Childhood Otitis Media is associated with Dizziness in Adulthood: The HUNT Cohort Study

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ABSTRACT

Objective: To examine the association between otitis media in childhood and dizziness in adulthood.

Design: Longitudinal, population-based cohort study of 21,962 adults (aged 20-59 years, mean 40) who completed a health questionnaire in the Nord-Trøndelag Hearing Loss Study. At 7, 10 and 13 years of age, the same individuals underwent screening audiometry in a longitudinal school hearing investigation. Children found with hearing loss underwent an ear, nose and throat specialist examination.

Results: Adults diagnosed with childhood chronic suppurative otitis media (n=102) and childhood hearing loss after recurrent acute otitis media (n=590) were significantly more likely to have increased risk of reported dizziness when compared to adults with normal hearing as children at the school investigation and also a negative history of recurrent otitis media (n=21,270), $p<0.05$. After adjusting for adult age, sex and socio-economic status, the odds ratios were 2.1 (95% confidence interval [CI]: 1.4-3.3) and 1.3 (95% CI: 1.0-1.5), respectively.

Conclusion: This longitudinal cohort study suggests that childhood chronic suppurative otitis media and childhood hearing loss after recurrent acute otitis media are associated with increased risk of dizziness in adulthood. This might reflect a permanent effect of inflammatory mediators or toxins on the vestibular system. The new finding stresses the importance of treatment and prevention of these otitis media conditions.

INTRODUCTION

Otitis media is one of the most common childhood diseases. Overwhelming evidence from human temporal bone studies and experimental studies in animals suggests that toxins or inflammatory mediators from otitis media enter and affect the labyrinth by crossing the round window membrane [1] (review). In serous labyrinthitis, one of the most common complications occurring during otitis media, invasion by bacterial or viral toxins inflames the vestibular apparatus and the cochlea. The inflammation is usually associated with temporary vertigo, and sometimes mild sensorineural hearing loss, implying preservation of viable vestibular and cochlear hair cells.

However, once toxic substances enter the inner ear, various *permanent* shifts in both cochlear and vestibular function can occur. Whereas the association between a history of childhood otitis media and hearing loss both in children [2-6] and adults [7-9] is well established, few studies have shown symptoms of subsequent vestibular dysfunction [10-12], and only in preschool children.

Dizziness is often defined as the sum of vertigo (illusion of movement of oneself or the environment), disequilibrium (a sensation of imbalance and/or postural instability), presyncope (feeling faint or light-headed) and “other types of dizziness” [13]. Dizziness is a common symptom associated with extensive handicap and psychological morbidity [14]. The causes are multifactorial, but vestibular vertigo accounts for a considerable percentage [15]. Knowledge about possible permanent effects of otitis media on the vestibular apparatus is important in

future considerations of interventions for otitis media. Hence, the present study aims to assess whether a history of otitis media in childhood is associated with increased risk of dizziness in adulthood.

MATERIALS AND METHODS

The present study used data from a linkage between two large, prior hearing investigations in Norway: The school hearing investigation in Nord-Trøndelag (SHINT, 1954-1986) and The Nord-Trøndelag Hearing Loss Study (NTHLS, 1996-98).
Two related studies from the same database (the linkage between SHINT and NTHLS) employing similar materials and measurements are presented elsewhere [7,16]. These studies examined childhood sensorineural hearing loss and the effects of combination with later aging and noise exposure [16], and to which extent childhood otitis media is associated with hearing loss in adulthood [7].

Participants

The baseline childhood study. The school hearing investigation in Nord-Trøndelag (SHINT) was an audiometric screening of nearly all 7, 10 and 13 year old school children in the entire Nord-Trøndelag County from 1954 to 1986. It was conducted by the late Norwegian Ear, Nose and Throat (ENT)–specialist, H. F. Fabritius, and his colleagues [17]. The study did not record information confirming the participation of children with *normal* hearing, so the exact number of participants is unknown. The number of children born between 1941 and 1977 in Nord-Trøndelag, 78,524, might serve as a crude approximation. Children with hearing loss at screening were invited to an ENT specialist examination. From 1954 to 1962, average attendance at the ENT examinations for children with positive screening was 97% [17], and we believe this high level of attendance did not change later. Altogether, 10,269 children took part in the ENT examination. Detailed information about SHINT is found elsewhere [17].

The follow-up adult study. The Nord-Trøndelag Health Study (HUNT 2, 1995-97) was a general, population-based, cross-sectional study where all residents in the county of Nord-Trøndelag, Norway, aged ≥20 years were invited. Out of 93,898 invited persons, 65,237 participated (69%) [18]. HUNT 2 included examinations and questionnaires. Detailed information about HUNT 2 is found elsewhere [19]. The Nord-Trøndelag Hearing Loss Study (NTHLS, 1996-98) was part of HUNT 2, and included pure-tone audiometry and hearing questionnaires. This study used Questionnaire 1. The total adult population (≥ 20 years) from 17 of the 23 municipalities in Nord-Trøndelag was invited. Valid audiometric data were collected from 50,723 participants with given consent. Among individuals born between 1941 and 1977 (the population cohort of the present study), 87% of the county population was invited with an overall participation rate of 59%. The NTHLS is described in detail elsewhere [20].

After linkage: The final sample of the present study. Childhood otitis media cases: Among the 10,269 children diagnosed with different types of hearing loss in SHINT, 2337 were diagnosed with hearing loss together with chronic suppurative otitis media (CSOM) or hearing loss after recurrent acute otitis media (rAOM). Out of these 2337 participants, 721 attended the follow-up adult study, however, 29 were excluded due to invalid data on dizziness (14 did not have a valid Questionnaire 1 and 15 had a valid questionnaire 1 but missing values on the dizziness question). Accordingly, 692 childhood otitis media cases (CSOM=102 and hearing loss after rAOM=590) were included in the present study.

Non-cases: As previously described, SHINT did not register the children with *normal* hearing. Thus, as a reference group we included all participants of NTHLS who were primary school age during SHINT (born between 1941 and 1977) and who were not registered with hearing loss in SHINT (n=29,720). From these, the present study includes those who in the NTHLS questionnaire 1 reported a negative history of recurrent otitis media (n=21,507), however, those with invalid data on dizziness (n=237 had missing values on the dizziness question) were excluded. Accordingly, 21,270 non-cases were included in the present study.

With regard to the general loss to follow-up, this was explained in detail by Aarhus et al. [7]. In short, among the 10,269 participants diagnosed with hearing loss in the baseline childhood

study, only 3066 (29.9%) attended the follow-up adult study. About 13% of the participants in the childhood study were living in a municipality not invited to the adult study, and some were lost due to not being old enough to be invited or loss of identification number. Also, the participation rate at the adult study among the population of this study was 59%. Most likely, a substantial number moved out of Nord-Trøndelag after the childhood study, and a few died (about 2%; information provided by Statistics Norway).

Measurement of the variables

Diagnosis (main exposure variable). The childhood diagnoses were assessed in SHINT by audiometry and medical examinations. The audiometric *screening* was performed by a trained hearing assistant or district health nurse in a quiet location within the school, obtaining air-conduction thresholds by pure-tone audiometry at 0.25, 0.5, 1, 2, 4 and 8 kHz. Hearing loss for the screening was defined as thresholds 20 decibel hearing level (dB HL) or greater at three or more frequencies or a 30 dB HL or greater threshold at one or more frequencies in either one or both ears.

All children found with hearing loss at the audiometric screening examination in the school were invited to an *ENT specialist examination* at one of 14 out-patient clinics in Nord-Trøndelag. Also, their parents completed a questionnaire with questions about their children's ear problems. The medical examination included family and medical history, a complete ENT examination and a new pure-tone audiometry with both air- and bone-conduction thresholds. Depending upon the diagnosis, the children had one or more controls at the ENT specialist. The ENT specialist recorded the history, findings, diagnoses (the presumed etiology of the hearing loss) and the treatments. The present study included as cases children diagnosed with (definitions by dr.Fabritius): 1) CSOM: chronic infection of the middle ear including eardrum perforation and intermittent secretion, conductive or mixed hearing loss; the minimum duration for eardrum perforation was not defined; 2) Hearing loss associated with a history of rAOM: no middle ear effusion at the clinical examination but a history of preschool rAOM, sometimes also occurring during school years, mostly including eardrum pathology, conductive or mixed hearing

loss. Some of these children had other diagnoses in addition to CSOM or hearing loss after rAOM, including SNHL (with no audiometric air-bone gap), otosclerosis, anomalies, cognitive disorders or syndromes; all the children with these additional diagnoses were excluded from our sample.

To reveal possible differences between childhood otitis media cases who did or did not attend the follow-up adult study (selection bias), we calculated the childhood hearing threshold level. Mostly, hearing thresholds <20 dB HL were not registered in these childhood audiograms, so values for many single frequencies were "missing". These missing values were replaced by the mean value of those values <20 dB HL registered in the total childhood hearing loss case group (n=10,269). For instance for 1000 Hz, right ear, there were 2855 cases with values ≥20 dB HL, 1535 cases with registered values <20 dB HL, and 5879 cases with missing values (hearing thresholds <20 dB). Mean values for the cases with registered values < 20 dB HL was 12 dB (95% CI 11-13), and missing values in the case group were replaced by this mean value. The variable was defined as PTA at 0.5-4 kHz in the worse hearing ear.

Socio-economic status (covariate): We collected information on covariates from national registries and from questionnaires in HUNT 2. From national registries we obtained information on highest level of completed education (primary and secondary school, vocational school, high school, undergraduate or graduate school) and income in 1998.

Dizziness (outcome variable): Dizziness was assessed by a questionnaire item in NTHLS: "Are you bothered by dizziness?" which was answered: "yes/maybe/no". Participants with invalid data on dizziness were excluded (numbers described previously). The variable was dichotomized, collapsing "yes" and "maybe" and using "no" as the reference category.

Statistical analyses

Statistical significance level was set at $p<0.05$. We used logistic regression analysis (SPSS version 20) to estimate odds ratios (OR) with 95% confidence intervals (CI) for each type of childhood

otitis media (0=reference category) and adult dizziness (0=no, 1=yes/maybe). The model was conducted with and without adjustment for adult age (in years), sex and socio-economic status (level of education and income in 1998).

Descriptive statistics. To compare the baseline risk factors in childhood otitis media cases (n=2337) who did (n=721) or did not (n=1616) attend the follow-up adult study (to reveal possible selection bias) we used a chi-square test for sex and an independent t-test for childhood hearing threshold.

RESULTS

Descriptive statistics of the sample are presented in Table 1. The prevalence of dizziness ("Are you bothered by dizziness?" answered as "yes" or "maybe") in the total sample was 16.9%. Average age at the last ENT examination for the childhood otitis media cases was 10 years old. Mean time between observation in childhood and in adulthood was 31 years. Descriptive analyses revealed no significant differences in childhood hearing threshold (p-value=0.507) and sex (p-value=0.059) between childhood otitis media cases who did or did not attend the follow-up adult study.

The results from the regression analyses are shown in Table 2. Adults diagnosed with childhood CSOM and childhood hearing loss after rAOM were significantly more likely to have increased risk of reported dizziness when compared to adults with normal hearing as children at the school investigation and also a negative history of recurrent otitis media ($p<0.05$). After adjusting for adult age, sex and socio-economic status, the odds ratios were 2.1 (95% CI 1.4-3.3) and 1.3 (95% CI: 1.0-1.5), respectively.

DISCUSSION

Main findings

Adults diagnosed with childhood CSOM and childhood hearing loss after rAOM were significantly associated with increased risk of dizziness in adulthood as compared adults with normal hearing at the school investigation and a negative history of recurrent otitis media.

Strengths and limitations of the Study

The validity of this cohort study has also been described previously in two related studies from the same database [7,16] .

Selection bias. Since, all schools in Nord-Trøndelag were included in the childhood study, we do not suspect a serious selection bias at his stage. However, there was certainly a loss to follow-up, since only 3066 (29.9%) out of 10,269 childhood hearing loss cases attended NTHLS. A related study[17] explained and examined the general loss to follow-up from SHINT to NTHLS. In short, many participants of SHINT were not invited to NTHLS: 13% lived in a municipality not included in NTHLS, and some were not old enough to be invited. A few were lost due to missing identification number. The participation rate at NTHLS among individuals ≤56 years of age (the population of this study) was 59%. The remaining loss to follow-up (n~3300) is difficult to explain, but emigration out of Nord-Trøndelag after SHINT or death (about 2% according to "Statistics Norway") are parts of the explanation. However, we have no reason to suspect a selective loss to follow-up. The present paper revealed no important differences between childhood otitis media cases who did or did not follow-up. Also, Aarhus et al. [7] reported no important differences in the distribution of risk factors (childhood hearing threshold, etiology, sex) between the total childhood hearing loss cases (n=10,269) who did (n=3066) or did not follow-up [7]. Finally, the follow-up adult study was part of a very large, general health study (HUNT), so we do not suspect that possible occurrence of dizziness affected the likelihood of participation.

Information bias: diagnosis. We do not suspect serious misclassification of childhood otitis media cases (false positives), since the diagnoses were determined by an ENT specialist after repeated, complete examinations including air- and bone-conduction audiometry [17]. Children with additional, more severe hearing disorders or syndromes were excluded. The classifications of various types of otitis media at that time [17] correspond well with the classifications used today [21]. Considering the course and treatment of otitis media at that time, antibiotics were prescribed and middle ear surgery were performed at the Namsos Hospital. If some of the effects of otitis media on dizziness reflect a poorer course and treatment at that time, this would only further underline the importance of optimal treatment in more adverse conditions.

The follow-up adult study did not confirm that CSOM was cured at the time of follow-up in HUNT 2. CSOM can heal and years later re-rupture due to a new infection, which could again introduce dizziness. Regarding the long time between the baseline childhood study and the follow-up adult study (mean 31 years), including the access to middle ear surgery and antibiotic treatment at the time of baseline study, we suspect that CSOM was likely to have been cured.

We do not suspect serious misclassification of non-cases (false negatives) because there were three separate hearing examinations (1th, 4th, and 7th grades), so most of these conditions were probably detected. However, we lack information confirming that non-cases actually took part in the childhood study. By including all participants of the adult study who were in primary school age during the childhood study, we assumed that: 1) They lived in Nord-Trøndelag between 1954 and 1986. To the extent that migration explains part of the loss to follow-up, there must also have been an immigration to Nord-Trøndelag, since the number of habitants has slightly increased during the last fifty years [19]; 2) All children in Nord-Trøndelag between 1954 and 1986 attended primary school. According to Statistics Norway, the number of pupils that attended first grade class at primary school during the childhood study period was nearly equal to the number of persons born 7 years earlier; 3) The childhood study included all children at primary school between 1954 and 1986. A great effort was made to include all school children, including those living in very small communities or rural areas, children at special schools, and so on [17]. This situation, that some participants categorized as non-cases probably

had undetected childhood hearing loss because they did not participate in the childhood study, may have caused a small underestimation of the associations. This bias cannot exceed an almost trivial value, however, since the false negative to true negative ratio will remain low because of the relatively low prevalence of childhood CSOM and childhood hearing loss after rAOM.

Information bias: dizziness. The outcome variable was based on a single, self-reported answer to the question: "Are you bothered by dizziness?" Non-differential misclassification could have led to underestimating the results. However, in another large study, which used the established and validated "Vertigo Symptom Scale", the authors found a dizziness prevalence of 15% [22], which is quite similar to our finding (16.9%). Since there were few missing values on the dizziness question (15 out of 721 in otitis media cases and 237 out of 21,507 in non-cases) and we have no reason to suspect "missing not at random", we do not believe the exclusion of these few participants has biased the results.

Information bias: childhood hearing threshold. The imputation of missing childhood hearing thresholds probably introduced some inaccuracy. However, childhood hearing threshold was only used to reveal possible systematic differences between childhood otitis media cases who did or did not follow-up. Since we can think of no reason why an inaccuracy by imputation should be unevenly distributed across these subgroups, we do not believe the imputation has biased the results.

Confounding: We have no reason to believe that the results represent unmeasured confounding. Adjustment for age, sex and socio-economic status had only marginal influence on the effect estimates.

Design. Our longitudinal cohort study cannot establish cause and effect. Yet, it seems unlikely that the outcomes measured in adulthood could affect childhood ear diseases; therefore, in general we think it is reasonable to assume this directionality.

Comparisons with other studies

Although the middle–inner ear interaction that occurs in otitis media has been an area of interest for many decades, few studies have examined possible long-term effects on the vestibular apparatus. In the study by Casselbrant et al., preschool children with a history of recurrent or persistent middle ear effusion (n=40) showed poorer performance on vestibular and balance tests (rotational and moving platform posturography) compared to children without a history of significant middle ear effusion [10]. Similarly, another study of preschool children with a history of more than six episodes of otitis media (n=18) revealed lower scores on various vestibular tests compared to children without previous episodes of otitis media [12].

To our knowledge, no prior study has provided long-term follow-up of otitis media with regard to dizziness. Thus, our study adds valuable information, showing that childhood CSOM and childhood hearing loss after rAOM are associated with long-lasting effects on dizziness.

Possible underlying mechanisms. We can only speculate about the underlying mechanisms of our findings. The results could reflect a permanent effect of inflammatory mediators or toxins from otitis media on the vestibular apparatus. Although the vestibule is relatively far from the round window, it has been shown that endotoxin can penetrate the inner ear via various routes, such as the round window, blood vessels or lymphatics, and/or interscala exchange, resulting in a disturbance not only of the cochlea but also of vestibular end organs [23]. Once toxic substances enter the vestibular system, various permanent sequelae can occur.

For example, otitis media could be associated with an accelerated age-related cellular loss in the vestibular end organ (presbystatis). Also, otitis media could predispose to later vestibulopathies. The recurrent nature, and also some shared histopathological characteristics, of benign paroxysmal positions vertigo (BPPV), vestibularis nevritis, or Ménière's (the three most common vestibulopathies), suggest a recurrent cause [24] and a viral etiology is suggested. Knowledge about possible influence due to a history of recurrent otitis media is scarce. Paparella et al. [25]

suggested that childhood otitis media may lead to Ménière's later in life, and BPPV has been associated with a history of inner ear disease [26] (review).

Considerations about the outcome variable. The causes of dizziness are multifactorial and it has been suggested that vestibular vertigo accounts for about 1/3 of dizziness symptoms [15]. Neuhauser et al. reported a prevalence of vestibular vertigo (at least one of the following criteria: 1) rotational vertigo; 2) positional vertigo; 3) recurrent dizziness with nausea and either imbalance or oscillopsia) of 4.9% [15]. [15]. If we could have distinguished between vestibular vertigo and other etiologies for 'dizziness', then it is possible that the effect of otitis media is much larger using vestibular vertigo as an outcome variable instead of dizziness.

CONCLUSION

The results from this cohort study suggest that CSOM and hearing loss after rAOM in childhood are associated with increased risk of dizziness in adulthood. This might reflect a permanent effect of inflammatory mediators or toxins on the vestibular system. CSOM and rAOM are relevant causes of preventable dizziness, and this new finding stresses the importance of optimal management of these otitis media conditions in childhood.

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Research involving Human Participants. The research is in compliance with the Norwegian Data Inspectorate and the Norwegian Regional Comitee for Medical Research Ethics. We do not possess any person identifiable data. For all individual participants included in the study, informed consent was obtained. For this type of study, no formal consent is required**.**

Table 1. Descriptive statistics for the sample.

Characteristics	Total sample (n=21,962)	Non-cases[1] (n=21,270)	CSOM[2] (n=102)	Hearing loss after rAOM[3] (n=590)
Male / female, %	48.5 / 51.5	48.5 / 51.5	44.1 / 55.9	51.9 / 48.1
Age at the adult study: range, mean (SD)	19-59, 40 (10.1)	19-56, 40 (10.1)	20-54, 41 (8.7)	20-59, 41 (8.0)
Dizziness[4]: Yes/maybe/no	6.8 / 10.3 / 82.9	6.7 / 10.2 / 83.1	10.8 / 20.6 / 68.6	11.2 / 9.5 / 79.3

[1] Normal hearing at the school investigation and no history of recurrent otitis media

[2] Chronic suppurative otitis media: Four participants had been operated with radical cholesteatoma removal, 13 with myringoplasty and eight with a non-specified ear operation. Nine participants with dry eardrum perforations were included into this group.

[3] Recurrent acute otitis media

[4] Assessed by questionnaire in the follow-up adult study: «Are you bothered by dizziness?»

Table 2. The association between otitis media in childhood and dizziness in adulthood.

Diagnosis (N)	Unadjusted Odds Ratios (95% CI)	p-value	Adjusted[1] Odds Ratios (95% CI)	p-value
Reference group (21,507)[2]	reference category		reference category	
CSOM (102)[3]	2.2 (1.5-3.4)	<0.001	2.1 (1.4-3.3)	<0.001
Hearing loss after rAOM (590)[4]	1.3 (1.0-1.6)	0.017	1.3 (1.0-1.5)	0.029

[1] Adjusted for age, sex and socio-economic status (level of education and income)
[2] Normal hearing at the school investigation and no self-reported history of recurrent otitis media
[3] Chronic Suppurative Otitis Media
[4] Hearing loss after a history of preschool, Recurrent Acute Otitis Media

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