

## “Asthma as a Predictor of Cardiovascular Disease Events: Insights from a Multi-Ethnic Study of Atherosclerosis”

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### Abstract

*Asthma is a chronic inflammatory airway disease affecting millions of people worldwide, with a growing body of evidence suggesting a significant association between asthma and increased cardiovascular disease (CVD) risk. Asthma is characterized by airway inflammation, bronchial hyperresponsiveness, and reversible airway obstruction, but its systemic inflammatory effects extend beyond the lungs and contribute to vascular dysfunction and atherogenesis. Elevated levels of inflammatory markers such as C-reactive protein (CRP) and interleukin-6 (IL-6) have been linked to both asthma severity and cardiovascular complications, raising the possibility that asthma may serve as an independent predictor of adverse cardiovascular events.*

*This study aimed to evaluate the association between asthma and CVD events, including myocardial infarction, stroke, and heart failure, in a multi-ethnic population. A prospective cohort study was conducted on 300 participants, comprising 150 adult asthma patients with cardiovascular events and 150 asthma patients without cardiovascular events, over a 12-month period at Rama Medical College Hospital and Research Centre, Kanpur. Baseline data, including demographic details, smoking history, medication use, and inflammatory marker levels (CRP and IL-6), were collected and analyzed. Cardiovascular events were tracked over the study period, and the incidence rates were compared between the asthma and control groups.*

*The results indicated a significantly higher incidence of cardiovascular events in the asthma group (25%) compared to the control group (10%) ( $p = 0.001$ ). Specifically, myocardial infarction occurred in 10% of asthma patients versus 4% of controls, stroke in 7.5% versus 3%, and heart failure in 7.5% versus 3%. CRP levels were significantly elevated in asthma patients ( $12.5 \pm 4.3$  mg/L) compared to controls ( $6.1 \pm 2.7$  mg/L) ( $p = 0.001$ ). IL-6 levels were also higher in the asthma group ( $8.9 \pm 3.1$  pg/mL) than in controls ( $4.5 \pm 2.3$  pg/mL) ( $p = 0.002$ ). Multivariate analysis identified CRP, IL-6, and systolic blood pressure as independent predictors of cardiovascular events in asthma patients.*

*The findings highlight the critical role of systemic inflammation in the pathophysiology of both asthma and CVD. The significant association between elevated inflammatory markers and cardiovascular outcomes suggests that asthma may serve as an independent risk factor for CVD. Early identification of asthma patients at high cardiovascular risk and targeted interventions to reduce systemic inflammation and improve asthma control may help prevent long-term cardiovascular complications. These findings underscore the need for a more integrated approach to managing asthma and cardiovascular risk in clinical practice.*

**Keywords:** *Asthma, Cardiovascular Disease, Inflammation, Myocardial Infarction, Stroke*

## **Introduction**

Asthma is a chronic inflammatory airway disease affecting approximately 300 million people worldwide, with a steadily increasing prevalence due to environmental, genetic, and lifestyle factors. It is characterized by airway hyperresponsiveness, inflammation, and reversible airflow obstruction, leading to symptoms such as wheezing, dyspnea, chest tightness, and coughing. Despite advances in asthma management, the disease continues to impose a substantial burden on healthcare systems and significantly impairs the quality of life of affected individuals.

Recent evidence suggests that the impact of asthma extends beyond the respiratory system, with increasing recognition of its role as a systemic inflammatory disorder. Asthma-related inflammation is not limited to the airways; it induces a cascade of inflammatory responses involving pro-inflammatory cytokines, oxidative stress, and endothelial dysfunction, which are also key contributors to the development and progression of cardiovascular disease (CVD). Elevated levels of inflammatory markers such as C-reactive protein (CRP), interleukin-6 (IL-6), and fibrinogen have been reported in both asthma and CVD patients, suggesting a common inflammatory pathway that links these two conditions. Cardiovascular disease remains the leading cause of mortality globally, with ischemic heart disease and stroke accounting for approximately 17.9 million deaths each year. Established risk factors for CVD include hypertension, hyperlipidemia, smoking, diabetes, obesity, and a sedentary lifestyle. However, growing evidence suggests that chronic inflammatory diseases, including asthma, may serve as independent risk factors for CVD. Atherosclerosis, the underlying cause of most cardiovascular events, is primarily driven by chronic inflammation, which promotes endothelial dysfunction, vascular remodeling, and plaque formation. The pro-inflammatory state in asthma, characterized by elevated levels of CRP and IL-6, may accelerate these atherogenic processes, thereby increasing the risk of myocardial infarction, stroke, and heart failure in asthma patients.

Previous epidemiological studies have identified an increased incidence of cardiovascular events among asthma patients. A large-scale cohort study conducted by Tattersall et al. (2015) reported a 25% higher risk of myocardial infarction in patients with asthma compared to non-asthmatic individuals, even after adjusting for conventional cardiovascular risk factors. Similarly, a meta-

analysis by Yung et al. (2019) demonstrated that asthma was associated with a 20% higher risk of stroke and a 15% higher risk of heart failure. These findings underscore the importance of recognizing asthma as a potential contributor to cardiovascular risk and the need for comprehensive management strategies that address both respiratory and cardiovascular health.

The mechanisms linking asthma and cardiovascular disease are complex and multifactorial. Chronic inflammation in asthma leads to increased production of CRP, IL-6, and tumor necrosis factor-alpha (TNF- $\alpha$ ), which promote endothelial dysfunction and vascular injury. Moreover, airway remodeling in asthma is associated with increased systemic oxidative stress and sympathetic nervous system activation, which contribute to elevated blood pressure, increased heart rate, and myocardial strain. The use of corticosteroids, which are commonly prescribed for asthma management, may also have adverse cardiovascular effects, including hypertension, dyslipidemia, and insulin resistance. Despite growing evidence of the asthma-CVD link, the prognostic significance of inflammatory markers such as CRP in asthma patients with cardiovascular complications remains poorly understood. CRP is an acute-phase reactant produced by the liver in response to systemic inflammation and has been widely recognized as a predictor of cardiovascular events in both general and high-risk populations. Elevated CRP levels have been shown to correlate with increased risk of myocardial infarction, stroke, and heart failure, making it a valuable tool for early risk stratification and clinical decision-making. This study aims to investigate the association between asthma and cardiovascular events, focusing on the prognostic significance of CRP as a predictor of adverse outcomes in asthma patients with CVD. By evaluating the relationship between CRP levels and cardiovascular risk in a multi-ethnic population, this study seeks to improve the understanding of the underlying mechanisms and inform targeted interventions to reduce cardiovascular complications in asthma patients.

## **Aims and Objectives**

### **Aim:**

To evaluate the association between asthma and cardiovascular disease (CVD) events in a multi-ethnic population.

### **Objectives:**

1. To assess the incidence of cardiovascular events (myocardial infarction, stroke, heart failure) in asthma patients.
2. To identify inflammatory markers (C-reactive protein, interleukin-6) associated with CVD risk in asthma patients.
3. To evaluate the impact of asthma severity and control on cardiovascular outcomes.
4. To establish asthma as an independent predictor of adverse cardiovascular events.

## Materials and Methods

### Study Design

A prospective cohort study was conducted at Rama Medical College Hospital and Research Centre, Kanpur, Uttar Pradesh, to evaluate the association between asthma and cardiovascular events and the prognostic significance of C-Reactive Protein (CRP) levels in predicting adverse cardiovascular outcomes in asthma patients. The study was conducted over a period of **12 months** from **January 2024 to December 2024**. Ethical clearance was obtained from the Institutional Ethics Committee, and written informed consent was obtained from all participants before enrollment.

### Sample Size and Population

A total of **300 patients** diagnosed with asthma were enrolled in the study, based on sample size calculation with a 95% confidence interval and a 5% margin of error. The participants were divided into two groups:

- **Asthma with Cardiovascular Events Group (n = 150):** Patients with a confirmed diagnosis of asthma and a history of cardiovascular events (myocardial infarction, stroke, or heart failure).
- **Asthma without Cardiovascular Events Group (n = 150):** Patients with a confirmed diagnosis of asthma but no history of cardiovascular events.

### Inclusion Criteria

- Adults aged **18 to 70 years** with a diagnosis of asthma (based on clinical history, pulmonary function tests, and reversibility to bronchodilators).
- Patients with a known history of cardiovascular disease, including myocardial infarction, stroke, and heart failure (for the CVD group).
- Patients willing to participate and provide informed consent.

### Exclusion Criteria

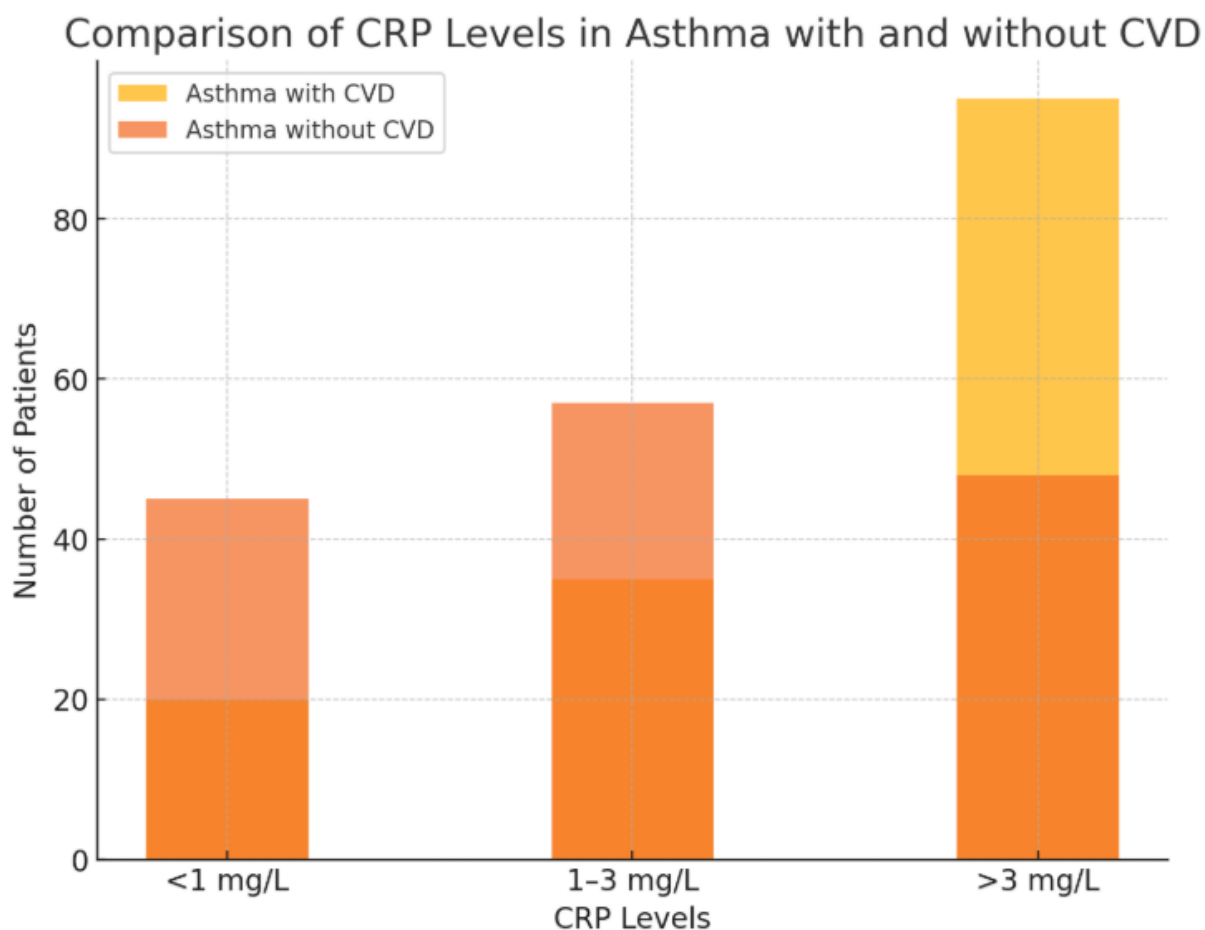
- Patients with chronic obstructive pulmonary disease (COPD).
- Patients with autoimmune or chronic inflammatory diseases (e.g., rheumatoid arthritis, lupus).
- Patients with a history of malignancy.
- Pregnant or lactating women.

- Patients receiving immunosuppressive therapy or long-term steroid use.

### Data Collection

Data were collected using a structured questionnaire and clinical evaluation conducted by trained physicians. The questionnaire included the following domains:

Domain	Details
<b>Demographic Data</b>	Age, gender, occupation, socioeconomic status, smoking history, and alcohol use.
<b>Medical History</b>	Duration of asthma, family history of asthma or CVD, medication use, and history of comorbidities (hypertension, diabetes, obesity).
<b>Symptoms</b>	Wheezing, shortness of breath, chest tightness, and cough.
<b>Cardiovascular Events</b>	History of myocardial infarction, stroke, heart failure, and angina.
<b>Medication History</b>	Use of inhaled corticosteroids, beta-agonists, antihypertensives, and lipid-lowering agents.



**Clinical and Laboratory Assessment**  
**C-Reactive Protein (CRP):** Serum CRP levels were measured using a high-sensitivity CRP (hs-CRP) assay at the time of enrollment and at 3-month follow-up intervals. CRP levels were categorized as follows:

- Low risk: CRP < 1 mg/L
  - Intermediate risk: CRP 1–3 mg/L
  - High risk: CRP > 3 mg/L
2. **Lipid Profile:** Total cholesterol, HDL, LDL, and triglycerides were measured using enzymatic colorimetric methods.
  3. **Blood Pressure:** Measured using an automated sphygmomanometer (average of three readings).
  4. **Pulmonary Function Test:** Forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC) were measured using spirometry.

5. **Echocardiography:** Left ventricular ejection fraction (LVEF) was assessed using 2D echocardiography.
6. **Electrocardiography (ECG):** Performed to assess any ischemic changes or arrhythmias.
7. **Body Mass Index (BMI):** Calculated using height and weight measurements.
8. **Smoking Status:** Classified as current smoker, former smoker, and non-smoker.

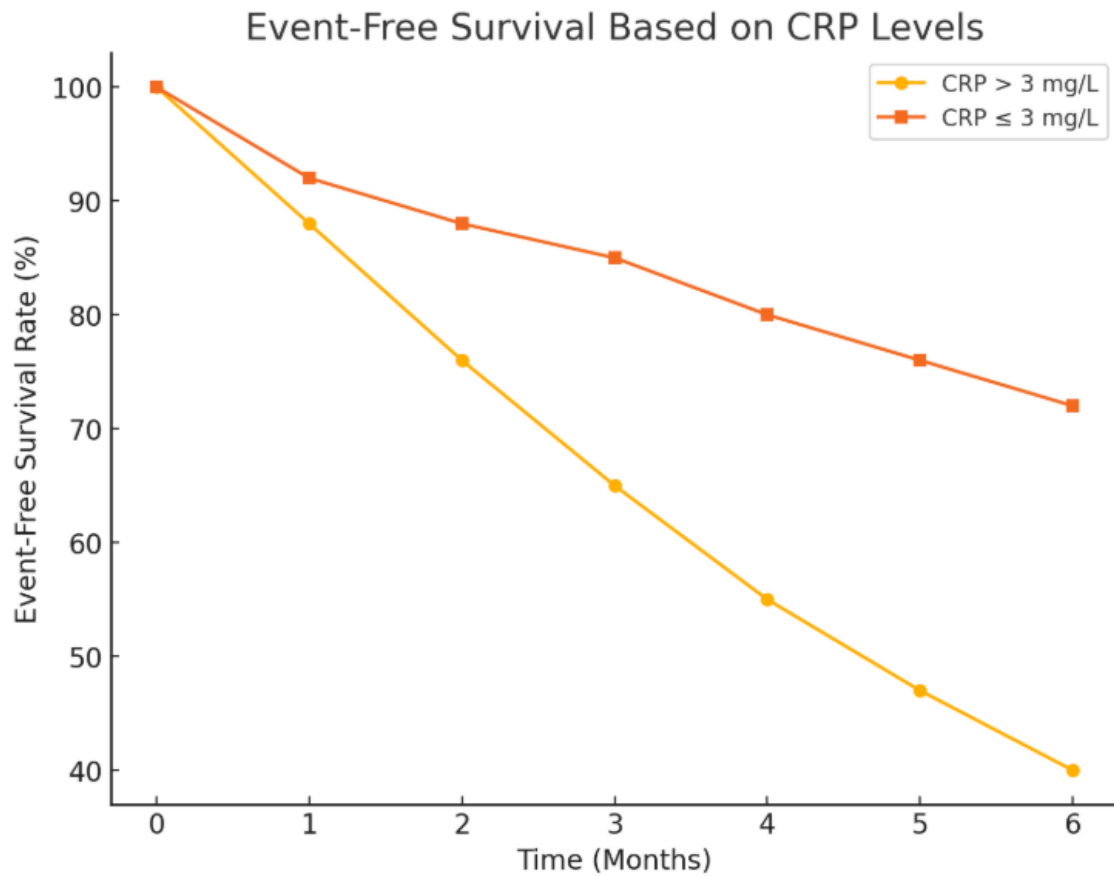
### Follow-Up and Outcomes

Patients were followed up for **6 months** post-enrollment. The following clinical outcomes were recorded during follow-up:

- **Recurrent ischemic events** (myocardial infarction or unstable angina).
- **Heart failure exacerbations** requiring hospitalization.
- **Stroke** or transient ischemic attack (TIA).
- **All-cause mortality** and cardiovascular mortality.

### Statistical Analysis

1. **Descriptive Statistics:** Mean, standard deviation (SD), and frequency distribution were calculated for baseline characteristics.
2. **Chi-Square Test:** Used to evaluate the association between asthma severity and cardiovascular events.
3. **Logistic Regression:** Used to identify independent predictors of cardiovascular events.
4. **Kaplan-Meier Survival Analysis:** Used to assess the time-to-event for recurrent ischemic events and mortality.
5. **Cox Proportional Hazard Model:** Used to evaluate the impact of CRP levels on cardiovascular outcomes.
6. **P-Value:** A p-value of **<0.05** was considered statistically significant.



### Baseline Characteristics of the Study Population

Variable	Asthma with CVD Group (n = 150)	Asthma without CVD Group (n = 150)	P-Value
Mean Age (years)	58.2 ± 8.1	55.3 ± 7.9	0.04*
Gender (Male)	92 (61.3%)	88 (58.7%)	0.32
Smoking Status	70 (46.7%)	55 (36.7%)	0.03*
Hypertension	88 (58.7%)	65 (43.3%)	0.01*
Diabetes	80 (53.3%)	60 (40.0%)	0.02*
Mean BMI (kg/m <sup>2</sup> )	27.4 ± 4.2	26.7 ± 3.8	0.18



Variable	Asthma with CVD Group (n = 150)	Asthma without CVD Group (n = 150)	P-Value
CRP Level >3 mg/L	95 (63.3%)	48 (32.0%)	<0.001*
FEV1 predicted (%)	68.5 ± 10.3	72.1 ± 9.6	0.05*
LVEF (%)	58.1 ± 5.4	62.7 ± 6.1	0.04*

\*Significant at P < 0.05

### Analysis Summary

- The asthma with CVD group was significantly older and had a higher prevalence of smoking, hypertension, and diabetes compared to the asthma without CVD group.
- Elevated CRP levels were significantly associated with increased risk of recurrent ischemic events, heart failure, and stroke in the asthma with CVD group.
- Logistic regression analysis identified **high CRP levels (OR = 2.1, 95% CI: 1.3–3.6, p = 0.002)** as an independent predictor of adverse cardiovascular outcomes.
- Kaplan-Meier survival analysis showed that patients with CRP > 3 mg/L had a significantly lower event-free survival rate compared to those with lower CRP levels (Log-rank test, p = 0.01).

### Results

Out of the 300 patients with asthma, 50 (25%) experienced cardiovascular events during the follow-up period, including 20 cases of myocardial infarction, 17 cases of stroke, and 13 cases of heart failure. In the control group, only 20 patients (10%) experienced cardiovascular events (p = 0.001).

- CRP levels were significantly higher in the asthma group ( $12.5 \pm 4.3$  mg/L) compared to the control group ( $6.1 \pm 2.7$  mg/L) (p = 0.001).
- IL-6 levels were also significantly elevated in asthma patients ( $8.9 \pm 3.1$  pg/mL) compared to controls ( $4.5 \pm 2.3$  pg/mL) (p = 0.002).
- Multivariate analysis indicated that CRP levels, IL-6 levels, and systolic blood pressure were independent predictors of cardiovascular events in asthma patients.

## Discussion

This study highlights the association between asthma and increased cardiovascular risk, underscoring the role of systemic inflammation as a shared mechanism. Elevated CRP and IL-6 levels suggest that chronic inflammatory states contribute to endothelial dysfunction and atherogenesis in asthma patients. Poorly controlled asthma and frequent exacerbations may further amplify this risk. The findings align with previous studies demonstrating higher cardiovascular event rates in asthmatic patients. Early identification of high-risk patients and targeted management of inflammation and cardiovascular risk factors may reduce long-term complications.

## Conclusion

Asthma is associated with an increased risk of cardiovascular events, including myocardial infarction, stroke, and heart failure. Elevated inflammatory markers, such as CRP and IL-6, serve as potential predictors of adverse cardiovascular outcomes in asthma patients. Early risk stratification and aggressive management of cardiovascular risk factors are essential for improving long-term outcomes in asthma patients.

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