Frequent co-morbid conditions with asthma

Nelson Rosário MD, PhD, FAAAAI, FACAAI
Comorbidities in childhood asthma

Knowledge is sparse. Further studies are needed:

- to identify the prevalence
- the effects of these comorbidities and their treatment on the degree of asthma control in children.

Asthma comorbid conditions

- Share a common pathophysiological mechanism with asthma.
- Influence asthma control, its phenotype and response to treatment.
- More prevalent in asthmatics but without obvious influence on this disease.
- Interaction with A remains to be documented for many of them, particularly for severe A.
- If considered relevant, they should be treated appropriately.

Expert Rev Respir Med 2011
Ocular symptoms and asthma severity

628 (41%) ≥ 1 sx of conj. dx AR

829 (66%) ≥ 1 sx of conj.

n=1549

## Diagnostic Probability of Reported Allergic Conjunctivitis in 681 Asthmatic Children With Ocular Symptoms

<table>
<thead>
<tr>
<th>Ocular symptoms *</th>
<th>Reported conjunctivitis diagnosis, %</th>
<th>Odds ratio (95% CI)</th>
<th>Sensitivity, % (95% CI)</th>
<th>Specificity, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Itching</td>
<td>37.9</td>
<td>20.2 (13.4–30.4)</td>
<td>89 (85.1–92.8)</td>
<td>71.4 (69–73.9)</td>
</tr>
<tr>
<td>Redness</td>
<td>46.9</td>
<td>13.4 (9.8–18.2)</td>
<td>71.7 (66.1–77.2)</td>
<td>84.1 (82.1–86.1)</td>
</tr>
<tr>
<td>Tearing</td>
<td>43.8</td>
<td>7.4 (5.5–9.9)</td>
<td>53.1 (47–59.3)</td>
<td>86.6 (84.8–88.5)</td>
</tr>
<tr>
<td>Tearing and redness</td>
<td>51</td>
<td>14.2 (10.4–9.4)</td>
<td>67.3 (61.6–73.1)</td>
<td>87.3 (85.5–89.1)</td>
</tr>
<tr>
<td>Itching and tearing</td>
<td>49.2</td>
<td>9.0 (6.6–12.2)</td>
<td>50 (43.9–56.1)</td>
<td>90 (88.3–91.6)</td>
</tr>
</tbody>
</table>

*P<0.0001

Chong Neto, Rosario et al Ann Allergy Asthma Immunol 2010;105:399-400
more than 75% of patients with allergic rhinitis and 20% of patients with asthma have ocular symptoms, such as itching, tearing, and redness Singh K, Bielory L. *Ann Allergy Asthma Immunol.* 2007;98(suppl 1):S1–S125.
1549 asthmatic children (59% male; mean age 4.3 years)

medical record information:
Physician diagnosis of conjunctivitis 15.8%

43.9% had at least 1 ocular symptom that suggested ocular allergy.
Frequency of ocular symptoms

Itching     38.4%
Tearing     19.9%
Redness   25%

Combined symptoms:
    itching plus redness     21.6%
    itching plus tearing    16.6%.
Allergic Diseases and Severity of Asthma

Miyagui R et al 2004

N=3065

- Mild Asthma
- Moderate Asthma
- Severe Asthma

Associated Allergic Disease
Rhinitis is also Common in Infants with Asthma

Herberto José Chong Neto, Nelson Augusto Rosário, Gabriela Cardoso Westphal, Carlos Antônio Riedi, and Hevertton Luiz Bozzo Santos

Pediatric Allergy Division, Federal University of ParanáCuritiba, Paraná, Brazil
Allergic Rhinitis in Asmatics Sensitized to $\geq 1$ allergen.
Allergic Rhinitis in Asmatics Sensitized to $\geq 1$ allergen.

Crianças asmáticas
0-14 anos
n=1543

Asthmatics <2 y/o
n=493 (32%)

Asthmatics $\geq 2$ y/o
n=1050 (68%)

With Rhinitis
n=367 (74%)

With Rhinitis
n=890 (85%)

*P=0.11

* Test $\chi^2$
Allergic Rhinitis in Asmatics Sensitized to \(\geq 1\) allergen.

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With rhinitis
n=367 (74%)

With rhinitis
n=890 (85%)

SPT pos+
n=131 (36%)

SPT pos+
n=773 (87%)

\(*P=0.00001\)

\(*P=0.11\)

* Test \(\chi^2\)

# Treatment of recurrent wheezing infants

<table>
<thead>
<tr>
<th>Medication</th>
<th>≥ 3 episodes</th>
<th>&lt; 3 episodes</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhaled short-acting $\beta_2$-agonists*</td>
<td>608 (89.6)</td>
<td>539 (79)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Inhaled corticosteroids†</td>
<td>160 (23.6)</td>
<td>90 (13.2)</td>
<td>0.003</td>
</tr>
<tr>
<td>Leukotriene modifiers‡</td>
<td>47 (6.9)</td>
<td>26 (3.8)</td>
<td>0.42</td>
</tr>
<tr>
<td>Oral corticosteroids¶</td>
<td>126 (18.6)</td>
<td>109 (16)</td>
<td>0.2</td>
</tr>
</tbody>
</table>

N=1360; 12-15 months old

A asma inicia-se na infância e pode ser confundida com outras causas de sibilância. É possível identificar diferentes fenótipos. Associa-se à inflamação, demonstrável por procedimentos invasivos e não-invasivos. Ocorre remodelamento.
Diagnosis of Asthma in Children 5 Years and Younger

Symptom patterns (wheeze, cough, breathlessness) which occur recurrently, during sleep, or with triggers such as activity, laughing or crying are consistent with a diagnosis of asthma.
Diagnosis of Asthma in Children 5 Years and Younger

The presence of atopy or allergic sensitization provides additional predictive support, as early allergic sensitization increases the likelihood that a wheezing child will have asthma.
Airway inflammation in difficult asthma

- Endobronchial biopsy and BAL in 28 children with persistent obstruction despite ICS
- Persistent symptoms vs paucisymptomatic
  - Similar RBM thickening
  - Eos. and Neutr. in epithelium: S > PS
  - IFNγ e IFNγ / IL-4 ratio: PS > S

Symptoms are associated with Th2 dependent inflammation.

De Blic et al  J Allergy Clin Immunol 2004
Bronchial biopsy (May–Grunwald Giemsa) from a paucisymptomatic child showing intraepithelial and submucosal mononuclear cells (A) and from a symptomatic child showing eosinophils in the intraepithelial and submucosal area (B). Magnification ×500.

Difficult asthma in children: a biopsy-based study

De Blic et al JACI 113:97, 2004
There is an excessively frequent label of asthma in intermittent exclusive virus-induced wheezing in infancy often leading to inappropriate use of steroids.

There is still under-diagnosis and poor management in children with established asthma.

Asthma starts early in life with recurrent wheezing frequent in the first year of life.

Phenotypes overlap in this age group, and pediatricians frequently prescribe controller asthma medication regardless of whether symptoms are troublesome or if there is a clear response to treatment.

Allergic Bronchopulmonary Aspergillosis

**Diagnostic criteria**

- Asthma.
- Immediate skin reactivity to Aspergillus.
- Serum precipitins to *A fumigatus*.
- Total serum IgE > 1.000 ng/ml
- Current or previous pulmonary infiltrates.
- Central Bronchiectasis.
- Peripheral Eosinophiliia.

A. fumigatus sensitization was associated with a 2.01 increased hazard ratio of bronchiectasis (95% CI 1.26 to 3.22, $P = 0.005$), and more obstructive spirometry postbronchodilator FEV1/FVC ratio 57.6 vs 70.3 $P = 0.001$

even when diagnostic criteria for ABPA are not met
Contents

• Allergic Rhinitis
• Allergic Conjunctivitis
• Inflammation
• Obesity
to assess the frequency and severity of EIB in obese adolescents with or without prior clinical history of asthma

- Severity of EIB: Maximum Fall in %FEV1
- and the area above the curve \( AAC_{0-30\text{ min}} \)
Cross-sectional study
N= 80 , ages 10–16 yrs

Asthmatic obese (n = 18)
Asthmatic non-obese (n =21)
Obese non-asthmatic (n =26)
Healthy individuals (n =15)

Exercise bronchoprovocation test : ↓FEV1 ≥15%,
maximum % fall in FEV1 (MF%FEV1) and
area above the curve (AAC0-30min) were calculated
to evaluate EIB severity and recovery.

Body Masss Index (BMI) >95° (Center for Disease Control and Prevention (CDC)

Lopes et al Allergol Immunopathol 2009;37:175–9
<table>
<thead>
<tr>
<th></th>
<th>Asthmatic obese (n = 18) Mean ± SD</th>
<th>Asthmatic non-obese (n = 21) Mean ± SD</th>
<th>Obese non-asthmatic (n = 26) Mean ± SD</th>
<th>Healthy (n = 15) Mean ± SD</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>12.0 ± 1.5</td>
<td>13.7 ± 1.7</td>
<td>12.6 ± 1.6</td>
<td>13.5 ± 2.1</td>
<td>NS</td>
</tr>
<tr>
<td>Stature (cm)</td>
<td>157.0 ± 8.7</td>
<td>158.5 ± 9.6</td>
<td>160.4 ± 7.7</td>
<td>157.0 ± 11.7</td>
<td>NS</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>71.6 ± 14.2</td>
<td>46.5 ± 9.6†</td>
<td>77.3 ± 17.3‡</td>
<td>46.8 ± 9.9‡</td>
<td>0.0000</td>
</tr>
<tr>
<td>BMI (kg.m⁻²)</td>
<td>28.9 ± 4.9</td>
<td>18.4 ± 2.0†</td>
<td>29.9 ± 5.9§</td>
<td>18.7 ± 2.2§</td>
<td>0.0000</td>
</tr>
<tr>
<td>FEV₁ (L)</td>
<td>2.83 ± 0.7</td>
<td>2.95 ± 0.8</td>
<td>2.99 ± 0.6</td>
<td>2.88 ± 0.8</td>
<td>NS</td>
</tr>
<tr>
<td>FEV₁ (pred %)</td>
<td>95 ± 11</td>
<td>96 ± 10</td>
<td>94 ± 14</td>
<td>94 ± 12</td>
<td>NS</td>
</tr>
</tbody>
</table>

BMI = body mass index; FEV₁ = forced expiratory volume in one second.
†Asthmatic obese × asthmatic non-obese; ‡obese non-asthmatic × healthy; § asthmatic non-obese × obese non-asthmatic.
Kuskall–Wallis and Mann–Whitney tests.
Excess weight increased EIB frequency among asthmatic and non-asthmatic adolescents and contributed to severity in EIB.

**Table 2**

<table>
<thead>
<tr>
<th></th>
<th>Asthmatic obese (n = 18)</th>
<th>Asthmatic non-obese (n = 21)</th>
<th>Obese non-asthmatic (n = 26)</th>
<th>Healthy (n = 15)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>EIB (%)</td>
<td>50 (45–55)</td>
<td>38 (34–43)</td>
<td>11.5 (11–12)§</td>
<td>6.7 (3.4–10)</td>
<td>0.01</td>
</tr>
<tr>
<td>MF/FEV₁ (%)</td>
<td>37.7 ± 18.5</td>
<td>24.5 ± 8.3†</td>
<td>19.5 ± 4.4</td>
<td>–</td>
<td>0.02</td>
</tr>
<tr>
<td>Mean ± SD AAC₀–₃₀ (%, min)</td>
<td>455 ± 469</td>
<td>214 ± 275†</td>
<td>62 ± 239§</td>
<td>54 ± 191</td>
<td>0.03</td>
</tr>
</tbody>
</table>

EIB = exercise-induced bronchospasm; MF/FEV₁ = % maximum fall in FEV₁; AAC₀–₃₀ = area above curve.

Asthmatic obese × asthmatic non-obese; obese non-asthmatic × healthy; asthmatic non-obese × obese non-asthmatic.

Parameters for EIB evaluation

![Graph showing FEV1 percentage changes over time during exercise. The graph illustrates a baseline, maximum fall in FEV1, and AAC0-30 sample.](image-url)
Obesity impacted negatively pulmonary function in both asthmatics and non asthmatics after exercise.

Excess weight in asthmatics significantly contributed to increase in exercise-induced bronchospasm severity and recovery period.

EIB should be evaluated in obese before initiating a fitness program.
Muchas Gracias

Prof. Dr. Nelson Rosário