Selecting persistent glue ear for referral in general practice: a risk factor approach

Medical Research Council Multi-centre Otitis Media Study Group

SUMMARY

Background: *Glue ear (otitis media with effusion) is the most common reason for surgical intervention in children.*
Aim: *To determine the yield and predictive value of a set of risk factors that predict persistence of glue ear over the interval from general practice referral to ear, nose and throat (ENT) consultation to ensure the appropriateness of referrals.*
Design of study: *Nested case control study.*
Setting: *Sixteen ENT departments in the UK.*
Method: *With the aid of audiometry and tympanometry, diagnostic information was collected on 548 children from 16 ENT departments after referral by their general practitioner (GP), as a lead-in to a clinical trial, the Trial of Alternative Regimens in Glue Ear Treatment (TARGET). Using cases and controls, children were classified as either having or not having persistent glue ear. Parental reports on an extensive list of risk factors were also collected.*
Results: *After adjustment for time waiting to be seen from GP referral and age at referral, four main significant factors emerged for persistence of glue ear. These were: referral between July and December (OR [odds ratio] = 1.73, 95% CI = 1.15 to 2.6); having a mother who smokes ten or more cigarettes per day (OR = 1.7, 95% CI = 1.1 to 2.8); multiple upper airway symptoms (OR = 2.2, 95% CI = 1.5 to 3.2; and siblings with a history of glue ear (OR = 1.6 for one sibling versus none).*
Conclusion: *For a child who is referred between July and December, who has two or more upper airway symptoms, who has a sibling who has had glue ear, and who has a mother who smokes ten or more cigarettes per day, the odds of having persistent glue ear are over ten times that of a child without adverse values on these factors.*
Keywords: *risk factors; glue ear; otitis media with effusion; middle ear; child health.*

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Introduction

GLUE ear (otitis media with effusion) is the most common reason for surgery in children and by far the main cause of hearing loss in children. Resolution occurs in about 50% of cases after 12 weeks and 75% after 24 weeks,[1] although groups of cases can be defined that show slower resolution. The condition is most prevalent between the ages of two and five years, and in most instances it begins to regress between six and seven years of age.

Although the diagnosis is straightforward, glue ear can be difficult for doctors to suspect and to refer appropriately because of its semi-symptomatic fluctuating nature and diverse presentation. A set of risk factors for persistence of glue ear would be useful in helping general practitioners (GPs) in deciding which children might benefit from referral with possible subsequent specialist intervention. They could function either as a filter preceding audiometric assessment or in conjunction with it. Informing parents about risks and their modification could also help reduce the likelihood of their child developing glue ear, although no rigorous intervention study has yet reported positive results.

An overview of the literature on risk factors for the occurrence of glue ear shows the main risk factors to be parental smoking,[2-5] attending day care,[5-7] and having siblings with a history of glue ear.[8,9] Breastfeeding as a protective factor is less consistently found.[10,11] Other factors reported less frequently are: season of consultation; allergic conditions (for example, asthma); sex; and race.[12] Studies may show differing views on particular risk factors for glue ear, mainly because of small sample sizes, but sometimes because of differences in the study populations and in the methodologies used. Unfortunately, most studies examine risk factors for occurrence of glue ear, which could be considered subclinical, rather than for its persistence. Those considering persistence specifically have identified few specific predictive factors,[6,13] or have adopted a rather short-term definition by United Kingdom (UK) standards. As most research has been performed in a secondary or tertiary setting, the issue arises of risk factors specifically applicable in primary care.[14] We have previously shown[13] that referrals from the community audiological services had higher positive predictive values (PPVs) — a measure of the appropriateness of referral — than those from GPs, probably owing to their much greater access to audiometry.

There is wide variation in referral rates at the level of individual clinicians rather than at the level of whole practices,[15] suggesting that guidance on referral is required. The recruitment stages of the UK national Trial of Alternative Regimens in Glue Ear Treatment (TARGET) has given us the opportunity to quantify the strength of risk factors for persistence of glue ear as applicable in general practice, drawing on a representative database of over 3000 referrals as a basis for

HOW THIS FITS IN

What do we know?

The main risk factors for the occurrence of glue ear are reported as parental smoking, attendance at day care, and having siblings with a history of glue ear. Few studies have examined persistence of glue ear.

What does this paper add?

The study confirms two of the risk factors for occurrence as specific to persistence, but adds season and multiple upper airways symptoms as predictive of persistence.
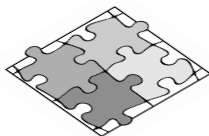
such guidance. This advances beyond mere listing of risk factors to a proposal for their systematic use, with numerical implications attached.

Method

This study presents data on children who were referred from their GP with suspected ear or hearing problems in association with glue ear, to 16 ear, nose and throat (ENT) departments in the UK, as part of TARGET, a large multi-centre clinical trial evaluating surgical treatment. There are 4000 subjects on the database, but the data required for this study was only present for 548 of them. For reasons of efficiency, the protocol did not require full audiometry unless the tympanogram, a sensitive but non-specific objective test of fluid in the ear, was abnormal. Data available from all 16 ENT departments were used, including data from six departments that performed full audiometry on all children seen. These six departments were typical, for example, in terms of the tympanometric confirmation rate, hence caseload severity. All data were collected at the first visit of the child to the ENT department after GP referral. Children were also referred from community audiological services, but these are not considered further here. Glue ear was defined as having a bilateral B or B+C2 tympanogram associated with an air–bone gap >10 dB and a hearing level (HL) (averaged over 0.5, 1, 2, and 4 kHz in each ear) of 20 dB HL in the better ear. Children not fulfilling these criteria were allocated to the 'control' group (i.e. no glue ear).

After giving informed consent to participate in the study, parents or guardians of children attending the clinic completed a 'Hearing and Predictive Factors' questionnaire. This contained information on risk factors that are known or suggested to be associated with glue ear, in the following areas: duration of hearing problem when seen at ENT consultation; number of ear infections in the previous 12 months; head circumference; height and weight (between 12% and 15% of data were missing on anthropometric variables); occupation and social class of parents; history of colds and respiratory infections; diagnosis of asthma and other allergic conditions; sleeping position as a baby; number of siblings with a history of glue ear; number of siblings living at home; birthweight in kg; mother's age at birth of the child; whether breast or bottle fed and duration; parental smoking habits, including smoking during pregnancy; and frequency of

snoring, mouth breathing, and blocked nose. The last three factors were pooled according to whether the child had zero or one, versus two or three, 'upper airway symptoms', scored dichotomously as 'often or always' versus 'less frequently'. Attendance at day care was not examined, as 98.9 % of the children attended some type of day care such as a crèche, playgroup, nursery, or school, permitting no comparison. The child's age and sex, date of referral, and date of consultation in the ENT department, were used, and the time in weeks between the GP referral and the ENT consultation was calculated. The time spent waiting to be seen is adjusted for in the analyses because a longer interval is accompanied by a higher rate of remission in glue ear. Clinically, this time serves as an extra 'watchful waiting' stage.

Statistical analysis

The restriction in the trial protocol for the use of audiometry only in those children failing a tympanometric criterion meant that the majority of the children having full data did have persistent glue ear, which was the inclusion criterion for the trial. This is not representative of the usual ENT workload or GP referrals. Analysis was performed as for an unmatched case control study. First, univariate analyses for glue ear as defined above were performed. Factors that were significant in the univariate analysis ($P<0.10$) were entered into a logistic regression (backwards elimination), to identify the main independent factors ($P<0.10$). Interactions were only tested for significant main effects. The number of weeks between the GP referral and the ENT consultation, and the age of the child at referral, were entered into each model for control purposes only. To compute the expected probabilities of glue ear by the risk factors identified, the constant term in the logistic regression equation was adjusted to correspond to a case control study[16] with an uneven distribution of cases to controls. An adjustment was made to weight cases to controls in the ratio of one to three, to give the proportion of cases being persistent as 25%, similar to that in a separate study of GP referral.[17] This assumes that the study sample of non-persistent cases is a random sample from the larger clinic population. This is the population referred to, not the unaffected population. There is no specific reason to question the sampling assumption, as the inclusion of audiometry is an arbitrary element which differs between local clinical pathways. The percentages of children with the various risk factors are presented for the sample used and predicted for the expected GP referral workload, based on weighting cases and controls in the sample to the ratio of one to three. The study is powered (80%), with the smallest $n = 180$ in the 'no glue ear' group, to detect (at $\alpha = 0.05$) an odds ratio (OR) of 1.68 on a baseline proportion of 0.5. To make a checklist of about five factors useful in practice, risk factors need to be of this strength or greater.

Results

Of the 548 children with complete data on risk factors and glue ear status, 53% were boys and 47% were girls. The age when first seen at the ENT department was restricted by the protocol to between 3.25 and 6.75 years, and the mean age

at referral was 4.8 years standard deviation = 0.83). The number of children with persistent glue ear as defined above was 347, with 201 non-persistent 'controls'.

Univariate analysis

The following variables were predictive (at $P<0.10$) of persistent glue ear: age when referred ($P = 0.002$); season of referral ($P = 0.004$); nasal symptoms ($P<0.001$); mother's smoking habits ($P = 0.016$); siblings with a history of glue ear ($P = 0.071$); and manual versus non-manual parental occupation ($P = 0.096$).

Multivariate analysis

The above factors were entered into a logistic regression model, using backwards elimination, to predict diagnosis at ENT consultation. Odds ratios and 95% confidence intervals from the final main-effects logistic regression model are given in Table 1. The main significant factors identified were: month when referred; having two or more of the upper airway symptoms; siblings with a history of glue ear; and having a mother who smoked ten or more cigarettes per day. The ORs lie between 1.7 and 2.2; similar to those observed in other studies.[9] There was only one significant interaction, which was between the mother's smoking habits and the referral age ($P = 0.038$); a higher rate of persistent glue ear was found in older children whose mothers smoked.

The probability of bilateral glue ear being found at ENT consultation after GP referral, measured as positive predictive value (PPV), assuming the main effects (i.e. no interaction) model, is presented for simplicity in Table 2. Probabilities are adjusted for the differences in sampling fractions between cases and controls in our sample and the predicted population. To simplify the table, average values are assumed for the period of weeks waiting to be seen, i.e. 12 weeks, and for the average number of brothers and sisters with a history of glue ear, i.e. 0.19. Also given is the proportion of the study sample to which each risk factor combination, and hence the PPV, applies. In these analyses, a child with two or more of the upper airway symptoms, whose mother smokes ten or more cigarettes per day, who has a

sibling with a history of glue ear, and who is referred by their GP between July and December, has an odds of persistent glue ear over ten times that of an index child with non-risk values. Slightly greater predictive power would occur if the risk factors were expressed as continuous variables, but Table 2 uses dichotomies to permit reasonable accuracy.

Discussion

From an extensive list of risk factors considered for predicting bilateral persistent glue ear, the main factors found in the unweighted analysis were: frequent upper airway symptoms, mother's smoking habits, and being referred by the GP during the months between July and December. This is after statistical adjustment for weeks waiting to be seen (mean = 12.12 weeks), and for the age of the child at the time of GP referral (mean = 4.8 years). As the average waiting time in the UK to be seen at an ENT department is about three months, a child referred between July and December will, on average, be seen at the ENT department between October and March, when glue ear is most likely to recur in the short term or in persistent form.[9]

This study is based on a large number of cases with objective measures of glue ear status, as defined by tympanometry and audiometry of both ears. The study does not address the presence of fluid in the ears at the time of GP referral, owing to the lack of diagnostic equipment available and/or used in general practice, as this reflects real-life circumstances.[18] Referral is currently based upon history and examination, and the relevant policy issue concerns whether using present and other findings can improve referral quality within the existing system. The reporting of risk factors by parental questionnaire, as performed in this study, is highly cost-effective but obviously prone to reporting biases. Under-reporting of parental smoking is particularly likely. Therefore, the issue that directly relates to practice is whether any such biases are sufficiently small or adjustable to represent an improvement over informal history taking, which is also bias prone.

Children were also referred to TARGET via the community. This did not rule out GP involvement, but in effect meant

Table 1. Odds ratios and 95% confidence intervals for factors predicting persistent bilateral glue ear in GP referrals.

Factor	OR (95% CI)	P-value
Season of referral		0.009
Between January and June	1.0	
Between July and December	1.73 (1.15–2.59)	
Number of nasal symptoms		<0.001
0 to 1	1.0	
2 to 3	2.18 (1.49–3.21)	
Number of cigarettes smoked by mother		0.022
<10 per day	1.0	
≥10 per day	1.74 (1.08–2.81)	
Siblings with history of glue ear, per sibling (continuous variable)	1.63 (1.04–2.57)	0.034
Controlled for in the analysis		
Age at referral		0.001
≤5 years	2.05 (1.37–3.08)	
>5 years	1.0	
Weeks until seen, per week (continuous variable)	0.972 (0.95–0.99)	0.006

Table 2. Probability of persistent glue ear by significant risk factors identified by logistic regression.[a]

Time of year of referral	Age at referral	Number of upper airway symptoms	Number of cigarettes per day smoked by mother	Predicted probability of persistent glue ear (95% CI)	Percentage of sample	Predicted percentage of GP referral workload[b]
January to June	≤5 years	0 to 1	<10	0.21 (0.09–0.33)	8.0	9.5
			≥10	0.31 (0.04–0.60)	2.0	2.6
January to June	≤5 years	2 to 3	<10	0.36 (0.23–0.49)	9.7	7.8
			≥10	0.50 (0.28–0.71)	3.8	3.0
January to June	>5 years	0 to 1	<10	0.11 (0.04–0.19)	13.5	18.2
			≥10	0.18 (0.0–0.36)	3.3	3.4
January to June	>5 years	2 to 3	<10	0.22 (0.13–0.30)	15.9	17.1
			≥10	0.33 (0.17–0.48)	6.2	5.2
July to December	≤5 years	0 to 1	<10	0.31 (0.14–0.48)	5.3	3.6
			≥10	0.44 (0.0–1.0)	0.5	0.5
July to December	≤5 years	2 to 3	<10	0.50 (0.33–0.66)	6.2	4.3
			≥10	0.63 (0.37–0.89)	2.4	1.8
July to December	>5 years	0 to 1	<10	0.18 (0.07–0.55)	8.9	10.7
			≥10	0.28 (0.0–0.29)	1.8	1.9
July to December	>5 years	2 to 3	<10	0.32 (0.19–0.46)	8.4	8.1
				0.46 (0.25–0.66)	4.0	2.2

[a]Assuming the average number of weeks to be seen = 12.1, and average number of siblings with a history of glue ear = 0.19. [b]Cases and controls in the sample weighted in ratio 1:3.

that audiometry was one factor used for referral that was used in very few GP referrals. The proportion of children with persistent bilateral glue ear at ENT consultation was significantly higher for community referrals than GP referrals, despite the former having to wait longer (mean = 14.2 weeks) to be seen (*t*-test, $P = 0.012$). This difference shows that incorporating audiometry over three to six months in referrals of suspected glue ear improves the appropriateness of referral; it suggests that there would be some improvement in referral specificity if there was greater access in primary care to audiometry or other instrumental testing, either through community audiological services or through other sources, Upper airway symptoms, such as frequent snoring, mouth breathing and blocked nose, are known to be associated with enduring glue ear, probably because they mark a second and independent complex of risk factors acting between primary infection and long-term mucosal secretions. The association with the mother's smoking habit was not particularly strong, but displayed the expected dose–response relationship of longer persistence with the increasing number of cigarettes smoked, which is consistent with the literature on middle ear problems[2-3] and general health.[19] The interaction between the age of the child at referral and parental smoking ($P = 0.038$) could possibly be owing to cumulative environmental exposure or to differences between smokers and non-smokers bringing ear problems to their GP. We did not find the expected protective effect of breast-feeding,[11] which is known to be a little unstable over samples and definitions.

The rate of diagnostic confirmation of glue ear at ENT consultation suggests that simple risk factor questioning with standard wording may be useful for GPs in helping to make decisions as to whether to refer immediately or delay until the end of the summer. This would not necessarily override parental concerns regarding their child's hearing problem, or the results of any diagnostic testing, but would provide additional information for consideration at the time of the decision about referral. This additional information could help compress differences in referral rates among GPs and improve efficiency and consistency in the primary care system as a whole. However, any case-finding system that includes existing referral practice produces false negatives. Although much harder to define, the number of false negatives is probably unacceptable. The study findings justify using these risk factors as a supplement to existing criterion and documenting the predictive value of a prospective checklist. The latter may be precise enough to reduce the false-negative problem to an acceptable level.

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