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How common is sensorineural hearing loss after neonatal meningitis?

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Keywords:	Audiology, Deafness, Neonatology, Microbiology, Epidemiology

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TITLE:

How common is sensorineural hearing loss after neonatal meningitis?

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ABSTRACT

Babies in intensive care are at higher risk for meningitis and sensorineural hearing loss (SNHL). The rate of SNHL associated with neonatal meningitis is unclear. We undertook a retrospective review of admissions to our neonatal intensive care unit over a 16-year period (2006-2021). We identified only 16 definite meningitis cases among 16,070 admissions, an incidence of 0.1%. Diagnostic audiology showed 80% (8/10) surviving infants tested had normal/satisfactory hearing while 20% (2/10) had SNHL: both were extremely preterm and received potentially-ototoxic antimicrobials. Larger studies are needed to clarify whether SNHL occurs mainly due to meningitis itself or its antimicrobial drug treatment.

Neonatal meningitis is a well-recognised risk factor for sensorineural hearing loss (SNHL).[1] Meningitis indicates automatic referral for formal audiological testing at age 8 months in the UK.[2] There are no recent UK data reporting detailed hearing outcomes of neonates who suffered neonatal meningitis. Our aim was to study the incidence of SNHL in neonates admitted to our tertiary-level neonatal intensive care unit (NICU) with proven meningitis.

We reviewed electronic neonatal records (BadgerNet, Clevermed, UK) and our local microbiology database for the 16-year period 1/1/2006 to 31/12/2021 to identify all neonates diagnosed with unequivocal bacterial or fungal meningitis. We defined proven meningitis cases as those with positive bacterial or fungal growth on culture of cerebrospinal fluid (CSF) obtained from infants with clinical signs of suspected meningitis/sepsis and who had received at least 2 weeks of antibiotic therapy for the episode. We excluded any neonates with meningitis who were never admitted to our NICU and also those treated for suspected meningitis despite a negative CSF culture. Babies with CSF isolates of a coagulase-negative Staphylococcus plus a concomitant CSF leucocyte count $<20x10^6$/L were considered false positive cases and so also excluded.[3] For all confirmed cases we reviewed isolates, concomitant blood cultures, CSF cell counts, newborn hearing screening results, and later diagnostic audiological testing at 0.5, 1, 2, and 4 kHz pure tone audiometry thresholds. SNHL was diagnosed for infants with hearing loss thresholds >20 dB.[4]

We had 16,070 neonatal admissions to our NICU during the 16-year study period. Twenty-eight babies had a culture-positive CSF result and of these 16 were confirmed as definite meningitis cases (Table). Overall, the definite meningitis rate was 16/16,070 (0.1%), or 1 case per 1000 admissions. Fifteen were bacterial meningitis cases and one fungal. Three babies had meningitis caused by a Coagulase-negative Staphylococcus. All except four babies (cases 8, 9, 12, 16) had concomitant blood cultures positive with the same organism.

CSF specimens showed very wide variation in white to red blood cell ratios. The incidence of meningitis was three-fold higher among preterm compared with term admissions, 12/7,185 (0.17%) vs. 4/8,885 (0.05%), p=0.02, Chi^2 test). Two infants did not undergo newborn hearing screening (1 deceased, 1 contraindicated). Of 14 who underwent the screening, 9/14 (64%) had clear responses and 5/14 (36%) required referral (1 bilateral, 4 unilateral screen fails).

Definitive follow-up audiology outcomes were unavailable for six babies (2 died in infancy before completion of diagnostic testing; 2 had no formal testing despite meningitis history; 2 failed to attend appointments).

Diagnostic audiology outcome data were available for 10/14 (71%) surviving infants: 8/10 (80%) had hearing within normal limits (normal/satisfactory); 2/10 (20%) have SNHL (1 severe bilateral; 1 moderate mixed bilateral), a rate of SNHL among surviving neonatal meningitis cases of at least 14% (2/14) (95% confidence limits: 2%, 43%). Both SNHL cases were infants born extremely preterm at 24 weeks' gestation who suffered meningitis in their second postnatal week: one had fungal meningitis caused by *Candida albicans*; one had bacterial meningitis caused by *Staphylococcus epidermidis*. Their antimicrobial treatments included the potentially-ototoxic agents flucytosine, vancomycin, and rifampicin.

Our single centre series covering a 16-year period showed that the incidence of definite neonatal meningitis among neonatal admissions was very low overall. SNHL caused by neonatal meningitis (or its treatment) was relatively rare, with only two confirmed cases in 16 years in our NICU. However, for cases of proven meningitis, the associated rate of SNHL was not insignificant (at least 14%). Larger studies are required to clarify whether SNHL occurs mainly due to meningitis itself, or to its antimicrobial drug treatment in extremely preterm neonates.

Contributorship

PC devised this project. AS, ST and PC collected clinical data, JML, CC, and JF collected audiological data, and CS interrogated the microbiological database. PC and CT reviewed and adjudicated the meningitis cases, and JF provided audiological expertise. PC analysed the data. PC and AS wrote the first manuscript draft and PC wrote the final draft. All authors contributed to manuscript revisions. PC is guarantor.

Patient and Public Involvement statement

The research question arose as a direct result of a parent's question.

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Competing interests

The authors have no relevant competing interests to declare.

Ethics approval

This study reviewed routinely collected clinical data and did not require formal ethics review.

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Table: CSF isolates, microscopy, and hearing outcomes of 16 neonates with definite meningitis

Case No.	Birth gestation, weeks	Postnatal age, days	CSF isolate	CSF cell count, x10^6/L		CSF ratio WCC:RCC	Audiological Outcome*
				WBC (% polymorphs)	RBC		
1	24	8	*Candida albicans*	100 (75%)	21600	1:216	Severe bilateral SNHL
2	24	39	Group B Streptococcus	840 (90%)	7580	1:135	N/A
3	24	8	*Staphylococcus epidermidis*	56 (0%)	7540	1:135	Moderate mixed bilateral permanent hearing loss
4	24	9	*Pseudomonas aeruginosa*	4970 (80%)	850	1:0.17	Satisfactory†
5	25	61	*Escherichia coli*	7420 (75%)	390	1:0.05	N/A (died, untested)
6	25	15	Coagulase-negative Staphylococcus‡	398 (75%)	4580	1:12	Normal
7	27	13	*Escherichia coli*	3180 (90%)	360	1:0.11	N/A
8	27	25	*Enterobacter cloacae complex*	18 (5%)	4320	1:240	N/A (died, prior testing attempts unsuccessful)
9	28	30	*Escherichia coli*	6 (% N/A)	6	1:1	Satisfactory§
10	29	89	Group B Streptococcus	650 (80%)	2220	1:3	N/A
11	31	40	*Escherichia coli*	3210 (95%)	2	1:6x10^{-4}	Normal
12	36	6	*Escherichia coli*	960 (60%)	690	1:0.72	Satisfactory†
13	40	8	Group B Streptococcus	2030 (30%)	11310	1:6	Satisfactory†
14	40	2	Group B Streptococcus	10 (% N/A)	5500	1:550	Normal
15	41	5	Group B Streptococcus	2850 (40%)	1300	1:0.46	N/A
16	41	49	*Staphylococcus haemolyticus*	620 (90%)	2830	1:5	Satisfactory§

CSF, cerebrospinal fluid; WCC, white blood cell count; RCC, red blood cell count; SNHL, sensori-neural hearing loss; N/A, test not available (not done or lost to follow up before determined).
*Normal hearing ≤20 dB; mild hearing loss 21-40 dB minimum detectable threshold; moderate 41-70 dB; severe loss 71-95 dB; profound loss >95 dB
†Satisfactory hearing, based on oto-acoustic emissions and visual reinforcement audiometry with sound field testing down to 25 dB (no audiogram), unable to rule out mild loss
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References

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Sensorineural hearing loss after neonatal meningitis: a single centre retrospective study

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Word count: 633

ABSTRACT

Babies in intensive care are at higher risk for meningitis and sensorineural hearing loss (SNHL). We reviewed the rate of SNHL among definite cases of bacterial/fungal meningitis in our neonatal intensive care unit over a 16-year period (2006-2021). We identified 16 confirmed meningitis cases among 16,070 admissions: 8 of 10 surviving infants with available diagnostic audiology had normal/satisfactory hearing while 2 of 10 had SNHL. Both infants with permanent hearing loss had been born extremely preterm and received potentially-ototoxic antimicrobials. Larger studies are needed to clarify whether SNHL occurs mainly due to meningitis itself or to its antimicrobial drug treatment.

Neonatal meningitis is a well-recognised risk factor for sensorineural hearing loss (SNHL),[1] and indicates automatic referral for early auditory brainstem response testing and other formal audiological testing.[2] There are no recent UK data reporting detailed hearing outcomes of neonates who suffered neonatal meningitis. Our aim was to study the incidence of SNHL in neonates admitted to our tertiary-level neonatal intensive care unit (NICU) with proven meningitis.

We reviewed electronic neonatal records (BadgerNet, Clevermed, UK) and our local microbiology database for the 16-year period 1/1/2006 to 31/12/2021 to identify all neonates diagnosed with unequivocal bacterial or fungal meningitis. We defined proven meningitis cases as those with positive bacterial or fungal growth on culture of cerebrospinal fluid (CSF) obtained from infants with clinical signs of suspected meningitis/sepsis and who had received at least 2 weeks of antibiotic therapy for the episode. We excluded any neonates with meningitis who were never admitted to our NICU, those treated for suspected meningitis despite a negative CSF culture, and cases of viral meningitis. Babies with CSF isolates of a coagulase-negative Staphylococcus plus a concomitant CSF leucocyte count $<20x10^6$/L were considered false positive cases and also excluded.[3] For all confirmed cases we reviewed isolates, concomitant blood cultures, CSF cell counts, newborn hearing screening results, and later diagnostic audiological testing at 0.5, 1, 2, and 4 kHz pure tone audiometry thresholds. SNHL was diagnosed for infants with hearing loss thresholds >20 decibels.[4]

We had 16,070 neonatal admissions to our NICU during the 16-year study period. Twenty-eight babies had a culture-positive CSF result and of these 16 were confirmed as definite meningitis cases (Summary Table). Twelve infants were born preterm (cases 1-12) and four were born at term (cases 13-16). Overall, the definite meningitis rate was 16/16,070 (0.1%), or 1 case per 1000 admissions. Fifteen were bacterial meningitis cases and one fungal. Three babies had meningitis caused by a Coagulase-negative Staphylococcus. All

except four babies (cases 8, 9, 12, 16) had concomitant blood cultures positive with the same organism. CSF specimens showed very wide variation in white to red blood cell ratios. The incidence of meningitis was three-fold higher among preterm compared with term admissions, 12/7,185 vs. 4/8,885, p=0.02, Chi^2 test). Two infants did not undergo newborn hearing screening (1 deceased, 1 contraindicated). Of 14 who underwent the screening, 9 had clear responses and 5 required referral (1 bilateral, 4 unilateral screen fails).

Definitive follow-up audiology outcomes were unavailable for six babies (2 died in infancy before completion of diagnostic testing; 2 had no formal testing despite meningitis history; 2 failed to attend appointments).

Diagnostic audiology outcome data were available for 10 of the 14 surviving infants: 8 had hearing within normal limits (normal/satisfactory), and 2 have SNHL (1 severe bilateral; 1 moderate mixed bilateral). Both SNHL cases (cases 1 and 3) were infants born extremely preterm who had suffered meningitis in their second postnatal week: one had fungal meningitis caused by *Candida albicans*; one had bacterial meningitis caused by *Staphylococcus epidermidis*. Their antimicrobial treatments included the potentially-ototoxic agents flucytosine, vancomycin, and rifampicin.

Our single-centre series covering a 16-year period showed that the incidence of definite neonatal meningitis among neonatal admissions was very low overall. SNHL caused by neonatal meningitis (or its treatment) was relatively rare, with only two confirmed cases in 16 years in our NICU. However, for cases of proven meningitis, the associated rate of SNHL was not insignificant. A large epidemiological study, for example one linking meningitis cases contained in large infection surveillance databases with hearing outcomes as logged in national audiological databases would provide a more accurate indication of SNHL risk after neonatal meningitis. Such linking, along with related biochemical antimicrobial therapeutic

drug monitoring data, may also help to clarify whether SNHL occurs mainly due to meningitis itself or to its antimicrobial drug treatment in extremely preterm neonates.

Contributorship

PC devised this project. AS, ST and PC collected clinical data, JML, CC, and JF collected audiological data, and CS interrogated the microbiological database. PC and CT reviewed and adjudicated the meningitis cases, and JF provided audiological expertise. PC analysed the data. PC and AS wrote the first manuscript draft and PC wrote the final draft. All authors contributed to manuscript revisions. PC is guarantor.

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Competing interests

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Ethics approval

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CSF, cerebrospinal fluid; WCC, white blood cell count; RCC, red blood cell count; SNHL, sensori-neural hearing loss; N/A, test not available (not done or lost to follow up before determined).
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ABSTRACT

Babies in intensive care are at higher risk for meningitis and sensorineural hearing loss (SNHL). We reviewed the rate of SNHL among definite cases of bacterial/fungal meningitis in our neonatal intensive care unit over a 16-year period (2006-2021). We identified 16 confirmed meningitis cases among 16,070 admissions: 8 of 10 surviving infants with available diagnostic audiology had normal/satisfactory hearing while 2 of 10 had SNHL. Both infants with permanent hearing loss had been born extremely preterm and received potentially-ototoxic antimicrobials. Larger studies are needed to clarify whether SNHL occurs mainly due to meningitis itself or to its antimicrobial drug treatment.

Neonatal meningitis is a well-recognised risk factor for sensorineural hearing loss (SNHL),[1] and indicates automatic referral for early auditory brainstem response testing and other formal audiological testing.[2] There are no recent UK data reporting detailed hearing outcomes of neonates who suffered neonatal meningitis. Our aim was to study the incidence of SNHL in neonates admitted to our tertiary-level neonatal intensive care unit (NICU) with proven meningitis.

We reviewed electronic neonatal records (BadgerNet, Clevermed, UK) and our local microbiology database for the 16-year period 1/1/2006 to 31/12/2021 to identify all neonates diagnosed with unequivocal bacterial or fungal meningitis. We defined proven meningitis cases as those with positive bacterial or fungal growth on culture of cerebrospinal fluid (CSF) obtained from infants with clinical signs of suspected meningitis/sepsis and who had received at least 2 weeks of antibiotic therapy for the episode. We excluded any neonates with meningitis who were never admitted to our NICU, those treated for suspected meningitis despite a negative CSF culture, and cases of viral meningitis. Babies with CSF isolates of a coagulase-negative Staphylococcus plus a concomitant CSF leucocyte count $<20x10^6$/L were considered false positive cases and also excluded.[3] For all confirmed cases we reviewed microbiological isolates, concomitant blood cultures, CSF cell counts, newborn hearing screening results, and later diagnostic audiological testing at 0.5, 1, 2, and 4 kHz pure tone audiometry thresholds. SNHL was diagnosed for infants with hearing loss thresholds >20 decibels.[4]

We had 16,070 neonatal admissions to our NICU during the 16-year study period. Twenty-eight babies had a culture-positive CSF result and of these 16 were confirmed as definite meningitis cases (Table 1). Twelve infants were born preterm and four were born at term. Overall, the definite meningitis rate was 16/16,070 (0.1%), or 1 case per 1000 admissions. Fifteen were bacterial meningitis cases and one fungal. Three babies had

meningitis caused by a Coagulase-negative Staphylococcus. All except four babies had concomitant blood cultures positive with the same organism. CSF specimens showed very wide variation in white to red blood cell ratios (Table 1). The incidence of meningitis was three-fold higher among preterm compared with term admissions, 12/7,185 vs. 4/8,885, p=0.02, Chi^2 test). Two infants did not undergo newborn hearing screening (1 deceased, 1 contraindicated). Of 14 who underwent the screening, 9 had clear responses and 5 required referral (1 bilateral, 4 unilateral screen fails).

Definitive follow-up audiology outcomes were unavailable for six babies (2 died in infancy before completion of diagnostic testing; 2 had no formal testing despite meningitis history; 2 failed to attend appointments).

Diagnostic audiology outcome data were available for 10 of the 14 surviving infants: 8 had hearing within normal limits (normal/satisfactory), and 2 have SNHL (1 severe bilateral; 1 moderate mixed bilateral), a rate of SNHL among surviving neonatal meningitis cases of at least 14% (2/14) (95% confidence limits: 2%, 43%). Both SNHL cases were infants born extremely preterm who had suffered meningitis in their second postnatal week: one had fungal meningitis caused by *Candida albicans*; one had bacterial meningitis caused by *Staphylococcus epidermidis*. Their antimicrobial treatments included the potentially-ototoxic agents flucytosine, vancomycin, and rifampicin.

Our single-centre series covering a 16-year period showed that the incidence of definite meningitis among neonatal admissions was very low overall. SNHL caused by neonatal meningitis (or its treatment) was thus relatively rare, with only two confirmed cases in 16 years in our NICU. However, among cases of proven meningitis, the associated rate of SNHL was not insignificant. A large epidemiological study - for example one linking meningitis cases contained in large infection surveillance databases with hearing outcomes as logged in national audiological databases - would provide a more accurate indication of

SNHL risk after neonatal meningitis. Such linking, along with related biochemical antimicrobial therapeutic drug monitoring data, may also help to clarify whether SNHL occurs mainly due to meningitis itself or to its antimicrobial drug treatment in extremely preterm neonates.

Contributorship

PC devised this project. AS, ST and PC collected clinical data, JML, CC, and JF collected audiological data, and CS interrogated the microbiological database. PC and CT reviewed and adjudicated the meningitis cases, and JF provided audiological expertise. PC analysed the data. PC and AS wrote the first manuscript draft and PC wrote the final draft. All authors contributed to manuscript revisions. PC is guarantor.

Patient and Public Involvement statement

The research question arose as a direct result of a parent's question.

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Competing interests

The authors have no relevant competing interests to declare.

Ethics approval

This study reviewed routinely collected clinical data and did not require formal ethics review.

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Table 1: Summary of baseline characteristics, CSF isolates and microscopy, and hearing outcomes of the 16 neonates with definite meningitis

Birth gestational age, completed weeks	28 (24 to 41; 25 to 38)
Birth weight, grammes	935 (589 to 3630; 740 to 2280)
Postnatal age at diagnosis, days	14 (2 to 89; 8 to 40)
Isolate, n cases:	
Escherichia coli	5
Group B Streptococcus	5
Coagulase-negative Staphylococcus	3*
Pseudomonas aeruginosa	1
Enterobacter cloacae complex	1
Candida albicans	1
CSF cell counts	
WCC, $x10^6$/L	745 (6 to 7420; 78 to 3015)
% polymorphs of total WCC	75% (0 to 95%; 40 to 90%)
RCC, $x10^6$/L	2525 (2 to 21600; 540 to 6520)
CSF ratio WCC:RCC	1:4 (1:550 to 1:$6x10^{-4}$; 1:135 to 1:0.32)
Hearing outcomes†, n	
Sensorineural hearing loss	2
Normal	3
Satisfactory‡	5
N/A	6

Data are median (range; interquartile range).

CSF, cerebrospinal fluid; WCC, white blood cell count; RCC, red blood cell count; N/A, test not available (not done, died, or lost to follow up before determined).

*1 *Staphylococcus haemolyticus*. 1 *Staphylococcus epidermidis*, 1 not further speciated

†Normal hearing ≤20 dB; mild hearing loss 21-40 dB minimum detectable threshold; moderate 41-70 dB; severe loss 71-95 dB; profound loss >95 dB

‡Satisfactory hearing, based on oto-acoustic emissions and visual reinforcement audiometry with sound field testing down to 25 dB (no audiogram), but unable to rule out mild loss (n=3) or based on tone pip auditory brainstem responses/oto-acoustic emissions (no audiogram) (n=2)

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