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Repeated Audiometry After Bacterial Meningitis: Consequences for Future Management

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Objective: Sensorineural hearing loss is a common sequela of bacterial meningitis. The objective of this study is to delineate the incidence and course of hearing loss after bacterial meningitis.
Study Design: Retrospective cohort study.
Setting: Tertiary referral center.
Patients: Data of 655 patients who suffered from bacterial meningitis between 1985 and 2015 were analyzed.
Interventions: None.
Main Outcome Measurements: Availability of audiometric data, incidence of hearing loss, and onset and course of hearing loss.
Results: In this cohort the incidence of hearing loss (>25 dB) was 28% (95% confidence interval 23–34%). The incidence of profound hearing loss (>80 dB) was 13% (95% confidence interval 10–18%). Normal hearing at the first assessment after treatment for meningitis remained stable over time in all these patients. In 19 of the 28 patients with diagnosed hearing loss, the hearing level remained stable over time. Hearing improved in six patients and deteriorated in two patients. One patient showed a fluctuating unilateral hearing loss.
Conclusion: Audiological tests in patients with bacterial meningitis, especially children, should be started as soon as possible after the acute phase is over. As we found no deterioration of initial normal hearing after bacterial meningitis, repeated audiometry seems indicated only for those with diagnosed hearing loss at first assessment. **Key Words:** Audiology—Bacterial meningitis—Follow-up—Hearing loss.

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One of the most common sequelae of bacterial meningitis with high impact on general functioning is hearing loss, either unilateral or bilateral, and varying from mild to profound. Timely administration of dexamethasone or other steroids, preferably before hearing loss, is diagnosed, generally reduces the risk of hearing loss (1).

As cochlear inflammation can progress into ossification of the cochlear lumen, early diagnosis will enable placement of a cochlear implant before ossification takes place and electrode insertion becomes impossible.

There is international consensus on the need for early audiological testing (2–5), but not about the extent of audiological follow-up. In the Netherlands, the Cochlear Implant Group protocol prescribes audiological assessment as soon as the patient's condition permits this, and advises audiological follow-up at 1, 2, 6, and 12 months when the first test showed normal hearing (5).

A recent systematic review could include only a few studies addressing the course of hearing loss after bacterial meningitis (6). From the results of these studies it was concluded that late onset hearing loss is very rare (7–12). A general downside to all studies included is the basic, sometimes nonquantitative, description of the audiometric results. Also, the exact time of onset of hearing loss remained unclear in most studies.

Therefore, additional research is needed. In this study, we analyzed data from the medical records of patients with bacterial meningitis in our own hospital to first clarify the incidence, course and onset of hearing loss after bacterial meningitis. Secondly, we established compliance to audiometric testing protocol.

The results of this study can help improve current recommendations for audiological follow-up.

METHODS

Study Design

Data collected in the Erasmus University Medical Center (Erasmus MC, Rotterdam, The Netherlands) was used for this

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retrospective cohort study. This hospital accounts for 25% of pediatric intensive care hospitalizations and 3.5% of adult IC hospitalizations in the Netherlands. Its audiological department has a regional function for audiological tests of babies and young children.

Patient Inclusion

Patients with bacterial meningitis were identified via the Erasmus MC financial registration system, the diagnosis codes in the electronic medical records, and the Dutch Reference Laboratory for Bacterial Meningitis database (NRLBM: ''*Nederlands Referentielaboratorium voor Bacteriële Meningitis*''). The NRLBM receives cerebrospinal fluid and blood samples of about 90% of all patients with bacterial meningitis in the Netherlands (13) and provided us with a list of patients with bacterial meningitis treated in Erasmus MC between 1985 and 2015. All these patients were considered to be confirmed cases. The medical records of the patients identified through the financial registration system or diagnosis code were screened for information on lumbar puncture, symptoms, and treatment. Patients were excluded if they had not been treated for bacterial meningitis or if lumbar puncture had shown negative culture results and low number of leukocytes. Another exclusion criterion was pre-existing hearing loss or recurrent meningitis with an unclear relation between the episodes of meningitis and hearing loss.

We distinguished three cohorts, data of each of which served to answer specific questions (Fig. 1).

Cohort 1: Patients treated for bacterial meningitis in our hospital; their data was used to answer the questions on pathogen distribution and adherence to the audiometry follow-up protocol.

Cohort 2: A subgroup of patients identified through the Erasmus MC audiometry database. These patients had been diagnosed with bacterial meningitis in another hospital and referred to our hospital for audiological assessment. Those with adequate audiometry and those with adequate audiometry from Cohort 1 together formed Cohort 2. Their data was used to answer the questions on the incidence of hearing loss and pathogen distribution.

Cohort 3: A subgroup of patients from Cohort 2 for whom repeated audiometry was available; their data was used to study the course and timing of hearing loss after meningitis (Fig. 1).

Data Extraction

From each medical record the following information was retrieved: date of birth, date of meningitis, type of pathogen, and audiometric data. Audiometric data was discarded if more than 1 year had elapsed between the treatment of meningitis and the audiometric testing, or if the last assessment had been performed less than 3 months or more than 2 years after the first assessment.

Sensorineural hearing loss was classified according to the World Health Organisation grades of hearing impairment (14). Hearing loss was defined as a sensorineural loss of 25 dB, based on the high-frequency pure-tone average or auditory brainstem response (ABR) threshold. The high-frequency pure-tone average is the average hearing threshold at 1, 2, and 4 kHz in dBHL, and it was calculated using the bone conduction thresholds. In case of ABR data (click-stimulation), the response threshold corresponds to the hearing threshold around 3 kHz plus 10 dB. Conductive hearing losses were estimated by one of the researchers (L.R.) from the shape of the latency-intensity function and the results of tympanometry. Only sensorineural hearing losses were included in the analysis. Hearing loss was considered stable when the difference between the results of two consecutive assessments was less than 15 dB.

Results

Patient Selection and Audiometric Data

Cohort 1 consisted of 655 patients. As to age distribution, 246 were < 4 years old, 107 from 4 to 17 years old, and 302 ≥ 18 years old. Lumbar puncture was positive for bacterial meningitis in 584 patients; in the other 71, treatment for bacterial meningitis was started based on clinical presentation ($n = 31$), number of leukocytes in the cerebrospinal fluid ($n = 24$), or a diagnosis made in a referring hospital ($n = 16$), see Figure 1.

Most patients of meningitis in Cohort 1 were caused by *S. pneumoniae* (164 patients, 25%), followed by *N. meningitides* (163 patients, 25%), and Haemophilus influenzae type B (56 patients, 9%). In total 183 patients (28%) were caused by other (less frequently occurring) pathogens and in 89 patients (14%) no pathogen was identified but cerebrospinal fluid showed pleiocytosis.

Audiometric data were available for 174 of the 655 patients (27%) in Cohort 1. The younger the age, the higher the availability: 56% of the babies had audiometry data available against 14% of the adults. The most frequent reasons for missing audiometric data were: rapid death or bad condition (19%, 89/481) and transfer to another hospital (13%, 63/481), with various other reasons in 8% (22/481). In 64% (307/481) reasons for missing audiometry were not clear from the medical record, but seemed related to age in particular: in 34% of the babies without audiometry the reason for the lack of audiometry was unknown against 71% of the adults.

Cohort 2 consisted of 252 patients, that is 174 from Cohort 1 and 78 identified from the ABR database of the audiological department with both a history of meningitis and available audiometric data (74 (<4 yr old and 4 from 4 to18 yr old). Audiometry had been performed at a median interval of 43 (interquartile range [IQR] 19–105) days after meningitis.

Cohort 3 consisted of 110 patients whose hearing had been tested twice or more (Cohort 3, Fig. 1). The median interval between first and last test was 217 (IQR 168–355) days.

Incidence of Hearing Loss and Determinants

Hearing loss had been diagnosed in 69 of the 252 patients in Cohort 2 (27%, 95% CI 22–33%). The mean incidence of profound hearing loss (in at least one ear) was 13% (33/252 patients, 95% CI 10–18%), which was bilateral in almost half of these patients (6% of all patients, 16/252, 95% CI 4–10%).

Hearing loss was significantly age-related with an incidence of 63% (15/24, 95% CI 43–79%) in the over 17-year-olds and 24% (54/228, CI 19–30%) in children. In the latter group it was significantly more often

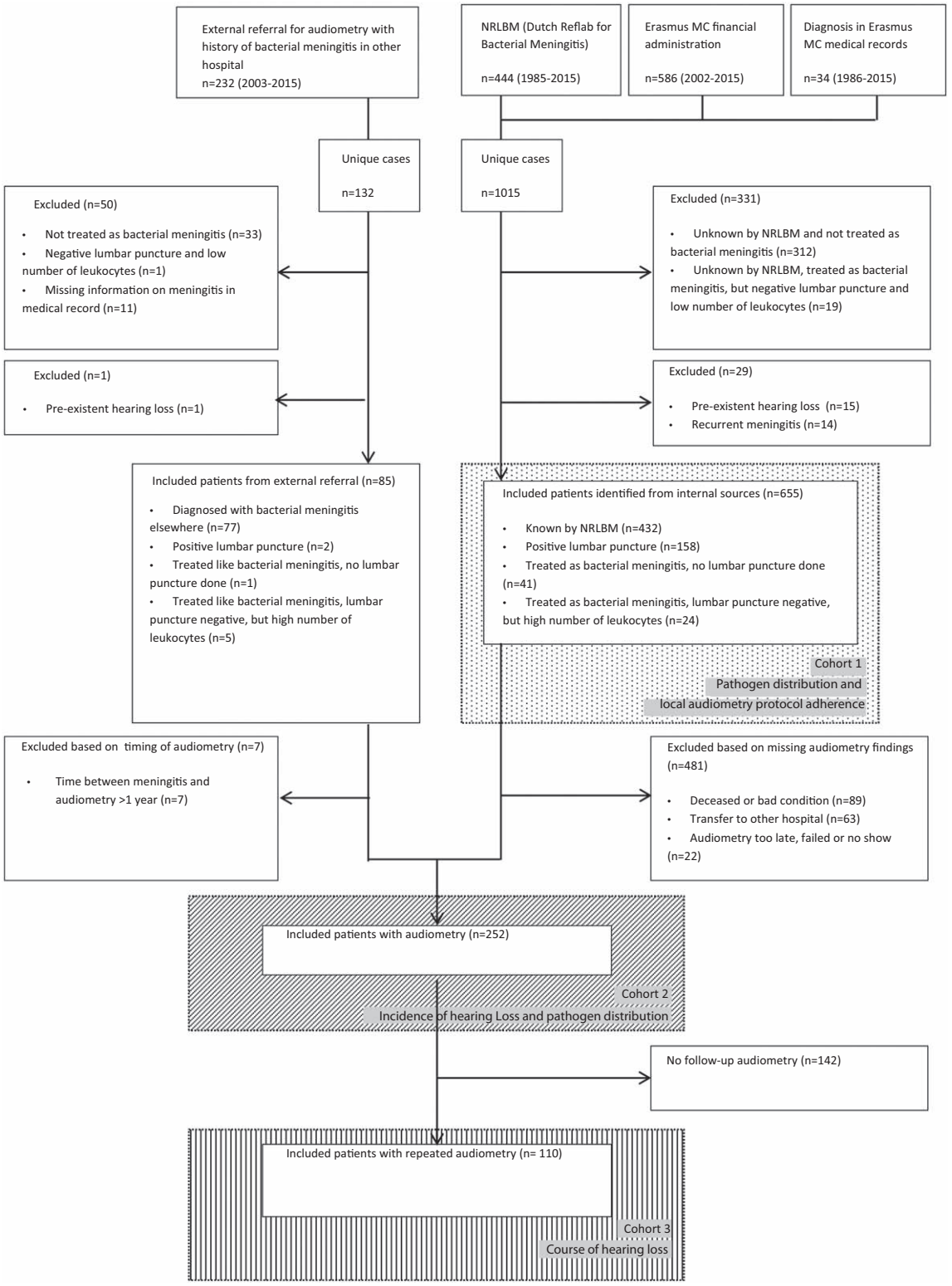

FIG. 1. Patient inclusion scheme.

profound than in the adult population (56% against 20%, odd's ratio 5, 95% CI 1, 3–20) (Table 1).

The distribution of pathogens in Cohort 2 was not significantly different from that of Cohort 1. In the subgroup of Cohort 2, patients diagnosed with hearing loss suffered significantly more frequently from pneumococcal meningitis than those without hearing loss (Table 2).

TABLE 1. *Grades of hearing loss per age category*

Hearing at First Test	Young Children (0-3 yr)		Children (4–17 yr)		Adults (>18yr)	
Normal hearing	153	(77%)	21	(75%)	9	(38%)
Slight hearing loss	14	(7%)	0	(0%)	4	(17%)
Moderate hearing loss	6	(3%)	1	(4%)	2	(8%)
Severe hearing loss	3	(2%)	0	(0%)	6	(25%)
Profound hearing loss	24	(12%)	6	(21%)	3	(13%)
total	200	(100%)	28	(100%)	24	(100%)
total hearing loss	47	(24%)	7	(25%)	15	(63%)

Course of Hearing Loss

Of 110 patients with repeated audiometry in Cohort 3, 82 (75%, 95% CI 66–82%) had normal hearing at the first assessment. Follow-up audiometry in these 82 patients did not reveal deterioration of hearing, although in 6 patients only data for one ear was available. In 19 of the 28 patients with diagnosed hearing loss after meningitis (20 unilateral, 8 bilateral) audiometry results remained stable, although in one patient only data for one ear was available (Fig. 2). Nine patients showed changes in hearing over time (Fig. 2). For six of them the hearing improved: in four patients even from mild hearing loss to normal hearing. One had a unilateral profound hearing loss after an infection with an unknown pathogen around birth, which showed fluctuations to a severe unilateral hearing loss. Two had a unilateral hearing loss (one moderate, one profound) with deterioration of the normal hearing ear to a moderate hearing loss in both, progressing to bilateral hearing loss.

Both patients who developed a hearing loss in the other ear had neonatal meningitis; in one patient due to an infection of a group B streptococcus and in the other due to *E. coli* infection. The patient with a group B streptococcus infection initially had a normal response on the ABR in one ear, including a normal I-V interval although both I and V-latency were lengthened, and otoacoustic emissions were present. However, after 70 days, the otoacoustic emissions had disappeared while the tympanogram was normal. The ABR result 15 days later showed a hearing loss of 60 dB HL and a delayed I-V interval. The patient with an infection due to *E. coli* had delayed latencies at the first ABR, which took place 61 days after the meningitis, and the otoacoustic emissions were present in some frequency bands for both ears. In follow-up assessments (246 and 402 days after meningitis) the latencies were almost conform age. From pure-tone audiometry, taken at older ages, the hearing loss seemed stable at 60 to 65 dB in both ears.

Onset

In the two patients from Cohort 3 who developed hearing loss in the contralateral ear, results of the audiological test at 4 and 8 weeks, respectively, after meningitis were normal, and deterioration was detected at 3 and 8.5 months, respectively.

DISCUSSION

The incidence of documented hearing loss in the studied population of 655 patients with bacterial meningitis in a tertiary referral center was established at 28%. Only the patients with initially diagnosed hearing loss after meningitis showed deterioration of hearing over time. A review on this topic found a mean incidence of 11%, with a large variation from 2 to 35% in the individual studies (6). A possible explanation for the high incidence in our series is the low percentage of available audiometry data. Cohort 2, which was used to calculate the incidence of hearing loss, might therefore be subject to selection bias. Those without complaints of hearing loss—especially adults—are less likely to be tested and were excluded from the analysis when audiometric information was lacking. As an additional reasoning, the incidence of

TABLE 2. *Cohort description: pathogen distribution, age, year of meningitis, and follow-up time*

	Cohort 1	655	Cohort 2	252	Cohort 2—With HL	69
Pathogen distribution						
S. pneumoniae	164	25% (CI 22–28%)	67	27% (CI 22–32%)	31	45% (CI 34–57%)
N. meningitides	163	25% (CI 22–28%)	57	23% (CI 18–28%)	11	16% (CI 9–26%)
Haemophilus influenzae B	56	9% (CI 7–11%)	30	12% (CI 8–16%)	8	12% (CI 8–16%)
Other pathogen	183	28% (CI 25–31%)	63	25% (CI 20–31%)	11	16% (CI 9–26%)
Not identified	89	14% (CI 11–16%)	35	14% (CI 10–19%)	8	12% (CI 8–16%)
Total	655	100%	252	100%	69	100%
age (median, yr)	15 (IQR 1–51)		0 (IQR 0–3)		1 (IQR 0–15)	
year of meningitis (median)	1999 (IQR 1991–2008)		2005 (IQR 1993–2010)		2006 (IQR 1993–2011)	
time between audiometry and meningitis (median, d)	n.a.		43 (IQR 19–105)		24 (IQR 11–101)	

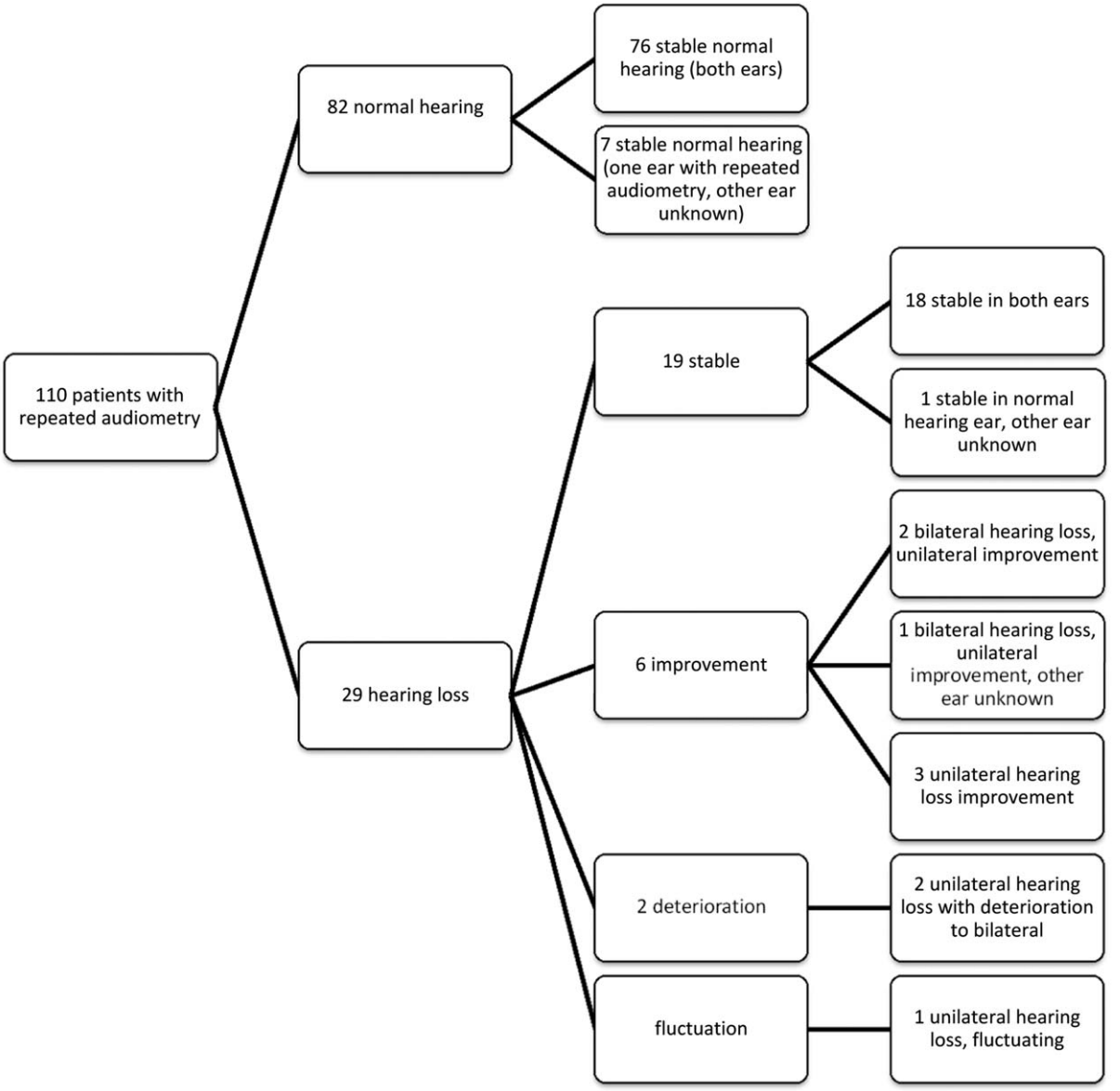

FIG. 2. Course of hearing capacity after meningitis.

hearing loss in our adult population was higher than that in the younger population. Given that the oldest person in our cohort was aged 69 years, we think it is unlikely that the high incidence of hearing loss in the adult population can be explained by an age-dependent, clinically not relevant hearing loss (15).

Patient selection could be a second possible explanation for the high incidence of post meningitis hearing loss we found. In a previous study it was suggested that hearing loss after meningitis is related to the severity of meningitis (8). Although we lacked information on the disease severity for a number of patients, the fact that the Erasmus Medical Centre is a tertiary referral center with potential selection of higher severity meningitis patients may have resulted in an overestimation of the hearing loss risk.

In our series, changes in hearing loss were observed between 4 weeks and 8 months after meningitis. A systematic review has found earlier onset of hearing loss, which nevertheless often improved in the early phase of the meningitis (9,10).

An important finding is that normal hearing at first audiometric assessment remained stable over time in all patients. Hence, patients with normal hearing immediately after the infection run little risk of developing hearing loss. This observation is confirmed by our systematic review on this subject, in which only one patients of deterioration of normal hearing is described: a young baby developed a bilateral severe hearing loss. However, no further information was available for this patients (6,12). We can conclude that repeated audiometry is

unnecessary for this group. However hearing loss occurring immediately after the infection should be regularly monitored with hearing tests for both ears.

A remarkable finding is that two patients with unilateral hearing loss developed hearing loss in the contralateral, initially normal hearing, ear. The question could be raised, therefore, whether this supports the proposition that initial normal hearing can deteriorate over time after meningitis, or whether this is a different situation with another origin? Patients of this kind have been described in the literature, but these were not caused by bacterial meningitis (16). We did not find an explanation for this in our data or in the literature, apart from some suggestions that endolymphatic hydrops can lead to fluctuating hearing loss after meningitis (17) or that it could be explained by autoimmunity (18).

A major limitation of this study is that audiometric data was available for only 30% of the patients in our hospital. Conversion to a noncompliance ratio is not possible, as a number of patients were transferred to another hospital before audiometry was done. However, for the majority of patients the reason for the absence of audiometric data was unclear, especially for the adult patients, which may point to flawed protocol adherence. For that matter, adherence to the audiometry follow-up protocol in our hospital seems to be lower than reported elsewhere (19). Also, the number of patients with repeated audiometry was relatively small: 110 out of 252 patients.

Furthermore, clinical characteristics of patients were not taken into account. Therefore, we cannot confirm hearing loss due to known associations with clinical characteristics, such as ataxia, *S. pneumoniae* as causative pathogen, low cerebrospinal fluid glucose level, absence of petechial, or longer duration of symptoms before admission (20).

CONCLUSION

Hearing loss after meningitis is difficult to study: although we started with a large pool of included meningitis patients, we ended up with only a small portion for which enough audiometric data were available. In future research this could be overcome by conducting a prospective study, and ensuring better adherence to the audiological follow-up protocol. We hope that our findings will help create more awareness of the importance of audiological testing after meningitis. These should be started as soon as the acute phase is over. This is most important for (young) children, who are less likely to complain about hearing loss and who more often suffer from a profound hearing loss. Repeated audiometry is only needed for those who show hearing loss at the first test.

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