

(RESEARCH ARTICLE)



## The Relationship between Congenital Hearing Loss Risk Factors and Outcomes of Otoacoustic Emission Screening Test in Neonates at Dr. Zainoel Abidin Hospital (RSUDZA) Banda Aceh

Srifia Wardianti <sup>1,\*</sup>, Dina Alia <sup>1</sup>, Lily Setiani <sup>1</sup>, Darnifayanti <sup>2</sup>, Azwar Ridwan <sup>1</sup>, Fadhlia <sup>1</sup> and Rachmad Suhanda <sup>3</sup>

<sup>1</sup> Department of Otorhinolaryngology-Head and Neck Surgery, Faculty of Medicine, Universitas Syiah Kuala/Dr. Zainoel Abidin Hospital, Banda Aceh, Indonesia.

<sup>2</sup> Department of Pediatric, Faculty of Medicine, Universitas Syiah Kuala/Dr. Zainoel Abidin Hospital, Banda Aceh, Indonesia.

<sup>3</sup> Department of Public Health and Community Medicine, Faculty of Medicine, Universitas Syiah Kuala/Dr. Zainoel Abidin Hospital, Banda Aceh, Indonesia.

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### Abstract

**Background:** Congenital hearing loss is deafness that occurs before childbirth. Infant hearing impairment can affect speech, language, cognitive, social, and emotional problems. Otoacoustic Emission (OAE) screening test was used for early detection of hearing function.

**Objective:** To determine the relationship between congenital hearing loss risk factors and outcomes of Otoacoustic Emission screening test in neonates at RSUDZA Banda Aceh.

**Methods:** Case control study in Perinatology and Neonatology Intensive Care Unit RSUDZA on April-Jun 2022. Study sample carried out on 80 respondents consist of 40 case group (pass) and 40 control group (refer). The risk factors which were researched including Low Birth Weight (LBW), premature, hyperbilirubinemia, low APGAR score, craniofacial anomalies, staying in NICU more than 5 days, and family history of congenital deafness. Each group was analyzed using Chi-Square test or Fisher's exact test and the Ods ratio was calculated.

**Result:** There were four risk factors that had a significant relationship ( $p < 0.05$ ), such as Low Birth Weight (OR=0.294), hyperbilirubinemia (OR=0.103), low APGAR score (OR=0.107), and craniofacial anomalies ( $p=0.026$ ). LBW is the most significant risk factor.

**Conclusion:** Low birth weight, hyperbilirubinemia, low APGAR scores, and craniofacial anomalies are risk factors for referral results on OAE screening test in neonates.

**Keywords:** Congenital hearing loss; Otoacoustic emission; Risk factor of congenital hearing loss; Early detection

### 1. Introduction

The function of ear as a hearing organ is often not paid attention to a new baby born because generally what parents pay attention is physical perfection<sup>1</sup>. Hearing loss ignored frequently because parents are not immediately aware that their child is suffering from a disorder, sometimes it considered as an autistic or hyperactive child because an uncontrolled attitude<sup>2</sup>. Parents often start looking for solutions while their children could not speak compared to children in their age<sup>3</sup>. Congenital hearing loss is a deafness that occurs before childbirth caused by genetic or non-

\* Corresponding author: Srifia Wardianti

genetic abnormalities<sup>4</sup>. Hearing function is closely related to speech and language processes. It will affect speech, language, cognitive, social, emotional and academic abilities, if it is not recognized immediately and gets appropriate intervention<sup>1,5</sup>. Newborn hearing screening is needed as a program to reduce the number of congenital deafness in children<sup>3</sup>. The target of this screening program is diagnosis at the age of 3 months and intervention given before the age of 6 months<sup>6</sup>. Brain development in the golden period requires optimal nutrition and stimulation to determine the child's life<sup>7,8</sup>. Early recognition of babies with hearing loss in the golden period range will optimize language, cognitive, motoric, social, and emotional development<sup>9</sup>. Gestational age from 25 weeks to 6 months is a critical period for the development of the neurosensory part of the hearing and speech systems<sup>10</sup>. Hearing loss could be reduced and detected, if early intervention is conducted<sup>11</sup>. World Health Organization (WHO) states that the number of people suffering hearing loss have been increased quite significantly in 2010. There were 7.5 million cases of hearing loss in children under 5 years. The incidence of newborn hearing loss in the United States ranges from 1 to 3 of every 1.000 live births. There were 374 out of 552 patients had referral Otoacoustic Emission Examination (OAE) results and mostly 12 to 36 month age group (237 patients) were found at RSU dr. Soetomo Surabaya in 2018<sup>12,13</sup>. Data from ORL-HNS polyclinic at RSUD dr. Zainoel Abidin Banda Aceh from 2018 to 2021, there were 203 children with hearing impairments, while the distribution according to age over 36 months was 99 children, 12-18 months (15 children), and 6-12 months (6 children). A study of risk factors in 203 children found congenital abnormalities in 23 children (11.33%) and 12 children (5.9%) with a close family history of congenital hearing loss. This data explained that children with deafness were on average over 3 years whose golden age of development has already passed.

The Joint Committee on Infant Hearing (JCIH) published a guideline in 1994. This program was also recommended by the American Academy of Pediatrics (AAP) through the Centers for Disease Control and Prevention which has launched the Early Hearing Detection and Intervention (EHDI) program<sup>14,15</sup>. Otoacoustic Emission (OAE) is one of the hearing function tests for hearing screening in neonates with the sensitivity level of 85-100% and the specificity of 91-95%<sup>15</sup>. JCIH mentioned several classifications of risk factors associated with hearing loss which reported in 2007 such as; prenatal, perinatal, and postnatal risk factors include the use of ototoxic drugs, prematurity, low birth weight, low Appearance, Pulse, Grimace, Activity, Respiration (APGAR) scores, hyperbilirubinemia, craniofacial abnormalities, and prolonged duration of mechanical ventilation<sup>14,16,17</sup>. Data obtained from the Perinatology and Neonatal Intensive Care Unit (NICU) registration book for the period October to December 2021 recorded 308 children receiving treatment, 109 children in the NICU room (35.4%), and 199 children (64.6%) in the Perinatology room.

Based on the explanation and data above, the researchers wanted to assess the relationship between risk factors for congenital hearing loss and the results of OAE screening examinations in neonates at RSUDZA Banda Aceh. Furthermore, we can expand collaboration with the Pediatric Health Department in making the hearing screening program recommended by the AAP so that intervention can be conducted before the age of 6 months.

## 2. Methods and materials

### 2.1. Study Design and Research Location

This research is an analytical observational study with a case control design to determine the relationship between risk factors for congenital hearing loss and the results of the first OAE screening examination in neonates (babies less than 1 month old) in the Perinatology and NICU rooms at RSUDZA Banda Aceh. The research was conducted from October 2021 to June 2022 after being approved by the RSUDZA Ethics Committee.

### 2.2. Population Research Study

The study populations were all neonates from April to June 2022 in the Perinatology and NICU rooms at RSUDZA. The samples for this study were the entire population that fulfill the inclusion and exclusion criteria. Inclusion criteria for the study included;

- Neonates with a gestational age of  $\geq 32$  weeks, and a stable hemodynamic condition,
- The subject's parents were willing to be interviewed and agreed to conduct an oae examination on their child by signing an informed consent,
- Neonates with examination results were bilateral oae.

Meanwhile, research exclusion criteria included;

- Neonates with microtia abnormalities,
- External acoustic canal atresia,
- Neonates with oae examination results of "no seal and noise",
- Neonates with unilateral oae examination results.

### 2.3. Sample Research Study

The subjects in the Perinatology population were 111 neonates and 70 neonates in NICU so that the total population for this study were 181 subjects. In this study, the sample proportion of perinatology subjects were 25 neonates for the case group (refer), and 25 neonates for the control group (pass). Meanwhile, the sample proportion of NICU subjects were 15 neonates for the case group (refer), and 15 neonates for the control group (pass). Therefore, the number of samples in the case group were 40, and control group were 40.

### 2.4. Sampling Method

The sampling technique used was proportional random sampling, a method of taking samples by proportioning members of the population, which obtained a representative sample according to the proportions.

### 2.5. Data Collection Tools and Research Procedures

The instruments used in this research including; Patient medical records, research status, research inform consent form, GSI Corti brand OAE and accessories, head lamp, stationery and laptop. Every neonate aged  $\geq 32$  gestation weeks who was more than 24 hours old defined as the target population. The neonate's parents were explained about the examination procedure, and researcher conducted a guided interview about risk factors for a family history of congenital deafness. The results of the OAE examination were interpreted by the community ORL-HNS specialist. If the results of the OAE examination showed "Pass" meaning "passed" then they are used as a control group. If the results of the OAE examination showed "Refer" meaning "did not pass" then they are used as a case group. The samples were determined by proportional random sampling technique to obtain the proportion number of samples both Perinatology room and NICU.

### 2.6. Data Analysis

The data was presented in the form of tables and graphs, and analyzed using Statistical Product and Service Solutions (SPSS) software. Univariate analysis was used to describe the characteristics of each research variable. Meanwhile, Chi Square test was used for bivariate analysis. Fisher's exact test was used if the Chi Square requirements were not fulfill in finding the relationship between 2 variables.

## 3. Results

### 3.1. Characteristics of the research sample

Research data collection was conducted from April to June 2022, and 80 research samples were obtained consisting of 40 case group samples (refer), and 40 control group samples (pass) who fulfill the research criteria. The characteristics of the research sample are presented in table 1 below:

**Table 1** Characteristics of the Research Sample Based on Gender and Parent's Occupation

Characteristic	Otoacoustic Emission		P-value
	Case (Refer) (n = 40)	Control (Pass) (n = 40)	
Gender, n (%)			0,370
Male	17 (42,5)	21 (52,5)	
Female	23 (57,5)	19 (47,5)	
Body Length (cm), Median (min – max)	48,5 (35 – 54)	48 (43 – 52)	0,480
Head Circumference (cm), Median (min –max)	33,5 (25 – 48)	34 (30 – 37)	0,472
Gestasional Age (Weeks), Median (min – max)	38 (32 – 42)	38 (35 – 41)	0,244
Father's Job, n (%)			0,108
Civil Servants	4 (10)	9 (22,5)	
Private	25 (62,5)	24 (60)	
Soldier/Police	3 (7,5)	2 (5)	

Farmer	3 (7,5)	2 (5)	
Laborer	3 (7,5)	2 (5)	
BUMN Employee	1 (5)	1 (2,5)	
Mother's Job, n (%)			0,244
Civil Servants	5 (12,5)	11 (27,5)	
Private	6 (15)	3 (7,5)	
Farmer	0	1 (2,5)	
Housewife	29 (72,5)	25 (62,5)	

Based on Table 1, the gender of the case group (refer) is dominated by female (57.5%) and the control group (pass) is dominated by male (42.5%). The total sample had an average body length of 48.5 cm, head circumference of 33.5 cm, and gestational age of 38 weeks. The father's job is dominated by the private sector while the mother's job is dominated by the housewife. Table 2 below shows that the average of education in both parents are high school graduates.

**Table 2** Sample Characteristics Based on Parent's Education

Characteristics	Otoacoustic Emission		p-value
	Case (Refer) (n = 40)	Control (Pass) (n = 40)	
Father's Education, n (%)			0,568
Elementary School	3(7,5)	0	
Junior High School	2(5)	3(7,5)	
Senior High School	16(40)	15(37,5)	
Diploma Program	9 (22,5)	8 (20)	
Undergraduate Program	11(27,5)	13(32,5)	
Mother's Education, n (%)			
Elementary School	1 (2,5)	0	0,149
Junior High School	4 (10)	0	
Senior High School	21 (52,5)	24 (60)	
Diploma Program	6 (15)	2 (5)	
Undergraduate Program	8 (20)	14 (35)	

### 3.2. Risk factor of Low Birth Weight (LBW)

Table 3 presents an analysis of the relationship between low birth weight and the results of OAE screening in neonates at RSUDZA. The number of samples with low birth weight were 21 neonates (26.3%). The percentage of the case group (refer) was 18.8% and the control group (pass) was 7.5%.

**Table 3** Analysis of the relationship between LBW risk factor and the results of OAE screening in neonates

Low birth weight	OAE		OR	p-value*
	Case (Refer) (n = 40)	Control(Pass) (n = 40)		
Yes (< 2.500 gr)	15 (18,8)	6 (7,5)	0,294	0,022
No (> 2.500 gr)	25 (31,3)	34 (42,5)		

\* Chi-squared test

Statistically using the Chi-squared test, it is known that there is a significant relationship between neonates who have risk factor of LWB and the results of OAE screening examinations with a value of  $p = 0.022$

( $p < 0.05$ ) with an odds ratio value of 0.294 ( $OR > 1$ ), meaning that LWB is truly a risk factor of congenital hearing loss and babies with LWB are 3 times more likely to be referred to an OAE examination.

### 3.3. Risk factor of prematurity

Based on Table 4 showing the analysis of the relationship between risk factor of prematurity and the results of OAE screening examinations, there were 12 (15%) samples for the case group.

**Table 4** Analysis of the relationship between risk factor of prematurity and the results of OAE screening in neonates

Prematurity	OAE		p-value*
	Case (Refer) (n = 40)	Control(Pass) (n = 40)	
Yes	12 (15)	7 (8,8)	0,189
No	28 (35)	33 (41,3)	

\* Chi-squared test

Based on Chi-squared analysis, it is known that there is no significant relationship between neonates born prematurely and the results of OAE screening examinations with a p-value = 0.189 and an odds ratio value of

0.495 ( $OR > 1$ ), meaning that prematurity is a risk factor for congenital deafness. Premature babies are 5 times more likely to be referred to an OAE examination.

### 3.4. Risk factor of hyperbilirubinemia

Based on Table 5, the analysis of the relationship between risk factor of hyperbilirubinemia and the results of OAE screening examinations in neonates at RSUDZA is presented in the Table 5. The case group consisted of 8 people (10%) from the total sample.

**Table 5** Analysis of the relationship between risk factor of hyperbilirubinemia and the results of OAE screening in neonates

Hyperbilirubinemia	OAE		OR	p-value
	Case (Refer) (n = 40)	Control(Pass) (n = 40)		
Yes	8 (10)	1 (1,3)	0,103	0,029
No	32 (40)	39 (48,8)		

\* Fisher's exact test

Fisher's exact test was used in this Table, because the Chi-squared test does not fulfill the requirements. It was found that there was a significant relationship between the condition of hyperbilirubinemia and the results of OAE screening examinations in neonates at RSUDZA with a value of  $p = 0.029$  ( $p < 0.05$ ) and an odds ratio value of 0.103, meaning that hyperbilirubinemia is a risk factor of congenital deafness and babies with hyperbilirubinemia have a probability of 1 time higher risk of referral in OAE examination.

### 3.5. Risk factor of low APGAR score

Table 6 presents an analysis of the relationship between the risk factor of low APGAR scores and the results of OAE screening examinations using Chi-squared test. The sample in the case (refer) group was found 11 neonates (13.7%).

**Table 6** Analysis of the relationship between risk factor of low APGAR scores and OAE screening in neonates

Low APGAR Score	OAE		OR	p-value*
	Case (Refer)(n = 40)	Control(Pass)(n = 40)		

Yes	11 (13,7)	1 (1,3)	0,107	0,037
No	29 (36,3)	39 (48,7)		

\* Chi-squared test

Statistically, there is a significant relationship between the condition of low APGAR score and the results of OAE screening examinations with a value of  $p = 0.037$  ( $p < 0.05$ ) and an odds ratio value of 0.107, meaning that a low APGAR score is a risk factor of congenital deafness. Low APGAR scores are 1 time more likely to be referred for an OAE examination.

### 3.6. Risk factor of craniofacial disorders

Table 7 presents an analysis of the relationship between craniofacial abnormalities and the results of OAE screening examinations in neonates at RSUDZA. The number of cases (refer) group were 6 (7.5%) samples.

**Table 7** Analysis of the relationship between risk factor of craniofacial abnormalities and the results of OAE screening in neonates

Craniofacial Disorders	OAE		Nilai p-value*
	Case (Refer) (n = 40)	Control(Pass) (n = 40)	
Ya	6 (7,5)	0	0,026
Tidak	34 (42,5)	40 (50)	

\* Fisher's exact test

Based on Fisher's exact test analysis, there is a significant relationship between craniofacial abnormalities and the results of OAE screening examinations in neonates at RSUDZA with  $p = 0.026$  ( $p < 0.05$ ). The Ods ratio value of this risk factor could not be calculated because there is a value of zero in the control group.

### 3.7. Risk factor of family history of deafness since birth

Table 8 presents the analysis of the relationship between a family history of deafness since birth and the results of OAE screening examinations in neonates at RSUDZA. The case group obtained were 3 (3.8%) samples.

**Table 8** Analysis of the relationship between a family history of deafness since birth and the results of neonatal OAE screening

Family history of deafness since birth	OAE		p-value*
	Case (Refer) (n = 40)	Control (Pass) (n = 40)	
Yes	3 (3,8)	0	0,241
No	37 (46,3)	40 (50)	

\* Fisher's exact test

Statistically using Fisher's exact test, it was found that there was no significant relationship between a family history of deafness since birth and the results of OAE screening examinations in neonates at RSUDZA with  $p\text{-value}=0.241$ .

## 4. Discussion

### 4.1. Characteristics of the research sample

This research was conducted in the Perinatology and NICU rooms by selecting samples according to research criteria and then examined at least 24 hours after birth. According to Balkany as quoted from Chang et al, neonates aged less than 24 hours had their ear canals filled with vernix caseosa. All vernix caseosa would be drained within 24-48 hours after birth, so that the referral result was 5-20% if screening was carried out less than 24 hours after birth. A referral rate of <3% was achieved if screening was carried out along 24-48 hours after birth. Bonfils et al reported that outer hair cell maturation occurs completely after 32 weeks of gestation<sup>18</sup>. The characteristics of the study sample reviewed based on gender are presented in Table 1. The case group was dominated by female (57.5%) and the control group by male (52.5%). This condition was also found in research at Columbia Asia Hospital, Medan, North Sumatra in 2017.

There were 2 girls and 1 boy out of 17 babies (10 boys and 7 girls) who had referral results in OAE<sup>19</sup>. Research by Bashiruddin J (2009), found that 18 girl babies (56.3%), and 14 boy babies (43.8%) had referral results in OAE screening at six hospitals in Jakarta<sup>20</sup>.

There were 237 boys (50.9%) had a higher incidence of hearing loss than girls (229/49.1%) out of 466 research samples at Kariadi Hospital Semarang from January 2019 to December 2020. The same as the retrospective research results period 2011 until 2013 which conducted at Dr. Soetomo Hospital on 556 samples of babies and children showed that 293 (52.79%) were boys<sup>21</sup>. Although boy babies are epidemiologically more experiencing brain maturation disorders, white matter development of the brain and nerve dysfunction, but there is no mechanism that states gender is susceptible to hearing loss<sup>22</sup>. The dominance of male subjects may be an incidental finding and still unknown whether differences in the anatomy of male and female ears<sup>23</sup>. Factors which contribute to potential hearing loss are called risk factors of hearing loss<sup>24</sup>. Research by Davis A et al, found that Babies who had one risk factor were 10.1 times more likely suffering hearing loss. Babies with two risk factors had 12.7 times probability, whereas the probability increased to 63.2 times if there were three risk factors<sup>18</sup>.

Hearing screening is designed only detecting the occurrence of hearing loss (could not differentiate the type of deafness)<sup>25</sup>. In this study the tool used is OAE screening which principle is to measure the emissions emitted by the ear when sound is stimulating the cochlea. This technique is sensitive for detecting damage in the outer hair cells of the cochlea. If there are OAE waves, the baby can pass the OAE test (pass), meaning it is likely that the baby will not experience hearing loss. If there are no OAE wave (refer), it means that there is a possibility that the baby is suffering hearing loss, so that further tests must be conducted according to the hearing screening process recommended by the Indonesian Ministry of Health and JCIH. The referral results allow hearing loss of more than 30-40 dB. The results of the OAE are influenced by vernix caseosa, debris, and the condition of the middle ear (cavum tympani)<sup>26</sup>.

#### **4.2. Analysis the relationship between risk factors of low birth weight and the results of OAE**

Body weight is an indicator of a newborn's health. The average weight of a normal baby with a gestational age of 37-41 weeks is 3200 grams. In general, babies with low birth weight (< 2500 grams) and babies with excess weight (≥ 3800 grams) have greater risk of experiencing problems<sup>27</sup>. Various complications arise due to low birth weight, including hearing loss. The prevalence of neonates with LBW who receive referral results at the first screening are higher than neonates with normal birth weight, because neonates with LBW experience higher levels of fluid collection in the middle ear than normal neonates, this hearing loss is usually temporary<sup>28</sup>. Observational research at RSUP Dr. Kariadi Semarang using a cross sectional approach, data taken from medical records of all children diagnosed with hearing loss from January to December 2020. It was found 33 (7.1%) of the sample with LBW, different from previous research which reported that 453 babies in the NICU had hearing loss as many as 62.5%, and 3.9% with a history of prematurity and LBW. This difference is due to the sample study of babies treated in the NICU which tend having other risk factors so that the tendency for hearing loss is greater<sup>29</sup>. Other research which was also conducted at RSUP Dr. Kariadi Semarang with a case control design, found that there were 62 people with speech delay. LBW could influence Sensorineural Hearing Loss (SNHL) in speech delay sufferers which have a risk 14 times greater than speech delay sufferers without LBW risk factor (OR=14.190). Chien Ho Wang's research at the NICU of Chang Gung Chikdren'a Hospital Taiwan for 2 years, found that 3.9% (12/309) of babies with LBW experienced hearing loss<sup>15</sup>.

LBW indicates regarding intrauterine fetal development could not occur optimally. This is in line with research by Muyassaroh which showed the risk factor that most influenced SNHL in newborns was LBW<sup>30</sup>. Rahayuningrum (2016) independently stated that LBW was a risk factor that influences SNHL in speech delay sufferers with a risk of 27 times greater than speech delay sufferers without LBW<sup>30</sup>. Research by Chang Myeon regarding very low birth weight babies in the Korean Neonatal Network, found that a statistically significant relationship with hearing loss and retinopathy of prematurity<sup>31</sup>. This study illustrates that babies with LBW have 3 times more likely being referred in OAE compared to babies with normal birth weight. These are caused by (1) Disorders of mesenchymal which can interfere with the pneumatization formation of the temporal bone and the vibrational function of the ossicles, (2) Changes the position and structure of the tympanic membrane in the first postnatal year, (3) The incomplete formation of the ear canal bone part which causes disturbances transmission of sound vibrations to the cochlea<sup>32</sup>.

#### **4.3. Analysis the relationship between premature risk factor and OAE screening results**

Prematurity is a risk factor for hearing loss in infants and children<sup>21,29</sup>. This study did not show a significant relationship between risk factor of prematurity and the possibility of referral results on OAE, because the gestational age which was classified as a premature sample<sup>33</sup>. This was in accordance with research conducted at RSUP Dr. Kariadi Semarang which assessed the relationship between prematurity and LBW with the degree of hearing loss in children. It was found that there was no significant relationship between prematurity and the degree of hearing loss<sup>29</sup>. Similar to research by

Tri Kartika Setyarini, there were no significance statistically between the incidence of hearing loss and OAE results at the first and the second<sup>31</sup>. The same results was also presented by Ramzan Shahid's research at Loyola University Medical Center that the factor of premature births did not have a significant relationship to a possibility of hearing loss<sup>34</sup>. Research by Amir and Elena showed that prematurity had no correlation statistically using Chi-squared test ( $p$ -value=0.001) with the incidence of hearing loss in 530 neonates at the NICU Abuzar Hospital Iran. Most of the premature babies referred at the first OAE showed a normal hearing at audiological screening test. Apart from that, several studies reported that maturation of the hearing organ could influence the results of hearing tests<sup>35</sup>. It can be explained that the changes in the hearing threshold which depend on auditory maturity both in the peripheral and central pathways so that the deafness are temporary in children with prematurity<sup>35</sup>.

#### 4.4. Analysis the relationship between risk factor of hyperbilirubinemia and OAE screening results

Hyperbilirubinemia is one of the most common clinical phenomena in newborn babies. Neonatal hyperbilirubinemia is a condition where the total bilirubin level is  $> 5$  mg/dl ( $86 \mu\text{mol/L}$ ). Hyperbilirubinemia appears clinically as jaundice<sup>36</sup>. The conditions of hyperbilirubinemia in neonates that are not handled properly will have neurotoxic effects on their development. In term babies, the symptoms of hyperbilirubinemia are weak and reluctant to drink which will progress to choreoathetoid cerebral palsy, mental retardation, Sensorineural hearing loss and gaze paresis<sup>36</sup>. Table 5 shows a significant correlation between the condition of hyperbilirubinemia and the results of OAE examination. This is in accordance with the theory that bilirubin metabolism disturbances through intrahepatic circulation causing an increased of bilirubin levels in the blood<sup>30</sup>. Hyperbilirubinemia causes selective damage to the auditory nucleus, thereby damaging the auditory nerve and spiral ganglion cells by disrupting the concentration of intracellular neuronal calcium ions<sup>37</sup>. There is an evidence that moderate increased of bilirubin levels will affect cognitive, perceptual, motor, and auditory disorders<sup>36</sup>.

Research conducted at Mnazi Mmoja Hospital (MMH) Zanzibar Tanzania, found that there was a significant risk factor for hearing loss ( $p=0.001$ ) about 2.7% hyperbilirubinemia sufferers from 600 subjects along 8 months<sup>37</sup>. Research by Wickremasinghe in California with a cohort design, showed that hyperbilirubinemia had an effect on SNHL while blood bilirubin levels were more than the Exchange Transfusion Thresholds (ETT)<sup>38</sup>. Hyperbilirubinemia is not only associated with SNHL but also with a certain type of hearing dysfunction called auditory dyssynchrony or Auditory Neuropathy Spectrum Disorder (ANSND). Individuals with ANSD have abnormal auditory nerve function but normal cochlear function, therefore they have abnormal results on ABR examination but normal results on OAE. Children with ANSD had at higher risk of experiencing language and speech disorders<sup>38</sup>.

#### 4.5. Analysis the relationship between risk factor of low APGAR scores and OAE screening results

APGAR scores is a quickly method in diagnosing and classifying the degree of asphyxia. According to the AAP and the American College of Obstetricians and Gynecologists (2004), perinatal asphyxia in neonates will show APGAR scores of 0-3 at 5 minutes. Based on Table 6, there was a significant relationship between low APGAR scores and the results of OAE screening. The cause of hearing loss in neonatal asphyxia is damage to brain cells due to hypoxia and ischemia so that oxygen distribution to various tissues decreased. This was in accordance with research by Tri Kartika Setyarini, the degree of severe hearing loss occurred in severe asphyxia<sup>34</sup>. Apart from affecting the peripheral components, neonatal asphyxia also affects the central components of the auditory system, which are indicated by damage to the brain stem. Jiang et al reported that neonatal asphyxia affects the peripheral and central components of hearing<sup>34</sup>. Research by Schmitzhard et al found that caspase 3 was a marker of apoptosis hair cells, spiral ganglion cells, and marginal cells of the stria vascularis in asphyxiated neonates. It was showed that the influence of hypoxia causing cochlear damage formerly<sup>34</sup>.

This is in accordance with the prospective cohort research conducted by Tri Kartika Setyarini at Dr. Hospital Kariadi Semarang in 2009-2010, there were 34 asphyxia neonates out of 68 neonates with 35% referral OAE examination results, stating that neonatal asphyxia is a risk factor for hearing loss. Cohort study by Ellen Kvestad in Norway, stated that low APGAR scores were associated with the incidence of SNHL hearing loss in 2014.<sup>39</sup> Watcharapol's research in Northern Thailand (2016) stated that babies with low APGAR scores had a 2.2 times risk of hearing loss compared to babies with normal APGAR scores<sup>26</sup>.

#### 4.6. Analysis the relationship between risk factor of craniofacial abnormalities and OAE screening results

Table 7 shows that there is a significant relationship between craniofacial abnormalities and the results of OAE screening in neonates ( $p = 0.026$ ). The craniofacial abnormalities found in this study were hydrocephalus and microcephaly. This research is in accordance with Watcharapol's research in Northern Thailand (2016) stated that babies with craniofacial abnormalities were 2.5 times more likely being the occurrence of hearing loss compared to



babies without craniofacial abnormalities<sup>26</sup>. Research by Vartianien showed that the degree of head trauma was correlated with the incidence of SNHL in children, especially head trauma involving the temporal bone which could be result in damage to the inner ear components. In this study, the effect of head trauma on SNHL was not significant.<sup>30</sup> Data from Chien Ho Wang's research at the NICU of Chang Gung Chikdren'a Hospital for along 2 years, found that 3.9% risk factor of craniofacial abnormalities were significant to the incidence of hearing loss<sup>15</sup>.

#### **4.7. Analysis the relationship between a family history of deafness since birth and the results of OAE screening**

Based on Table 8, it shows that there is no significant relationship between a family history of deafness since birth and the results of OAE screening examinations in neonates ( $p = 0.241$ ). This is in line with Amir and Elena's research at the NICU Abuzar Hospital Iran involving 530 neonates. It was found that the family history of deafness since birth did not have a significant correlation with the incidence of hearing loss, but the marriage history of relatives was one of them<sup>35</sup>. Study in Zambia involving 600 neonates, stated that the most significant risk factor was hyperbilirubinemia, but babies with hyperbilirubinemia also had a history of congenitally deaf families. This explained the synergistic role of risk factors for neonatal hearing loss<sup>37</sup>. In contrast to Ramzan Shahid's research at Loyola University Medical Center, the family history of deafness had a significant relationship with the incidence of hearing loss ( $OR=11.35$ )<sup>40</sup>. In this case, it is important to ask about family history of hearing loss because this factor could influence the referral results in the OAE examination<sup>40</sup>.

There are various classifications of hearing loss, including genetic and acquired. This classification involves many genetic and environmental interactions<sup>41</sup>. Deafness is caused by genes found on the X chromosome which are usually inherited as X linked recessive. Deafness is rarely seen in women even though they are "carriers", but deafness will have an impact on some of the men. If the affected gene is inherited through the father, no offsprings are affected even all the daughters are carriers. Deafness is inherited as an X-linked recessive only through the mother also has the same effect on girls and boys<sup>41</sup>.

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## **5. Conclusion**

In this study, seven risk factors were analyzed, those that had a significant relationship with the results of the OAE screening examination, including Low Birth Weight, hyperbilirubinemia, low APGAR score), and craniofacial abnormality. Low birth weight is the most influential risk factor.

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## **Compliance with ethical standards**

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### *Disclosure of conflict of interest*

The authors have declared that no competing interests exist in this study.

### *Statement of ethical approval*

The study has been approved by the Health Research Ethics Committee of the Faculty of Medicine at Universitas Syiah Kuala with a number of ethical contributions KEPPKN registration number 1171012P (Description of ethical expedited number: 046/EA/FK-RSUDZA/2022)

### *Statement of informed consent*

All authors declare that informed consent was obtained from all individual participants included in the study.

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