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A review of the audiological risk factors in Neonatal Intensive Care Unit's population in Albania

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Abstract

Objective: This study aims to evaluate the impact of audiological risk factors on the neonatal population in Neonatal Intensive Care Units (NICU) in Albania over time.

Methodology: To compare the data, neonates born in the two maternity hospitals in Tirana during the period 2018-2019 were studied, specifically those in NICUs. Since true NICUs exist only in Tirana's maternity hospitals, this study essentially provides an overview of the situation across Albania. Data collected from a similar study in 2006-2007 were used for comparison. Thus, the study periods in both cases covered two years, with a time gap of approximately 10 years.

An extensive database of 22,814 recordings was filtered, and 985 cases with complete data were selected. All of this group had one or more risk factors. The risk factor analysis was based on the completed data for this group.

Results: The dominant risk factors in the study population were NICU stay, the use of ototoxic medication, low birth weight, prematurity, hyperbilirubinemia and mechanical ventilation.

Conclusions: The weight of risk factors in the Albanian NICU population remains significant, and many of the subjects who fail the hearing screening tests or with hearing loss have risk factors. Careful monitoring of pregnancy and the accurate selection of antibiotics for perinatal infections are two elements that can and should remain the focus of attention to reduce hearing loss in newborns. The risk of later-onset hearing loss in subjects with multiple risk factors necessitates close follow-up for this category.

Keywords: Universal Neonatal Hearing Screening; Audiological Risk Factors; NICU; Low Birth; Aminoglycosides

1. Introduction

Neonatal hearing screening has become a standard of care for newborns through universal neonatal hearing screening (UNHS) programs in many countries [1,2]. Unfortunately, in some countries like Albania, this program is not yet universally available to all neonates [3]. As a result, delays in diagnosing hearing loss persist, leading to well-documented consequences for language development, academic performance, and psychosocial well-being of the children [4,5,6].

Another significant challenge with early-stage or inconsistent programs is the high rate of loss to follow-up (LTFU) cases [7,8]. As a result, many well babies and Neonatal Intensive Care Unit (NICU) subjects miss follow-up testing and present

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at a later age with varying degrees of hearing loss and language delays. The effectiveness of rehabilitation in these cases often depends on the timing of intervention and the severity of hearing loss, which can impact overall outcomes [9].

The Committee on Infant Hearing (1994, 2007, 2019 and 2000) [10,11,12] has identified a list of audiological risk factors that, if present, can increase the likelihood of permanent hearing loss in children by up to tenfold. The estimated risk of hearing loss in neonates with these factors is significantly higher compared to healthy infants [13]. Generally, neonates who spend time in neonatal intensive care units (NICU) are more likely to have one or more of these risk factors, making them more susceptible to permanent hearing loss than healthy newborns. Key risk factors include the duration of NICU stay, prematurity, low birth weight, neonatal hypoxia, hyperbilirubinemia, and others [12].

Various studies highlight the prevalence of audiologic risk factors, which vary from one country to another [14,15] . A study by Kozmidou et al. (2022) found that the most common risk factors in the NICU at their hospital, were the use of ototoxic drugs, low Apgar scores, and prematurity. Ototoxicity as a prevalent risk factor is also discussed in other studies [16], which aim to improve the protocol for treating neonatal infections in the NICU.

A previous study conducted in Albania (2003-2004) [17] found that the most prevalent risk factor in the NICU population was prematurity, followed by respiratory distress (including asphyxia and hypoxia). However, the study was conducted on a small number of neonates and the data collected was sometimes scarce.

The identification of neonates with risk factors is an important element, as it draws attention to the need for continued monitoring of these cases, or to consider approaches and policies that reduce the rate of LTFU. It is noteworthy that the risk of hearing loss in neonates who do not attend follow-up tests is high.

On the other hand, monitoring audiological risk factors in the NICU is crucial, as it evaluates the trends of these factors and can raise alarms for issues related to pregnancy care, antibiotic use, or TORCH infections. If these factors are addressed correctly and in a timely manner, they reduce the prevalence of risk factors, thus minimizing their impact on the normal development of the auditory system of the newborns.

The aim of this recent study is to monitor the prevalence of risk factors in NICU settings in Albania and analyze the trends of changes over a 10-year period.

2. Material and methods

This is a retrospective study based on data collected from the neonatal hearing screening program conducted between 2018 and mid-2020 in four maternity hospitals (EUSCREEN study): two located in Tirana and two in other cities. The data taken for further analysis belonged to infants born in 2018 and 2019 only.

The implementation of newborn hearing screening (NHS) in Albania was not classified as a clinical trial by the Albanian ethics committee, nor was it considered a novel procedure. As a result, ethical committee approval was not required for its implementation. However, the EUSCREEN study received formal approval from the University of Medicine in Tirana and the Albanian Ministry of Health and Social Protection. In addition, informed consent was obtained from parents prior to screening their infants.

For this analysis, data from maternity hospitals outside Tirana, as well as from well babies, were excluded. Notably, Tirana maternity hospitals are equipped with advanced NICU services, and neonates with risk factors are typically treated there.

Additionally, normal newborns who spent up to 36 hours in the NICU without receiving any treatment (e.g., those admitted to the NICU due to maternal medical conditions) or well babies with a family history of hearing loss who were referred directly for audiological evaluation were also excluded. Neonates discharged previously and then returned later to NICU were also excluded.

The screening protocols for NICU babies included two automated auditory brainstem response (aABR) tests conducted at two-week intervals from each other. The devices used for screening were Interacoustics Titan with ABRIS module built in.

After the selection of the data, only 985 subjects from a database of 22,814 subjects, were accepted for further analyses.

The information regarding the risk factors was collected by trained midwives who conducted the screening tests and also from medical files of the subjects. The parents were asked about any family history of hearing loss and this information was also filed. The neonates were registered in a database with a numerical code therefore there is no possibility to identify a subject along the study. Independently, parental consent for hearing screening and data collection were also requested.

The risk factors taken into analysis were; birth weight, prematurity (pregnancy duration), length of stay in NICU, mechanical ventilation, use of aminoglycosides, family history of hearing loss, APGAR score 1st, 5fth and 10th minute, meningitis, hyperbilirubinemia, chronic hypoxia and aABR test results.

The information was coded in Statistical Package for Social Sciences (SPSS) Statistics version 26 (IBM Corp., Armonk, NY, USA) software and analyzed at the significance level of 0.05. For evaluation of the risk factors were used frequency distribution for descriptive statistics and the Chi-square test.

3. Results

Only 985 subjects met the study's criteria from an extensive database. The majority were male, 561 subjects (51.9%), while the remaining subjects were female.

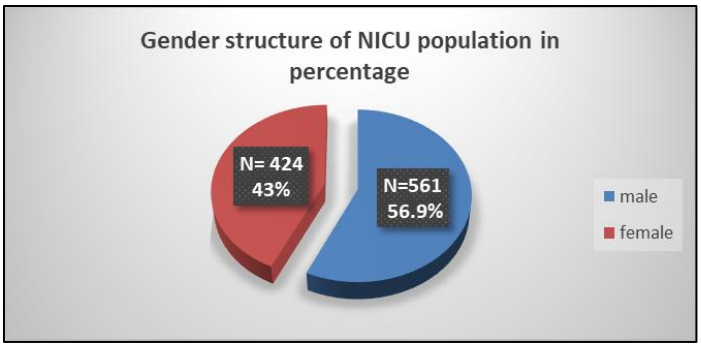

Figure 1 Gender distribution of the population in study

The following table presents the risk factors considered in the study, along with the corresponding number of subjects in both absolute values and percentages.

Table 1 Number of NICU subjects who presented each of the risk factors studied, both in absolute number and percentage

Risk factor	Number of subjects	Percentage total
APGAR 1st min (<3)	33	3.4
Premature	607	61.6
Low birth weight (<2500 gr)	608	61.7
Family history for hearing loss	12	1.2
Meningitis	1	0.1
Hyperbilirubinemia	440	44.7
Intrauterine infections	4	0.4
Exsanguinotransfusion	86	8.7
Use of ototoxic medications	679	68.9
Chronic hypoxia	4	0.4
Mechanical ventilation	145	14.7
Day NICU > 5 days	791	80

One of the most prominent risk factors identified in the study was low birth weight, which was often associated with prematurity. A birth weight below 1250 grams has long been associated with an increased risk of hearing loss [10,11,12]. Therefore, within the group of low-birth-weight neonates, we specifically identified those born weighing ≤1250 grams. Out of the 608 neonates with low birth weight (defined as under 2500 grams), only 63 had a birth weight of ≤1250 grams. Meanwhile, 608 neonates or 61.7% of the total number are born underweight.

The use of ototoxic medications is prevalent among a significant percentage of newborns in NICU settings. The most common ototoxic drugs used, were amikacin, gentamycin and furosemide.

According to our data, some infants received not just one but a combination of furosemide and an aminoglycoside. In some cases, the duration of aminoglycoside therapy was prolonged. Regarding the latter, the data is scarce because the duration of therapy was not a mandatory parameter to be recorded. However, in cases where the data was available, the average duration of the therapy with aminoglycosides was 6.3 days. In some instances, the use of gentamicin was followed by amikacin. In total, 679 neonates representing 68.9% of all subjects received at least one ototoxic medication during their stay in the NICU.

Again, data on the exact levels of serum bilirubin or the use of phototherapy is limited, although 44.7% of NICU patients in the study population had high bilirubin levels. The use of phototherapy depends on serum bilirubin levels, particularly if they exceed five times the birth weight. However, the bilirubin levels associated with an increased risk of hearing loss vary between different studies [18], as such, the study did not establish a cutoff value when evaluating this factor.

Out of 145 (14.7%) subjects on mechanical ventilation, 108 were on mechanical ventilation for five or more days. Interestingly, only one case of meningitis was reported. Regarding intrauterine infections, two mothers had syphilis, and two others had CMV infections. The first two neonates passed the screening test, but data is missing for the infants whose mothers had CMV infections. Independently, these cases have to be followed and monitored after discharge from the maternity hospitals.

A NICU stay of five or more days is also considered a risk factor for hearing loss in neonates. In this study, the average NICU stay was 27 days. Twelve neonates had syndromes or craniofacial dysplasia that could increase the risk of hearing loss, such as cleft palate and Down syndrome. Of these, seven failed the screening tests and were referred for further evaluation and diagnosis.

The graph below summarizes the presence of 1, 2, 3, or more risk factors in the study subjects who failed the 1st aABR test.

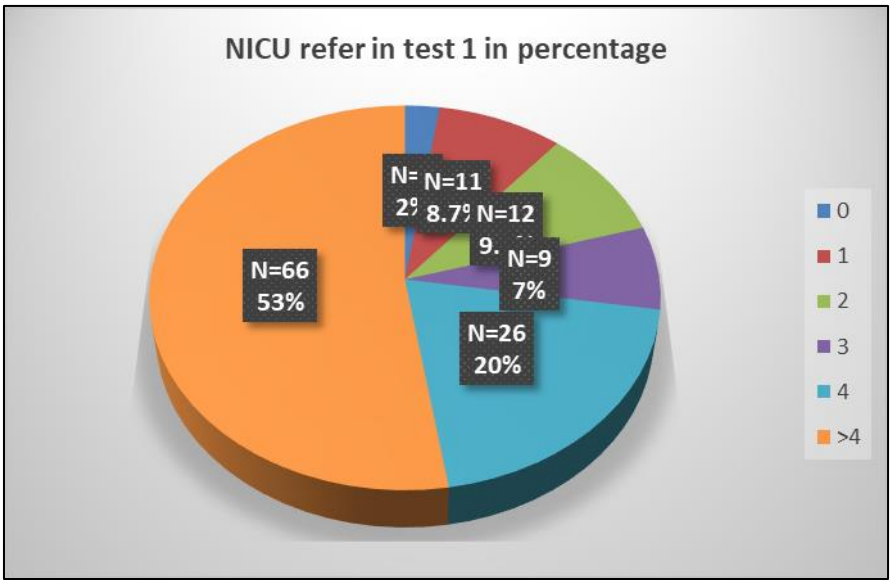

Figure 2 The number of risk factors present in the NICU subjects who failed the first screening test in percentage

The majority of subjects 66 neonates (53%) presented with more than four risk factors. Eleven babies (8.7%) had only one risk factor, while just three subjects (2%) had no risk factors at all. It is clear that most NICU subjects presented with multiple audiologic risk factors.

A linear regression analysis was conducted to determine whether there is a significant statistical correlation between the main risk factors and the failure results of the first aABR test. This analysis identified exsanguinotransfusion as a statistically significant factor influencing the negative outcome of the screening test. The table 2 below summarizes the results of the statistical tests.

Table 2 Linear regression test results. P value < 0.05 is considered statistically significant

Variables	Standardized coefficient Beta	t value	P value
Gender	-0.006	-0.160	0.888
Status at birth	-0.010	-0.264	0.792
Ototoxic medications	-0.049	-1.337	0.182
APGAR 1st min	-0.043	-1.179	0.239
Day NICU	0.013	0.354	0.723
Birth weight	-0.003	-0.094	0.925
Ex-sanguino transfusion	0.150	3.254	0.001

This was also cross-checked with non-parametric tests, leading to the same conclusion. It is understandable that ex-sanguine transfusion indicates extremely high bilirubin levels.

4. Discussion

Hearing loss is the most common congenital condition, with an incidence of 1–3 per 1,000 well babies. This figure is ten times higher in NICU neonates [19,20]. The increased incidence of hearing loss in this population is associated with various factors, some related to pregnancy and others that come into effect after birth.

This is now a well-established fact, as it is the theoretical possibility to reduce the incidence of neonatal hearing loss by controlling some of these factors.

The audiologic risk factors are listed in various statements, with minor differences between documents [10,11,12]. These risk factors may vary between populations and likely evolve over time. The aim of this study was to analyze these variations. This study focused on the NICU population in two maternity hospitals over two consecutive years. It analyzed factors such as prematurity<36 weeks of gestation age), low and very low birth weight (<1500 g), mechanical ventilation, APGAR scores, bilirubin levels, and the need for exchange transfusion, use of ototoxic medications, TORCH infections, and family history of hearing loss. The gender distribution was already equal between the two.

The study found that a significant number of neonates had more than four risk factors, with NICU admission being the most prevalent independent risk factor, present in 80% of cases. This was followed by the use of aminoglycosides, prematurity, and low birth weight. Some neonates received both aminoglycosides and Lasix (a diuretic), both of which are well-known ototoxic drugs.

Approximately 61% of NICU subjects were premature and had a low birth weight, with around 10% of this group classified as having very low birth weight (<1500g). It is expected that these neonates spend a considerable amount of time in the NICU, often requiring antibiotics, mechanical ventilation, and other interventions, which in turn increases the risk factors affecting their auditory system.

Our study found that audiologic risk factors are still prevalent in NICUs in Albania, although their distribution has slightly changed. The 2006–2007 study, despite focusing only on "fail" cases and using a smaller sample, identified largely the same dominant audiologic risk factors. However, the impact of aminoglycoside use appears to have slightly increased in more recent data. The remaining factors have remained mostly unchanged. What has significantly changed compared to the previous study is the increased percentage of the population presenting with multiple risk factors.

The increase in risk factors in this specific population may be associated with a higher maternal age at first delivery, demographic and social changes in the country, as well as the continued improper use of antibiotics and the rising resistance of several bacterial strains. Each of these possible influencing factors has to be further investigated.

Numerous studies in the scientific literature [21, 22] suggest that the presence of multiple risk factors is associated with an increased likelihood of developing hearing loss, even later in life. These findings, combined with the high percentage of neonates presenting with multiple risk factors in our study, highlight the importance of continued monitoring of at-risk infants even after discharge from the maternity hospital. This approach is crucial to ensure the timely identification of late-onset hearing loss. Until a comprehensive national hearing screening program is implemented, a well-maintained high-risk registry could serve as a valuable interim strategy.

Finally, only a few cases of intrauterine infections were observed in the study population two babies were born to mothers with syphilis, and two others were born to mothers with CMV. The first two passed the screening tests, while the other two failed and were referred for audiological assessment. It appears that neonatal infection is not a dominant risk factor in the Albanian population, but when present can influence the hearing status of the newborns.

Several studies have linked late-onset hearing loss to various risk factors such as CMV infection [23,24], mechanical ventilation and NICU stay [25] . Dumanch et al. [26] highlight craniofacial anomalies and CMV infection as factors that increase the risk of hearing loss later in life. Van Noort-van der Spek [27] suggests that a normal screening test at birth does not exclude hearing loss at two years of age, particularly in preterm infants. Other studies [28,29] have reached similar conclusions.

A limitation of the study is the lack of final audiologic results for the subjects who failed the screening test, or the absence of audiologic test results for all subjects at the age of two. This gap hinders the ability to establish a stronger link between hearing status in childhood and the audiologic risk factors present at birth.

5. Conclusion

The recent study on audiologic risk factors in the Albanian population aimed to identify and compare the most prevalent risk factors over time. It was conducted both on subjects who failed the screening tests, as well as on all NICU subjects due to their increased risk of later-onset hearing loss. The most prevalent risk factor was the length of NICU stay, followed by prematurity, low birth weight, and the use of ototoxic medications. The high percentage of subjects with one or more risk factors highlights the need for a structured follow-up regimen for these neonates to identify any later-established hearing loss in a timely manner.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest to be disclosed.

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