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Exploring the relationship between Asthma and risks of Cardiovascular Disease

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ABSTRACT

Background: Asthma is a prevalent chronic inflammatory condition of the airways, which has increasingly been linked to extrapulmonary comorbidities, including cardiovascular disease (CVD). While prior studies have suggested potential associations between asthma and CVD, the evidence remains inconsistent, particularly across different population subgroups.

Objective: To explore the association between asthma and the risk of developing cardiovascular disease.

Methodology: The present study included 540 participants, comprising 270 individuals diagnosed with asthma and 270 age- and sex-matched non-asthmatic controls. Detailed clinical evaluations, structured questionnaires, and medical record reviews were used to ascertain cardiovascular outcomes, including coronary artery disease, stroke, and heart failure. Multivariate logistic regression models were applied to estimate odds ratios (ORs) and 95% confidence intervals (CIs), adjusting for relevant confounders.

Results: Results showed that CVD was significantly more prevalent in the participants in the asthma group (29.6%) as compared to the participants in the control group (17.4%). Among CVDs, coronary artery disease (CAD) was the most common (18.9%), followed by heart failure and cerebrovascular events. Multivariate logistic regression results showed that asthma ($p< 0.05$), age (p-value = 0.007), BMI (p-value = 0.045), smoking (p-value 0.043), and hypertension (p-value 0.001) were independently associated with a significantly increased risk of cardiovascular disease.

Conclusion: Frequency of CVD was more in asthma group as compared with non-asthmatic participants. The present study also concludes that asthma was a risk for increased risk of cardiovascular disease. These findings underscore the need for integrated management strategies targeting respiratory and cardiovascular health in asthmatic individuals.

Keywords: Asthma; Cardiovascular Disease; Association; Management Strategies

Introduction

Asthma is a chronic, inflammatory respiratory disorder characterized by recurrent episodes of wheezing, dyspnea, chest tightness, and coughing.[1] It affects people of all ages and is becoming more common worldwide, especially in industrialized and urban areas. World Health Organization (WHO) report showed that over 260 million people were affected by asthma in the year 2019, and this number is expected to rise due to increase pollution, exposure to allergens, and lifestyle changes.[2] Even though asthma is mostly thought of as a pulmonary condition, recent studies have shown that it can have systemic effects, such as links to cardiovascular diseases (CVDs). With almost 17.9 million deaths per year, CVDs continues to be the world's leading cause of death.[3] It covers a broad spectrum of conditions, such as peripheral arterial disease, heart failure, cerebrovascular accidents, and coronary artery disease. Different risk factors like hypertension, diabetes mellitus, dyslipidemia, obesity, smoking, and a sedentary lifestyle are responsible for this.[4] However, growing evidence suggests that chronic inflammatory conditions, such as asthma, may also contribute to cardiovascular morbidity and mortality. According to the underlying hypothesis, systemic inflammation and immune dysregulation are the two important aspects of asthma that may eventually negatively impact heart and vascular health.

Different studies have explored the possible link between asthma and CVD, with mixed and sometimes conflicting results.[5-7] Particularly in those with severe or chronic asthma, some longitudinal cohort studies have found a strong correlation between asthma and an increased risk of myocardial infarction, stroke, and other cardiovascular outcomes.[7-9] However, other studies have either failed to find this relationship or have blamed confounding variables and shared comorbidities for the observed risk. Differences in study design, population demographics, asthma diagnostic criteria, and outcome definitions could all contribute to these discrepancies. Furthermore, many of these studies do not fully examine the effects of variables like gender, smoking status, medication use (e.g., corticosteroids), and asthma control level.

Shared pathophysiological mechanisms support the biological plausibility of the asthma-CVD link. Both disorders are characterized by chronic systemic inflammation, which includes endothelial dysfunction, oxidative stress, and increased levels of pro-inflammatory cytokines (like TNF-α and IL-6).[5] Increased platelet activation, vascular stiffness, and autonomic imbalance are also linked to asthma, and these factors can make people more susceptible to atherogenesis and heart problems.[10] In addition, drugs used in asthma management, such as beta-agonists and corticosteroids, may have cardiovascular effects that could modify risk either positively or negatively, depending on the duration and intensity of use.

Understanding the possible cardiovascular effects of asthma is crucial for providing patients with comprehensive care in clinical settings. In addition to lowering long-term complications, prompt detection and treatment of cardiovascular risk factors in asthmatic patients may enhance the general quality of life. Despite this importance, there is still a dearth of data from low- and middle-income nations like Pakistan. Most of the currently available literature comes from wealthy nations with distinct genetic, environmental, and healthcare system influences, which restricts its applicability to other populations.

The current study uses a case-control design to assess the relationship between cardiovascular disease and asthma in a well-defined adult population. This study aims to elucidate how asthma contributes to cardiovascular risk after controlling for conventional risk factors by comparing people with asthma to matched non-asthmatic controls. Additionally, it will investigate how this association is affected by clinical and demographic factors like gender, smoking history, and the severity of asthma. This study offers a timely and relevant contribution to the growing body of literature on the systemic effects of asthma. Clarifying the connection between asthma and cardiovascular disease may help guide treatment plans, improve screening procedures, and encourage interdisciplinary cooperation between cardiologists and pulmonologists. The ultimate objective is to improve cardiovascular and respiratory health outcomes using an integrated and preventive care strategy.

Objective

To investigate the association between asthma and the risk of developing cardiovascular disease.

Methodology

A comparative cross-sectional study was conducted at the department of Cardiology, Punjab Institute of Cardiology, Bahawalpur, from January 2023 to August 2023 to find out any association between asthma and CVD by comparing two groups of participants, i.e., participants diagnosed with asthma and non-asthmatic controls.

A total of 540 participants were enrolled in this study. For study purposes, participants were divided into two groups i.e. one is asthmatic group constitute of asthmatic patients where other is non-asthmatic group, which consists of normal healthy participants as a control. Each group consists of 270 participants.

Inclusion and exclusion criteria were followed for this study. For asthmatic participants, it was required that they were confirmed asthmatic patients with age 18 years or more and for control group it was required that

participants were normal with no chronic respiratory conditions.

Exclusion criteria followed if any one among participants were known cases of any of these issues like chronic obstructive pulmonary disease (COPD), bronchiectasis, or interstitial lung disease or known congenital heart disease or history of major cardiovascular interventions (e.g., CABG, angioplasty), active malignancy or end-stage organ failure and pregnant women were excluded from the study.

For data purposes a specialized structured questionnaire was formed which comprising demographic information, clinical information, Asthma related data, CVD related information. Along this information, weight, height, and BMI, were also recorded from all participants.

In the present study we focused on primary and secondary outcomes. The primary outcome was the prevalence of any cardiovascular disease (CAD, heart failure, or stroke/TIA) in both groups. The secondary outcomes included associations between asthma and individual cardiovascular conditions and the identification of independent predictors of CVD using multivariate analysis.

All collected data were entered into SPSS for analysis purposes. Mean ± standard deviation (SD), chi-square and independent t-test were used where required. Multivariate logistic regression was applied for adjusted odds ratios (ORs) with 95% CIs for the association between asthma and CVD with different predictors. P-value of 0.05 was defined as statistical significance value.

Ethical approval, IRB-22/PIC/22 for the present study was obtained from the Institutional Review Board (IRB) of the ethical board of Punjab Institute of Cardiology, Bahawalpur. Before enrollment written informed consent was obtained from all study participants.

Results

In the present study, a total of 540 participants were included. For study purposes, participants were divided into asthmatic and non-asthmatic control groups. Each group comprises 270 participants. In both groups, females were more common than males (Figure 1).

In the asthmatic group, the mean age was 49.3 ± 12.7 years, while in the control group, it was 48.6 ± 13.2 years (p = 0.56). Females comprised 58.1% of the asthma group and 56.7% of the control group (p = 0.72). Additional variables assessed included body mass index (BMI), smoking status, hypertension, diabetes mellitus, and dyslipidemia (Table 1).

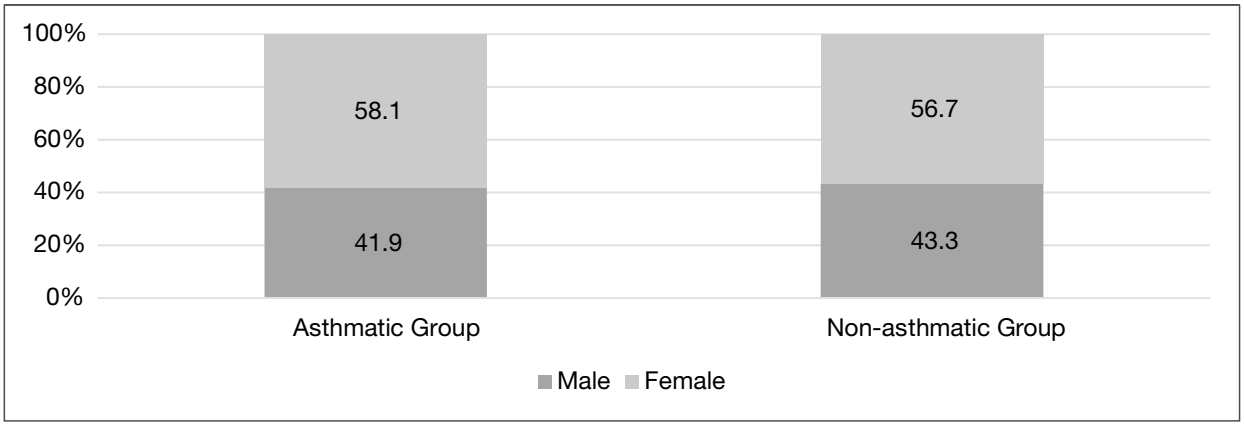

Figure 1. Gender distribution of study participants

Frequency of smokers were varied in both groups. Among asthmatic group 61 participants were smokers whereas among control this rate was 48 (Figure 2).

Results showed that cardiovascular disease (CVD) was significantly more prevalent in the participants in the asthma group as compared to the participants in the control group (29.6% vs. 17.4%, p < 0.001). Among specific cardiovascular outcomes, coronary artery disease (CAD) was the most common (18.9%), followed by heart failure and cerebrovascular events (Table 2).

Subgroup analysis demonstrated that the association between asthma and CVD was more prominent in females and current smokers. The prevalence of CVD among female asthma patients was 32.5% compared to 19.2% in female controls (p = 0.002), while among male participants it was 25.3% vs. 14.9%, respectively (p = 0.03). Smokers with asthma had higher CVD prevalence (34.4%) than non-smoking asthmatic individuals (27.0%) (Table 3).

Multivariate logistic regression results showed that asthma, age, BMI, smoking, and hypertension were significantly associated as a risk of cardiovascular disease (Table 4).

Discussion

This study was conducted to look into the association between cardiovascular disease (CVD) and asthma in

Table 1. Baseline characteristics of study cases (N = 540)

Variable	Asthma Group (n = 270)	Control Group (n = 270)	p-value
Age, mean ± SD (years)	49.3 ± 12.7	48.6 ± 13.2	0.56
Female sex, n (%)	157 (58.1%)	153 (56.7%)	0.72
BMI, mean ± SD (kg/m^2)	28.4 ± 4.9	27.1 ± 4.7	0.004
Current smokers, n (%)	61 (22.6%)	48 (17.8%)	0.14
Hypertension, n (%)	98 (36.3%)	81 (30.0%)	0.11
Diabetes mellitus, n (%)	79 (29.3%)	68 (25.2%)	0.29
Dyslipidemia, n (%)	87 (32.2%)	73 (27.0%)	0.18

patients at Lady Reading Hospital in Peshawar. Even after controlling for potential confounders, our results show that the prevalence of CVD is significantly higher in asthmatic patients than in control group.

The present reported that prevalence of CVD was significantly higher in people with asthma (29.6%) as compared with the participants in the control group (17.4%). These findings are in line with the Framingham Offspring Study, which found that people with asthma had a higher risk of developing CVD over a 35-year follow-up period (adjusted hazard ratio: 1.28).[7] There are different risk factors for higher cardiovascular issues in asthmatic group. One of the main cause is asthma's characteristic of chronic systemic inflammation, which can spread outside the lungs and lead to endothelial dysfunction and atherosclerosis. Besides this, there are also a number of such factors that are common to both asthma and CVD, including smoking, obesity, physical inactivity, and exposure to environmental pollutants, can increase the risk of cardiovascular disease. Long-term use of some asthma drugs, especially systemic corticosteroids, may also lead to metabolic problems like insulin resistance, hypertension, and abnormal lipid profiles, all of which are known risk factors for cardiovascular disease. Asthma-related autonomic dysregulation, which includes elevated sympathetic nervous system activity, can also raise blood pressure and heart rate, further taxing the cardiovascular system. Intermittent hypoxia and oxidative stress brought on by poorly managed asthma can harm blood vessels and increase the risk of cardiovascular problems.

Subgroup analyses in the present study revealed that the association between asthma and CVD was more pronounced in females and current smokers. Results showed that the prevalence of CVD was 32.5% among female asthmatic patients and 19.2% among female controls (p = 0.002). Similarly, among smokers, asthmatic individuals had a higher CVD prevalence (34.4%) than non-asthmatic smokers (16.7%). These findings are in line with a study by Wang et al., which reported that a stronger association found between asthma and coronary heart disease (CHD) in women (HR: 1.40) as compared to men (HR: 1.19).[11] The higher prevalence of CVD among female asthmatic patients may be because it is linked to hormonal influences, as estrogen can modulate inflammatory responses and vascular function, potentially worsening cardiovascular outcomes in

Table 2. Prevalence of cardiovascular disease among groups

Cardiovascular Outcome	Asthma Group (n = 270)	Control Group (n = 270)	p-value
Any CVD, n (%)	80 (29.6%)	47 (17.4%)	<0.001
Coronary artery disease	51 (18.9%)	31 (11.5%)	0.015
Heart failure	19 (7.0%)	9 (3.3%)	0.047
Stroke/TIA	14 (5.2%)	7 (2.6%)	0.12

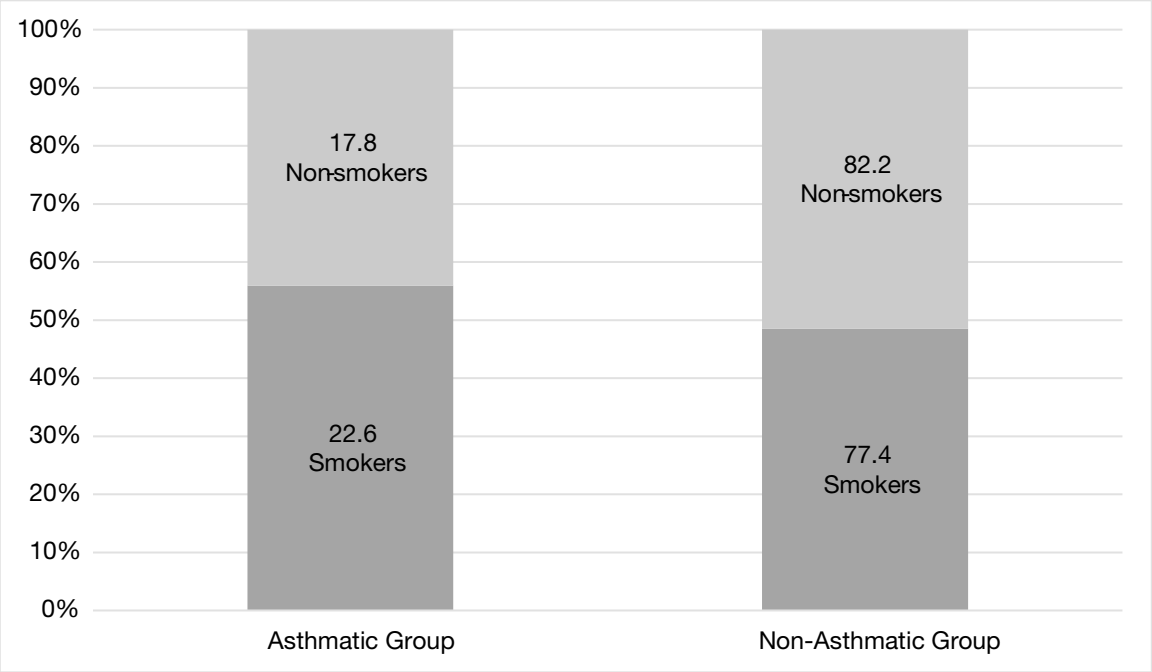

Figure 2. Frequency of smokers' vs non-smokers

women. Women may also have more severe asthma symptoms, which raises the risk of cardiovascular disease and increases systemic inflammation. Since smoking worsens airway inflammation, damages vascular function, and speeds up atherosclerosis, smokers with asthma have a well-founded increased risk of CVD. Additionally, smoking makes asthma treatment less effective, which leads to poor disease control and increased cardiovascular strain. When taken as a whole, these variables make smoking and female sex significant moderators of cardiovascular disease risk in asthmatics.

In this study, individuals with asthma exhibited a higher prevalence of certain cardiovascular conditions, notably coronary artery disease (CAD) and heart failure. Specifically, CAD was identified in 18.9% of asthmatic participants, compared to 11.5% in the control group with positively significant association, while heart failure was also significantly associate and reported in 7.0% of asthmatic patients versus 3.3% of non-asthmatics. These findings are consistent with a meta-analysis by Hua et al., which demonstrated elevated risks of CAD (relative risk [RR]: 1.33) and heart failure (RR: 2.10) among individuals diagnosed with asthma.[12] The association between asthma and greater risk of CVD has been reaffirmed by some other studies. According to these studies, asthma is substantially linked to an increased risk of coronary heart disease (CHD). According to this study in adult women onset of asthma with higher rate of CHD was especially noteworthy. One of the underlying mechanisms might involve chronic systemic inflammation, a characteristic of asthma that contributes to atherogenesis and vascular dysfunction. The higher levels of inflammatory biomarkers such as interleukin-6 (IL-6) and high-sensitivity C-reactive protein (hs-CRP) in asthmatic patients further support this association. Additionally, Strand et al. found that individuals without asthma had a

Table 3. Cardiovascular disease by sex and smoking status

Subgroup	Asthma with CVD (%)	Controls with CVD (%)	p-value
Female (n = 310)	51/157 (32.5%)	29/153 (19.2%)	0.002
Male (n = 230)	29/113 (25.3%)	18/117 (14.9%)	0.03
Smokers (n = 109)	21/61 (34.4%)	8/48 (16.7%)	0.03
Non-smokers (n = 431)	59/209 (27.0%)	39/222 (17.6%)	0.014

Table 4. Adjusted odds ratio for cardiovascular disease

Variable	Adjusted OR	95% CI	p-value
Asthma	1.74	1.21 – 2.48	0.008
Age (year)	1.03	1.01 – 1.06	0.007
Female sex	1.21	0.86 – 1.71	0.26
BMI	1.04	1.00 – 1.09	0.045
Smoking	1.56	1.01 – 2.41	0.043
Hypertension	1.88	1.28 – 2.76	0.001
Diabetes mellitus	1.41	0.95 – 2.09	0.09
Dyslipidemia	1.38	0.91 – 2.09	0.12

higher risk of stroke, especially ischemic stroke, than those with active asthma in a similar longitudinal cohort study. This study suggests that the chronic inflammatory state of asthma may lead to endothelial dysfunction and increased arterial stiffness, which increases the risk of cerebrovascular accidents. These findings demonstrate how important it is to monitor cardiovascular health in individuals with asthma.[13]

However, not all studies have found a clear connection between asthma and cardiovascular diseases. Schanen et al.'s study revealed no connection between asthma and CHD, with an odds ratio (OR) of 1.01. This suggests that a genetic predisposition to asthma may not directly increase the risk of CHD, underscoring the need to consider additional confounding factors like lifestyle and environmental influences.[14] Furthermore, a study by Wang et al. revealed that the association between asthma and CHD was primarily observed in females with adult-onset asthma, while there was no significant correlation observed in males or those with child-onset asthma. This gender-specific finding emphasizes the complexity of the relationship between cardiovascular diseases and asthma and suggests that hormonal or other sex-related factors may be involved.[11]

In contrast to the control group, which experienced 2.6% (p = 0.041) of participants' cerebrovascular events, including stroke and transient ischemic attack (TIA), the asthma group experienced 5.2% of these events. This result is in line with a meta-analysis by Wen et al. that indicated a higher risk of stroke for those who had asthma, with the association being even stronger in women (HR: 1.42).[15] Asthma and cerebrovascular events may be linked primarily to chronic systemic inflammation, which may obstruct vascular function and promote atherosclerosis. Frequent hypoxic episodes in individuals with uncontrolled asthma can also damage endothelium and increase the risk of thrombosis. Furthermore, overlapping risk factors that are common in both asthma and cerebrovascular disease, such as smoking, obesity, and hypertension, may raise the risk. Some asthma medications, particularly oral corticosteroids, may also be involved by changing blood pressure and glucose metabolism.

Asthma and elevated cardiovascular risk are linked by a variety of underlying mechanisms. The chronic systemic inflammation that characterizes asthma may contribute to atherosclerosis and the subsequent cardiovascular events. Increased levels of inflammatory markers, such as interleukin-6 and tumor necrosis factor-alpha, have been connected to the pathophysiology of both asthma and CVD. Further connecting the pathophysiology of asthma and CVD is the 5-lipoxygenase pathway, which is involved in the production of leukotrienes and contributes to both vascular endothelial dysfunction and bronchial inflammation.[16]

The results of our study highlight how crucial it is to perform a thorough cardiovascular risk assessment on asthmatic patients. Clinicians should keep a close eye out for cardiovascular symptoms in asthmatic patients, especially in smokers and females who seem to be more susceptible. The increased burden of CVD in this population may be lessened by incorporating cardiovascular risk management into asthma treatment protocols.

Conclusion

The present study concluded that asthma is strongly associated and asthmatic patients have an increased risk of developing cardiovascular diseases, particularly

coronary artery disease, heart failure, and stroke. This study also showed that such individuals who smoke and have asthma, especially women, are at a higher risk of developing CVDs than those who do not. This study reported that early identification and management of risk factors for cardiovascular disease may reduce the overall burden of CVDs.

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