

Risk factors for hearing loss in neonates

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Abstract

Background An estimated 6 of 1,000 children with live births suffer from permanent hearing loss at birth or the neonatal period. At least 90% of cases occur in developing countries. Hearing loss should be diagnosed as early as possible so that intervention can be done before the age of 6 months.

Objective To determine risk factors for hearing loss in neonates.

Methods We performed a case-control study involving 100 neonates with and without hearing loss who were born at Sanglah Hospital, Denpasar from November 2012 to February 2013. Subjects were consisted of 2 groups, those with hearing loss (case group of 50 subjects) and without hearing loss (control group of 50 subjects). The groups were matched for gender and birth weight. We assessed the following risk factors for hearing loss: severe neonatal asphyxia, hyperbilirubinemia, meningitis, history of aminoglycoside therapy, and mechanical ventilation by Chi-square analysis. The results were presented as odds ratio and its corresponding 95% confidence intervals.

Results Seventy percent of neonates with hearing loss had history of aminoglycoside therapy. Multivariable analysis revealed that aminoglycoside therapy of 14 days or more was a significant risk factor for hearing loss (OR 2.7; 95%CI 1.1 to 6.8; P=0.040). There were no statistically significant associations between hearing loss and severe asphyxia, hyperbilirubinemia, meningitis, or mechanical ventilation.

Conclusion Aminoglycoside therapy for ≥ 14 days was identified as a risk factor for hearing loss in neonates. [Paediatr Indones. 2015;55:328-32].

Keywords: hearing loss, neonates, risk factors

The Indonesian Health Surveys (1993-1996) in 8 provinces on loss of hearing reported a prevalence of 0.4% for deafness and 16.8% for hearing loss (HL). The toddler age group had a deafness prevalence of about 0.4%, higher than the pre-school and school aged groups. Early identification of HL is important, as the ages of 0 to 6 years are a critical period of speech and language development.^{1,2}

Sensorineural HL and deafness occur in 2 to 4% of neonates who receive treatment in neonatal intensive care unit (NICU). This incidence of HL is higher than in normal neonates, but the underlying cause is still controversial.³ Some proposed risk factors for congenital or acquired neonatal HL include family history of permanent sensorineural HL, craniofacial anomalies, intrauterine infections, physical anomalies or other related syndrome, birth weight <1,500 grams, low Apgar scores (0-3 at 5 minutes, or 0-6 at 10 minutes), NICU admission, respiratory distress, mechanical ventilation for 5 days or more, hyperbilirubinemia at levels that require exchange transfusion, bacterial meningitis, and use of ototoxic drugs.⁴⁻¹¹ Given this uncertainty, we aimed to identify risk factors associated with HL in neonates.

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Methods

We performed a case-control study to determine the risk factors for HL in neonates at Sanglah Hospital, Denpasar from November 2012 to February 2013. The case group consisted of neonates admitted to the Neonatology Ward and diagnosed with HL by *Interacoustic*[®] distortion product otoacoustic emissions (DPOAE), while the controls were gender- and birth weight-matched neonates with no HL who were also admitted to the hospital. Exclusion criteria were congenital craniofacial abnormalities, suspected neonatal disorder related to neurofibromatosis, osteopetrosis, Usher syndrome, Hunter syndrome, Friedreich ataxia, Charcot-Marie-Tooth syndrome, family history of congenital deafness, and suspected intrauterine infection such as cytomegalovirus or congenital syphilis. Sample size was calculated based on the rule of thumb that for each independent variable, there should be at least 10 children with outcome of interest (HL).¹²

Outcome of this study was HL confirmed by “refer” result with DPOAE examination, whereas the independent variables were severe neonatal asphyxia, hyperbilirubinemia, meningitis, aminoglycoside therapy, and mechanical ventilation. Birth weight was measured within 1 hour of birth, and subjects were categorized into <1,500 grams, 1,500 to 2,499 grams, and ≥2,500 grams. Severe neonatal asphyxia was defined as an Apgar score of 0 to 3 at 1 minute. Hyperbilirubinemia was defined as total bilirubin ≥20 mg/dL. Neonates were diagnosed with meningitis according to medical services guidelines at Sanglah Hospital. Aminoglycoside therapy was defined as aminoglycosides given to neonates for ≥14 days. Mechanical ventilation was defined as mechanical ventilation given for ≥5 days.

We routinely did DPOAE examinations in subject at the time of hospital discharge. Parents provided informed consent before examination. Neonates with a “refer” result were included in the case group, while those with a “pass” result were included in the control group. Data were collected from medical records.

The associations between potential risk factors and hearing loss were initially analyzed by Chi-square and Fisher’s exact tests. The strength of the associations was expressed as odds ratio (OR)

with corresponding 95% confidence interval (CI). A P value <0.05, corresponding to 95% CI not including 1, was considered statistically significant.. Multivariable logistic regression analysis was further performed. The *SPSS version 16* software was used for statistical analysis. This study was approved by the Research Ethics Committee at Udayana University Medical School and Sanglah Hospital, Denpasar.

Results

During the study period, 124 patients met the eligibility criteria. Two patients were excluded because of microcephaly. Of the remaining 122 subjects, 53 subjects were in the case group and 69 subjects were in the control group. At the final analysis, we had 50 subjects in each group matched for gender and birth weight (**Figure 1**). Baseline characteristics of the study subjects are presented in **Table 1**. The median of age subjects was 10 [interquartile range (IQR) 6 to 20] days. The age range of subjects was 2 to 90 days. Mean birth weight was 2,732 (SD 7.365) grams with a median hospital stay of 9 (IQR 6 to 15) days. The case group had more subjects with severe asphyxia, meningitis, and mechanical ventilation than the control group. However, the control group had more subjects with hyperbilirubinemia. The use of aminoglycoside therapy, which was amikacin, was the most common potential risk factor in the case group

Table 1. Characteristics of subjects

Characteristics	Case group (n=50)	Control group (n=50)
Male gender, n (%)	27 (54)	27 (54)
Median age (IQR), days	11 (5 to 26)	8 (6 to 15)
Median hospital stay (IQR), days	8 (5 to 18)	8 (6 to 12)
Birth weight, n (%)		
≥2,500 grams	31 (62)	31 (62)
1,500 – 2,499 grams	16 (32)	16 (32)
<1,500 grams	3 (6)	3 (6)
Gestational age, n (%)		
Full term	30 (60)	33 (66)
Preterm	20 (40)	17 (34)
Severe asphyxia, n (%)	3 (6)	2 (4)
Hyperbilirubinemia, n (%)	8 (16)	14 (34)
Meningitis, n (%)	5 (1)	1 (2)
Aminoglycoside therapy, n (%)	21 (42)	9 (18)
Mechanical ventilation, n (%)	4 (8)	0 (0.0)

IQR=interquartile range

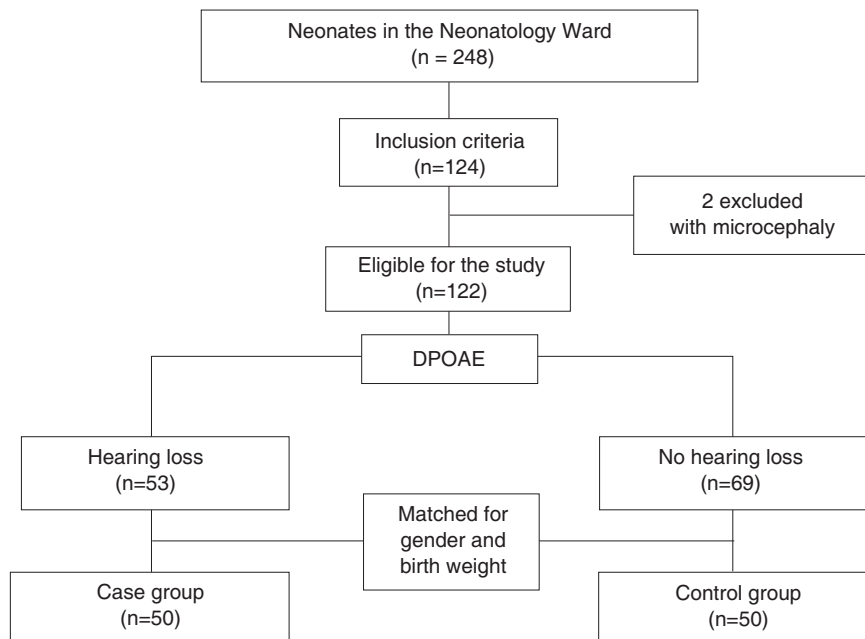


Figure 1. Study outline

Table 2. Potential risk factors for hearing loss in neonates

Risk factors	Crude OR			Adjusted OR		
	OR	95% CI	P	OR	95% CI	P value
Aminoglycoside therapy	3.3	1.3 to 8.2	0.009*	2.7	1.1 to 6.8	0.040
Severe asphyxia	1.5	0.2 to 9.6	1.000**			
Hyperbilirubinemia	0.5	0.2 to 1.3	0.148*	0.6	0.2 to 1.6	0.265
Meningitis	5.4	0.6 to 48.4	0.204**	1.6	0.1 to 18.4	0.696
Mechanical ventilation	NA	NA	0.117**	NA	NA	0.999

* Chi square test; **Fisher's exact test; NA= not available

(70%), and in all study subjects (30%).

Table 2 shows that on univariable analysis, hyperbilirubinemia, meningitis, and mechanical ventilation were not significantly associated with HL, neither did severe asphyxia (P=1.00). Both univariable and multivariable analyses revealed that aminoglycoside therapy was statistically significant as a risk factor of HL (crude OR 3.3; 95%CI 1.3 to 8.2; P=0.009; adjusted OR 2.7; 95%CI 1.1 to 6.8; P=0.040).

Discussion

We found that aminoglycoside therapy, specifically amikacin, given for ≥ 14 days was associated with an almost 3-fold increased risk of HL in neonates.

Aminoglycosides can cause HL by damaging the cochlea or outer hair cells, due to the concentration of the drug in the perilymph fluid. An animal study showed that concentration and duration of amikacin may cause HL by increasing perilymph amikacin levels.¹³ The duration and dose of the amikacin have been suggested to influence toxicity.¹⁴ A previous study however showed that aminoglycoside treatment for >5 days in the NICU was associated with HL in univariable, but not in multivariable analysis.¹⁵ Other studies that investigated ototoxic drugs, without specifying the type of drugs, dose, and duration of exposure, found no association between ototoxic drugs and HL.^{16,17} A diagnosis of HL in our study was made on the same day as the termination of aminoglycoside therapy. A study in animals reported that HL was

usually not detected at the time of termination of ototoxic drugs, but more detectable after 7 days of drug termination.¹⁸

Hyperbilirubinemia that requires exchange transfusions may be a risk factor for HL. In our study, hyperbilirubinemia of ≥ 20 mg/dL was more common in the group without HL, though the difference was not statistically significant. Hyperbilirubinemia reportedly increased the risk of HL by 4 times in neonates in the intensive unit.¹⁶ The pathophysiology of HL due to hyperbilirubinemia is through an auditory neuropathy in the central nervous system. Auditory neuropathies reveal a normal result on DPOAEs.^{19,20}

Mechanical ventilation ≥ 5 days was not a significant risk factor for HL in our study. However, another study showed that mechanical ventilation ≥ 5 days increased the risk of HL in the NICU by approximately 2 fold, whereas asphyxia increased the risk by 3.5 fold.¹⁶ The use of oxygen also increased the risk of HL by about 9 times.²¹ Asphyxia may lead to HL as hypoxia may damage the cochlea.^{22,23} We were not able to assess the association between mechanical ventilation and HL as none of our controls were mechanically ventilated.

Meningitis and bacterial infections were found to increase the risk of hearing loss by about 2.5 fold in neonates.¹⁷ Meningitis can cause hearing loss due to bacterial infections in labyrinth of the inner ear. The labyrinth membrane in the cochlea and vestibule may be replaced with fibrous tissue during bacterial infection.²⁴ In our study, meningitis exposure was not significantly associated with HL, which may be due to a small number of subjects with meningitis.

Our study was mainly limited by the relatively small sample size that a full assessment of certain risk factors, such as mechanical ventilation, was not possible. However, we believe that recall bias was very unlikely as data about proposed risk factors were taken from medical records without any knowledge of the outcome (HL), which was measured at discharge.

In conclusion, aminoglycoside therapy for at least 14 days is associated with a 3-fold increased risk of HL in neonates.

Conflict of interest

None declared.

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