

The role of atopy in otitis media with effusion among primary school children: audiological investigation

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Abstract The objective of this study was to evaluate the role of atopy in otitis media with effusion (OME) in children attending primary school in western Sicily focusing on the audiological characteristics among atopic and non-atopic subjects suffering from OME. A total of 310 children (5–6 years old) were screened by skin tests and divided into atopics (G1) and non-atopics (G2). The samples were evaluated for OME by pneumatic otoscopy, tympanogram and acoustic reflex tests. The parameters considered were: documented persistent middle ear effusion by otoscopic examination for a minimum of 3 months; presence of B or C tympanogram; absence of ipsilateral acoustic reflex and a conductive hearing loss greater than 25 dB at any one of the frequencies from 250 Hz through 4 kHz. A total of 56 children (18.06%) resulted to be atopics while 254 were non-atopics. OME was identified in

24 atopic children and in 16 non-atopic children for a total number of 40 children; the overall prevalence rate was 12.9% (42.85% for G1 and 6.30% for G2). OME was bilateral in 28 children (70%), with a significant difference between G1 (79.17%) and G2 (56.25%). The prevalence of B tympanogram was 70.59%, corresponding to 79.07% for G1 and 56% for G2. The mean air conduction pure tone was, respectively, 31.97 dB for G1 and 29.8 dB for G2. The prevalence value of OME in atopic children, also supported by the higher predominance of bilaterality, B tympanogram and hearing loss among this group, could suggest the important role of allergy in the pathogenesis of OME.

Keywords OME · Otitis media with effusion · Allergy · Eustachian tube dysfunction

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Introduction

Otitis media with effusion (OME) describes an inflammatory process within the middle ear space that is generally associated with the accumulation of fluid. Persistent middle ear fluid from OME results in decreased mobility of the tympanic membrane and serves as a barrier to sound conduction. It is a common disease in children with an incidence range from 6 to 64%, depending on the methods used and population characteristics, and which may lead to hearing loss, learning difficulties and delay of language development [1–6]. Approximately, 90% of children (80% of individual ears) have OME sometimes before school age, most often from 6 months to 4 years of age. In the first year of life, >50% of children experience OME, increasing to >60% by 2 years. Many episodes resolve spontaneously within 3 months, but ~30 to 40% of children have

recurrent OME, and 5–10% of episodes last 1 year or longer [7–9]. The pathogenesis of OME is clearly related to the dysfunction of the eustachian tube [10]. Upper respiratory tracts infections (URTI) are one of the most common causes of eustachian tube dysfunction and thus OME among children 1 year old or younger than among 2- or 3-year-old children. Mechanical obstruction of the nasopharyngeal opening of the eustachian tube by adenoid hypertrophy or craniofacial malformations, such as cleft palate deformities and Down syndrome, also cause OME in younger children [11]. The involvement of IgE-mediated allergic reactions in the pathogenesis of OME has been suggested by clinical observations of a high prevalence of OME among patients with allergies [12–14]. In fact, several studies evidenced that 40–50% of children with OME, older than 3 years, had nasal allergy, whereas 21% of allergic children had OME. Other studies showed no association with allergic disease during the first 3 years of life, suggesting that allergy did not play a dominant role in OME at a younger age [11]. It is known that middle ear mucosa itself is rarely a target organ for allergy and the release of biologic mediators of inflammation from basophils and mast cells occurs in the nasal and nasopharyngeal mucosa. These mediators most likely produce eustachian tube edema and inflammation. Over a long period this chronic inflammatory response, along with viral or bacterial infection, produces middle ear effusion [15]. A recent clinical practice discussion and literature review states that “the relation between allergy and OME will remain controversial until well-controlled clinical studies are conducted documenting that in select populations anti-allergy therapy is efficacious in preventing or limiting the duration of OME” [16].

Although in the last few years, there has been a great consensus among the studies with respect to the role of atopy in OME, the knowledge of the audiological characteristics of OME among atopic and non-atopic subjects is yet incomplete.

The aim of this study, carried out on primary school children aged 5–6 years who underwent skin prick tests, was to evaluate the prevalence of OME among the screened population to determine any difference either in OME incidence or in audiological characteristics between atopic and non-atopic subjects suffering from OME.

Materials and methods

This study was carried out by the Department of Audiology, University of Palermo, together with the District of Sciacca, examining a group of children attending primary schools in Sciacca from September 2006 to June 2007. The subject group consisted of 313 patients, 155 males and 158

females, ranging from 5 to 6 years of age. The study protocol was fully explained to patients or their guardians, and written informed consent was obtained from each patient. Children with skull–facial malformations, Down syndrome, perforated drums and ventilation tubes were excluded from the study. At the time of the first screen, all the children underwent skin prick tests and otoscopic examination. Skin tests were performed using 12 common perennial and seasonal allergens: *Alternaria*, *Aspergillus*, *Cladosporium*, *Penicillium*, ragweed, grass mix, trees mix, cockroach, dust mites, *Dermatophagoides farinae*, *Dermatophagoides pteronyssinus* and cat and dog epithelium. The food allergens tested were: dairy, egg, peanut, tree nut, seafood, shellfish, soy and wheat. Solutions of histamine and saline were used as positive and negative controls, respectively. The results were evaluated after 10 min. Wheals ≥ 3 mm in diameter than wheals at the site of the negative control were considered positive. Children with at least one positive skin prick test to any antigen were classified as atopic and included in group 1 (G1), while children with negative skin prick test served as non-atopic controls and were included in group 2 (G2). Patients in both groups were evaluated for OME and underwent pneumatic otoscopy. When abnormalities suggestive of OME, which included presence of retracted tympanic membranes, fluid level, bubbles or hypervascularity, were noted, tympanogram and ipsilateral acoustic reflex were performed. The instrument used was a tympanometry machine, model Amplaid 766, with a probe frequency of 220 Hz and an air pressure range of -400 to 100 mmH₂O with automatic recording. Tympanograms were divided into the following types: type A ($+99$ to -99 mmH₂O), type C1 (-100 to -199 mmH₂O), type C2 (>-200 mmH₂O) and type B (flat curve without peak identification). For ipsilateral acoustic reflex, the same machine was used: an Amplaid 766, with a signal of 105 dB HTL and pure tone stimulus at 1,000 and 2,000 Hz. Children with otoscopic appearance of OME and abnormal tympanogram (type B or C with no stapedial reflex) were regarded as positive screens and given a follow-up appointment within 3 months after the initial screening. The criteria for diagnosis of OME in the study were as follows: documented persistent middle ear effusion by otoscopic examination for a minimum of 3 months; presence of B or C tympanograms; absence of ipsilateral acoustic reflex and a conductive hearing loss greater than 25 dB at any one of the frequencies from 250 Hz through 4 kHz. Audiogram was performed if the child had a type B or C tympanogram. Audiometric tests were performed using a duly calibrated pure tone audiometer and were applied to each ear at frequencies of 0.5, 1.0, 2.0 and 4.0 kHz.

Statistical analysis were performed using the Matlab[®] computer program.

Results

The total number of children examined was 313, but 3 children were excluded from the study because of skull–facial malformations and perforated drums. A total of 310 children were analyzed. The age of children ranged from 5 to 6 years, with a mean age of 5.56 years (5.59 for male and 5.53 for female). Of the children, 155 (50%) were boys and 155 girls.

At the time of the first examination, based on skin tests, children were classified into two groups: G1 (atopics) including 56 children (18.06%) with positive skin tests and G2 (non-atopics) including 254 controls (81.94%) with negative skin tests.

Of the 56 children belong to G1, 29 patients (51.78%) had positive skin tests for both inhalant and food allergens; 17 patients (30.36%) had a positive test only for food allergy; 10 (17.86%) patients had an allergy only against inhalant allergens.

During pneumatic otoscopy, a total of 44 children were found with suspected OME. Of these, four were found without any evidence of OME in the follow-up appointment after 3 months and were excluded from the study. A total of 40 children (overall prevalence rate of 12.9%) who suffered from persistent OME were studied (≥ 3 months), of which 12 were boys and 28 were girls.

Of the 40 children with OME, 24 (60%) were atopic (G1), while 16 (40%) were non-atopic (G2) (Fig. 1a, b).

Of the 56 children belonging to G1, 24 (42.85%) were found to suffer from OME while 32 (57.15%) were healthy. Of the 254 non-atopic children belonging to G2, 16 (6.29%) were diagnosed with OME while the others (93.71%) were healthy (Table 1) (Fig. 2).

Of those suffering from OME, 12 were boys (7 G1 and 5 G2) and 28 were girls (17 G1 and 11 G2). The rate of OME was 30% for boys (29.16% for G1 and 31.25% for G2) and 70% for girls (70.83% for G1 and 68.75% for G2).

A total of 28 subjects had bilateral OME (70%) and 12 had unilateral OME (7 right ear and 5 left ear) for a total of 68 ears. In G1, OME was found as bilateral in 19 cases

Table 1 Distribution of 310 children according to atopy and OME

Groups	Otitis media with effusion				Total N
	Yes		No		
	N	%	N	%	
G1	24	42.85	32	57.15	56
G2	16	6.30	238	93.7	254
	40	12.9	270	87.1	310

$\chi^2 = 54.56, df = 1, P = 1.50^{-13}, OR = 11.16$

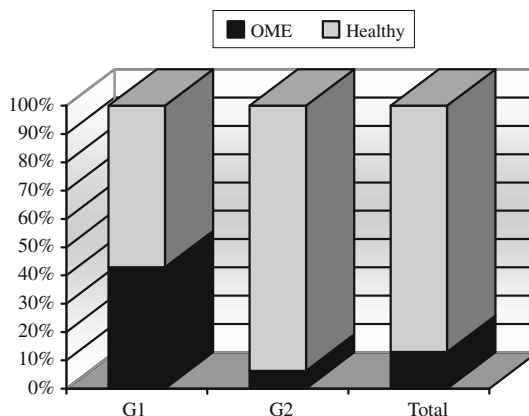


Fig. 2 Percentage values of OME in the population

(79.17%) and unilateral in 5 cases (20.83%) for a total of 43 ears, while in G2, OME was found as bilateral in 9 cases (56.25%) and unilateral in 7 cases (43.75%) for a total of 25 ears (Fig. 3a, b).

Of the total of 68 ears, 48 ears (65%) had B tympanogram with negative reflex test and 20 had C tympanogram with negative reflex test (35%). As for atopic children with OME (G1), 34 ears (79.07%) had B tympanogram and 9 had C tympanogram (20.93%), while in G2, 14 ears (56%) had B tympanogram and 11 had C tympanogram (44%) (Fig. 3c, d).

Regarding the audiometric threshold observed in the OME population, 42 ears (61.76%) had a hearing loss between 25 and 30 dB; 22 (32.35%) between 35 and

Fig. 1 Distribution of pediatric population according to OME and atopy; **a** absolute values; **b** relative values

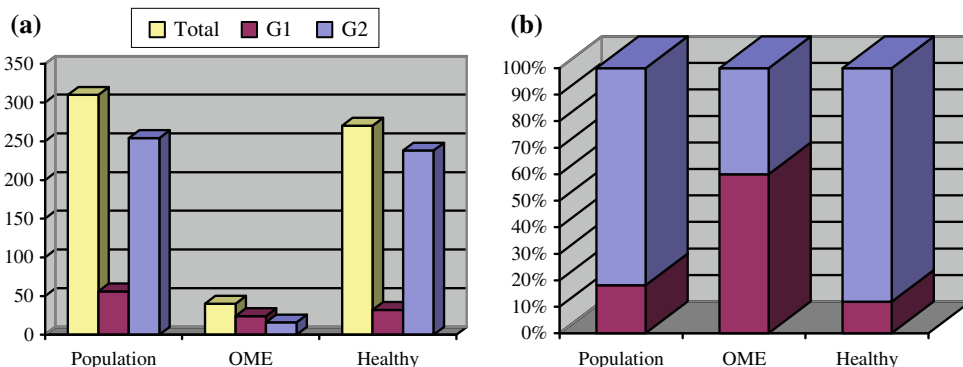
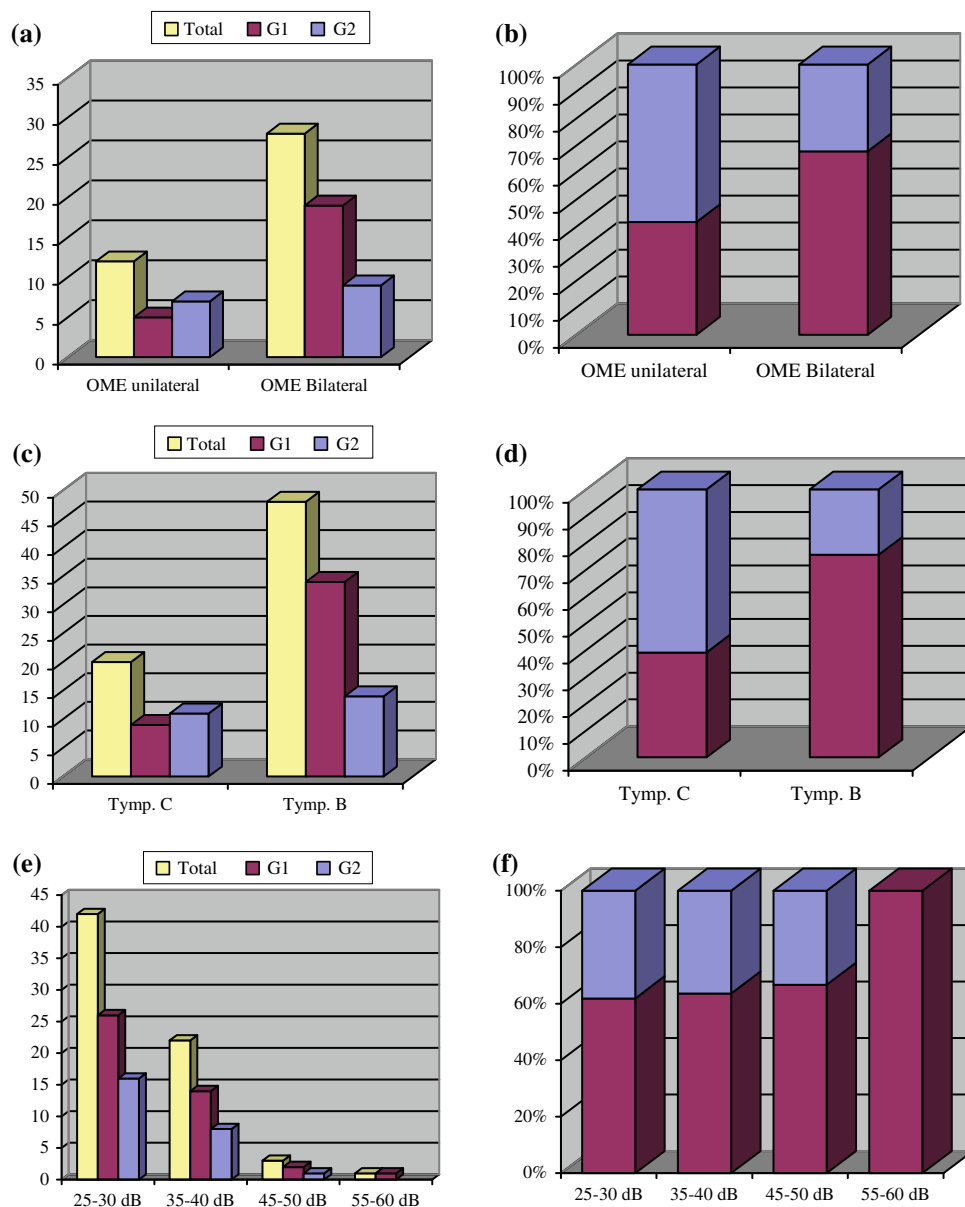


Fig. 3 Audiological characteristics of the OME population



40 dB; 3 (4.41%) between 45 and 50 dB; 1 (1.47%) between 55 and 60 dB. The mean air conduction pure tone according to diagnosis at frequencies 500 Hz–4 kHz was, respectively, 31.97 dB for G1 and 29.8 dB for G2 (Fig. 3e, f).

Discussion

OME is defined as the presence of fluid in the middle ear without signs or symptoms of acute ear infection. It is a common disease in children, which may lead to hearing loss or surgical intervention. In most children, OME improves spontaneously and has a good prognosis, but approximately 10% of pediatric patients experience

repeated or chronic OME. In addition to hearing loss, chronic OME may be associated with learning difficulties and delay of language development.

The reported prevalence rates of OME among primary school children in literature were as follows: 10.4% in a study from Turkey including 912 children between 6 and 8 years of age [17]; 6.8% in Italy (2,132 children, 5–14 years old) [18]; 9.5% in the Netherlands (1,004 children, 5–8 years old) [19]; 13.8% in Saudi Arabia (4,124 children, 1–8 years old) [20]; 6.5% in Greece (5,121 children, 6–12 years old) [21].

The prevalence rate of OME in our study including 310 children between 5 and 6 years of age is 12.9%. Our results are higher than those in most other studies. Many factors may explain the differences between these prevalence

rates. Irrespective of the researcher's method, age is one of the most important risk factors for the disease. On reviewing some articles about the issue, Zielhuis et al. [22] used an age-specific prevalence rate and came to the conclusion that the rate has two peaks: one around 2 years of age, probably leading both to immaturity of function of the immune system and to anatomical and functional diversity of the eustachian tube (i.e., nearly horizontal orientation), and the other around the age of 5 years, probably leading to a higher percentage of URTI among children attending the same class. Our population presents an age range of 5–6 years that coincides with the second peak reported by Zielhuis, confirming the important role of age as risk factor for OME. In fact, our prevalence was lower than that reported in the study conducted in Saudi Arabia (13.8%) in which the age range was 1–8 years that includes both the peaks reported by Zielhuis. As for sex, some previous studies found that OME was encountered more frequently in boys than in girls, whereas others found no sex-related differences. In our study, the number of girls with OME significantly exceeded the number of boys ($\chi^2 = 7.384$; $P = 0.0067$).

Besides the methods used and the age considered, the different prevalence rates may also depend on the high percentage of atopy among the population screened. In fact, controlled studies have shown an increase in the prevalence of OME in children with an atopic history or positive skin prick tests compared with normal children [23]. Atopy has been defined as the sensitization or predisposition to hyperreactivity to a normal non-reactive antigen. Allergic patients are considered to be those who express symptoms related to exposure and are not merely sensitized. Approximately, 20–30% of the general population and 10–15% of children are atopic [24]. In our study, to value the role of atopy, all the pediatric population was screened by means of routine skin testing; of 301 subjects ranging from 5 to 6 years of age, atopy was evidenced in 18.06% (56 subjects) (Fig. 1b). Allergy may be related to OME etiology through different mechanisms. Experiments indicated that the middle ear mucosa was capable of sustaining an allergic reaction; however, the extent and duration of inflammation were limited, and OME was not observed. Given that the middle ear space is an anatomical extension of the airway by way of the eustachian tube, the middle ear may be considered a component of the united airway in atopic individuals. The allergic inflammation is not isolated to the middle ear, but occurs uniformly in the nasopharynx, middle ear and eustachian tube, leading to the development of OME [25].

Our epidemiologic data seem to support the existence of a relationship between OME and atopic disease. In fact, of 310 children ranging in age from 5 to 6 years old, OME was diagnosed in a total of 40 children (overall prevalence

rate 12.9%). Of these, 60% were atopic (24 children), while 40% (16 children) were non-atopic. Of a total of 56 atopic children, 24 (42.85%) were found to suffer from OME, while 16 of 254 non-atopic children (6.29%) were diagnosed with OME (Figs. 1b, 2). Other investigators, using objective intradermal and in vitro testing, have demonstrated that 72–100% of the children with OME are atopic: Tomonaga (72%) [26], Nsouli (78%) [27], Hurst (81%) [28], McMahan (93%) [29], Hall (100%) [30]. Statistical analysis evidenced a significant correlation between atopy and OME with a correlation index of $r = 0.998$ ($\chi^2 = 54.56$; $P = 1.50^{-13}$; OR = 11.16).

The role of atopy in the development and persistence of OME may be supported by the different audiological characteristics between atopic and non-atopic subjects suffering from OME. In our study, we found a predominance of bilateral OME in atopic subjects with respect to non-atopics. In fact, of a total of 40 children suffering from OME, 28 subjects had bilateral OME and of these 67.86% were atopic (19 children corresponding to 79.17% of the whole G1). This hypothesis is also supported by the statistically significant predominance of B tympanograms in atopic children (79.07%) with respect to non-atopics (56%) ($\chi^2 = 4.053$, $P = 0.044$, OR = 2.97). Besides, our study shows that atopy may contribute to the severity of hearing loss; the mean air conduction pure tone was, respectively, 31.97 dB for atopics and 29.8 dB for non-atopics (index

Table 2 Distribution of OME suffered according to atopy, sex and audiological characteristics

Factors	OME populations			
	Atopics G1		Non-atopics G2	
	N	(%)	N	(%)
Children				
Boys	7	(29.16)	5	(31.25)
Girls	17	(70.83)	11	(68.75)
OME				
Unilateral	5	(20.83)	7	(43.75)
Bilateral	19	(79.17)	9	(56.25)
Ears				
Right	22	(51.16)	13	(52)
Left	21	(48.84)	12	(48)
Tympanogram				
Tymp. C	9	(20.93)	11	(44)
Tymp. B	34	(79.07)	14	(56)
Hearing threshold				
25–30 dB	26	(60.46)	16	(64)
35–40 dB	14	(32.56)	8	(32)
45–50 dB	2	(4.65)	1	(4)
55–60 dB	1	(2.33)		

correlation $r = 0.99$; $P < 0.0001$). In particular in four ears, three of which belong to G1, a moderate hearing loss was evidenced. It was related to the contemporary presence of atelectasis that could be facilitated by chronic allergic reaction of the upper airway (Table 2).

In sum, we concluded that the point prevalence rate of OME among primary school children aged 5–6 years, in our series, was 12.9%. The results clearly identify a group of variables as risk factors for OME. In particular, the present study showed that age and allergy may be important risk factors for OME. Of children with OME, 60% were atopic, whereas 42.85% of children with allergy were found to suffer from OME. These results, also based on the audiological measurements, seem to support the hypothesis that allergic inflammation could have a role in the genesis and recurrence of OME indirectly by causing a persistent blockage of the eustachian tube or directly by means of middle ear mucosa inflammation, but need further investigation with other studies.

Conflict of interest statement The authors report no conflict of interest. The authors alone are responsible for the content and writing of the paper.

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