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Hearing Loss in Bacterial Meningitis Revisited—Evolution and Recovery

Elisa Skovgaard Jensen,[1] Per Cayé-Thomasen,[2,3] Jacob Bodilsen,[4] Henrik Nielsen,[4] Lennart Friis-Hansen,[3,5] Thomas Christensen,[6] Malina Christiansen,[1] Malene Kirchmann,[1] and Christian Thomas Brandt[3,7,8]

[1]Department of Otorhinolaryngology, Nordsjællands Hospital, University of Copenhagen, Hillerød, Denmark, [2]Department of Otorhinolaryngology Head & Neck Surgery and Audiology, University Hospital Copenhagen Rigshospitalet, Copenhagen, Denmark, [3]Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark, [4]Department of Infectious Diseases, University Hospital Aalborg, Aalborg, Denmark, [5]Department of Clinical Biochemistry, Bispebjerg Hospital, University of Copenhagen, Copenhagen, Denmark, [6]Department of Neurology, University Hospital Copenhagen Rigshospitalet, Copenhagen, Denmark, [7]Department of Pulmonary and Infectious Diseases, Nordsjællands Hospital, University of Copenhagen, Hillerød, Denmark, and [8]Department of Infectious Diseases, Zealand University Hospital, University of Copenhagen, Roskilde, Denmark

Background. Hearing loss and deafness are well-known sequelae from bacterial meningitis (ABM) and may result in social dysfunction and learning difficulties. Yet, the timely development of hearing loss and restitution is poorly studied, especially among adults. Hearing loss was revisited using otoacoustic emissions (OAEs) to determine the occurrence, magnitude, and development of hearing loss among adults with ABM.

Methods. Distortion product OAEs were measured in patients with ABM the day of admission and days 2, 3, 5–7, and 10–14 and at follow-up 30–60 days after discharge. Frequencies were categorized as low (1, 1.5, 2 kHz), mid (3, 4, 5 kHz), mid-high (6, 7, 8 kHz), and high (9, 10 kHz). Audiometry was performed on discharge and 60 days after. Results were compared with 158 healthy controls.

Results. OAE was obtained in 32 patients. ABM was due to *S. pneumoniae* in 12 patients (38%). All patients were treated with dexamethasone. OAE emission threshold levels (ETLs) were significantly decreased upon admission and at follow-up in all frequencies compared with healthy controls. A substantial and significant decrease in ETLs was found in *S. pneumoniae* meningitis. Sensorineural hearing loss (SNHL) >20 dB was present in 13 of 23 (57%) at discharge and in 11 of 18 patients (61%) 60 days after discharge. Hearing recovery decreased from day 3.

Conclusions. Hearing loss in ABM still affects >60% of patients despite treatment with dexamethasone. In *S. pneumoniae* meningitis, SNHL is profound and permanent. A window of opportunity for systemic or local treatments aiming to preserve cochlear function is proposed.

Keywords. bacterial meningitis; OAE; cochlea; hearing loss; otoacoustic emissions.

Acute bacterial meningitis (ABM) is one of the most common causes of acquired sensorineural hearing loss (SNHL), reported to occur in up to 54% of survivors, with the highest incidence among adults with *S. pneumoniae* meningitis [1–3]. SNHL is closely associated with long-term complications, including poor academic performance, depression, and impaired psychosocial adjustment [4].

Even though hearing loss and deafness are the most common sequelae from meningitis, clinical studies addressing new treatment strategies addressing this complication are sparse, and anti-inflammatory treatment with dexamethasone is essentially the only treatment currently available [1, 5–9]. Studies that were primarily carried out in children with *H. influenzae* and *N. meningitidis* documented the presence of hearing loss early during disease [1, 10, 11]. Still, the pattern is not well described, with highly variable SNHL either declining, fluctuating, or resolving with time intervals ranging from 1 month to 12 years [11–16]. Previously, the cause of SNHL was proposed to be secondary to brain damage or direct injury to nerve fibers [17, 18]. Subsequent experimental studies demonstrated the site of lesions showing suppurative labyrinthitis with cochlear damage and spread of infection from the subarachnoid space or directly from otitis media [19–23].

Cochlear inflammation has been shown to cause fibrosis and cochlear ossification developing 3–4 weeks after the onset of meningitis, increasing the risk of not being able to implant cochlear electrodes [24, 25]. This underlines the importance of timely identification of hearing loss and the need for further studies of preventive treatment strategies.

The present study targeted cochlea-derived hearing loss by measuring otoacoustic emissions (OAEs), which are

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Correspondence: Christian T. Brandt, MD, DMSc, Zealand University Hospital Roskilde, Vestermarksvej 9, 4000 Roskilde, Denmark (chtb@regionsjaelland.dk); or Malene Kirchmann, MD, PhD, Department of Ear-Nose and Throat Diseases, Nordsjællands Hospital, University of Copenhagen, Denmark (malene.kirchmann.01@regionh.dk).

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low-intensity sounds generated by outer hair cells in the cochlea in response to sound stimuli [26, 27].

The aim of the present study was to clarify the temporal development and extent of SNHL in adults with ABM by repeated OAE measurements.

METHODS

In this prospective observational cohort study, SNHL was evaluated by audiometry and repeated measures of distortion product otoacoustic emissions (DPOAEs) in adults with ABM. Patients were recruited consecutively at the Department of Infectious Diseases, Nordsjællands Hospital, from November 2016 to July 2019 and from November 2016 to April 2017; patients were also recruited at the Department of Infectious Diseases, Aalborg University Hospital.

Control Cohort

A control group of healthy subjects aged 18–80 years (n = 158) with even gender distribution divided into 8 groups in decennials were recruited for the assessment of age- and sex-related DPOAE loss (Figure 1). Subjects aged 18–65 years were recruited among blood donors at Nordsjællands Hospital. Subjects aged >65 years were recruited in the Department of Orthopedics at Nordsjællands Hospital among candidates for elective surgery (Figure 1).

Exclusion criteria were familial deafness, head trauma requiring admission, significant history of noise exposure, ear surgery, previous administration of known ototoxic agents (eg, gentamycin), and prior central nervous system disease including meningitis. All subjects underwent otoscopy and tympanometry to rule out external and middle ear pathology.

Patient Cohort

Patients with ABM were enrolled prospectively on admission and follow-up as outpatients. Otoscopy and tympanometry were performed to rule out external and middle ear pathology.

Inclusion Criteria

Patients were ≥18 years of age, had a clinical presentation strongly suggesting bacterial meningitis (headache, fever, stiffness of the neck, petechiae, confusion or impaired level of consciousness), and had ≥1 of the following:

(a) Positive cerebrospinal fluid (CSF) culture.
(b) Positive blood culture and ≥1 of the following CSF findings: >10 leukocytes ($\times 10^6$ cells/L); glucose index <0.3; CSF glucose <1.9 mmol/L or CSF lactate >3.5 mmol/L; CSF protein >2.2 g/L.
(c) Presence of bacteria in gram stain of CSF or nonculture identification of bacteria in CSF by either gene amplification or antigen test.
(d) >100 leukocytes ($\times 10^6$ cells/L) in CSF with neutrophil predominance (>50%) in combination with low CSF glucose or CSF/blood glucose ratio (<1.9 mmol/L and 0.3, respectively) or CSF lactate >3.5 mmol/L.

Exclusion Criteria

Exclusion criteria were nosocomial meningitis, concomitant endocarditis, brain abscess, and viral meningitis or encephalitis. Patients were screened by a structured interview to exclude hearing loss due to other causes as described above for healthy controls.

Patient Data

Patients were divided into 5 groups based on CSF bacteriological results: *Streptococcus Pneumoniae, Haemophilus influenzae,*

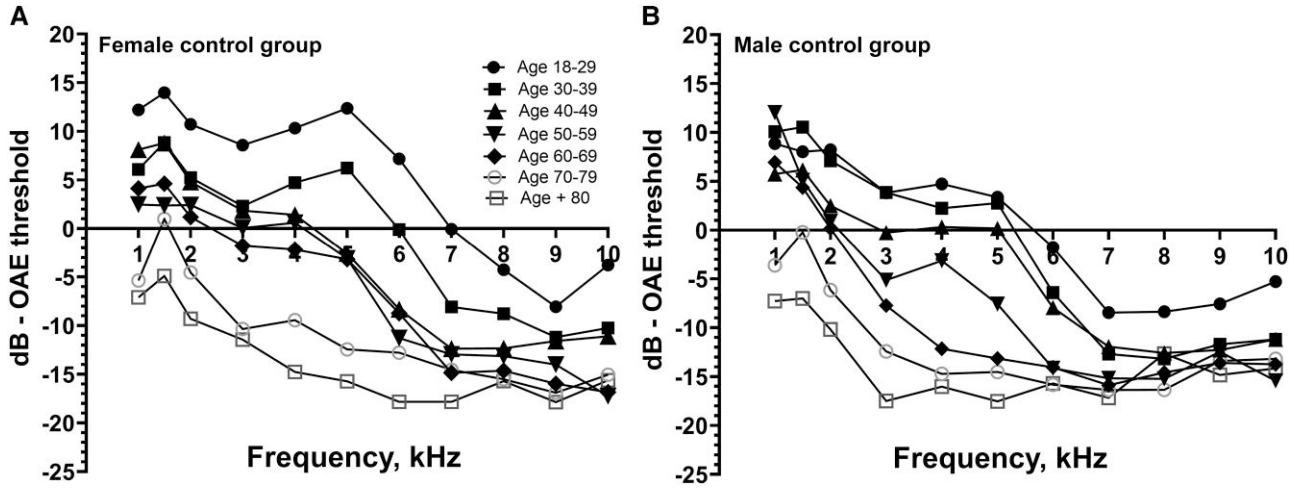

Figure 1. Emission threshold levels among healthy control group participants. Graph (*A*) shows ETLs among females, and graph (*B*) shows ETLs among males. The age groups are divided into decennials from 18 to 80+ years. Abbreviation: ETL, emission threshold level.

Neisseria meningitidis, other pathogen (*Staphylococcus aureus, Listeria monocytogenes, Escherichia coli,* non- and β-hemolytic streptococci), and unidentified pathogen. Clinical, biochemical, and microbiological data were recorded on admission.

Audiological Assessment

OAE (DPOAEs) was measured in both ears (excluding ears with middle ear pathology, eg, otitis media) on the day of admission (day 1), days 2 and 3, and between days 5 and 7 and 10 and 14. Patients were followed up in the outpatient clinic at least 30 days after discharge. OAEs were recorded using the Interacoustics Titan DPOAE 440 module. Eleven frequencies were measured in each ear: 1, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, and 10 kHz. The frequency ratio (f2/f1) was fixed at 1.22. OAE was performed with patients lying down with a 30° tilted head position. Frequencies were categorized as low (1, 1.5, 2 kHz), mid (3, 4, 5 kHz), mid-high (6, 7, 8 kHz), and high (9, 10 kHz). The emission threshold level (ETL) in each frequency category was calculated as the mean of the included frequencies.

A signal-to-noise ratio (SNR) of +3 dB was applied to the noise floor in low to mid-high frequencies and +6 dB in high frequencies. The distribution of final noise floor, and thus border of OAE detection, within each frequency category was low −10 dB, mid −15 dB, mid-high −13 dB, high −16 dB [28].

OAE Repeatability

Seven control group participants (median age [interquartile range {IQR}], 34 [30–52] years) were tested on 3 occasions (days 1, 14, and 90). From days 1 to 14, the mean variation ranged from 1.1 (+/−1.3 dB) to 1.4 dB (+/−0.9 dB). From days 1 to 90, mean variation ranged from 0.8 dB (+/−0.6 dB) to 0.7 dB (+/−1.1 dB). A change in ETL was determined to be ≥2.5 dB to be significant and a change <2.5 dB was registered as 0 (zero) [29].

Pure-Tone Audiometry

Patients were tested upon discharge and 60 days after discharge. Patients underwent pure-tone audiometry at the frequencies 0.125–8 kHz. Both air conduction and bone conduction were measured (Madsen Astera 2 Clinical Audiometer). The pure-tone average (PTA) was calculated as the average of the thresholds at 0.5, 1, 2, and 4 kHz. In case of a conductive hearing loss, bone conduction was applied. Hearing was classified in each ear as no hearing loss (≤20 dB HL), mild (21–40 dB HL), moderate (41–55 dB HL), moderately severe (56–70 dB HL), severe (71–90 dB HL), or profound (> 90 dB HL) [24]. The PTA of each patient was compared with PTA from an age- and sex-matched normative data set provided by ISO-7029 [30].

Statistical Evaluation and Data Handling

Statistical analyses were done in R studio, version 1.4.1717. The Fisher exact test and Mann-Whitney *U* test were used to compare groups, and a stratified Wilcoxon-Mann-Whitney combined analysis was used to perform comparisons of emissions with respect to age and sex. Spearman's rank test was applied for the correlation analysis between PTA and ETL levels. A *P* value <.05 was considered significant.

Loss of (otoacoustic) emissions upon admission (in dB) was calculated as the difference between the patient's ETL (mean of both ears) and the mean ETL in the age- and sex-matched control group.

Changes in ETL during admission were calculated as the difference from the patient's own ETL on admission. A recovery or decline of ≥2.5 dB was considered significant, and changes <2.5 dB were registered as 0 (zero). A recovery or decline in ETL was only registered at the first interval where this was observed (days 1–3, days 5–7, or days 10–14).

Patient Consent

The study was approved by the Danish Data Protection Agency (2012–58-0004, I-Suite 03637). Informed, written consent was obtained from subjects or relatives before enrollment. The study did not interfere with patient treatment, and OAE testing is harmless. The Committees on Biomedical Research Ethics for the Capital Region of Denmark (vek@regionh.dk) therefore did not require any registration (j.no. h-1-2012-086). The study was registered on clinicaltrials.gov (identifier: NCT03715569).

RESULTS

Patient Characteristics

In total, 32 patients with community-acquired ABM were included. The median age (IQR) was 67 (54–72) years, and 11 (34%) were female (Table 1). Etiology was confirmed in 28 (88%) patients and is presented in Table 1. Three patients were excluded because of bilateral otitis media (n = 1), preexisting hearing loss (n = 1), and deafness from previous *S. pneumoniae* meningitis (n = 1). Four patients were transferred to our hospital during disease, and DPOAE was only available at follow-up. Four patients did not attend scheduled follow-up. Mortality was 13% (n = 4/32). Data from 28 patients were therefore available on admission and for 24 patients at follow-up.

Treatment

Initial antimicrobial treatment consisted of a combination of penicillin and a third-generation cephalosporin in 30 (94%) patients and carbapenem monotherapy in 2 (6%) patients. Adjunctive dexamethasone was administered to all patients, although it was tapered in 1 (Figure 1, Table 2).

In total, 158 healthy subjects were included in the control group. Measurements were conducted on both ears. No ETL difference between the right and left ear was found (Mann-Whitney test, *P* = .4) (Figure 2, Table 3).

Table 1. Patient Demographics

Variables	Included Patients (n = 32)
Age, y	67 [55–72]
Male sex	21 (66)
Mortality	4 (13)
Clinical findings	…
Duration of symptoms before admission, d	2 [1–3]
Glasgow Coma Scale score[a]	11 [10–14]
Admission temperature, °C	38.5 [37.5–39.2]
Focus of infection (otitis media)	9 (30)
Focus of infection (pneumonia)	3 (10)
Seizures before or on admission	4 (13)
Brain imaging pathology	…
No. of patients with brain imaging pathology	4 (13)
Brain infarction or hemorrhage	2 (6.7)
Subdural empyema	1 (3.3)
Brain edema	1 (3.3)
Microbiology	…
Patients with positive CSF culture	28 (88)
Streptococcus pneumoniae	12 (38)
Neisseria meningitidis	4 (13)
Haemophilus influenzae	4 (13)
Staphylococcus aureus	2 (6)
Listeria monocytogenes	1 (3)
Other streptococci	4 (13)
Escherichia coli	1 (3)
Laboratory results	…
CRP, mg/L	174 [89–278]
B-leukocytes, 10^9/L	14.3 [11.6–22.2]
B-thrombocytes, $\times 10^9$/L	198 [158–261]
CSF leukocytes, $\times 10^6$/L	2520 [7762–7425]
CSF glucose, mmol/L	2.8 [0.2–3.7]
CSF protein, g/L	2.8 [1.5–5.3]
CSF lactate, mmol/L	6.9 [3.9–15]

Data are presented as No. (%) or median [IQR].

Abbreviations: CRP, C-reactive protein; CSF, cerebrospinal fluid.

[a]Characteristics of 32 patients with bacterial meningitis.

Admission

On admission, 22 (79%) of 28 patients had decreased ETL in ≥1 frequency group compared with healthy controls. ETL was significantly decreased in all frequency groups compared with age-matched and sex-matched healthy controls (male patients: Wilcoxon-Mann-Whitney test, $P < .0001$ in low and high frequencies; $P = .003$ in the mid frequency area; and $P = .0001$ in the mid-high frequency area; female patients: Wilcoxon-Mann-Whitney test, $P < .0001$ in low, mid, mid-high, and high frequencies). ETLs were below detection in all frequencies in 9 (32%) patients (5 *S. pneumoniae*, 2 *H. influenzae*, 2 other pathogens [*E. coli*]).

Nine (90%) of 10 female patients presented with decreased ETL on admission compared with 13 (72%) of 18 male patients (Fisher exact test, $P > .05$). Emission loss in dB was not different between female and male patients in any frequency category (Mann-Whitney test, $P > .05$).

Emission loss in dB was not different between pathogen groups in any frequency category and also not when comparing *S. pneumoniae* with all other pathogens combined (Kruskal-Wallis test, $P > .05$).

Follow-up

At final follow-up after discharge, 17 (71%) of 24 patients had decreased ETLs in ≥1 frequency group. ETLs remained significantly decreased in all frequency groups compared with controls (male patients: Wilcoxon-Mann-Whitney test, $P < .0001$ in low frequencies; $P = .0003$ in the mid frequency area; $P = .001$ in the mid-high frequency area; and $P = .0002$ in the high frequency area; female patients: Wilcoxon-Mann-Whitney test, $P < .0001$ in low, mid, mid-high, and high frequencies). ETL was below the border of detection in all frequencies in 5 (21%) of 24 patients (3 *S. pneumoniae*, 1 *H. influenzae*, 1 other pathogen [*E. coli*]). Eight (80%) of 10 female patients had decreased ETLs in ≥1 frequency area at the final follow-up compared with 9 (64%) of 14 male patients (Fisher exact test, $P > .05$).

Emission loss in dB was not different between pathogens in any frequency area (Kruskal-Wallis test, $P > .05$). Comparing *S. pneumoniae* meningitis with the other pathogen groups combined, yielded significantly higher emission loss in *S. pneumoniae* meningitis in the low (median [IQR], 8.5 [3.5–13.8] dB; vs median [IQR], 1.8 [0–13.3] dB; Mann-Whitney test, $P = .021$) and mid frequency areas (median [IQR], 4.3 [1.1–13.6] dB; vs median [IQR], 0 [0–3.7] dB; $P = .046$).

Cochlear Dynamics—Recovery and Decline in OAE

Changes in ETLs, defined as an increase or decrease >2.5 dB in any frequency area, were found in 17 (63%) of 27 patients between admission and day 3; 6 (22%) patients from days 5 to 7; 1 (4%) patient from days 10 to 14. Two patients had emissions below the border of detection from admission to follow-up. Data from 1 patient were only available on admission and follow-up (Supplementary Tables 1 and 2).

Audiometry

Audiometry at discharge was available in 23 (82%) of 28 patients, and audiometry after discharge was available in 18 (64%) of 28 patients (median, 60 days) (Table 4). The 5 patients who did not show up for their second audiometry had either no hearing loss (n = 3) or mild hearing loss (n = 2) in the first audiometry. SNHL was present in 13 (57%) of 23 patients upon the first audiometry and 11 (61%) of 18 patients upon the second audiometry. Cases with severe or profound hearing loss were all due to *S. pneumoniae* meningitis. SNHL was bilateral in all cases except for 1 patient. In the 18 patients who underwent the second audiometry, hearing was unchanged in 14 patients, improved in 3 patients, and deteriorated in 1 patient.

Table 2. Maximum Detectable Hearing Loss Based on Control Group Mean to Lowest Detectable OAE

… …	Frequency Group Lowest OAE Level	Low 1, 1.5, 2 kHz −10 dB	Mid 3, 4, 5 kHz −15 dB	Mid-high 6, 7, 8 kHz −13 dB	High 9, 10 kHz −16 dB
Age group	Sex	…	…	…	…
18–29 y	F	**22.3 db**	**25.4 dB**	**14 dB**	**11.1 dB**
	M	**18.4 dB**	**19.0 dB**	**6.8 dB**	**9.6 dB**
30–39 y	F	**16.7 dB**	**19.4 dB**	**7.4 dB**	**5.3 dB**
	M	**19.2 dB**	**18.0 dB**	**2.3 dB**	**4.7 dB**
40–49 y	F	**17.2 dB**	**15.2 dB**	**2.0 dB**	**4.7 dB**
	M	**14.8 dB**	**15.1 dB**	**2.4 dB**	**4.3 dB**
50–59 y	F	**12.5 dB**	**14.8 dB**	0.5 dB	0.4 dB
	M	**16.0 dB**	**9.7 dB**	0 dB	**2.1 dB**
60–69 y	F	**13.3 dB**	**13.6 dB**	0.2 dB	0 dB
	M	**13.8 dB**	**4.0 dB**	0 dB	**2.4 dB**
70–79 y	F	**7.0 dB**	**4.3 dB**	0 dB	0 dB
	M	**6.8 dB**	**1.1 dB**	0 dB	**2.7 dB**
>80 y	F	**2.9 dB**	**1.1 dB**	0 dB	0 dB
	M	**2.2 dB**	0 dB	0 dB	0.5 dB

Only values in bold were included in the data-analysis of hearing loss in meningitis patients.
The range from the control group mean emission threshold levels to the noise floor with an added SNR of 3 dB for the low to mid-high frequencies and 6 dB in the high frequency spectrum is shown for both sexes in decennials from 18 y to 80+.

Abbreviations: OAE, otoacoustic emission; SNR, signal-to-noise ratio.

Two patients with *S. pneumoniae* meningitis were candidates for cochlear implants (but declined).

PTA from the first audiometry had significantly higher thresholds compared with the PTA from the age- and sex-matched control data set (mean, 29 dB vs 14 dB; Mann-Whitney test, $P = .008$).

OAE Correlation With Pure Tone Audiometry

The mean ETLs at the final follow-up in frequencies 1–4 kHz were significantly correlated to PTA results of the first audiometry ($P = .003$; Spearmann rank, −0.63).

DISCUSSION

The present study is the first to measure otoacoustic emissions through the course of disease in adult patients with bacterial meningitis. Our findings confirm that cochlear injury is the primary cause of hearing loss and deafness in meningitis. Compared with a healthy age- and sex-matched control group, we found that decreased cochlear emissions affected 79% of patients on admission and still 71% at final follow-up.

Repeated OAE measurements revealed that 60% of emission changes—recoveries and declines—occurred within 72 hours of admission, thus suggesting a narrow window for additional preventive measures. This finding is consistent with a previous study in children demonstrating early loss of click stimulus response [1, 10, 11].

Dexamethasone has both clinically and experimentally been shown to significantly reduce hearing loss [31–33]. Still, SNHL was marked among our patients, all of whom received dexamethasone.

Our control group data were in accordance with previous data showing better hearing among women and declining hearing with age [34]. Gender differences were not further analyzed given the higher baseline emission threshold levels observed among healthy female controls.

The limited recovery of cochlear function in patients with *S. pneumoniae* meningitis is likely related to obliteration of cochlear lumen that may occur in the weeks after hearing loss has developed [24, 25]. Also, ossification of cochlea following bacterial meningitis has been demonstrated experimentally [22]. Experimental studies have greatly improved our understanding of the pathophysiology of suppurative labyrinthitis in ABM and hearing loss, elucidating the spread of bacterial and inflammatory debris from the cerebrospinal fluid and vice versa [20–23]. A bilateral open cochlear aqueduct or hematogenic spread is supported by our data, in which hearing loss was observed in both ears with no significant difference between the right and left ears.

SNHL, defined by PTA, was present in 13 (57%) patients in the first audiometry. This is higher than previously reported but is supported by recent data from a retrospective study [35]. Another recent systematic review reported a much lower incidence of hearing loss of 14% and an incidence of 5% for profound hearing loss following bacterial meningitis [31]. The high frequency of SNHL may by the result of the high number of patients with *S. pneumoniae* meningitis, which is known to result in the highest incidence of meningitis-related hearing loss [3]. This is consistent with our results, where severe or profound hearing loss was observed predominantly among patients surviving *S. pneumoniae* meningitis (Figure 2). However, cases due to other pathogens were few,

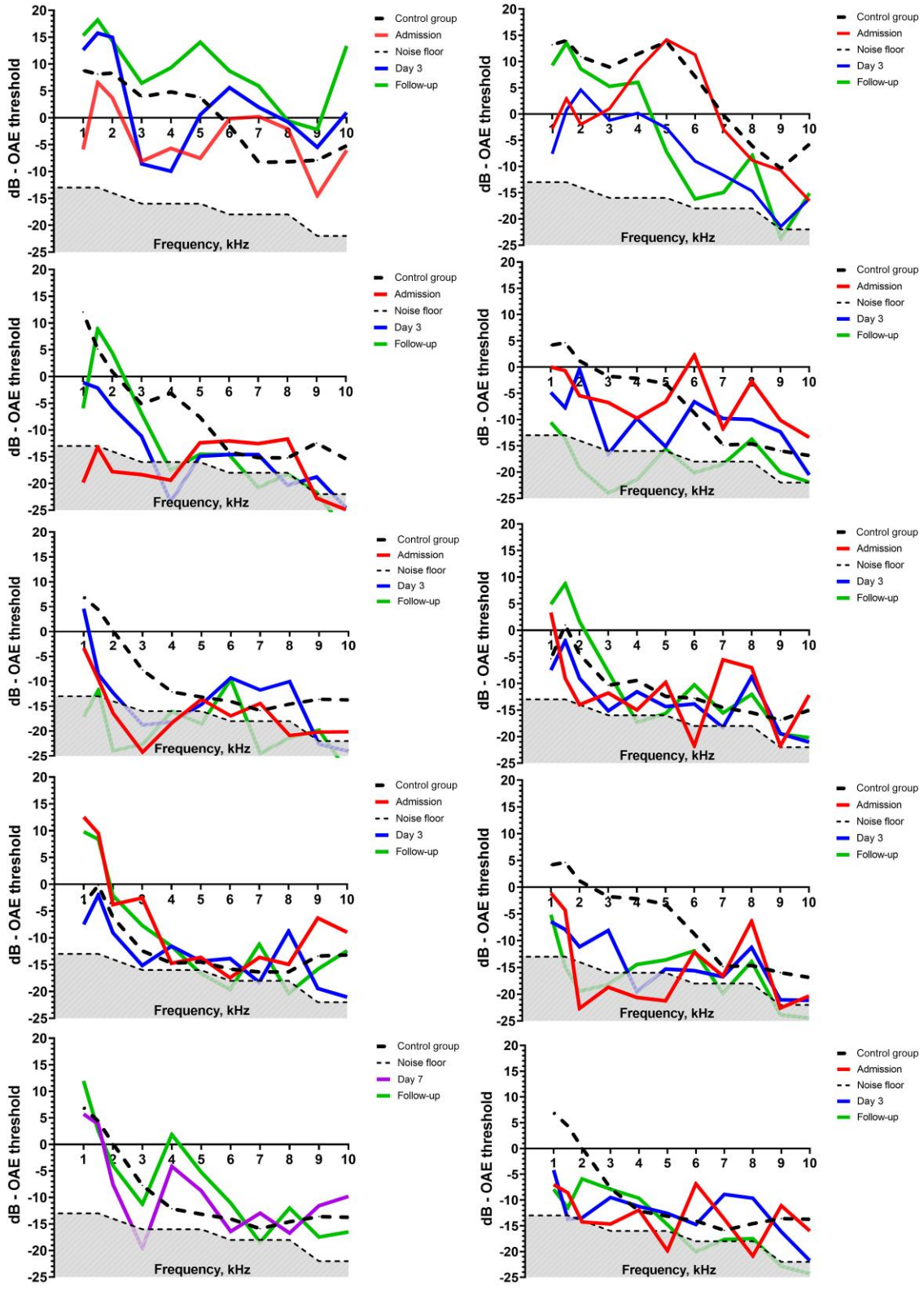

Figure 2. Changes in ETLs from admission to follow-up showing the dB level of each frequency measured (1–10 kHz). The red line shows admission ETL; the blue line shows ETLs on day 3 (72 h after admission); the green line shows ETLs at final follow-up. The black dotted line shows the mean ETL level of age- and sex-matched controls. The gray scattered area at the bottom of each graph is the noise floor. The ETL level of detection was calculated from the noise floor with the addition of SNR +3 dB (low, mid, and mid-high frequencies) and +6 dB (high frequencies). A and B, A male (age 20) and female (age 18) with *N. meningitidis* meningitis. C and D, A male (age 50) and female (age 61) with *S. pneumoniae* meningitis. E and F, A male (age 65) and female (age 75) with *H. influenzae* meningitis. G and H, A male (age 71) and female (age 64) with other pathogens (*S. aureus* and *E. coli*, respectively). I and J, A female (age 67) and male (age 64) with meningitis with unidentified pathogens. Abbreviations: ETL, emission threshold level; SNR, signal-to-noise ratio.

Table 3. Loss and Recovery of Emissions From Admission to Follow-up

…	…	…	No. With Emission Loss	Age	Admission Emission Loss—ETLs in Db Compared With Mean Control Group Level, Median (Min/Max)				Emission Loss Follow-up	Final Follow-up Emission Loss—ETLs in Db Compared With Mean Control Group Level, Median (Min/Max)			
Pathogen	Sex	No.	No./No.	Median and Range	Low Frequency 1, 1.5, 2 kHz	Mid Frequency 3, 4, 5 kHz	Mid-High Frequency 6, 7, 8 kHz	High Frequency 9, 10 kHz	No./No.	Low Frequency 1, 1.5, 2 kHz	Mid Frequency 3, 4, 5 kHz	Mid-High frequency 6, 7, 8 kHz	High Frequency 9, 10 kHz
All	F	10	9/10 (90)	67 (17 to 81)	7.0 (2.4 to 13.3)	7.6 (1.7 to 13.6)	0.0[a] (0.0 to 1.2)	0.0[a] (0.0 to 8.8)	8/9 (72)	7.0 (0.0 to 13.3)	13.0 (0.0 to 14.0)	14.0[b] (–)	11.1[b] (–)
	M	18	13/18 (72)	68 (19 to 82)	10.3 (2.2 to 16.0)	6.9 (1.1 to 12.4)	0.0[c] (0.0 to 2.3)	2.4[d] (0.0 to 4.7)	7/11 (72)	3.5 (0.0 to 13.8)	1.8 (0.0 to 4.0)	0.0[a] (–)	2.4 (0.0 to 2.7)
Streptococcus pneumoniae	F	5	5/5 (100)	67 (61 to 73)	7.0 (5.1 to 13.3)	4.3 (4.3 to 13.6)	*BD*	*BD*	4/4 (100)	7.9 (7.1 to 13.3)	13.3 (6.9 to 13.6)	*BD*	*BD*
	M	4	3/4 (75)	70 (50 to 82)	13.8 (2.2 to 16.0)	6.9 (4.0 to 9.7)	*BD*	2.3 (2.1 to 2.4)	3/3 (100)	9.2 (3.5 to 13.8)	1.8 (1.1 to 4.0)	*BD*	2.1 (1.7 to 2.4)
Haemophilus influenzae	F	1	1/1 (100)	75 (–)	3.3 (–)	1.2 (–)	*BD*	*BD*	1/1 (100)	0.0 (–)	2.7 (–)	*BD*	*BD*
	M	3	3/3 (100)	65 (64 to 66)	13.6 (3.8 to 13.8)	4.0 (4.0 to 4.0)	*BD*	1.2 (0.0 to 2.4)	3/3 (100)	6.7 (2.3 to 13.3)	0.0 (0.0 to 4.0)	*BD*	2.4 (0.0 to 2.4)
Neisseria meningitidis	F	1	1/1 (100)	18 (–)	12.9 (–)	7.6 (–)	0.0 (–)	8.8 (–)	1/1 (100)	1.8 (–)	14.0 (–)	14.0 (–)	11.1 (–)
	M	2	2/2 (100)	20 (19 to 20)	3.5 (0.0 to 6.9)	5.5 (0.0 to 11.1)	0.0 (0.0 to 0.0)	2.8 (0.0 to 4.6)	0/2 (0)	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)
Other pathogen	F	2	1/2 (50)	73 (64 to 81)	12.7 (–)	13.6 (–)	*BD*	*BD*	1/2 (50)	13.3 (–)	13.6 (–)	*BD*	*BD*
	M	6	3/6 (50)	73 (50 to 79	6.5 (0.0 to 6.8)	1.4 (1.1 to 6.3)	*BD*	2.3 (2.1 to 2.4)	1/3 (33)	9.3 (–)	1.8 (–)	0.0 (–)	2.4 (–)
Unidentified pathogen	F	1	1/1 (100)	67 (–)	2.5 (–)	9.1 (–)	*BD*	*BD*	1/1 (100)	1.0 (–)	2.5 (–)	*BD*	*BD*
	M	3	1/3 (33)	69 (37 to 69)	15.8 (–)	12.4 (–)	2.3 (–)	0.0 (–)	0	*NA*	*NA*	*NA*	*NA*

Data are shown as No. (%) or median with full range (min/max) in each frequency category. The emission loss in dB was calculated as the difference from the control group mean ETL to the patients' ETLs. In cases with absent emissions, the difference was calculated from control group mean to the noise floor, where the SNR was +3 dB (low, mid, and mid-high frequencies) and +6 dB (high frequencies).

Abbreviations: BD, below level of detection; ETL, emission threshold level; NA, data not available; SNR, signal-to-noise ratio.

[a]ETL was below age-related level of detection (BD) in 6 patients.

[b]ETL was below age-related level of detection (BD) in 7 patients.

[c]ETL was below age-related level of detection (BD) in 10 patients.

[d]ETL was below age-related level of detection (BD) in 3 patients.

Table 4. Results of Audiometry

No. Patients		
Severity of Hearing Loss	First Audiometry, No. (%)	Second Audiometry, No. (%)
No HL	10 (43)	7 (39)
Mild HL	5 (22)	5 (28)
Moderate HL	5 (22)	3 (17)
Severe HL	2 (9)	2 (11)
Profound HL	1 (4)	1 (5)

Classification of sensorineural hearing loss in patients with bacterial meningitis with and without age and sex adjustment. Classification is based on PTA and ΔPTA in the worse ear. No hearing loss (≤20 dB HL), mild (21–40 dB HL), moderate (41–55 dB HL), moderately severe (56–70 dB HL), severe (71–90 dB HL), profound (>90 dB HL). Audiometries were performed 13 days (median) and 60 days (median) after hospitalization. First audiometry (n = 23), second audiometry (n = 18).

Abbreviations: HL, hearing loss; PTA, pure-tone average.

and not all our patients underwent audiometry; this may have biased our results. Although the worst hearing outcome was observed in *S. pneumoniae* meningitis, not all patients had SNHL defined by PTA. Therefore, DPOAE measurements in patients with normal hearing defined by PTA may provide an early indication of hearing loss in patients at risk of presbycusis.

Our study was limited by the ability of OAE to detect emission loss in the frequencies above 5 kHz due to age-related hearing loss naturally occurring in our study group. The limited sample size restricted further analysis of factors associated with emission loss. Calculating emission loss as the mean value from both ears and not only the "worse ear" may also contribute to lower levels of emission loss. The clinical impact of the measured changes in ETLs may be subclinical, and a definite border of significance was not clarified. With respect to this, our application of SNR +3 to +6 dB reduced the predefined spectrum of detectable emissions. However, an analysis of reproducibility of emissions close to the noise floor was beyond the scope of this study. Lastly, we cannot exclude preexisting hearing loss, and despite careful interview the number of patients excluded due to preexisting hearing loss was low. Essentially, only a premorbid hearing test could fully clarify this issue.

CONCLUSIONS

In ABM, hearing loss is the result of cochlear dysfunction and injury. Emission loss is bilateral, affecting 70% of patients determined by OAE and 56% by audiometry. Hearing loss was primarily observed in *S. pneumoniae* meningitis, but all pathogens can lead to permanent hearing loss. Our data suggest that local or systemic treatment strategies aimed at preserving cochlear function should be initiated upon admission and no later than day 3.

Our findings underline the importance of audiological evaluation in patients with ABM and provide a framework for future clinical studies.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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