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RESEARCH ARTICLE

Interleukin-6 Gene Promoter Region Polymorphism in Patients with Dilated Cardiomyopathy: A Prospective Observational Study

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ABSTRACT

Background: Dilated cardiomyopathy (DCM) is characterized by enlargement of the ventricular chambers with reduced myocardial contractility, leading to impaired cardiac performance. Its pathogenesis is multifactorial, involving a complex interplay between genetic susceptibility and inflammatory mechanisms. Interleukin-6 (IL-6), a pro-inflammatory cytokine, plays a key role in myocardial remodeling, and polymorphisms in its promoter region may influence disease susceptibility and severity.

Objective: To examine the relationship between IL-6 promoter gene polymorphism and clinical outcomes among patients with DCM.

Methods: This study was conducted at a tertiary care center inPawapuri, over 10 months (April 2025–January 2026). A total of 110 patients diagnosed with DCM were included. IL-6 promoter polymorphism (−174 G/C) was analyzed using PCR-based techniques. Clinical parameters and outcomes were recorded and statistically analyzed.

Results: The GG genotype was most prevalent (52.7%), followed by GC (34.5%) and CC (12.8%). Patients with the CC genotype showed significantly reduced left ventricular ejection fraction (LVEF) and higher NYHA class. The CC genotype was associated with increased hospitalization and mortality.

Conclusion: IL-6 promoter polymorphism is significantly associated with disease severity and outcomes in DCM patients, suggesting its potential role as a prognostic biomarker.

Keywords: Gene Promoter, Polymorphism, Cardiomyopathy.

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Introduction

Dilated cardiomyopathy (DCM) is characterized by dilation of the ventricular chambers and impaired systolic function in the absence of abnormal loading conditions or coronary artery disease [1]. It represents one of the leading causes of heart failure and accounts for a significant proportion of cardiac transplantation cases worldwide [2]. The etiology of DCM is multifactorial, involving genetic predisposition, viral infections, autoimmune mechanisms, and environmental factors [3].

Recent research has highlighted the role of inflammation in the progression of DCM. Pro-inflammatory cytokines, particularly interleukin-6 (IL-6), are elevated in patients with heart failure and contribute to myocardial remodeling, fibrosis, and contractile dysfunction [4]. IL-6 is a multifunctional cytokine involved in immune regulation, hematopoiesis, and inflammatory responses [5].

Genetic polymorphisms in cytokine genes have been increasingly studied for their role in cardiovascular diseases. The IL-6 gene is located on chromosome 7p21, and variations in its promoter region, especially the −174 G/C polymorphism, influence transcriptional activity and circulating IL-6 levels [6]. Individuals carrying the C allele have been reported to exhibit altered inflammatory responses and disease susceptibility [7].

Several studies have demonstrated an association between IL-6 polymorphisms and cardiovascular conditions such as coronary artery disease, hypertension, and heart failure [8]. Elevated IL-6 levels have been correlated with poor prognosis and increased mortality in heart failure patients [9].

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In DCM, inflammatory activation is considered a key mechanism contributing to disease progression. Increased cytokine levels lead to myocardial damage, ventricular dilation, and impaired cardiac function [10]. Genetic predisposition involving cytokine gene polymorphisms may explain inter-individual variability in disease severity and outcomes [11].

The −174 G/C polymorphism has been widely investigated in different populations, but results have been inconsistent, possibly due to ethnic variations and sample size differences [12]. Understanding the genetic basis of DCM can help identify high-risk individuals and improve personalized treatment strategies [13].

In India, data on IL-6 gene polymorphism in DCM patients are limited. Given the rising burden of cardiovascular diseases, exploring genetic factors associated with disease progression is essential [14].

Therefore, this study aims to evaluate the association between IL-6 promoter region polymorphism and clinical profile and outcomes in patients with dilated cardiomyopathy.

Materials And Methods

Study Setting

Bhagwan Mahavir Institute of Medical Sciences, Pawapuri

Study Duration

April 2025 to January 2026 (10 months).

Sample Size

110 patients.

Inclusion Criteria

- Patients aged ≥18 years
- Diagnosed with dilated cardiomyopathy (echocardiographic criteria)

Exclusion Criteria

- Ischemic heart disease
- Congenital heart disease
- Acute infections or inflammatory disorders

Data Collection

- Demographic data
- Clinical profile (NYHA class, LVEF)
- Laboratory parameters
- Genetic analysis

Statistical Analysis

Data were analyzed using SPSS version XX. Continuous variables were expressed as mean ± SD. Categorical variables were compared using Chi-square test. ANOVA was used for comparing means across genotypes. A p-value <0.05 was considered statistically significant.

Results

A total of 110 patients were included.

Demographic Characteristics

Mean age was 56.2 ± 11.4 years. Males constituted 60% of the population (Table 1).

Genotype Distribution

The GG genotype was most common (52.7%), followed by GC (34.5%) and CC (12.8%) (Table 2, Figure 1).

Association with LVEF

Patients with CC genotype had significantly lower LVEF (32.1 ± 5.4) compared to GG (38.5 ± 6.2) and GC (35.7 ± 5.9) (ANOVA, p = 0.021) (Table 3).

Association with NYHA Class

Higher NYHA class (III/IV) was more common in CC genotype (71.4%) compared to GG (34.5%) and GC (47.3%) (p = 0.034) (Table 4).

Clinical Outcomes

Hospitalization and mortality were significantly higher in CC genotype (Table 5, Figure 2).

Table 1: Demographic Profile

Variable	*Frequency*	*Percentage*
Male	66	60.0
Female	44	40.0

Table 2: IL-6 Genotype Distribution

Genotype	*Frequency*	*Percentage*
GG	58	52.7
GC	38	34.5
CC	14	12.8

Table 3: Genotype vs LVEF

Genotype	*Mean LVEF (%)*
GG	38.5 ± 6.2
GC	35.7 ± 5.9
CC	32.1 ± 5.4

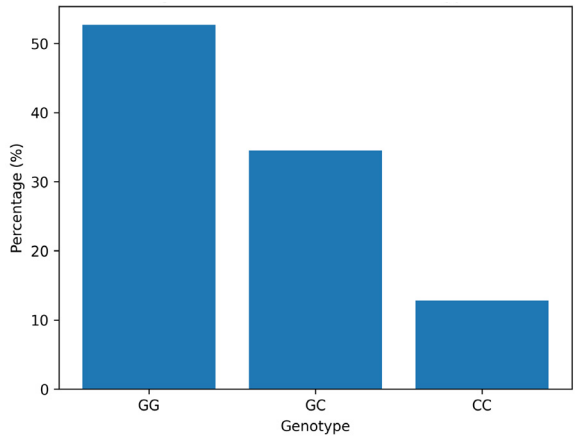

Figure 1: Distribution of IL-6 Genotypes

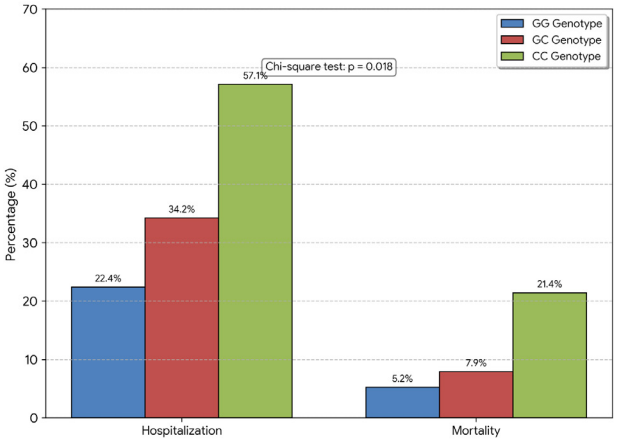

Figure 2: Outcome Distribution by Genotype

Table 4: Genotype vs NYHA Class

Genotype	*NYHA III/IV (%)*
GG	34.5
GC	47.3
CC	71.4

Table 5: Genotype vs Outcomes

Genotype	*Hospitalization (%)*	*Mortality (%)*
GG	22.4	5.2
GC	34.2	7.9
CC	57.1	21.4

Chi-square test: p = 0.018

Discussion

This study evaluated the association between IL-6 promoter polymorphism and clinical outcomes in patients with DCM. The findings suggest a significant relationship between genetic variation and disease severity.

The predominance of the GG genotype observed in this study is consistent with previous reports in various populations [15]. However, the CC genotype, although less frequent, was associated with more severe disease manifestations.

Patients with the CC genotype demonstrated significantly reduced LVEF, indicating worse cardiac function. Similar findings have been reported in earlier studies where IL-6 polymorphism influenced myocardial remodeling and contractility [16].

The association between CC genotype and higher NYHA class further supports the role of IL-6 in disease progression. Elevated cytokine levels are known to contribute to ventricular dysfunction and symptomatic heart failure [17].

Increased hospitalization and mortality among CC genotype patients highlight the prognostic significance of IL-6 polymorphism. Previous studies have shown that higher IL-6 levels are associated with adverse outcomes in heart failure [18].

Inflammation plays a central role in DCM pathogenesis. Cytokines such as IL-6 promote fibrosis, apoptosis, and ventricular dilation, leading to progressive cardiac dysfunction [19]. Genetic variations affecting cytokine expression may therefore influence disease trajectory.

The findings of this study align with global research demonstrating the impact of cytokine gene polymorphisms on cardiovascular diseases [20]. However, ethnic differences in genetic distribution may influence results, emphasizing the need for region-specific studies [21].

In India, limited research has been conducted on genetic factors in DCM. This study contributes valuable data and highlights the importance of incorporating genetic analysis into clinical evaluation [22].

The clinical implications of this study include the potential use of IL-6 polymorphism as a biomarker for risk stratification and personalized management of DCM patients [23].

Conclusion

IL-6 gene promoter polymorphism is significantly associated with clinical severity and outcomes in patients with dilated cardiomyopathy. The CC genotype is linked to poorer cardiac function and increased mortality, indicating its potential role as a prognostic marker.

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