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Rate and correlates of deafness in a sample of neonates in a Lebanese university hospital

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ABSTRACT

Background: Neonatal deafness is a silent disability that can lead to severe impairments, particularly in a child's linguistic and cognitive development, especially if diagnosis and treatment are delayed. If deafness is identified before three months of age and therapies are initiated before six months, the newborn may achieve good cognitive and language development.

Objective: This paper aims to determine the prevalence of deafness in high-risk infants and identify factors associated with deafness in a sample of Lebanese neonates.

Methods: This is a prospective study conducted at the University Hospital Center of Notre Dame des Secours (CHUNDS) in Jbeil, Lebanon, between January 2017 and December 2019, enrolling 180 children. For multivariable analysis, a stepwise backward likelihood ratio logistic regression was performed, using the presence or absence of hearing problems as the dependent variable and including all factors with a p-value < 0.2 from the bivariate analysis as independent variables.

Results: The prevalence of hearing problems (in either ear) was 10% [95% CI 0.056-0.144]. The variables included in the multivariable model explained 61.3% of the variance (Nagelkerke R^2 = 0.215). The results of the logistic regression showed that in vitro fertilization (ORa = 5.23) was significantly associated with higher odds of hearing problems, whereas the presence of a materno-fetal infection (ORa = 0.17) was significantly associated with lower odds of hearing problems.

Conclusion: This study sheds light on factors associated with hearing loss/deafness among Lebanese neonates. By identifying two new risk factors for the universal screening of deafness, we conclude that there may be other undiscovered factors at play.

Introduction

Neonatal deafness is a silent disability that can result in severe impairments, mostly, in a child's linguistic and cognitive development especially if the diagnosis and treatment were delayed. In fact, its prevalence is one of the highest among other neonatal pathologies (such as hypothyroidism, cystic fibrosis and phenylketonuria) detected in children in France (3/1000 newborns). Adding to this and according to the WHO, the prevalence of permanent neonatal hearing loss is generally between 0.5 and 1 per 1000 infants, and even higher in low and middle-income countries (1). Also, for newborns with one or more risk factors, the prevalence increases from 1% to 3%(2). Therefore, systematic screening for newborns deafness is a necessity.
The Joint Committee of Infant Hearing (JCIH) defined risk factors in newborns who cause neonatal deafness in 1999 and 2007 (3). Those include the length of stay in the incubator for more than 2 weeks, low birth weight (less than 1500g), prematurity (4), hyperbilirubinemia and phototherapy, Apgar score of 0-4 at 1 minute or 0-6 at 5 minutes of life, craniofacial abnormalities, head trauma, ototoxic drugs: aminosides with or without furosemide(5, 6) respiratory distress, familial consanguinity, congenital malformations, materno-fetal infection (MFI) : TORCH infections (Toxoplasmosis, other STDs such as syphilis, rubella, CMV, herpes, parvovirus B19) and other bacterial infections (2). Maternal risk factors such as in vitro fertilization, multiple pregnancy, intrauterine growth retardation, obstetric complications and premature rupture of amniotic membrane have been also incriminated in increased deafness in children as well. Therefore, identifying deafness through neonatal auditory screening (NHS) is essential for early intervention. Several procedures for audiological screening and evaluation have been described and advocated around the world, in particular acoustic otoemissions (AEAP) and auditory evoked potentials (AABR) (7).
If deafness is identified before the age of three months and therapies are started before the age of six months, the newborn may achieve a good cognitive and language development (8). This study has two objectives: to determine the rate of deafness in high-risk infants and determine factors associated with deafness in a sample of Lebanese neonates.

Methods

Ethics approval and consent to participate

This study protocol was approved by the ethics committee of the Psychiatric Hospital of the Cross (HPC-026-2020). A written informed consent was obtained from the parents.

Study design and sample

This is a prospective study conducted at the University Hospital Center of Notre Dame des Secours (CHUNDS) in Jbeil, Lebanon between January 2017 and December 2019. The study was led using a sample of new born infants from the neonatal intensive care unit (NICU) based on the risk factors of deafness criteria listed by the joint committee of infant hearing in 2014. The selected newborns were all tested for acoustic otomissions before discharge from the NICU. Inclusion criteria with the risk factors related to the newborn included (1) a prolonged stay in the incubator for more than 2 weeks was studied to determine if it increases the risk of ototoxicity, (2) prematurity was divided into the following ranking: low (35-37 SA), Moderate (32-34 SA), Grande (27-31 SA), Extreme (22-26 SA) (4), (3) low birth weight less than 1500 g that may increase the risk of hyperbilirubinemia, (4) infants with very high levels of bilirubin requiring

treatment and phototherapy were only included, (5) a low Apgar score of 0-4 at 1 minute or 0-6 at 5 minutes of life were included. Normally, this score must be between 7 and 10 to predict that the child is in good general condition at birth (9). The 1-minute APGAR score determines how the child tolerates childbirth, while at 5 minutes it reflects the child's condition outside the mother's uterus, (6) any craniofacial malformation may be associated with problems with the anatomy of the ear and therefore was tested in our study, (7) ototoxic drugs: The use of a few drugs that have an ototoxic effect is sometimes essential in neonatology such as antibiotics (aminoglycosides), diuretics, etc (5, 6), (8) respiratory distress causes a lack of oxygen to the neurological tissue, or even to the hearing centre and/or sensitive inner ear. We divided this group into four categories: the ones that needed O2 mask, CPAP, intubation and intubation with chest drain, (9) cardiac problems were added because they may reflect the presence of a syndrome that also includes a malformation of the auditory system, or a lack of oxygenation of the brain, (10) transfusion: Whether it is blood, platelet or PFC, with or without hyperbilirubinemia, (11) parenteral Consanguinity: In addition to many consequences, this factor greatly elevates the incidence of congenital and genetic hearing loss (10), (12) Mateno-Fetal Infection (MFI): TORCH infections (Toxoplasmosis, Other STDs (such as Syphilis), Rubella, CMV, Herpes, Slapped cheek (Parvovirus B19) that typically affect the prenatal fetus, and other bacterial or non-bacterial infections are noted(11), and (13) Familial malformations: A malformation of the auditory, craniofacial or any system of the body can in most cases be hereditary and affects the hearing of the child. Children with a presence of a severe birth defect and children dismissed from the NICU before undergoing a hearing screening test were excluded from this study. Other inclusion criteria related to the mother included: (1) In Vitro fertilization (IVF): No previous studies in the literature on this subject, but in the clinic there has been an increase in the rate of children born after IVF with hearing problems. Which suggests making the statistics on that, (2) Multiparous pregnancy: Multiple pregnancy can affect a fetus by delaying the maturation of several systems, especially the auditory system, (3) a Delayed Antenatal Intrauterine Growth diagnosed by a fetal prenatal ultrasound is included for because it can affect the maturation of the sensitive hearing system, (4) Multiple complications during any period of the pregnancy can have adverse consequences for an individual's hearing. Many of these problems will be analyzed individually afterwards, and (5) Premature rupture of membrane is a source of infection and fetal suffering.

Minimal sample size calculation

According to the Epi info sample size calculations, a sample of 135 newborns was targeted to allow for adequate power for bivariate and multivariable analyses, with a 3% (2) expected frequency of deafness, a 95% confidence limit, and a design effect of 3.

Data collection and measurement

Children in the NICU were examined by the ear, nose and throat (ENT) physician before their discharge, who did a complete ENT examination followed by an acoustic otoemission test. Children who showed hearing impairment in one or both ears were sent to do the auditory evoked potentials (PEA). Data was collected regarding maternal risk factors of deafness such as in vitro fertilization, multiple pregnancy, intrauterine growth retardation, obstetric complications and premature rupture of amniotic membrane.

Statistical analysis

Data entry and analysis were performed using SPSS statistical software, version 23. A p-value less than 0.05 was considered significant. Descriptive statistics were calculated for all study variables. This includes the mean and standard deviation for continuous measures, counts and percentages for categorical variables. The Chi-square test was used for comparison between categorical variables, whereas the Student t-test was used to compare two means. For multivariable analysis, a stepwise backward likelihood ratio logistic regression was performed using the presence/absence of hearing problems as the dependent variable and taking all factors that had a p<0.2 in the bivariate analysis as independent variables; this would decrease confounding factors. A p<0.05 was considered statistically significant.

Results

A total of 180 children was enrolled in this study, among whom 14 (7.8%) had hearing problems in one of the two ears, and 4 children (2.2%) had hearing problems in both ears. The rate of hearing problems (in any of the two ears) was 10% [95% CI 0.056-0.144]. In addition, 43.3% children were females and 53 (30.6%) were conceived via IVF. The mean weight at birth was 1005.11 ± 1167.97 grams. The sociodemographic and other characteristics of the children and their mothers are summarized in Tables 1 and 2 respectively.

Table 1. Characteristics of the children (N=180).

Variable	N (%)
Gender	
Male	(%56.7) 102
Female	(%43.3) 78
Test for the left ear	
Absence of hearing problems	(%95.5) 169
Presence of hearing problems	(%4.5) 8
Test for the right ear	
Absence of hearing problems	(%92.1) 163
Presence of hearing problems	(%7.8) 14
Hyperbilirubinemia + phototherapy (yes)	(%42.7) 76
Carniofacial abnormalities (yes)	(%4.4) 8
Head trauma (yes)	(%2.2) 4
Ototoxic drugs (yes)	(%50.8) 91
Abnormal APGAR 1 min (yes)	(%9.4) 16
Abnormal APGAR 5 min (yes)	(%11.0) 19
Intubation	
No	(%73.9) 133
Yes	(%19.4) 35
CPAP	(%2.2) 4
O2 masque	(%3.9) 7
Int + Drain thoracique	(%0.6) 1
Respiratory distress (yes)	(%42.5) 76
Cardiac problems (yes)	(%32.6) 58
Materno-Fetal infection (yes)	(%34.1) 60
Prematurity	(%37.2) 67
Late preterm	(%26.7) 48
Moderate preterm	(%43.9) 79
Very preterm	(%15.1) 27
Extremely preterm	(%1.7) 3
Term infant	(%13.9) 25
NICU hospitalization >2 weeks	(%44.6) 79
Weight (<2600 g)	(%67.8) 122
Weight (<1500 g)	(%18.9) 34
Transfusion (yes)	(%28.3) 51
Consanguinity (yes)	(%7.3) 13
Family history of malformations (yes)	(%12.3) 22
Hearing problems	
None	(%90.0) 162
Only in right ear	(%2.2) 4
Only in left ear	(%5.6) 10
In both ears	(%2.2) 4
	Mean ± SD
APGAR score at 1 min	1.54 ± 7.12
APGAR score at 5 min	1.37 ± 8.00
Weight at birth (in grams)	1167.97± 1005.11

Table 2. Characteristics of the children's mothers.

Variable	N (%)
In-vitro fertilization (yes)	(%30.6) 53
Delivery type	
Vaginal delivery	(%10.8) 19
Cesarean section	(%89.2) 157
Multiple pregnancies (yes)	(%46.7) 84
Prenatal anomalies (yes)	(%27.0) 48
Infections and antibiotics intake before delivery (yes)	(%21.1) 38
Maternal cardiac problems (yes)	(%18.3) 33
Uterine problems (yes)	(%18.3) 33
Preterm rupture of the membranes (yes)	(%22.2) 40
Complications during pregnancy (yes)	(%15.0) 27
Rupture of the membranes (yes)	(%22.2) 40
Maternofetal infections (yes)	(%34.1) 60
	Mean ± SD
Number of pregnancies	1.40 ± 2.14
Parity	1.00 ± 2.28
Number of abortions	0.92 ± 0.41

Bivariate analysis

The results of the bivariate analysis are summarized in Table 3. A significantly higher percentage of children born with an in-vitro fertilization method (20.8% vs 5.0%; $p < 0.001$), without premature rupture of the membranes (12.9% vs 0%; $p = 0.017$) and without a materno-fetal infection (12.9% vs 3.3%; $p = 0.041$) had hearing problems. No significant difference was found between the presence/absence of hearing problems and severe hyperbilirubinemia requiring

phototherapy and transfusion ($p = 0.064$).

Table 3. Bivariate analysis of factors associated with hearing problems.

Variable	Absence of hearing problems	Presence of hearing problems	p-value
In-vitro fertilization			**0.001>**
No	(%95.0) 114	(%5.0) 6	
Yes	(%79.2) 42	(%20.8) 11	
Premature rupture of the membranes			**0.017**
No	(%87.1) 122	(%12.9) 18	
Yes	(%100.0) 40	(%0) 0	
Severe hyperbilirubinemia requiring phototherapy and transfusion			0.064
No	(%86.3) 88	(%13.7) 14	
Yes	(%94.7) 72	(%5.3) 4	
Materno-Fetal infection			**0.041**
No	(%87.1) 101	(%12.9) 15	
Yes	(%96.7) 58	(%3.3) 2	

Some numbers do not add up to the total sample (N=180) because of missing values.

Multivariable analysis

The variables included in the model were able to explain 61.3% of the variations of the model (Nagelkerke R^2=0.215). The results of the logistic regression, taking the presence vs. absence of hearing problems as the dependent variable, showed that in-vitro fertilization (ORa=5.23) was significantly associated with higher odds of hearing problems, whereas the presence of a materno-fetal infection (ORa=0.17) was significantly associated with lower odds of hearing problems (Table 4). It is noteworthy that severe hyperbilibinemia requiring phototherapy and transfusion (ORa=0.27) was associated with lower odds of hearing problems, but this association was not significant.

Table 4. Multivariable analysis: Logistic regression taking the presence/absence of hearing problems as the dependent variable.

Variable	p-value	ORa	Confidence Interval %95	
In vitro fertilization (yes vs no*)	0.004	5.23	1.694	16.140
Severe hyperbilibinemia requiring phototherapy and transfusion (yes vs no*)	0.054	0.27	0.069	1.026
Materno-fetal infection (yes vs no*)	0.031	0.17	0.036	0.853

*Reference group; ORa=adjusted odds ratio; numbers in bold indicate significant p values.

Discussion

Even though studies have been conducted worldwide in this field, this is the first one in our country studying neonatal deafness in our population and factors associated with it. Indeed, by comparing it with several old studies, our study revealed many interesting results.

In a total of 180 children with one or more risk factors for deafness as identified by the Joint Commitee of Infant Hearing (JCIH) in 2014, our study found 18 children (10%) having had a test of negatively provoked acoustic otoemissions in any of the two ears, or even a neonatal hearing problem. The percentage of hearing loss we had in our study is much higher than the average prevalence of international hearing loss in high-risk infants (2-5%) (12) and higher than the one found in a Polish study of 2986 children at high risk of deafness that showed hearing loss in 128 newborns (4.29%)(13). This very high difference in the percentage is significantly important for Lebanese records. However, these results should be interpreted with caution since this study was conducted in one hospital only; further multicenter studies are needed to investigate the prevalence of deafness in neonates and the reasons behind this high percentage.

Based on the review of the available studies, JCIH has compiled a list of all risk factors that put newborns in a significant risk of hearing loss (14). Despite the fact that deafness criteria identified by the JCIH seem understandable and logical, several investigations have reported the presence of other variables affecting hearing in newborns (15). Actually, in our study, we collected the data based on a few risk factors identified by JCIH and other factors that we believe to be possibly significant. In-vitro fertilization was significantly associated with higher deafness in the neonates. In our study, 79.2% of children with absent acoustic otoemissions were born after IVF. We hypothesize that this can be correlated with the effects of IVF in the laboratory on the genetic map of the embryo, or even its effect on the normal development of the fetus later in utero or during the life of the infant. No studies have evaluated the relationship between IVF and hearing loss in newborns. This result is important to the health registry in Lebanon, and to the neonatal deafness screening standards in the world. Because IVF and multiple pregnancy variables are not included in the JCIH's published risk factors register, the results of this study provide more factors that can be used in the selection of newborns at high risk of being deaf.

The results of the bivariate, but not the multivariable analysis, showed that severe hyperbilibinemia requiring phototherapy and transfusion was associated with less deafness in newborns. Hyperbilirubinemia in newborns leads to a central deficit and a pathology of the nervous system secondary to kernicterus, resulting in hearing loss as confirmed by previous findings (16). Although, these results are inconsistent with international standards, especially the JCIH register (2), they may be explained by the high frequency of hyperbilirubinemia found in our children.

The type of delivery, whether vaginal or caesarean section, was not significantly associated with deafness in our study, in agreement with previous results (17, 18). Controversially, one study suggests that delivery by normal method or emergency caesarean section were associated with higher odds of having sensorineural hearing loss (19); those authors speculated that "the incidence of fetal distress and the associated risks are less likely to be pronounced in pregnancies already considered as high risk" (19). More studies are needed to decipher the causes behind this association.

Early rupture of the membranes and antenatal infections, especially TORCH, are considered a cause of infant deafness. These infections are part of JCIH's list of risk factors (20). In our study, there was no relationship between antenatal infections and newborn hearing loss problems and this may be because all our cases were treated early with antibiotics. The rapid access to medical treatment and early diagnosis by lab workouts and cultures made the treatment possible early and decreased the complications.

Clinical implications

Our results have important clinical implications for parents and healthcare providers. Neonates conceived through IVF should be closely monitored for hearing problems. It is important for parents to be aware of this potential risk and discuss any concerns with their healthcare provider. Additionally, healthcare providers should act appropriately to ensure early detection and intervention if necessary.

On another note, the early detection of maternal infections and accurate intervention can help mitigate the severity of hearing loss in neonates. Awareness among healthcare providers can help guide appropriate screening, diagnosis and management strategies, highlighting the importance of close monitoring and appropriate treatments.

Limitations

This study has some limitations. Although the Otoacoustic emissions (OAE) and auditory brainstem responses (ABR) are required to be done according to the guidelines, however, these tests do not exist at the hospital and therefore, were not done. A selection bias is possible since the sample was taken from a single hospital. This pilot study targeted newborns at high risk of developing neonatal hearing loss only. Despite the long period, the sample is rather small and may not be representative of the Lebanese neonatal population. A residual confounding bias is also possible since not all factors associated with deafness were taken into consideration in this study. However, this study is the first to be conducted in Lebanon and to take a large number of factors associated with deafness in children.

Conclusion

This study was able to shed light on factors associated with hearing loss/deafness among Lebanese neonates. Since we were able to add two new risk factors to the universal list of deafness screening, it is concluded that many risk factors are not yet revealed.

Ethics approval and consent to participate

This study protocol was approved by the ethics committee of the Psychiatric Hospital of the Cross (HPC-026-2020). A written informed consent was obtained from the parents.

Consent for publication

Not applicable.

Availability of data and materials

There is no public access to all data generated or analyzed during this study to preserve the privacy of the identities of the individuals. The dataset that supports the conclusions is available to the corresponding author upon request.

Competing interests

The authors disclose no conflicts of interest.

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None.

Authors' contributions

HM conceived and designed the study. MI and HM performed the data collection and entry. HM and MS wrote the manuscript. SH involved to data interpretation and statistical analysis, edited the paper and revised the paper for intellectual content. All authors critically revised the manuscript for intellectual content. All authors read and approved the final manuscript.

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