Prognostic Factors for Persistent Otitis Media With Effusion in Infants

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Objective: To study prognostic factors for persistent otitis media with effusion (OME) in a birth cohort of 30,099 children born in the eastern part of the Netherlands between January 1, 1996, and April 1, 1997.

Design: Case-referent study.

Subjects: Children who failed a triple hearing test before their first birthday and were subsequently diagnosed with bilateral OME during 3 of the 4 bimonthly visits to an ear, nose, and throat (ENT) department (n = 372). The persistent cases were compared with 3 referent groups: (1) all the children who attended the first of 3 hearing tests; (2) all the children of the birth cohort who were referred to an ENT department after the third hearing test; and (3) all the children who were diagnosed with bilateral OME during the first visit to an ENT department.

Results: When all the children who participated in the first hearing test were taken as referents, persistent OME was associated with upper respiratory tract infections, attending a day-care center, having older siblings, and a family history of otitis media. When all the children who were referred to an ENT department were taken as referents, only attending a day-care center was associated with persistent OME. When the children diagnosed with bilateral OME during the first visit to an ENT department were taken as referents, no prognostic factors were found for OME persistence.

Conclusion: When a child is referred early, an otolaryngologist can ask the parent about the presence of prognostic factors to decide which policy to follow.


In the literature, many prognostic and risk factors have been described for otitis media with effusion (OME) in children. The main factors considered responsible for the development of OME are infections and eustachian tube dysfunction. Other factors that may influence the occurrence of OME are race, sex, acute otitis media, the presence of siblings, family history of otitis media, respiratory tract infections, Down syndrome, cleft palate, allergies, season, bottle feeding, attending a day-care center, passive smoking, low birth weight, blood group A Rh+, and socioeconomic status.

Some studies have investigated the risk factors specific for persistent OME such as male sex, sibling history of ear infection, bottle feeding, group A Rh+, day-care attendance, and season. The results of these studies have been contradictory, probably owing to differences in methods and study populations. In addition, the definition of persistent OME varies between studies. In most studies, persistent OME was defined as a minimum of 2 months of effusion, while the present guidelines for treatment with ventilation tubes recommend waiting 4 to 6 months.

The aim of this study was to analyze prognostic factors for persistent OME of at least 4 months’ duration in a large population. Children with these factors might benefit from early detection, more frequent checkups, and/or early intervention.

RESULTS

The results of the univariate analyses are given in Table 1. In the analysis with the referent children who participated in the first screening, 5 factors were associated with persistent OME: sex (OR = 1.4 [95% CI, 1.0-1.8]), URTIs (OR = 2.6 [95% CI, 2.0-3.6]), older siblings (OR = 3.2 [95% CI, 2.3-4.4]), attending a day-care center (OR = 1.9 [95% CI, 1.3-2.6]), and a family history of otitis media (OR = 1.9 [95%
PATIENTS AND METHODS

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The population in this study comprised all the infants born in the eastern part of the Netherlands between January 1, 1996, and April 1, 1997 (N = 30,099). These children were screened for hearing impairment (Ewing method) at age 9 months. Those who failed 3 screening tests were referred to an ear, nose, and throat (ENT) outpatient clinic for diagnosis with tympanometry and otoscopy. During this visit the parents were asked to complete a questionnaire with a number of items about prognostic factors. Infants with bilateral OME (determined by a type-B tympanogram and/or fluid found during the otoscopy procedure) were recalled 2 months later, while the children with unilateral or no OME were not further observed. Otitis media with effusion was considered to be persistent when the diagnosis was made during 3 of the 4 bimonthly visits (over the subsequent 6 months). Those infants with persistent OME composed the cases in this study (n = 372).

To make a valid estimate of the relative risk, we performed a case-referent study.31 This meant that controls needed to be selected from the source population. As a consequence, it was possible for a child in the referent group to be a case as well as a control.

Our study had 3 possible source populations: (1) the children who participated in the first of 3 hearing tests (a random sample of 450 children [366 respondents] born between March and July 1996 was taken from this population to serve as controls, and the parents of these control children completed the same questionnaire on prognostic factors); (2) the children who were referred to an ENT department after failing the third hearing test (n = 1083); and (3) the children who were diagnosed with bilateral OME during their first visit to the ENT department (n = 757). Comparing the persistent cases with these 3 referent populations enabled us to study the effect of the prognostic factors over time.

PROGNOSTIC FACTORS

Day-care attendance, breastfeeding, prematurity, and passive smoking were all studied as dichotomous variables (yes/no) and as continuous variables (days per week, number of weeks, and number of cigarettes). An infant was considered to have a history of acute otitis media if the child ever had an earache with fever or if a general practitioner had prescribed treatment for earache in the past 3 months. An infant was considered to have a family history of otitis media if a sibling or parent had acute otitis media or OME once. There was a history of respiratory illness if upper respiratory tract infections (URTIs) had occurred more than 4 times in the first year of life.

STATISTICAL PROCEDURES

For each prognostic factor, the risk ratio for persistent OME was estimated by means of an odds ratio (OR) with a 95% confidence interval (CI). Multiple logistic regression was used to examine prognostic factors simultaneously. Only prognostic factors that showed an association with OME in univariate analysis were selected for the multivariate models.

The prognostic value of the models was evaluated using the c-index. This c-index is equal to the area under a receiver operating characteristic curve32 and has a range of 0.5 (no prognostic value) to 1.0 (maximum prognostic value).

Because ORs do not show the absolute difference in risk of OME in children with and without the prognostic factors, we estimated the baseline prevalence of persistent OME in the referents who participated in the first screening, using the method described by Schouten et al31: corrected $\beta_0 = \beta_0 + \log (f)$, where $f$ represents the probability that a subject in the cohort was selected from the random sample (assuming that sampling was independent of the outcome). All analyses were performed using the statistical package SAS (SAS Institute, Cary, NC, version 6.12, 1996).

CI, 1.4-2.5). Other variables such as prematurity, number of days in day care, breastfeeding, duration of breastfeeding, atopy, educational level of the parents, AOM, and passive smoking and number of cigarettes did not show an association with persistent OME. When all the infants who were referred to an ENT department were selected as referents, none of the factors was associated with persistent OME in children with and without the prognostic factors, we estimated the baseline prevalence of persistent OME in the referents who participated in the first screening, using the method described by Schouten et al31: corrected $\beta_0 = \beta_0 + \log (f)$, where $f$ represents the probability that a subject in the cohort was selected from the random sample (assuming that sampling was independent of the outcome). All analyses were performed using the statistical package SAS (SAS Institute, Cary, NC, version 6.12, 1996).
center, and a family history were associated with persistent OME (Table 2). The final logistic model can therefore be described by:

$$P(\text{Persistent OME}) = \frac{1}{1 + e^{-(-1.5 + 0.7 URTIs + 1.1 \text{Older Siblings} + 0.6 \text{Day Care} + 0.4 \text{Family History})}}.$$ 

The c-index of this model was 0.70. When we adjusted for the above effect modification by adding 2 interaction factors (day care × URTIs and older siblings × URTIs) the c-index did not improve.

Table 2 indicates that after correction for URTIs, day-care attendance, and a family history of otitis media, a child with older siblings was 3 times more likely to develop persistent OME than one without. After correction for the other factors, a child with URTIs was 2.1 times more likely to develop persistent OME than one without. After correction for URTIs, day-care attendance, and a family history of otitis media, a child with URTIs was 2.1 times more likely to develop persistent OME than one without. After correction for URTIs, day-care attendance, and a family history were associated with persistent OME when all these factors were present.

Prevalences of OME, calculated using the method described by Schouten et al,31 are given in Table 3. In the sample of 352 referents who could be used in the multivariate analysis, 3 children were both case and referent. If we assume that the 360 cases without missing values also represent all the children who participated in the first screening, the total cohort can be calculated by (360 cases/5) × 352 referents = 25,344 infants. In this case, \( f = 352/25\,344 = 0.0139, \) and \( \beta_0 = 1.48 + \log(0.0139) = -5.75. \) The prevalence is given by \( \exp(\beta_0 + 0.7 \text{URTI} + 1.1 \text{older siblings} + 0.6 \text{day care} + 0.4 \text{family history}). \) The prevalence of persistent OME in children without URTIs, older siblings, a family history of otitis media, or attendance at day care was 0.3%, while the prevalence was 5.5% when all these factors were present.
In accordance with other studies, we found that a history of URTIs, day-care attendance, having older siblings, and a family history of otitis media were prognostic factors for persistent OME.\textsuperscript{2,7,28} However, this was only the case when a sample of the original screening population served as referents. When the children with persistent OME were compared with the children referred to an ENT department after the third screening, only day-care attendance was associated with persistent OME. When the children diagnosed with bilateral OME during the first visit to an ENT department served as referents, no factors were associated with persistent OME.

Having older siblings seemed to modify the effect of a history of URTIs on persistent OME. Children without older siblings but with a history of URTIs were at higher risk for persistent OME than children with both older siblings and a history of URTIs. Moreover, children attending day care who did not have older siblings were at higher risk for persistent OME than children attending day care who did have older siblings. This suggests an important role of immune status: children with older siblings have probably been exposed to pathogens that cause URTIs and OME, so their immune system may be stimulated to protect them against these pathogens.\textsuperscript{33}

After the third hearing test, 318 children (23\%) were not referred to an ENT department for a variety of reasons (mostly because the parents did not want it). This might have caused some bias if the infants lost to follow-up formed a select group. For example, if these children did not have persistent OME and did not score on the prognostic factors either, the calculated ORs would overestimate the true rates. But as it is unlikely that this was the case in a large proportion of the children lost to follow-up, the amount of bias can be considered small.

It is possible that all the children referred to an ENT department had already been suffering from OME for at least 3 months, since they failed the hearing test 3 times. This might explain the lesser effect of the prognostic factors when the children referred to an ENT department and the children diagnosed with bilateral OME at an ENT department served as referents.

Data on prognostic factors were based on questionnaires completed by the parents. Although parental recall of prognostic factors also forms the source of information in clinical practice, it should be noted that recall errors and misclassification will lead to some degree of underestimation of the ORs.

Children from the referent group who participated in the first of the 3 hearing tests were used as controls in an earlier study.\textsuperscript{34} These children were born between March and July 1996. We do not expect that the presence of prognostic factors depends on the month of birth, but we know that the prevalence of persistent OME is highest during the winter months and lowest during the summer months. The children born between March and July had their conditions first diagnosed at the ENT department at age 12 months. Therefore, fewer of the referents might have been diagnosed with OME, and the calculated ORs might be a little overestimated.

To show the absolute difference in risk of persistent OME, we estimated the prevalences. The risk of OME in children without a history of URTIs, older siblings, a family history of otitis media, or day-care attendance was 0.3\%, while the estimated risk in children with a history of URTIs, older siblings, a family history of OME, and day-care attendance was 5.5\%. These differences show that information on prognostic factors does not wholly discriminate between those who develop persistent OME and those who do not, but the differences seem to be substantial enough to be used.

In conclusion, this study showed that children with all 4 prognostic factors at the time of screening were at higher risk for persistent OME. However, when these children were older and had been suffering from OME for some months, these factors were no longer prognostic. So when a child is referred early to a general practitioner, pediatrician, or otolaryngologist, and if these physicians must decide which policy to follow, they can ask the parents about the presence of the prognostic factors and decide accordingly.

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