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PRESIDENT'S MESSAGE

Dear seniors, colleagues and friends

It is with great pride and immense pleasure that we present to you the latest edition of the Quarterly Journal of the Pediatrics Respiratory Society, Delhi, being released on the momentous occasion of Delhi Respicon 2025. This annual flagship conference of our society continues to serve as a platform where science meets collaboration, and where innovative ideas translate into improved care for our young patients.

The field of pediatric respiratory medicine is evolving rapidly. Our mission as a society has always been to bridge the gap between evidence-based medicine and practical, patient-centric care. This journal is an embodiment of that mission—an academic forum to share clinical experiences, research findings, and evolving guidelines that shape our practice.

Delhi Respicon 2025 is not just a conference; it is a celebration of our collective commitment to children's respiratory health. This year's program brings together leading experts, researchers, and clinicians, promising an exchange of knowledge that will inspire us to push the boundaries of excellence in pediatric respiratory care. I am confident that the insights gained here will pave the way for improved outcomes and holistic well-being for our young patients.

I would like to express my heartfelt gratitude to all contributors, reviewers, and the editorial team led by Dr. Anil Sachdev who has worked tirelessly to bring this journal to life. Your dedication and passion for academic pursuit have made this publication a valuable resource for every pediatrician and postgraduate student alike.

As we release this issue during the inaugural function of Delhi Respicon 2025, I extend my warmest wishes to all participants. May this conference and our journal continue to ignite curiosity, foster collaboration, and strengthen our resolve to provide the best respiratory care to children.

With warm regards,

Dr. Rakesh K. Dogra
President
Pediatrics Respiratory Society, Delhi

INDIAN PERSPECTIVES ON PEDIATRIC ANAPHYLAXIS: DIAGNOSIS, TREATMENT, AND PREVENTION.

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Abstract

Purpose: This review provides an updated overview of pediatric anaphylaxis, focusing on its epidemiology, clinical features, diagnostic strategies, and management, with a special emphasis on challenges specific to low- and middle-income countries like India.

Overview: Anaphylaxis is a rapid-onset, multisystem hypersensitivity reaction that can be lifethreatening if not promptly recognized and treated. The incidence of pediatric anaphylaxis has been rising globally over the last two decades, with food allergens such as milk, eggs, peanuts, and tree nuts being the most common triggers in children. Drug-induced and insect venomrelated anaphylaxis are also significant contributors, particularly in hospital-based settings. The clinical manifestations vary with age, often making diagnosis more difficult in infants and young children. While the NIAID/FAAN criteria remain the cornerstone for clinical diagnosis, laboratory tools such as serum tryptase and allergen-specific IgE can offer supportive evidence. Intramuscular epinephrine remains the cornerstone of anaphylaxis management and must be administered promptly, as any delay significantly increases the risk of severe outcomes or fatality. This should be accompanied by airway support and circulatory stabilization as part of initial resuscitation. Adjunctive therapies, such as corticosteroids, antihistamines, and inhaled bronchodilators, may aid in symptom relief but must not substitute for or delay epinephrine administration.

Problems in India: India faces unique challenges in the diagnosis and management of pediatric anaphylaxis. National epidemiological data are scarce, and underdiagnosis is common due to poor awareness among frontline healthcare providers. Most reported cases come from urban tertiary centers, overlooking the burden in rural and underserved areas. Access to epinephrine auto-injectors remains limited due to cost and availability, leading to delayed treatment. Cultural factors, traditional medicine use, and dietary diversity further complicate allergen identification. Moreover, structured emergency protocols and follow-up care, including action plans and allergen testing, are inconsistently implemented.

Conclusion: Pediatric anaphylaxis is a growing public health concern that requires heightened clinical vigilance, especially in young children, where symptoms may be atypical. While advances in diagnosis and treatment exist, gaps in awareness, access, and standardized care remain, particularly in India. Strengthening healthcare provider training, improving access to epinephrine, and implementing structured follow-up plans are essential steps toward reducing morbidity and mortality associated with pediatric anaphylaxis.

Keywords: Pediatric anaphylaxis, Hypersensitivity reaction, Epinephrine, Food allergy, Biphasic anaphylaxis, Anaphylaxis Diagnosis

Introduction

Anaphylaxis is a severe, systemic hypersensitivity reaction that is rapid in onset and potentially fatal. It typically involves multiple organ systems, most notably the skin, respiratory tract, cardiovascular system, and gastrointestinal tract. The World Allergy Organization **(WAO)** defines anaphylaxis as "a serious allergic reaction that is rapid in onset and may cause death" [1]. The National Institute of Allergy and Infectious Diseases/Food Allergy and Anaphylaxis Network **(NIAID/FAAN)** criteria describe it as an acute illness with involvement of the skin or mucosal tissue accompanied by respiratory compromise, hypotension, or signs of end-organ dysfunction following exposure to a likely allergen [2]. In the pediatric population, common triggers include food allergens, insect venom, medications, and latex [3]. Globally, the incidence of anaphylaxis has shown a rising trend over the past two decades, with pediatric cases contributing significantly to this increase [4–6]. Although fatalities are rare in children, delayed recognition and sub optimal administration of intramuscular epinephrine are recognized contributors to morbidity and mortality [7,8]. In India, the burden of pediatric anaphylaxis is likely underestimated due to limited epidemiological data, poor awareness among healthcare providers, and under reporting. [9,10]. Given the potential for rapid deterioration, timely recognition and appropriate first-line treatment are critical. This review aims to provide an updated overview of the epidemiology, clinical features, and management of pediatric anaphylaxis, with an emphasis on the unique challenges encountered in low- and middle-income countries.

Epidemiology

Anaphylaxis is increasingly recognized as a significant public health concern worldwide, with rising incidence in both adult and pediatric populations. However, data specific to children reveal unique epidemiological patterns influenced by age, geography, allergen exposure, healthcare access, and diagnostic practices.

The global incidence of anaphylaxis is estimated to range between 50 and 112 episodes per 100,000 person-years, with children accounting for a substantial proportion of these cases [11]. In pediatric populations, the incidence appears lower than in adults but is on a consistent upward trajectory. In a report from the United Kingdom, hospital admissions for anaphylaxis in children increased by over 600% between 1992 and 2012, particularly among those under 5 years of age [4]. Similar trends have been reported in Australia and the United States, where emergency department visits and hospitalizations for anaphylaxis in children have more than doubled in the last two decades [6,12]. The incidence is highest in children aged 0–4 years and adolescents, likely reflecting patterns of food introduction and risk-taking behavior. A systematic review reported that the pooled global incidence in children was approximately 20–50 per 100,000 person-years, with higher estimates in North America and Europe than in Asia or Africa

[5]. Mortality due to pediatric anaphylaxis remains low, estimated at <1 per million annually in most developed countries [5,7]. However, deaths do occur, often due to delayed epinephrine administration, coexisting asthma, or unrecognized biphasic reactions.

Common Triggers

In children, food allergens are the most frequent cause of anaphylaxis, accounting for more than 80% of cases in many high-income countries. The most common triggers vary with age: cow's milk and egg predominate in infants and toddlers, while peanuts, tree nuts, and shellfish are more frequently implicated in older children and adolescents. Non-food triggers include insect stings, medications—particularly antibiotics, nonsteroidal anti-inflammatory drugs (NSAIDs), and vaccines—as well as latex, especially among children who have undergone multiple surgeries. Less commonly, exercise-induced, idiopathic, and immunotherapy-related anaphylaxis are reported, particularly in adolescents [13].

In the Indian context, there is a paucity of nationally representative data on pediatric anaphylaxis. Most published literature originates from urban tertiary care centers and likely underestimates the true burden, especially in rural and underserved areas[14]. Food allergens such as milk, egg, wheat, and seafood are increasingly recognized as important triggers [15]. Iatrogenic causes, including antibiotics (notably penicillins and cephalosporins), NSAIDs, and intravenous contrast agents, are prominently featured in hospital-based case series [10]. In contrast, insect stings and environmental allergens appear to be underreported, possibly due to limited recognition or inadequate clinical documentation. A multicentric study conducted by Kumar et al. involving several tertiary care centers across India revealed that 30% of pediatric anaphylaxis cases were attributed to food allergens, while over 40% were drug-induced [9].

Geographical and cultural factors further influence allergen profiles across the country. In northern India, wheat and lentils have been reported as emerging food allergens, whereas shellfish allergy appears more prevalent in coastal southern regions. Cultural practices such as the use of traditional or alternative medicines and religious dietary restrictions may also modulate exposure patterns and complicate the clinical identification of allergens [9,10].

Pathophysiology of Anaphylaxis

Anaphylaxis is a rapid-onset, life-threatening hypersensitivity reaction resulting from systemic activation of mast cells and basophils. These immune cells release potent mediators such as histamine, tryptase, leukotrienes, prostaglandins, and cytokines, leading to widespread vasodilation, increased vascular permeability, bronchoconstriction, and mucosal edema, manifesting clinically as multi-organ dysfunction.

In children, the predominant mechanism is immunoglobulin E (IgE)-mediated, or type I hypersensitivity. Initial allergen exposure activates T-helper 2 (Th2) cells, stimulating B cells to produce allergen-specific IgE.

These IgE antibodies bind to high-affinity FcεRI receptors on mast cells and basophils, sensitizing them. Upon re-exposure, allergen-induced cross-linking of IgE leads to degranulation and release of preformed and newly synthesized mediators. Histamine, a primary preformed mediator, induces vasodilation, capillary leakage, and bronchial smooth muscle contraction, responsible for urticaria, angioedema, hypotension, and bronchospasm. Leukotrienes (LTC , LTD) and prostaglandin D (PGD) enhance bronchoconstriction and vascular permeability, while platelet-activating factor (PAF) has been associated with severe and fatal reactions [16]. Cytokines such as TNF-α and interleukins (IL-4, IL-5, IL-13) further contribute to sustained inflammation and tissue infiltration [17].

Non-IgE-mediated anaphylaxis, often referred to as "non-immunologic" or "anaphylactoid," does not involve prior sensitization. Instead, it results from direct mast cell activation or complement pathways, commonly triggered by agents such as radiocontrast media, opioids, vancomycin, and physical stimuli like cold or exercise. These reactions may be mediated via the Mas-related G protein–coupled receptor X2 (MRGPRX2), bypassing the classical IgE-FcεRI pathway [18].

Several factors influence the severity and rapidity of anaphylactic reactions, including the dose and route of allergen exposure, the patient's age, comorbid conditions such as asthma, and the presence of cofactors like physical exertion, alcohol consumption, and nonsteroidal anti inflammatory drug (NSAID) use. [19] Among these, poorly controlled asthma significantly increases the risk of severe and potentially fatal respiratory compromise in children. Biphasic anaphylaxis, characterized by a recurrence of symptoms after initial resolution without further exposure to the allergen, has been reported in approximately 4% to 20% of pediatric cases. This phenomenon is thought to result from a secondary, delayed immune response following the initial IgE-mediated mast cell degranulation. Proposed mechanisms include persistent or resensitized mast cells, sustained synthesis of late-phase mediators such as cytokines and eicosanoids, and recruitment of inflammatory cells, including eosinophils and basophils. Protracted anaphylaxis, although relatively rare, presents as a prolonged episode lasting several hours to days and often necessitates intensive care support. It is believed to arise from ongoing mast cell activation, delayed allergen clearance, and immune dysregulation, leading to persistent clinical manifestations despite timely and appropriate therapeutic intervention. [20]

Clinical Manifestations of Anaphylaxis in Children (Age-wise Presentation)

The clinical presentation of anaphylaxis varies with age, influenced by immune system maturity, communication ability, and organ system dominance. While the patho-physiological processes are similar across age groups, the manifestations differ in both frequency and form. Prompt recognition requires a high index of suspicion, especially in infants and young children, where classical symptoms may be absent or atypical.

Infants (<1 year): Anaphylaxis in infants is frequently underdiagnosed due to nonspecific signs. Cutaneous features, such as **facial flushing, urticaria, or angioedema**, are commonly seen but may be subtle or misattributed to benign rashes.

Persistent irritability, inconsolable crying, sudden pallor, hypotonia, and refusal to feed are red flags that may suggest an anaphylactic reaction in this age group (21). Respiratory signs include **stridor, wheeze, grunting, and nasal flaring.** Vomiting and diarrhea can occur but are often underappreciated as allergic signs. Importantly, **hypotension and cardiovascular collapse** may be late or sole presentations, particularly in rapidly progressing cases (22).

Toddlers (1–3 years): Toddlers frequently present with **urticaria, angioedema (especially of the face, lips, and periorbital region), vomiting, and respiratory distress,** including wheezing and coughing. As in infants, cardiovascular signs such as pallor, tachycardia, or lethargy should not be overlooked (23).

Preschool and School-aged Children (4–10 years): In this age group, children are better able to describe their symptoms, allowing for earlier identification. Common complaints include an **itchy mouth, throat tightness, chest tightness, or difficulty breathing.** They usually present with **generalized urticaria, facial and periorbital edema, wheezing, hoarseness, stridor, and vomiting.** Respiratory symptoms are prominent and may dominate, especially in children with comorbid asthma. Cardiovascular manifestations, such as **dizziness, syncope, or altered mental =status**, occur in more severe cases but remain less frequent than in adults (24). Gastrointestinal symptoms, including **abdominal cramps, diarrhea, and nausea,** are common and may precede more serious respiratory or cardiovascular involvement.

Adolescents (11–18 years): Adolescents present with a broader range of symptoms, often mirroring adult patterns. They may exhibit **multi-system involvement:** generalized urticaria, **bronchospasm, hypotension, and syncope** are all common. Due to greater allergen exposure, reactions can be more severe and rapid onset. They are more likely to engage in behaviors that act as cofactors (e.g., exercise, NSAID use, alcohol), increasing the risk of **biphasic or severe anaphylaxis** (19). They can accurately describe symptoms like **anxiety, palpitations, or chest tightness**, which can aid in early recognition.

Clinical Diagnostic Criteria

Anaphylaxis is primarily a **clinical diagnosis**, especially in the pediatric age group, where rapid recognition and treatment are vital. The most widely accepted clinical diagnostic criteria are those proposed by the **NIAID/FAA**, endorsed by the **WAO,** and followed in pediatric guidelines globally (13,17). These criteria require **any one of the three clinical scenarios** to establish the diagnosis. **(Table 1)** These criteria are estimated to have a sensitivity of >95% for clinical diagnosis in children. In pediatric practice, especially in infants and toddlers, clinicians should be aware that **cutaneous manifestations may be absent,** and presentations may include **isolated hypotonia, sudden behavioral changes, or respiratory distress.**

Table 1. The National Institute of Allergy and Infectious Diseases (NIAID) criteria for diagnosing Anaphylaxis.

NIAID Clinical Criteria (2006)

Anaphylaxis is highly likely when any one of the following 3 criteria are fulfilled:

1. Acute onset of illness (minutes to several hours) involving the skin, mucosa, or both (e.g., hives, pruritis, flushing, swollen lips-tongue-uvula, angioedema), plus at least one of the following:
- ➤ Respiratory compromise (e.g., dyspnea, wheeze, stridor, reduced PEF, hypoxemia)
- ➤ Reduced blood pressure or symptoms of end-organ dysfunction (e.g., hypotonia, collapse, syncope)

2. Two or more of the following occurring rapidly after exposure to a likely allergen:
- ➤ Skin-mucosal involvement
- ➤ Respiratory compromise
- ➤ Reduced blood pressure or associated symptoms
- ➤ Persistent gastrointestinal symptoms (e.g., crampy abdominal pain, vomiting)

3. Reduced blood pressure after exposure to a known allergen:
- ➤ For infants and children: age-specific low systolic blood pressure (e.g., <70 mmHg in infants, <(70 + 2 × age in years) mmHg in children aged 1–10 years) or >30% decrease from baseline

Laboratory Diagnosis of Pediatric Anaphylaxis:

Tools and Clinical Significance Although the diagnosis of anaphylaxis in children is primarily clinical, laboratory investigations can provide supportive evidence, especially when the diagnosis is uncertain, when medicolegal documentation is needed, or in atypical presentations. In pediatric populations, lab markers also play a role in distinguishing anaphylaxis from mimicking conditions, identifying high-risk patients, and confirming mast cell activation after the acute episode has resolved. However, the timing and interpretation of these tests are critical, and their use must be tailored to the clinical context

1. Serum Tryptase: Serum tryptase is the most widely used laboratory marker of mast cell activation. It is a protease stored in mast cell granules and released into circulation during degranulation. Tryptase levels peak 1 to 2 hours after symptom onset and usually return to baseline within 6 to 8 hours. In children, particularly in food-induced anaphylaxis, tryptase may not rise significantly, whereas it is more likely to be elevated in insect venom, drug, or perioperative reactions (1,2). A clinically meaningful elevation is defined using the formula recommended by the World Allergy Organization: Post-event tryptase > (1.2 × baseline tryptase + 2 ng/mL).

2. Plasma Histamine and Urinary Histamine Metabolites: Plasma histamine rises rapidly within 5–15 minutes after mast cell activation and declines within 30–60 minutes, making timely collection challenging. Alternatively, 24-hour urinary excretion of histamine metabolites such as N-methylhistamine may provide supportive evidence but has limited clinical availability. (2)

3. Platelet-Activating Factor (PAF) and PAF-Acetylhydrolase (PAF-AH): PAF is a potent lipid mediator released during anaphylaxis, and high levels correlate with reaction severity. Low activity of its degrading enzyme, PAF-AH, has been associated with fatal and near-fatal anaphylactic episodes (16). However, no commercial test is yet available for clinical use.

4. Baseline Serum Tryptase: Measuring baseline tryptase (at least 24–48 hours after resolution) is recommended in children with severe or recurrent anaphylaxis or when symptoms are disproportionately intense. Helps recognize patients more likely to develop profound hypotension or protracted anaphylaxis and may guide the need for more intensive emergency preparedness and long-term management planning. Persistently elevated baseline tryptase may suggest mastocytosis or hereditary alpha-tryptasemia. (2)

5. Allergen-Specific IgE and Skin Prick Testing: These are not diagnostic of anaphylaxis per se, but are essential for identifying the culprit allergen. Testing is typically performed 2–3 weeks after the acute episode, when mast cell reactivity normalizes. However, both can yield false positives due to sensitization without clinical allergy, and false negatives in cases of cofactordependent anaphylaxis or mast cell desensitization post-reaction.

Severity Grading in Pediatric Anaphylaxis: Systems

Severity grading in pediatric anaphylaxis is essential for standardized diagnosis, clinical decision-making, and risk stratification. Several grading systems have been proposed, but two are predominantly used in pediatric practice. (Table 2) First and the most commonly used classification is the Brown Grading System (Australia), developed by Simon G. A. Brown. This system categorizes anaphylaxis into three severity grades—mild, moderate, and severe—based on clinical involvement of different organ systems. (17) The second commonly used system is the Ring and Messmer Classification, originally developed in Europe for perioperative anaphylaxis. It provides a more detailed, four-tiered grading of severity and is particularly useful in settings requiring a more detailed assessment. (24)

Table 2. Common Anaphylaxis Severity Grading System

Brown Grading System

Mild reactions are limited to skin and subcutaneous tissue (e.g., urticaria, angioedema).
Moderate reactions include respiratory symptoms (e.g., wheezing, stridor) or gastrointestinal symptoms (e.g., vomiting, abdominal pain).
Severe anaphylaxis involves hypoxia, hypotension, neurological impairment, or cardiovascular collapse.

Ring and Messmer Classification

Grade I: Generalized cutaneous symptoms (e.g., flushing, urticaria)
Grade II: Moderate systemic symptoms (e.g., tachycardia, dyspnea, nausea)
Grade III: Life-threatening symptoms (e.g., shock, arrhythmias, severe bronchospasm)
Grade IV: Cardiac and/or respiratory arrest

Clinical Significance of Severity Grading

The clinical utility of severity grading extends beyond diagnosis. In acute care, grading guides the urgency of epinephrine administration, the need for hospital or ICU admission, and the duration of observation (particularly in moderate to severe reactions where biphasic anaphylaxis is a concern). Grading also helps identify children at risk for future severe episodes, influencing allergen avoidance strategies and decisions about prescribing self-injectable epinephrine.

In India, no single national guideline mandates a specific grading system, but the Brown grading system is the most commonly adopted in pediatric emergency settings, especially in tertiary hospitals and allergy centers. Its ease of use, clinical relevance, and compatibility with WHO's emergency triage protocols make it a pragmatic choice (26).

Treatment of Pediatric Anaphylaxis: A Comprehensive Clinical Approach

Basic Emergency Care: Airway and Circulatory Stabilization Early recognition of anaphylaxis must be followed immediately by supportive care, focusing on airway, breathing, and circulation (ABC). The child should be placed in a supine position with legs elevated to enhance venous return, unless respiratory distress or vomiting necessitates another posture. High-flow oxygen should be administered via a face mask in all moderate to severe cases. In cases with stridor, hoarseness, or significant tongue/laryngeal swelling, early airway intervention, including intubation, may be required. Simultaneously, intravenous access should be established to deliver 20 mL/kg boluses of isotonic fluids, particularly in hypotensive children (27-29).

Epinephrine: The First-Line and Life-Saving Treatment

Epinephrine remains the single most critical intervention in the treatment of anaphylaxis, acting on alpha and beta adrenergic receptors to reverse vasodilation, reduce mucosal edema, and alleviate bronchospasm. It should be administered intramuscularly in the mid-anterolateral thigh as soon as anaphylaxis is suspected. The recommended dose is 0.01 mg/kg of 1:1000 solution (1 mg/mL), with a maximum single dose of 0.3 mg for children and 0.5 mg for adolescents. If symptoms persist or recur, doses can be repeated every 5 to 15 minutes. Delay in epinephrine use is strongly associated with poorer outcomes, including respiratory failure and biphasic reactions. Intravenous epinephrine may be considered only in cases of refractory hypotension and must be administered as a controlled infusion with cardiac monitoring (2,24,27).

Role of Corticosteroids

Corticosteroids, such as methylprednisolone (1–2 mg/kg IV) or prednisolone (1–2 mg/kg orally), are often administered in pediatric anaphylaxis to reduce the risk of biphasic or protracted reactions. However, their onset of action is delayed (4–6 hours), and they do not play a role in acute symptom relief. While widely used, current evidence supporting their efficacy in preventing biphasic reactions is

weak, and they should never delay epinephrine administration. Their utility lies more in cases with severe, prolonged symptoms or where there is a history of recurrent biphasic reactions (23,28).

Role of Antihistamines

Antihistamines, including H1 receptor blockers such as diphenhydramine or cetirizine, provide symptomatic relief from urticaria, pruritus, and angioedema. They are not effective in treating respiratory or cardiovascular symptoms and should only be used as adjuncts after epinephrine administration. H2 blockers, like ranitidine, may be added in cases with persistent gastrointestinal or cutaneous symptoms. These agents do not prevent life-threatening manifestations and should not be used as monotherapy for anaphylaxis (27).

Nebulized Therapy in Respiratory Symptoms

Inhaled bronchodilators are indicated for children presenting with symptoms such as wheezing or bronchospasm. Salbutamol administered via nebulizer or metered-dose inhaler with a spacer can relieve bronchoconstriction. In cases of upper airway edema or stridor, nebulized epinephrine may reduce mucosal swelling and improve airway patency. These therapies are supportive and should be used alongside, not instead of, systemic epinephrine (2).

Discharge Planning and Allergy Action Plan

Upon stabilization, all children should be observed in a healthcare setting for a minimum of 4 to 6 hours, or longer if they had severe reactions, required multiple doses of epinephrine, or have risk factors for biphasic anaphylaxis. Families should be provided with a written anaphylaxis action plan, detailing the child's allergen(s), early warning signs, and emergency steps, including epinephrine administration. Parents and caregivers must be trained in the recognition of anaphylaxis and the use of epinephrine devices (23,29).

Who Should Be Prescribed Epinephrine Auto-Injectors?

Children who have experienced a prior anaphylactic reaction, particularly to food, venom, or idiopathic triggers, should be prescribed an epinephrine auto-injector. Additional criteria include those with asthma and food allergies, mast cell disorders, or a history of biphasic or severe reactions. Devices such as EpiPen Jr (0.15 mg/Green package) are recommended for children weighing 15–30 kg, and EpiPen (0.3 mg/Yellow package) for those over 30 kg. Prescriptions should always be accompanied by detailed demonstration and return demonstration to ensure correct usage (2,27). In India, where auto-injectors may be expensive or unavailable, caregivers can be trained to use preloaded epinephrine syringes.

Identification and Avoidance of Allergens: An essential component in both acute management and long-term prevention of pediatric anaphylaxis is the identification and strict avoidance of the inciting allergen. A thorough clinical history is vital, followed by confirmatory testing, such as serum allergen-specific IgE assays or skin prick testing, which should be conducted at least 2–3 weeks after the resolution of the acute episode to avoid false negatives. (23,24)

CONCLUSION

Pediatric anaphylaxis constitutes a rapidly progressive and potentially fatal hypersensitivity reaction necessitating prompt recognition and timely administration of intramuscular epinephrine, which remains the definitive first-line therapy. Although the global incidence is increasing, especially among children, significant disparities in awareness, diagnosis, and management persist, particularly in low- and middle-income countries. Food allergens represent the most common triggers, with notable variations based on age and regional dietary practices. Enhancing healthcare provider education, ensuring the availability of epinephrine auto-injectors, and implementing individualized anaphylaxis action plans are imperative. A coordinated, evidence-based approach is essential to mitigate morbidity, prevent recurrenc e, and improve overall clinical outcomes in the pediatric population.

KEY MESSAGES

- Food allergens are the most common cause of pediatric anaphylaxis, with age-specific trigger patterns.
- Clinical manifestations vary by age, necessitating tailored recognition strategies.
- Prompt diagnosis and timely intramuscular epinephrine administration are critical for optimal outcomes.
- Delayed recognition and limited epinephrine use significantly increase the risk of morbidity.
- Long-term management requires allergen identification, caregiver education, and a personalized action plan.

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GINA 2025: KEY UPDATES FOR THE DIAGNOSIS AND MANAGEMENT OF ASTHMA IN CHILDREN

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Abstract: Asthma remains a prevalent chronic respiratory disease in children, with significant health implications. The 2025 Global Initiative for Asthma (GINA) guidelines introduce several key updates, particularly emphasizing diagnostic and management strategies for children under five years of age. Notably, the new guidelines permit a definitive asthma diagnosis in this age group based on a syndromic approach requiring recurrent wheezing, absence of alternative diagnoses, and a timely response to asthma therapy. Treatment updates include a stepwise approach centered around daily low-dose inhaled corticosteroids (ICS) and as-needed shortacting beta-agonists (SABA), with careful reassessment of diagnosis, inhaler technique, and adherence before stepping up therapy. The use of ICS-formoterol as a reliever therapy is under investigation for preschoolers. For acute exacerbations, intravenous magnesium sulfate is emphasized, while nebulized magnesium is no longer recommended. In adolescents and adults, diagnostic criteria are refined to clarify that fixed airflow limitation is not required, and biomarkers such as FeNO and blood eosinophils are increasingly incorporated to guide diagnosis and therapy. Treatment continues to prioritize ICS-formoterol over SABA for better outcomes, with further emphasis on personalized care and risk stratification. The 2025 guidelines reflect a shift towards precision medicine, highlighting the importance of early diagnosis, appropriate biomarker use, and individualized management across all age groups.

Asthma is one of the most common chronic respiratory conditions in childhood and is a serious health issue. The Global Initiative for Asthma (GINA) publishes a strategy report every year containing recommendations on diagnosis and management of asthma based on the latest evidence. The 2025 GINA guidelines continue to emphasize a syndromic approach to diagnosis based on history of characteristic symptom patterns and evidence of variable flow limitation.

While, the long term goals of asthma management in all age groups remain the same (long term asthma symptom control and risk minimization), this review is a summary of the most important updates in the 2025 edition of GINA related to diagnosis and management strategies for childhood asthma.

Key Changes in GINA 2025

1. Diagnosis of asthma in children less than 5 years There has been an extensive review and revision of this section in GINA 2025 guidelines. The most important change is that children under five years of age can be diagnosed as asthma. The diagnostic criteria for asthma in children younger than five years include: 1. Recurrent acute episodes of wheezing with or without interval asthma symptoms 2. Alternative diagnosis is unlikely to cause these symptoms and 3. Timely clinical response to acute short acting beta agonist (SABA) or long term inhaled corticosteroid (ICS) asthma treatment. All three criteria must be fulfilled for diagnosis of asthma in this age group. If only 1 or 2 criteria are fulfilled describe as 'suspected asthma' and continue follow up.

The recurrent acute wheezing episodes are defined as at least two acute episodes lasting >24 hours in last 12 months with asthma-like symptoms i.e wheezing on expiration, accessory muscle use, difficult and/or fast breathing with wheezing confirmed during at least one episode or at least one wheezing episode lasting > 24 hours with wheezing confirmed and presence of asthma-like symptoms in between the wheezing episodes (interval symptoms). Episodes may occur with or without upper respiratory tract infections and /or in response to other triggers e.g. exposure to allergens or irritants. The alternative diagnosis for respiratory symptoms should be ruled out on the basis of thorough medical history, examination and investigations if required. The younger the child, the greater the likelihood of an alternative diagnosis. If there is suboptimal response to a trial of bronchodilator particularly in an infant, consider alternative diagnosis and refer to an expert. The differential diagnosis to be considered are depicted in Table 1. The key indicators for referral include failure to thrive, neonatal or very early onset of symptoms, vomiting associated with respiratory symptoms, continuous wheezing, recurrent stridor, barking cough, no association of symptoms with typical triggers, focal lung or cardiovascular signs or finger clubbing or hypoxemia < 95%. Timely clinical response is considered if there is an appropriate response to inhaled SABA including symptomatic improvement to SABA within 20-60 minutes of administration or decrease in frequency of wheezing episodes/ asthma like symptoms with a diagnostic trial of daily ICS for 2-3 months via pMDI and spacer.

Table 1: Differential diagnosis of asthma in children 5 years and younger

➤ Mainly cough and congested nose without wheezing or difficulty breathing.	➤ Viral respiratory tract infections
➤ Coughing/choking while feeding with recurrent chest infections	➤ Gastroesophageal reflux
➤ Protracted paroxysms of coughing	➤ Pertussis
➤ Noisy breathing while crying, barking seal like cough	➤ Tracheomalacia
➤ Cardiac murmurs, failure to thrive	➤ Congenital heart disease
➤ Preterm, symptoms since birth	➤ Bronchopulmonary dysplasia
➤ Wet Cough, mucus production, FTT, gastrointestinal symptoms	➤ Cystic Fibrosis
➤ Wet cough, recurrent chest infections, neonatal respiratory distress, chronic ear infections, persistent nasal discharge	➤ Primary Ciliary Dyskinesia
➤ Noisy breathing, feeding difficulties	➤ Vascular Ring
➤ Recurrent fever, other site infections	➤ Immunodeficiency

2. Tests to assist in diagnosis: No test can diagnose asthma in under 5 children. However, following tests are useful adjuncts.

a. Tests for allergic sensitization: Sensitizations to allergens can be assessed using a skin prick test or allergen specific IgE test. The presence of allergen sensitization can aid in diagnosis, however the absence of this does not rule out a diagnosis of asthma,

b. Chest X-Ray: A plain radiograph can aid to exclude structural abnormalities such as congenital lobar emphysema, vascular ring, tuberculosis, inhaled foreign body, etc. Other imaging can be considered depending on the condition being considered.

c. Lung function tests: Most under 5 children are not able to perform the expiratory maneuvers. Alternative tests such as impulse oscillometry may help in diagnosis in children above three years of age.

d. Exhaled Nitric Oxide: This test is not widely available and is currently limited to research purpose. However, an elevated FeNO in a preschool child with coughing and wheezing predicted an increased odds of asthma by school age.

3. Treatment of asthma in children less than 5 years: The management goals for children under 5 years are similar to those in older patients. These include 1. To achieve best possible control of symptoms and maintain normal activity. 2. To minimize the risk of flare ups, impaired lung development and medication side effects. This is achieved through the continual cycle: Assess, Adjust and Review response. The GINA Strategy Report 2025 updates the therapeutic approach to asthma in children under 5 years of age with a confirmed diagnosis. A step-wise treatment approach is recommended. Treatment typically involves long-term, daily low-dose ICS to keep asthma well controlled, and reliever medications can be used for as-needed symptom relief. The recommended reliever among preschoolers with asthma is SABA as needed when symptoms occur, using a pressurized metered-dose inhaler (pMDI) with a mouthpiece or facemask as appropriate. Symptoms more than twice a week over a 1 month period indicates the need for a trial of low dose ICS treatment (Step 2). When symptoms are not well controlled after 2 to 3 months on initial treatment with low-dose ICS, or if there are continued exacerbations, clinicians may consider doubling the low daily ICS dose plus as-needed SABA (Step 3). However, before stepping up, confirm the diagnosis, check and correct inhaler technique, confirm good adherence and control the risk factors such as environmental allergens or snoke. If asthma symptoms are still not well controlled, the patient's inhaler technique and medication adherence should be reassessed, along with environmental factors, reconsider the diagnosis of asthma and the patient can be referred to a specialist for advice (Step 4). New alternatives are currently being investigated, such as low-dose ICS-formoterol as an anti-inflammatory reliever therapy in this age group.

4. Asthma exacerbations in children less than 5 years:

➤ The recommendation to use intravenous magnesium sulfate in moderate or severe exacerbations is reinforced.

➤ The use of nebulized magnesium sulfate is no longer recommended.

➤ Changes to the dosing of inhaled medications during intensive care have been included. Treatment with bronchodilator and oxygen if needed: SABA, 4 to 6 puffs of salbutamol (albuterol) 100 mcg/actuation by pMDI with spacer or 0.25 mg by nebulizer, given once for mild exacerbations and every 20 minutes for 3 total doses during the first hour, for moderate or severe exacerbations; and oxygen, if needed, to maintain saturation at least 94%. Consider adding ipratropium bromide (250 mcg) by nebulization every 20 minutes with SABA and oral corticosteroids (1-2mg/kg of oral prednisolone or 0.3-0.6 mg/kg of oral dexamethasone or 1 mg/kg 6 hourly of intravenous methylprednisolone)

➤ The target oxygen saturation has changed from 94-98% to ³94%, with a reminder to consider skin color and to make altitude adjustments if relevant (for this and all age groups).

5. Diagnosis of asthma in adults and adolescents: The diagnostic algorithm for asthma in adults and adolescents has been revised to make it clearer. The term variable expiratory airflow limitation has been replaced by variable expiratory airflow. It has also been clarified that airflow limitation is not a necessary criteria for diagnosis of asthma since it is characteristically variable in a patient of untreated asthma and may not be present at the time of diagnostic assessment. The limited role of biomarkers was added (Appendix A of GINA guidelines 2025). While the lung function assessment with spirometry or peak expiratory flow rate remains the first choice to confirm the diagnosis, in patients with typical asthma symptoms, if these tests are not available or the testing is negative, elevated FeNO (adults/adolescents>50ppb;children>35ppb) or blood eosinophils above national/regional reference range can support the diagnosis of Type 2 asthma. However, lower levels of FeNo or blood eosinophil counts does not rule out asthma.

6. Treatment recommendations in adults and adolescents:

➤ GINA 2025 maintains the two-track treatment strategy for adolescents and adults, prioritizing Track 1 with ICS-formoterol as the anti-inflammatory reliever medication (when available), since it reduces the risk of severe exacerbations, corticosteroid exposure, and urgent care needs compared to SABA (Short-Acting Beta 2-Agonist)based regimens.

➤ In Track 2, Step 4 has changed from medium-to-high dose ICS-LABA to medium dose ICS-LABA (Inhaled corticosteroid Long-acting beta 2-agonist) to minimize adverse effects associated with high doses of ICS. If high-dose ICS-LABA is needed, its use should be limited to 3-6 months whenever possible.

➤ The daily doses of fluticasone furoate have been reclassified: 100 mcg as low-medium and 200 mcg as medium-high.

➤ In the GINA 2025 edition, the "other controller options" (add- on LAMA at step 4 and add-on LTRA) that previously appeared in gray boxes under each step were removed. These options, which had lower evidence of efficacy and/or safety than tracks 1 and 2, were replaced by explanatory text. The goal is to prevent delays in referring patients with difficult-to-control asthma to a specialist by avoiding trials of multiple additional treatments without proven effectiveness.

7. Risk factors for severe exacerbations in adults and adolescents: The ORACLE2 study supports GINA's recommendation to assess multiple factors—including type 2 biomarkers—to estimate the risk of future exacerbations2. The meta-analysis was based on data from patients in the placebo groups of multiple clinical trials, although the risk associated with SABA overuse could not be assessed due to lack of data. Similar studies are needed in real-world populations, along with risk-reduction strategies based on the identified factors. The significant reduction in asthma exacerbations during COVID-19 lockdown highlights the important role of environmental factors, such as air quality, in reducing exacerbations.

8. Biomarkers for Type 2 inflammation: In the GINA 2025 Guidelines, Type 2 inflammation biomarkers take on greater importance and are specifically addressed in Appendix A. This appendix states that Type 2 inflammation biomarkers in patients with asthma (measured in blood, urine, induced sputum, exhaled air, and bronchoalveolar lavage) should always be interpreted within an appropriate clinical context. For asthma management, the most useful and widely used biomarkers are those indicating Type 2 airway inflammation and allergy, such as:

- Blood eosinophil count (BEC)
- Fractional exhaled nitric oxide (FeNO)
- Total serum immunoglobulin E (IgE)
- Allergen-specific IgE

These biomarkers are helpful for diagnosis, phenotype identification, monitoring, prognosis, and predicting patient response to asthma treatment. It also notes that sputum eosinophil count can guide corticosteroid therapy in patients with moderate to severe asthma, although this test is not commonly available in clinical practice. It is also helpful in assessing the patients eligibility for Type-2 targeted biologic therapy.

9. Personalized asthma care: Personalized asthma management involves a continual cycle of assessment, adjustment of treatment and review. The role of biomarkers is again highlighted in this section and 'consider biomarkers' has been added for reviewing the response to therapy. If the patient remains uncontrolled, consider assessing Type 2 biomarkers especially FeNO since an elevated FeNO is due to poor adherence with ICS.

In summary the GINA 2025 guidelines give a clear diagnostic and treatment protocols for diagnosis and management in preschool children. The use of ICS–formoterol as reliever to reduce severe exacerbations is reiterated and re-emphasized. The new guideline highlights the expanded use of T2 biomarkers for refined diagnosis and therapy guidance and the integration of risk-informed tools, climate awareness, and shared decision aids.

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ALL-ORAL REGIMENS FOR DRUG-RESISTANT TUBERCULOSIS IN CHILDREN UNDER 5 YEARS: A REVIEW OF CURRENT EVIDENCE AND FUTURE DIRECTIONS

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Abstract

The emergence of drug resistance is a major threat to global efforts to end TB. Early diagnosis and prompt treatment will prevent the patient from spreading the disease to others, developing resistance to more drugs, progressing to chronic state of permanent lung damage and ultimately prevent mortality due to disease. There has been a paradigm shift in the management of DR TB. To begin with the regimes were prolonged and included injectable drugs. This reduced the compliance and also increased morbidity due to adverse effects. Recent advances have been made in the management and now all oral regimes are available to manage DR- TB and we are also slowly progressing to reduce the duration of treatment, This review summarises the recent advances and recommendation of the WHO in the with regard to the newer shorter oral regimes that are now available.

Introduction

Tuberculosis (TB) continues to be one of the most significant global public health challenges, particularly in vulnerable populations such as young children under five years of age. Despite being a preventable and curable disease, TB remains the leading infectious cause of death globally, accounting for approximately 1.25 million deaths in 2023, with children bearing a disproportionate burden of morbidity and mortality. According to the WHO Global TB Report 2024, children and adolescents account for approximately 12% of the global TB burden, equating to over 1.3 million cases annually. India continues to carry the highest burden of tuberculosis (TB) globally, accounting for 26% of the world's cases, with an estimated 2.7 million cases in 2023. The country has made notable progress, with treatment coverage improving to 89% and TB incidence rates declining by 17.7% since 2015. Mortality has also reduced by 21.4% over the same period. However, India remains off-track to meet its 2025 TB elimination goals, particularly in reducing incidence and mortality further. Rifampicin-resistant TB (RR-TB) is rare among first-time diagnosed patients but is increasing in some regions. The global burden of multidrug-resistant TB (MDR-TB) remains stable, with 3-4% of firsttime diagnosed patients having MDR/RR-TB and 18-21% among previously treated cases. In India, drug-resistant TB (DR-TB) constitutes 27% of global MDR-TB cases. Resistance to FQ in new TB patients without rifampicin resistance is rare (1.0–1.2%). Isoniazid-resistant TB is the most common form of drug resistance globally, with rates of 7% in newly diagnosed and 8–11% in previously treated patients. Isoniazid resistance increases the risk of developing multidrug-resistant TB (MDR-TB).

Accurate and timely diagnosis of DR-TB in young children remains a critical bottleneck. Children under five often present with paucibacillary disease and are unable to produce sputum for microbiological confirmation. Despite advancements in molecular diagnostics such as Xpert MTB/RIF Ultra, access remains inconsistent, especially in lowresource settings. In many regions, presumptive diagnosis based on clinical and radiological findings, combined with epidemiological links, is still necessary. This reliance on probable rather than confirmed diagnoses can delay the initiation of appropriate DR-TB treatment and contribute to under-reporting of pediatric DR-TB cases.

Historically, pediatric treatment regimens for DR-TB have been adapted from adult protocols, frequently involving injectable agents associated with significant toxicities such as irreversible hearing loss and nephrotoxicity. These regimens pose substantial challenges in young children, including issues with palatability, adherence, and the need for hospitalization. The paradigm shift towards all-oral, shorter, and less toxic regimens, as reflected in the recent WHO 2025 consolidated guidelines, offers a promising advancement in pediatric TB care. All-oral regimens incorporating newer drugs such as Bedaquiline, Delamanid, Pretomanid, and linezolid have been shown to improve treatment outcomes in adults and older children, with emerging evidence supporting their use in younger age groups.

However, despite these advances, data specific to children under five years of age remain limited. Pharmacokinetic differences, safety profiles, and the availability of childfriendly formulations are critical considerations that continue to shape treatment recommendations. The WHO's emphasis on scaling up all-oral regimens and eliminating injectable agents aligns with the broader goals of improving adherence, reducing toxicity, and enhancing treatment outcomes in this vulnerable population.

DR TB treatment regimens:

Standardized definitions for TB treatment outcomes are essential for monitoring and public health strategies. New definitions include "cured," "treatment completed," and "treatment failed," applicable to both drug-susceptible and drug-resistant TB. The definitions aim to facilitate practical clinical monitoring and implementation of treatment strategies. The concept of "sustained treatment success" is proposed for operational research to assess long-term outcomes post-treatment. The management of drug-resistant tuberculosis (DR-TB), particularly multidrug-resistant TB (MDR-TB), has evolved significantly over the past two decades. Treatment regimens for MDR-TB were long, toxic, and complex, typically extending over 18–24 months and relying heavily on injectable agents such as aminoglycosides (kanamycin, amikacin). These regimens were associated with poor adherence, high rates of adverse events and variable treatment success rates, particularly in resource-limited settings. Treatment outcomes in young children were even more challenging, owing to difficulties in diagnosis, lack of child-friendly formulations, and limited pharmacokinetic data to guide dosing.

In 2016, the WHO endorsed a 9–12 month "short-course" regimen, which included a combination of first-line drugs, a fluoroquinolone, and injectable agents. While this approach reduced treatment duration, it still carried significant toxicity and was not widely studied in children under five.

The advent of newer drugs—bedaquiline, delamanid, and pretomanid—and the repurposing of linezolid and clofazimine marked a paradigm shift towards all-oral, injectable-free regimens. Landmark trials such as NIX-TB, ZeNix, TB-PRACTECAL, BEAT-TB, and end TB demonstrated that shorter, all-oral regimens could achieve high treatment success with fewer adverse events in adults and older children. Building on this evidence, the WHO 2022–2025 guidelines recommend 6–9 month all-oral regimens, such as BPaL/BPaLM and BDQ-DLM-based combinations (BDLLfxC), as the preferred standard of care for most forms of DR-TB, including in children where feasible.

Despite these advancements, specific data on children under five remain limited, and much of the current pediatric practice relies on extrapolation from adult studies and emerging pharmacokinetic data. Programs are increasingly moving toward childfriendly, dispersible formulations and weight-band dosing to facilitate the safe and effective use of these regimens in younger age groups. This evolution towards all-oral, shorter, safer regimens represents a significant advancement in pediatric TB care, addressing long-standing challenges of adherence, toxicity, and treatment access.

Under the current National Tuberculosis Elimination Programme (NTEP) guidelines in India, the management of drug-resistant TB (DR-TB) in children under 5 years remains cautious and distinct from adult and older pediatric protocols. While WHO recommends all-oral, bedaquiline- and delamanid-based regimens for children of all ages, India's NTEP has not fully adopted these for children under 5 due to regulatory limitations and lack of national approvals for this age group. As a result, young children are typically treated with longer, modified all-oral regimens, often lasting 12 months or more, with drugs selected based on susceptibility and tolerability, occasionally including injectables like amikacin when necessary. This cautious approach reflects a gap between international recommendations and national implementation, pending further evidence and regulatory approvals to align Indian practice with global standards for shorter, safer, all-oral regimens in young children.

WHO RECOMMENDED SHORTER MDR REGIMES:

Treatment of drug-resistant TB using 6-month regimens

the 6-month bedaquiline, pretomanid, linezolid and moxifloxacin (BPaLM) regimen;

the 6-month bedaquiline, delamanid, linezolid, levofloxacin and clofazimine (BDLLfxC) regimen

➤ **Treatment of drug-resistant TB using 9-month regimens**

Table1: Comparison of NTEP and WHO with regard DR TB Regimes

Aspect	NTEP (India) Guidelines	WHO 2025Guidelines
Eligibility for Short, All-Oral Regimens	**Not applicable for <5 years;** Bedaquiline (Bdq) and Delamanid (Dlm) not approved under NTEP.	**Recommended for all ages,** including <5 years, if weight and drug susceptibility allow. BPaLM/BPaL preferred.
Preferred Treatment Duration	**12–18 months** (longer, modified oral regimens)	**6–9 months** (short, all-oral regimens preferred where possible).
Injectables	**Avoided where possible;** used only in exceptional cases with strict monitoring (e.g., amikacin).	**Injectables not recommended**; all-oral regimens standard.
Core Drugs	**Group A/B drugs where possible:** - Linezolid -Levofloxacin/Moxifloxacin - Pyrazinamide - Ethionamide - PAS - Ethambutol - Amikacin (exceptional) - Carbapenems (meropenem preferred if CNS TB)	**Group A prioritized:** - Bedaquiline - Linezolid - Fluoroquinolones Group B: - Clofazimine - Cycloserine **Group C only when necessary.**
Use of Bedaquiline / Delamanid	**Not approved for <5 years** under NTEP.	**Approved and recommended for all ages** with child-friendly formulations available.
Formulations	Pediatric dispersible formulations preferred where available; Bdq suspension not routinely available.	Pediatric-friendly (dispersible, scored tablets) formulations recommended and increasingly available.
Monitoring Requirements	Monthly clinical review; strict ototoxicity monitoring if injectables used; active adverse effects monitoring	Regular clinical and laboratory monitoring; pharmacovigilance integrated.
Special Populations (CNS, Osteoarticular TB)	Longer regimens (up to 18 months) recommended; carbapenems preferred for CNS involvement.	Tailored regimens but preference for shorter, all-oral protocols whenever possible.
Approval Oversight	Requires pediatric DR-TB committee review and approval.	National programmatic oversight; no additional restriction for <5 age group.

Regimen for Rifampicin-Susceptible and Isoniazid-Resistant TB

A 6-month regimen with rifampicin, ethambutol, pyrazinamide, and levofloxacin is recommended. H mono/poly DR-TB regimen is of 06 or 09 months with no separate IP/CP. The addition of injectable agents like streptomycin is not advised

Table 2: Replacement sequence of drugs to modify Hr-TB regimen

Situation	Sequence of using replacement drugs
1. If Lfx or Z can't Be Used	Replace with Lzd. If Lzd also cannot be given, replace with Cfz* + Cs.
2. If both Lfx and Z can't be used	Add 2 drugs of the 3-Lzd, Cfz", Cs in order of preference based on resistance, tolerability & availability.
3. If R resistance	Switch to appropriate shorter or longer oral regimen

Six-Month Regimens

BPaLM/BPaL: [Bedaquiline (Bdq), Pretomanid (Pa), Linezolid (L/Lzd), Moxifloxacin (M/Mfx)]

BPaLM regimen must be the first choice of treatment in eligible patients ≥14 years age with MDR/RR- TB regardless of their FQ resistance status or HIV status.

(i) Person with age 14 years & above with new microbiologically confirmed MDR/ RRTB requiring a new course of treatment or probable MDR-TB who failed H mono/poly DR-TB treatment

(ii) H/o of Drug Exposure: Person with exposure of less than one month intake of Bdq,Lzd and/ or Pa in the past
or
Person with exposure of more than one month intake of Bdq, Lzd and/ or Pa and documented sensitivity to these drugs
or
Person who had not failed treatment with Bdq or Lzd containing shorter or longer regimen, and sensitivity to these drugs are documented

(iii) QTcF in ECG is ≤450 ms in males and ≤470 ms in females
or
when serum electrolytes are abnormal and QTcF is >450 ms in males & QTcF is >470 ms in females in baseline ECG, after correcting the electrolytes, QTcF in repeat ECG is ≤450 ms in males and ≤470 ms in females

(iv) Non-lactating women, lactating women but not breast-feeding, non-pregnant women, pregnant women with <20 or <24 weeks gestation and who is willing for medical termination of pregnancy (as per latest MTP gazette notification, as applicable) Patients < 14 years of age, documented resistance to Bdq, Lzd and/ or Pa, with severe liver dysfunction, with severe forms of extrapulmonary disease (CNS TB/ Spinal TB) or disseminated TB and patients with sevre cardiac conduction abnormalities are not eligible for BPaLM regime

BDLLfxC: [Bedaquiline (Bdq), Delaminid (D), Linezolid (L), Levofloxacin (Lfx), Clofazimine (C/Cfz)]

The WHO consolidated guidelines on tuberculosis recommend a novel, all-oral, 6-month regimen – BDLLfxC – for the treatment of MDR/RR-TB, with or without additional resistance to fluoroquinolones (pre-XDR-TB).

- This can be an alternative regimen for children, pregnant women, or where pretomanid is unavailable/contraindicated.
- Initial regimen includes all five drugs; levofloxacin or clofazimine may be stopped after DST.
- Allows for programmatic flexibility ("tapering down" approach). Subgroup Considerations:
- Pregnant or breastfeeding: Prefer BDLLfxC over BPaLM/BPaL.
- Children: BDLLfxC preferred; BPaLM/BPaL not recommended in children < 14 years.
- PLHIV: Most regimens effective if ART initiated; avoid drug–drug interactions.

Nine-Month Regimens

WHO suggests the use of the 9-month all-oral regimen rather than longer (18-month) regimens in patients with MDR/RR-TB and in whom resistance to fluoroquinolones has been excluded. It is recommended in patients without extensive TB disease and without severe extrapulmonary TB. It can also be used in children (and patients in other age groups) who do not have bacteriological confirmation of TB or resistance patterns but who do have a high likelihood of MDR/RR-TB (based on clinical signs and symptoms of TB, in combination with a history of contact with a patient with confirmed MDR/RR-TB). It comprises of bedaquiline, linezolid and pyrazinamide in different combinations with levofloxacin/moxifloxacin, clofazimine and delamanid.

Modified All-Oral Regimens (BLMZ, BLLfxCZ, BDLLfxZ): [Pyrizinamide (Z)]

- Use in MDR/RR-TB without FQ resistance.
- BLMZ is generally preferred due to lowest cost, pill burden, and favorable side effect profile.
- Adverse events similar across regimens; all include linezolid, which may require dose modification.
- Not for severe extrapulmonary forms (CNS, osteoarticular, disseminated).
- If culture remains positive at 4 months, extend initial phase or total duration up to 11 months.

Linezolid- or Ethionamide-based Regimens:

- Replace ethionamide with linezolid for pregnancy/females of reproductive age.
- Monitor for linezolid toxicity and manage accordingly.

Longer, Individualized Regimens

➤ Reserved for those who are not candidates for shorter regimens (e.g., XDR-TB, severe forms, drug intolerance, failed prior regimens).
➤ Constructed using a stepwise, priority-based approach, starting with Group A, then B, and adding Group C drugs as needed.
· More intensive monitoring and a patient-centered approach are necessary due to higher risk for toxicity, poor adherence, and treatment failure.

Special Populations & Clinical Scenarios

➤ Children and Adolescents: Shorter regimens (BDLLfxC, modified 9-months) are recommended where possible; use child-friendly formulations.
➤ Pregnant/Breastfeeding Women: BDLLfxC and 9-month regimens are preferred; close monitoring is required due to limited data on safety.
➤ PLHIV: All regimens can be used, but be cautious of ART interactions—avoid efavirenz with bedaquiline/pretomanid, avoid zidovudine with linezolid.
➤ Comorbidities (Diabetes, Renal/Liver Failure, Anaemia): Regimens require dose adjustments and more intensive monitoring; linezolid-containing regimens should not be used if severe anaemia or myelosuppression is present. Table 3 summarises the common DR TB regimes recommended in different age groups by the WHO and table summarises the common adverse effects of the commonly used drugs.

Monitoring:

Clinical assessments at month 4 and 6 are crucial for evaluating treatment response.

➤ If no improvement is observed by month 4, investigations for treatment failure or drug resistance should be conducted.
➤ Treatment should be stopped if there is no improvement by month 6.

Adverse Effects

Monitoring for side effects is a critical component of managing drug-resistant tuberculosis (DR-TB), especially due to the toxicity and prolonged duration of second-line anti-TB drugs (Table 2). If FQ resistance develops during treatment, it should be declared a failure, and a new regimen should be initiated. Discontinuation of pyrazinamide or linezolid due to AEs may be considered, but multiple drugdiscontinuations necessitate regimen cessation. The common adverse effects are summarised in table 3.

General Monitoring Protocol

· Monthly clinical review: symptoms, adherence, and adverse events.
· Routine labs: CBC, LFTs, RFTs every 1–3 months depending on the regimen.
· Audiometry: especially when injectable drugs are used.
· ECG: regularly if patient is on QT-prolonging drugs like bedaquiline, moxifloxacin, or clofazimine.

Conclusion

The management of drug-resistant tuberculosis (DR-TB) in children presents unique challenges due to limited pediatric-specific data, variable drug tolerability, and the complexity of prolonged treatment regimens. Recent advances, including the introduction of all-oral, shorter regimens and newer agents such as bedaquiline and delamanid, have significantly improved treatment outcomes and reduced toxicity. However, individualized regimens must be carefully tailored based on drug susceptibility patterns, age, weight, and potential side effects. Close monitoring for adverse events, nutritional support, psychosocial care, and adherence strategies are critical to ensure treatment success. Continued research, robust pharmacovigilance, and expanded access to child-friendly formulations are essential to optimize outcomes and reduce the global burden of DR-TB in the pediatric population

Table 3: Summary Table: Major DR-TB Regimens

Regimen Type	Indications	Eligible Populations	Key Exclusions/Notes
6-mo BPaLM/BPaL	MDR/RR/pre-XDR-TB (≥14y)	Adults/adolescents (not pregnant)	CNS, bone, disseminated TB excluded; not in pregnancy; FQ DST recommended
6-mo BDLLfxC	MDR/RR/pre-XDR-TB, any age	All ages, incl. kids, pregnancy	Not for severe extrapulmonary (CNS, bone, disseminated)
Modified 9-mo	MDR/RR-TB FQ-susceptible)	All ages	Not for CNS, bone, disseminated TB
Longer (18+ mo)	XDR - TB/failed/NTM/multiple exclusions	Extensive disease, severe extrapulmonary disease	Individualized; higher toxicity, pill burden

Table 4: Summary of key side effects of commonly used DR-TB medications and the parameters that should be regularly monitored:

Drug Group	Examples	Major Side Effects	Monitoring
Aminoglycosides / Polypeptides	Kanamycin, Amikacin, Capreomycin	Ototoxicity (hearing loss, tinnitus)- Nephrotoxicity	Audiometry- Serum creatinine/Urea
Fluoroquinolones	Levofloxacin, Moxifloxacin	QT prolongation- GI upset- Tendon rupture	ECG (baseline + periodic)- LFTs (if needed)
Thioamides	Ethionamide, Prothionamide	Hepatotoxicity- Hypothyroidism- GI intolerance	LFTs- TSH (every 3 months)
Cycloserine		Neurotoxicity- Psychosis- Seizures	Mental status exams- Monitor for mood changes or psychosis
Linezolid		Myelosuppression- Optic neuritis- Peripheral neuropathy	CBC (every 2 weeks initially)- Visual acuity and color vision- Monitor for neuropathy
Clofazimine		Skin pigmentation- GI upset	Clinical monitoring
Bedaquiline		QT prolongation- Hepatotoxicity	ECG (baseline, 2, 12, 24 weeks)- LFTs
Delamanid		QT prolongation- GI intolerance References:	ECG- Electrolytes

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HOUSE DUST MITE - ALLERGEN EXTRACTS AND ITS CLINICAL SIGNIFICANCE

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Introduction

House dust mites (HDMs) are a major source of indoor allergens worldwide.(1) During the 1960s, several surveys reported large populations of the Dermatophagoides genus in household dust, indicating their possible role as a key contributor to indoor allergen exposure. Many studies in recent years have also proven that the house dust mite is the commonest allergen causing allergic symptoms. They are known to cause allergic rhinoconjunctivitis and allergic asthma, and they also contribute in atopic eczema and other allergic skin conditions(2) . There are many species of house dust mites known to cause allergic symptoms. Till date, 82 mite allergens have been identified across 10 different species both in developing and developed countries. These allergens are categorized into 36 groups based on similarities in their amino acid sequences and biochemical functions.

The allergen extracts of house dust mites starts from culturing the mites in large quantities in regulated environment with suitable culture medium. Ensuring optimal growth parameters is vital for achieving the desired allergenic profile in the final product. To verify consistency between batches, each lot must undergo immunochemical analysis.

The aim of the article is to emphasize on the methods used for culturing and processing mites, as well as the procedure of production of allergen extracts which are used in the diagnosis and treatment of individuals with mite sensitization.

Process of House Dust Mite Allergen extract preparation

The process of preparing allergen extract is very tedious, every step is crucial for good quality of allergen. The type of source material used to prepare mite allergen extracts plays a significant role, but several other factors can also impact mite cultivation, resulting in variations in the final extract obtained. This variation is reflected in the differing allergen content and composition seen among commercial products, including those from the same producer(3). Therefore, careful monitoring and optimization of all steps in the production process are crucial to ensure the quality and uniformity of mite allergen extracts.

Step 1: Preparation of Raw Mite Material (figure 1)

A. Culture Medium

The culture medium is important for the proper growth of the mite. House dust mites (HDMs) were originally grown using human skin scales, which served as their natural food source(4). Over time, alternative culture media have been developed, including animal skin scales, dried daphnia, ox liver, fish flakes, dog food, rodent feed, wheat germ, and fungal cultures, often supplemented with yeast (5,6). Currently, manufacturers of mite allergen extracts use a combination of various food sources such as pork liver, brine shrimp eggs, wheat germ, and yeast to support mite growth.(7) In addition, vitamin or amino acid supplements that mimic the composition of the human stratum corneum are also sometimes incorporated (8,9). According to European and U.S. regulatory guidelines, mite culture media must not include ingredients that could pose allergenic risks. If human or animal-derived components are used, their inclusion must be thoroughly justified to ensure they do not introduce potential pathogens. Gamma irradiation may be applied to the culture media as a safety measure to facilitate their use.

B. House dust mite culturing method

The standard approach for cultivating mites involves introducing starter cultures into flasks containing an appropriate growth medium. The flasks should provide adequate ventilation while remaining securely sealed to prevent the escape of mites and ensure sterile conditions. To avoid cross-contamination, especially in facilities where multiple mite species are cultured, it is crucial to separate species either by room or designated areas within the same facility. The mite species may require unique environmental conditions to thrive. Certain conditions, such as temperature between 20°C and 30°C and relative humidity (RH) levels between 70% and 80% — are generally suitable for the growth of house dust mites (HDMs) (10,11). While higher temperatures (above 30°C) and RH levels (above 80%) can boost mite population growth but both may also promote fungal contamination, which can be harmful to mite survival and its allergenicity. Therefore, for optimal cultivation, key environmental factors—especially temperature and humidity—should be tailored to the requirements of each mite species, as these conditions directly affect both population growth and the allergenic composition of the final extract.

C. Inactivation and Drying

Mite cultures must be inactivated prior to harvesting to preserve their immunological characteristics and eliminate any viable mites. The most commonly employed method is to freeze the cultures at temperatures below –20°C for atleast 24 hours. Once inactivated, the cultures are typically subjected to drying under precisely controlled conditions to achieve the desired moisture reduction. Regardless of the approach taken, it is essential that both the inactivation and drying procedures are well-documented and rigorously monitored to ensure product consistency and high quality.

D. Purification: Obtaining Fractions

The obtained culture of mites is a complex mix that includes mite bodies, eggs, shed skins, fecal matter, and remnants of the culture medium. In this step, the main target is to separate the components using different techniques. The most commonly used method by manufacturers is mechanical sieving, which

which utilizes meshes of varying pore sizes to segregate materials based on particle dimensions (12). This process aims to isolate fractions enriched in specific mite components. For instance, it is possible to obtain fractions predominantly composed of mite bodies (ranging from 90-350 µm) and fecal particles (less than 50 µm), which are then retained for further extraction. Alternative fractionation techniques includes – the use of air classifiers, which separate particles based on both size and density, and the heat-escape method, which captures live mites that move away from a mildly heated culture environment (13). Another strategy involves using the entire culture as the source material (14). Careful selection of the mite fraction is a key step in producing standardized and clinically relevant allergen extracts. Current evidence supports the use of both mite bodies and fecal particles as suitable raw materials to generate comprehensive extracts that reflect the full range of sensitizing mite allergens.

E. Mite Raw Material

High-quality raw material is identified by qualified personnel with expertise in mite morphology and taxonomy. It is essential to define the specific fraction(s) of the mite culture used, as well as to implement appropriate quality control measures and set clear acceptance criteria regarding purity and the presence of foreign material in the raw material. According to the U.S. Food and Drug Administration (FDA), the raw material should not contain more than 1% detectable foreign matter (15). In contrast, the European Pharmacopoeia does not specify a quantitative limit but requires that no foreign mite species shall be present (16). Till date there is no set criteria in India or in neighboring countries.

Step 2 : Production of Mite Allergen Extracts from raw mite material (figure 2)

As outlined earlier, the initial step in producing mite allergen extracts involves obtaining suitable raw mite material. This is followed by the extraction and purification of allergens, where undesired contaminants and non-relevant substances are removed using various physicochemical techniques (17). To ensure the quality and consistency of the final product, the entire manufacturing process must be continuously monitored and strictly controlled. The house dust mite allergen extracts contain highly active enzymatic proteins, it is essential for the manufacturing process to incorporate measures that limit allergen degradation as much as possible. The extraction process typically begins with the use of an aqueous solution to extract proteins from mite raw material. To facilitate allergen release, the mite bodies and fecal particles are disrupted through methods such as stirring, homogenization, or sonication. This enhances the overall protein yield in the final product. Key variables in the extraction process include the composition of the extracting fluid, extraction speed, pH, temperature, and duration. For optimal preservation of protein integrity, the temperature should be maintained between 2°C and 8°C to reduce enzymatic activity, and the extraction time should be kept to a minimum (18,19). Following extraction, clarification techniques like filtration or centrifugation are used, along with purification methods such as dialysis, ultrafiltration, or chromatography, to eliminate unwanted components such as nucleic acids, carbohydrates, lipids, and salts. A final sterile filtration step using a 0.2-µm filter ensures sterility of the extract. The final protein-rich extract is obtained after filtration.

Step 3: Preparation of final products

In extracts intended for in vitro use, enzyme inhibitors may be added to help maintain both stability and allergenic activity. However, this practice is discouraged for preparations intended for direct human use unless further purification steps are planned to remove the inhibitors. The protein-rich extracts are generally stabilized in aqueous solutions containing 50% glycerin or between 0.01% and 0.05% human serum albumin. To prevent microbial contamination, preservative such as phenol (0.3%–0.5% volume/volume) is commonly added, making the extracts suitable for both diagnostic and therapeutic use. In United States, only standardized extracts of Dermatophagoides farinae and Dermatophagoides pteronyssinus in 50% glycerin are approved for clinical application. In contrast, European practices favor aqueous extracts for in vivo diagnostic purposes, while extracts intended for subcutaneous immunotherapy are typically freeze-dried to extend their shelf life.

Some European manufacturers also polymerize mite allergen extracts to reduce their allergenic potential. This polymerization process produces highmolecular-weight compounds (>300 kDa), which results in reduced IgE-binding activity while maintaining the extract's immunogenicity. Upon reconstitution, these freeze-dried extracts can be formulated with aluminum hydroxide or combined with other adjuvants such asmonophosphoryl lipid A.

Polymerized extracts require advanced analytical techniques, such as mass spectrometry, for allergen profiling, since traditional immunological assays like ELISA are often insufficient for their characterization. Regardless of whether extracts are used for diagnosis or therapy, the qualitative allergen composition remains largely consistent.

Standardization of Mite Allergen Extracts

In the United States, mite allergen extracts are biologically standardized by evaluating the size of the skin erythema produced when serial dilutions of the extract are administered intradermally to individuals with high mite sensitivity. This approach, known as ID50EAL (intradermal dilution for a 50 mm sum of erythema), is used to determine the potency of reference extracts. Licensed manufacturers then compare their products to these reference preparations using a validated IgE enzyme-linked immunosorbent inhibition assay. A parallel-line bioassay is employed to calculate the relative potency, which is used to assign potency values to each batch of standardized extract (21).

In contrast, Europe relies on skin prick testing and wheal size to assess the biological potency of mite extracts. In some cases, further adjustments during manufacturing are required to reach predefined potency targets expressed in biological units.

Additional distinctions exist between standardization practices in the United States and Europe. In the U.S., potency is labeled in allergy units (AU), and standardization is overseen by the FDA's Center for Biologics Evaluation and Research (CBER), which supplies reference extracts and approves product release. This centralized process ensures that standardized extracts from different U.S. manufacturers are qualitatively consistent and comparable.

In Europe, however, allergen activity labeling varies by manufacturer. Some companies have begun incorporating major allergen quantification into their standardization methods. European standardization is typically based on in-house references and national or international guidelines. Potency units differ across manufacturers, and product release is regulated on a country-bycountry basis. As a result, allergen extracts from different European manufacturers are often not interchangeable.

Discrepancies in biological potency have been noted between U.S. and European mite extracts. For instance, standardized diagnostic extracts of Dermatophagoides pteronyssinus produced in Europe have shown approximately 50% lower relative potency compared to those produced in the U.S. This variation is clinically significant because skin test results guide patient selection for immunotherapy. Differences in extract potency could lead to misdiagnosis or inappropriate treatment.

Clinical Importance:

Allergen extracts are commonly used for both skin prick testing and allergen immunotherapy. Subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT) have proven to be safe and effective treatment options for managing allergic conditions (22,23,24). Recently, sublingual immunotherapy (SLIT) tablets containing mite allergen formulations have been introduced in Europe for the treatment of allergic rhinitis and asthma (20). The SLIT tablet was launched in India a few months ago.

Among the two, SLIT offers a better safety profile. In recent years, SLIT tablets with defined dosages have been introduced in several countries. However, the clinical efficacy of SLIT in liquid form remains uncertain, primarily due to the lack of well-established dosing guidelines.

Conclusions:

The manufacturing process plays a critical role in determining the final composition of allergen extracts. Standardized mite allergen extracts are vital for ensuring the safety and effectiveness of allergen immunotherapy, including both subcutaneous (SCIT) and sublingual (SLIT) routes. Enhancing the quality and uniformity of these extracts is key to providing reliable treatment options for clinicians. To achieve this, regulatory frameworks and guidelines are applied throughout the entire production chain—from the initial raw materials to the finished product. This standardization becomes especially important considering the limited effectiveness of
allergen avoidance strategies and pharmacological treatments alone.

Figure 1 : Flowchart demonstrating Steps involved in production of mite raw material

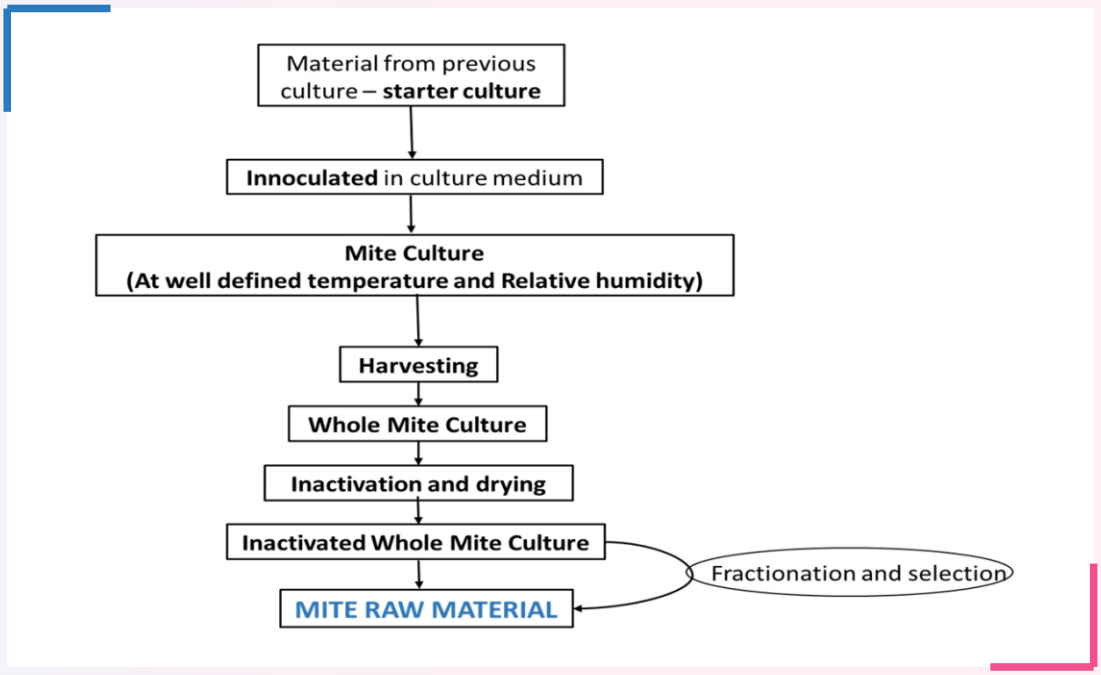
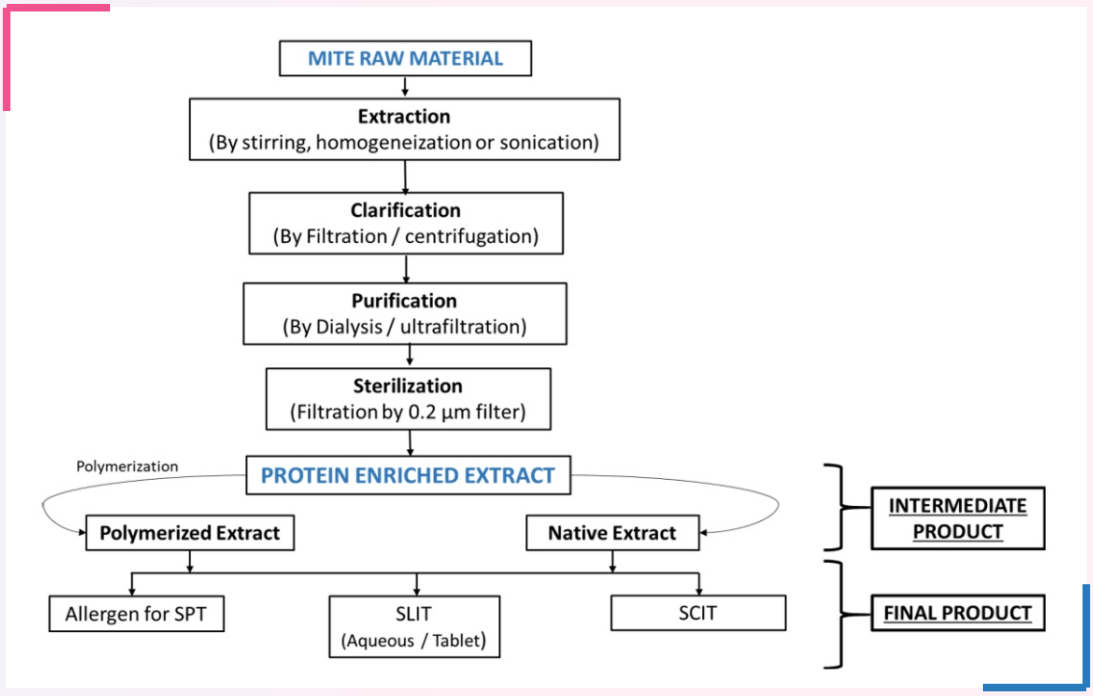


Figure 2: Flowchart showing Production of allergen extract from mite raw material



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From Lungs to Larynx: a rare case of pediatric TB unveiling laryngeal involvement

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Background: Laryngeal tuberculosis (TB) is a rare manifestation of tuberculosis, with an incidence of 1% in adult patients of pulmonary TB. No case has been reported inpediatric population in recent literature. It typically arises from direct infection via bronchial spread or hematogenous dissemination. Early recognition and differentiation from other potential causes of laryngeal symptoms are crucial for appropriate management.

Case Presentation: An 8-year-old female presented with a 15-day history of fever and a 7-day history of shortness of breath. Clinical examination revealed tachypnea, tachycardia, and decreased air entry with crepitations on the left side of the chest, although the patient-maintained oxygen saturation on room air. Chest radiography revealed left-sided consolidation and pleural effusion. Sputum CBNAAT detected rifampicin resistant M. Tuberculosis.

Intervention and Course: The patient was initiated on an MDR anti-tuberculosis treatment (ATT). Post-initiation, the patient became afebrile but subsequently developed hoarseness of voice and persistent shortness of breath. This deterioration led to an emergency department admission with respiratory distress. Diagnostic bronchoscopy was performed, revealing laryngeal edema and laryngeal tubercles.

Management and Outcome: The treatment regimen was adjusted to include oral prednisolone along with MDR regiment ATT. Currently, the patient's respiratory symptoms resolved, she is currently asymptomatic and thriving well.

Discussion: Laryngeal TB, though rare, presents with distinct clinical features such as hoarseness of voice, which may be accompanied by odynophagia, dysphagia, cough, otalgia, and stridor. It is essential to differentiate these symptoms from other causes of hoarseness and respiratory distress, such as foreign body aspiration, inhalational burns, laryngeal papilloma, or laryngeal hematoma. Early diagnosis and tailored treatment are critical in managing this rare but potentially serious complication of TB.

Conclusion: This case illustrates the importance of considering laryngeal TB in the differential diagnosis of hoarseness and respiratory symptoms in pediatric patients with a history of TB. Timely recognition and comprehensive treatment are key to achieving favorable outcomes in such cases.

Utility of Stool-CBNAAT Testing for the Diagnosis of Pulmonary Tuberculosis In Children: A Cross-Sectional Study

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Background: Paediatric tuberculosis (TB) is among one of the major health issues globally and poses diagnostic challenges in children. Collecting respiratory sample for analysis
is traumatic for kids. Therefore, non-respiratory samples are being studied as a non-invasive method of diagnosis. This study focussed on evaluating cartridge-based nucleic acid amplification test (CBNAAT) using stool sample in clinically suspected cases for diagnosing paediatric pulmonary tuberculosis (PTB) and analysing its accuracy with that of gastric aspirates (GA) CBNAAT.

Methods: This single-centric cross-sectional study included 50 children aged 0.25-16 years, suspected as PTB. GA and stool sample were obtained from the enrolled patients and CBNAAT diagnosis was performed. Statistical analysis was done for results of both the groups.

Results: Out of 50 patients, 28 were microbiologically confirmed, 7 were clinically diagnosed as TB and 15 were diagnosed other than TB. All microbiologically confirmed cases were GACBNAAT positive, but only 18 patients were stool-CBNAAT positive. Both GA and stool
CBNAAT had strong relation with high Cohen's kappa value of 0.613 and highly acceptable significant value 0.0001. Stool-CBNAAT had sensitivity, specificity, PPV, NPV and diagnostic accuracy of 64.3%, 100%, 100%, 68.8%, and 80%, respectively as compared to GA-CBNAAT test.

Conclusion: The stool CBNAAT can be considered as a feasible, reliable, and non-invasive diagnostic tool for PTB. In this study Stool-CBNAAT was found to have comparable accuracy with that of GA-CBNAAT.

The impact of COVID-19 on routine home-based care of children with Cystic Fibrosis and the utility of teleconsultation in enforcing home-based care

Background

COVID-19 severely impacted patients with chronic diseases. The study assessed the pandemic's effect on psychosocial aspects and routine care of children with cystic fibrosis (CF). We also explored the role of teleconsultation in enforcing the routine care since educational programs and mental health screening can enhance adherence. Teleconsultation also reduces hospital visits thereby preventing cross infections.

Materials and Methods

To assess the impact of COVID-19 on the psychosocial aspects and home-based care of children with CF, we used the Patient Health Questionnaire-9 (PHQ-9) and a questionnaire to evaluate self-reported changes in CF treatment, focusing on oral medicine, nebulization, chest physiotherapy, and nutrition. To evaluate the utility of teleconsultation, participants completed the Cystic Fibrosis Questionnaire-Revised (CFQ-R), tailored for different age groups. After initial counseling on CF home-based care, the cohort was contacted again after one month to reassess adherence and Health Related Quality of Life (HRQoL) using the CFQ-R.

Results

In the study population of 30 patients, 83.33% of participants strictly adhered to COVID-19 protective measures. Hospital admissions decreased from an average of 1.8 per year pre-COVID to 1.2 post-COVID. No significant change was observed in depression levels (mean PHQ-9 score increased by 0.57, p=0.1), medication adherence (mean score increased by 0.01, p=0.76), or overall nutrition (mean score increased by 0.03, p=0.36). However, participants reported healthier eating habits. Chest physiotherapy quality improved, and nebulization quality also improved, with more frequent nebulization. However, no significant difference was noted in the overall scores for chest physiotherapy (mean score increased by 0.08, p=0.16) and nebulization (mean score increased by 0.03, p=0.44). No significant difference was noted in mean CFQR scores post teleconsultation.

Conclusion

The study found that the COVID-19 pandemic did not significantly impact the mental health or home-based treatment of children with CF, likely due to existing routines of social isolation and hygiene and increased parental presence. While teleconsultation was feasible, our study did not find significant improvement probably due to the small sample size or short duration (1 month) between assessments.

nters and the rest, pMDIs without dose counters. Of the total caregivers, 44% said they knew about

Assessing Knowledge of Caregivers of Asthmatic Children to Identify Empty Metered Dose Inhaler

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Introduction

Asthma is the most common chronic respiratory disease among children.1 Pressurised metered dose inhalers (pMDIs) are the most commonly used drug delivery devices in children with asthma. However, one of the disadvantages of pMDIs is inability to identify amount of medication remaining in it and when the device is empty. Only a single recent study is available from UK which assesses the knowledge of caregivers of asthmatic children on when to know their inhalers are empty.2 This study was conducted in the Indian setup to assess the same.

Material and methods

This observational cross sectional study was done in paediatric chest clinic of a tertiary care hospital in north India. Asthmatic children (6-12years) attending the paediatric chest clinic and using pMDI for more than 3months were included after taking informed consent from their parents. Knowledge of caregivers regarding identification of empty pMDI and factors associated with correct awareness to identify empty pMDI were assessed using pre designed proforma. Technique of using pMDI was assessed using checklist available in GINA guidelines.

Results

A total of 135 asthmatic children, (Males :60%, females: 40%), with mean age 8.51 (6-12 years). All children were using pMDIs with spacers. 40% (n=54) were using pMDIs with dose counters and the rest, pMDIs without dose counters. Of the total caregivers, 44% said they knew about the number of manufacturer quoted doses, 76.2% said they were aware on how to identify empty pMDIs and 60.7% responded they were routinely checking whether their pMDIs were empty or not. Corresponding figures for those using pMDIs with dose counters and without dose counters were 68.5%, 92.5%, 70% and 27.1%, 65.4%, 54.3% respectively. However, on evaluating the methods used by caregivers to assess the doses remaining in the pMDIs, only 32.5% were using the correct methods i.e. using dose counters/ keeping track of doses used. Upon analyzing this data separately for those using pMDIs with dose counters and those using pMDIs without dose counters, these numbers were 77.7% and 2.4% respectively. Overall, a majority were using the wrong methods to identify empty pMDIs, i.e. 51.8% checking mist during actuation, 39.5% shaking the inhaler and 1.23% floating the cannister in a bowl of water. We also found that correct awareness regarding identification of empty pMDIs was associated with using pMDIs with dose counter and routinely checking the doses remaining in the pMDI. Moreover, being able to correctly identify empty pMDI was associated with better asthma control. Thus, awareness among caregivers of asthmatic children regarding identification of empty pMDI is poor especially among those using pMDI without dose counters. Addition of dose counter to pMDI better enables the caregivers to identify empty pMDI and leads to better asthma control.

Conclusion

Our study showed that knowledge of caregivers regarding assessment of empty pMDIs is generally poor with only 32.5% or caregivers using the correct methods to identify empty pMDIs. This knowledge is ever poorer in those using pMDIs without dose counters. Incorporation of dose counters enhances the ability of the caregivers to identify empty pMDIs and this results in better asthma control.

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The diagnostic utility and clinical implications of Flexible fiberoptic bronchoscopy in Pediatric Hematology oncology and Hematopoietic stem cell transplant patients -A Decade of experience

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Background: Patients treated for hematological malignancies and those undergoing hematopoietic stem cell transplantation (HSCT) have an increased risk of infections. Pulmonary complications are a common cause of significant morbidity and mortality for immunosuppressed patients of all ages with up to 60% developing pulmonary infiltrates during treatment. Flexible fibreoptic bronchoscopy(FFB) and bronchoalveolar lavage (BAL) are a well-established method for identifying the causative organisms of pulmonary infiltrates. Currently, there is less confidence in performing BAL on young and sick children, the presence of thrombocytopenia and risk of bleeding, risk of introducing new infections secondary to mucosal injury, risk of sedation and inadequate yield thereby failure of the procedure. With this study, we aim to evaluate the impact of FFB and BAL in influencing the management of paediatric haematology oncology and hematopoietic stem cell transplant patients at our tertiary care centre over 10 years.

Methods: This retrospective study was conducted in the department of Pediatric Pulmonology at Sir Ganga Ram Hospital, Delhi. All patients admitted under the paediatric haematology oncology and BMT unit undergoing FFB over 10 years from January 2012 to December 2021 were identified from the PHO and bronchoscopy database. Data were analysed using descriptive methods and presented as mean, median and range. Categorical variables and diagnostic yields were expressed as frequencies and percentages.

Results: In total, 57 BAL examinations were performed over a decade in 49 patients of haematology, oncology and immunodeficiency with mean age of 6.49 ± 5.05 years and M:F ratio of 2.2:1. Most common indication of doing BAL was cough(87.7%), fever(77.2%) , chest findings(66.7%), abnormal CT scan(84.2%). The median duration of symptoms in our cohort was 17.4 days. The bacterial yield was comparable amongst timing of BAL (early(<7days)-8/16, late(>7days)8/16, p=0.84), respiratory symptoms (present 62.5% vs absent 37.5%,p=0.677), chest findings (present 62.5% vs absent 37.5%,p=0.174), neutropenic and non-neutropenia patients(50% vs 50%,p=0.678). The yields were comparable amongst haematological vs oncological diagnosis(p=0.489) and solid malignancy patients (90.9%,10/11) comparable to hematologic malignancy patients (17/27,63%, P=0.124). The bacterial yield was significantly better in PICU vs Ward (11/26 vs 5/31, p=0.028). GNB positivity was found in 13 BAL done in 11 patients. Seven out of 16 (43.7%) of fungal positive patients were neutropenic and 10/16 (62.5%) had received steroids in prior 7 days. Fourteen (14/57(24.6%)) were on prophylactic antifungal (7 voriconazole, 7 fluconazole), 6 had positive fungal yield.

There was no difference in fungal yield on patients on prophylactic antifungal vs not on any prophylaxis (p=0.314). The positivity rate of serum galactomannan was 6/12 and 50% similarity with BAL fungal culture. 9/31(29%) of serum galactomannan negative had BAL fungal positivity. The sensitivity of BAL galactomannan was 60% and specificity was 72.2%. BAL led to microbiological diagnosis in 39/57(68.4%) and a change in management in 75.4% (43/57) either by establishing a microbiological diagnosis or aiding cessation of ongoing agents. Noninvasive and radiological testing could pick only 30% of microbiologically positive cases. Complications were reported in 5 cases and were mainly mild. The BAL yield and bacterial yield improved over the years 2012 to 2017 (16/28,57.1%) and 2018 to 2021(23/28,79.3%) (p=0.072).

Conclusion: BAL is well tolerated, safe and accurate procedure in immunocompromised cohort. Standardized procedures for BAL sampling should be continuously revised to exclude unnecessary microbiological tests. The low rate of complications combined with the high diagnostic yield support the use of bronchoscopy as a diagnostic tool in this population.