided into two groups: stable CHF (n=28) and acutely decompensated CHF (ADCHF) (n=28). Laboratory assessment included TNF-α, IL-6, and IL-1β levels measured via ELISA. Clinical data, NYHA class, BNP/NT-proBNP, CRP, and ESR levels were also collected. Statistical analysis was performed using SPSS v25.0, with $p < 0.05$ considered significant.

Results: The ADCHF group showed significantly elevated cytokine levels compared to the stable group. TNF-α was 14.2 ± 4.1 pg/mL in ADCHF vs. 6.5 ± 2.2 pg/mL ($p<0.01$), IL-6 was 12.6 ± 3.7 pg/mL vs. 5.8 ± 2.0 pg/mL ($p<0.01$), and IL-1β was 9.8 ± 2.6 pg/mL vs. 4.2 ± 1.3 pg/mL ($p<0.05$). These increases correlated with elevated NYHA class, NT-proBNP, CRP, and ESR levels.

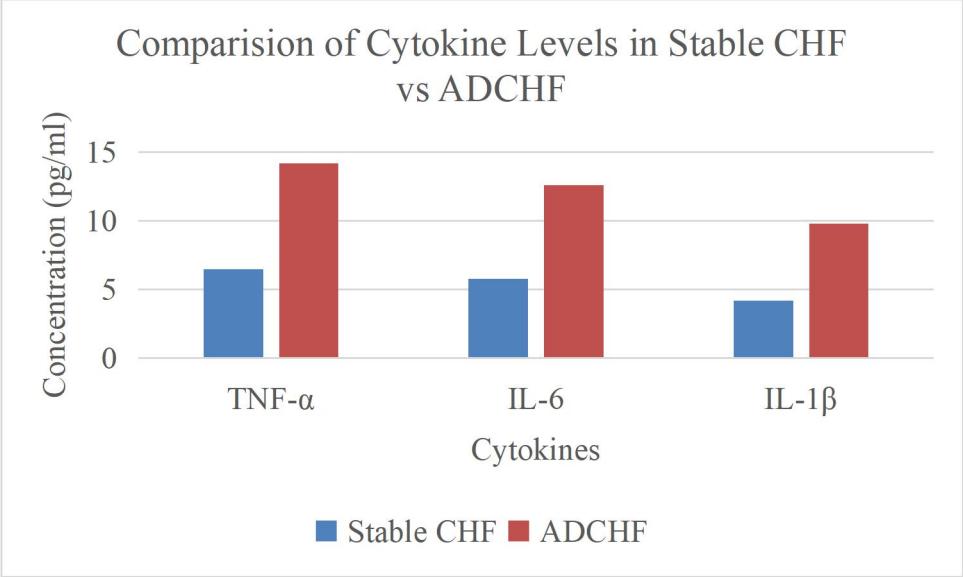

Figure 1. Comparision of cytokine levels in stable CHF vs ADCHF

A positive correlation was observed between IL-6 and NT-proBNP ($r = 0.67$, $p<0.01$), suggesting a link between inflammation and myocardial stress. The most common comorbidities included hypertension (75%), ischemic heart disease (64%), and diabetes mellitus (39%).

Discussion: This study supports current evidence linking cytokine activation to acute heart failure episodes. Elevated TNF-α contributes to cardiomyocyte apoptosis and contractile dysfunction, IL-6 is associated with disease severity and fibrotic remodeling, while IL-1β exacerbates endothelial damage and hypotension [1]. Emerging biomarkers like soluble ST2 (sST2) further enhance risk prediction, and therapies targeting IL-1 show promise in reducing inflammatory burden [2,3]. Our findings

reinforce the value of cytokine profiling for clinical assessment and personalized care in heart failure patients.

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Recent clinical trials support the therapeutic potential of interleukin-1 (IL-1) inhibition in heart failure management. A randomized controlled trial by Van Tassell et al. demonstrated that administration of anakinra—an IL-1 receptor antagonist—reduced systemic inflammation and improved exercise tolerance in patients with acute decompensated heart failure [2]. In another study focused on heart failure with preserved ejection fraction (HFpEF), IL-1 blockade led to a significant reduction in CRP and improved cardiorespiratory fitness, suggesting a direct link between cytokine suppression and myocardial performance [2]. These findings suggest that IL-1 plays a pathogenic role in both systolic and diastolic dysfunction.

Furthermore, sST2, a biomarker of myocardial stress and inflammation, has gained attention as a predictor of outcomes in CHF. sST2 acts as a decoy receptor for IL-33, interrupting its protective signaling and facilitating myocardial fibrosis and remodeling [3]. Studies show that combining sST2 with NT-proBNP enhances prognostic accuracy and improves patient risk stratification beyond traditional markers [3]. Therefore, incorporating inflammatory biomarkers like sST2 alongside cytokine profiling may refine diagnostic and therapeutic strategies in managing acute decompensated CHF.

Conclusion:

Elevated inflammatory cytokines are closely associated with acute decompensation in CHF and reflect both disease severity and inflammatory activity. Cytokine profiling could improve prognostication and guide targeted interventions, offering a potential breakthrough in heart failure management strategies.

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