

Recurrent Wheezing and Asthma – Epidemiology and Environmental Determinants

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Abstract

Wheeze is the musical continuous sound produced by oscillations in any critically narrowed airways, and heard mostly on expiration. It is common in preschool age, about half of all children will experience an episode of wheezing by their sixth birthday. Asthma is usually characterized by cough, wheeze, chest tightness and fast breathing. It is a significant global health issue and affects both children and adults. The prevalence is on the increase, especially in LMIC. Studies from different populations have revealed the key role influencing the progression from preschool wheezing to childhood asthma. Recurrent wheezing is four or more episodes in the preceding year and has a spectrum of phenotypes and with heterogeneous features. Phenotypes of wheezing were proposed to facilitate the identification of young children who are at risk of subsequent development of asthma. The epidemiology and environmental determinants of recurrent wheezing and asthma are discussed.

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Introduction

Wheeze is the musical continuous sound produced by oscillations in any critically narrowed airways, and heard mostly on expiration. It is common in preschool age, about half of all children will experience an episode of wheezing by their sixth birthday.

Asthma is usually characterized by cough, wheeze, chest tightness and fast breathing. It is a significant global health issue and affects both children and adults. The prevalence is on the increase, especially in LMIC. Studies from different populations have revealed the key role influencing the progression from preschool wheezing to childhood asthma.

Recurrent wheezing is four or more episodes in the preceding year and has a spectrum of phenotypes and with heterogeneous features. Phenotypes of wheezing were proposed to facilitate the identification of young children who are at risk of subsequent development of asthma. The epidemiology and environmental determinants of recurrent wheezing and asthma are discussed.

Recurrent preschool wheeze- What do we know?

Many have clinical symptom resolution by school age and do not develop allergic asthma. Transient wheezers are usually non atopic, resolves during the preschool years suggesting non-allergic drivers. Corticosteroids are thus not as beneficial compared to allergic asthma. The pathogens associated with acute episodes of wheezing in preschool children may be distinct from those in school-age asthma. Acute wheeze episodes associated with hypopharyngeal bacterial infection; 85% of the time *Streptococcus pneumoniae*, *Haemophilus influenzae*, or *Moraxella catarrhalis*; as well as nasopharyngeal viral infection.¹

Airway epithelium and structural cells

The respiratory system airway epithelium has defence mechanisms to protect itself. The physical barrier that stops penetration by inhaled microbes/allergens is maintained by intercellular epithelial junctions. Only extremely small particles, less than 3 to 5 microns (0.000118 to 0.000196 inches) in diameter, penetrate to the deep lung. Any compromise on epithelial integrity predisposes to aeroallergen sensitization and ongoing inflammation by allergens and microbes.¹

The airway epithelial cell innate immune function is however impaired in children with persistent wheeze compared with healthy children. Airway remodelling from inflammation increased thickness of the subepithelial reticular basement membrane, increased airway smooth muscle angiogenesis. The airway remodelling linked with abnormal lung function in older children with asthma and likely associated with early lung function changes.

Recurrent preschool wheeze and role of Eosinophils

Eosinophils are increased number in established severe recurrent wheeze by 3 years of age and this notable in the submucosa, while there is increase in urinary eosinophil activation markers during acute wheeze episodes.

In the INFANT Study, the RCT study Individualized Therapy for Asthma in Toddlers, daily ICS vs daily LTRA vs intermittent ICS were given to 300 children aged 12–59 months old. Children who had aeroallergen sensitization and/or blood eosinophils >300 cells/ μ l had the greatest reduction in asthma symptoms in children receiving daily ICS.²

Recurrent wheeze and the role of Neutrophils & Microbiome

Neutrophilic inflammation was noted in the bronchoalveolar lavage sample (BAL), of preschool children with neutrophilic, steroid refractory wheeze. Furthermore severe wheezers with neutrophilia had lower airway positive bacterial culture and *Moraxella*-dominant airway microbiome profile.¹

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Risk factors for progression from wheeze to asthma

Lower respiratory tract illness (LRTI) in early life

Wheezing illnesses are frequently triggered by respiratory viral infections in children. LRTI from RSV affects about 70% children in the first year of life, with bronchiolitis, affecting 10–30% of preschool children. These wheezing episodes may precede the subsequent diagnosis of asthma.¹

Allergens

Multiple early aeroallergen sensitization: house dust mite, cat, dog, cockroach, mouse. In a Multicentre Allergy Study children were followed from birth to 13 years, sensitization by age 3 years was associated with persistent wheeze and reduced lung function at school age.¹

Vitamin D

Vitamin D plays important roles in immune regulation and fetal lung maturation. Low maternal intake of vitamin D and long-chain polyunsaturated fatty acids (LC-PUFAs) during pregnancy have been linked to risk of wheezing in their offspring.¹

Breastfeeding

Benefits of breastfeeding include early life immunity and reduction in respiratory infections. Dogaru et al³ showed strong protective association with wheezing in the first 2 years of life, ie protects against transient early wheezing by reducing RTIs known to trigger wheeze attacks. Ayuk et al showed that early introduction of non-breast milk foods were associated with allergic sensitization and subsequent development of food allergy and asthma.

Conclusion

Key Studies from different populations have revealed the role of epidemiological and environmental influencers for progression from preschool wheezing to childhood asthma.

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