

Clinicopathological, epidemiological, and immunological relationship between allergic rhinitis and bronchial asthma

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Abstract

INTRODUCTION: Allergic rhinitis and bronchial asthma are thought to be sequela of the same allergic airway disease. The relationship between both diseases has been confirmed by various clinicopathological epidemiological and immunological studies. In this study, we tried to establish a different relationship between both diseases and strengthen the concept of “One-airway one disease.”

MATERIALS AND METHODS: A total of 100 patients visiting ear, nose, and throat and respiratory medicine outpatient department were taken. They were divided into two groups of fifty each and were studied for various mediators of inflammation. Group 1 consisted of patients of allergic rhinitis and Group 2 consisted of patients of bronchial asthma.

RESULTS: Most of the patients in Group 1 were in the age group of 21–30 years (40%) and in Group 2, in the age group of 11–20 years (38%) with a mean age 28.4 ± 1.3 years. The most common symptoms in Group 1 patients were sneezing (90%) and rhinorrhea (68%) and in Group 2 wheezing (86%), followed by shortness of breath (66%). The most common sign in Group 1 was B/L inferior turbinate hypertrophy (70%), while in Group 2, it was rhonchi (76%). Mean absolute eosinophil count was 575.35 in Group 1 and was 446.61 in Group 2. Nasal smear for eosinophil was positive for 86% of patients in Group 1 and bronchial lavage showed eosinophilia in 64% of Group 2 patients. Mean total serum immunoglobulin E was 777.23 IU/ml in Group 1 and 662.08 IU/ml in Group 2. The incidence of bronchial asthma in patients of allergic rhinitis was 36%, while the incidence of allergic rhinitis in patients in bronchial asthma was 74%.

CONCLUSION: Thus, in our study, we found that both the diseases were closely linked clinicopathologically epidemiologically as well as immunologically pointing toward the concept one-airway one disease.

Keywords: Absolute eosinophil count, allergic rhinitis, bronchial asthma, immunoglobulin E

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Introduction

Allergic rhinitis is a very common comorbid condition associated with asthma. It is defined as inflammation of the lining of the nose and is characterized by nasal symptoms including rhinorrhea, sneezing, nasal blockage, and/or itching of the nose. Bronchial asthma is a reversible chronic inflammatory disorder of airways that causes recurrent episodes of wheezing, breathlessness, chest tightness, and cough. The connection between the upper and lower airways has become a topic of great interest over the past many years. It is now well established that nasal allergy and asthma frequently occur together, with approximately 20%–50% of allergic rhinitis patients having concomitant asthma and 80% of asthmatic patients having chronic nasal symptoms. Not only this mediators of inflammation in both disease and the management of one greatly affects the other thus leading to the concept of one airway one disease. In this study, we tried to establish clinicopathological, epidemiological, and immunological relationship between both diseases.

Materials and Methods

This study was prospective in nature and has been carried out in the Department of Otorhinolaryngology and Respiratory Medicine, Jawaharlal Nehru Medical College, AMU, Aligarh from December 2016 to November 2018. Patients attending the outpatient department and indoor patients in the hospital were included in this study. The total number of patients included in the study was 100 after taking proper informed consent. The patients who were selected for the study were evaluated with proper history, detailed examination, diagnostic nasal endoscopic examination, blood sample were taken for serum immunoglobulin (Ig) E level, smears from nasal and bronchial secretions were made, pulmonary function tests were done and radiological investigations were done which included X-ray paraNasal sinuses (water's view with open mouth) chest X-ray or computed tomography scan-nose and paranasal sinuses in some patients. The patients were divided into two groups of fifty each. Proper ethical clearance was taken from the Institutional Ethic Committee.

- Group 1 – All patients of allergic rhinitis only or patients of allergic rhinitis having asthma symptoms also. (In which allergic rhinitis proceeds bronchial asthma symptoms)
- Group 2 – All patients of bronchial asthma only or patients of bronchial asthma having allergic rhinitis symptoms also. (In which bronchial asthma proceeds allergic rhinitis symptoms).

Inclusion criteria

Patients >11 years of age of both sexes were included in the study. Patients who did not give consent for the study and patients with systemic diseases such as diabetes mellitus, hypertension, and cardiovascular diseases were excluded from the study.

All patients of allergic rhinitis (GROUP 1) underwent spirometry to access the pulmonary symptoms. If spirometry showed obstruction (forced expiratory volume [FEV] 1/forced vital capacity < 0.75) then reversibility was done. If FEV1 increases by 12% or by 200 ml postbronchodilation, they were diagnosed with patients of allergic rhinitis having bronchial asthma also (GINA guidelines). All patients of bronchial asthma (GROUP 2) were inquired about typical history of allergic rhinitis and diagnosis of allergic rhinitis was made according to ARIA guidelines. If allergic rhinitis was also present, they were classified as patients of bronchial asthma having allergic rhinitis also.

Smears from nasal secretions of patients of allergic rhinitis and bronchial secretions of patients of bronchial asthma were made. The smears were stained with hematoxylin and eosin and were examined under light microscope. Nasal smear was considered as positive if there is the presence of eosinophils and negative if there is the absence of eosinophils as it was found that majority (87.6%) of the normal population have negative nasal smear for eosinophils.^[1] Bronchial smears were made from samples obtained after bronchoscopy from asthma patients and were examined for morphology of cell. Absolute eosinophil count (AEC) was done in all patients of both groups. Cell counts of >440/cumm was considered to be the presence of eosinophilia.

Total IgE level were compared in patients of allergic rhinitis and bronchial asthma using ELISA technique. The total IgE level in normal, allergy-free adults is <150 IU/mL in the serum. However, variations in total IgE concentrations may be expected in certain age groups and clinical conditions.

Results



Out of 100 patients of allergic rhinitis and bronchial asthma taken into the study 54 were male and 46 were female. Most of the patients in Group 1 were in the age group of 21–30 years (40%) and in Group 2, in the age group of 11–20 years (38%) with a mean age 28.4 ± 1.3 years as shown in [Table 1]. The youngest patient included in the study was 12 years old and the eldest patient was 50 years old.

Age	Number of patients (%)	
	Group 1	Group 2
11-20	15 (30)	19 (38)
21-30	20 (40)	15 (30)
31-40	10 (20)	7 (14)
41-50	4 (8)	6 (12)
>50	1 (2)	3 (6)
Total	50 (100)	50 (100)

Table 1: Age wise distribution of both groups

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Symptoms

In Group 1, almost all the patients presented with sneezing (98%) followed by rhinorrhea (68%). In Group 2, most patients presented with wheeze (86%) followed by the shortness of breath (66%) as shown in [Table 2].

Symptoms	Group 1 (%)	Group 2 (%)
Sneezing	98	40
Rhinorrhea	68	36
Nasal blockage	64	22
Nasal itching	44	8
Wheeze	32	86
Shortness of breath	16	66
Cough	16	46

Table 2: Different symptoms of both groups

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Examination findings

The most common sign in Group 1 was B/L inferior turbinate hypertrophy (70%) followed by deviated nasal septum (DNS) with Inferior turbinate hypertrophy (ITH). Most common sign in Group 2 was rhonchi (76%) followed by DNS with ITH [Table 3].

Signs	Group 1 (%)	Group 2 (%)
B/L ITH	70	36
DNS with ITH	62	46
Rhonchi	32	76
Polyp	12	10
Spur	8	6

DNS=Deviated nasal septum, ITH=Inferior turbinate hypertrophy

Table 3: Different examination findings of both groups

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Bronchial asthma in patients of allergic rhinitis

Pulmonary function of all patients of Group 1 were assessed and if any obstruction was found to be present reversibility was done. If reversibility was present at least once they were diagnosed with patients of allergic rhinitis having asthma also according to the GINA guidelines.

In this study, we found that out of 50 patients 18 patients (36%) of allergic rhinitis also had bronchial asthma. Two-third of patients developing bronchial asthma had history of perinéal allergic rhinitis.

Allergic rhinitis in patients of bronchial asthma

All patients of Group 2 were accessed for signs and symptoms of allergic rhinitis. If present they were diagnosed with patients of bronchial asthma having allergic rhinitis also (ARIA guidelines).

In our study, we found that out of 50 patients, 38 patients (76%) of bronchial asthma also developed allergic rhinitis.

Mediators of inflammation

AEC-Absolute eosinophil count was done in all patients of both groups. Cell counts of >440/cumm was considered to be the presence of eosinophilia. In Group 1, 37 (74%) patients of and in Group 2, 27 (54%) patients were found to have eosinophilia [Table 4].

	Smear eosinophilia	Blood eosinophilia	Mean absolute eosinophil count
Group 1 (%)	43 (86)	37 (74)	575.34
Group 2 (%)	32 (64)	27 (54)	446.61

Table 4: Smear eosinophilia, blood eosinophilia, and mean absolute eosinophil count of both groups

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Nasal and bronchial smear

Nasal smear from nasal secretions in Group 1 and bronchial smear from bronchoalveolar lavage in Group 2 patients were made and eosinophils were seen. Forty-three patients (86%) in Group 1 and 32 patients in Group 2 (64%), the smear showed abundance of eosinophils [Table 4].

Mean blood absolute eosinophil count

Mean AEC in Group 1 was found to be 575.34 cells/cumm highest being 930 cells/cumm and lowest being 250 cells/cumm. In Group 2, it was 446.61 cells/cumm highest being 850 cells/cumm and lowest being 200 cells/cumm [Table 4]. In patients of allergic rhinitis having bronchial asthma also it was 593.21 cells/cumm and in patients of bronchial asthma having allergic rhinitis also it was 500.33 cells/cumm.

Total serum immunoglobulin E

Total serum IgE was measured in patients of both groups and in twenty healthy control. DRG ELISA kit no RN-58888 was used to determine the value of IgE in each sample using the standard curve obtained.

In Group 1, 46 patients had value >200 IU/ml, highest value being 1485 IU/ml and lowest being 55 IU/ml and mean value being 777.23 IU/ml. In Group 2, 43 patients had value greater 200 IU/ml, highest value being 1410 IU/ml and lowest being 28 IU/ml and mean value being 662.08 IU/ml. In 20 healthy controls, 9 had value >200 IU/ml highest being 855 IU/ml and lowest being 24 IU/ml and mean being 252.21 IU/ml [Figure 1].

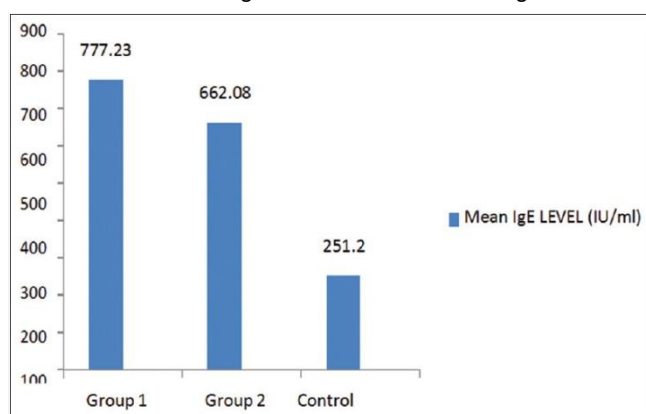


Figure 1: Immunoglobulin E Level in both groups and control

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Discussion



Allergic rhinitis and bronchial asthma are a common health problem accounting for a large number of cases in otorhinolaryngology outpatient departments. Many different studies have been done to study the relationship of both diseases in terms of clinical and pathophysiological and immunological aspects. In our study, we have taken 100 patients and divided them into two groups, Group 1 consisted of patients of allergic rhinitis and Group 2 consisted of patients of bronchial asthma.

Epidemiological link

Incidence of allergic rhinitis in bronchial asthma and bronchial asthma in allergic rhinitis was seen. Different mediators of inflammation were studied in both groups and compared.

Out of 50 patients of allergic rhinitis, 18 patients (36%) had symptoms of bronchial asthma also. They were diagnosed with patients of allergic rhinitis having bronchial asthma also. Of these, 66.67% patients developing bronchial asthma had history of perinatal allergic rhinitis.

Out of 50 patients of bronchial asthma, 38 patients (76%) had symptoms of allergic rhinitis also. They were diagnosed with patients of bronchial asthma having allergic rhinitis also.

Many studies have been done to see the epidemiological relationship between allergic rhinitis and asthma which have shown similar results.

In another study done by Masuda *et al.*^[2] in children, they found that persistent nasal symptoms were present in 83.8% of the asthmatic children. The incidence of allergic rhinitis was 77.7% based on the objective findings.

However, the reported prevalence of allergic rhinitis in patients with asthma, shows a wide range ranges from 6.2% to 95% as diagnosis is mostly based on a questionnaire to the patients which is a subjective criteria.^[3] The high coincidence of both disease can be explained by various anatomical physiological and pathological basis. The respiratory tract can be considered as a single morphofunctional. It is covered by ciliated epithelium and mucinous glands and an extensive

vasculature and innervation similar in the upper and lower airways.^[4] The respiratory mucosa is rich in mast cells which are important effector and immunoregulatory and these cells are thought to significantly contribute to nose-bronchi connection through cytokine release.^{[5],[6]}

Moreover, the lymphoid tissue constitutes the bronchial associated lymphoid tissue-mucosal associated lymphoid tissue, which is largely represented in both the nose and bronchi.

The mechanisms that connect upper and lower airway allergies are under active investigation. Proposed pathogenetic mechanisms include a nasobronchial reflex, mouth breathing caused by nasal congestion, and pulmonary aspiration of nasal contents.^[7] In children, viruses were detected in 80% of reported episodes of asthma exacerbations.^[8] Upper airway rhinovirus infection is an important risk factor for asthma exacerbation through various pathophysiologies to cause allergic inflammation in the lower airway, such as ICAM1 expression.^[9] It has also been demonstrated that rhinovirus could directly infect lower airways.^[10] Spreading of allergic inflammation from the upper airway to the lower airway may be induced since local allergic sensitization causes systemic production of allergen specific IgE and T-cells are able to migrate from regional lymph nodes and “home in” on other tissues.^[11]

Pathological link

In our study, we studied the mediators of inflammation (blood eosinophil level, smear eosinophil, and total serum IGE) in both groups. Smears from nasal secretions in allergic rhinitis patients (Group 1) and smears of bronchoalveolar secretions from bronchial asthma patients (Group 2) were made and eosinophils were seen. Eosinophils were found to be present in significant amount in smears made from both nasal secretions (in Group 1) and from bronchial lavage (in Group 2). In Group 1, 86% and in Group 2, 64% showed smear eosinophilia.

AEC was raised in both groups (cut-off value >440 cells/cumm). In Group 1, 74% of patients and in Group 2, 54% had raised value.

Mean AEC in Group 1 was 573.34 and in Group 2, it was 446.61. The value was still higher in patients having both disease.

A number of studies have been done to see the AEC, relationship of it with smear eosinophilia level in patients of allergic diseases showing similar results.

Kelly *et al.*^[12] have shown a significant increase in the number and activity of inflammatory cells in bronchoalveolar lavage fluid in asthma the numbers of eosinophils and lymphocytes obtained in lavage fluid from patients with stable asthma; the increase in lavage fluid neutrophils was nonsignificant, though the absolute numbers of neutrophils were much greater than the numbers of eosinophils.

Patel and Nagpal^[13] Kumar *et al.*,^[14] Sonawane *et al.*^[15] and Chanda *et al.*^[16] found that the mean values of blood AEC, nasal eosinophilia were higher in patients of allergic rhinitis and much higher in group of patients having nasal and respiratory system as compared to nasal symptom.

However, in contrary to above studies, Chowdary *et al.*^[17] had found their >90% of patients with allergic rhinitis had blood AEC <440.

In our study, we found that in Group 1, 74% and in Group 2, 54% showed eosinophilia. However, it should be recalled that the absence of peripheral eosinophilia does not rule out the possibility of eosinophilic inflammation of the lung tissue.^{[18],[19]} Serum eosinophils are more dependent on interleukin-5 (IL-5) for their maturation and survival, whereas tissue eosinophils are more responsive to the granulocyte and macrophage colony-stimulating factor originating from innate immunity or derived from the Th1 axis. Besides that, eosinophil count can be normal in peripheral blood but active and filled with active granules with major basic protein, eosinophil cationic protein, and other mediators.^[20] Another explanation for normal serum eosinophil count in 50% of these patients could be the presence of a mild inflammatory process, without any effects at the peripheral blood level, which may result from the use of medications to control the allergy or from the downregulation of the number of eosinophils in circulating blood, and is a common finding in chronic intestinal parasitic infections.^[21]

Immunological link – in our study, total serum IgE value was found to be raised in both group. In Group 1, mean value was 772.3 IU/ml and in Group 2, it was 662.08 IU/ml as compared to control normal healthy individuals 252.21 IU/ml.

In general, the concentration of serum IgE increases from birth until the age of 15 years, and then decreases during adulthood.^[22] Furthermore, males tend to have a higher level of serum IgE than females.^{[23],[24]} Some authors have suggested that a higher prevalence of smoking in men could explain this phenomenon.^[25]

There is a wide variation in normal serum IgE levels documented. Because of the wide range of serum IgE levels, it has been extremely difficult to establish reliable ranges or 95% confidence limits for this Ig. The variation in values are probably related to a different technique used for measuring IgE, to different populations studied and possibly to the use of a different standard.

In this study, we found the normal control level of IgE 252.21 IU/ml which is slightly higher as compared to other studies. This may be contributed various factors such as high prevalence of parasitic infection and smoking ^[25] in the study area. Moreover, males have higher values of IgE level as compared to females ^{[23],[24]} and in our study healthy controls consisted of 70% males.

In our study, mean IgE value in allergic rhinitis was 772.3 IU/ml and in bronchial asthma patients it was slightly lower 662.3 IU/ml. However, they were much greater when compared to the normal healthy controls (252.51).

Many studies have been done previously showing similar results.

In a study done by Grundbacher and Massie ^[26] geometric mean values for asthmatics were about twice as high as in nonallergic individuals. Sandeep *et al.* ^[27] compared the mean IgE levels in healthy controls and bronchial asthma patients and found to be 151.95 IU/L and 756.26 IU/L, respectively. They also found that the mean serum IgE value of bronchial asthma patients was 374.3 IU/ml that is higher than the general population as noted by previous studies.

Borish *et al.* ^[28] the mean total IgE level of the population was found to be 106.6 IU/ml, whereas higher mean total IgE level was observed patients with severe asthma have a higher mean IgE level (280.2 IU/ml). Several other studies have also shown significant elevation of IgE levels in allergic subjects. ^{[26],[27],[28],[29]}

In this study, we found that same inflammatory mediators to be raised in both group indicating toward a common pathology. This can be explained by the fact that both upper and lower respiratory airway share common anatomical structure including pseudostratified columnar epithelium, basement membrane, lamina propria, and goblet cells along the whole length. Many studies have described the presence of systemic allergic inflammatory response after nasal provocation and shown that in inflammatory changes as indicated by elevated IL-5 and eosinophils in bronchoalveolar lavage occurred both in nasal and bronchial mucosa. ^[30] There is also a strong association of IL-4 cytokines with IL-5 in most cases of allergic rhinitis and asthma as shown by different studies. ^[31] Cytokines play a central role in chronic inflammation and orchestrating the allergic inflammatory response. Cytokine IL-4 present in allergic diseases plays important role in Th2 differentiation which causes a switch to IgE production by differentiating B-cells, thus explaining the increased level of IgE in both disease. The presence of high amount of eosinophil in both diseases is related to cytokine IL5 and tumor necrosis factor alpha. The role of IL-5 in eosinophilic inflammation has been confirmed by the use of anti-IL-5 antibody which almost depletes the circulating eosinophils and prevents the eosinophil recruitment into the airway after allergen exposure.

Conclusion



Thus, from our study, we can say that both the diseases are closely related to each other clinicopathologically epidemiologically as well as immunologically. The inflammatory mediators involved in both the diseases were found to same pointing out toward the common pathophysiology strengthening the concept of “One airway one disease.”

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Conflicts of interest

There are no conflicts of interest.

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