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## REGULAR ARTICLE

# Prevalence and independent risk factors for hearing loss in NICU infants

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**Keywords**

Hearing loss, Hearing screening, NICU population, Risk factors

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**Abstract****Aim:** To determine the prevalence and independent relationship between hearing loss and risk factors in a representative neonatal intensive care unit (NICU) population.**Methods:** Automated auditory brainstem response (AABR) hearing screening has been introduced since 1998 in the Dutch NICUs. After a second AABR failure, diagnostic ABR was used to establish diagnosis of hearing loss. Newborns who died before the age of 3 months were excluded. In the present study only the NICU infants who were born with a gestational age <30 weeks and/or a birth weight <1000 g between October 1, 1998 and January 1, 2002 were included. Risk factors included in the study were familial hearing loss, in utero infections, craniofacial anomalies, birth weight <1500g, hyperbilirubinemia, ototoxic medications, cerebral complications, severe birth asphyxia, assisted ventilation  $\geq 5$  days and syndromes.**Results:** A nationwide cohort of 2186 newborns were included. Mean gestational age was 28.5 weeks (SD 1.6) and mean birth weight was 1039 g (SD 256). Prevalence of uni- or bilateral hearing loss was 3.2% (71/2186; 95% CI 2.6–4.1). Multivariate analysis revealed that the only independent risk factors for hearing loss were severe birth asphyxia (OR 1.7; 95% CI 1.0–2.7) and assisted ventilation  $\geq 5$  days (OR 3.6; 95% CI 2.1–6.0).**Conclusion:** The prevalence of hearing loss in a representative NICU population was 3.2%. Independent risk factors for hearing loss were severe birth asphyxia and assisted ventilation  $\geq 5$  days.**INTRODUCTION**

Hearing loss is apparent in approximately 0.1% of the normal population and is much higher in a defined at-risk population (1–2%; 1–3). Because of the high risk of hearing impairment the National Institutes of Health recommends hearing screening of all infants at a neonatal intensive care unit (NICU) before discharge (4). Prior studies have shown the successful use of automated auditory brainstem response (AABR) hearing screening in the neonatal intensive care setting (5,6).

Most NICU infants fulfil the at-risk criteria of the Joint Committee on Infant Hearing (JCIH). Over the years these risk criteria shift (7,8). There are a few papers studying the association between risk factors and hearing loss in high-risk populations (9–13). These populations differ in characteristics, resulting in different risk estimates for hearing loss of the JCIH risk criteria. Worldwide there are no clear criteria which newborns should enter the NICU. In the Netherlands all infants with a gestational age <30 weeks and/or a birth weight <1000 g are referred to a NICU.

The aim of the present study in a nationwide cohort of Dutch NICU infants was to determine the prevalence and independent relationship between hearing loss and risk factors according to the JCIH 1994 guidelines. In order to obtain independent relations for a representative group of the NICU population, comparable between NICUs, only the newborns born with a gestational age <30 weeks and/or a birth weight <1000 g were analysed.

**SUBJECTS AND METHODS****Subjects**

In the Netherlands neonatal intensive care has been centralised in 11 NICUs. In all NICUs approximately 70% of children are inborn, 30% outborn. Newborns who fulfilled at least one of the criteria according to the JCIH were included in this study (Table 1). Also, if an included child was one of a multiple birth, the other child (or children) although not fulfilling the JCIH criteria was screened as service. The characteristics of the population of infants on a NICU may differ between the different hospitals. In order to obtain independent relations between risk factors and hearing loss, a representative (definite) group of the NICU population, comparable between NICUs in general, were included in the present study; namely, the newborns who were born with a gestational age <30 weeks and/or a birth weight <1000 g.

Data concerning the neonatal hearing screening programme on all NICU infants were centrally registered at the Netherlands Organisation for Applied Research (TNO Quality of Life) in Leiden. The study period started on October 1, 1998 and was limited to those newborns born till January 1, 2002. During the study period the screeners recorded the JCIH criteria on the AABR hearing screening form. Newborns who died before the age of 3 months were excluded, because diagnosis of hearing loss could never be established. All medical ethical committees of the participating NICUs approved the study protocol. All parents were informed prior to the AABR hearing screening with a brochure in their

**Table 1** Risk factors for hearing loss in the neonatal period according to the American Joint Committee on Infant Hearing 1994(7)

Familial history of permanent childhood sensorineural hearing loss
In utero infections, such as cytomegalovirus, herpes, toxoplasmosis or rubella
Craniofacial anomalies, including morphological abnormalities of the pinna, ear canal, nose and throat
Birth weight less than 1500 g
Hyperbilirubinemia at serum levels requiring exchange transfusion
Ototoxic medications, including but not limited to aminoglycosides alone or in combination with loop diuretics
Cerebral complications (bacterial meningitis)
Severe birth asphyxia (APGAR scores <5 at 1 min or <7 at 5 min.)
Assisted ventilation lasting 5 days or longer
Syndromes: stigmata or other findings associated with a syndrome known to include a sensorineural and/or conductive hearing loss

pre-admission packet. Also, parents were informed for the need to return for rescreening after discharge from the hospital in case of a first referral.

### Procedures

The neonatal hearing screening programme in the NICUs is a two-stage hearing screening programme. A first test is performed as late as possible before discharge from the NICU. In failed cases at the first screening with an unexpected prolonged stay in the NICU a 'repeated first test' is performed before discharge. Both the first test and the repeated first test are the first stage of this screening programme. When a child has failed at the first stage, a second test is performed in an outpatient setting with an interval of at least 4 weeks provided that the child has reached the term age. After a failure at the second screening the child is referred for further diagnostic procedures to an audiological centre.

Methods used and quality control have been extensively described in Van Straaten (2003; 14). AABR hearing screening is safe, simple to operate and quick to administer to large populations. It results in an objective 'refer' or 'pass' and can be used by personnel who have no special audiological training (5).

### Monitoring of the project

This study was designed as part of a future universal hearing screening programme consisting of hearing screening in all NICUs as well as hearing screening in the healthy newborn in the Netherlands. Central registration provides the opportunity of integration between both hearing screening systems. Of more importance is the tracking of NICU children frequently moving between centres and local hospitals. The monitoring function embedded a recall function, described in Van Straaten (2003; 14).

### Statistical analyses

Data were registered in a central database and analysed with SPSS version 14.0 (SPSS Inc, Chicago, IL). We performed univariate analyses (Pearson's chi-square) to identify the contribution of each risk factor for hearing loss. The significance of single risk factors was further assessed by multivariate analyses (logistic regression). Multivariate analysis

of this representative NICU population determines independent risk factors for hearing loss, independent of the hospital.

### RESULTS

A nationwide cohort of 2186 newborns who were born with a gestational age <30 weeks and/or a birth weight <1000 g have been included. Mean gestational age was 28.5 weeks (SD 1.6) and mean birth weight was 1039 g (SD 256). AABR hearing screening revealed an overall prevalence of uni- or bilateral hearing loss after diagnostic ABR of 3.2% (71/2186; 95% CI 2.6–4.1; Table S1). Mean gestational age and mean birth weight did not significantly differ between the NICUs. The prevalence of hearing loss differed significantly between the NICUs from 0.7% to 7.0% (Table S1).

In the study population 95% (2068/2086) of the NICU infants had a birth weight <1500 g (5% <30 weeks, but not <1500 g), 37% (815/2086) required assisted ventilation  $\geq 5$  days and 26% (566/2086) had severe birth asphyxia. Furthermore in 8% (171/2086) and 7% (148/2086) of the NICU infants, respectively, cerebral complications and ototoxic medications were recorded as risk factors. Infants with hyperbilirubinemia, craniofacial anomalies, in utero infections, familial hearing loss or syndromal manifestations were almost absent in the study population (Table S2). Hearing loss was determined in NICU infants with familial hearing loss, birth weight <1500 g, ototoxic medications, cerebral complications, severe birth asphyxia or assisted ventilation  $\geq 5$  days. The risk for hearing loss significantly increased in infants with severe birth asphyxia (OR 1.7; 95% CI 1.0–2.7) or assisted ventilation  $\geq 5$  days (OR 3.6; 95% CI 2.1–6.0; Table S2).

Severe birth asphyxia and assisted ventilation  $\geq 5$  days are independent risk factors for hearing loss: There is no significant interaction between severe birth asphyxia and assisted ventilation  $\geq 5$  days as risk factors for hearing loss (Table S3). In infants with neither severe birth asphyxia nor assisted ventilation  $\geq 5$  days the prevalence for hearing loss was 1.3% (95% CI 0.7–2.3). Infants with both severe birth asphyxia and assisted ventilation  $\geq 5$  days revealed a prevalence for hearing loss of 7.8% (95% CI 4.9–12.1; Table S3).

### DISCUSSION

This study revealed independent risk factors for hearing loss in a nationwide cohort of NICU infants who were born with a gestational age <30 weeks and/or a birth weight <1000 g. These high-risk infants will all be treated in one of the 11 NICU in the Netherlands. The described risk factors will therefore be representative for a definite NICU population in general. The overall prevalence of hearing loss in the study population was 3.2% (95% CI 2.6–4.1). However, there was a significant difference in the prevalence of hearing loss between the Dutch NICUs. We expect one of the reason to be different base populations in the different NICUs (different ethnic groups cluster in parts of the Netherlands). But we cannot completely exclude that another reason may be differences in treatment of these high-risk infants.

Compared to the supposed prevalence of hearing loss in the general population (0.1%; 1,2) means that being a definite NICU infant in itself already gives a more than 30 times higher risk. On top of that independent risk factors for hearing loss in this group were severe birth asphyxia, OR 1.7 (95% CI 1.0–2.7) and assisted ventilation  $\geq 5$  days, OR 3.6 (95% CI 2.2–6.0). Ototoxic medications, cerebral complications, hyperbilirubinemia, craniofacial anomalies, in utero infections, familial hearing loss and syndromal manifestations may not be independent risk factors in a definite NICU population: There was no significantly increased risk for hearing loss in infants with ototoxic medications or cerebral complications. Infants with hyperbilirubinemia, craniofacial anomalies, in utero infections, familial hearing loss or syndromal manifestations were almost absent in this cohort.

Compared to other studies describing the association between risk factors and hearing loss in high-risk infants (9–13), the current study investigated a definite NICU population. This influenced the presence of the JCIH 1994 risk factors and their relative importance for hearing loss. In our cohort 95% of the NICU infants had a birth weight  $< 1500$  g (5%  $< 30$  weeks, but not  $< 1500$  g), 26% had severe birth asphyxia and 37% required assisted ventilation for 5 or more days. On the other hand, only in 7% of the NICU infants ototoxic medications were mentioned as a risk factor.

Our findings are in accordance with the study by Suzuki (2004; 12) who found that ABR examinations are especially important in extremely low birth weight infants who have received assisted ventilation. In addition, Suzuki described an increased risk for hearing loss for NICU children receiving five or more different antibiotics. Furthermore, the study by De Capua (2003; 10) stressed the importance of prolonged assisted ventilation, ototoxic medications and severe birth asphyxia as risk factors for hearing loss. In our cohort ototoxic medications did not reveal additional hearing loss. This might be due to careful monitoring of the pharmacotherapeutic levels of these drugs.

The study by Meyer (1999; 11) found that 5% of the high-risk neonates revealed a pathologic AABR hearing screening. Almost 25% of these infants appeared normal during follow-up. This study suggested a change in the risk profile for neonatal hearing loss related to changes in perinatal and neonatal care. Craniofacial malformations, familial hearing disorders and neonatal bacterial infections were significant factors, whereas a very low birth weight and complications of prematurity were not independent risk factors. Our results could not confirm their conclusions. This might be due to the characteristics of the high-risk population.

Also, the retrospective study by Chu (2003; 9) found other independent risk factors for hearing loss. Congenital structural and chromosomal anomalies appeared to be the most significantly associated risk factors for the development of newborn hearing loss. However, only half of the neonates with hearing loss were from the NICU population and had one or more of the JCIH 1994 risk factors. Furthermore, the prevalence of hearing loss in their NICU population was only 1.6% (compared to 3.2% in our study).

Our hearing screening programme in the NICUs started in 1998 using the JCIH 1994 risk factors. Meanwhile the JCIH risk factors had been modified. However, NICU infants with severe birth asphyxia who require NICU admission and those who need assisted ventilation for 5 or more days will adhere to the JCIH 2000 risk factors (requiring admission of 48 h or greater to a NICU).

The current report distinguishes itself from other studies on hearing loss in high-risk populations, because our cohort is a representative nationwide sample with clear inclusion criteria. The overall prevalence of hearing loss was 3.2% (95% CI 2.6–4.1). However, NICU infants with neither severe birth asphyxia nor assisted ventilation  $\geq 5$  days had a prevalence of 1.3% (95% CI 0.7–2.3), whereas those having both had a prevalence of 7.8% (95% CI 4.9–12.1). The effect of familial hearing loss, craniofacial anomalies and syndromal malformations on hearing loss could not be shown in our study, because these conditions were almost absent in our cohort. Furthermore, the frequent use of ototoxic medications is a known risk factor for hearing loss, but may be limited with strict determination of blood levels.

We conclude that severe birth asphyxia and assisted ventilation for 5 or more days are independent risk factors for hearing loss in infants born with a gestational age  $< 30$  weeks and/or a birth weight  $< 1000$  g.

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All authors have seen and approved the final version and have no conflicts of interest in the study.

Dr ETM Hille contributed to the study design, coordinated the data collection, performed and interpreted the data analyses and drafted the manuscript.

Dr HLM van Straaten and Dr PH Verkerk initiated and supervised the design and the execution of the study, and contributed to the interpretation of the data analyses and the drafting of the manuscript.

#### APPENDIX

The members of the Dutch NICU neonatal hearing screening working group are: Irma van Straaten MD (co-ordinator: Isala clinics, Zwolle); Paul Verkerk MD, Elysee Hille PhD (TNO Quality of Life, Leiden); W Baerts MD, Carin Bunkers, Enna Smink (Isala Clinics, Zwolle); Ruurd van Elburg MD (VU University Medical Centre, Amsterdam); Martin de Kleine MD (Máxima Medical Centre, Veldhoven); Joke H Kok MD, Adri Ilsen MD (Academic Medical Centre, Amsterdam); Dianne Visser MD, Katerina Steiner MD (University Medical Centre St Radboud, Nijmegen); Linda S de Vries MD (Wilhelmina Children's Hospital, Utrecht); Nynke Weisglas-Kuperus MD (Erasmus Medical Centre,



Sophia Children's Hospital, Rotterdam); Arwen Sprij MD (Juliana Children's Hospital, Den Haag); Enrico Lopriori MD (Leiden University Medical Centre, Leiden); Jan Brokx MD, Danilo Gavilanes MD (University Hospital Maastricht, Maastricht); Wil Geven MD, Arie Bos MD (University Medical Centre Groningen, Groningen).

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## Supplementary material

The following supplementary material is available for this article:

**Table S1** Number of infants born with a gestational age <30 weeks and/or a birth weight <1000 grams in each NICU, and mean gestational age, mean birth weight and prevalence of hearing loss.

**Table S2** Contribution of risk factors on hearing loss in infants born with a gestational age <30 weeks and/or a birth weight <1000 grams and ORs from univariate and multivariate analyses.

**Table S3** Percentage of hearing loss and ORs for each combination of the independent risk factors assisted ventilation  $\geq 5$  days (AV) and severe birth asphyxia (APGAR in infants born with a gestational age <30 weeks and/or a birth weight <1000 grams

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