International Journal of Pediatric Otorhinolaryngology (2005) xxx, xxx–xxx

International Journal of Pediatric Otorhinolaryngology

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# Factors influencing the presence of otitis media with effusion 16 months after initial diagnosis in a cohort of school-age children in rural Greece: A prospective study

John Xenellis [a], John Paschalidis [a], Christos Georgalas [b,*], Dimitris Davilis [a], Antonis Tzagaroulakis [a], Eleftherios Ferekidis [a]

[a] *Academic Department of Otolaryngology — Head and Neck Surgery, Ippokration Hospital, National University of Athens, Athens, Greece*
[b] *Department of Otolaryngology — Head and Neck Surgery, Southend Hospital, Westcliff-On-Sea, Essex SS0 0RY, UK*

Received 24 November 2004; accepted 29 March 2005

**KEYWORDS**
Otitis media with effusion;
Etiology;
School-age population

**Summary**

*Objective:* Few studies have specifically assessed the risk factors for persistence or recurrence of OME in a cohort of school-age children. The generally accepted etiological factors for OME occurrence may not apply in the same way when the presence of OME over a year from original diagnosis is assessed.
*Methods:* A cohort of 250 school-age children with unilateral or bilateral OME, identified through screening of 5121 asymptomatic children was re-examined 16 months later. All were assessed for a variety of demographic, family and medical factors. Measures included tympanometry, acoustic reflexes and a complete otolaryngologic examination.
*Results:* At 16 months after initial confirmation of OME, 56 out of 250 children (22.4%) suffered from OME, 21 bilateral and 31 unilateral. Presence of OME at 16 months was not associated with gender, blood group, gestational age and weight, history of breast feeding, paternal education level and smoking history, history of allergy, previous use of antibiotics, or with surgery (myringotomy, insertion of ventilation tubes or adenotonsillectomy). In multiple backward-eliminating logistic regression, the only factors associated with OME presence after 16 months were episodes of AOM during the study period (odds ratio 2.75 (95% CI: 1.13—8.17), $p = 0.04$) and younger age (odds ratio 0.53 (95% CI: 0.32—0.79), $p = 0.002$ for each 2 years of increase in age).
*Conclusion:* Seventy-eight percent of school-age children identified with OME through screening will be free of disease 16 months later. The threshold for referral,

* Corresponding author. Tel.: +44 7881504522; fax: +44 2085356834.
*E-mail address:* cgeorgalas1@yahoo.co.uk (C. Georgalas).

0165-5876/$ — see front matter 
doi:10.1016/j.ijporl.2005.03.047

or surveillance could however justifiably be lower in children who (a) have once been identified with OME and (b) are (relatively) younger, or have experienced an episode of acute otitis media.


## 1. Introduction

Otitis media with effusion (OME) is the commonest cause of hearing loss in children: screening studies using monthly tympanometry and pneumatic otoscopy of children aged 2–6 years showed that the incidence of OME was between 53 and 61% during a 1-year period [1]. Seven-year-old children showed a much lower incidence (26%) [2]. In most cases, OME presents as an episodic, self-limiting process, with approximately 65% of OME episodes in children 2–7 years old resolving within 1 month [3]. The main symptom of concern in OME is a mild to (rarely) moderate hearing loss seen in about half with tympanometric or otoscopic diagnosis. Whether this could lead to lasting impairments of speech, language, cognitive, and psychosocial development is debatable. A recent study from Pittsburgh showed negligible effects of early treatment for OME in children less than 3 years old on the developmental outcomes at three [4] and 4 years of age [5]. This study however has been criticized for a failure to select more seriously affected children for study and the inclusion of children with only episodic OME. This highlights the importance of identifying the small group of children with persistent OME. This would allow treatment to be targeted towards the chronically and more severely affected children while avoiding over-treating the large majority of children.

Although many studies have assessed the causes of OME, relatively few studies have analyzed the factors leading to its persistence: Tos et al. [6] assessed a cohort of 4-year-old children with OME over 12 months and found that season at diagnosis was the only factor correlating with effusion persistence. Daly et al. [7] followed up for 6 weeks children between 10 months and 6 years of age and identified day care attendance as a factor predicting persistence but the staging of this study still points to relatively mild and non-persistent cases. A study from the Netherlands assessing risk factors for OME persistence in infants [8] demonstrated that the presence of older siblings (with or without OME), day care attendance, multiple upper respiratory tract infections could predict the persistence of OME. A large-scale study of the recruitment lead-in to the Medical Research Council Multi-Centre Otitis media Study Group's Trial of Alternative Regiments for Glue Ear Treatment (TARGET) [9] provided an opportunity to look at 3-month persistence in children that had met criterion ($\geq$20 dB HL) after a delay from referral in children aged 3–6 years old [10]. The degree of hearing loss and season of referral were the only factors predicting (non-) resolution of OME. While these studies have shed light on significant areas of the natural course of OME on children, only the TARGET study included large numbers of school-age children in whom OME problems are longstanding and are causing concern in relation to educational progress. Although lower rates of OME apply in this older group, many of the common etiological factors for OME may not apply (such as day care attendance, as all children go to school). We felt that there was a need for a study of a cohort of school-aged OME children identified through screening (thus avoiding the biases associated with referral). We chose a longer period before reassessment (16 months compared to 3 or 6 of other studies) taking into consideration particular developmental and educational circumstances in this age group.

## 2. Patients and methods

### 2.1. Background

We studied a cohort of 250 children (144 boys and 106 girls) aged 6–12 years diagnosed with unilateral or bilateral otitis media with effusion. This cohort was identified from the screening of 5121 children for OME from May to June 1996, performed as part of a study on point prevalence of otitis media with effusion in Greece [3]. The screening study took part in the municipality of Argolida a municipality in south east of Greece. This is a mainly rural area, with two urban centers, where resides approximately one-fifth of the total population. The level of medical services is average, generally representative of Greece, with two main hospitals and four health centers. However, for the purpose of this study ENT doctors from the Otolaryngology Department of Athens University performed all the otolaryngology examinations.

## 2.2. Patients

### 2.2.1. Inclusion criteria

Unilateral or bilateral OME during the initial screening period (May—June 1996) as defined by positive tympanometry and otoscopy (see criteria for OME presence, Section 2.3).

### 2.2.2. Exclusion criteria

Children with craniofacial abnormalities, cleft palate, Down syndrome or other significant co-morbidity as well as sensorineural hearing loss were excluded from the study.

## 2.3. Methods

All 250 patients identified diagnosed with OME were contacted through their parents and local schools 16 months later. As it was not an intervention study, Regional Ethics Committee approval was not required and was not sought. However, the hospital's board approved this study, and informed consent was obtained from the children's parents prior to re-examination. Of these children 148 (59%) had unilateral disease, and 102 (41%) had bilateral disease at baseline. Parents were handed a questionnaire one week prior to their appointment, with questions on parental education level and smoking status, number of siblings and history of otitis media of the siblings, previous medical history of the child including attacks of acute otitis media (AOM), operations (myringotomy and ventilation tube insertion, tonsillectomy or adenoidectomy) as well as the presence of allergy.

All children who attended and fulfilled the inclusion criteria underwent a complete otolaryngologic examination, including pneumatic otoscopy (after removal of wax plugs) and tympanometry with measurement of acoustic reflexes.

Tympanometry was performed using the MAICO 630-C and Medical QI Master tympanometers, using a probe tone of 226 Hz.

### 2.3.1. Criteria for presence of OME

Otoscopic evidence of fluid (air fluid level, bubbles, reduced mobility on pneumatic otoscopy).
Type B (compliance $<0.2$ ml) or C2 (compliance $>0.2$ ml and pressure $<200$ mm$H_2O$) tympanogram and absence of acoustic reflexes.

All tympanometry recordings were repeated after swallowing (the test) retest variability of tympanometry recordings was minimal ($<5\%$), however, when there was a discrepancy between repeated measurements, the least abnormal were accepted.

## 2.4. Statistical analysis

All data were entered into an SAS data file and analyzed using SAS [11]. For univariate analysis, we used simple comparison of proportions by the Chi-squared test and Fischer exact test as required. Multiple logistic regression was used to adjust for confounding factors and multicollinearity of the independent variables, and so to create a predictive model of OME persistence (backward elimination).

# 3. Results

At re-examination, 16 months later, 56 out of 250 children (22.4%) were found to meet the definition of otitis media with effusion, hence to be persistent or recurrent. Twenty-five of these 56 children (45%) had bilateral OME and 31 (55%) had unilateral OME. In checking possible factors in OME persistence or recurrence via univariate analysis, children with unilateral and bilateral disease were grouped together.

## 3.1. Demographic factors

OME persisted in 32 boys (22.2%) and 24 girls (22.6%). There was no difference in persistence rates between boys and girls ($p = 0.31$). Persistence of OME was much more likely in younger children: 15 out of 34 children younger than 7 years old had evidence of persisting OME, compared with only 3 out of 29 children older than 11 years old. The difference in persistence rates and the trend towards reduced recurrence as children grew older was consistent across the age range, and was highly statistically significant ($p < 0.001$) (Table 1).

## 3.2. Parental factors

Parental education level was assessed separately for mother and father. Paternal and maternal education levels were found to be very closely correlated and as a result, only paternal education level was used for the study's purposes (Table 1). Persistence or recurrence seemed to be more prevalent in children of parents with higher education, although this was far from being statistically significant ($p = 0.31$).

## 3.3. Patient factors

Four factors in the epidemiology of occurrence were examined. Three of them showed trends in the expected direction, but all failed by a considerable

**Table 1** Persistence rates of OME in our cohort of school-age children 16 month after diagnosis: the effect of demographic/patient factors

| Categorical variable | Persistence of OME (%) | Odds ratio | 95% CI | *p*-value |
|---|---|---|---|---|
| Sex | | | | |
| Male | 22.2 | 0.98 | 0.53–1.77 | 0.93 |
| Female | 22.6 | | | |
| Age | | | | |
| <7 years | 44.1 | 6.84 | 1.82–25.07 | 0.001 |
| 7–9 years | 22.3 | 2.48 | 0.74–8.27 | |
| 9–11 years | 16.7 | 1.73 | 0.47–6.24 | |
| >11 years | 10.3 | 1 | | |
| Paternal education | | | | |
| Basic | 20.2 | 1 | | 0.31 |
| High school | 26.4 | 1.4 | 0.49–4.04 | |
| University | 26.3 | 1.39 | 0.48–4.04 | |
| Parental smoking | | | | |
| Yes | 23.1 | 1.14 | 0.59–2.18 | 0.68 |
| No | 20.1 | | | |
| Preterm delivery | | | | |
| Yes | 10 | 0.37 | 0–2.35 | 0.33 |
| No | 22.9 | | | |
| Birth weight (g) | | | | |
| <3000 | 22.5 | 1.43 | 0.58–3.52 | 0.24 |
| 3000–3499 | 30.6 | 2.18 | 1.06–4.48 | |
| 3500–3999 | 16.8 | 1 | | |
| >4000 | 20 | 1.23 | 0.49–3.11 | |
| Breastfeeding at infancy | | | | |
| Yes | 26.5 | 0.93 | 0.39–2.16 | 0.86 |
| No | 27.9 | | | |

margin to achieve significant effects on persistence/recurrence: exposure to parental smoking ($p = 0.68$); too low or too high birth weight ($p = 0.24$); and absence of breast feeding ($p = 0.87$). Surprisingly, in our sample children who had been delivered pre-term showed a trend towards reduced presence of OME, although it was non-significant ($p = 0.30$) (Table 1).

### 3.4. Medical history

History of allergy was not associated with higher OME persistence or recurrence after 16 months. However, the occurrence of an episode of acute otitis media (as reported by the parents) was associated with higher rates of glue ear: 45% of children who had at least an episode of AOM during the watchful waiting period had OME 16 months later, compared with 20% of AOM-free children ($p = 0.01$). Equally important was the reported presence of middle ear effusion (MEE) at least once during the study period as evidenced by the fact that it was associated with 29% persistence rates at 16 months, compared to 18% in the remaining children ($p = 0.04$) (Table 2).

### 3.5. Interventions

Children diagnosed with OME during the screening program were advised to see an otolaryngologist. As the children were not randomized to different treatments, analysis of the influences of subsequent interventions are restricted to weak observational conclusions, although they do illustrate the impact of screening-related interventions in practice. Use of antibiotics during the study period appeared to be correlated with persistence of OME, as it was a feature of the history of 43% of children with persistent OME versus only 30% of children in which OME resolved. The difference was not significant ($p = 0.08$) and it could reflect more prescriptions for the apparently worse-affected. Myringotomy and ventilation tube insertion, either during the study time or previously was not associated with any difference in rate of persistence of OME, while the same was true for adenoidectomy or tonsillectomy (Table 2).

**Table 2** Persistence rates of OME in our cohort of school-age children 16 months after diagnosis: the effect of medical conditions and external interventions

| Categorical variable | Persistence of OME (%) | Odds ratio | 95% CI | *p*-value |
|---|---|---|---|---|
| Blood group | | | | |
| A | 35 | 1.25 | 0.24 | 0.68 |
| B | 16.7 | 1 | | |
| AB | 25 | 1.66 | 0—19.2 | |
| O | 33 | 2.5 | 0.45—13.1 | |
| History of allergy | | | | |
| Yes | 23.6 | 1.08 | 0.49—2.42 | 0.83 |
| No | 22.1 | | | |
| Reported history of AOM | | | | |
| Yes | 45.2 | 3.18 | 1.27—7.95 | 0.001 |
| No | 20.1 | | | |
| Reported history of MEE episode during the study period | | | | |
| Yes | 29.5 | 1.84 | 1.01—3.36 | 0.04 |
| No | 18.2 | | | |
| Antibiotic use | | | | |
| Yes | 28.9 | 1.71 | 0.93—3.14 | 0.18 |
| No | 19.1 | | | |
| Myringotomy anytime during the past | | | | |
| Yes | 32.1 | 1.76 | 0.76—4.08 | 0.18 |
| No | 21.2 | | | |
| Ventilation tube insertion | | | | |
| Yes | 23.7 | 1.04 | 0.29—3.65 | 0.59 |
| No | 22.1 | | | |
| Tonsillectomy | | | | |
| Yes | 33.3 | 1.75 | 0—8.48 | 0.4 |
| No | 21.2 | | | |
| Adenoidectomy | | | | |
| Yes | 36.3 | 2.32 | 0.93—5.8 | 0.06 |
| No | 19.7 | | | |
| Adenotonsillectomy | | | | |
| Yes | 35 | 2.19 | 0.84—5.7 | 0.06 |
| No | 19.7 | | | |

### 3.6. Unilateral versus bilateral disease

All univariate comparisons were repeated separately for the group of children with persistent unilateral ($n = 31$) and the group of children with persistent bilateral ($n = 25$) disease. There were no significant differences, although children with bilateral disease were more likely to have had episodes of AOM and to have undergone myringotomy. The rates of unilateral versus bilateral disease were not significantly different at baseline and 16 months later (41% at baseline versus 45% 16 months later, $p = 0.3$). Unfortunately we did not assess unilaterality, bilaterality and persistence of effusion in the same or contralateral ear, so we cannot comment on the natural history of a specific ear in unilateral cases.

### 3.7. Multivariate analysis

In order to account for inter-correlation and confounding variables, multiple backward-eliminating logistic regression was performed, assessing all the factors studied. Two factors remained in the model and emerged as being independently associated with the risk of persistence of OME. The estimates from this back-deleted model were as follows: age of the child, with odds ratio 0.53 (95% CI: 0.32—0.79), $p = 0.002$ for each 2 years of increase in age and history of AOM, odds ratio 2.75 (95% CI: 1.13—8.17), $p = 0.04$.

## 4. Discussion

Improvements in understanding of otitis media with effusion come from two sources: improved quality of data from increasingly well-designed randomized controlled trials, prospective and epidemiological studies and better understanding of the basic processes in OME pathophysiology. Data from these two sources appears to converge.

The incidence of OME depends very much on the age of the child [12,13]. Our study shows that in children of school age, irrespective of treatment used, the chance of OME persisting beyond 16 months decreases with age—by 47% for every 2 years.

All of these considerations point towards the importance of the infective origin of otitis in enabling small differences in occurrence, or recurrence to be shown, but making it hard to throw detailed light on the risk factors in the anatomy and the immune system that are involved in converting AOM into OME or which govern OME persistence. An episode of acute otitis media, here increased the risk of OME with an odds ratio of almost three. Recorded OME during the assessment period of 16 months also increased the probability of persistent/recurrent OME but the predictor variable here was not systematically recorded on all children by a second screen so detailed interpretation is not possible. We are thus left with only age as an easy gross marker of the complex of risk factors that convert infection into secretion and persistent secretion. It is not questioned that such factors do exist but two considerations make them inaccessible to small-scale clinical epidemiology: (a) the partly random nature of the triggering infection; and (b) the lack of markers for the underlying biological variables. Large-scale studies with biological markers are required to show differences in the absolutely low contingent probabilities of recurrence or persistence that would show the factors in play.

The design of our study (mass screening of a cohort of school-age children in two separate occasions) precludes serial assessments for the presence of OME. As a result, we can only comment on prevalence of OME on two occasions, 16 months apart. This, strictly speaking, does not distinguish between recurrence and persistence of OME, as the child could theoretically have been free of disease in the interim. At the public health level, this may not matter, whether it is an indicator chiefly of persistence or of recurrence in this sample. The lack of distinctive findings suggests that future studies will need to make this distinction.

Any epidemiological study is most likely to be relevant to practice in the country and health system where it took place—in Greece, the majority of otolaryngologists tend to manage OME conservatively. The children for this study were not selected via a GP referral or self-referral process, but were identified following general screening. In this population of children, and especially in children older than 6 years old, watchful waiting is warranted, as the chances of persistent bilateral OME are less than 13%. There is no reliable way at present of defining in which children the effusion will persist, however, it appears that in older school-age children, with no intermittent episodes of AOM recurrence or persistence are not a major concern. In the future, biological markers may well prove useful in defining the subgroup of children with persistent effusions. Meanwhile, a conservative policy in this population may be justified.

## References

[1] M.L. Casselbrant, L.M. Brostoff, E.I. Cantekin, et al. Otitis media with effusion in preschool children, Laryngoscope 95 (1985) 428—436.
[2] J. Lous, M. Fiellau-Nikolajsen, Epidemiology of middle ear effusion and tubal dysfunction: a one-year prospective study comprising monthly tympanometry in 387 non-selected seven-year-old children, Int. J. Pediatr. Otorhinolaryngol. 3 (1981) 303—311.
[3] M.L. Casselbrant, Mandel EM, Epidemiology of otitis media with effusion, in: R.M. Rosenfeld, C.D. Bluestone (Eds.), Evidence-Based Otitis Media, second ed., BC Decker, Hamilton, London, 2003, p. 150.
[4] J.L. Paradise, H.M. Feldman, T.F. Campbell, C.A. Dollaghan, D.K. Colborn, B.S. Bernard, H.E. Rockette, J.E. Janosky, D.L. Pitcairn, D.L. Sabo, M. Kurs-Lasky, C.G. Smith, Effect of early or delayed insertion of tympanostomy tubes for persistent otitis media on developmental outcomes at the age of three years, N. Engl. J. Med. 344 (16) (2001) 1179—1187.
[5] J.L. Paradise, C.A. Dollaghan, T.F. Campbell, et al. Otitis media and tympanostomy tube insertion during the first three years of life: developmental outcomes at the age of four years, Pediatrics 112 (2003) 265—277.
[6] M. Tos, S. Holm-Jensen, C.H. Sorensen, Mogensen C.Spontaneous course and frequency of secretory otitis in 4-year-old children, Arch. Otolaryngol. 108 (1) (1982) 4—10.
[7] K. Daly, G.S. Giebink, C.T. Le, B. Lindgren, P.B. Batalden, R.S. Anderson, J.N. Russ, Determining risk for chronic otitis media with effusion, Pediatr. Infect. Dis. J. 7 (7) (1988) 471—475.
[8] M.M. Rovers, G.A. Zielhuis, H. Straatman, K. Ingels, G.J. van der Wilt, P. van den Broek, Prognostic factors for persistent otitis media with effusion in infants, Arch. Otolaryngol. Head Neck Surg. 125 (11) (1999) 1203—1207.

[9] MRC Multi-centre Otitis Media Study Group, Risk factors for persistence of bilateral otitis media with effusion, Clin. Otolaryngol. 26 (2) (2001) 147–156.
[10] F.A. van Balen, R.A. de Melker, Persistent otitis media with effusion: can it be predicted? A family practice follow-up study in children aged 6 months to 6 years, J. Fam. Pract. 49 (7) (2000) 605–611.
[11] http://www.sas.com/software, accessed March 2005.
[12] C. Suarez Nieto, R. Malluguiza Calvo, P. Barthe Garcia, Aetiological factors in chronic secretory otitis in relation to age, Clin. Otolaryngol. 8 (3) (1983) 171–174.
[13] G.A. Gates, C. Wachtendorf, G.R. Holt, E.M. Hearne, Medical treatment of chronic otitis media with effusion (secretory otitis media), Otolaryngol. Head Neck Surg. 94 (3) (1986) 350–354.