

ORIGINAL ARTICLE

Acute otitis media in schoolchildren: allergic diseases and skin prick test positivity

YNGVILD E. BENTDAL^{1,2}, PER NAFSTAD^{3,4}, GUNNHILD KAREVOLD^{1,2} & KARI J. KVÆRNER^{1,2}

¹Faculty Division of Akershus University Hospital, University of Oslo, ²Department of Otorhinolaryngology, Akershus University Hospital, ³Department of General Practice and Community Medicine, Medical Faculty, University of Oslo, and ⁴Division of Epidemiology, Norwegian Institute of Public Health, Oslo, Norway

Abstract

Conclusions. Single and repeated episodes of acute otitis media (AOM) in 10-year-old children were associated with reported allergic disease. Further, skin prick test (SPT)-negative children with reported asthma and allergic rhinoconjunctivitis had increased risk of AOM. We suggest that optimal treatment of allergic symptoms may have an effect on AOM in school children. **Objective.** The objective of the study was to estimate associations between AOM, allergic diseases and SPT positivity in 10-year-old children. **Material and methods.** Population-based cross-sectional study of 3406 10-year-old children living in Oslo. Main outcome measures were questionnaire-based information on AOM and reported physician-diagnosed allergic diseases with symptoms during the last year. In addition, 2657 children were skin prick tested. Logistic regression analyses were performed to estimate associations and control for potential confounders. **Results.** One or more episodes of AOM were present in 13.8% ($n=470$) of the children; 9.7% ($n=331$) had single episodes, while 4.1% ($n=139$) had two or more infections. We found a statistically significant association between AOM and reported allergic diseases, strongest for AOM and asthma with odds ratio 2.7 (95% confidence interval 1.8–4.0) and 2.3 (95% confidence interval 1.3–4.3) for single and two or more episodes of AOM, respectively. The risk for AOM was increased in asthmatic SPT-negative children compared with asthmatic SPT-positive children, the odds ratios were 3.0 (1.7–5.4) and 1.5 (0.8–2.8), respectively. The same tendency was found for allergic rhinoconjunctivitis.

Keywords: Acute otitis media (AOM), allergic diseases, skin prick test (SPT), children

Introduction

Otitis media is one of the most common childhood diseases [1] and the most frequent reason for children to consume antibiotics or undergo surgery [2]. A recent report has documented that acute otitis media (AOM) remains prevalent also in school children [3]. Eustachian tube dysfunction is a key factor in the pathogenesis of the disease, and nasal inflammation due to allergic rhinitis or upper respiratory infection are suggested contributing risk factors [4].

Both clinical [5–8] and epidemiological [9–11] studies have addressed the relation between otitis media and allergic diseases, and allergy co-occurring with otitis media has been reported to range from

10% to 80% [7,12]. The latter discrepancy calls for a more precise understanding of the relationship between otitis media and allergic diseases. Epidemiological studies using well-accepted diagnostic criteria for atopy, such as skin prick tests (SPTs), have been specifically requested [13]. The present study has enabled us to study the relation between AOM and allergic disease using both questionnaire-based information on allergic diseases and AOM and the SPT as an objective measure of allergic (IgE-mediated) sensitization. The aim of the study was to estimate associations between parental reported AOM and allergic diseases and results of SPTs in a population-based sample of 10-year-old children in Oslo, Norway.

Material and methods

Study population

In 2001–2002 a population-based cross-sectional study of children born in 1992 and living in Oslo was carried out. In all, 5125 children were sent an invitation to participate in the study; 3406 of their parents responded positively by completing and returning the self-administered questionnaire (response rate 66%).

The participants were also offered a clinical examination that included SPTs. A mobile unit of trained research nurses visited the schools and conducted the examinations. SPT results were available for 2657 children, collected in the period between October 2001 and December 2002. For safety reasons, children who reported earlier severe allergic reactions ($n=69$) were not skin prick tested. Increased prevalence of both allergic diseases and respiratory infections was found in the latter group. Another 55 children refused to be tested due to anxiety. The clinical testing was conducted under medical supervision after parental consent. The study was approved by the Regional Ethics Committee and the Norwegian Data Inspectorate.

Health outcomes

The outcome of interest was the frequency of AOM episodes in the past 12 months. In the questionnaire the questions were formulated as follows: 'Has the child had otitis media the past 12 months? If yes, how many episodes in the past year?'. Other outcome measures were allergic rhinoconjunctivitis, asthma and atopic eczema. The allergic diseases had to be physician-diagnosed and with the presence of symptoms during the previous 12 months. Parental atopy was defined as reports of maternal or paternal asthma, hay fever or eczema. Information on current medication was not collected.

Skin prick test

The SPTs were performed and standardized as recommended by the ISAAC (International Study of Asthma and Allergies in Childhood) phase II protocols [14]. Standardized perennial allergens used were: cat, dog, house dust mite (*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*), moulds (*Cladosporium herbarum* and *Alternaria tenuis*), horse and the seasonal allergens – birch and grass (timothy). Histamine chloride solution (10 mg/ml) was used as a positive control and NaCl (9 mg/ml) as a negative control. Weal size was measured after 15 min. A positive SPT corresponded to a weal with mean diameter (half the

value of the horizontal plus the vertical diameter) exceeding the negative control by at least 3 mm, in accordance with the ISAAC protocol [14]. Children with at least one positive SPT were considered SPT-positive. The children who were skin prick tested were asked not to use antihistamines before the test procedure. The SPTs are described more detailed elsewhere [15].

Statistics

Prevalence was used as a measure of disease occurrence. Logistic regression analyses were performed to estimate associations and odds ratio (OR) with 95% confidence interval (95% CI) was used as a measure of effect and precision. When the association between AOM and allergic disease and SPT positivity was estimated, no episode was compared to one episode and with two or more episodes of AOM during the past year. Due to lack of statistical power, AOM was dichotomized into no episode and one or more episodes during the past year, when allergic children were stratified by SPT positivity. Based on previous knowledge, gender and parental atopy were included in multivariate logistic regression analyses for adjustment of odds ratios. Missing information was given a separate value and analyses were performed with and without the missing category. Both approaches gave consistent results and only results with the missing category are presented. To optimize statistical power of the analyses, associations between AOM and allergic diseases were assessed in the total material, while analyses including SPT results had to be performed in a subsample. There were no significant differences in disease and gender distribution between the total study population and those with valid SPT (Table I). SPSS version 13.0 for Windows (SPSS Inc., Chicago, IL, USA) was used for statistical analyses.

Results

The distribution of AOM during the study year is presented in Figure 1. One or more episodes of AOM were present in 13.8% ($n=470$) of the children; 9.7% ($n=331$) had single episodes, while 4.1% ($n=139$) had two or more infections. Figure 2 shows the distribution and overlap between the allergic diseases; 11.1% ($n=378$) had allergic rhinoconjunctivitis, 10.5% ($n=358$) had atopic eczema and 5.0% ($n=171$) had asthma. Of the skin prick tested children, 23.9% ($n=634$) were positive to one or more allergens. There was only partial overlap between SPT positivity and the different allergic diseases as reported in the questionnaire. Among children with asthma, 52.4% had a positive test to

Table I. Reported respiratory infections, allergic diseases and characteristics in the total study population ($n=3406$) and among children with valid skin prick test ($n=2657$).

Characteristics	All children ($n=3406$)%	Children with valid skin prick test ($n=2657$)%
AOM ≥ 1 episode	13.8	13.0
1 episode AOM	9.7	9.4
≥ 2 episodes AOM	4.1	3.6
Tonsillopharyngitis ≥ 1	21.6	21.3
Common cold ≥ 1	85.3	86.2
Lower respiratory infections ≥ 1	8.1	7.7
Asthma	5.0	4.7
Allergic rhinoconjunctivitis	11.1	10.9
Atopic eczema	10.5	10.6
All three atopic diseases	1.0	0.7
Gender (boys)	50.9	50.9
Parental atopy	56.8	59.8

Missing information in the total material: current infection, 52; allergic diseases, 30. AOM, acute otitis media.

one or more allergens. Comparable numbers for allergic rhinoconjunctivitis and atopic eczema were 74.8% and 42.9%, respectively.

Significant associations were found between AOM and allergic diseases, strongest for asthma (Table II). Children with two or more episodes of AOM were not more prone to allergic diseases compared to those with single infectious episodes (Table II). Girls had a higher risk of AOM than boys with adjusted odds ratio 1.1 (95% CI 0.9–1.4) and 1.5 (95% CI 1.1–2.2) for one and two or more episodes, respectively. Parental atopy also increased the risk of AOM with odds ratio 1.3 (95% CI 1.0–1.7) for a single episode and 1.2 (95% CI 0.9–1.7) for two or more episodes.

We found an inverse association between single episodes of AOM and SPT positivity to any allergen with odds ratio 0.7 (95% CI 0.5–1.0). The same tendency was found for both seasonal and perennial allergen positivity (Table III). For children with

repeated AOM, corresponding negative associations were not found.

When the data were stratified by SPT positivity, we found the risk for one or more episodes of AOM increased in asthmatic SPT-negative children compared with SPT-positive children, odds ratios were 3.0 (1.7–5.4) and 1.5 (0.8–2.8), respectively (Table IV). The same tendency was found for allergic rhinoconjunctivitis.

Discussion

We found that AOM was significantly related to reported physician-diagnosed asthma, allergic rhinoconjunctivitis and atopic eczema, but not to SPT positivity. The frequency of infection did not influence the strength of the positive association found between AOM and reported allergic disease.

There are diverging reports as to how otitis media is associated with allergic diseases [7,12]. One reason may be differences in study designs and outcome measures in studies addressing this issue [5–11]. Both clinical and epidemiological studies have methodological challenges that could explain why there still is uncertainty about how these diseases are related. Associations found in clinical studies could be biased due to selection and epidemiological studies may have weaknesses related to precision and potential misclassification of outcomes. Clinical studies have mostly studied children with otitis media with effusion (OME) [5–8], with inconsistent definition of allergy [16]. Although the accuracy of questionnaire-based diagnosis of otitis media and allergic diseases may be challenged, retrospective parental-reported childhood AOM has been validated as a reliable disease measure [17]. For allergic diseases, self-reported physician-diagnosed asthma has correlated well with objective findings of asthma [18]. The present study has included both questionnaire-based health outcomes and SPT as a measure of allergic (IgE-mediated) sensitization.

We found increased risk of AOM in children with reported allergic diseases. This is in accordance with earlier epidemiological studies [9–11]. The strongest association was found between AOM and asthma. An underlying factor predisposing to both diseases may explain our finding, as indicated in two previous studies [19,20]. A common link between asthma and AOM could be respiratory syncytial virus (RSV), as it has been reported that respiratory infections caused by RSV during early childhood are associated with an increased risk of asthma [21], and RSV has been suggested to be the principal viral pathogen involved in AOM [22]. Although studies of otitis media pathogenesis have identified interactions

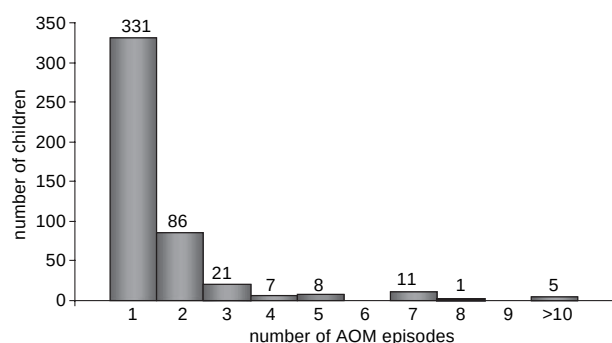


Figure 1. Number of acute otitis media episodes in study population in past year ($n=3406$).

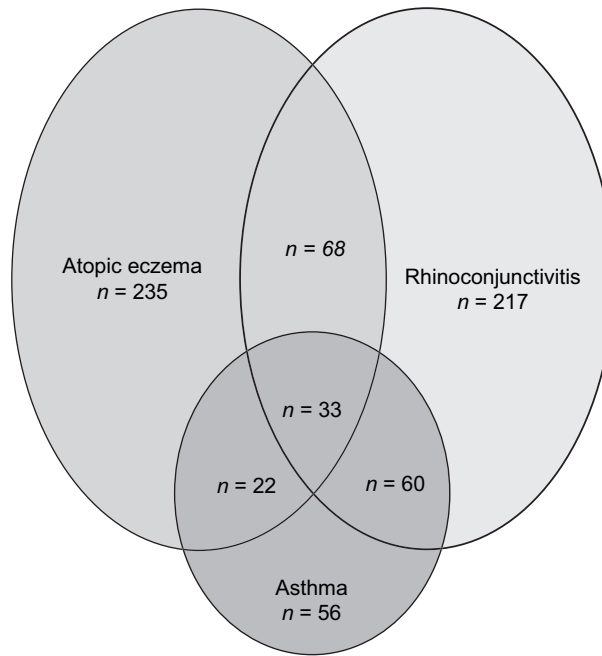


Figure 2. Distribution and overlap of the allergic diseases in the total material ($n=3406$).

among infection, allergic reactions, and eustachian tube dysfunction [4], it has been concluded from randomized studies that antihistamines do not have any beneficial effect on otitis media [16]. Nasal congestion induced by an allergic reaction and followed by reflux of nasopharyngeal secretions into the middle ear or blockage of the eustachian tube secondary to mucosal inflammation could induce otitis media [11]. Allergic rhinitis may predispose to upper respiratory infections by increased expression of intracellular adhesion molecule-1 (ICAM-1). This molecule in the nasal mucosa is a receptor for rhinoviruses, which cause 30% of childhood upper respiratory tract infections [23]. Further, a recent review found allergic disease and

gastro-oesophageal reflux to be two important contributors to tubal inflammation causing otitis media with effusion [24]. Recently Nguyen et al. identified allergic inflammation on both sides of the eustachian tube in atopic patients with OME [25] and concluded that the middle ear may be part of the united airway in atopic individuals.

In contrast to the relation between AOM and reported allergic disease, we found inverse associations between AOM and SPT positivity. Similar findings have been reported by Caffarelli et al. [5] and Alles et al. [6] for otitis media with effusion. As shown in this study and several others [26–30],

Table II. Risk (odds ratio with 95% confidence interval) of single and two or more episodes of acute otitis media (AOM) in schoolchildren with different allergic diseases ($n=3406$).

Allergic diseases*	1 AOM Odds ratio	(95% confidence interval)	≥2 AOM Odds ratio	(95% confidence interval)
Asthma				
No	Ref.		Ref.	
Yes	2.7	(1.8–4.0)	2.3	(1.3–4.3)
Allergic rhinoconjunctivitis				
No	Ref.		Ref.	
Yes	1.3	(1.0–1.9)	1.4	(0.9–2.3)
Atopic eczema				
No	Ref.		Ref.	
Yes	1.5	(1.1–2.1)	1.3	(0.8–2.2)

*Missing = 70.

Table III. Risk (odds ratio with 95% confidence interval) of single and two or more episodes of acute otitis media in skin prick test-positive schoolchildren in Oslo ($n=2657$).

Skin prick test positivity*† (≥1 allergens)	1 AOM Odds ratio	(95% confidence interval)	≥2 AOM Odds ratio	(95% confidence interval)
For any allergen				
Negative	Ref.		Ref.	
Positive	0.7	(0.5–1.0)	1.2	(0.8–2.0)
For any seasonal allergen				
Negative	Ref.		Ref.	
Positive	0.5	(0.4–0.8)	1.2	(0.7–2.0)
For any perennial allergen				
Negative	Ref.		Ref.	
Positive	0.9	(0.6–1.3)	1.6	(0.9–2.6)

*Allergens included in the study: seasonal (birch, timothy), perennial (cat, dog, horse, house dust mite, moulds).

†Missing = 53.

Table IV. Prevalence (%) and risk (odds ratio with 95% confidence interval) of one or more episodes of acute otitis media (AOM) in children with positive or negative skin prick test (SPT) and allergic disease ($n=2657$).

Allergic disease*	AOM in children with allergic disease			
	%	<i>n</i>	Odds ratio	(95% confidence interval)
Asthma				
No asthma, SPT-negative = 1915	13.2	253	Ref.	
Asthma, SPT-negative = 57	31.6	18	3.0	(1.7–5.4)
No asthma, SPT-positive = 553	10.8	60	0.8	(0.6–1.1)
Asthma, SPT-positive = 65	18.5	12	1.5	(0.8–2.8)
Allergic rhinoconjunctivitis (ARC)				
No ARC, SPT-negative = 1902	13.3	253	Ref.	
ARC, SPT-negative = 70	25.7	18	2.3	(1.3–3.9)
No ARC, SPT-positive = 403	12.2	49	0.9	(0.7–1.3)
ARC, SPT-positive = 215	10.7	23	0.8	(0.5–1.2)
Atopic eczema (AE)				
No AE, SPT-negative = 1813	13.5	244	Ref.	
AE, SPT-negative = 159	17.0	27	1.3	(0.9–2.0)
No AE, SPT-positive = 497	11.1	55	0.8	(0.6–1.1)
AE, SPT-positive = 121	14.0	17	1.1	(0.6–1.8)

*Missing = 67.

allergic disorders only partially overlap with objective measures, including SPTs, serum allergen-specific or total IgE. A systematic review by Pearce et al. [28] showed that the proportion of asthma cases attributable to atopy was usually <50%. Our finding of only partial overlap between allergic disease and SPT positivity confirms that although such tests are important clinical tools, one needs to be aware that a substantial proportion of children with allergic diseases will test negative [29,30]. Further, it may explain the contrasting associations between AOM and allergy reports versus SPT positivity. In a cross-sectional study differential disease reporting cannot be ruled out when all the information comes from one source [31]. However, the SPT status was unknown to the participants and the distinction in associations between SPT-positive and -negative children makes such bias less likely. To optimize statistical power of the analyses, associations between AOM and allergic diseases were assessed in the total material, while analyses including SPT results could only be performed in a subsample. No significant differences were found in terms of gender, allergic diseases and reported respiratory infections, indicating no selection bias to either group. Furthermore, the association between AOM and allergic diseases showed no differences in the total material versus the subsample that was skin prick tested.

Although it reduced statistical power, the separate analyses among children with and without a positive SPT indicated that the risk of having AOM in asthmatic children was mainly increased in the SPT-negative children. The same tendency was

found for allergic rhinoconjunctivitis. Our findings indicate that non-IgE-mediated asthma and allergic rhinoconjunctivitis predispose to AOM. This corresponds with the findings in a primary care-based Dutch study [19]. In contrast to our study, the Dutch study was not able to distinguish IgE-mediated from non-IgE-mediated asthma, which makes our data and results stronger.

It has been hypothesized that a major proportion of asthma is due to neutrophilic airway inflammation, and that environmental exposure to bacterial endotoxin and air pollution, as well as viral infections, may play important roles as triggers of neutrophilic airway inflammation in asthma [32]. Similar mechanisms may contribute to the increased risk of AOM in non-IgE-mediated asthmatic children.

The current study demonstrates an association between reported allergic disease and both single and recurrent episodes of AOM. Further, SPT-negative children with reported asthma and allergic rhinoconjunctivitis had an increased risk of AOM. We suggest that optimal treatment of allergic symptoms may have an effect on AOM in schoolchildren.

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