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Review Article

Allergic rhinitis

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ABSTRACT

Asthma is a chronic airway inflammatory disorder, with variable severity. The mainstay of asthma management is to control symptoms. Sometimes, asthma symptoms will not be controlled in spite of optimal treatment. Many associated conditions such as allergic rhinitis, gastroesophageal reflux disease, obesity, obstructive sleep apnoea, and psychological disturbances are among a few conditions seen concomitantly in patients with asthma, which can directly/indirectly have an impact on the disease process. Influences of comorbid conditions are variable and still uncertain, but many a time alters asthma responses to treatment. Evaluation and appropriate treatment of these comorbidities should be part of asthma management.

Keywords: Asthma comorbidities, Gastroesophageal reflux, Allergic rhinitis, Obesity, Obstructive sleep apnoea

INTRODUCTION

Asthma is an airway inflammatory disorder characterised by airway obstruction. It is of variable severity and is recognised as a spectrum of diseases with varying phenotypes and endotypes, which may impact disease control.[1,2]

The main aim of asthma management is to control symptoms. It is mainly characterised by minimal/no symptoms, no nocturnal symptoms, normal activities, and most appropriate lung function test.[3,4]

Management includes patient education about pharmacotherapy and device use, avoidance measures about environmental triggers with periodic regular follow-ups. Several comorbidities can be associated with asthma as they may be responsible for appropriate disease management.

Asthma in children is unique in that comorbidities were less as compared to adults, but an increasing trend is of concern in recent times. This can impact the quality of life and increase medical expenditure.[5]

These comorbidities are associated with inadequate disease control with impacts the management of the condition.[6] The multipronged approach helps in the identification of these medical conditions, which can ameliorate patient sequelae.[7-9]

Comorbidities are underdiagnosed

Because of increasing awareness of some concomitant conditions such as allergic rhinitis (AR), obstructive sleep apnoea (OSA) is being more frequently diagnosed, than other medical

conditions. Hence, we should sensitise peers and patients alike with these conditions.

Most commonly associated comorbidities with asthma in children
Allergic rhinitis
Obesity
Obstructive sleep apnoea
Gastroesophageal reflux
Dysfunctional breathing
Psychological disturbances (especially depression and anxiety disorders)
Food allergy
Secondhand smoke exposures

Possible increased association mainly in adults and adolescents

1. Chronic rhinosinusitis – mainly in adolescents and adults
2. Hypertension, diabetes, ischaemic heart disease, and congestive heart disease – mainly in adults
3. Hormonal disturbances (adult females)
4. Vasomotor/non-AR
5. Nasal polyps and aspirin intolerance.

Only Allergic Rhinitis will be covered in detail here.

ALLERGIC RHINITIS (AR)

Rhinitis may be allergic or non-allergic.

Allergies are caused when our body's immune system reacts to certain substances (allergens) in an exaggerated manner. Allergies can develop at any age. They are more likely to develop if parents and siblings have allergy symptoms. Rarely one may outgrow the allergy over a period of time.

Nearly 20–30% of people in India suffer from allergic conditions including AR and asthma.

Mechanisms

United airway concepts point to the coexistence of upper and lower airway dysfunction.[10] Pathogenesis of AR is described in Figure 1.

The presence of rhinitis (allergic/non-allergic) increases the risk for asthma.[11] Rhinitis, severity, and sensitisation to allergens are associated with more airway dysfunction and severe asthma.[10,12]

IMPACT OF AR

a. Impaired quality of life
b. School absenteeism
c. Impeded learning
d. Decreased quality of sleep
e. Associated asthma, sinusitis, and otitis media.

RISK FACTORS FOR AR

- Family history of atopy
- Male sex
- Early use of antibiotics, in the first 12 months of life
- Maternal smoking exposure (passive/active) in the 1st year of life
- Presence of allergen-specific immunoglobulin E (IgE).[13]

CLINICAL MANIFESTATIONS

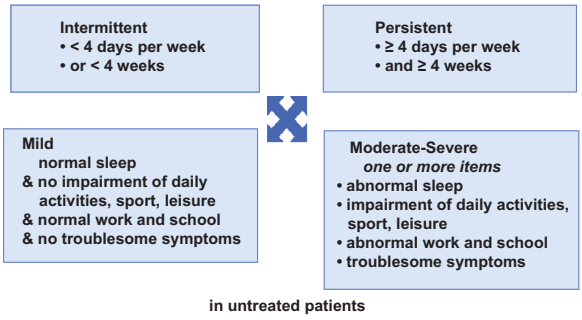
AR can be a combination of sneezing, rhinorrhoea, obstruction of the nose, and or itching. This can present in isolation or a combination of the symptoms mentioned above. In children, postnasal drip can be a presenting feature. Few people also experience itching in the ear or the palate. Many a time, AR can be associated with allergic conjunctivitis, which is overlooked when examining the patient. Always enquire about such symptoms and perform detailed upper and lower respiratory tract examinations.

Acute symptoms may alert the patients of the impairment but chronicity of symptoms may go unnoticed as patients adapt accordingly. Physical findings

- Oedema below the eyes and darkening of the skin are referred to as 'allergic shiners'
- Enhanced lines below the lower eyelid margins (Dennie-Morgan lines) can be associated with allergic conjunctivitis simultaneously
- A transverse nasal crease on the tip of the nose is caused by repeated rubbing with the hand – 'Allergic salute'
- The nasal mucosa of patients is boggy along with inferior turbinate hypertrophy

Clear rhinorrhoea may be visible anteriorly or postnasal drip.

Table 1: Allergic Rhinitis and its Impact on Asthma (ARIA) classification.



acc. to: Allergic Rhinitis and its Impact on Asthma: Allergy 2008; 63 (S86)

Table 2: Approach to allergic rhinitis clinically.[14,16]

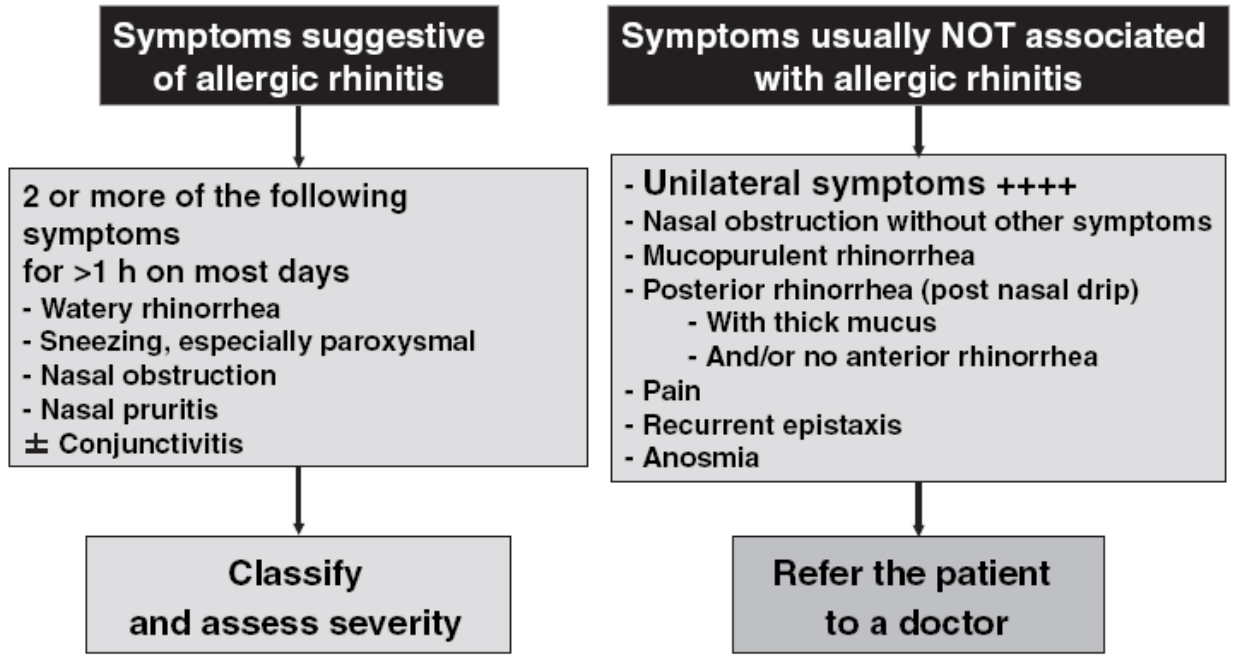


Table 3: Pharmacotherapy of allergic rhinitis.

The first line of treatment	Other possible treatments	Short term medications
Intranasal corticosteroids	Saline treatments	Decongestants (oral or intranasal)
Antihistamines (non-sedating-oral or intranasal)	Oral leukotriene antagonists	Systemic oral corticosteroids
Combination (Intranasal corticosteroids and antihistamines)	Intranasal chromones	Combination of intranasal decongestant and antihistamine sprays
	Intranasal anticholenergics	

Immune mechanisms

The World Health Organisation has created a working task force to address the issue of allergic rhinitis and its impact on asthma.[15]

ARIA classification of AR

Allergic Rhinitis and its Impact on Asthma classification is highlighted in Table 1.

Diagnostic tests in AR

In an IgE-mediated reaction; there are the following components to be considered for diagnosis.

1. Thorough clinical history for possible identification of causative allergens [Table 2]
2. Tests like allergen skin prick testing (SPT) or *in vitro,* blood tests (specific IgE immunoassay) will illustrate the presence of allergen-specific IgE.
3. To determine whether exposure to the causative allergens will result in symptoms, either by history or challenge if needed.

Investigations in AR

Skin prick tests and *in vitro*-specific IgE tests have many similarities. They demonstrate the presence of allergen-specific IgE, which is the same as saying that he or she is sensitised.

Sensitisation must precede the development of an allergic illness but is not sufficient in itself to justify a diagnosis of an allergy. Relevant history should always corroborate with the results. Skin prick tests are often used as screening tests as the advantages are many. They are cheaper (many allergens can be tested at a single sitting), results are obtained in 20 min and patients can see the results themselves which motivates them to do allergen avoidance measures. Serum IgE testing is the test of choice when:

Table 4: Intranasal steroids pharmacological properties.

Intranasal corticosteroids	First line of therapy recommended for persistent AR
Age	Different strengths have different recommendations
Frequency	Continuous is recommended, at least for 2–3 weeks. Intermittent-less effective
Advantages	1. Decreases sneezing, itchiness and runny nose 2. Decreases itchy and watery eyes 3. Decreases nasal congestion 4. Cost benefit in long-term
Disadvantages	Nasal dryness and occasional nasal bleeding

AR: Allergic rhinitis

Table 5: Different types of Intranasal steroids.

COMPOSITION OF INS	AGE ALLOWED
First-generation	
Beclomethasone	6 years and above
Flunisolide	
Second-generation	
Budesonide	
Third-generation	
Fluticasone propionate	4 years and above
Fluticasone furoate	2 years and above
Mometasone furoate	2 years and above
Triamcinolone acetonide	2 years and above
Ciclesonide	6 years and above
Budesonide dipropionate	6 years and above

a. The patient does not have enough healthy skin for SPT (e.g., severe atopic dermatitis or dermographism)
b. The patient's reaction was anaphylactic in the recent past
c. The patient cannot stop using antihistamines because it causes worsening/recurrence of symptoms.

Skin tests in AR

Skin prick test is usually more sensitive than specific IgE, though there may be a better correlation in the diagnosis of food allergies. Skin prick test may be particularly useful in:

- In uncontrolled symptoms in spite of adequate pharmacological treatment
- Inconsistent diagnosis based on history and examination
- Concurrent lower airway symptoms – Where the patient is willing to do allergen avoidance measures rather than opt for up dosing of pharmacotherapy

SPT should be avoided in symptomatic patients or during peak pollen season (in patients with known pollen allergy), as it can aggravate symptoms. Hence, it is preferred to treat the symptoms and schedule testing once better.

Table 6: Antihistamines pharmacological properties.

Anti-histamines (second-generation, non-sedating)	
Route-oral/intranasal	Rapid onset of action (may be used as a rescue medication
Frequency	1–2 times daily
Advantages	1. Decreases sneezing, itchiness, and runny nose 2. Decreases itchy and watery eyes 3. Limited effect on nasal congestion
Disadvantages	Cost

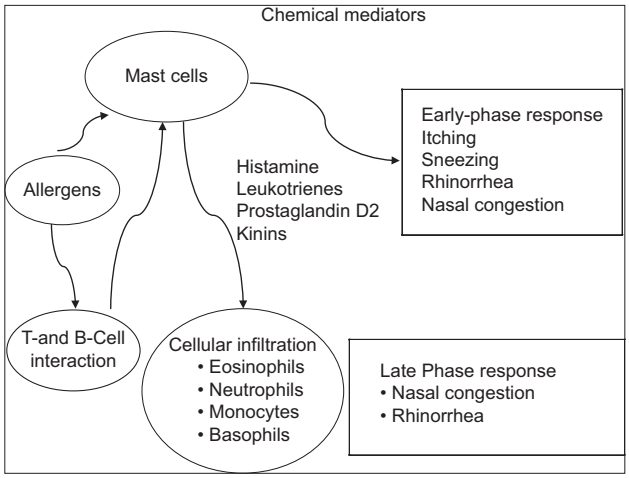


Figure 1: Pathogenesis of allergic rhinitis.[15]

1. There are certain prerequisites for a skin prick test. The patient must be off antihistamines at least 7–10 days before testing, based on the drug in action, to avoid histamine release necessary for demonstration of Type 1 hypersensitivity reaction to demonstrate degranulation of allergen-specific IgE on cutaneous mast cells
2. The patient must be well on the day of the test.

Standardised skin prick test allergen reagents are commercially available for many common aeroallergens. The allergen reagent is placed on the skin (usually the volar aspect of the forearm or the back in children) and the skin is pricked through the reagent epicutaneously involving only the dermis. The results are interpreted in 15–20 min. Positive histamine and negative controls are done in the test on each occasion [Figure 2].

For interpretation of the test, the wheal (swelling) and flare (redness) responses in 15 or 20 min are recorded. A wheel of >3 mm above the negative control is considered a positive test.

Skin prick tests for aeroallergens generally have better negative predictive value than positive predictive value. The general specificity of these tests is close to 90–95%.

Measurement of allergen-specific IgE

IMMUNOCAP is the standard test done presently to measure serum allergen-specific IgE.[17-20]

Sometimes, we do encounter a patient who has clinical features suggestive of AR, but the allergy test may be negative (both skin testing and *in vitro* testing). Such patients may be classified as chronic non-AR/or maybe having features of local AR.

Nasal challenges to an allergen or nasal cytology are tests that are limited to research and not routinely used in clinical settings.

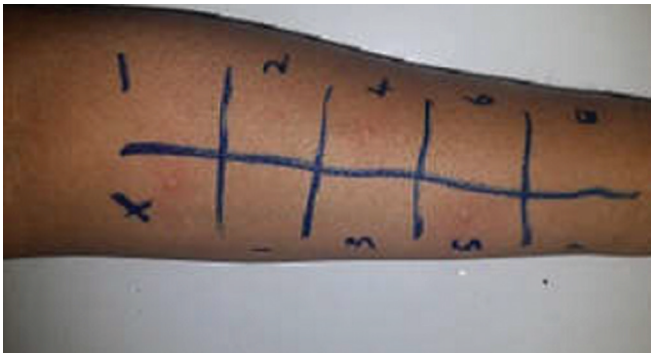


Figure 2: Allergy skin prick test for aeroallergens with histamine and saline controls.

In children <2 years of age, other differentials like adenoid hypertrophy, sinusitis, structural abnormalities like choanal atresia, and foreign body have to be considered.

PHARMCOTHERAPY

AR and its impact on Asthma classification will help in the initiation of appropriate pharmacotherapy for patients [Table 3].

The treatment principles include

- Treatment can be stepped up or stepped down according to the symptoms. Consistent use of prescribed drugs should be emphasised with proper technique of intranasal steroids [Tables 4 and 5].
- Non-sedating antihistamines are preferred as the first line of medication in mild-intermittent AR [Tables 6 and 7].

Correct administration of INS:

1. Prime the spray device (for the first time or after a period of non-use)
2. Shake the bottle after each use
3. Blow nose before spraying if blocked by mucus
4. Tilt head slightly and gently insert nozzle into the nostril
5. Aim the nozzle away from the septum (middle) of nose and direct the nozzle into the nasal passage (back or side of the nose)
6. Avoid sniffing blowing in/out for at least 15–20 min after spraying.

Table 7: Second-generation antihistamine dosage.[21]

Medication	Age range				
	6–11 mo	12–23 mo	2–5 year	6–11 years	≥12 years
Cetirizine	2.5 mg OD	2.5 mg OD/BID Or 5 mg OD	2.5–5 mg OD	5–10 mg OD	5–10 mg OD
Levocetirizine	1.25 mg OD	1.25 mg OD	1.25 mg OD	2.5 mg OD	5 mg OD
Loratadine	-	-	5 mg OD	10 mg OD	10 mg OD
Desloratadine	1 mg OD -	1.25 mg OD -	1.25 mg OD	2.5 mg OD	5 mg OD
Fexofenadine	15 mg bid (FDA USA)	15 mg bid (FDA USA)	30 mg bid	30 mg bid	60 mg bid or 180 mg OD
Bilastine	-	-	-	-	20 mg OD
Rupatadine	-	-	-	-	1 tablet (10 mg) once daily

Table 8: Efficacy of pharmacotherapeutic agents in symptom management.

Agent	EYE symptom	Itching	Sneezing	Runny nose	Nasal block
Corticosteroid (Intra nasal)	+	++	++	++	++
Decongestant (Intranasal)	-	-	-	-	++
Cromolyn (Mast Cell Stabiliser)	-	+	+	+	+
Anti-histamine (Oral)	++	++	++	++	+/-
Decongestant (Oral)	-	-	-	-	+
Anti-histamine (Nasal)	-	+	+	+	+/-
Anti-cholinergic (Topical)	-	-	-	++	-

Other treatment options [Table 8]

Saline nasal irrigation

- Clears the inflammatory mucus and thereby reduces nasal obstruction
- Usually well tolerated and acts as an adjunct with pharmacotherapy.

Intranasal chromones (e.g., sodium cromoglycate)

- Typically used for mild and intermittent rhinitis
- Mainly used for symptomatic treatment. For alleviation of symptoms for a short duration of time
- Less effective than intranasal corticosteroids.

Oral leukotriene antagonists

- Used in children/adolescents with concomitant asthma and AR
- No additional benefit if used in combination with antihistamines for the treatment of AR as it is less effective than intranasal corticosteroids
- Recently, FDA has issued a *black box* labeling of Montelukast as it may cause neuropsychiatric manifestations which are used for a long duration of time. Hence, the cost-effectiveness, duration and probable side effects must be discussed with the family and patient before initiation of the medication.

Decongestants

- Oral or nasal decongestants may be used short-term (up to 3–5 days) to reduce nasal congestion if severe
- Chronic use of intranasal decongestants may lead to a medical condition called ***Rhinitis medicamentosa, characterised by*** rebound nasal obstruction.

Allergen immunotherapy

- Allergen-specific immunotherapy – well-defined treatment for IgE-mediated allergic disease
- Administered by subcutaneous/sublingual routes
- Sublingual immunotherapy, approved in Europe and S America – in process in India; subcutaneous in India,
- Allergy immunotherapy-effective treatment for AR
- It is the only treatment modality that can change the course of allergic disease and induce allergen-specific immune response
- To be considered in patients not controlled by avoidance and medications.

WHEN TO REFER

1. Patients with persistent or recurrent symptoms, refractory to therapy
2. Concomitant asthma/sinusitis/polyp
3. Patients with impaired quality of Life.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Nil.

Conflicts of interest

There are no conflict of interest.

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ALLERGIC RHINITIS AS A COMORBID FACTOR FOR ASTHMA IN A NUTSHELL

- Allergic rhinitis is very common and causes considerable morbidity
- Adequate and appropriate treatment leads to significant improvement in quality of life in these patients
- Association with asthma is very common, warrants attention in evaluation of patients and appropriate treatment for better control of symptoms.
- Intranasal steroids are the first line of recommended treatment in moderate to severe cases
- Allergy evaluation and environmental manipulations may also have an important role in the control of disease