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OPTIMIZATION OF EARLY DIAGNOSIS AND AUDITORY REHABILITATION IN CHILDREN WITH SENSORINEURAL HEARING LOSS

321.16 - OTORHINOLARYNGOLOGY

Summary of Ph.D. Thesis in Medical Sciences

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THE RESEARCH CONCEPTUAL FRAMEWORK

Research actuality. Hearing impairment is beyond the scope of otology, since hearing underpins the auditory and cognitive development of the child, contributing to personality formation. Due to its incidence and serious complications that often lead to disability, hearing impairment continues to be an issue of interest for both researchers and multidisciplinary specialists. [1,2,13].

The data provided by the specialized literature reveal that hearing loss is diagnosed in 1-3 cases per 1,000 healthy newborns and one in 1000 might acquire it during childhood [4,11]. The incidence of neonatal hearing loss is 60 times higher than the incidence of congenital metabolic disorders, which is supported by a universal screening program, as for example in phenylketonuria, which might occur in 1/20 000 live births [6,28] .

Hearing loss complications are even more pronounced in earlier pediatric hearing impairment. Since the auditory centers develop only as they receive sensory impulses, deaf children do not develop nervous automatisms necessary for speech production, although they exhibit the same psychomotor and buccopharyngeal opportunities as the hearing children [3,7].

Hearing loss is a contributing factor affecting the child's mental development that is impossible without hearing. Moreover, a hearing-impaired child cannot form and develop conceptual thinking, thus intellectual development disorders might occur. The analysis of specialized literature, as well as the positive opinion of the experts from highly developed countries, which provide universal programs on “early hearing loss detection in children”, convincingly highlight the importance and practical usefulness of the hearing loss screening in newborns [6,9, 11,26,29].

Although the technical advance has provided new objective methods on auditory assessment of children even in the first days of life, late diagnosis is still quite common [12,25]. The lack of an early prosthetic and psycho-pedagogical rehabilitation support are the main causes for deaf children being institutionalized in special kindergartens and schools for hearing-impaired children. Early hearing loss rehabilitation is still a vulnerable issue among deaf children, as it requires collaboration between doctors, educators and social workers [18]. In the Republic of Moldova, over 1,400 children with different types of hearing impairment, as well as new cases are registered annually, ranking third among the disability –causing diseases. There are no statistical data on the incidence of deafness in newborns.

Modern methods of auditory rehabilitation by using conventional hearing aids or cochlear implant require early and accurate diagnosis of hearing deficiency in children, as well as a complex assessment of the auditory analyzer pathway [21,26]. This is not an easy task due to the anatomical and physiological patterns of the auditory analyzer in terms of age, particularities of neuropsychiatric development of the child, as well as lack of a universal assessment method [18]. The technical-scientific progress in the recent years has allowed a qualitative early diagnosis of hearing -impaired children. Therefore, the objective diagnostic methods such as otoacoustic emissions, auditory evoked potentials, and impedancemetry have contributed to the decrease of children’s mean age at which hearing impairment has been diagnosed [13,17]. However, the analysis of specialized literature reveal different, sometimes even contradictory, views on the diagnostic usefulness of certain auditory exploration techniques. To date, there is no single method

for assessing hearing function in infants and young children. The expert opinions differ regarding the audiological screening, the age of hearing testing and the methods used in auditory screening. The genetic diagnosis is carried out complementary to both anamnestic data and audiological evaluation and plays an important role in the detection of the causes of deafness. The main reasons for performing a mutational-genetic screening are as following: 1) to prove the etiology of hearing impairment; 2) to determine the carrier status 3) to develop a complex algorithm for diagnosing hearing loss in children. In order to clarify the aforementioned issues, the following study has been carried out.

The purpose of the study:

To provide an efficient early diagnosis of hearing loss and prosthetic rehabilitation in children, by developing and implementing a behavioral diagnostic and therapeutic algorithm in order to improve their quality of life and social inclusion.

Objectives:

1. To optimize the etiological diagnosis of hearing impairment in children based on anamnestic data, risk factors and molecular and genetic assessment.
2. To determine the diagnostic utility of transient evoked otoacoustic emissions in newborn hearing screening.
3. To highlight the characteristics of an early complex diagnosis of sensorineural hearing loss in newborns by using OAEs, ASSR, BERA and conditioned play and behavioral audiometry.
4. To study the effectiveness of the newborn hearing screening in the rehabilitation process of hearing-impaired children.
5. To provide an auditory function assessment in children with sensorineural deafness following a prosthetic rehabilitation via using hearing aids or cochlear implant.
6. To develop an algorithm for early diagnosis and auditory rehabilitation of sensorinural hearing loss in children.

The scientific novelty of the research:

This present clinical study was conducted for the first time in the Republic of Moldova and aimed at analyzing the newborn hearing screening findings by recording otoacoustic emissions. Moreover, the importance of newborn hearing screening associated with molecular and genetic screening has also been studied. We analyzed the particularities of rehabilitation process in children with sensorineural hearing loss, who were early diagnosed via the modified method compared to the patients diagnosed by the classical method. Furthermore, there was determined the difference of the audiologic rehabilitation parameters among sensorineural hearing-impaired children using conventional hearing prostheses compared with those with cochlear implants. The importance and usefulness of both neonatal and molecular-genetic hearing screening has been outlined, regarding the algorithm of an early diagnosis and rehabilitation of children with sensorineural hearing impairment.

Theoretical significance:

The research findings helped to facilitate the early diagnosis of pediatric sensorineural hearing loss. The previous methods of diagnosing sensorineural hearing loss in children allowed

to establish late diagnosis in multiple cases, currently, the results of the study helps to early diagnose sensorineural hearing impairment. Due to an early diagnosis of pediatric sensorineural hearing loss, the audiologic rehabilitation parameters following the use of conventional prosthesis or cochlear implant, have significantly improved, due to the neuroplasticity of the first five years of the children's life.

The analysis of risk factors in perinatal, intranatal and postnatal periods, enabled to outline the major risk factors for developing sensorineural hearing loss, thus the knowledge obtained might help avoid their impact, being considered as preventive measures for sensorineural hearing loss in children.

The molecular-genetic screening, associated with the newborn hearing screening, plays an important role in improving considerably the genetic counseling regarding the evolution of hearing loss disorder and the risk of a recurrent mutation events in children or within families who have already had a child diagnosed with hearing loss.

The applicative value of the research:

To identify the most important risk factors of sensorineural hearing loss in children during the perinatal, intranatal and postnatal periods, in order to improve deafness prevention in children. The study results confirm the usefulness of implementing otoacoustic emission testing as the first stage of newborn hearing screening. The use of diagnosis and auditory rehabilitation algorithm in sensoroneural hearing-impaired children might contribute to an early diagnosis and might optimize the rehabilitation of deaf children.

Implementation of research findings:

The study results were implemented within the clinical activity of The Republican Center for Audiology, Auditory Prosthesis and Medico-Pedagogical Rehabilitation, IMC Emilian Coţaga Clinic, as well as in the teaching activity at the Department of Otolaryngology, at “Nicolae Testemitanu" SUMPh.

1. RESEARCH MATERIAL AND METHODOLOGY

The present research was based on a controlled clinical trial. A methodological plan of the research was drafted prior to the study initiation , which involved the criteria selection for the eligibility of the patients included in the study, the development and completion of the study forms, analysis, synthesis and study findings interpretation, making conclusions and implementing the study results within the clinical practice. The research was conducted during the period of 2016-2018 in accordance with the Principles of Helsinki Declaration - WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects. The study was carried out, based on a written agreement signed by all participants (the information form and the acceptance form), who were informed about the assessment methods. All confidential data were respected at the time of research initiation and throughout the study.

The number of study subjects required for a research inclusion was evaluated according to the following formula:

$$n = \frac{1}{(1-f)} \times \frac{2(Z_\alpha + Z_\beta)^2 xP(1-P)}{(P_o - P_1)^2}$$

whereas:

P_o = according to specialized literature, the successful detection of sensorineural hearing impairment in children via traditional methods (hearing function assessment via behavioral and conditioned play audiometry, hearing balance components) makes up 60.0% (P0= 0.60) on average (P_0=0,60). This method might waste the precious time for hearing loss detection, since it is available only in advanced age, exceeding 36 months, after the parents observe a hearing deficiency.

P_1= patients from the study group L_1, will be diagnosed with sensorineural hearing loss via a modified method (newborn hearing screening by evoked otoacoustic emissions test performance), which reveals a detection efficiency of 80, 0 % (P_1=0, 80); the diagnosis is likely to be established at birth and confirmed in the first months of life.

$P = (P_0 + P_1)/2$=0, 75

$Z\alpha$ - table value. When the statistical significance is 95.0%, then the coefficient $Z\alpha = 1.96$

Z_β - table value. When the comparison statistical power is 80.0%, then $Z_\beta = 0.84$

f = the number of subjects, who may abandon the study for any other reasons besides the investigated ones

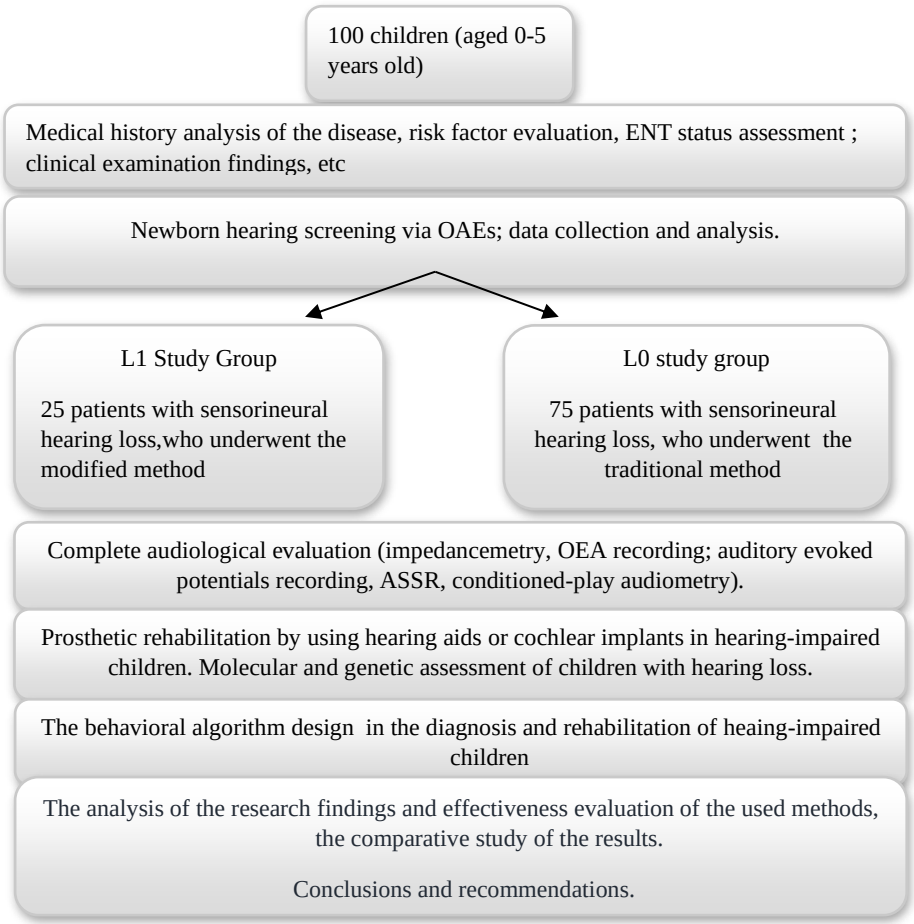
q = 1 / (1-f), f = 10,0% (0,1).

We obtained the following results by introducing data into the formula:

$$n = \frac{1}{(1-0.1)} \times \frac{2(1.96+0.84)^2 \, x0.775x0.225}{(0.60-0.95)^2} = 25$$

Therefore, the L_1 study group will include at least 25 patients with sensorineural hearing loss, diagnosed via a modified method (newborn hearing screening) and the L_0 control group will include at least 75 patients with sensorineural hearing loss, diagnosed via the traditional methodology.

THE STUDY DESIGN



Criteria for inclusion in the research group

• Newborns who underwent hearing screening and were detected as lacking OAEs (OAEs negative testing in suspected hearing impairment)

• Children of early age, who were diagnosed via the complex audiological evaluation when being referred to the audiologist or ENT doctor, without a prior hearing screening

Criteria for exclusion from the research group:

- Children whose parents refused undergoing hearing screening
- Children with congenital ear malformation (external auditory canal atresia)
- Children detected with hearing loss, due to the newborn hearing screening

The investigations conducted on the subjects enrolled within the study

• The subjects from the two study groups underwent the following investigations: 1. ENT status evaluation; 2. OAEs recording; 3. Impedancemetry; 4. auditory evoked potentials recording; 5. Reflexive and instrumental audiometry; 6. Cochlear implant fitting; 7. Questionnaire survey; 8. Genetic assessment ; 9. Specialists consultation: ophthalmologist, cardiologist, nephrologist, geneticist, speech therapist, psychologist.

1. RESEARCH RESULTS

1.1 Risk factors assessment for sensorineural hearing loss based on anamnestic data

Both research groups included a total of 100 patients with sensorineural hearing loss, aged between 0 and 60 months, most children were enrolled within the L1 study group (n = 25) , who were detected with sensorineural hearing loss due to the OAE hearing test performed within the newborn hearing screening, at the maternity units, at 2-3 days postpartum. The L0 research group (n = 75) included children with sensorineural hearing loss, diagnosed at the Republican Center for Audiology , and who underwent a complex hearing evaluation, or later on being referred by other specialists to ENT doctors or audiologists, as well as at parents' request , when a speech delay and hearing disorder were suspected. The gender-related distribution represented an absolute number of 30 female patients (40.0%) and 45 male (60.0%) within the L0 study group. 13 subjects were born by primiparous mothers (17.3%), 24 - from 2^{nd} gravid mothers; (32.0), 9 – from 3^{rd} gravid mothers (12.0%), 1 - from the 5th gravid ones. The L1 research group included an absolute number of 14 (56.0%) female patients and 11 (44.0%) male patients. 11 (44.0%) subjects were born by primiparous mothers, 6 (24.0%) - from 2^{nd}, 2 (12.0%) - from 3^{rd} and 1 - from the 4^{th} gravid mothers.

In order to elucidate the presence of risk factors for hearing loss within the patients' medical history, the research participants underwent a questionnaire survey regarding the occurrence of any risk factor antecedents for hearing loss. The child's personal health record included a series of questions to detect the presence of pre-, intra- or postnatal risk factors for hearing loss impairment. The child's parent or legal representative answered these questions. The data statistical analysis was carried out. Out of all the identified risk factors, the following ones were found to show true statistically significant results: low amniotic fluid period lasting for over 6h ($P < 0.05$), asphyxia with intubation ($P < 0.05$), preterm birth ($P < 0.05$), a child's delay in holding head up ($P < 0.05$), a delay in sitting up ($P < 0.05$), a child's walking delay ($P < 0.05$), meningitis ($P < 0.05$), influenza ($P < 0.05$), cytomegalovirus ($P < 0.05$), ototoxic antibiotic use ($P < 0.05$), intoxications ($P < 0 , 05$).

Table 1. Risk factors for pediatric sensorineural hearing loss.

Risk factor	**Number of subjects**		**%**		**x^2**	**gl**	**P**
	L0	**L1**	**L0**	**L1**			
Low amniotic fluid period of over 6h	26	2	34,6%	8,0%	18,96	2	0,015
Asphyxia with intubation	16	2	21,3%	8,0%	2,855	3	0,041
Preterm birth	9	4	12,0%	16,0%	23,213	6	0,001
A delay in holding head up	10	4	13,3%	16,0%	23,213	6	0,001
A delay in sitting up	14	3	18,6%	12,0%	17,612	9	0,040
A child's walking delay	15	4	20,0%	16,0%	16,526	10	0,040
Meningitis	1	2	1,3%	8,0%	6,042	1	0,014
Influenza	22	1	29,3%	4,0%	6,795	1	0,009
Cytomegalovirus	21	9	28,0%	36,0%	5,998	1	0,014

Use of ototoxic antibiotics	26	7	34,7%	28,0%	20,475	2	0,001
Intoxications	21	2	28,0%	8,0%	4,235	1	0,040

2.2. Important aspects of molecular and genetic screening

The molecular - genetic screening of the 35 delG mutation of GJB2 in 50 patients with deep non-syndromic sensorineural hearing impairment , who underwent cochlear implantation and were recruited within the study, revealed the following results: 9 (18.0%) patients exhibited the 35delG mutation in 2 alleles and 7 (14.0%) on 1 allele (Figure 2.1).

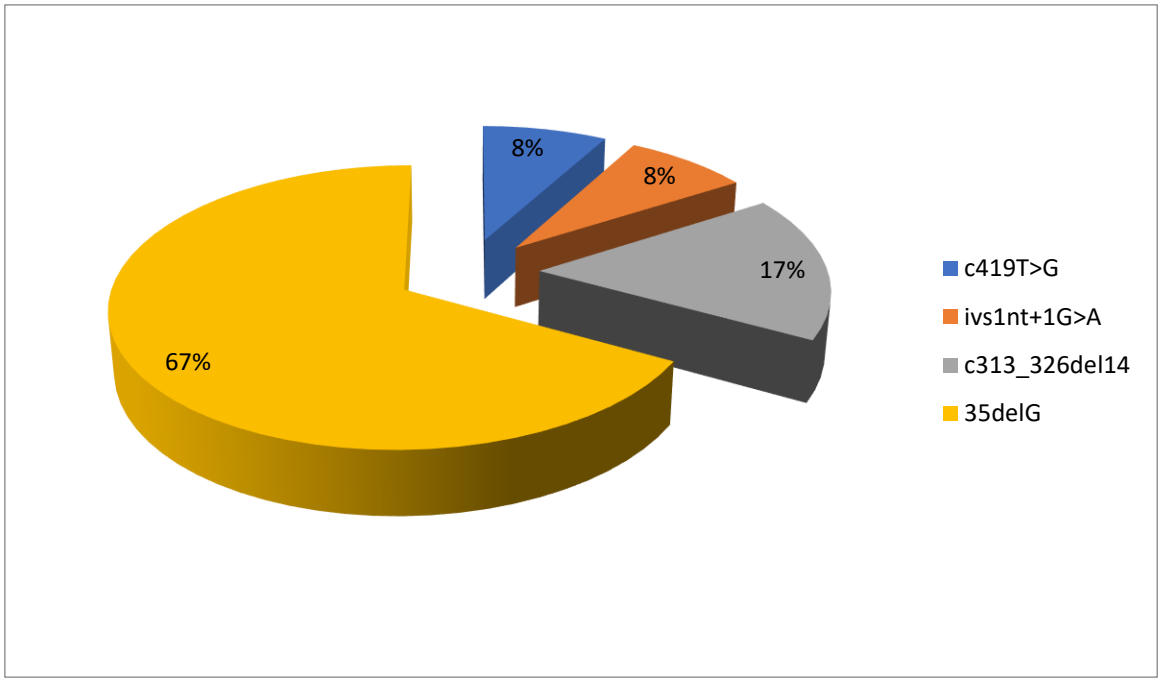


Figure 1. The study of cochlear implant patients for mutation screening

Figure 2.1 shows the predominance of the 35delG mutation in 67% of the 50 patients with deep non-syndromic sensorineural hearing loss, who underwent cochlear implantation and who were recruited within the study. The c313_326del14 mutation ranks second according to the incidence rate, and was detected in 17% of cochlear implant children with deep non-syndromic sensorineural hearing loss. Both c419T> G mutation and the ivs1nt + 1G> A mutation shared the same 8% of the total number of patients recruited in the molecular-genetic study

As referring to the sensorineural hearing loss of genetic origin, all types of transmission have been found present. The autosomal recessive pattern is the most commonly attested, although there are cases of dominant autosomal transmission pattern; the X-linked inheritance and mitochondrial DNA transmission are extremely rare.

Nevertheless, the 35delG mutation was predominantly attested in 67% of 50 cochlear implant patients with deep non-syndromic sensorineural hearing impairment. 17% of cochlear implant children with deep non-syndromic sensorineural hearing loss exhibited the c313_326del14 mutation, 8% of subjects had the c419T> G mutation and 8% - the ivs1nt + 1G> A mutation out of the total number of subjects involved in the molecular-genetic study

2.3. The role of OAEs in newborn hearing screening

The patients, diagnosed with sensorineural hearing loss via the audiological screening (n = 25), were recruited during the 2016-2019 years , by performing the otoacoustic emissions testing in 8,434 newborns from the perinatology centers from the Republic of Moldova.

The test results of the 8 434 newborns were classified into the following types: - Bilateral PASS results (both ears), - Bilateral Refer results (both ears), - Unilateral Pass result (right ear) , Unilateral Pass result (left ear), - Unilateral Refer results (right ear), - Unilateral Refer results (left ear), - No Seal (bilateral) result, - No Seal (unilateral) result (right ear), - No Seal (unilateral) result (left ear).

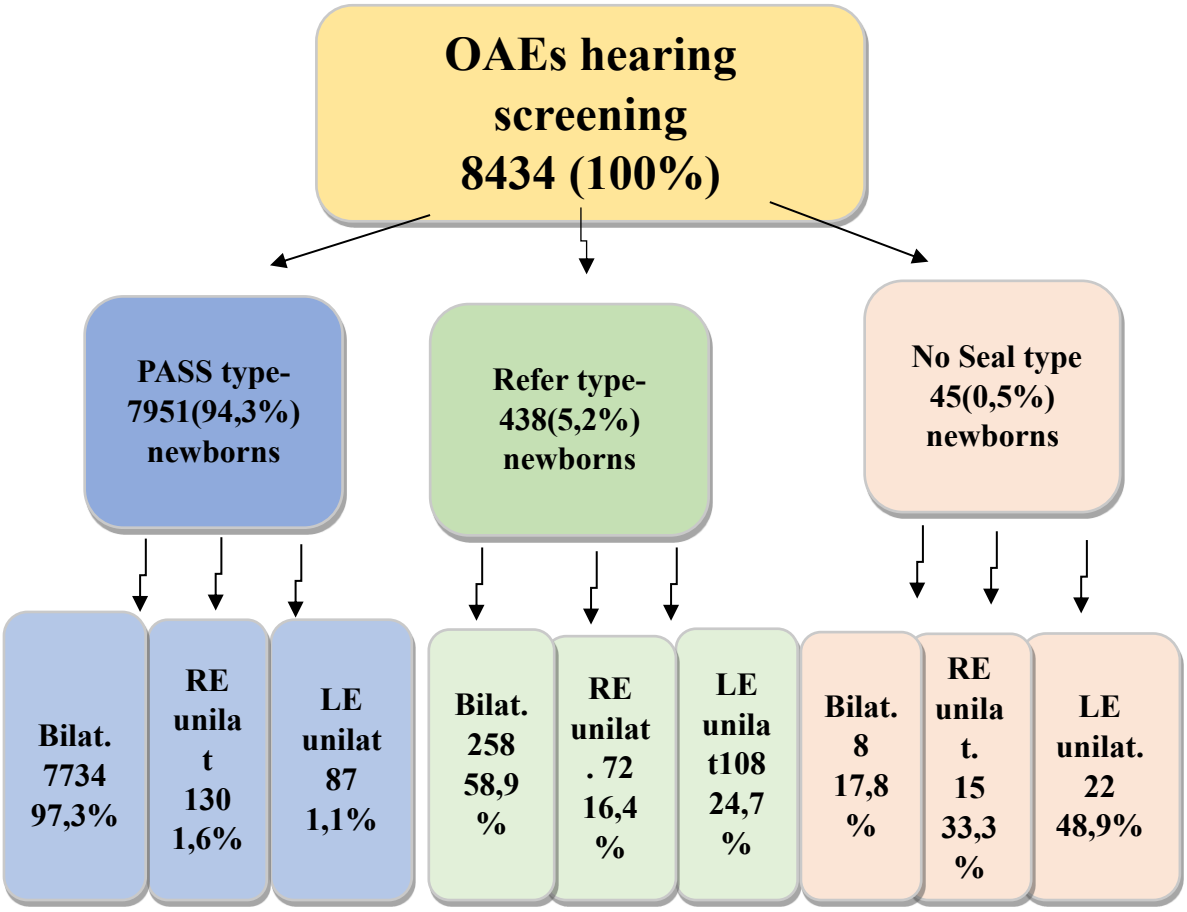


Figure 2. The OAEs screening findings.

The OAEs testing showed that most newborns included within the study (out of a total 8434), exhibited the Pass result - 7951 (94.3%) -Figure. 4.1. Unilateral or bilateral Refer results were found in 438 (5.2%) cases, whereas No Seal results, unilateral or bilateral results were found in 45 children. (0.5%).

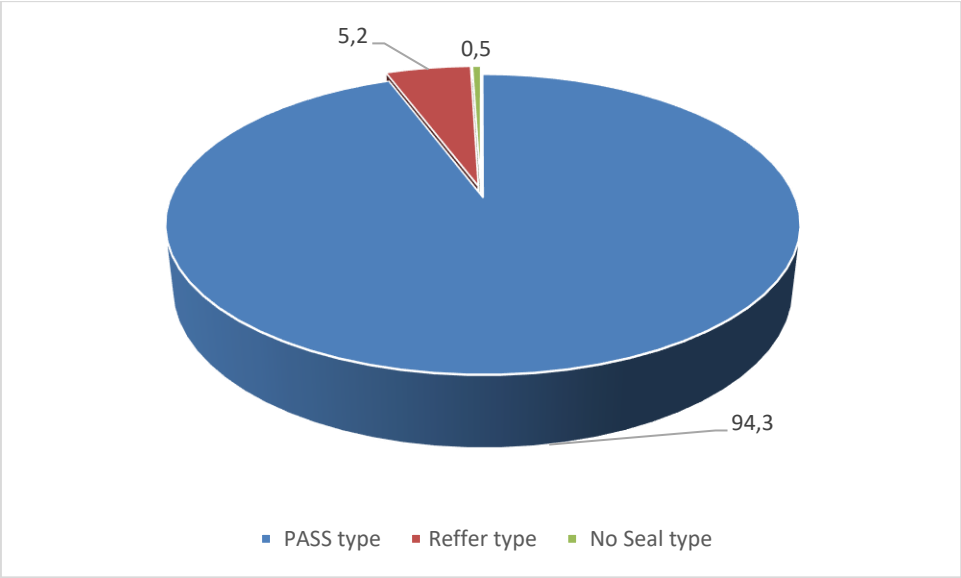


Fig. 3. The percentage of newborns based on OAEs findings

The comparative study of the OAEs parameters between the groups revealed that L1 research group (children who underwent newborn hearing screening was performed) showed statistically significant results, in case of OAEs of bilateral left ear PASS, Refer and No Seal type (table 1). According to the study findings of the right ear, the highlighted parameters did not present any statistical authenticity.

Table 1. Comparative analysis of OAEs findings

	PASS type		**Refer type**		**No Seal type**		**PASS/ Refer**	**PASS/ No Seal**	**Refer/ No Seal**
	Abs.	**P(%)**	**Abs.**	**P(%)**	**Abs.**	**P(%)**	**X^2, gl=1, p**	**X^2, gl=1, p**	**X^2, gl=1, p**
Bila-teral	7734	97,3	258	58,9	8	17,8	972.693, p < 0.0001	186.721, p < 0.0001	5.349, p = 0.0207
Right ear	130	1,6	72	16,4	15	33,3	15.774, p = 0.0001	28.917, p < 0.0001	2.249, p= 0.1337
Left ear	87	1,1	108	24,7	22	48,9	21.952, p < 0.0001	41.441, p < 0.0001	5.180, p = 0.0228
Total	7951	100,0	438	100,0	45	100,0			

The data statistical analysis regarding the mean age of children at the time of hearing assessment, according to the protocol, revealed a mean value of 2.27 months (standard deviation -1.438) in children from the L_1 research group (children diagnosed via the newborn hearing screening), compared with a mean age of 45, 15 months (standard deviation -10,340) in children from the L_0 research group. The results from table 2 confirm that children from L_1 group who underwent OAEs assessment during the newborn hearing screening, exhibited a 19.88 times higher opportunity for performing a complex hearing balance, followed by an early complex diagnosis, compared to children in the L0 research group (who did not undergo the newborn hearing screening).

Table 2. Comparative analysis of children's mean age at time of assessment.

Lot		**Child's age during assessment (months)**
L0	**Mean value**	45,15
	N	75
	Standard deviation	10,350
L1	**Mean Value**	2,27
	N	25
	Standard deviation	1,438
Total	**Mean value**	37,76
	N	100
	Standard deviation	18,822

2.4 The importance of hearing loss diagnosis by recording BAEP, ASSR and conditioned play and behavioral audiometry

According to the sensorineural hearing-impaired patient's health records, the complex audiological balance was performed within the Republican Center for Audiology. The investigation protocol of the patient, suspected of hearing impairment includes a series of objective and behavioral investigations, allowing to confirm the diagnosis. The recording of brainstem auditory-evoked potentials (BAEP) detected their presence or absence, as well as due to the V wave intensity in Db (tabs 3, 4).

Table 3. Comparative analysis of BAEP results on the left ear

	L0		**L1**		**Total**		**x^2**	**gl**	**P**
	Nr.	**%**	**Nr.**	**%**	**Nr.**	**%**			
V wave presence 50 dB	2	2,66%	0	0,0%	2		48,121	11	<0,0001
V wave presence 60 dB	13	17,33%	1	4,0%	14		48,121	11	<0,0001
V wave presence 65 dB	0	0,0%	1	4,0%	1		48,121	11	<0,0001
V wave presence 70 dB	5	6,66%	0	0,0%	5		48,121	11	<0,0001
V wave presence 80 dB	7	9,33%	2	8,0%	9		48,121	11	<0,0001

V wave presence 80 dB, 7,20/6,60	15	20,0%	0	0%	15		48,121	11	<0,0001
V wave presence 90 dB	9	12,0%	6	24,0%	15		48,121	11	<0,0001
V wave presence 90 dB, 6.28/6.32	1	1,33%	1	4,0%	2		48,121	11	<0,0001
V wave presence 90 dB, 6.68/6.52	5	6,66%	1	4,0%	6		48,121	11	<0,0001
V wave absence	19	25,33%	14	56,0%	33		48,121	11	<0,0001
Total	75	100%	25	100%	100		48,121	11	<0,0001

The statistical analysis of the BAEP right ear results (table 4) revealed the following values of the statistical parameters: $x^2 = 27.306$; gl = 7; P = 0.000, and for BAEP left ear: $x^2 = 48.121$; GL = 11; P = 0.000.

Table 3. Comparative analysis of BAEP results on the right ear

	L0		**L1**		**Total**		**x^2**	**gl**	**P**
	Nr.	**%**	**Nr.**	**%**	**Nr.**	**%**			
V wave presence 50 dB	4	5,33%	0	0,0%	4	4,0%	27,306	7	<0,0001
V wave presence 60 dB	13	17,33%	1	4,0%	14	14,0%	27,306	7	<0,0001
V wave presence 70 dB	18	24,0%	4	16,0%	22	22,0%	27,306	7	<0,0001
V wave presence 80 dB	21	28,0%	16	64,0%	37	37,0%	27,306	7	<0,0001
V wave presence 90 dB	17	22,66%	5	20,0%	22	22,0%	27,306	7	<0,0001
V wave absence	2	2,66%	0	0,0%	2	2,0%	27,306	7	<0,0001
Total	75	100%	25	100%	100	100%	27,306	7	<0,0001

All subjects involved in the research groups were subjected to ASSR *(auditory steady state response)* - early evoked auditory potentials with modulation and amplitude. The ASSR results showed the following: absent potentials, presence at 500 Hz, presence at 1000 Hz, presence at 2000 Hz, presence at 4000 hz (Tables 5 and 6). Both left and right ears were assessed separately.

Table 5. Comparative analysis of the right ear-ASSR results

	L0		L1		Total		x^2	gl	P
ASSR	**Nr.**	**%**	**Nr.**	**%**	**Nr.**	**%**			
Presence at 500 Hz, 1000 Hz, 2000 Hz	69	92,0%	24	96,0%	93	93,0%	17,303	3	0,001
Presence at 500 Hz, 1000 Hz, 2000 Hz,4000 Hz	6	8,0%	1	4,0%	7	7,0%	17,303	3	0,001
Total	75	100,0%	25	100,0%	100	100,0%	17,303	3	0,001

Table 5. Comparative analysis of left ear-ASSR results

	L0		L1		Total		x^2	gl	P
ASSR, Hz	**Nr.**	**%**	**Nr.**	**%**	**Nr.**	**%**			
Presence at 500,1000	2	2,66%	0	0,0%	2	2,0%	34,642	3	<0,001
Presence at 500,1000, 2000	66	88,0%	23	92,0%	89	89,0%	34,642	3	<0,001
Presence at 500,1000,2000,4000	7	9,33%	2	8,0%	9	9,0%	34,642	3	<0,001
Total	75	100,0%	25	100,0%	100	100,0%	34,642	3	<0,001

The statistical analysis of the right-ear ASSR results showed the following values of the statistical parameters: $x^2 = 17,303$; gl = 3; P = 0.001, and for left ear- ASSR results: $x^2 = 34.642$; gl = 3; P = 0.000.

The assessment of sensorineural hearing-impaired patients via the ASSR method allowed to both attest the diagnosis and define the hearing threshold in each patient. The hearing cut-off point values are presented in Table 6, which were established via ASSR method, for each individual, involved within the study and from both study groups.

Table 7. Hearing cut-off point according to ASSR results:

	L0		L1		Total		x^2	gl	P
ASSR	**Nr.**	**%**	**Nr.**	**%**	**Nr.**	**%**			
50 dB	8	10,66%	1	4,0%	9	98,0%	24,141	4	<0,001
60 dB	17	22,66%	1	4,0%	18	1,0%	24,141	4	<0,001
70 dB	11	14,66%	0	0%	11	1,0%	24,141	4	<0,001
80 dB	28	37,33%	6	24,0%%	35	100%	24,141	4	<0,001
90 dB	11	16,66%	17	68,0%	28		24,141	4	<0,001
Total	75	100%	25	100%	100	100%	24,141	4	<0,001

The statistical data processing of the ASSR results exhibited the following values of the statistical parameters: $x^2 = 24,141$; gl = 4; P <0.001.

The complex auditory assessment diagnosed the following disorders: bilateral sensorineural hearing loss, unilateral sensorineural hearing loss, a bilaterally mixed type hearing loss. Depending on the type of hearing impairment, the final diagnosis results are presented in table 7

2.5 Conventional prostheses and cochlear implants in hearing loss rehabilitation

All the patients involved within the study were diagnosed according to the international protocol on sensorineural hearing loss, approved by the *International Bureau of Pathology and Audiology Balance*. The sensorineural hearing-impaired patients were assessed in terms of recovery and rehabilitation efficiency, and who underwent a conditioned-play free-field audiometry, after being diagnosed, as well as over 1 year, following a prosthetic rehabilitation or cochlear implantation. The study results were compared in both research groups, which involved the patients who were diagnosed with sensorinural hearing loss, following the newborn hearing screening and patients, diagnosed at the Republican Center for Audiology, Auditory Prosthesis and Medico-Pedagogical Rehabilitation, as well as at parents' personal request or being referred by other specialists (Table 8).

Table 8. The comparative study of auditory rehabilitation in children diagnosed by screening according to reflective free- field audiometry data

Hearing parametres	„Newborn hearing screening" group (n=25)	„ complex assessment on request" (n=75)	P
RE 500 Hz	51,83	70,91	0,028
RE 1000 Hz	63,22	78,02	< 0,001
RE 2000 Hz	69,25	84,00	0,086
RE 4000 Hz	71,98	81,10	< 0,001
RE 6000 Hz	70,55	82,15	0,009
RE 500 Hz	63,25	79,27	0,004

RE 1000 Hz	71,75	83,31	< 0,001
RE 2000 Hz	72,62	86,10	0,014
RE 4000 Hz	69,64	79,18	0,021
RE 6000 Hz	66,14	76,53	< 0,001

The data analysis presented in table 8 shows a statistically significant difference of the results of the reflective audiometry in free field in children, who were early diagnosed and underwent an early prosthetic rehabilitation, compared to children who were much later diagnosed and, thus, showing poor auditory rehabilitation rate. The studied audiometric frequencies included: 500 Hz, 1000 Hz, 2000 Hz, 4000Hz, 6000 Hz, which were used in assessment of both ears, separately. The results were measured in dB for each individual ear, at each of the frequencies (see Figures 4 and 5).

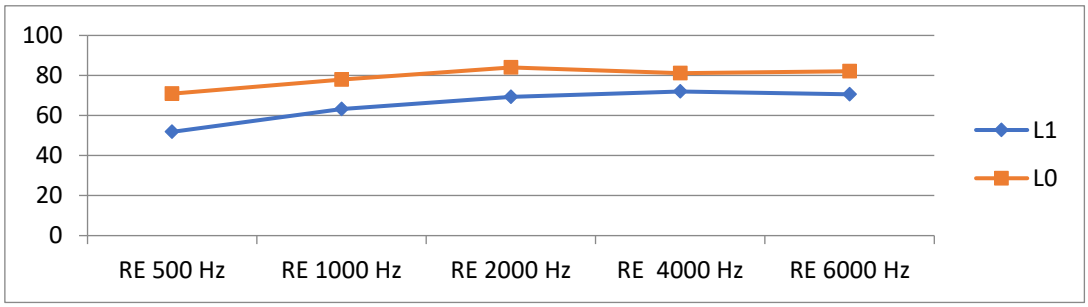


Figure 4. The comparative analysis of free- field reflective audiometry

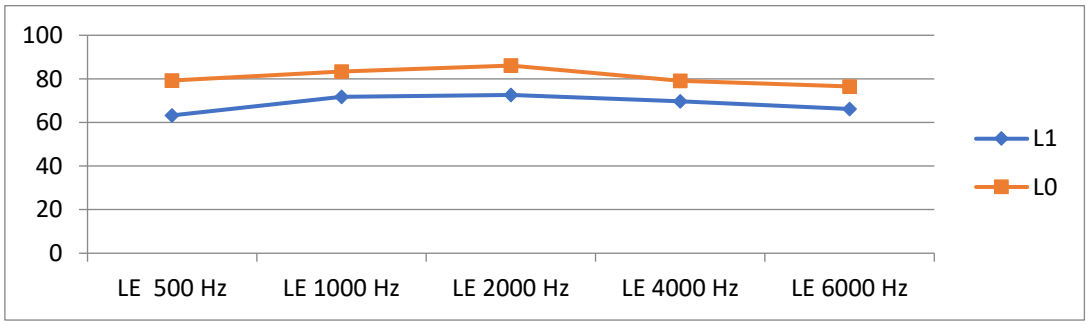


Figure 5. The comparative study of free-field reflective audiometry (Cochlear implants vs. hearing prostheses.)

Another research issue was related to the hearing-speech rehabilitation of unilateral cochlear implant patients, compared to those implanted bilaterally and those with digital prostheses. The results obtained are presented in table 9.

Table 9. Comparative analysis of auditory rehabilitation in cochlear implant patients and binaural hearing aids

	RE 500 Hz	**RE 1000 Hz**	**RE 2000 Hz**	**RE 4000 Hz**	**RE 6000 Hz**	**LE 500 Hz**	**LE 1000 Hz**	**LE 2000 Hz**	**LE 4000 Hz**	**LE 6000 Hz**	**gl**	**F**	**P**
Binaural hearing aids	63,09 dB	68,95 dB	72,17 dB	71,19 dB	70,73 dB	75, 87 dB	72,2 0 dB	76,2 7 dB	76,76 dB	78,5 4 dB	1	2,5 88	0,112

Unilateral Cochlear implant	56,15 dB	57,69 dB	56,67 dB	55,45 dB	63,46 dB	65, 54 dB	66,1 5 dB	66,1 7 dB	66,27 dB	67,1 3 dB	3	4,2 50	0,008
Bilateral Cochlear implant	38,75 dB	36,25 dB	36,25 dB	35,00 dB	33,75 dB	33, 75 dB	36,2 5 dB	33,7 5 dB	35,00 dB	35,2 5 dB	3	8,6 40	<0,001

SUMMARY OF THE RESEARCH FINDINGS

Due to the newborn hearing screening, by testing the presence of OAEs in children from the study group , who underwent the newborn hearing screening, the mean age for diagnosing sensorineural hearing loss was 4.33 months (standard deviation = 1.810), compared to 45.68 months (standard deviation = 10.074) of the study group, which was subjected to a traditional diagnostic method.

The research findings revealed a statistically significant difference between children with early prosthetic diagnosis, who followed a free-field reflective audiometry, compared with children in which the diagnosis was confirmed much later (P <0.001).

The present research results and data provided within our study and according to recommendations of the International Bureau for Audiophonology (BIAP), showed that early childhood is the optimal period for child's brain plasticity, thus , the conjugated effect of the earliest natural exposure might facilitate exposure to close and varying environmental sounds, which is provided by an early hearing aid, and thus optimizing the development of the child's hearing abilities. In the absence of early, regular, qualitative sound stimuli, the cortical auditory areas can be colonized by neurons from the other pathways. Therefore, early preventive measures should be carried out before these structural changes might occur and steadily install, or even become irreversible after a certain age.

Our study contributes to optimizing the early diagnosis of sensorineural hearing loss in children, thus enhancing its optimal rehabilitation. The research findings allow to conclude that the prosthetic rehabilitation in children with deep sensorinural hearing loss via cochlear implantation is obviously superior to the auditory prosthetic rehabilitation. Most concerned specialists share the same opinion, especially in recent years, when the cochlear implant recovery is widely applied in pediatric audiology. Thus, the present research data allow to affirm that treatment of deep sensorineural hearing loss in cochlear implant children can be widely used through a national program over the Republic of Moldova.

CONCLUSIONS AND RECOMMENDATIONS

GENERAL CONCLUSIONS

1. The detailed analysis of the anamnestic data, risk factors and genetic-molecular patterns , have outlined a number of risk factors that increase the hearing loss incidence among children, such as: : low amniotic fluid period for over 6h (P <0.05), asphyxia with intubation (P <0.05), preterm birth (P < 0.05), a child's delay in holding head up (P <0.05), a delay in sitting up (P <0.05), a child's walking delay (P <0.05), meningitis (P <0.05), influenza (P <0.05), cytomegalovirus (P <0.05), ototoxic antibiotic use (P <0.05), intoxications (P <0 , 05), whereas this information can be used as means of preventing hearing loss in children.

2. The recording of OAEs, is an objective, noninvasive method, easy to perform, and showing a high sensitivity and specificity, which can be used as a universal newborn hearing screening; thus, the comparative study of the mean age values, at which sensorineural hearing loss was diagnosed represented 4.33 months (standard deviation = 1.810), compared with 45.68 months (standard deviation = 10.074) in those children who did not undergo the newborn hearing screening.
3. The final diagnosis of deafness in infants and young children can be established only following a complex hearing assessment, which includes the use of objective electrophysiological methods: OAEs ($x^2 = 0.337$; gl = 1; P = 0.562), BAEP ($x^2 = 27.306$; gl = 7; P<0.001), BERA and ASSR ($x^2 = 24.141$; gl = 4; P <0.001), as well as due to the conditioned play and behavioral audiometry data.
4. Early auditory prosthesis exhibits a positive dynamics in hearing function development among children with moderate and moderate-severe hearing impairment (P <0.001).
5. Cochlear implant children showed a considerable improvement of the hearing function compared to children with auditory prostheses (P <0.001), which confirms a greater effectiveness of the cochlear implant prosthetic rehabilitation compared to auditory prosthesation in cases of deep severe hearing loss (P = 0.008).
6. The algorithm developed on the basis of the present study, requiring a complex medical assistance, allows to establish an early and proper diagnosis of pediatric hearing impairment, as well as determine an individual approach for subsequent prosthetic and psycho-pedagogical rehabilitation.

PRACTICAL RECOMMENDATIONS

1. To routinely apply the universal newborn hearing screening to all newborns within the maternity units via a national state program.
2. To carry out the molecular-genetic screening on all the subjects diagnosed with non-syndromic sensorineural hearing impairment.
3. ENT physicians and audiologists should use an algorithm for determining the diagnosis and for auditory rehabilitation of sensorineural hearing-impaired children.
4. To apply early auditory rehabilitation methods via conventional prosthesis or cochlear implantation.
5. To implement a national state program for cochlear implantation in all children diagnosed with deep sensorinural hearing loss.
6. All the practical recommendations outlined within the present research findings and data should be referred to the ENT doctors, audiologists, neonatologists, geneticists, family doctors, and therapists.

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- **Active participations at scientific forums:**

✓ **International attendance**

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ANNOTATION

Doina Chiaburu-Chiosa. Optimization of early diagnosis and auditory rehabilitation in children with sensorineural hearing loss. PhD thesis in Medical Sciences. Chisinau, 2019.

The research work comprises 112 edited pages, including introduction, 4 chapters, general conclusions, practical recommendations, and 255 bibliographic sources. The research findings were published within 32 scientific works, as well as used wihin national and international oral presentations.

Keywords: sensorineural hearing loss, deafness, otoacoustic emissions, newborn hearing loss screening, brainstem-evoked potentials, auditory prostheses, cochlear implants.

Research domain: Otolaryngology

Purpose of the study: To assess the etiological diagnosis of hearing loss in children based on the anamnestic data and molecular-genetic evaluations. To determine the diagnostic importance of transient otoacoustic emissions in newborn hearing screening. To highlight the diagnostic patterns of sensorineural deafness in newborns by recording OAEs, ASSR, BERA and conditioned play and behavioral audiometry. To study the effectiveness of newborn hearing screening in the auditory rehabilitation process of hearing-impaired children. To provide the auditory function assessment in children with sensorineural hearing loss following a prosthetic rehabilitation by means of hearing aids or cochlear implants. To develop an algorithm for early diagnosis and auditory rehabilitation of sensorineural hearing-impaired children.

The scientific novelty of the research: This present clinical study, aimed at assessing the newborn hearing screening findings was conducted for the first time in the Republic of Moldova, which included the recording of the otoacoustic emissions and the study of the risk factors for developing a diagnostic and rehabilitation algorithm for sensorineural hearing loss.

The scientific issue to be solved: Early diagnosis of sensorineural hearing loss in children, followed by an optimal early rehabilitation.

Theoretical significance: The study results will enable the early diagnosis of sensorineural hearing loss in children, as well as to improve the genetic counseling for patients with non-syndromic hearing loss.

The applicative value of the research: The results of the study encourage the use of the acoustic testing within the newborn hearing loss screening, providing reliable research findings

Implementation of the scientific results: The study results were implemented within the clinical activity at the Republican Center for Audiology, Auditory Prosthesis and Medico-Pedagogical Rehabilitation, and at IMC Emilian Coţaga Clinic, as well as in the teaching activity of the Department of Otolaryngology, at “Nicolae Testemitanu" SUMPh.

DOINA CHIABURU-CHIOSA

OPTIMIZATION OF EARLY DIAGNOSIS AND AUDITORY REHABILITATION IN CHILDREN WITH SENSORINEURAL HEARING LOSS

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