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Evaluating the Bidirectional Association Between Allergic Rhinitis and Bronchial Asthma

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ABSTRACT

Background: Allergic rhinitis (AR) and bronchial asthma (BA) are chronic inflammatory airway diseases that frequently coexist, reflecting the "united airway" concept. Patients with AR are at increased risk of developing asthma, while a significant proportion of asthmatics also suffer from AR. Understanding this bidirectional association is crucial for early diagnosis and integrated management.

Objective: To know association between allergic rhinitis (AR) and bronchial asthma (BA) by determining the incidence of BA in patients of AR and the incidence of AR in patients of BA.

Methodology: A cross-sectional observational study conducted in a tertiary care hospital over a period of twelve months enrolled a total of 240 patients, including 120 patients with clinically diagnosed AR and 120 with BA. The diagnosis of AR was made according to the ARIA guidelines, and asthma was diagnosed using the GINA criteria using a clinical assessment and spirometry. A detailed history, clinical examination, use of nasal endoscopy, an absolute eosinophil count, serum IgE, and spirometry were done. The incidence of BA in patients with AR and AR in patients with BA was ascertained. Factors triggering the disease and temporal sequence of the onset were also studied.

Results: Among 120 AR patients, 59.2% had coexisting asthma, while 76.7% of asthmatics had AR. In AR patients who developed asthma, the mean interval between disease onsets was 2.9 years, with AR preceding asthma in most cases. Dust (85.0%) and pollen (31.7%) were significantly more frequent triggers in AR compared to BA (65.0% and 13.3%; $p<0.01$).

Conclusion: This study confirms a strong bidirectional association between AR and BA, with AR often preceding asthma. Routine screening and integrated management of both conditions are recommended.

Keywords: Allergic Rhinitis; Bronchial Asthma; Bidirectional Association; Airway Disease

Introduction

Allergic rhinitis (AR) and bronchial asthma (BA) are diseases very closely related to each other in the respiratory tract and frequently occur together. AR implies an IgE-mediated inflammatory condition of the nasal mucosa due to airborne allergens, which cause symptoms like sneezing, rhinorrhea, nasal congestion, and itching. Bronchial asthma describes an inflammation of the lower airway associated with hyperresponsiveness and variable airflow obstruction that presents as wheezing, shortness of breath, chest tightness, and cough. The "united airway" concept states that the upper and lower respiratory tracts form one continuous airway system, with shared pathophysiological mechanisms, Type-2 immune responses, eosinophilic inflammation, and common triggers.[1,2]

There is much epidemiological significance for AR and asthma with some of the burden being global. One of the largest meta-analyses of cohort and case-control studies (n ≈ 274,000) has shown that AR previously had about 3.82 times the odds of being developed into asthma when compared to those without AR (95% CI: 2.92-4.99).[3] Also quite a few studies also revealed that many patients suffering from asthma could he have AR co-morbidity. For example, one multicenter study conducted in India with over 1,100 asthma patients showed 65% prevalence of co-existing AR.[4] Another cross-sectional survey conducted in China (n: approx. 4,700) revealed that 6.5% had both AR and asthma while 25.4% had AR, and 9.4% had asthma; this is showing a considerable overlap however different populations have varied figures of this status.[5]

AR not only increases the risk of developing asthma, but also affects its severity, control, and the patient's overall wellbeing. According to the results of Willows et al. in “The Impact of Allergic Rhinitis on Asthma and Its Effect on the Quality of Life of Asthmatic Patients” (2023), quality-of-life score was significantly lower in patients with both AR and asthma, as compared to patients with one of the two conditions. Moreover, AR medication in mild intermittent AR was significantly associated with better asthma control.[6] These results suggest that AR might have an impact on the prognosis of asthma if left untreated or unrecognized.

There are common risk factors that underline both AR and asthma, including sensitization to allergens (dust mites, pollen, mould), environmental factors (tobacco smoke, pollution), genetic factors, early life exposures (e.g. respiratory infections in childhood), and socioeconomic, geographical, and climatic factors.[2,5,7] In Asia, the prevalence of AR has been reported to be between 10-30% in discursive populations, but much variation depends on urban vs rural living, pollution, and density of living conditions.[7]

In addition, temporal relationships between AR and asthma are of clinical importance. Numerous studies report a temporal relationship where AR precedes a patient's asthma symptoms, thus potentially creating a window of opportunity for intervention in the future.[3,8] Some patients may present with concomitant AR and asthma, while in other patients, asthma could precede significant rhinitis symptoms. The relationship is likely dependent on age group, environmental exposures, and possible differences among physicians in diagnostic processes. The clinical implications of understanding the incidence of one of the diseases in patients with the other, when it occurs, how an inciting factor or factors play into the association, is important for preventative and therapeutic planning.

Despite extensive research, important knowledge gaps remain. Most studies are cross-sectional, limiting insights into incidence and trends. There is also scarce data from regions like South Asia, the Middle East, and Africa on the relationship between asthma and allergic rhinitis (AR), their triggers, and impact on disease severity. This study aims to address these gaps by recruiting 120 diagnosed AR cases and 120 asthma cases in a local context. The results will provide crucial regional data to improve understanding, aid in early diagnosis and integrated management, and ultimately reduce disease burden.

Objective

To know association between allergic rhinitis (AR) and bronchial asthma (BA) by determining the incidence of BA in patients of AR and the incidence of AR in patients of BA.

Methodology

This cross-sectional observational study was carried out in the Departments of Ear, Nose and Throat (ENT), Nishtar Medical University and Hospital, Multan, over the course of twelve months. A total of 240 participants were enrolled, consisting of 120 diagnosed cases of allergic rhinitis (AR) and 120 diagnosed cases of bronchial asthma (BA). The outpatients were included by consecutive hiring once the inclusion and exclusion criteria were met. A written informed consent form for participation was obtained from each participant before commencing the study process. The Institutional Ethics Review Committee, NMU, Multan, provided ethical clearance for the study in accordance with the Declaration of Helsinki (2013 revision).

Eligible patients were 18 years of age and older and had a confirmed diagnosis of AR or BA based on clinical assessment and standard guidelines. Diagnosis of allergic rhinitis was made on the basis of the ARIA (Allergic Rhinitis and its Impact on Asthma) criteria, which include having a history of recurrent nasal congestion, rhinorrhea, sneezing, nasal itch, and/or ocular symptoms in response to allergen exposure, as supported with findings from anterior rhinoscopy and diagnostic nasal endoscopy . A diagnosis of bronchial asthma was made in accord with the Global Initiative for Asthma (GINA) guidelines; the

diagnosis was based upon usual symptoms of episodic wheezing, breathlessness, cough, and shows variable airflow limitation on spirometry. Patients with a history of chronic obstructive pulmonary disease (COPD), interstitial lung disease, sequelae of extensive pulmonary tuberculosis or significant cardiac disease were excluded from taking part. To ensure that we did not have study population confounding, we excluded smokers and ex-smokers, as well as participants that had used systemic corticosteroids within the last 3 weeks, or bronchodilators less than 24 hours prior to the testing.

All participants were assessed in a structured clinical assessment using a pre-prepared proforma. Its main purpose was to collect descriptive demographic data, such as age, sex, residence (urban/rural), and occupation. Presenting symptoms, particularly nasal symptoms (sneezing, rhinorrhea, nasal obstruction, and nasal itch) and lower-lower airway symptoms (breathlessness, wheeze, cough, and chest tightness), were summarized. The duration of symptoms, a seasonal component of the symptoms, and if there was a family history of atopy, were captured. Environmental factors that may be contributors, such as dust, smoke, pollen, change in weather, and strong odors were systematically evaluated.

A full ENT examination was conducted, which included both anterior rhinoscopy and diagnostic nasal endoscopy, in order to search for signs of AR (e.g. mucosal edema, turbinate hypertrophy, nasal polyps, allergic mucosal changes), chest examination with emphasis on auscultation for ronchi, wheezing, and crepitations. Bloods were sent for AEC and total serum IgE. AEC was defined as greater than 500 cells/μL as "raised". IgE was considered elevated according to laboratory reference standards. These tests will be used to support the diagnosis of allergic disorders.

All patients completed spirometry with an electronic spirometer according to American Thoracic Society (ATS) standards. Spirogram measures included forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), and the FEV1/FVC ratio, with reversibility testing with a bronchodilator done when appropriate. An obstructive pattern was defined as an FEV1/FVC < 70% with ≥ 12% and ≥ 200 mL improvement in FEV1 after administering the bronchodilator. Spirometry confirmed asthma in patients with AR and identified obstructive airway involvement in patients without classic asthma symptoms.

In AR patients, asthma was diagnosed based on clinical symptoms, auscultatory findings, and/or obstructive spirometry. In BA patients, AR was diagnosed on the basis of clinical history and findings from nasal examination. The temporal pattern of onset of symptoms in patients with both conditions was categorized in one of three ways: (a) succeeding asthma (asthma developed after AR), (b) preceding asthma (asthma existed prior to (AR), and (c) concomitant (both diseases developed simultaneously). The time interval (years) between the onset of AR and asthma was also recorded.

The database was created in Microsoft Excel and then transferred and analyzed using SPSS software version 26.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were produced with the continuous variables presented as mean ± standard deviation (SD) and categorical variables as frequencies and percentages. The Chi-square test was used to compare proportions of triggering factors, co-morbidities and categorical variables between AR and BA groups. All analyses were considered statistically significant at p-values < 0.05. The analyses and results were displayed in tables and graphics for clarity.

Results

The present study included 240 patients, comprising 120 diagnosed cases of allergic rhinitis (AR) and 120 diagnosed cases of bronchial asthma (BA). The mean age was 32.8 ± 12.4 years in the AR group and 35.6 ± 13.1 years in the BA group. The age of patients ranged from 18 to 70 years. The majority of patients in the AR group were in the 18–30 years age bracket (52; 43.3%), followed by 31–40 years (28; 23.3%). Similarly, in the BA group, the largest proportion was also in the 18–30 years category

Table 1. Chief complaints of the study cases

Chief Complaint	Allergic Rhinitis (n=120)	Bronchial Asthma (n=120)
Excessive sneezing	68 (56.7%)	15 (12.5%)
Rhinorrhea	55 (45.8%)	14 (11.7%)
Nasal obstruction	15 (12.5%)	3 (2.5%)
Breathlessness	6 (5.0%)	102 (85.0%)
Cough	3 (2.5%)	28 (23.3%)
Nasal itching	2 (1.7%)	0 (0.0%)

Table 2. Factors responsible for AR and BA

Triggering Factor	Allergic Rhinitis (n=120)	Bronchial Asthma (n=120)
Dust	102	78
Smoke	52	40
Pollen	38	16

(45; 37.5%) followed by 31–40 years (30; 25.0%). Both conditions showed a male predominance, with male-to-female ratios of 2.3:1 in the AR group and 1.9:1 in the BA group (Figure 1).

Study cases experienced different complaints. In AR patients, the most common symptom was excessive sneezing (110; 91.7%), followed by rhinorrhea (106; 88.3%). In BA patients, the most frequent asthma-related symptom was breathlessness (112; 93.3%), followed by wheezing (96; 80.0%) and dry cough (89; 74.2%) (Table 1).

There are different factors for both issues among study cases. Results showed that dust was the most common aggravating factor in both AR (102; 85.0%) and BA (78; 65.0%) groups ($p<0.05$). Smoke exposure was reported by 52 (43.3%) AR patients and 40 (33.3%) BA patients. Pollen sensitivity was observed more frequently in AR patients (38; 31.7%) compared to BA patients (16; 13.3%) (Table 2).

Signs of allergic rhinitis were present in 92 (76.7%) of AR patients and 80 (66.7%) of BA patients. Conjunctival hyperemia was observed in 71 (77.2%) and 66 (82.5%) patients of AR and BA groups, respectively. Raised absolute eosinophil count (AEC) was detected in 61 (50.8%) AR patients and 67 (55.8%) BA patients. Elevated immunoglobulin E (IgE) levels were found in 57 (47.5%) and 62 (51.7%) of AR and BA patients, respectively (Table 3).

Obstructive spirometry patterns were found in 36 (30.0%) AR patients and 85 (70.8%) BA patients. In the AR group, 71 (59.2%) patients were diagnosed with concomitant bronchial asthma. Among these, 47 (39.2%) had both symptoms and clinical signs, while 24 (20.0%) demonstrated obstructive changes on spirometry without overt symptoms. In the BA group, 92 (76.7%) patients were found to have allergic rhinitis based on symptoms and clinical examination (Figure 2a & b) (Table 4).

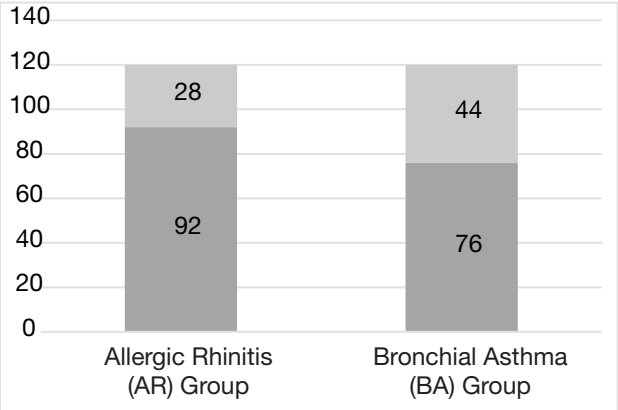

Figure 1. Gender based distribution of study cases

Among AR patients who developed asthma, the mean interval between onset of rhinitis and asthma symptoms was 2.7 ± 3.4 years. Conversely, in BA patients who developed AR, the mean interval was 0.8 ± 4.6 years. The majority of AR patients developed bronchial asthma after the onset of rhinitis (succeeding BA). In BA patients, concomitant onset of both diseases was more common than preceding rhinitis.

Dust was the most common precipitating factor in both groups, significantly higher in AR patients (85.0%) compared to BA patients (65.0%, $p=0.0006$). Pollen sensitivity was also significantly higher among AR patients (31.7%) compared to BA patients (13.3%, $p=0.0012$). Smoke exposure, change in weather, and strong odors were observed in both groups without significant differences ($p>0.05$) (Table 5).

Table 3. Response of immune system among study cases

Finding	Allergic Rhinitis (n=120)	Bronchial Asthma (n=120)
Raised AEC	61	67
Raised IgE	57	62

Discussion

The current study aimed to investigate the bidirectional relationship between Allergic Rhinitis (AR) and Bronchial Asthma (BA), which is commonly referred to as "united airway disease." Overall, our data provide compelling support for a strong, interdependent relationship between AR and BA that has substantial overlap in symptoms, triggers, and pathophysiology.

In our study cohort males outnumbered females in both the AR (2.3:1) and BA (1.9:1) groups, and participants fell within the third to fourth decades of life at the mean age for both groups. In particularly for AR this male predominance is consistent with some studies suggesting that hormonal and potentially genetic factors influence how atopic disease expressed. However, this is not always the case. A large population study by Papapostolou et al., (2021) was able to show men and women with adult AR had similar gender prevalence which supports the conjecture that environmental and regional considerations may impact the demographic data considerably.[9]

In opposition, our age demographic with the average

Table 4. Parameters found among study cases

Parameter	Allergic Rhinitis (n=120)	Bronchial Asthma (n=120)
Obstructive pattern	36	85
Comorbid diagnosis (AR→BA)	71	
Comorbid diagnosis (BA→AR)		92

person having at 18 and 40 (young adult) is in agreement with the typical age of onset for allergic disease. When analyzing the data globally, the Global Asthma Network study reported that asthma was diagnosed primarily in the early stages of life and showed consistent data to this.[10]

The chief complaints and symptom profiles certainly described the principal disease but also revealed a degree of comorbidity. Excessive sneezing and rhinorrhea were represented symptoms of AR while breathlessness and wheezing portrayed BA. Importantly, 5% of the AR patients documented breathlessness as a chief complaint, while 12.5% of BA patients presented excessive sneezing as a chief complaint, notes the clinical overlap that can exist when diagnosing a patient. Such symptomatic crossover is one of the cornerstones of the united airway theory. The work of Buzan et al. (2015) pointed out that nasal and bronchial inflammation often present at the same time, and that symptoms from one organ can worsen the other and treatment of the two organ systems independently is not as effective.[11] Our observation that 76.7% of BA patients on examination showed signs of AR is a powerful illustration of this relationship. This is greater than the 60-70% comorbidity rate cited, for example in the review of Small et al. (2018) and reinforces the importance for physicians to routinely assess for rhinitis in all asthma patients, and visa versa.[12]

Table 5. Factors responsible for issues among study participants

Factor	AR (n=120)	BA (n=120)	X^2	p-value
Dust	102	78	11.76	0.0006
Smoke	52	40	2.13	0.1442
Pollen	38	16	10.54	0.0012
Change in weather	22	34	2.82	0.0932
Strong odors	18	25	1.02	0.3125

Dust was the most relevant triggering factor for both conditions, and it was more prevalent in AR patients (85% vs 65%, p=0.0006). This is consistent with the contribution of perennial aeroallergens, especially house dust mites, in inducing chronic airway inflammation. Pollen sensitivities were similarly and significantly higher in AR patients (31.7% vs 13.3%, p=0.0012), which may be due to larger pollens, with greater nasal deposition primarily initiating symptoms in nasal airways. The shared response with dust, and diverging reactions with pollen support the notion of a spectrum of inflammation rather than two distinct diseases; pollen is generally tolerated by AR patients, whereas dust was showed in the cases to produce symptoms. There was evidence from Ceylan et al.'s (2019)[13] study that polysensitization to both perennial and seasonal allergens was a strong predictor for the development of asthma disease process in patients with rhinitis disease process. This anticipated positivity relates to the overall burden of allergenic load, and the mix of allergens is relevant considering AR and BA represents two distinct processes of 'non-asthmatic' and 'asthmatic', respectively, and would imply divergent outcomes as metaphors, but overall there is an implication for greater burden on the whole airways. The tests from triggers such as smoke and climate changes indicated no significant difference, but may reflect the non-specific irritant that augment already existent airway hyperresponsiveness, which is a shared characteristic for both AR and BA.

The laboratory findings further support shared allergic pathophysiology. Elevated Absolute Eosinophil Count (AEC) and IgE were found in almost half of the patients in both groups with slightly more in the BA group. Eosinophilia and IgE-mediated inflammation have been well documented as features of T-helper 2 (Th2) driven immunity in atopic disease. Our findings were in agreement with Matucci et al. (2021) who found high fractional exhaled nitric oxide (FeNO) and blood eosinophils are biomarkers of Th2 inflammation that predict positive response to inhaled corticosteroids in both upper and lower airway diseases.[14] The data obtained from spirometry provided important objective measures. An obstructive pattern was found in 30% of AR patients indicating subclinical bronchial involvement. This is a vital finding as this represents a high-risk population of AR patients that are predisposed to develop overt asthma. The high frequency of obstructive patterns in the BA patients (70.8%) was anticipated. Samitas et al. (2021), who studied small airway dysfunction in patients with AR without a diagnosis of asthma, although different from our study, offers a physiological rationale for this as they state inflammation infiltrates beyond the nasal mucosa into distal bronchi before symptoms manifest.[15]

The strongest support for the united airway disease model stems from our examination of comorbidity and

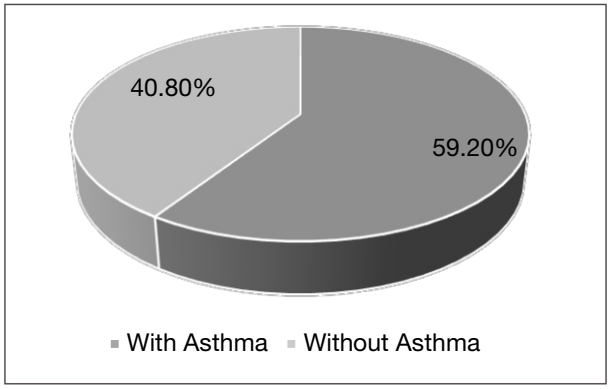

Figure 2a. Comorbidity in Allergic Rhinitis Patients

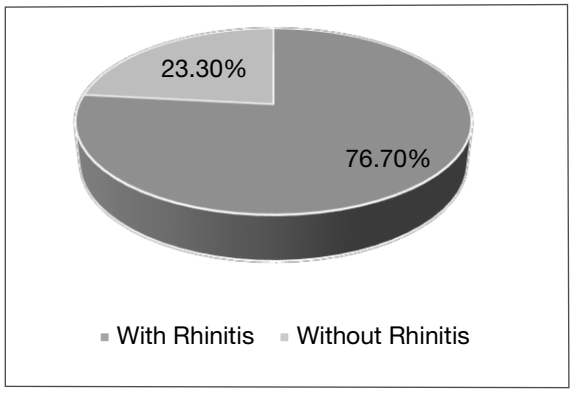

Figure 2b. Comorbidity in Bronchial Asthma Patients

temporal onset. Of those patients with allergies, 59.2% had concomitant bronchial asthma but, in the group with bronchial asthma, 76.7% had concomitant allergic rhinitis. The mean time from the onset of allergic rhinitis to the development of bronchial asthma was 2.7 years, while development of allergic rhinitis after bronchial asthma occurred at a mean time of 0.8 years. The temporal relationship suggests that allergic rhinitis is typically prior and is a significant risk factor for bronchial asthma where this has been well established in the literature. The sheer number of patients who had their allergic rhinitis and bronchial asthma with co-morbid onset as well as the co-morbid patients with bronchial asthma present prior to allergic rhinitis suggests that the relationship is not strictly linear but rather it is bidirectional, whereby either can serve as an initiator or an exacerbator of the other. Our analysis supports the seminal findings of a study by Leynaert et al, which found rhinitis is an independent risk factor for adult-onset asthma.[16] A more recent longitudinal study by Toppila-Salmi et al. (2020) confirmed that the risk of developing asthma is highest in the first years after the onset of rhinitis, which aligns with our observed mean interval of 2.7 years.[17] The bidirectional nature of the link was further elaborated by Côté et al. (2020), who stated that treating rhinitis improves asthma outcomes and, conversely, effective asthma control can reduce nasal symptoms, highlighting the need for a integrated management approach.[18]

The results of the current study strongly confirm the close association between allergic rhinitis and bronchial asthma. Demographic similarities and overlapping culprit triggers (particularly dust), inflammatory biomarkers of the Th2 pathway (including AEC and IgE), and spirometric abnormalities support this underlying pathophysiological model. High co-diagnosis rates and the natural history of allergic rhinitis often preceding asthma support a sequential atopic march model. Collectively our study highlights the importance of a holistic approach to patient management - a "one airway" approach. When one condition is diagnosed, the clinician must again search for the other.

Conclusion

This research also presents strong clinical evidence supporting the concept of "united airway disease" by

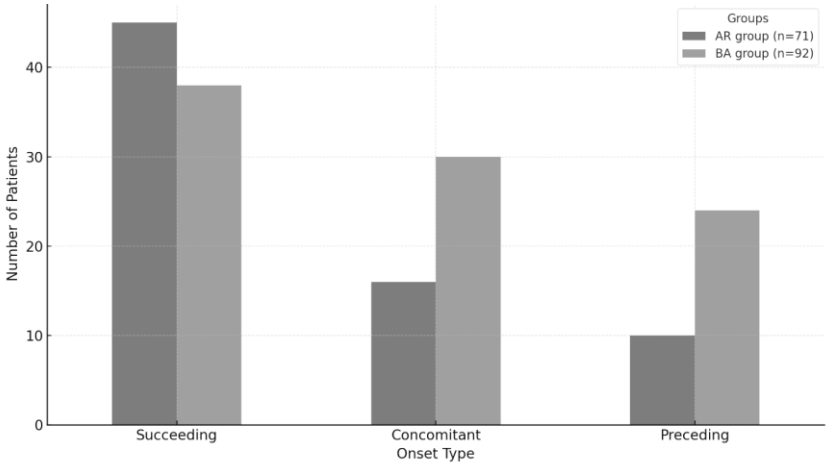

Figure 3. Temporal relationship of symptom onset in AR and BA patietns

demonstrating a strong, bidirectional association between allergic rhinitis (AR) and bronchial asthma (BA). In addition, AR often preceded BA, with the average time between the onset of AR and the presentation of BA being 2.7 years, which supports AR as a significant risk factor for the development of lower airway disease. The pathophysiological mechanism is shared as both AR and BA are T-helper 2 (Th2) mediated inflammatory responses, and we also share exposing triggers such as dust, and the themes of a shared increase in biomarkers including absolute eosinophil count (AEC) and IgE observed in both patient populations. Finally, the finding of obstructive spirometry patterns in 30% of AR patients with no clinical asthma reinforces the universal finding of subclinical bronchial involvement in the setting of AR, suggesting a pre-asthmatic state.

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