

SPECIAL ARTICLE

Allergic Rhinitis and Co-morbid Asthma: Perspective from India- ARIA Asia-Pacific Workshop Report

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SUMMARY In India, allergic rhinitis (AR) is considered to be a trivial disease, despite the fact that symptoms of rhinitis were present in 75% of children and 80% of asthmatic adults. Traditionally, AR was also divided into seasonal or perennial, based on the time of occurrence of symptoms during the year. The ARIA workshop report proposed that patients be categorized as "intermittent" and "persistent" while severity was classified as "mild" and "moderate-severe". Patients with AR, depending on their predominant symptom, can also be categorized as "sneezers-runners" and "blockers". On sketching their clinical profile, it was observed that "blockers" had significantly higher sinusitis and had higher sensitization to fungi. Skin allergy testing in Indian adults showed that in patients with AR house dust mite (*Dermatophagoides farinae*) was the most common allergen. Studies conducted in India have shown that AR often restricts the patient's quality of life (QOL). It can affect the physical, psychological and social aspects of the patients' life and can also impact their functions at work. Furthermore, AR adversely affects sleep related QOL. Topical corticosteroids are now considered as the cornerstone of the treatment for AR. In spite of causing a major impact on the QOL in Indian patients, AR is rarely given the importance it deserves.

Rhinitis is defined as inflammation of the membranes lining the nose and is characterized by nasal congestion, rhinorrhea, sneezing, itching of the nose and/or post-nasal drainage.¹ Atopy is an important risk factor for rhinitis and allergic rhinitis (AR) is the most common form.¹ Although a cause of significant and widespread morbidity, AR is often viewed, rather erroneously, as a trivial disease.² It may significantly affect the quality of life (QOL) of the patient by causing fatigue, headache, cognitive impairment and other associated symptoms.¹

A recent multicenter study³ by the Asthma

Epidemiology Study Group of the Indian Council of Medical Research found the prevalence of bronchial asthma in Indian adults to be 2.38%. They also observed that "recurrent coryza" occurred in 3.45%, "recurrent skin rashes" in 2.1%, and "recurrent eye itching" in 2.78% in Indian adults. Considering a population of 1.2 billion, these numbers suggest that the burden of rhinitis as well as asthma in India is

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immense. However, in India, AR still does not receive the attention it deserves by both patients as well as clinicians.

Epidemiology of allergic rhinitis in India

The International Study of Asthma and Allergies in Childhood (ISAAC)⁴ is a unique international initiative to monitor time trends and determinants of the prevalence of asthma and allergies in children. ISAAC developed simple methods for measuring the prevalence of childhood asthma, AR and atopic eczema for international comparisons, suitable for different geographical locations and languages. Data on nasal symptoms, hay fever and allergic rhinoconjunctivitis were obtained through a standardized questionnaire. Nasal symptoms were said to be present if the child ever had sneezing, or a runny, or a blocked nose in the absence of a cold or the flu. Since there were no widely agreed criteria for the diagnosis or classification of rhinitis then, the term 'hay fever' was applied for symptoms pertaining to seasonal allergic rhinitis (SAR). If nasal complaints were accompanied by itchy-watery eyes, it was classified as allergic rhinoconjunctivitis. The study comprised children in two age groups: 6-7 years age group and 13-14 years age group. For the 6-7 years age group, there were 91 collaborating centers in 38 countries while in the 13-14 years age group, 155 centers from 56 countries participated.

In India, ISAAC study was conducted in 14 centers. Phase 1 included 30,879 children in the 6-7 years age group, while there were 37,171 children in the 13-14 years age group. The ISAAC phase one data from India revealed that nasal symptoms alone were present in 12.5% children in the 6-7 years age group and 18.6% in the 13-14 years age group. Hay fever alone was present in 5.5% and 8%, respectively, while allergic rhinoconjunctivitis was seen in 3.3% and 5.6%, respectively.⁵

Classification of allergic rhinitis

In 1979, Mygind,⁶ for the first time, categorized patients with perennial rhinitis into two groups as per their predominant symptoms. Those who had sneezing and watery discharge as their most troublesome symptoms were classified as "sneezers", while those with nasal blockade and mucus secretion as their main symptoms were described as "blockers". In 1994, the International Consensus Report⁷ on di-

agnosis and management of rhinitis acknowledged the division of patients into "sneezers and runners" and "blockers", and provided clinical features to distinguish the two entities. In the first Allergic Rhinitis and its Impact on Asthma (ARIA) workshop report⁸, this subdivision was included in the diagnosis and assessment of severity of rhinitis and was advocated as an important part of clinical history. However, the epidemiological evidence for such a subdivision was lacking in literature. Traditionally, AR was divided into SAR and perennial allergic rhinitis (PAR), based on the time of occurrence of symptoms during the year.^{1,9} The ARIA workshop report⁸ proposed that the disease be categorized as "intermittent" and "persistent" while severity was classified as "mild" and "moderate-severe". This new classification is based on number of days per week and number of weeks per year during which the patient is symptomatic. The report stressed upon the need for use of this new categorisation for epidemiological studies. However, when proposed, this classification also lacked validation in daily practice.¹⁰

We compared the clinical and epidemiological profile of "sneezers and runners" and "blockers".¹¹ The older classification of patients into SAR and PAR was also compared with new categories, "intermittent" and "persistent", as proposed by the ARIA workshop report.⁸ The study distinguished 114 patients with AR into "sneezers and runners" and "blockers". Based on clinical history, almost two-thirds of these patients were classified as "sneezers and runners". Majority of them were categorized as SAR, while the ARIA report classified them as "moderate-severe/intermittent". However, a quarter of these patients, who were traditionally classified as PAR, were now categorized as "intermittent". "Blockers" had more perennial disease and more than half were "mild/persistent". Thus patients were better represented when they were classified according to the duration and severity of symptoms as per the ARIA workshop report.⁷ The updated ARIA document¹² reiterates that AR should be subdivided into "intermittent" or "persistent" and severity be classified as "mild" or "moderate/severe".

Patients who are predominantly "sneezers and runners" often report sneezing and anterior rhinorrhea along with itchy nose and itchy eyes as their main symptoms. More patients with SAR are cate-

gorized as “sneezers and runners”. A significant number of “sneezers and runners” described by us had an atopic family background.¹¹ In contrast, “blockers” are troubled by severe nasal blockage and thick nasal mucus which often leads to post nasal drip and breathlessness. The symptoms are constant day and night but may worsen during the night. Further, because of associated breathlessness, these patients could be mistakenly diagnosed as having asthma only, with the possibility of rhinitis being overlooked. Early identification of such patients assumes importance, since morbidity that results from misdiagnosis can be avoided. “Blockers” had significantly more sensitization to perennial allergens, such as fungi and house dust mite. More patients with PAR were categorized as “blockers”.

Co-existence of rhinitis and asthma: adults and children

Of all the atopic disorders, AR is most commonly associated with asthma.^{8,13,14} An editorial² entitled “*Rarely does one hear a wheeze without a sneeze*” succinctly described the close link between the two entities. Nasal symptoms have been reported to occur in 28-78% asthmatics while 17-38% of patients with AR have coexistent asthma.¹

A questionnaire-based study¹⁵ determined the co-occurrence of AR in 646 out patient asthmatics (405 children and 241 adults) reporting to our Institute. Symptoms of rhinitis were present in 75% of the children and 80% of the adults. Three-fourths of children and 55% of adults with asthma and associated AR had simultaneous onset of both diseases. It was thus observed that AR occurred commonly with asthma and could be an independent risk factor for the development of asthma. In another study¹⁶ in 111 children with AR and/or asthma, both diseases co-occurred in 83 (74%), while 9 (8%) had asthma only and 19 (17%) had AR alone. We also found that exposure to environmental tobacco smoke (ETS) led to significant feeling of suffocation in 7/9 (78%) patients with asthma, 73/83 (88%) patients with asthma and AR and 15/19 (79%) with AR alone.

Effect of sinusitis in patients with allergic rhinitis and/or asthma

The presence of sinusitis further aggravates the morbidity caused by rhinitis and/or asthma. We studied 216 patients with AR and/or asthma for the

occurrence of sinusitis.¹⁷ All patients underwent spirometry with reversibility and CT-PNS. As a part of the workup, both investigations were performed in all enrolled patients, prior to commencement of standard therapy. A CT staging system¹⁸ for noting the extent of rhinosinusitis, with the total score ranging from 0 to 24 depending on the number of sinuses involved, was adopted. Twenty-seven patients had asthma only (group 1), 131 had AR (group 2) and 58 had asthma with AR (group 3). On CT-PNS, sinusitis was present in 20 (74%), 88 (67%) and 48 (82%) of patients, respectively. Sinusitis on CT-PNS was present in more than two-thirds of the 189 patients with AR in groups 2 and 3 (136/189). Postnasal drip (62/88 vs. 15/43, $p < 0.05$) and sneezing (52/88 vs. 7/43, $p < 0.05$) were significantly higher in these patients as compared to those without sinusitis. Coexistent sinusitis increased the severity and morbidity caused by AR especially, in those who were predominantly “blockers”.¹⁹

Allergic rhinitis and quality of life

AR often restricts the patient’s QOL. It can affect the physical, psychological and social aspects of the patients’ life and can also impact their functions at work. These aspects or “quality of life” issues provide information that cannot be obtained using conventional clinical and functional measures and they provide a focus on patient’s own perception of disease. In an initial study²⁰ of its kind in India, we assessed the quality of life in 34 patients of AR with the help of the Rhinitis Quality of Life Questionnaire (RQLQ)²¹ and found that the disease caused significant practical problems, emotional distress and limitation in activities. The presence of AR adversely affected behaviour, work performance and life style of these patients. They were troubled by their disease, which caused hindrance at work due to repeated blowing of the nose and the need to rub their eyes and nose. However, appropriate treatment along with patient education resulted in significant improvement in quality of life at 4 weeks, which continued at 8 weeks. We observed that Indian adults were bothered by problems at work and by the fact that it affected their feeling of general well being. They were, however, less troubled by the lack of a good night’s sleep and the need to carry handkerchief. AR when occurring concurrently with asthma is likely to further affect the quality of life in such patients.²²

Recent studies suggest that AR adversely affects sleep related QOL of patients.²³⁻²⁵ We assessed the sleep related quality of life impairment in patients with AR by means of questionnaires.²⁶ Nocturnal sleep, excessive daytime sleepiness and sleep specific QOL disturbances were assessed using the Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Score (ESS) and Nocturnal Rhinoconjunctivitis Quality of Life Questionnaires (NRQLQ), respectively. The PSQI, ESS and NRQLQ scores significantly correlated with the presence of nasal obstruction, thick nasal discharge as compared to watery rhinorrhea, and postnasal drip. In addition, the NRQLQ score positively correlated with number of sneezing episodes per day as well as number of sneezes during each episode. All patients were subjected to CT-PNS for the presence of sinusitis. In 207 patients with AR, we found coexistent sinusitis in 132 (63.7%). Patients with concomitant sinusitis had significant impairment in their nocturnal sleep disturbances and had excessive daytime sleepiness as compared to those without sinusitis.

Skin test reactivity in allergic rhinitis in India

Seasonal AR, also known as hay fever, is caused by an IgE mediated reaction to seasonal aeroallergens like pollens and moulds. Length of seasonal exposure to these allergens is dependent on

geographical location. In India, there are mainly two pollen seasons *viz.* February to April, and September to December.²⁷ In the former season, trees are the dominant aeroallergens; while in the latter season, weeds and grasses are the dominant aeroallergens. Moulds do not show any definite seasonal trend and are present through out the year, but definitely show seasonal exacerbation in summer and winter months. Indoor fungi are, however, mainly perennial but depend on the source of the organism. Perennial AR is caused by aeroallergens, which are present all the year round in the environment. These aeroallergens are commonly found indoors. Apart from moulds, they also include dust mites, animal allergens or certain pollens and occupational allergens in areas where they may be predominantly present throughout the year.

Intradermal skin testing against locally prevalent common aeroallergens in our patients with AR showed that sensitivity was highest with pollens, fungi and house dust mite.^{11,17,28} Amongst aspergilli, sensitization to *A. flavus* was more common than other species (Fig. 1).²⁸ All patients were sensitive to at least three aeroallergens. In our study comparing “sneezers and runners” with “blockers”, we found that “blockers” had significantly more sensitization to fungi (62%) and house dust mite (40%) ($p = 0.04$).¹¹ Sensitivity to insects (66%), kapok cotton

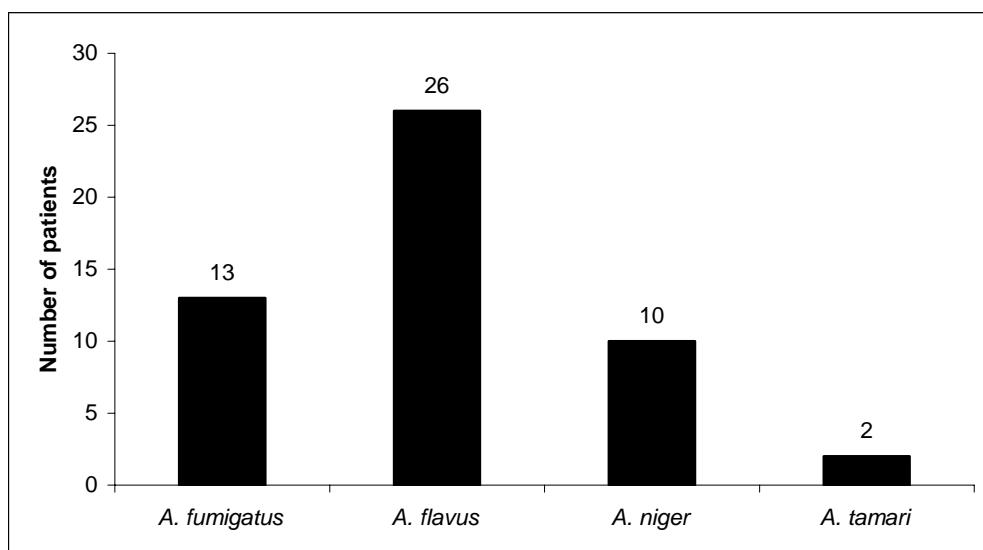


Fig. 1 *Aspergillus* skin testing in 207 patients with allergic rhinitis.

(5%) and wool (3%) was more in “sneezers-runners”, but the difference was not statistically significant (Table 1). Recently, in 207 patients with AR, we replicated that sensitization to pollens was significantly positive among patients with intermittent disease, while sensitivity to insects, fungi and house dust mite was significantly more among those with persistent disease.²⁸ Overall, house dust mite was demonstrated to be the most common allergen.^{11,28}

We also studied the relation between skin test reactivity to *Aspergillus* antigens and sinusitis in patients with AR.²⁹ Skin testing in 131 subjects demonstrated that *Aspergillus* sensitization was significantly higher in the “blockers” group as compared to “sneezers and runners”, and also significantly higher in those with associated sinusitis. Furthermore, the CT-PNS scores were significantly higher in *Aspergillus* positive “blockers” with sinusitis as compared to the *Aspergillus* negative. This comparison was not statistically significant in “sneezers and runners”. The fact that sensitization to *Aspergillus* antigens increases the severity of sinusitis associated with AR could have important clinical implications as these patients may possibly be at an increased risk for developing allergic *Aspergillus* sinusitis.

Management issues in India

In India, AR is a much overlooked disease with neither the patient nor the health care provider giving the disease the attention it deserves. The goals of management for AR include restoration of nasal patency, control of nasal secretions, treatment of nasal complications related to obstruction, and prevention of recurrent symptoms.⁷ Principles of

management are based on allergen avoidance, pharmacotherapy and immunotherapy in selected patients. The updated ARIA document¹² continues to advocate an evidence-based and step wise approach to the management of AR.

Allergen avoidance including house dust mite exposure reduction should be an integral component of management in AR. This reduces symptoms and the need for drug treatment but it may take several weeks to perceive the benefits. Topical corticosteroids are now considered as the cornerstone of the treatment for AR. Use of topical steroids has been an area of concern as undue fear, anxiety and misconception about steroid usage exists both among patients as well as treating physicians.³⁰ Most physicians rely primarily on drug safety and efficacy while prescribing these nasal sprays. Little attention has been paid to the patients’ perception and satisfaction with nasal sprays.³¹ Taking sensory attributes into consideration would enable physicians to prescribe nasal sprays that are more agreeable to their patients and thus can be given on long-term basis.³²

Currently available INCS differ little by way of efficacy and safety but vary in their sensory perceptions. In our country, physicians had a choice of four INCS to prescribe from, *viz.* beclomethasone dipropionate, budesonide, fluticasone propionate, and mometasone furoate. We also compared the preference and acceptability of these four INCS based on their sensory perceptions, in patients with AR.³³ We found that our patients preferred mometasone to other sprays due to less irritation, odour and aftertaste along with superior moistness. This led a greater acceptance and willingness to be pre-

Table 1 Skin testing with common aeroallergens among “sneezers and runners” and “blockers”

Aeroallergen	“Sneezers and runners” (n = 72)	“Blockers” (n = 42)	Statistical significance
Pollens*	61 (85%)	18 (43%)	$p < 0.05$
Insects	48 (67%)	27 (64%)	NS
Fungi	21 (29%)	26 (62%)	$p < 0.05$
Dusts	13 (18%)	18 (43%)	$p < 0.05$
House dust mite	11 (15%)	17 (40%)	$p < 0.05$
Kapok cotton	4 (6%)	2 (5%)	NS
Wool	3 (4%)	1 (2%)	NS

*includes grass, weed and tree pollens; NS, not significant.

scribed mometasone as compared to other sprays. Recently, in addition to the above four INCS, ciclesonide nasal spray was also introduced in the country. The added advantage of ciclesonide is that it can be given once a day. All INCS are reasonably priced and freely available in India. Adverse effects of INCS include transient symptoms of nasal stinging, throat irritation, dry nose, nasal bleeding and nasal septal perforation.³⁴

While categorising patients according to the ARIA classification, we found that “sneezers and runners” had a significant history of associated allergic manifestations, *viz.* eye, ear, throat, palate and skin itching.¹¹ It was thus postulated that due to these associated allergic symptoms, administration of oral antihistamines on long-term basis might possibly be required, in addition to INCS, for optimising the management. In contrast, “blockers” had a significant history of breathlessness, mouth breathing, loss of smell, and prior nasal surgeries without relief.¹¹ They also had significantly more sensitization to perennial allergens like fungi and house dust mite. Because of perennial allergen exposure, chronic persistent inflammation occurs in these patients; even during symptom-free periods.³⁵ This can have important clinical implications since “blockers” would require INCS throughout the year in view of persistent symptoms.

Conclusions

Atopic diseases often occur with associated conditions and AR is no exception. Even in India, AR is most commonly associated with asthma.^{15,16} An independent diagnosis of AR in our country is yet to be commonly accepted. In spite of causing a major impact on the quality of life in Indian patients, AR is rarely given the importance it deserves. Even patients fail to attribute the ill health to symptoms of AR and this disease continues to remain neglected.³⁶ In India, it is often treated as an ‘orphan’ disease as AR falls in the grey area between the otorhinolaryngologist and the pulmonologist resulting in lack of focus on research in AR by both the specialities.

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