VILNIUS UNIVERSITY

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The Functional Results and Prognostic Factors of Pediatric Cochlear Implantation

SUMMARY OF DOCTORAL DISSERTATION

Biomedical Sciences,
Medicine 06 B

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The doctoral dissertation was prepared at Vilnius University during the period of 2013–2018.

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Vaikų kochlearinės implantacijos funkciniai rezultatai ir prognostiniai veiksniai

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INTRODUCTION

Hearing loss (HL) is the most frequent congenital disability in developed countries. Out of every 1000 children, 1 to 3 are born with sensorineural hearing loss, and another 1 to 2 out of 1000 children develop hearing loss later. According to the World Health Organization, in 2018, approximately 466 million people all over the world were diagnosed with HL, 34 million of them being children. (*Deafness and Hearing Loss*, http://www.who.int/en/news-room/fact-sheets/detail/deafness-and-hearing-loss). According to the Compulsory Health Insurance Fund data, 2156 Lithuanian children were diagnosed with deafness or hearing loss in 2017 (4.25 of 1000 children) (*Lietuvos gyventojų sveikata ir sveikatos priežiūros įstaigų veikla 2016 m.*).

One third of congenital sensorineural hearing loss cases are profound or severe. Such a hearing loss has long-term consequences in both the child's and the family's life. Hearing loss has a distinct negative effect on the development of the spoken language, and that consequently affects everyday communication and limits learning and literacy; therefore, a child's achievements and abilities of employment suffer, causing psychosocial problems. (Schroeder et al. 2006; Marschark & Spencer 2010). A lack of auditory information in early childhood interrupts with the development of the auditory system of deaf children, as in the absence of acoustic stimulation, the auditory cortex reorganizes to receive information from other senses (vision, for example) – cross-modal reorganization occurs (Sharma & Glick 2016a). When the critical period of brain development ends, the auditory cortex can no longer process auditory information, even though primary centers frequently react to the stimulation of the cochlear nerve after cochlear implantation (CI) (Nishimura et al. 1999) It is essential that the period from the onset of bilateral deafness until medical intervention – hearing rehabilitation with hearing aids (HA) or cochlear implants (CI) – is as short as possible (Nicholas & Geers 2007). Universal hearing screening dramatically improved the

diagnosis of congenital hearing loss (CHL) and the speech and language results of children with hearing impairment (Shani J. Dettman, Pinder, Briggs, Dowell & Leigh 2007).

A cochlear implant is an electronic medical device used to restore hearing for deaf people. A CI processor transforms environmental sounds into an electric signal, and the electrode array inserted into the inner ear cochlea transmits this signal to the cochlear nerve. The impulse then travels to the cerebral cortex, and the implanted person is able to hear because of this. In recent decades, revolutionary solutions in HL diagnostics, implant technology, sound processing, surgical techniques, programming and special education gave the possibility for deaf children to not only understand spoken language but to speak as well. This progress proved cochlear implantation is a safe and effective method for restoring hearing (F. Forli 2011).

CI results are widely studied. CI gives the opportunity to hear, positively affects speech and language development, improves educational achievements, employment possibilities and quality of life. The effect on society manifests by the decreased expenses for the education of the deaf and increased work productivity (Bond et al. 2009). The results of cochlear implantation are assessed in steps: first – hearing and speech perception, later – speech and language development, and then – integration to the general education, quality of life and others. Based on the scientific literature, speech perception and speech intelligibility levels of half of children who are CI users can be the same as of their hearing peers (A. E. Geers, Moog, Biedenstein, Brenner, & Hayes 2009). In a 2016 review, Monteiro claims that the speech perception of 81% of children aged 12–48 months after implantation was within normal limits, and the speech and language development of 57% of children matched the results of their peers (C. G. Monteiro, Cordeiro, Silva & Queiroga 2016).

Individual results still differ a lot. A huge variability in speech perception and language development results is observed (Ann E. Geers, Strube, Tobey, Pisoni & Moog 2011a; Tobey et al. 2013). It

was proved that age at implantation is the most important prognostic factor of cochlear implantation – the earlier the implantation is performed, the better the results are. Other important factors are: internal and biological – the etiology of deafness, a child's intelligence; external and technical – implant characteristics, programming; social – the possibilities of speech and language therapy, parents' engagement in the learning process, and others (Driver & Jiang 2017). The establishment of prognostic factors helps to predict results for an individual patient and build real expectations for the family, plan implantation and rehabilitation process after the CI to achieve the maximal benefit (Peterson, Pisoni & Miyamoto 2010).

The first cochlear implantation in Lithuania was performed in 1998 in the Lithuanian University of Health Sciences by Professor S. Harris. Today, there are about 370 CI users in Lithuania.

Only early postoperative results of CI were evaluated in Lithuania (Byčkova, Gradauskienė, Lesinskas, Mikštienė & Utkus 2012). Long-term results, such as speech perception, speech and language development, integration into general education have not yet been studied in the Lithuanian population. Such factors as the etiology of deafness, the radiological anatomy of the inner ear and social factors that might affect the effectiveness of CI were not studied as well. The genomics of Lithuanian congenital hearing loss were recently studied by Violeta Mikstiene, in 2017. However, the etiology of pediatric deafness in general has not been studied yet. Half to two thirds of congenital HL cases are hereditary. The remaining cases are nonheritable – environmental or of unknown etiology. Mutations of the *GJB2* gene are found in 30% of cases of congenital deafness (Chan & Chang 2013). A congenital CMV (cCMV) infection is the second most frequent cause of CHL and accounts for 10–30% of CHL cases. Usually, a cCMV infection is asymptomatic; therefore, specific tests are not performed at birth. However, HL can develop after several months or even years. The detection of the prevalence of cCMV infection is still a relevant problem all over the world (Rawlinson et

al. 2017) Different populations have characteristic geographical, ethnic, social, medical, and genetic factors that generate a unique etiologic profile of HL. This is the first study to determine the etiological profile of deaf Lithuanian children who are CI users, and this study will enable the evaluation of the prevalence of genetic factors, cCMV infections and other risk factors as well as the establishment of recommendations for the creation of CI program guidelines.

It is known that best results are demonstrated in countries with a CI program, including early HL diagnostics, preoperative preparation, surgical implantation procedures and full postimplantation service: technical, medical, psychological, social, and financial support (Moeller, Carr, Seaver, Stredler-Brown & Holzinger 2013). Despite the fact that pediatric CI has been performed in Lithuania for already two decades, such a program is still lacking. This study attempts to prepare recommendations for developing a Lithuanian CI program. This program will help optimize the selection of candidates and postoperative rehabilitation, and improve the social integration of deaf children with CI.

In conclusion, it can be claimed that the evaluation of CI results and the establishment of prognostic factors is a relevant clinical and scientific problem. This study was the first in Lithuania to assess the etiology of hearing loss, postoperative results, and prognostic factors amongst pediatric CI users. The results of this doctoral dissertation might widen the clinical, social and educational means for optimizing the results of pediatric CI in Lithuania and improve indices of public health.

AIMS OF THE STUDY

To assess the functional results of cochlear implantation in children and determine their prognostic factors.

OBJECTIVES OF THE STUDY

1. To identify the etiology of hearing loss amongst pediatric cochlear implant users by performing genetic testing, detecting CMV DNA in dried blood spots, analyzing perinatal risk factors and, therefore, establishing the etiological profile of the study sample.
2. To evaluate the anatomical malformations of the inner ear of pediatric cochlear implant users by analyzing images of the temporal bone made by computed tomography.
3. To evaluate the speech perception results of deaf children after cochlear implantation.
4. To evaluate the results of speech and language development after pediatric cochlear implantation.
5. To determine prognostic factors for the outcomes of pediatric cochlear implantation.

1. MATERIALS AND METHODS

This multicenter, interdisciplinary, cross-sectional study was performed during 2013–2018 in Vilnius University, Faculty of Medicine, at the Clinic of the Ear, Nose, Throat and Eye Diseases, as well as in the Children's Hospital, affiliate of Vilnius University Hospital Santaros Klinikos (VUHSC), at the Children's Otorhinolaryngology and Ophthalmology Department. The local Vilnius Regional Biomedical Research Ethics Committee approved the protocol of this study (No. 158200-15-786-298)). An individual informed consent form was read and signed by parents or caregivers of each study participant prior to the inclusion to the study. The ethical principles of the Declaration of Helsinki for medical research involving human subjects were fulfilled.

The scheme of the study was planned at the beginning of the research, and data were collected based on the design of the cross-sectional study – the preoperative, surgical, and postoperative data of each participant were collected, etiologic factors tested, and postoperative hearing and speech results assessed all at the same time:

- In order to evaluate the *preoperative*, *surgical*, and *postoperative* factors that might influence CI results, the parents of participants were interviewed, and medical documentation reviewed: demographic, medical, audiological, surgical, and family data, as well as data regarding rehabilitation and education, were collected;
- To determine the *etiology* of hearing loss, anamnestic risk factors of hearing loss were assessed, genetic testing performed, and CMV DNA detected in dried blood spots;
- To determine any *inner ear malformations* that might influence CI results, a thorough analysis of preoperative temporal bone CT images was performed;
- Postoperative *hearing results* were evaluated using scales, the sound field warble tone and speech audiometry;

- Postoperative *speech and language results* were assessed during evaluations performed by teachers of the deaf.

After analyzing the collected demographic, medical, audiologic, surgical, and family data, as well as data about hearing rehabilitation, educational settings and postoperative results, the prognostic factors of pediatric CI were defined (Fig. 1).

The objectives of the scientific study were achieved in collaboration between an otorhinolaryngologist-audiologist (author of the study), a nurse audiometrist, a geneticist, radiologists, an otorhinolaryngologist, teachers of the deaf, speech and language therapists, a statistician, a laboratory medicine doctor and a medical student.

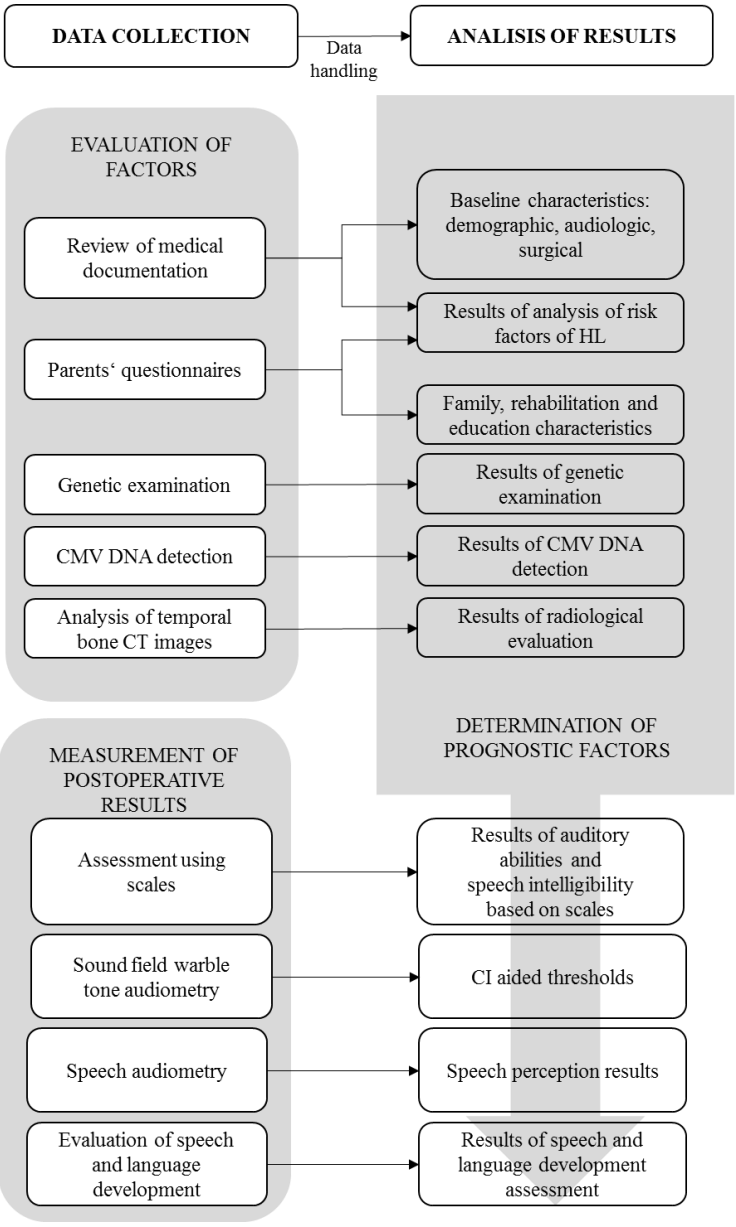


Figure 1. Scheme of the study.

1.1. Sampling

The sample of the study included children who underwent unilateral or bilateral cochlear implantations in Vilnius University Hospital Santaros Klinikos, in the Clinic of Ear, Nose, Throat and Eye Diseases. Participants were chosen from the list of CI surgeries performed in 2005–2017 in Vilnius University Hospital Santaros Klinikos, in the Department of the Ear, Nose and Throat Diseases. Patients who met the inclusion criteria were informed about the study and suggested to participate during a scheduled visit to an otorhinolaryngologist-audiologist in the Children's Hospital, affiliate of Vilnius University Hospital Santaros Klinikos. Families of children who did not come to a visit were invited to participate by contacting the parents or caregivers via a phone call, using contact data found in medical documentation. One hundred thirty children with CI were found, 122 of them met the inclusion criteria:

1. Deaf children, who underwent one or two cochlear implantation surgeries;
2. Participants aged 1–18 years;
3. Cochlear implantation surgery performed in Vilnius University Hospital Santaros Klinikos at the Clinics of the Ear, Nose, Throat and Eye Diseases;
4. Unilateral or the first one of the bilateral CI surgeries performed not later than prior to 6 months;
5. Parents or caregivers of children agreed for their child to participate in the study and signed the informed consent form.

Cochlear implantation was performed for all participants in Vilnius University Hospital Santaros Klinikos during the period from July 5, 2005 to July 10, 2017. Implantation surgery was performed according to a general procedure, when, based on the description of the CI reimbursement procedure, the necessity of surgery and an additional processor was ascertained by the medical consultation of three otorhinolaryngologists of the Santaros clinics. All surgeries were performed by one experienced otosurgeon. Processors were turned on

and regulated, and their technical support maintained according to the manufacturers' guidelines by the representatives of the CI manufacturers MED-EL, Cochlear and Advanced Bionics in Lithuania.

Data of all **122** participants were used to assess general, family, hearing rehabilitation and educational characteristics and to determine the etiologic profile. In addition to this, all children participated when performing sound-field audiometries and evaluations of auditory abilities and speech intelligibility according to scales. A sound-field speech audiometry was only performed for children older than 5 years who were implanted at least 2 years ago – they composed a group of **95** participants. Fourteen more participants (children with severe additional disabilities, and children with an onset of HL after their 3rd birthdays) were excluded when assessing speech and language development and determining prognostic factors for speech perception and speech and language development (N=81) (Fig. 2).

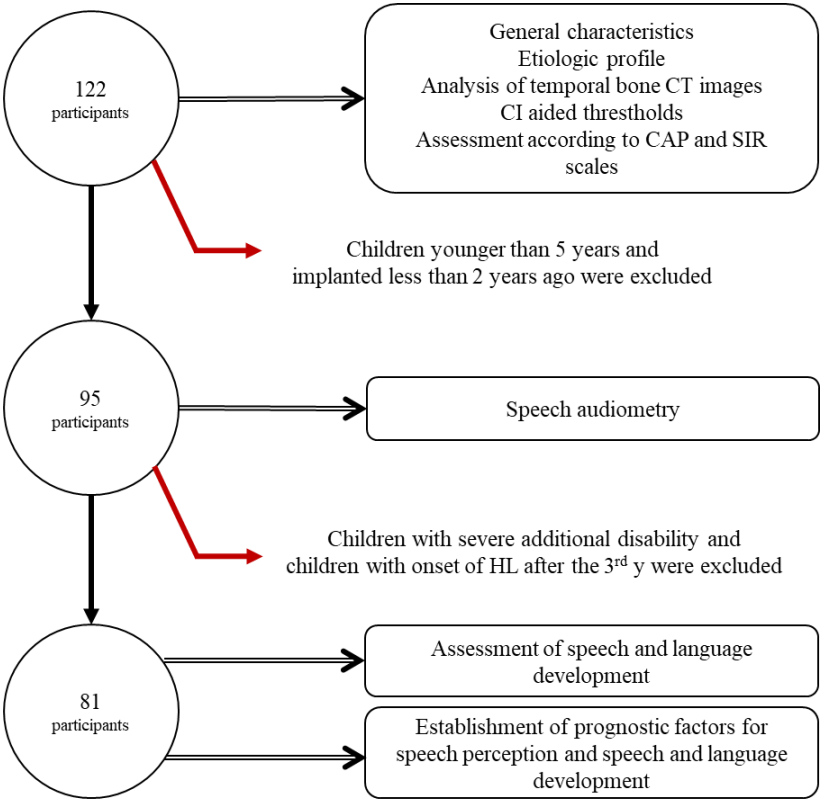


Figure 2. Flow-chart of the study.

1.2. Data Collection from Questionnaires and Medical Documentation

Questionnaires were filled in during the visit to an otorhinolaryngologist-audiologist; medical documentation reviewed from the in-patient and out-patient medical records, the electronic medical records of Vilnius University Hospital Santaros Klinikos and medical records from other healthcare institutions. According to the questionnaire prepared for the research, (a) medical, (b) hearing, (c)

surgical, (d) family, (e) hearing rehabilitation and education data were collected.

(a) **Medical documentation**. Prenatal, perinatal and postnatal risk factors for HL were recorded according to the list proposed by the Joint Committee of Infant Hearing from the medical documentation:

- Prematurity <32 weeks of gestation;
- Birth weight less than 1500 g;
- Severe perinatal hypoxia;
- Congenital TORCH infections: toxoplasmosis, syphilis, rubella, CMV, herpes;
- Newborn sepsis;
- Hyperbilirubinemia requiring blood transfusion;
- Ototoxic medication;
- Meningitis.

Data about any additional diseases that might have influence on postoperative results (visual impairment, cerebral palsy, epilepsy, developmental delay, autism, syndromes and other) were searched for as well.

(b) Audiological data were used to assess residual hearing before the implantation. Following hearing tests results and anamnesis, data were collected from the medical records:

- Age at diagnosis;
- Otoacoustic emission results;
- Brainstem Electric Response Audiometry (BERA) thresholds;
- Auditory Steady State Audiometry (ASSR) thresholds;
- Pure tone audiometry thresholds;
- HA aided thresholds;
- Duration of the hearing rehabilitation using HA;
- Onset and progression of HL.

Hearing thresholds prior to the CI were determined based on BERA results in case of the congenital HL, and based on age-appropriate last preoperative audiograms in case of acquired HL.

Mean hearing thresholds were calculated in a better hearing ear as well as in an implanted ear. Lower than 90dB hearing thresholds in the implanted ear (or in one of implanted ears) or in the contralateral ear were considered as residual hearing.

(c) Medical documents were reviewed for these **surgical and implant-associated** data:

- Date of the first/second implantation surgery;
- Side of the implantation/unilateral/bilateral;
- Age at first (second) implantation;
- CI device manufacture/processor/electrode array;
- Insertion of the electrode array;
- Complications (intraoperative, early and late postoperative);
- Programming of the speech processor;
- Speech coding strategy;
- Issues with the use of the CI processor (in case medical documentation included and/or parents declared about the inconsistent use of the processor or fitting problems during the first postoperative year).

(d) Family data were collected according to the Nottingham Children's Implant Profile (NChIP) using questionnaire:

- Size and structure of family;
- Parents' education level (different educational levels were grouped to three categories: higher education – at least 14 years of education (higher education); secondary education – 10 – 13 years of education (post-secondary, special secondary, secondary vocational, and secondary education); incomplete secondary education – less than 9 years of education (vocational school, lower-secondary and primary education)
- Parents' understanding of the CI process (based on the Pre-/Post-Implant Family Assessment Profile for PCI candidates (Hickson & Black 2012): parents understand the CI process when they have reasonable expectations consistent with hearing loss, demonstrate a good understanding of the CI

process and post-operative rehabilitation requirements, demonstrate good understanding of the level of commitment required and the impact this will have on the child's well-being; parents do not fully understand the CI process when they have some unreasonable post-operative expectations, demonstrate a sound understanding of CI processes and post-operative rehabilitation requirements, require additional information to aid understanding; parents do not understand the CI process when they demonstrate little understanding of the CI processes and post-operative rehabilitation requirements, have unreasonable high expectations and a reluctance to consider a professional's views, and are strongly reluctant to engage in the process);

- Frequency of follow-up (based on the recommendations for a follow-up of children after CI proposed by the Children's Hospital, affiliate of Vilnius University Hospital Santaros Klinikos, visits were considered sufficient if at least 5 visits were recorded over a 2-year period; insufficient – if 3–4 visits were recorded over a 2-year period; family did not attend consultations – 2 or less visits recorded during the first two years after the implantation);

(e) The following data about **hearing rehabilitation and education** were collected:

- Parents' engagement in the child's learning process (based on the NChIP profile: active participation – parents were interested in the child's outcomes and constantly communicate and interact with the child; passive participation – parents were interested with the result, but do not communicate with the child; no participation – parents were not interested with the result and do not communicate with the child);
- Communication mode (spoken language – when parents use only spoken language to communicate with the child, no additional visual cues are used; total communication – when

both, spoken and sign languages are used, child is lip-reading; sign language – when a child does not understand any words, signs only are used for communicating);

- The availability of speech and language therapy (based on the NChIP profile: available – there is a constant possibility to consult an experienced teacher of the deaf; moderately available – there is a possibility to consult an unexperienced teacher of the deaf; unavailable – there is no possibility to consult a teacher of the deaf);
- Intensity of the speech and language therapy (based on the frequency of visits to the teacher of the deaf per week during the two first years after the CI);
- Educational placement settings, program at school.

1.3. Evaluation of the Etiology of Hearing Loss

In order to establish all causes of hearing loss, risk factors were determined, genetic testing performed and CMV DNA extracted from dried blood spots.

1.3.1. Analysis of Risk Factors of Hearing Loss

An analysis of prenatal, perinatal and postnatal risk factors of hearing loss was performed using data retrieved from the questionnaires and medical records according to the aforementioned list of perinatal, prenatal and postnatal risk factors.

1.3.2. Genetic Examination

Genetic counselling and testing were performed by geneticist in Vilnius University Hospital Santaros Klinikos, at the Center for Medical Genetics (VUHSC CMG). Participants were divided into subgroups and examined based on the HL type. In case of isolated (non-syndromic) HL, *GJB2* gene sequencing was performed according to the procedure established by the VUHSC CMG. In the

absence of two pathogenic states, in case of signs of mitochondrial inheritance in genealogy or for patients with a complex perinatal anamnesis who were treated with aminoglycosides, the pathogenic state of the mitochondrial genome *MT-RNR1* 1555A>G was tested. Genes associated with a specific syndrome were tested for patients with a syndromic HL when a monogenic disease was suspected. *GJB2* gene sequencing was also performed for some patients with the syndromic HL to differentiate the cause of HL. When a chromosomal syndrome was suspected, karyotyping test or comparative genomic hybridization were performed. If the cause of HL remained unknown, a sequencing of 126 genes was performed in case of an isolated HL and positive genealogy (Fig. 3). Genomic DNA used for testing was extracted from the peripheral blood leukocytes using the standard phenol chloroform method.

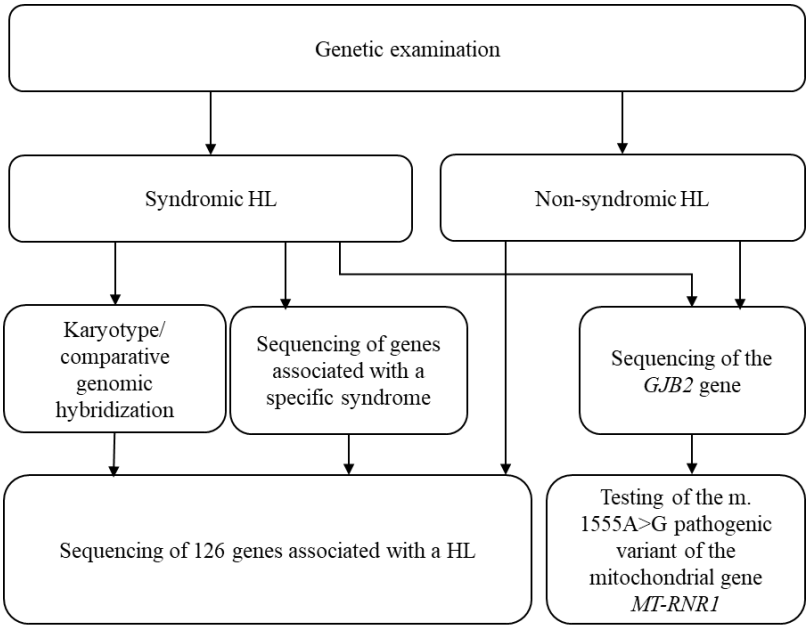


Figure 3. Scheme of the genetic examination.

1.3.3. Detection of the CMV DNA in Dried Blood Spot

In order to discover a possibly congenital cytomegalovirus (CMV) infection amongst the sample of the study, CMV DNA was detected in dried blood spots on the Guthrie cards. The examination was performed from September 2017 to April 2018 in Vilnius University Hospital Santaros Klinikos, at the Center of Laboratory Medicine (VUHSC CLM). Guthrie cards are filter-paper cards used for a universal neonatal screening of inherited metabolic disorders. The capillary blood of a newborn was collected onto a blood spot card on the 2^{nd} – 5^{th} day of life in a hospital. After screening for the metabolic disorder, cards with the remaining biologic content are kept in a VUHSC CLM archive. We used half of a dried blood spot for a every single DNA extraction (the diameter of a full spot is 10 mm), each sample was proceeded in triplicate. Scissors used for cutting the DBSs were cleaned with 70% ethanol between cards to avoid contamination. In each DNA extraction, blank DBSs were included for contamination control. CMV DNA was amplified using primers targeting the 105 bp region of the major immediate early (*MIE*) gene (artus CMV QS-RGQ, Qiagen). Real time PCR (Polymerase Chain Reaction) was performed on DNA triplicates. Results were assessed qualitatively. DBS sample considered positive when two or more DNA triplicates were CMV DNA positive (Fig. 4).

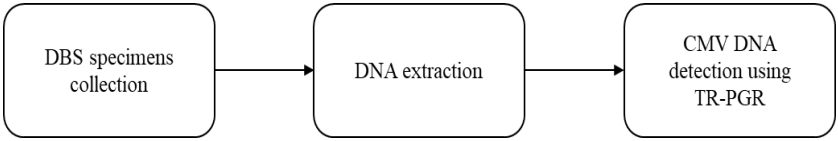


Figure 4. Scheme of the CMV DNA detection in dried blood spot.

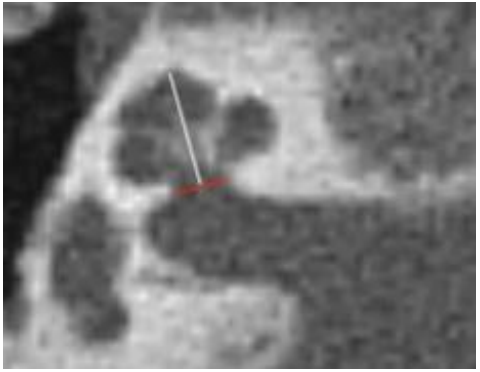
1.4. Evaluation of the Inner Ear Anatomy on Temporal Bone CT

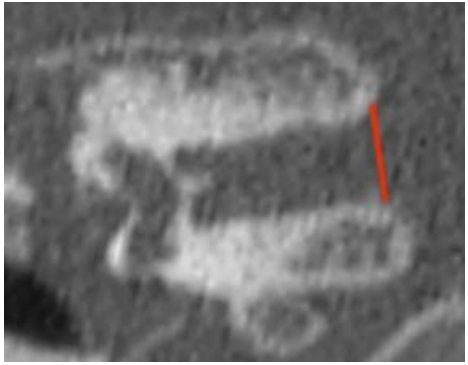
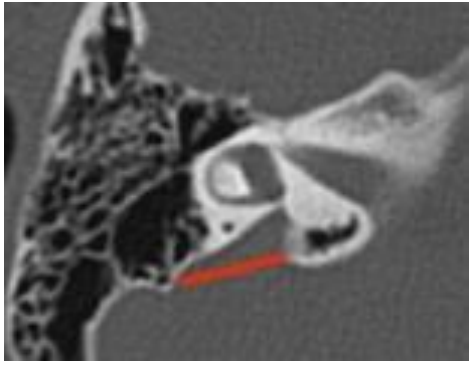
A retrospective analysis of preoperative temporal bone CT images, archived in the electronic medical system of VUHSC, was performed. High definition temporal bone CT images with <1-mm (0,7 mm on average) slice thickness were analyzed by an experienced radiologist in the VUHSC, at the Center of Radiology and Nuclear Medicine, using *Picture Archiving and Communications System* (PACS). *MultiPlanar Reconstructions* (MPR) of inner ear were performed as well. Evaluation was performed in two ways: major inner ear malformations (IEM) were assessed visually, small structures that might have effect on the CI results were measured additionally (Table 1). The architecture of the cochlea was considered abnormal in case of cystic cochlear changes and a decreased number of cochlear turns. The vestibule was considered abnormal in case it was dilated – when its transverse diameter was larger and the vestibule more rounded. Semicircular ducts were considered abnormal in case of defected integrity. Also, the radiologist measured all inner ear structures in detail in order to discover any delicate IEM that might have influence on postoperative results. All measurements were made in precisely described MPR planes – height of the cochlea, diameter of the bony cochlear nerve canal (BCNC), diameter of the internal acoustic meatus, diameter of the vestibular aqueduct. The descriptions by other authors about the technique of measurements were used to compare the result (Table 2). The cochlea was considered hypoplastic when its height was less than 3.3 mm. The BCNC was considered stenotic in case its diameter was equal or smaller than 1.4 mm. The internal acoustic meatus was considered stenotic when its diameter was smaller than 2 mm. The vestibular aqueduct was considered dilated when its width was more than 1.9 mm (D'Arco et al. 2017).

Table 1. An analysis of temporal bone CT images.

VISUAL EVALUATION	Architecture of the cochlea	Abnormal in case of decrease in number of turns, cystic cochlea
	Vestibule	Dilated in case transverse dimension is bigger, and vestibule rounder
	Semicircular canals	Abnormal in case of defected integrity
MEASUREMENTS	Height of the cochlea	Hypoplastic cochlea – height of the cochlear is smaller than 3.3 mm
	Diameter of the bony cochlear nerve canal	BCNC stenosis – diameter was equal or smaller than 1.4 mm
	Width of the internal acoustic meatus	Stenotic – when the width is smaller than 2 mm
	Width of the vestibular aqueduct	Dilated – when width is more than 1.9 mm

Table 2. Planes of radiologic measurements.

No	STRUCTURE	DESCRIPTION OF PLANES	IMAGES OF PLANES
1	Height of cochlea	The MultiPlanar Reconstruction depicts an X-shaped modiolus, cochlear nerve canal, cochlear canal. Measured is the distance from the center of the cochlear nerve canal to the apex of cochlea (Teissier, Van Den Abbeele, Sebag & Elmaleh-Berges 2010).	
2	Diameter of the cochlear nerve canal	Measured is the distance between the osseous parts of the canal aperture (Teissier, Van Den Abbeele, Sebag & Elmaleh-Berges 2010).	

3	Width of the internal acoustic meatus	The internal acoustic meatus is presented in the MultiPlanar Reconstruction. Perpendicularly measured is the distance between the osseous canal walls at the level of the *porus acusticus internus* (Shim, Snin, Chung, Lee, 2006).	
4	Width of the vestibular aqueduct	The MultiPlanar Reconstruction depicts the biggest width of the vestibular aqueduct. It is measured perpendicularly to the bony walls of the aqueduct (dilated vestibular aqueduct) (Vijayasekaran et al., 2007).	

1.5. Evaluation of Postoperative CI Results

A cross-sectional study was arranged to evaluate the postoperative results. All results, except for speech and language development, were assessed at the Children's Otorhinolaryngology and Ophthalmology Department of the Children's Hospital, affiliate of VUHSC. According to the hierarchic speech perception and speech and language development evaluation methodology, the assessment method was chosen based on the child's age. Hearing thresholds with CI in sound-field were tested for all participants as well as evaluated according to the CAP and SIR scales. Sound-field speech audiometry with CI, as well as an assessment of speech and language development, was performed only in the case the child was at least 5 years of age and was implanted at least 2 years ago.

1.5.1. Evaluation of Aided Thresholds and Speech Perception

CI-aided thresholds and open-set speech perception in quiet surroundings were evaluated during hearing assessments. Audiometric tests were performed with a diagnostic audiometer *Interacoustics AC 40* (Denmark), corresponding these standards: EN 60645-1/ANSI S3.6, 1 type, EN 60645-2/ANSI S3.6, A or A-E type, EN 60645 4/ANSI S3.6, EN 60601-1, I class, B type, EN 60601-1-2, calibrated according to ISO 389-1, ISO 389-3, ISO 389-7, IEC645-2. All hearing tests were performed in an audiometric booth, in which environmental noise did not exceed the permissible limits according to ISO 8253-2. All tests were performed by an audiometrist with long experience in pediatric audiology. The results were analyzed by the author.

The assessments of CI-aided thresholds were performed using warble tones following the standard procedure when the lowest sound intensity in 250, 500, 1000, 2000, and 4000 Hz frequencies is established for each ear separately. Loudspeakers were placed at a 45^{o} azimuth in a 1 m distance from the child. When testing binaurally, in

the case of bilateral CI, the loudspeaker was placed 1 m in front of the child at a 0° azimuth. Based on the child's age and psychomotor development, CI-aided sound field thresholds were assessed using visual reinforcement or play audiometry methods according to British Society of Audiology recommendations.

Open-set speech audiometry was performed in an audiometric booth according to standard procedure to assess speech perception levels using one or two CIs. Every child was presented with the list of 25 disyllabic phonetically balanced words at 65 dB SPL in quit with the loudspeaker positioned at a 0° azimuth in a 1 m distance from the child. The child was instructed to repeat words that he or she had heard. The speech perception score was calculated based on the number of correct words in percentages. Later, the results were classified according to speech perception levels (Table 3).

Table 3. Speech perception levels based on the results of speech audiometry.

Speech perception score (%)	Speech perception level
100–90	Excellent
89–75	Good
74–60	Average
59–50	Weak
<50	Very weak

Auditory abilities and the speech intelligibility of each child were assessed by an otorhinolaryngologist-audiologist during a visit using scales at least 6 months after surgery. Auditory abilities were evaluated using the *Categories of Auditory Performance* (CAP) scale proposed by Archbold and colleagues in 1995. CAP is a hierarchic scale reflecting the development of auditory abilities according to eight categories – from 0 to 7 (Table 4).

Table 4. Categories for auditory performance scale.

Category	Description
0	No awareness of environmental sounds
1	Awareness of environmental sounds
2	Responds to speech sounds
3	Recognizes environmental sounds
4	Discriminates at least two speech sounds
5	Understands common phrases without lipreading
6	Understands conversation without lipreading with a familiar talker
7	Can use the telephone with a familiar talker

Speech intelligibility was evaluated according to the *Speech Intelligibility Rating (*SIR) scale (Allen et al. 1998). SIR is a hierarchic scale, representing the development of speech intelligibility according to five categories – from 1 to 5 (Table 5).

Table 5. Speech intelligibility rating scale

Category	Description
5	Connected speech is intelligible to all listeners. The child is understood easily in everyday contexts.
4	Connected speech is intelligible to a listener who has little experience of a deaf person's speech. The listener does not need to concentrate unduly.
3	Connected speech is intelligible to a listener who concentrates and lip-reads within a known context.
2	Connected speech is unintelligible. Intelligible speech is developing in single words when context and lip-reading cues are available.
1	Pre-recognizable words in spoken language. The child's primary mode of everyday communication may be manual.

1.5.2. Evaluation of Speech and Language Development

In this study, the methodology for the evaluation of speech and language development, the *Book for Speech and Language Therapists* was used. It is designed for speech and language therapists working in educational psychological services and for teachers of the deaf working in Lithuanian Educational Center for the Deaf and Hard of Hearing (prepared by Gaulienė et al. in 2008). Speech and language development of children CI users was evaluated by speech and language therapists from educational psychological services according to the child's residence or by teachers of the deaf from the Lithuanian Educational Center for the Deaf and Hard of Hearing, who were taught the technique in specialized courses and are allowed to use this method. Six speech and language skills were assessed: speech intelligibility, vocabulary, grammar skills, pronunciation, phonological awareness and sound analysis. Speech and language therapists evaluated speech and language development by filling standard protocols of speech and language development. Final assessments were made by the group of independent experts – teachers of deaf with long experience in teaching and assessing deaf children with CIs. The experts had no interests associated with this study, they were only motivated to improve the integration of deaf Lithuanian children CI users. These experts analyzed the filled protocols taking into consideration the children's chronologic and hearing ages and described each speech and language area based on one out of four developmental levels: very good, good, satisfactory, and unsatisfactory. This was determined based on the nature of the mistakes the child made according to the qualitative analysis of results. The general speech and language development level was established after summarizing all 6 speech and language areas. In case of disagreement, a lower level was chosen. An agreement was reached when at least two out of three experts agreed. The speech and language development level was *very good* if a child's speech was developed, a child fulfilled all tasks covering different areas of speech and language

development without making any mistakes. Speech and language development was considered *good* when a child's speech was developed but the child pronounced one or several sounds incorrectly when performing given tasks, made one or several mistakes in phonemic perception, word building, word changing or combination in a sentence, mixed the meaning of infrequently heard words. Speech and language development was considered *sufficient* if a child's speech was developed sufficiently, the child made frequent, repeated mistakes in pronunciation, phonemic perception, vocabulary, grammatical speech structure, and speech perception. Speech and language development was considered *insufficient* when a child's speech was not developed: the child would not understand the majority of tasks and could not perform them. The *Book for Speech and Language Therapists* was chosen as it covers a wide age range; it is well mastered by speech and language therapists working in educational psychological services and is comprehensive as well. All evaluations were performed with the permission from the Lithuanian Bioethics Committee, when a collaboration agreement was signed between the National Center for Special Needs Education and Psychology, the Lithuanian Educational Center for the Deaf and Hard of Hearing and VUHSK, and only after the parents of participants signed the informed consent form.

1.6. Establishment of Prognostic Factors for Pediatric CI

The prognostic factors of pediatric CI were established using methods of statistical analysis meant to find dependence between different demographic, audiologic, surgical, etiologic, radiological, family, rehabilitation and educational variables and results of speech perception and speech and language development. Univariate and multivariate regression analyses were used to establish and evaluate factors that might be prognostic as significantly associated with the results of CI.

1.7. Statistical Analysis

Descriptive statistics (mean, standard deviation, minimal and maximal values, median, and mode) were used to systematize the results. The distribution normality of qualitative indices was verified by carrying out the Kolmogorov-Smirnov test and evaluating the histogram.

Possible associations between variables were determined using the Pearson correlation coefficient for nominal variables, and the Spearman correlation coefficient – for categorical variables. The nonparametric Mann-Whitney-Wilcoxon test (two independent samples) or the Kruskal-Wallis test (more than two independent samples) were used to verify the hypotheses concerning intergroup differences among variables. The results were considered significant when p value is <0.05.

The logistic regression analysis was used to define the influence of individual factors which were used in the case of the binary categorical dependent variable. The logistic regression model was considered appropriate if the χ^2 and Wald criterion p-value was less than 0.05, at least 50 percent of values were correctly classified and the chosen determination coefficient R^2 was equal or greater than 0.2. The Odds Ratio indicated the likelihood of *Y* to reach 1 varies.

Data handling and analysis were performed with MS Excel, IBM Statistical Package of the Social Sciences (SPSS) version 21.0 software (SPSS Inc., Chicago, IL) and the MedCalc 18.11.3 software.

2. RESULTS

2.1. General Characteristics of the Participants

The study population consisted of 122 children (70 male, 57% and 52 female, 43%) who underwent one or two cochlear implantation surgeries in Vilnius University Hospital Santaros Klinikos (VUHSC), at the Center of the Ear, Nose, Throat and Eye Diseases. The study population constituted 43.1% of the general population of deaf Lithuanian children who had underwent CI surgery during the years 1999 to 2017 (N=283) (Mataitytė-Diržienė et al. 2018).

Sixty-five (53.3%) children received unilateral CIs (the right ear was implanted in 47 cases, the left – in 18 cases). Fifty-seven (46.7%) – bilateral CIs (sequential surgeries were performed in 34 (59.6%) cases, simultaneous CI – in 23 (40.4%) cases). Three participants underwent reimplantation due to the malfunction of an implant (2 of them – after a head trauma). An electrode array was inserted fully in all 179 ears implanted.

The mean age of children at the time of inclusion to the study was 7.6 ± 3.3 years (Table 6, Fig. 5). The majority of the participants – 86 (70.5%) – were preschoolers and primary school-age children.

Table 6. The demographic characteristics of the participants.

	Age at first implantation, months	Age at second implantation, months	Duration of the implant use, years	Age at the time of the study, years
N	122.0	57.0	122.0	122.0
Mean	32.5	32.3	4.9	7.6
Median	21.0	23.0	5.0	8.0
Mode	11.9	12.0	5.0	8.0
Standard deviation	26.9	22.1	2.6	3.3
Minimum	10.3	10.0	0.6	2.0
Maximum	162.7	112.0	12.0	17.0

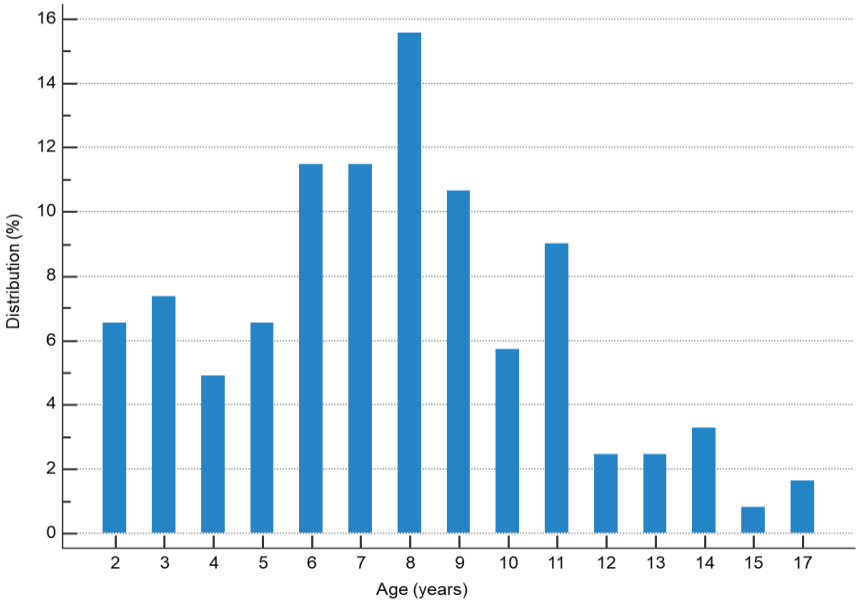


Figure 5. Age distribution amongst participants at the time on inclusion to the study (years).

Mean age during the first CI surgery was 32.5 ± 26.9 months. The youngest implanted child was 10 months of age, the oldest – 162 months old (Table 6, Fig. 6). The mean age of children born after 2014, when universal newborn hearing screening was introduced in Lithuania, was 14.56 ± 4.91 months during the first CI surgery and differed significantly compared to the age at first implantation of children born before 2014 (36.47 ± 28.1 months), $p<0,001$. On average, participants used their CI for 4.9 ± 2.6 years (Table 6, Fig. 7).

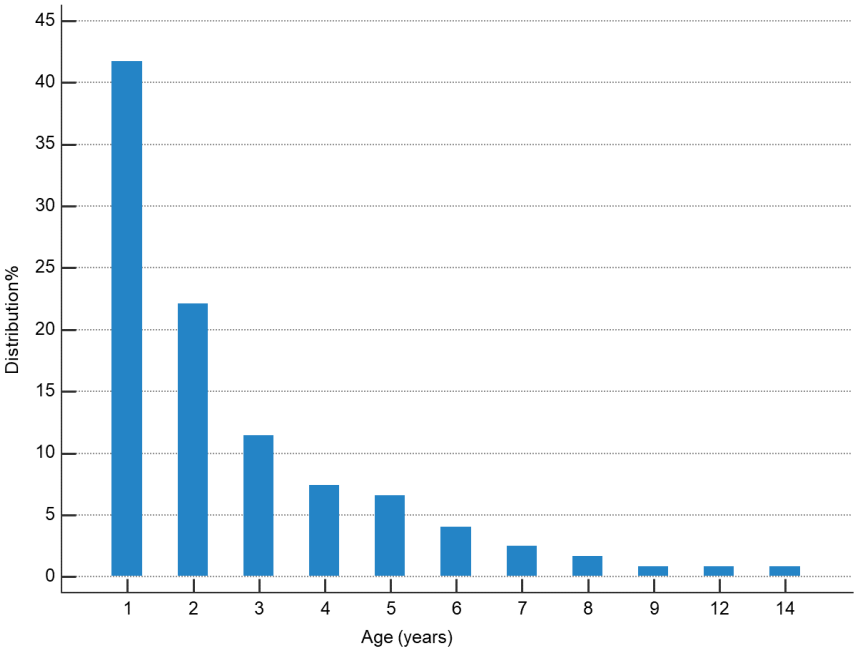


Figure 6. Distribution of age at first cochlear implantation amongst participants (years).

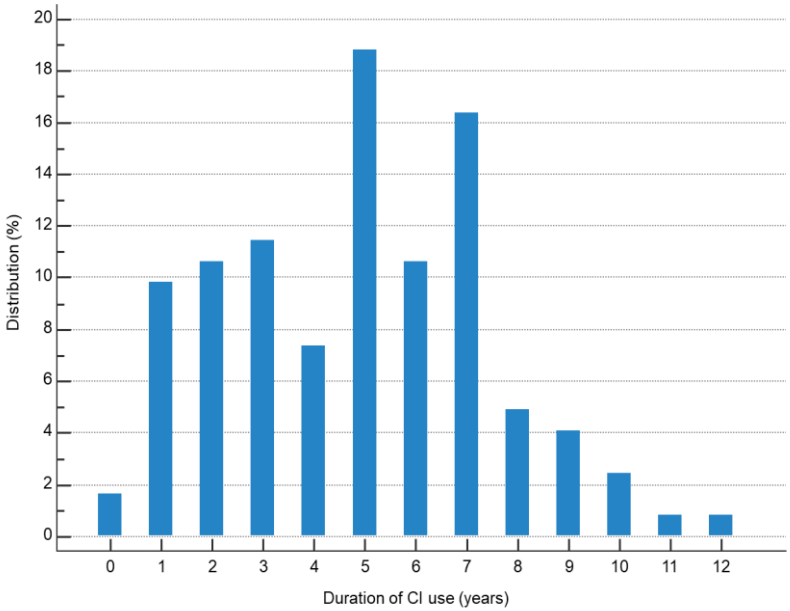


Figure 7. Distribution of the duration of the implant use amongst participants (years).

The majority of the participants (66 children) lived in five biggest Lithuanian cities; 11 children lived in cities with a population of 20 000 to 99 000 inhabitants; 4 – in cities with 10 000 to 19 900 inhabitants; 3 – in cities with less than 10 000 inhabitants in municipality centers; 13 – in other cities with less than 10 000 inhabitants; the last 25 participants resided in the rural areas (Fig. 8).

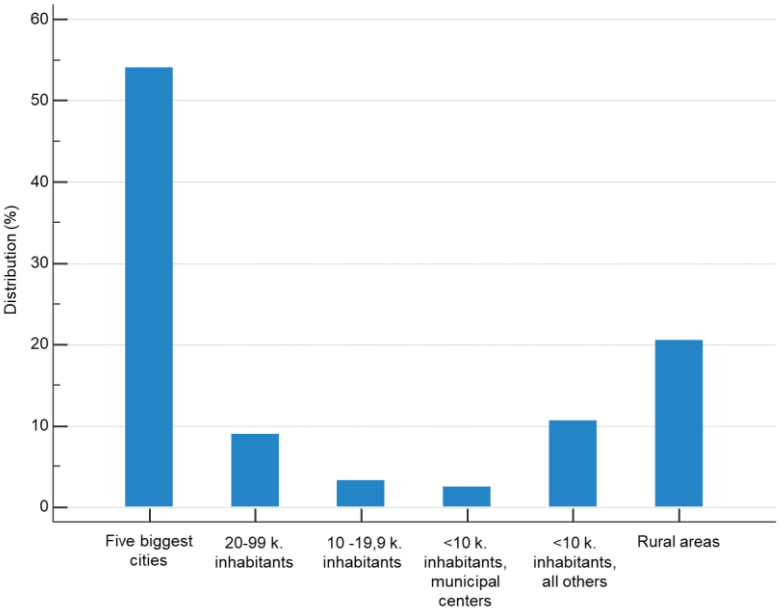


Figure 8. Distribution of a residential location amongst participants.

Analyzed was the distribution of participants based on the manufacturer of the cochlear implant: 103 (84%) children used MED-EL, 18 (14.8%) children – Cochlear, and 1 (0.8%) child – Advanced Bionics implants.

Forty-four (36%) participants were diagnosed during the newborn hearing screening, 23 (52.3%) of them were born in 2014 or later, when newborn hearing screening was implemented in Lithuania. Of all children, 118 (96.7%) were diagnosed with congenital hearing loss (HL) or their hearing loss progressed before 3 years of age; in 4 (3.3%) cases, the onset of hearing loss occurred after 3 years of age. Progressive HL was diagnosed in 21 (17.2%) cases. Congenital or prelingual HL was diagnosed at a mean age of 19.4 ± 16.5 months. When comparing the age of diagnosis between children born in 2014 and later, as well as children born earlier than 2014, a significant

difference was observed (7.7 ± 3.4 months and 24.6 ± 22.5 months, respectively (p <0,001)).

Eighty-four (68.9%) of children were diagnosed with HL in the Children's Hospital, affiliate of VUHSC, and 38 (31.1%) – in the Lithuanian University of Health Sciences. Hearing thresholds before the CI were determined based on BERA results in case of congenital HL or based on the last preoperative audiogram and were 95,5 ± 7,8 dB in the better hearing ear and 97.7 ± 4.8 dB in the implanted ear, or one of the implanted ears in case of a bilateral CI (Fig. 9).

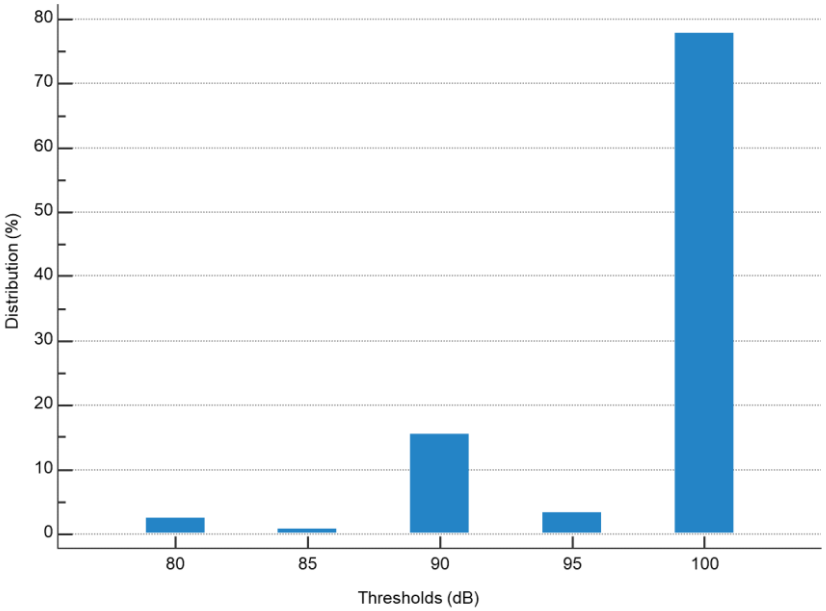


Figure 9. The distribution of hearing thresholds in the implanted ear before the surgery amongst participants (dB).

Average hearing thresholds were equal to or higher than 100 dB in the better hearing ear in the majority of cases (83 cases, 68%) (Fig. 10). Twenty (16.4%) children had residual hearing in the implanted or one of the implanted ears. Twenty (30.8%) participants with unilateral CI had residual hearing in the contralateral ear.

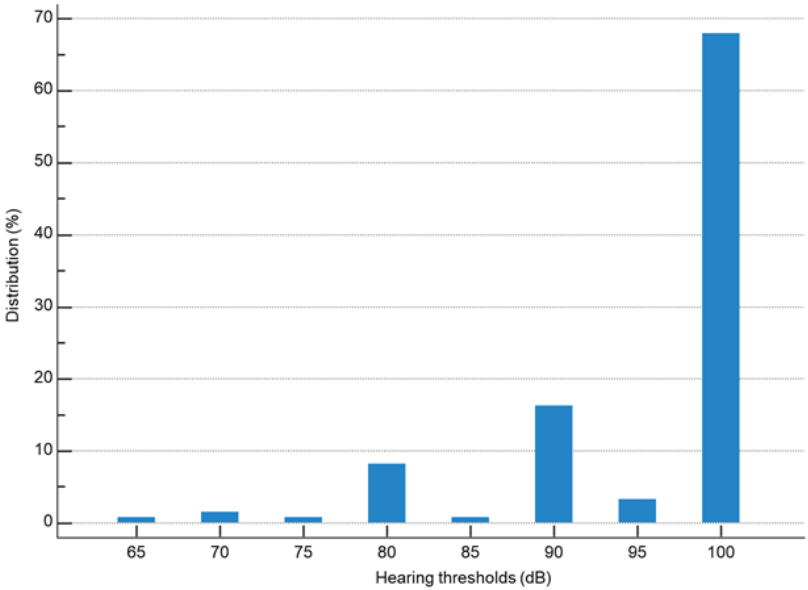


Figure 10. The distribution of hearing thresholds in the better hearing ear before the surgery participants (dB).

Seventy-nine (64.8%) children used two hearing aids at least 3 months prior to CI surgery. After the implantation, out of 65 unilateral CI users, 20 (30.8%) children permanently used hearing aids in the contralateral ear and the mean of aided thresholds using only HA was 51 ± 13 dB.

After analyzing the use of the CI processor, it was noticed that 63 (96.9%) unilateral CI users wore the device constantly, 2 children with an additional disability wore the device inconsistently, one bilaterally implanted recipient wore only one speech processor. During the first year after the surgery, 18 (14.8%) children reported issues with the processor (for example: inconsistent use of the device, programming issues of the device). Seven (38.9%) of these 18 children had severe additional disabilities.

2.2. Family Characteristics of Participants

Of all children, 13.1% lived in single-parent families, 0.8% were raised by caregivers, and the remaining 85.2% lived in a nuclear family. Of all children, 42.6% of children had no siblings, 44.3% lived in two-children families, and 13.1% had two or more siblings.

The mothers of 52.5% of children had acquired higher education, 44.2% – secondary education, and 3.3% – incomplete secondary education. The fathers of 40.2% of participants had acquired higher education, 46.7% – secondary education, and 11.5% – incomplete secondary education.

When analyzing the understanding of the CI process, 43.4% of families were assessed to understand the process, 36.9% – to partially understand it, and 19.7% of families did not understand the CI process at all. After the implantation surgery, the majority of the participants' families (41%) visited the CI centers sufficiently, 36.9% – insufficiently, and 22.1% did not visit the CI centers at all (Table 7).

Table 7. The family characteristics of the participants.

Variable	Number of participants (percent)
Family composition	
Nuclear family	104 (85.2)
Single-parent	16 (13.1)
Caregivers	1 (0.8)
Number of children in family	
One	52 (42.6)
Two	54 (44.3)
Three or more children	16 (13.1)
Education of mother	
Higher education level	63 (52.5)
Secondary education level	53 (44.2)
Incomplete secondary education level	4 (3.3)
Education of father	
Higher education level	49 (40.2)
Secondary education level	57 (46.7)
Incomplete secondary education level	14 (11.5)
Parents' understanding of the CI process	
Sufficient	53 (43.4)
Insufficient	45 (36.9)
Do not understand	24 (19.7)
Visits to the CI center (N=108)	
Sufficient	46 (42.6)
Insufficient	41 (38.0)
Did not visit	21 (19.4)

2.3. Rehabilitation and Education Characteristics of Participants

An analysis of hearing rehabilitation and educational placement settings of CI users revealed that 49.8% of families were

actively engaged in their children's learning process, 33.6% participated passively, and 17.2% of families did not participate in their children's learning. The majority of the parents (71.3%) used spoken language to communicate with their children, 23.8% of families used both spoken and sign languages, and 4.9% communicated only in sign language. Speech and language therapy was accessible in 53.3% of cases, moderately accessible in 27.9% of cases, and not accessible in 18.9% of cases. Of all children, 12.3% attended speech and language therapy 5 times per week, 9.8% – 3 times per week, 36.9% – twice per week, and 28.7% – once per week. Lastly, 12.3% of children did not attend speech and language therapy for the first two years after the surgery.

Of all children, 48.4% attended general kindergartens, 36.1% – specialized kindergartens for deaf and hard of hearing, 5.7% of preschoolers did not go to any kindergarten, and 9.8% were too young at the time of the study to attend kindergarten. Out of 74 participants, 67.6% attended regular schools, and 28.4% – specialized schools for deaf and hard of hearing; 4.1% had been home-schooled. Seventy% of children who attended regular schools followed the mainstream educational program, 26% followed an adapted program, and 4% – an individual program. In general, 59% of study participants attended general, and 28.7% – specialized kindergartens or schools; 2.5% had been home-schooled, while 9.8% were too young to attend any educational institution (Table 8, Fig. 11).

Table 8. The characteristics of hearing rehabilitation and education.

Variable	Number of participants (percent)
Parents' engagement in the learning process	
Active	60 (49.8)
Passive	41 (33.6)
Do not participate	21 (17.2)
Communication mode	
Spoken language	87 (71.3)
Total communication	29 (23.8)
Sign language	6 (4.9)
Accessibility of speech and language therapy	
Good	65 (53.3)
Moderate	34 (27.9)
Poor	23 (18.9)
Intensity of speech and language therapy	
5 times per week	15 (12.3)
3 times per week	12 (9.8)
2 times per week	45 (36.9)
Once per week	35 (28.7)
Did not attend	15 (12.3)
Preschool	
General	59 (48.4)
Special	44 (36.1)
Do not attend	7 (5.7)
Too young to attend	12 (9.8)
School N=74	
General school	50 (67.6)
Specialized school	21 (28.4)
Home-schooling	3 (4.1)
Educational institution attended at the time of the study	
General	72 (59.0)
Specialized	35 (28.8)
Home-schooling	3 (2.5)
Too young to attend	12 (9.8)

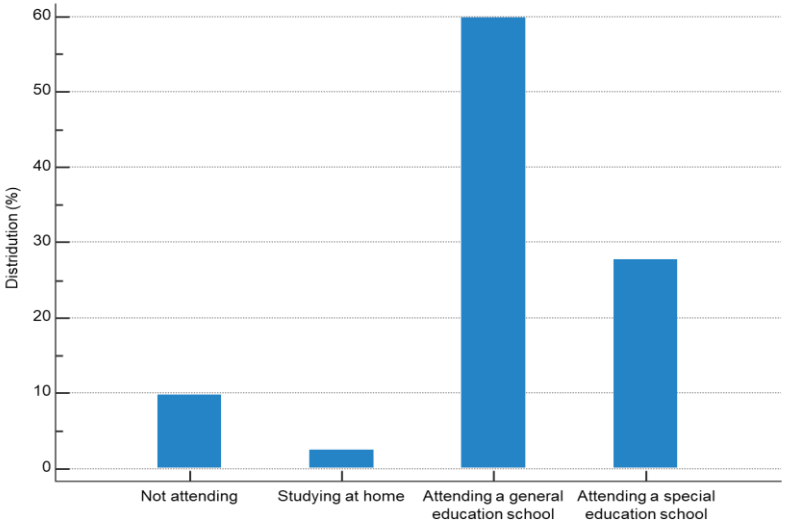


Figure 11. The distribution of educational institutions attended at the time of the study.

2.4. Etiologic Profile of HL amongst Lithuanian Children CI Users

2.4.1. Results of Genetic Testing

Of 122 children, 104 (85.2%) were consulted and examined by the geneticist (101 children had genetic testing, 3 children were only consulted), and the remaining 18 (14.8%) children were not consulted by the geneticist.

Out of 101 children consulted by the geneticist, 91 (90.1%) were attributed to the isolated HL group, 10 (9.9%) – to the syndromic HL group. In the isolated HL group, 13 (14.8%) children had perinatal risk factors for a HL (prematurity, hypoxia, sepsis), and 2 (2.2%) children were clinically diagnosed and confirmed by laboratory tests to have a congenital citomegalovirus (cCMV) infection. *GJB2* sequencing was performed in all 91 cases of isolated HL. Pathogenic homozygous or compound heterozygous variants of the *GJB2* gene

were determined in 58 (63.7%) individuals in the isolated HL group, one (1.1%) child was diagnosed with only one heterozygous variant of the *GJB2* gene (which is not enough to confirm the molecular diagnosis), and 32 (35.2%) children were not found to have any pathogenic variants of the *GJB2* gene (Fig. 12). 35delG was the most frequent pathogenic variant of the *GJB2* gene found – the frequency of its allele composed 68.9% of all pathogenic alleles. The second most frequent pathogenic variant of the *GJB2* gene was c.313_326del14, its frequency composed 29.3% of all pathogenic *GJB2* alleles. Other pathogenic variants of the *GJB2* gene were identified on a much rarer basis – the frequency of the alleles was less than 2%.

In the group of isolated HL, 7 participants with a positive genealogy and negative *GJB2* gene mutation underwent the next generation sequencing analysis of 126 genes. Alterations in other genes causing non-syndromic HL were identified in 5 participants (Table 9). The *MT-RNR1* gene of the mitochondrial genome was tested in 3 children treated with aminoglycosides in the anamnesis, 1555A>G pathogenic variants were not identified. In the group of syndromic HL, 8 syndromes were confirmed, and genetic testing in 2 children still remains unfinished; therefore, the exact syndrome is not yet identified (Table 10).

In conclusion, after the genetic examination of 101 children, 63 (62.4%) cases of non-syndromic HL and 10 (9.9%) cases of the syndromic HL were identified. Generally, 73 (59.8%) of children out of the study population (122 participants) were diagnosed with genetic causes of the congenital HL.

Table 9. The distribution of pathogenic variants causing non-syndromic deafness in the group of isolated HL (N=63).

Gene	Number of participants (%)
GJB2, two pathogenic variants	58 (92.1)
MYO15A, two pathogenic variants	3 (4.8)
TMPRSS3, two pathogenic variants	2 (3.2)

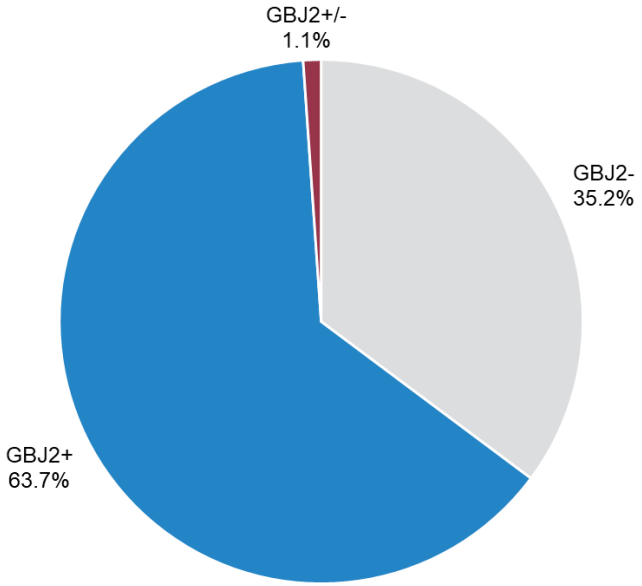


Figure 12. *GJB2* gene mutations testing results in the group of isolated HL.

Table 10. Number of hereditary syndromes in the study sample.

Syndrome	Number of cases
Pendred syndrome	2
Usher syndrome	2
Roger syndrome	1
Jacobsen syndrome	1
CHARGE syndrome	1
Coffin-Lowry syndrome	1
Unidentified syndrome	2

2.4.2. Results of the CMV DNR Testing

Dried blood spots were able to be received in 117 cases out of 122 (95.9%), and CMV DNA PCR tests performed. A retrospective DBS-based real-time PCR analysis showed 14 patients being positive for CMV DNA at birth. All 5 children who were diagnosed with a cCMV infection in newborn period were confirmed with a positive CMV DNA from a dried blood spot. Nine new cases of a cCMV infection were detected. Seven of these children had no confirmed etiologic factor of a HL prior to this research – *GJB2* gene mutations, a perinatal pathology, infection or postnatal infection were all unconfirmed. One child suffered a severe perinatal pathology; however, a cCMV infection was detected only during our research. Two children were confirmed with a positive CMV DNA and a pathologic *GJB2* gene mutation. In total, 14 new cases of a cCMV infection were detected; a symptomatic form was diagnosed in 6 (42.9%) cases, asymptomatic – in 8 (57.1%) cases (Fig. 13). Three children with a symptomatic form of the disease underwent the treatment specific in infancy.

When analyzing annual data presented by the Center for Communicable Diseases and AIDS, from the beginning of 2003 to the end of 2016, cCMV was registered only 3 times, whereas we found 13

cases of a cCMV infection in the study population in the same time period (*Lietuvos gyventojų sveikata ir sveikatos priežiūros įstaigų veikla 2017 m.*, 2018).

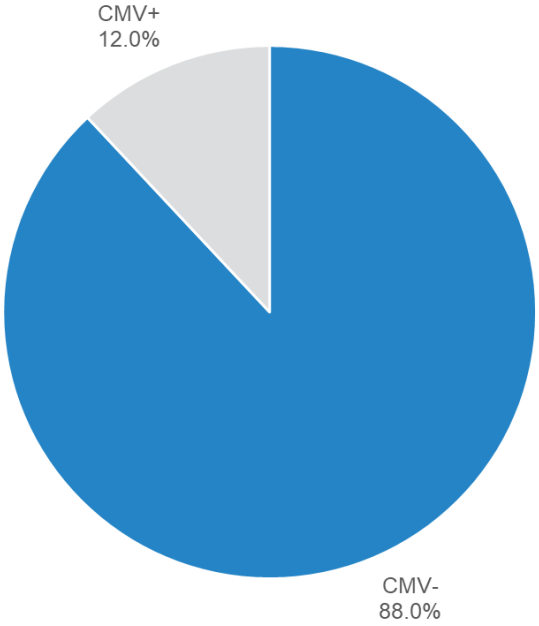


Figure 13. CMV DNA testing results amongst study participants.

2.4.3. Results of the Analysis of Risk Factors of HL

An analysis of the distribution of *perinatal* risk factors of HL amongst participants revealed that 11 (9%) children were premature, born before 32 weeks of gestation, 11 (9%) children weighed less than 1500g, 16 (13.1%) suffered severe perinatal hypoxia, 2 (1.6%) were diagnosed with hyperbilirubinemia requiring blood transfusion, 16 (13.1%) were diagnosed with sepsis, 16 (13.1%) were prescribed with ototoxic medication in infancy, and 1 (0.8%) was diagnosed with

meningitis in infancy. All these children had more than one perinatal risk factor that could have been the cause of the HL, and all were treated for more than 5 days in the Newborn Intensive Care Unit.

Five children were diagnosed with a symptomatic cCMV infection in infancy. No other *prenatal* risk factors, except for the cCMV infection, were discovered.

An analysis of *postnatal* risk factors showed 3 participants suffered purulent meningitis in infancy or early childhood; 1 child was diagnosed with severe pulmonary hypertension and sepsis. Two of these children were prescribed with ototoxic medication (Table 11).

Table 11. Prenatal, perinatal and postnatal risk factors of the HL amongst study participants.

Risk factor	Number of participants
Prematurity <32 weeks of gestation	11
Newborn weight <1500g	11
Severe perinatal hypoxia	16
Congenital TORCH infections: Toxoplasmosis, Rubella, CMV, Herpes, Syphilis	5 cases of CMV infection diagnosed in infancy
Newborn sepsis	16
Hyperbilirubinemia requiring blood transfusion	2
Ototoxic medication in infancy	16
Ototoxic medication in early childhood	2
Newborn meningitis	1
Meningitis in infancy or early childhood	3

2.4.4. Results of the Etiological Profile of HL

In order to thoroughly evaluate the etiologic profile of deaf children who are CI users, the causes of HL were estimated after genetic molecular testing, CMV DNA detection and analysis of prenatal, perinatal and postnatal risk factors. Out of 33 participants who did not have any pathologic mutations of the *GJB2* gene, 12 children were found to have severe perinatal risk factors in their medical histories (prematurity, hypoxia, newborn sepsis), 1 child suffered post-meningitis deafness, 6 children were diagnosed with a cCMV infection after the CMV DNA analysis, 2 cases of clinically diagnosed cCMV infections were confirmed after the CMV DNA analysis, and 5 children were diagnosed with other than GJB2 gene pathogenic mutations. Therefore, only 7 cases out of 33 *GJB2* negatives were left with the unknown cause of their HL.

By concluding results of the genetic testing, CMV DNA analysis, and data of the analysis of perinatal, prenatal and postnatal, risk factors, the etiology of deafness of all participants was attributed to one of the 6 following categories: non-syndromic HL, syndromic HL, prenatal HL (caused by a cCMV infection), perinatal HL, postnatal HL, and HL of unknown origin.

Most frequently diagnosed was the non-syndromic HL. It was diagnosed in 63 (51.6%) of cases. The second most frequent cause were the perinatal risk factors – they were found in 16 (13.1%) children. The third most common cause was a cCMV infection occurring in 12 (9.8%) cases. The fourth place was taken by the syndromic HL – 10 (8.2%) cases, and the fifth – by the postnatal risk factors, which caused HL in 4 (3.3%) children, 3 (2.5%) of whom had meningitis. In the final etiological classification, children diagnosed with several etiological factors (i.e., *GJB2* gene mutations and prenatal risk factors) were attributed to one of the factor that was most probable cause of a child's HL. HL of unknown origin was observed in 17 (13.9%) cases (Fig. 14). It is possible that the number of patients in this group will decrease as the etiologic examination continues.

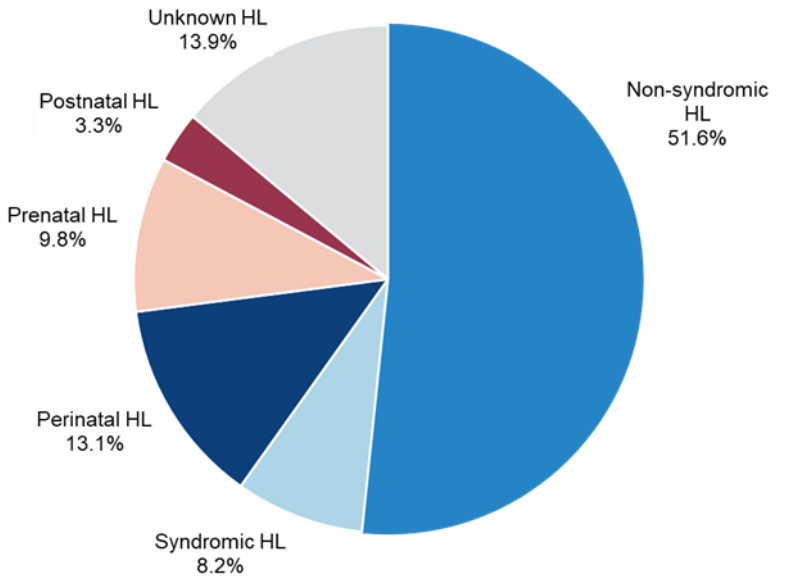


Figure 14. The etiologic profile of hearing loss amongst participants.

2.5. Results of an Analysis of Temporal Bone CT Images

We had CT images of 109 children; 13 images were excluded due to the insufficient quality. Measurements were performed on 103 cases (205 ears). Cochlear ossification was found in 3 patients. Complex anatomical radiological changes of the inner ear (such as an incomplete cochlear partition) were classified separately for the analysis of CT images. Minor unclassified malformations were described as cases per study population, as one child might have several minor anomalies. In general, inner ear malformations were found in 34 cases (21 of them were bilateral, 16 – unilateral) (Table 12).

Table 12. Inner ear malformations amongst participants.

Anatomical changes detected by visual inspection		**Number of cases (bilateral)**	**Prevalence (percent)**
Abnormal architecture of cochlea	Incomplete cochlear partition IP type I	2 (2) cases	3.9
	Incomplete cochlear partition IP type II	2 (2) cases	
Malformation of vestibule / semicircular canals		2(1) / 16(10) cases	18.9
Anatomical changes detected after the measurements		**Number of cases (bilateral)**	
Hypoplastic cochlea		16 (8) cases	15.5
Bony cochlear nerve canal stenosis		14 (8) cases	13.6
Internal auditory canal stenosis		0	0
Enlarged vestibular aqueduct		2 (1) cases	1.9
In total		**34 patients (21 bilateral changes)***	**33%**

*Some of the participants were found to have several inner ear malformations; therefore, a general number of patients with at least one malformation is presented.

Calculated were the average dimensions of inner ear structures of the study population (Table 13). We also calculated the average dimensions of observed anatomical changes: the average height of the hypoplastic cochleae found in 24 ears (16 children) was 3.11 ± 0.13 mm. The average width of the bony cochlear nerve canal in case of the bony cochlear nerve canal stenosis found in 22 ears (14 patients) was 1.08 ± 0.53 mm. We found no cases of the internal auditory canal stenosis.

Table 13. The average dimensions of the inner ear structures of participants.

Inner ear structure	Average dimensions (±SD)
Height of the cochlea	3.73 mm (± 0.32mm)
Diameter of the bony cochlear nerve canal	1.76 mm (± 0.35mm)
Width of the internal auditory canal	4.22 mm (± 0.85mm)
Width of the vestibular aqueduct	0.84 mm (± 0.7mm)

After excluding 3 cases of cochlear ossification, in the sample of 103 participants, an analysis of temporal bone CT images revealed a 33% general prevalence of inner ear malformations.

Assessed was the distribution of inner ear malformations in different etiological groups. Two cases of the IP were associated with the Pendred syndrome, one – with an unidentified syndrome, and another one – with pathogenic *GJB2* gene mutations (Table 14).

Table 14. The distribution of inner ear malformations amongst different etiologic groups.

Malformation	Non syndromic HL	Syndromic HL	Prenatal HL	Perinatal HL	Postnatal HL	HL of unknown origin
IP type I	–	2	–	–	–	–
IP type II	1	1	–	–	–	–
Malformation of vestibule/semicircular canals	-/4	3/5	–/–	1/2	1/3	-/4
Hypoplastic cochlea	8	2	–	2	–	4
Bony cochlear nerve canal stenosis	4	3	2	1	1	3
Enlarged vestibular aqueduct	1	3	–	1	–	1
Cochlear ossification	–	–	–	–	3	–

2.6. Postoperative Hearing Results

Mean aided thresholds with one or two CI in the sound field were 36.3 ± 7.8 dB. Assessing children with one and two implants separately, the average CI aided thresholds were 38.1 ± 8.2 dB and 34.3 ± 6.8 dB, respectively, and the difference was statistically significant (p=0,033).

2.6.1. Results of Auditory Abilities and Speech Intelligibility

Auditory abilities, according to the CAP scale, were assessed on average 4.9 ± 2. 6 years after the CI – it was found that 41.8% of children reached the scale's ceiling and can easily talk to a familiar person on the phone. The results of the auditory abilities are presented in Table 15 and Fig. 15.

Table 15. An evaluation of listening skills according to the CAP scale (N=122).

Category	Description	Number of participants (%)
0	No awareness of environmental sounds	0
1	Awareness of environmental sounds	0
2	Responds to speech sounds	3 (2.5)
3	Recognizes environmental sounds	9 (7.4)
4	Discriminates at least two speech	24 (19.7)
5	Understands common phrases without lipreading	23 (18.9)
6	Understands conversation without lipreading with a familiar talker	12 (9.8)
7	Can *use the telephone with* a familiar	51 (41.8)

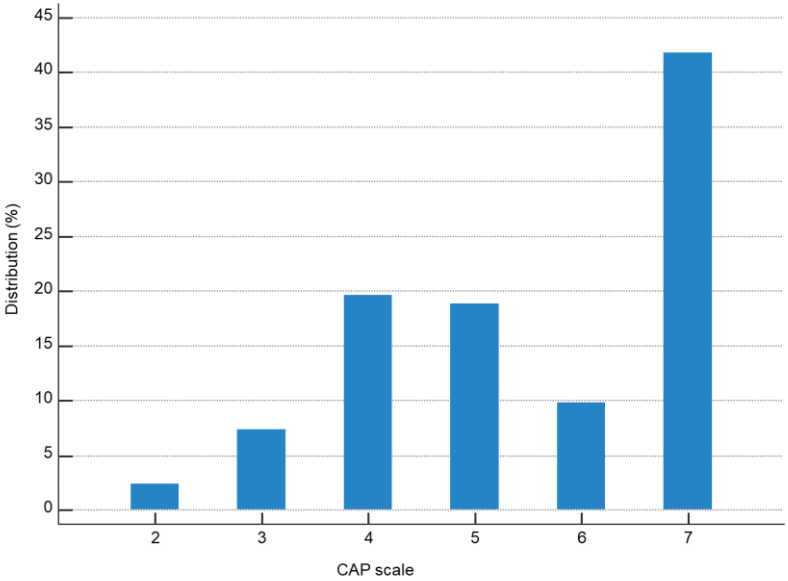


Figure 15. The distribution of the auditory abilities score according to the CAP scale.

Speech intelligibility, according to the SIR scale, was assessed on average 4.9 ± 2.6 years after the CI; it was found that 41% of 122 children reached the highest category in the scale – they developed such a speech that is easily understood by all listeners during casual activities (Table 16, Fig.16).

Table 16. Speech intelligibility categories according to the SIR scale (N=122).

Category	Description	Number of participants (%)
5	Connected speech is intelligible to all listeners. The child is understood easily in everyday contexts	50 (41)
4	Connected speech is intelligible to a listener who has little experience of a deaf person's speech. The listener does not need to concentrate unduly.	17 (13.9)
3	Connected speech is intelligible to a listener who concentrates and lip-reads within a known context.	17 (13.9)
2	Connected speech is unintelligible. Intelligible speech is developing in single words when context and lip-reading cues are available.	28 (23)
1	Pre-recognizable words in spoken language. The child's primary mode of everyday communication may be manual.	10 (8.2)

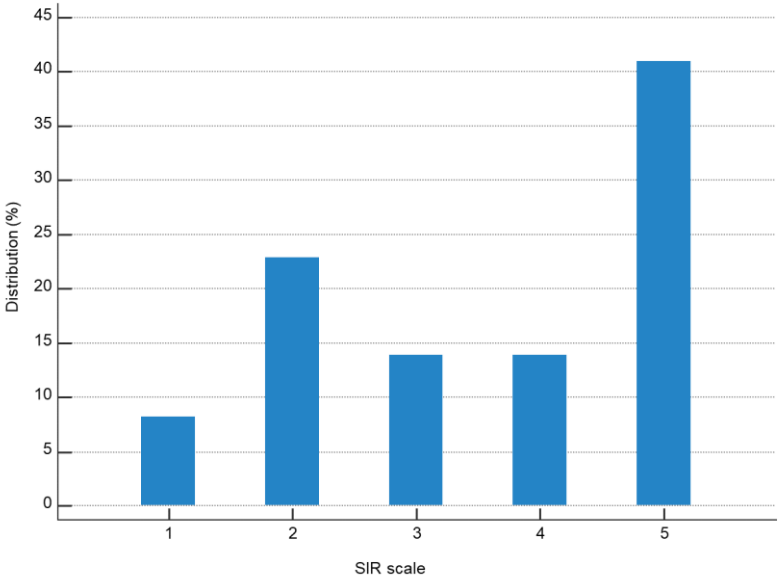


Figure 16. The distribution of the speech intelligibility category based on the SIR scale.

2.6.2. Results of Speech Audiometry

The speech audiometry results of 95 children were estimated to evaluate postoperative speech perception. The average score of the speech audiometry of these children was 63.9 ± 29.3%. The distribution of the participants, based on the speech perception level, is presented in Table 17.

Table 17. Speech recognition levels (N=95).

Speech perception level	Speech perception score in %	Number of participants (%)
None	Patient could not be tested with an open-set speech audiometry	11 (11.6)
Very weak	<50	14 (14.7)
Weak	59–50	5 (5.3)
Moderate	74–60	18 (18.9)
Good	89–75	30 (31.6)
Excellent	100–90	17 (17.9)

After excluding children with severe additional disabilities and patients with an onset of HL after 3 years of age, this group decreased to 81 children, whose speech perception levels were distributed as follows: excellent speech perception was reached by 16 (19.8%) children, good – 29 (35.8%), moderate – 16 (19.8%), weak – 5 (6.2%), and very weak – 11 (13.6%) children; 4 (4.9%) children could not be tested using open-set speech audiometry (Fig. 17). The average speech perception level in this group was 69.6 ± 24.2%. The average age at first implantation of these children was 33,1 ±22,2 months, age at the time of the study - 8,7 ±2,7 years and duration of the implant use 5,9 ±2,2 years.

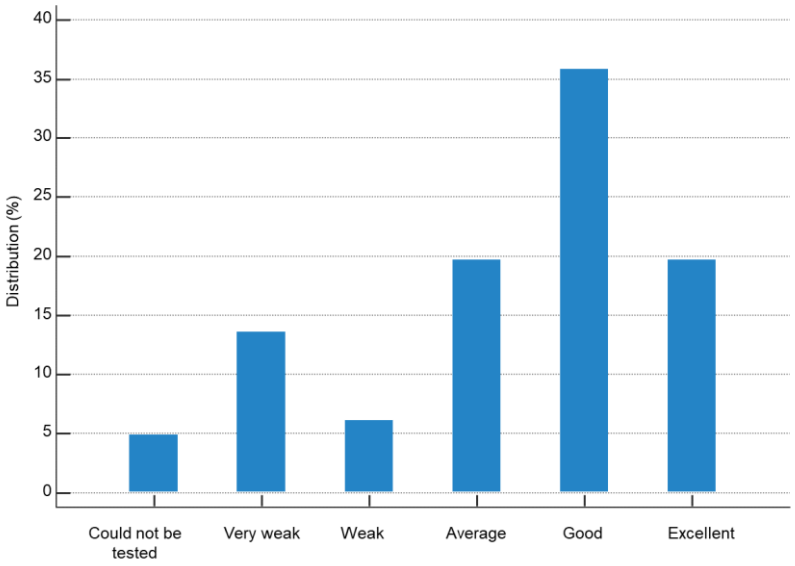


Figure 17. The distribution of patients based on the speech perception level (N=81).

2.6.3. Results of the Speech and Language Assessment

The results of the speech and language development assessment of 81 children were analyzed in order to evaluate postoperative speech and language achievement. Of them, 20 (24.7%) participants reached a very good speech and language development level, 22 (27.2%) – a good level, 21 (25.9%) – a satisfactory one, and 18 (22.2%) – an unsatisfactory level (Fig. 18).

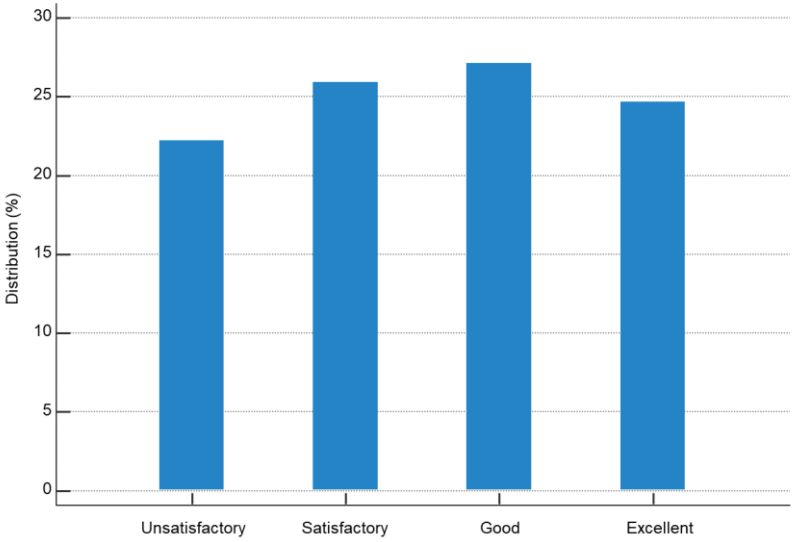


Figure 18. The distribution of participants based on speech and language development levels (N=81).

2.6.4. Relations between Etiological Factors and Age at Diagnosis and Operation

An analysis of the age at diagnosis and first implantation surgery amongst 6 different etiologic groups of participants (after excluding children with the postlingual HL) revealed that age at diagnosis and surgery differed significantly between different etiological groups (p=0,003 and p=0,023, respectively). Children with the non-syndromic HL were diagnosed and implanted earlier compared to children with HL of other etiologies (syndromic, perinatal, prenatal, postnatal, and unknown) (Figs. 19, 20).

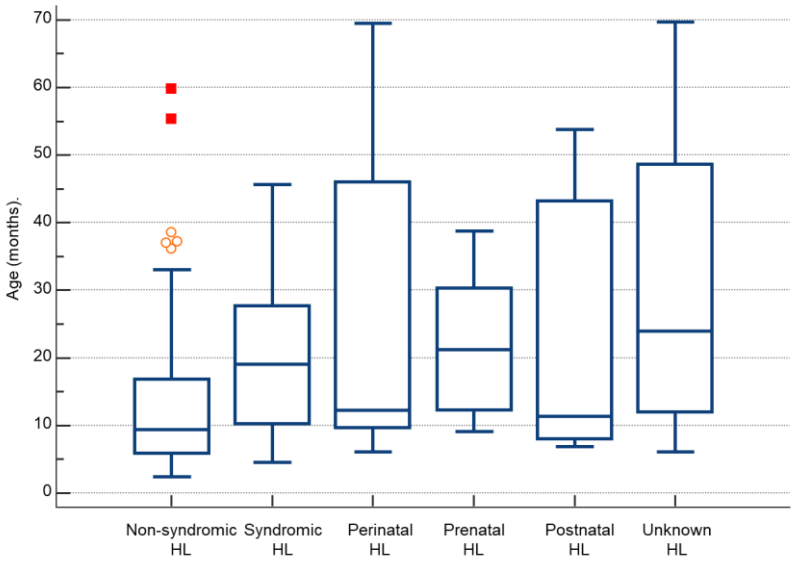


Figure 19. The distribution of age at diagnosis amongst different etiologic groups.

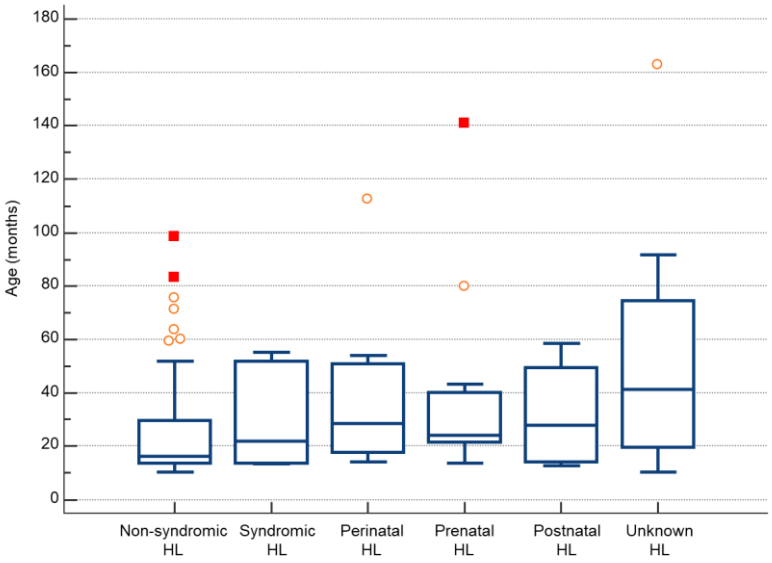


Figure 20. The distribution of age at implantation amongst different etiologic groups.

2.6.5. Relations between Etiological Factors and Speech Perception

In order to assess whether speech perception, evaluated using speech audiometry, differed comparing children with non-syndromic HL and children with HL of other etiologies, two etiological groups were picked – non-syndromic HL and HL of other etiologies (syndromic, prenatal, perinatal, postnatal, and unknown). The influence of the age at implantation on the speech perception results was reduced by including into the analysis only children implanted before 3.5 years of age (period of maximal neuroplasticity). Excluded were children with postlingual hearing loss. The "Non-syndromic HL" group included 38 participants, and the group "HL of other etiologies" included 30 children. It was found that the results of the speech recognition of children with "non-syndromic HL" were significantly better compared to children with the "HL of other etiologies" (p=0,013) (Fig. 21). However, this difference became insignificant

when children with severe additional disabilities were excluded from the analysis (p=0,21).

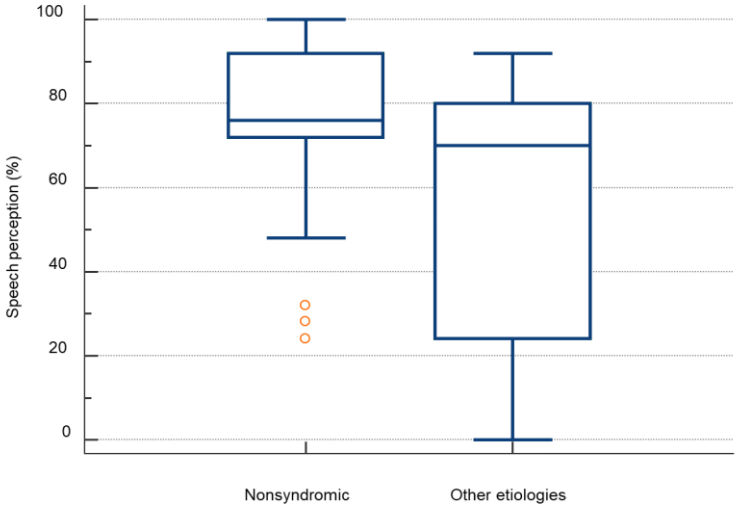


Figure 21. The distribution of speech perception results in "nonsyndromic hearing loss" and "hearing loss of other etiologies" groups.

2.6.6. Postoperative Results of Children with Additional Disability

Fourteen (11.5%) out of 122 children had severe additional disability, such as cerebral palsy, autism, epilepsy and others. All of them were diagnosed with developmental delay (Table 18). Twelve (85.7%) had more than two additional diagnoses. Severe additional disabilities were as follows: a CMV infection in 2 cases; congenital syndromes – in 5 cases; profound prematurity – in 2 cases; severe hypoxia at birth – in 1 case; severe postnatal infection – in 1 case; an unknown cause of severe additional disability – in 3 cases (2 of them were diagnosed with a GJB2 gene mutation that had caused HL).

Table 18. The distribution of the severe additional disability amongst study population (N=14).

Severe additional disability	Number of cases (percent)
Autism	4 (28.6)
Cerebral palsy	4 (28.6)
Hereditary syndrome	5 (35.7)
Severe isolated developmental disorder	1 (7.4)

In addition to this, 20 (16.4%) more children were diagnosed with minor additional disabilities that had no big influence on the child's psychomotor development, for example: Pendred syndrome, balance disorder, renal polycystosis, heart defect and others. In general, there were 34 (27.9%) of children CI users diagnosed with additional disabilities.

The general characteristics of children with severe additional disabilities revealed that these children were implanted at the mean age of 24.8 ± 12.8 months, used their CI on average 4.71 ± 2.3 years, and their mean age at the time of the study was 6.86 ± 2.2 years. Twelve (85.7%) of participants with severe additional disability use their CI permanently.

An analysis of postoperative auditory abilities of children with severe additional disabilities revealed that 4 (28.6%) children reached the 5^{th} category on the CAP scale, 5 (37.7%) – the fourth scale; 3 (21.4%) – the third scale; and 2 (14.3%) children managed only the second category. Speech intelligibility scores according to the SIR scale were as follows: 8 (57.1%) children managed the second category; remaining 6 (42,7%) had the lowest – first – category (Table 19). A comparison of the group of children with severe additional disabilities with the group of children without a severe disability based on CAP and SIR scales revealed significant differences between the two groups ($p=0,007$ and $p<0,001$, respectively).

Table 19. The results of auditory abilities and speech intelligibility amongst children with additional disabilities.

Case	Age at implantation, months	Duration of CI use, years	Additional disability	Other diseases	Cause of additional disability/hearing loss	CAP	SIR
N1	27	7.4	Autism	–	Prematurity	4	2
N2	15	6.6	Jacobsen syndrome	Vision impairment	Syndrome	4	1
N3	17	7.5	Autism	–	Unknown/*GJB2*	5	2
N4	25	7.1	CP	Epilepsy	cCMV	2	1
N5	16	6.9	Autism	–	Unknown/*GJB2*	5	2
N6	35	5.1	CP	Epilepsy	Unknown	3	2
N7	13	5.9	Unknown syndrome	–	Syndrome	3	1
N8	19	4.8	CP	Epilepsy	Hypoxia	4	2
N9	22	4.5	Roger syndrome	Diabetes mellitus, anaemia, vision impairment	Syndrome	5	1

N10	58	3.5	Severe postnatal infection	Pulmonary hypertension	Severe postnatal infection	4	2
N11	41	3.3	CHARGE syndrome	Multiple developmental defects	Syndrome	5	2
N12	22	1.1	CP	Epilepsy	cCMV	2	1
N13	29	2.1	CP	Epilepsy, blindness	Prematurity	3	2
N14	22	1.1	Coffin-Lowry syndrome	Hipothyreosis	Syndrome	4	1

Notes: CP – cerebral palsy.

2.7. Determination of Prognostic Factors of CI

2.7.1. Comparison of Groups with Different Speech Perception Results

In order to determine which factors determine worse speech perception, two groups were formed: children with a speech perception score of ≥ 60% were included into the "good speech perception group," and the remaining – with the speech perception score less than 60% – into the "poor speech perception" group. Therefore, the "good speech perception" group included participants with excellent, good, and moderate speech perception levels; the "poor speech perception" group included participants with poor, very poor speech perception levels and children who could not be tested with an open-set speech audiometry. Sixty children formed the "good speech perception" group, the and 21 – the "poor speech perception" group.

Thirty prognostic factors (demographic, audiologic, surgical, implant-associated, etiological, radiological, family, rehabilitation and educational) were analyzed in this study in order to find the relation to postoperative results of speech perception.

Comparing *demographic* data, groups did not differ neither based on the gender (p=0,837) nor on the age at the time of the study (p=0,057). However, groups differed significantly based on the residential location – the majority of children in the "good speech perception" group lived in the main cities (60%), whereas 47.6% of children from the "poor speech perception" group resided in small cities and the rural areas (p=0,034).

An analysis of the influence that *audiologic* factors have on speech perception results showed that in the group of "poor speech perception," congenital HL was diagnosed significantly later (p<0,001). The two groups did not differ neither in comparing preoperative hearing thresholds (p=0,767) nor in comparing residual preoperative hearing in the implanted ear (p=0,467), nor comparing use of HA in the contralateral ear after surgery (p=0,261) or in

comparing the number of children in each group diagnosed with progressive HL (p=0,675). Postoperative mean CI-aided thresholds were significantly worse in the group of "poor speech perception" (p<0,001) (Fig. 22)

In evaluating *surgical, implant-associated and processor-associated* factors, it was revealed that age at implantation was significantly older in the group of "poor speech perception" (p<0,001). The two groups did not differ neither based on the duration of CI use (p=0,723) nor based on the number of bilateral cochlear implantations (p=0,19). However, children with the worse speech perception had significantly more issues with CI use (p<0,001).

After assessing the influence of the *etiologic factors*, it was found that the groups did not differ in comparing the number of *GJB2* gene mutations (p=0,754) or comparing all six etiologic groups of HL (p=0,552).

An analysis of the *radiologic factors* revealed that the patients with the worse speech perception tended to have a significantly narrower BCNC (p=0,021). The groups did not differ according to the cochlear height (p=0,114) and the diameter of the internal acoustic meatus (p=0,093) (Fig. 23).

An evaluation of the influence of *family factors* demonstrated that these groups did not differ comparing family structure (p=0,061). The education of the fathers and mothers was poorer in the group of children with the worse speech perception (p<0,001 and p<0,001, respectively), their parents tended to misunderstand the CI process more often (p<0,001), and their families visited the CI center less frequently after surgery (p<0,001).

A comparison of the *rehabilitation and educational factors* revealed that the parents of children with a worse speech perception participated in the child's learning process less (p<0,001). Children with "poor speech perception" attended special kindergartens and schools more often as well (p<0,001 and p<0,001, respectively); in addition to this, they used total communication more often (p<0,001). The groups differed significantly based on the accessibility of speech

and language therapy: children with poor speech perception were less exposed to speech and language therapy ($p<0,001$), and it was significantly less intensive ($p=0,029$) (Table 20).

Table 20. A comparative analysis of the "good speech perception" and "poor speech perception" groups.

Variable	Good speech perception group (N=60) N (%) or M (±SD)	Poor speech perception group (N=21) N (%) or M (±SD)	P value
Demographic factors			
Gender			
Male	30 (50)	14 (66.7)	0,837
Female	30 (50)	7 (33.3)	
Residential location:			
Five biggest cities	36 (60.0)	7 (33.3)	
Cities with 20 000–99 000 inhabitants	6 (10.0)	1 (4.8)	0,034
Cities with 10 000–19 900 inhabitants	1 (1.7)	3 (14.3)	
Cities with <10 000 inhabitants and rural areas	17 (21.0)	10 (47.6)	
Age at the time of the study, years	8.32 (±2.56)	9,67 (±2.9)	0,057
Audiological factors			
Age at diagnosis, months	16.89 (±13.1)	32,10 (±17.3)	**<0,001**
Mean preoperative hearing thresholds, dB	94.25 (±9.2)	95,24 (±7.5)	0,767

Residual preoperative hearing in the implanted ear:			
Present			0,467
Absent	13 (21.7)	3 (14.3)	
	47 (78.3)	18 (85.7)	
Use of the residual hearing in the contralateral ear with the HA after CI:			0,261
Yes	14 (46.7)	4 (28.6)	
No	16 (53.3)	10 (71.4)	
Progression of HL:			
Yes	11 (18.3)	3 (14.3)	0,675
No	49 (81.7)	18 (85.7)	
CI aided thresholds, dB	33.23 (±5.0)	40.5 (±9.4)	**<0,001**
Surgical, implant and processor-associated factors			
Age at implantation, months	28.19 (±21.2)	47.16 (±19.4)	**<0,001**
Duration of the CI use, years	5.95 (±2.1)	5.62 (±2,4)	0,723
Unilateral CI	30 (50)	14 (66.7)	0,190
Bilateral CI	30 (50)	7 (33.3)	
Issues with the usage:			
Present	1 (1.7)	10 (47.6)	**<0,001**
Absent	59 (98.3)	11 (52.4)	

Etiologic factors			
GJB2 gene mutation (N=68):			
Positive	33 (63.5)	10 (62.5)	0,754
Negative	19 (36.5)	6 (37.5)	
Non-syndromic	34 (56.7)	11 (52.4)	0,552
Syndromic	4 (6.7)	1 (4.8)	
Prenatal cCMV	6 (10.0)	2 (9.5)	
Perinatal	8 (13.3)	3 (14.3)	
Postnatal	1 (1.7)	0 (0)	
Unknown	7 (11.7)	4 (19.0)	
Radiological factors (N=64)			
Diameter of the bony cochlear nerve canal, mm	1.8 (±0.2)	1.5 (±0.6)	**0,021**
Cochlear height, mm	3.6 (±0.3)	3.5 (±0.3)	0,114
Width of the internal acoustic meatus, mm	5.0 (±0.9)	4.9 (±1.9)	0,093
Family factors			
Family composition:			0,061
Nuclear family	52 (86.7)	15 (71.4)	
Single-parent	7 (11.7)	6 (28.6)	
Caregivers	1 (1.7)	0 (0)	
Family size:			0,738
One child	23 (38.3)	10 (47.6)	

Two children	29 (48.3)	7 (33.3)	
3 or more children	8 (13.3)	4 (19.0)	
Father's education level:			
Higher education	32 (55.2)	1 (4.8)	**<0,001**
Secondary education	23 (39.7)	15 (71.4)	
Incomplete secondary education	3 (5.2)	5 (23.8)	
Mother's education level:			
Higher education	39 (66.1)	5 (23.8)	**<0,001**
Secondary education	20 (33.9)	14 (66.7)	
Incomplete secondary education	0 (0)	2 (9.5)	
Parents' understanding about the CI process:			
Sufficient	37 (61.7)	1 (4.8)	**<0,001**
Insufficient	23 (38.3)	8 (38.1)	
Did not understand	0 (0)	12 (57.1)	
Family visits to the CI center:			
Sufficient	34 (56.7)	1 (4.8)	**<0,001**
Insufficient	24 (40.0)	4 (19.0)	
Did not visit	2 (3.3)	16 (76.2)	
Rehabilitation and educational factors			
Parents' engagement in the learning process:			
Active	42 (70.0)	1 (4.8)	**<0,001**
Passive	18 (30.0)	8 (38.1)	

Did not participate	0 (0)	12 (57.1)	
Communication mode:			
Spoken language	59 (98.3)	4 (19.0)	**<0,001**
Total communication	1 (1.7)	14 (66.7)	
Sign language	0 (0)	3 (14.3)	
Accessibility of speech and language therapy:			
Good	46 (76.7)	4 (19.0)	**<0,001**
Moderate	12 (20)	10 (47.6)	
Bad	2 (3.3)	7 (33.3)	
Intensity of speech and language therapy:			
Did not attend	0 (0)	7 (33.3)	
Once per week	12 (20)	3 (14.3)	**0,029**
2 times per week	32 (53.3)	6 (28.6)	
3 times per week	7 (11.7)	3 (14.3)	
5 times per week	9 (15)	2 (9.5)	
Educational placement settings:			
General education	56 (93.3)	5 (23.8)	
Special education	4 (6.7)	16 (76.2)	**<0,001**
Home-schooling	0	0 (0)	
Does not attend yet	0	0 (0)	
Kindergarten:			**0,001**
General	41 (68.3)	6 (28.6)	

Special education	19 (31.7)	13 (61.9)	
Did not attend	0 (0)	2 (9.5)	
Does not attend yet	0 (0)	0 (0)	
School/program (N=57):			
General school/mainstream program	31 (79.5)	1 (5.6)	
General school/adapted program	7 (17.9)	5 (27.8)	**<0,001**
Special education school	1 (2.6)	12 (66.7)	
Home-schooling	0 (0)	0 (0)	

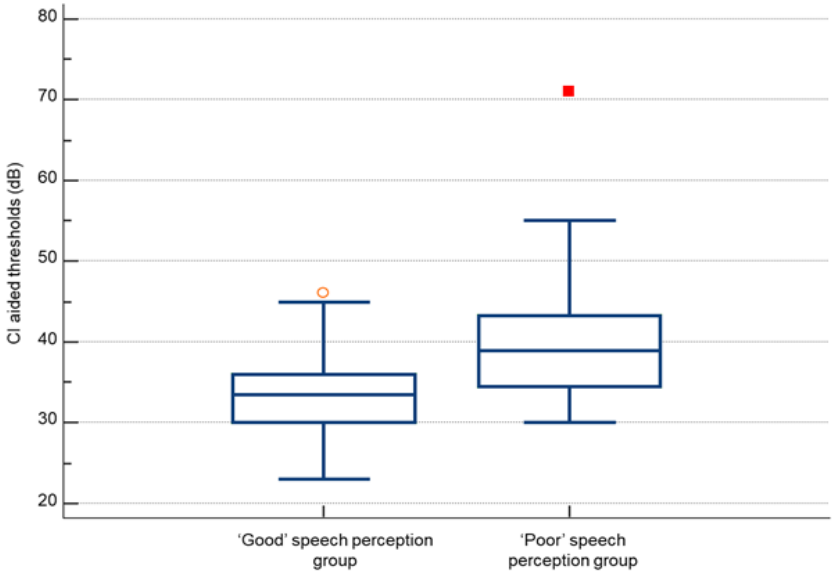


Figure 22. CI-aided thresholds with CI in different speech perception groups.

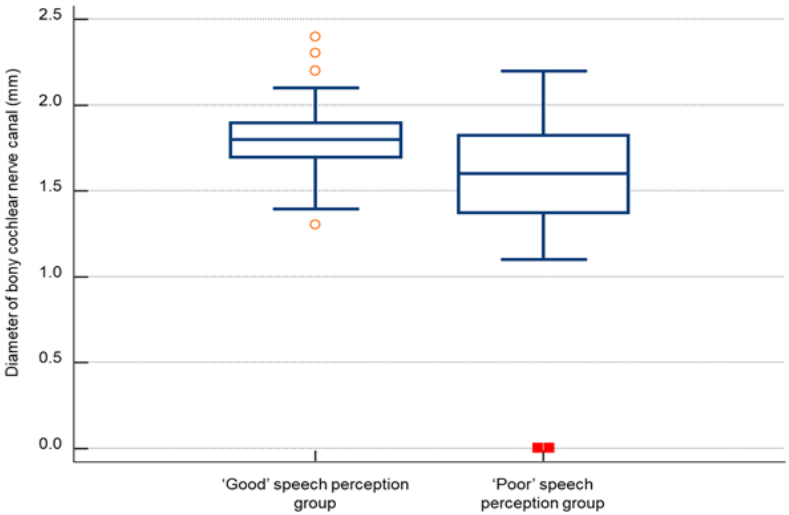


Figure 23. The diameter of the bony cochlear nerve canal in different speech perception groups.

A comparison of the "good" and "poor" speech perception groups based on other CI results revealed that children with poor speech perception showed significantly worse auditory abilities ($p<0,001$) and speech intelligibility ($p<0,001$) as estimated using CAP and SIR scales. In addition to this, children with poor speech perception showed significantly worse language development levels ($p<0,001$) (Table 21).

Table 21. Auditory abilities, speech intelligibility and and speech and language development amongst two grups of children with different speech perception levels.

Variable	Good speech perception N (%)	Poor speech perception N (%)	P value
CAP category			
1	0 (0)	0 (0)	**<0,001**
2	0 (0)	1 (4.8)	
3	0 (0)	3 (14.3)	
4	1 (1.7)	6 (28.6)	
5	4 (6.7)	10 (47.6)	
6	8 (13.3)	1 (4.8)	
7	47 (78.3)	0 (0)	
SIR category			
1	0 (0)	2 (9.5)	**<0,001**
2	2 (1.7)	6 (28.6)	
3	2 (3.3)	10 (47.6)	
4	11(18.3)	3 (14.3)	
5	46 (76.7)	0 (0)	
Language development levels			
Very good	20 (33.3)	0(0)	**<0,001**
Good	22 (36.7)	0(0)	
Sufficient	16 (26.7)	5 (23.8)	
Insufficient	2 (3.3)	16 (76.2)	

2.7.2. Determination of Prognostic Factors for Speech Perception Using Logistic Regression

The detection of prognostic factors for the speech perception of children who are CI users was performed using logistic regression analysis. The univariate analysis included all demographic, surgical/implant-associated, audiological, radiological, family,

rehabilitation and educational variables that differed significantly between the "good" and "poor" speech perception groups.

A univariate logistic regression demonstrated that speech perception is influenced by the residential location (OR: 1,506, CI: 1,044–2,173, p=0,029). Age at diagnosis (OR: 1,064, CI 1,027–1,101, p=0,001), age at implantation (OR: 1,038; CI: 1,014–1,064; p=0,002) and CI-aided thresholds (OR: 1,203; CI: 1,078–1,342; p=0,001) are all factors that have an effect on speech perception diagnosed using speech audiometry. Children who have issues with CI use have a 53-times bigger risk of insufficient speech perception (OR: 53,636; CI: 6,223–462, 33; p<0,001).

The diameter of the bony cochlear nerve canal is also associated with the speech perception results – as the diameter decreases by 1 mm, the risk for a child to have poor speech perception increases 12 times (OR: 11,928; CI: 1,292–110,129; p=0,029).

In the group of family factors, variables that have influence when predicting speech perception results are: the father's education (OR: 6,944; CI: 2,403–20,066; p<0,001), the mother's education (OR: 6,416; CI: 2,170–18,968; p=0,001), the parents' understanding of the CI process (OR: 42,745; CI 5,765–316,933; p<0,001) and the frequency of family visits to the CI center (OR: 24,444; CI: 6,234–95,855; p<0,001). The parents' engagement in a child's learning (OR: 44,230; CI: 6,069–322,372; p<0,001), the accessibility of speech and language therapy (OR: 7,076; CI: 2,837–17,652; p<0,001), intensity of speech and language therapy (OR: 1,639; CI: 1,030–2,609; p=0,037) and type of the preschool institution (OR: 5,067; CI: 1,812–14,171; p=0,002) were educational variables that were associated with speech perception results (Table 22).

Table 22. A univariate logistic regression analysis for detecting factors associated with postoperative speech perception.

Variable	Odds ratio		P
	Value	95% confidence interval	
Residential location	1,506	1,044–2,173	0,029
Age at diagnosis	1,064	1,027—1,101	0,001
Postoperative hearing thresholds with CI	1,203	1,078–1,342	0,001
Age at implantation	1,038	1,014–1,064	0,002
Issues with the use of CI	53,636	6,223–462,33	<0,001
Diameter of the bony cochlear nerve canal, mm	11,928	1,292–110,129	0,029
Father's education	6,944	2,403–20,066	<0,001
Mother's education	6,416	2,170–18,968	0,001
Parents' understanding of the CI process	42,745	5,765–316,933	<0,001
Family visits to the CI center	24,444	6,234–95,855	<0,001
Parents' engagement in the learning process	44,230	6,069–322,372	<0,001
Accessibility of speech and language therapy	7,076	2,837–17,652	<0,001
Intensity of speech and language therapy	1,639	1,030–2,609	0,037
Pre-school educational institution	5,067	1,812–14,171	0,002

After assuring a significant relation between postoperative speech perception and different chosen variables in a univariate regression analysis, the following variables were chosen in the multivariate regression analysis: age at implantation, aided thresholds,

the diameter of the bony cochlear nerve canal and the mother's education. Age at diagnosis was not included in the multiple regression analysis despite its statistical significance, because it is associated with the age at implantation and depends on it. The father's education, the parents' understanding of the CI process, family visits to the CI centers and the parents' engagement in the learning process were not included in the multivariate analysis as well – they were related to and dependent on the mother's education.

The multivariate regression analysis revealed that age at implantation (OR: 0,927: CI: 0,877– 0,980; p=0,008), postoperative aided thresholds with CI (OR: 0,721; CI 0,570–0,911; p =0,006) and the diameter of the bony cochlear nerve canal (OR: 24,215; CI: 1,227–477,77; p=0,036) are all independent prognostic factors for speech perception after pediatric CI.

2.7.3. Comparison of Groups of Children with Different Speech and Language Development Levels

In order to find the factors that determine better or worse speech and language development results, two groups were formed: children who demonstrated very good and good speech and language development levels were attributed to the "good speech and language development" group, and children who demonstrated satisfactory or unsatisfactory language development levels were attributed to the "insufficient speech and language development" group. The "good speech and language development" group included 42 children; the "insufficient speech and language development" group included 39 children.

Thirty prognostic factors (demographic, audiological, surgical, implant-associated, etiological, radiological, family, rehabilitation and educational) were analyzed in this study in order to find their relation to the postoperative results of speech and language development levels.

An analysis of the *demographic* factors showed no significant difference between the groups neither based on the gender (p=0,212) nor on the age at the time of the study (p=0,394). Two groups differed significantly based on the residential location (p=0,013) – children included into the "good speech and language development" group more frequently lived in big cities (69%), while children from the "insufficient speech and language development" group – in small cities and rural areas (41%).

After analyzing influence of the *audiological* factors, it was found that age at the time of diagnosis is significantly lower in a "good speech and language development" group compared to the "insufficient speech and language development" group (p=0,011). The two groups did not differ based on the mean preoperative hearing thresholds (p=0,465), preoperative residual hearing in the implanted ear (p=0,344), or based on the number of progressive HL cases (p=0,309). However, children with estimated "insufficient speech and language development" tended to not use residual postoperative hearing in the contralateral ear by using HA (p=0,039). CI-aided thresholds were significantly higher in the "insufficient speech and language development" group (p=0,001).

An evaluation of *surgical, implant-associated and processor-associated* factors revealed that age at implantation was significantly older in the "insufficient language development" group (p=0,005). Groups did not differ comparing duration of the implant use (p=0,612) or the number of bilateral CIs performed (p=0,421). However, children with estimated "insufficient speech and language development" had significantly more issues with CI use (p<0,001).

No significant difference was observed between groups comparing the effect of the *etiologic* factors: neither comparing the number of GJB2 positive cases (p=0,947), nor other causes of HL (p=0,723).

An analysis of the *radiologic* factors showed no difference between two groups based on the diameter of the bony cochlear nerve

canal (p=0,448), cochlear height (p=0,324) and the diameter of the internal acoustic meatus (p=0,145).

After analyzing *family-related* factors, it was observed that groups did not differ based on the family structure (p=0,185) and size of the family (p=0,793). In the "insufficient speech and language development" group, the father's and mother's education were significantly worse (p<0,001 in both cases), the parents' understanding of the CI process was poorer (p<0,001), and their families tended to significantly less frequently visit the CI center after the implantation surgery (p<0,001).

A comparison of groups based on *educational and hearing rehabilitation-related* factors revealed a significantly poorer parents' engagement in the child's learning process (p<0,001) in the "insufficient speech and language development" group. These children also attended specialized educational kindergartens more often (p=0,002), used total language to communicate more often (p<0,001), found it more difficult to reach speech and language therapy services (p<0,001), the latter also being less intensive (p=0,029) (Table 23).

Table 23. A comparative analysis of “poor” and “good” speech and language development groups.

Variable	Good speech and language development group N=42 N (%) or Mean	Insufficient speech and language development group N=39 N (%) or Mean	P value
Demographic factors			
Gender			
Male	20 (47.6)	24 (61.5)	0,212
Female	22 (52.4)	15 (38.5)	
Residential location:			
Five biggest cities	29 (69)	14 (35.9)	**0,013**
Cities with 20 000–99.000 inhabitants	1 (2.4)	6 (15.4)	
Cities with 10 000–19 900 inhabitants	1 (2.4)	3 (7.7)	
Cities with <10 000 inhabitants and the rural areas	11 (26.2)	16 (41)	
Age at the time of the study, years	8.36 (±2.3)	9.01 (±3.0)	0,394
Audiological factors			
Age at diagnosis, months	16.67 (±13.8)	25.32 (±16.6)	**0,011**

Preoperative mean hearing thresholds, dB	94.05 (±8.9)	95.0 (±8.7)	0,465
Residual preoperative hearing in the implanted ear:			0,344
Present	10 (23.8)	6 (15.2)	
Absent	32 (76.2)	33 (84.6)	
Use of residual hearing in the contralateral ear with the HA after CI:			0,039
Yes	12 (57.1)	6 (26.1)	
No	9 (42.9)	17 (73.9)	
Progression of hearing loss			
Present	9 (21.4)	5 (12.8)	0,309
Absent	33 (78.6)	34 (87.2)	
Postoperative hearing thresholds with CI, dB	32.60 (±5)	37.85 (±8)	**0,001**
Surgical, implant and processor-related factors			
Age at implantation, months	28,38 (±22.7)	38,20 (±20.7)	**0,005**
Duration of CI use, years	5,95 (±1.8)	5,77 (±2.5)	0,612
Unilateral CI	21 (50)	23 (59)	0,421
Bilateral CI	21 (50)	16 (41)	
Issues with the use of CI			**<0,001**
Present	0 (0)	11 (28.2)	

Absent	42 (0)	28 (71.8)	
Etiologic factors			
GJB2 (N=68)			
Positive	22 (62.9)	22 (63.6)	0,947
Negative	13 (37.1)	12 (36.4)	
Non-syndromic	23 (54.8)	22 (56.4)	0,723
Syndromic	4 (9.5)	1 (2.6)	
Prenatal cCMV	6 (14.3)	5 (12.8)	
Perinatal	4 (9.5)	4 (10.3)	
Postnatal	0 (0)	1 (2.6)	
Unknown	5 (11.9)	6 (15.4)	
Radiological factors N=64			
Diameter of the bony cochlear nerve canal, mm	1.77 (±0.2)	1,63 (±0.5)	0,448
Cochlear height, mm	3.62 (±0.3)	3,53 (±0.3)	0,324
Width of the internal acoustic meatus, mm	5.07 (±0.9)	4,87 (±1.5)	0,145
Family factors			
Family composition:			
Nuclear family	38 (90.5)	29 (74.4)	0,185
Single-parent	4 (9.5)	9 (23.1)	

Caregivers	0 (0)	1 (2.6)	
Family size:			
One child	17 (40.5)	16 (41)	0,793
Two children	20 (47.6)	16 (41)	
3 or more children	5 (11.9)	7 (17.9)	
Father's education level:			
Higher education	28 (70)	5 (12.8)	**<0,001**
Secondary education	12 (30)	26 (66.7)	
Incomplete secondary education	0 (0)	8 (20.5)	
Mother's education level:			
Higher education	31 (75.6)	13 (33.3)	**<0,001**
Secondary education	10 (24.4)	24 (61.5)	
Incomplete secondary education	0 (0)	2 (5.1)	
Parents' understanding of the CI process:			
Sufficient	31 (73.8)	7 (17.9)	**<0,001**
Insufficient	11 (26.2)	20 (51.3)	
Did not understand	0 (0)	12 (30.8)	
Family visits to the CI center:			
Sufficient	30 (71.4)	5 (12.8)	**<0,001**
Insufficient	11 (26.2)	17 (43.6)	
Did not visit	1 (2.4)	17 (43.6)	
Rehabilitation and educational factors			

Parents engagement in the learning process:			
Active	34 (81)	9 (23.1)	**<0,001**
Passive	8 (19)	18 (46.2)	
Do not participate	0 (0)	12 (30.8)	
Communication mode:			
Spoken language	42 (100)	21 (53.8)	**<0,001**
Total communication	0 (0)	15 (38.5)	
Sign language	0 (0)	3 (7.7)	
Accessibility of speech and language therapy:			
Good	37 (88.1)	13 (33.3)	**<0,001**
Average	4 (9.5)	18 (46.2)	
Poor	1 (2.4)	8 (20.5)	
Intensity of speech and language therapy:			
Did not attend	0 (0)	7 (17.9)	**0,029**
Once per week	4 (9.5)	11 (28.2)	
2 times per week	28 (66.7)	10 (25.6)	
3 times per week	4 (9.5)	6 (15.4)	
5 times per week	6 (14.3)	5 (12.8)	
Educational placement settings:			
General education	41 (97.6)	20 (51.3)	**<0,001**
Special education	1 (2.4)	19 (48.7)	
Home-schooling	0(0)	0(0)	

Does not attend yet	0(0)	0(0)	
Kindergarten:			
General education	31 (73.8)	16 (41)	**0,002**
Special education	11 (26.2)	21 (53.8)	
Too young to attend	0(0)	2 (5.1)	
School/program N=57			
General/mainstream program	27 (96.4)	4 (13.8)	**<0,001**
General/adapted program	1 (3.6)	11 (37.9)	
Special education school	0	14 (48.3)	
Home schooling	0	0	

Comparing groups based on speech perception, listening and speech recognition skills (measured using CAP and SIR scales), it was noticed that children with better speech and language developments demonstrated better speech perception (p<0,001) and higher scores of CAP and SIR scales (p<0,001) (Fig. 24)

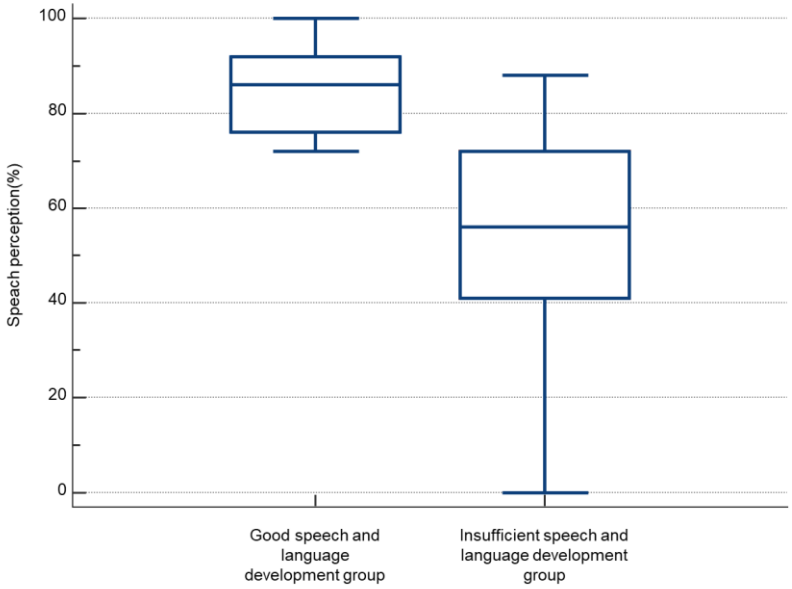


Figure 24. Speech perception amongst different speech and language development groups.

2.7.4. Determination of Prognostic Factors for Speech and Language Development Using Logistic Regression

The abovementioned variables, which differed significantly between two language development groups, were tested using the logistic regression analysis in order to determine associations between them and postoperative language development results

A univariate logistic regression analysis demonstrated that residential location (OR: 1,450; CI: 1,042-2,017; p=0,028), age at the

time of diagnosis (OR: 1,039; CI: 1,007-1,072; p=0,017) and CI aided thresholds (OR: 1,166; CI: 1,057-1,286; p=0,002) are the factors that influence postoperative language development results. They are also affected by the father's education (OR: 13,679; CI: 4,508- 41,508; p<0,001), mother's education (OR: 6,013, CI: 2,319-15,596, p<0,001), parents' understanding about the CI process (OR: 10,306; CI: 3,867-27,466; p<0,001) and the frequency of visits to the CI center (OR: 9,742; CI: 3,822- 24,834; p<0,001). Language development is also influenced by the parents' engagement in the learning process (OR: 8,310; CI: 3,037-22,738; p<0,001), accessibility of the speech and language therapy (OR: 8,310; CI: 3,037 - 22,738 0,370; p<0,001) and preschool institution (OR: 3,175; CI: 1,558-9,522; p=0,006) (Table 24).

Table 24. Univariate regression analysis to determine variables associated with postoperative language development results.

Variable	Odds ratio		P
	Value	95% CI	
	Univariate		
Residential location	1,450	1,042 - 2,017	0,028
Age at diagnosis	1,039	1,007 - 1,072	0,017
Postoperative hearing thresholds with CI	1,166	1,057 - 1,286	0,002
Age at implantation	1,022	1,000 - 1,044	0,053
Father's education	13,679	4,508 - 41,508	<0,001
Mother's education	6,013	2,319 - 15,596	<0,001

Parents' understanding about the CI process	10,306	3,867 - 27,466	<0,001
Family visits at the CI center	9,742	3,822 - 24,834	<0,001
Parents' engagement in the learning process	10,544	3,917 - 28,381	<0,001
Accessibility of the speech and language therapy	8,310	3,037 - 22,738	<0,001
Intensity of the speech and language therapy	1,353	0,958 - 1,909	0,086
Preschool institution	3,175	1,558 - 9,522	0,006

After assuring a significant relation between postoperative language development and the different chosen variables in a univariate regression analysis, the following variables were chosen for the multivariate regression analysis: age at the time of diagnosis, postoperative hearing thresholds with CI, parents' engagement in the learning process, and accessibility of speech and language therapy. Education and understanding about the CI process of the parents, family visits to the CI center were not included in the multiple regression analysis despite their statistical significance, as they were associated with the parents' engagement in the learning process and depend on it.

A multivariate regression analysis revealed that only parents' engagement in the learning process (OR: 6,255; CI: 1,846-21,191; p=0,003) and accessibility of speech and language therapy (OR: 3,295; CI: 1,112- 9,763; p=0,031) are two independent prognostic factors in language development after pediatric CI.

CONCLUSIONS

1. A unique etiologic profile of Lithuanian children who are CI users was established. The most common etiologic factor amongst children who are CI users was non-syndromic HL (63 cases, 51.6%). The second most common cause were perinatal factors (16 cases, 13.1%). Prenatal factors – a congenital CMV infection – were in the third place (12 cases, 9.8%). Syndromic HL was in the fourth place (10 cases, 8.2%) children; postnatal factors – in the fifth place (4 cases, 3.3%). The cause of HL remained unknown in 17 (13.9%) cases.

2. The prevalence of inner ear malformations in the group of pediatric CI users was established after performing an analysis of temporal bone CT images; the prevalence of inner ear malformations was at 33%.

3. Speech perception results after CI were evaluated. On average, 5.9 years after the CI surgery, excellent and good speech perception levels were demonstrated by 19.8 and 35.8% of children, respectively; average levels – by 19.8%, weak and very weak – by 6.2 and 13.6%, respectively; speech perception without any visual cues of 4.9% of children was equal to 0. The mean speech perception level of the study sample was 69.6 ± 24.2%.

4. Speech and language results after the CI were evaluated: out of 81 children examined, on average, 5.9 years after the CI surgery, 24.7% of participants reached a very good speech and language development level; 27.2% – a good level; 25.9% – a sufficient level; 22.2% – an insufficient level of speech and language perception.

5. A univariate logistic regression analysis revealed that results of speech perception and language development of pediatric CI users

are mostly associated with family, education and rehabilitation – related factors.

A multivariate regression analysis proved that age at implantation, postoperative CI aided thresholds and the diameter of the BCNC are three independent prognostic factors of speech perception after pediatric CI. Results of speech and language development depend on parents' engagement in child's learning process and accessibility of speech and language therapy.

RECOMMENDATIONS

1. The preoperative preparation for CI should include the evaluation of etiologic, medical, anatomical, audiologic, surgical, implant–associated, family, education and rehabilitation–related factors that might influence results after CI.
2. The preoperative parental counselling should accentuate family's role in the CI process, and the influence of family–related factors on the postoperative results.
3. The evaluation of the etiology of congenital hearing loss should begin with the genetic counselling, and a retrospective diagnosis of a cCMV infection should be established by the detection of CMV DNA from a dried blood spot.
4. The preoperative evaluation of the temporal bone should include a detailed measurement of delicate inner ear structures, such as the cochlear height and the diameter of the bony cochlear nerve canal, on CT scan images.
5. Pediatric CI users should regularly visit specialists after the implantation to measure postoperative results. When insufficient CI results are identified, it is recommended to determine factors that might have influenced it, inform the family, and discuss with the CI team changes should be made in the intervention manner.
6. The CI program should be established to coordinate collaboration between different institutions and ensure the long term monitoring of pediatric CI users.

SUMMARY IN LITHUANIAN

ĮVADAS

Klausos sutrikimas (KS) yra dažniausia įgimta patologija išsivysčiusiose šalyse. Iš 1000 naujagimių 1–3 gimsta turėdami neurosensorinį klausos sutrikimą, dar 1–2 vaikų klausa sutrinka vėliau.

Trečdaliu atvejų įgimtas neurosensorinis klausos sutrikimas yra sunkus bei ypač sunkus (gilus). Toks KS turi ilgalaikių padarinių vaiko ir jo šeimos gyvenimui. Labiausiai kurtumas veikia sakytinės kalbos raidą, tai riboja kasdienį bendravimą, menkina mokymosi galimybes ir raštingumą, dėl to ne tik nukenčia vaiko mokymosi pasiekimai ir galimybė ateityje įsidarbinti, bet ir kyla psichosocialinių problemų. Svarbu, kad laikotarpis nuo abipusio kurtumo pradžios iki medicininės intervencijos – klausos reabilitacijos klausos aparatais arba kochleariniais implantais – būtų kuo trumpesnis.

Kochlearinis implantas (KI) – tai elektroninis medicininis prietaisas, kuriuo kurtiesiems grąžinama klausa. KI procesorius transformuoja aplinkos garsus į elektroninį signalą, o implanto elektrodas, įstatytas į vidinėje ausyje esančią sraigę, perduoda šį signalą klausos nervui. Toliau impulsas keliauja į smegenų žievę ir asmuo ima girdėti. Tyrimais įrodyta, kad kochlearinė implantacija – saugus ir efektyvus būdas kurtumui gydyti.

Kochlearinės implantacijos rezultatai vertinami etapais: pirmiausia – girdėjimas ir kalbos suvokimas, tuomet – kalbos įgūdžiai, vėliau – integracija į bendrojo lavinimo įstaigą, gyvenimo kokybė ir kiti. Mokslinės literatūros duomenimis, pusės vaikų, besinaudojančių KI, kalbos suvokimo ir kalbinių įgūdžių lygis gali siekti normaliai girdinčių bendraamžių.

Vis dėlto pastebima didelė individualių pasiekimų įvairovė kalbos suvokimo ir kalbos išsivystymo srityse. Įrodyta, kad vaiko amžius KI operacijos metu yra svarbiausias veiksnys, lemiantis pooperacinius rezultatus, – rezultatai geresni tuomet, kai operacija atliekama kuo jaunesniam vaikui. Ne mažiau svarbūs veiksniai yra

vidiniai biologiniai – kurtumo etiologija ir vaiko intelektas; išoriniai techniniai – implanto savybės, implanto programavimas; socialiniai – specialiojo ugdymo galimybės, tėvų įsitraukimas padedant vaikui mokytis ir kiti. Įvardijus įtaką darančius veiksnius, lengviau prognozuoti konkretaus paciento rezultatus, o šeimai tai leidžia išsikelti realius lūkesčius bei planuoti gydymą ir reabilitaciją po kochlearinės implantacijos taip, kad būtų pasiekta maksimali nauda

Lietuvoje pirmąją kochlearinę implantaciją atliko švedų profesorius S. Harris 1998 m. Kauno medicinos universiteto klinikose. Dabar Lietuvoje yra daugiau kaip 370 KI naudotojų

Iki šiol Lietuvoje vaikų KI ilgalaikiai rezultatai – kalbos suvokimas, kalbos raida, integracija į bendrojo lavinimo įstaigas – nebuvo tiriami. Iki šio tyrimo nebuvo analizuojami ir tokie galimi KI efektyvumo veiksniai, kaip kurtumo etiologija, ausies radiologinė anatomija, socialiniai aspektai. Žinoma, kad nuo pusės iki dviejų trečdalių įgimto klausos sutrikimo (ĮKS) atvejų lemia paveldėjimas. Likusią dalį sudaro nepaveldėtas, t. y. aplinkos veiksnių sukeltas arba nežinomos kilmės, klausos sutrikimas. Įgimta citomegalo viruso (ĮCMV) infekcija yra antra pagal dažnį ĮKS priežastis ir lemia apie 10–30 proc. ĮKS atvejų. Dažniausiai ĮCMV infekcija yra besimptomė, todėl specifiniai tyrimai naujagimiams neatliekami, tačiau KS gali išsivystyti po kelių mėnesių ar metų. Todėl tebėra aktualu nustatyti ĮCMV infekcijos paplitimą įvairiose populiacijose.

Žinoma, kad geriausi KI rezultatai yra pasiekiami tose šalyse, kuriose yra sukurta KI sistema, apimanti ankstyvą KS diagnostiką, priešoperacinį pasiruošimą, chirurginę implantacijos procedūrą bei visapusišką medicininę, pedagoginę, techninę, psichologinę, socialinę bei finansinę pagalbą po implantacijos. Nors Lietuvoje vaikų KI atliekama beveik du dešimtmečius, tačiau iki šiol tokios sistemos mūsų šalyje nėra. Šiuo tyrimu siekta parengti rekomendacijas Lietuvos KI sistemai kurti. Remiantis KI sistema bus galima optimizuoti kandidatų atranką bei pooperacinę reabilitaciją, savo ruožtu pagerinti kurčiųjų vaikų socialinę integraciją.

Apibendrinant galima teigti, kad vaikų KI rezultatų vertinimas ir prognostinių veiksnių nustatymas išlieka svarbi klinikinė ir mokslinė problema. Šiame tyrime pirmą kartą Lietuvoje buvo vertinama KI naudojančių vaikų bendrosios, šeimos ir lavinimo charakteristikos, kurtumo etiologija, pooperaciniai rezultatai bei juos lemiantys veiksniai. Manoma, kad disertacinio darbo rezultatai padės išplėsti klinikines, socialines, pedagogines priemones, leidžiančias optimizuoti vaikų KI rezultatus.

DARBO TIKSLAS

Nustatyti vaikų kochlearinės implantacijos funkcinius rezultatus ir jų prognostinius veiksnius.

DARBO UŽDAVINIAI

1. Nustatyti kochlearinius implantus naudojančių vaikų kurtumo priežastį, atliekant genetinius, CMV DNR sauso kraujo lašo tyrimus, klausos sutrikimo rizikos veiksnių analizę, bei įvertinti gautą etiologinį profilį.
2. Įvertinti kochlearinius implantus naudojančių vaikų vidinės ausies anatominius pokyčius, atliekant smilkinkaulių kompiuterinės tomografijos vaizdų analizę.
3. Nustatyti kurčių vaikų kalbos suvokimo rezultatus po kochlearinės implantacijos, atliekant kalbinę audiometriją.
4. Nustatyti kurčių vaikų kalbos raidos rezultatus po kochlearinės implantacijos, atliekant kalbos raidos vertinimą.
5. Nustatyti vaikų kochlearinės implantacijos rezultatų prognostinius veiksnius.

DARBO METODIKA

Mokslinis daugiacentris tarpdisciplininis skerspjūvio tyrimas atliktas 2013–2018 metais VU MF Ausų, nosies, gerklės ir akių ligų

klinikoje bei VUL SK filialo Vaikų ligoninės Vaikų ausų, nosies, gerklės ir akių ligų skyriuje. Tiriamieji – kurtieji vaikai, kuriems atlikta KI. 122 vaikai atitiko numatytus įtraukimo į tyrimą kriterijus: kurtieji vaikai, kuriems buvo atlikta viena arba dvi KI operacijos; tiriamieji 1–18 metų amžiaus; KI operacija(-os) atlikta(-os) VUL SK Ausų, nosies, gerklės ir akių klinikoje; vienpusė arba pirmoji iš dviejų KI atlikta ne vėliau nei prieš 6 mėn.; vaikų tėvai ar globėjai sutiko, kad jų vaikas dalyvautų tyrime, ir pasirašė informuoto asmens sutikimo formą.

Pagal numatytą skerspjūvio tyrimo dizainą – priešoperaciniai, operacijos ir pooperaciniai tiriamojo duomenys rinkti bei etiologiniai kurtumo veiksniai tirti ir pooperaciniai klausos ir kalbos rezultatai vertinti lygiagrečiai tuo pačiu metu:

- siekiant nustatyti tiriamojo *priešoperacinius, operacijos ir pooperacinius veiksnius*, galinčius veikti KI rezultatus, apklausti tiriamųjų tėvai bei peržiūrėta medicininė dokumentacija – surinkti tiriamojo demografiniai, medicininiai, audiologiniai, operacijos, šeimos, lavinimo ir ugdymo duomenys;
- siekiant nustatyti *kurtumo priežastį*, vertinti kurtumo rizikos veiksniai, atliktas genetinis ištyrimas bei CMV DNR tyrimas sauso kraujo lašo ėminyje;
- siekiant nustatyti *anatominius vidinės ausies pokyčius*, galinčius veikti KI rezultatus, atlikta išsami prieš operaciją atliktos smilkinkaulių KT vaizdų analizė;
- siekiant nustatyti pooperacinius *klausos rezultatus*, atliktas vertinimas pagal skales, toninė audiometrija ir kalbinė audiometrija laisvame garso lauke naudojant KI;
- siekiant nustatyti pooperacinius *kalbos rezultatus*, buvo atliktas kalbos raidos vertinimas.

Vėliau, įvertinus turimus demografinius, medicininius, audiologinius, operacijos, šeimos, lavinimo ir ugdymo duomenis bei pooperacinius rezultatus, nustatyti vaikų KI rezultatų *prognostiniai veiksniai*.

Tyrimų rezultatams sisteminti naudota aprašomoji statistika, vidurkis, standartinis nuokrypis, minimali ir maksimali reikšmės, mediana, moda. Hipotezėms apie kintamųjų tarpgrupinius skirtumus tikrinti taikyti neparametriniai Mano, Vitnio ir Vilkoksono (dviem nepriklausomoms imtims) arba Kruskalo ir Voliso (daugiau negu dviem nepriklausomoms imtims) kriterijai. Rezultatai laikyti statistiškai reikšmingais, kai $p<0,05$. Ryšiams tarp kintamųjų nustatyti buvo skaičiuojami Pirsono ir Spirmeno koreliacijos koeficientai. Norint apibrėžti atskirų rodiklių priklausomybę ir prognozuoti analizuojamų rodiklių reikšmes, taip pat buvo naudotas logistinės regresijos metodas. Statistinė duomenų analizė atlikta naudojant MS Excel, IBM SPSS 21.0 ir MedCalc 18.11.3 programas.

REZULTATAI

Tiriamųjų grupę sudarė 122 vaikai, kuriems buvo atlikta viena arba dvi KI operacijos VUL SK Ausų, nosies, gerklės ir akių ligų centre. Tiriamųjų imtis sudarė 43,1 proc. bendros Lietuvos kurčiųjų vaikų, kuriems KI operacija buvo atlikta nuo 1999 m. iki 2017 m. pabaigos, populiacijos. 65 (53,3 proc.) vaikams buvo atlikta vienpusė KI), 57 (46,7 proc.) vaikams – abipusė KI, iš jų 34 (59,6 proc.) vaikai operuoti nevienmomentiškai, 23 (40,4 proc.) – vienmomentiškai. Vidutinis tiriamųjų amžius tyrimo metu buvo 7,6 ± 3,3 metų. Didžiausią imties dalį 86 (70,5 proc.) sudarė priešmokyklinio amžiaus vaikai ir pradinukai. Vidutinis tiriamųjų amžius pirmos operacijos metu buvo 32,5 ± 26,9 mėn. Vaikų, gimusių 2014 m. ir vėliau, kai Lietuvoje pradėta visuotinė naujagimių klausos patikra, amžius pirmos KI metu buvo 14,56 ± 4,91 mėn. ir statistiškai reikšmingai skyrėsi nuo vaikų, gimusių iki 2014 m., amžiaus pirmos operacijos metu – 36,47 ± 28,1 mėn. ($p<0,001$). Dauguma tiriamųjų vaikų, naudojančių KI, gyveno penkiuose Lietuvos didmiesčiuose. Klausos slenksčių vidurkiai prieš KI vidutiniškai sudarė 95,5 ± 7,8 dB geriau girdinčioje ausyje, 97,7 ± 4,8 dB operuotoje arba vienoje iš operuotų ausų abipusės operacijos atveju. 16,4 proc. vaikų turėjo likutinę klausą

operuotoje arba vienoje iš operuotų ausų. Po operacijos iš 65 vienpusių KI naudotojų 30,8 proc. vaikų nuolat naudojo KA kontralateralinėje ausyje. Pirmais pooperaciniais metais 14,8 proc. vaikų pasireiškė procesoriaus naudojimo problemų. Tiriamųjų vaikų šeimos po operacijos KI centre dažniausiai lankėsi pakankamai – 42,6 proc., 38 proc. šeimų lankėsi nepakankamai ir 19,7 proc. nesilankė KI centre, vertinant apsilankymų skaičių per pirmus 2 metus po KI. Vertinant vaikų, KI naudotojų, klausos ir kalbos lavinimo ir ugdymo aspektus nustatyta, kad 49,8 proc. vaikų šeimos aktyviai dalyvavo lavinant vaiką, 33,6 proc. šeimų dalyvavimas buvo pasyvus ir 17,2 proc. šeimų nedalyvavo vaiko lavinime. Dauguma tėvų bendraudami su vaiku vartojo tik sakytinę kalbą (71,3 proc.), 23,8 proc. šeimų vartojo ir sakytinę kalbą, ir gestus, 4,9 proc. šeimų su vaiku bendravo gestų kalba. Surdopedagoginė pagalba buvo gerai prieinama 53,3 proc. vaikų, vidutiniškai – 27,9 proc. ir blogai – 18,9 proc. vaikų. Tyrimo metu 59 proc. vaikų lankė bendrojo lavinimo ir 28,7 proc. – specialiojo lavinimo darželį ar mokyklą, 2,5 proc. mokėsi namuose ir 9,8 proc. vaikų dar nelankė ugdymo įstaigos dėl amžiaus.

GJB2 koduojančios sekos tyrimas atliktas visiems izoliuotą KS turintiems tiriamiesiems – 91 vaikui. Patogeniniai homozigotiniai arba sudėtiniai heterozigotiniai *GJB2* geno variantai nustatyti 58 (63,7 proc.) izoliuoto KS atvejais. 5 pacientams nustatyti kitų genų patogeniniai variantai, lemiantys nesindrominį KS. Atlikus 101 vaiko genetinį ištyrimą, nustatyti 63 (62,4 proc.) nesindrominio KS ir 10 (9,9 proc.) sindrominio KS atvejų.

117 vaikų buvo gauti sauso kraujo lašo ėminiai ir atlikti CMV PGR tyrimai, 14 (12 proc.) ėminių nustatyta CMV DNR.

Ištirtas vaikų, naudojančių KI, etiologinis profilis. Dažniausias etiologinis veiksnys – paveldimas nesindrominis klausos sutrikimas – nustatytas 51,6 proc., perinataliniai veiksniai – 13,1 proc., prenataliniai veiksniai, t. y. įgimta CMV infekcija, – 9,8 proc., sindromai – 8,2 proc., postnataliniai veiksniai – 3,3 proc. vaikų. Kurtumo priežastis liko neaiški 13,9 proc. vaikų.

Analizuojant smilkinkaulių KT vaizdus, 4 vaikams rastos sraigės nebaigtinio pasidalijimo anomalijos, 18 vaikų – prieangio ir pusratinių kanalų anomalijų, 16 vaikų – sraigės hipoplazija, 14 vaikų – kaulinio sraigės nervo kanalo stenozė ir 2 vaikams – prieangio vandentiekio išsiplėtimas. Bendras įgimtų vidinės ausies anomalijų dažnis buvo 33 proc.

Vertinant KI efektyvumą, laisvame garso lauke nustatytų klausos slenksčių vidurkis su vienu arba dviem KI buvo 36,3 ±7,8 dB. Vertinant klausymosi įgūdžius pagal KAK skalę, praėjus vidutiniškai 4,9 ±2,6 metų po KI operacijos, nustatyta, kad 41,8 proc. vaikų pasiekė skalės „lubas“ ir gali kalbėtis telefonu su pažįstamu pašnekovu. Vertinant kurčiųjų vaikų, KI naudotojų, kalbos suprantamumą pagal KSS skalę, praėjus vidutiniškai 4,9 ±2,6 metų po KI, paaiškėjo, kad iš 122 vaikų 41 proc. pasiekė aukščiausią skalės kategoriją – jiems išsivystė kalba, kuri yra suprantama visiems klausytojams kasdienės veiklos metu.

Vertinant kalbos suvokimą vaikų be sunkios negalios, vyresnių nei 5 metų amžiaus ir operuotų mažiausiai prieš 2 metus, nustatyta, kad puikų kalbos suvokimo lygį pasiekė –19,8 proc. tiriamųjų, gerą – 35,8 proc., vidutinį – 19,8 proc., silpną – 6,2 proc., labai silpną – 13,6 proc. vaikų; 4,9 proc. vaikų negalėjo būti tiriami atvirojo tipo kalbinės audiometrijos metodu. Šios grupės kalbos suvokimo vidurkis buvo 69,6±24,2 proc.

Vertinant kalbėjimo ir kalbos pasiekimus vaikų be sunkios negalios, vyresnių nei 5 metų amžiaus ir operuotų mažiausiai prieš 2 metus, nustatyta, kad 24,7 proc. tiriamųjų pasiekė labai gerą kalbos raidos lygį, 27,2 proc. – gerą, 25,9 proc. – patenkinamą ir 22,2 proc. – nepatenkinamą.

Nesindrominį KS turintiems vaikams diagnozė buvo nustatyta bei pirma KI operacija atlikta anksčiau nei kitų etiologijų (sindrominės, perinatalinės, prenatalinės, postnatalinės ir nežinomos) grupių vaikams (atitinkamai p=0,003 ir p=0,023). Iš 122 vaikų 14-ai (11,5 proc.) diagnozuota sunki gretutinė negalia: vaikų cerebrinis paralyžius, autizmas, epilepsija ir kt.

Siekiant išsiaiškinti, kokie veiksniai lemia blogesnį kalbos suvokimą, nustatytą kalbinės audiometrijos metodu, buvo suformuotos dvi grupės: gero ir silpno kalbos suvokimo. Tyrime nagrinėta 30 (demografinių, audiologinių, operacijos ir implanto, etiologinių, radiologinių, šeimos, lavinimo bei ugdymo) veiksnių, siekiant išsiaiškinti sąsajas su pooperaciniais kalbos suvokimo rezultatais. Visi kintamieji, kurie patikimai skyrėsi gero ir silpno kalbos suvokimo grupėse, buvo įtraukti į vienaveiksnės regresijos analizę. Regresinė analizė atskleidė, kad vaikų po KI prastesni *kalbos suvokimo* rezultatai yra susiję su gyvenamąja vieta kaime, vyresniu amžiumi nustatant diagnozę, vyresniu amžiumi operacijos metu, didesniais klausos slenksčiais po KI, siauresniu kauliniu sraigės nervo kanalu, KI naudojimo problemomis, žemesniu tėvų išsilavinimu, prastesniu tėvų supratimu apie KI procesą, retu šeimos lankymusi KI centre, mažesniu tėvų dalyvavimu lavinant vaiką, specialiojo lavinimo darželio lankymu ir nepakankamu surdopedagoginės pagalbos prieinamumu ir intensyvumu. Daugiaveiksnės žingsninės regresijos metodu nustatyta, kad amžius operacijos metu, pooperaciniai klausos slenksčiai naudojant KI ir kaulinio sraigės nervo kanalo spindis yra nepriklausomi kalbos suvokimo prognostiniai veiksniai po KI operacijos.

Siekiant išsiaiškinti, kokie veiksniai lemia geresnius arba blogesnius kalbos raidos rezultatus, buvo suformuotos dvi grupės: geros ir nepakankamos kalbos raidos. Visi demografiniai, operacijos ir implanto, audiologiniai, radiologiniai, šeimos bei lavinimo ir ugdymo kintamieji, kurie patikimai skyrėsi geros ir nepakankamos kalbos raidos grupėse, įtraukti į vienaveiksnės regresijos analizę. Regresinė analizė parodė, kad vaikų po kochlearinės implantacijos nepakankami *kalbos raidos* rezultatai yra susiję su gyvenamąja vieta kaime ar mažame miestelyje, vyresniu amžiumi nustatant diagnozę, didesniais klausos slenksčiais po KI, žemesniu tėvų išsilavinimu, nepakankamu tėvų supratimu apie KI procesą, retesniu šeimos lankymusi KI centre, mažesniu tėvų dalyvavimu lavinant vaiką, specialiosios ikimokyklinės ugdymo įstaigos lankymu ir

nepakankamu surdopedagoginės pagalbos prieinamumu. Daugiaveiksnės žingsninės regresijos metodu nustatyta, kad kalbos raidos rezultatai priklauso nuo tėvų įsitraukimo į mokymo procesą ir surdopedagoginės pagalbos prieinamumo.

IŠVADOS

1. Nustatytas unikalus Lietuvos vaikų, naudojančių KI, etiologinis profilis. Dažniausias etiologinis veiksnys – paveldimas nesindrominis klausos sutrikimas – nustatytas 51,6 proc., perinataliniai veiksniai – 13,1 proc., prenataliniai veiksniai, t. y. įgimta CMV infekcija, – 9,8 proc., sindromai –8,2 proc., postnataliniai veiksniai – 3,3 proc. vaikų. Kurtumo priežastis liko neaiški 13,9 proc. vaikų.

2. Kurčiųjų vaikų, naudojančių kochlearinius implantus, vidinės ausies anomalijų dažnis, nustatytas analizuojant smilkinkaulių KT vaizdus, siekia 33 proc.

3. Praėjus vidutiniškai 5,9 metų po kochlearinės implantacijos, kurčiųjų vaikų kalbos suvokimo vidurkis buvo 69,6 proc. Puikų ir gerą kalbos suvokimo lygį pasiekė atitinkamai 19,8 proc. ir 35,8 proc. vaikų, vidutinį – 19,8 proc., silpną ir labai silpną – atitinkamai 6,2 proc. ir 13,6 proc. vaikų, naudojančių KI. Po kochlearinės implantacijos 4,9 proc. vaikų atvirojo tipo kalbos suvokimas be vizualinių užuominų buvo lygus nuliui.

4. Iš kurčiųjų vaikų, kuriems vidutiniškai prieš 5,9 metų atlikta kochlearinė implantacija, labai gerą kalbos raidos lygį pasiekė 24,7 proc., gerą kalbos raidos lygį – 27,2 proc., o patenkinamą ir nepatenkinamą – atitinkamai 25,9 proc. ir 22,2 proc. tiriamųjų.

5. Vienaveiksnė regresinė analizė parodė, kad KI naudojančių vaikų ir kalbos suvokimo, ir kalbos raidos rezultatai daugiausia yra

susiję su vaiko šeimos bei ugdymo ir lavinimo veiksniais. Daugiaveiksnės žingsninės regresijos metodu nustatyta, kad amžius operacijos metu, pooperaciniai klausos slenksčiai naudojant KI ir kaulinio sraigės nervo kanalo spindis yra nepriklausomi kalbos suvokimo prognostiniai veiksniai po KI operacijos, o kalbos raidos rezultatai priklauso nuo tėvų dalyvavimo lavinant vaiką ir surdopedagoginės pagalbos prieinamumo.

REKOMENDACIJOS

Remdamiesi atlikto darbo rezultatais ir kitų autorių duomenimis, suformulavome šias praktines rekomendacijas Lietuvos kochlearinės implantacijos sistemai kurti:

1. Ruošiant vaiką kochlearinei implantacijai, priešoperaciniame etape rekomenduojame vertinti etiologinius, medicininius, anatominius, audiologinius, su operacija ir implantu, su šeima bei lavinimu ir ugdymu susijusius veiksnius, galinčius turėti įtakos implantacijos rezultatams.
2. Prieš operaciją reikėtų informuoti tėvus apie šeimos vaidmenį šiame procese ir pooperacinių rezultatų priklausomybę nuo šeimos veiksnių.
3. Vertinant kurtumo priežastis, etiologinę diagnostiką rekomenduojame pradėti nuo genetiko konsultacijos, o įgimtos citomegalo viruso (CMV) infekcijos retrospektyviajai diagnostikai atlikti rekomenduojame sauso kraujo lašo CMV DNR tyrimą.
4. Vertinant vidinės ausies anatomiją, į priešoperacinį smilkinkaulių kompiuterinės tomografijos vaizdų vertinimo protokolą rekomenduojame įtraukti detalų vidinės ausies struktūrų – sraigės aukščio ir kaulinio sraigės nervo kanalo spindžio matavimą.
5. Vertinant kochlearinės implantacijos rezultatus, reikėtų užtikrinti reguliarų pooperacinį lankymąsi KI centre. Identifikavus nepakankamus rezultatus, siūlome įvertinti veiksnius, kurie gali

turėti tam įtakos, informuoti šeimą, kartu su KI komandos specialistais spręsti dėl intervencijos būdo pakeitimo.

6. Tikslinga sukurti ir įdiegti tarpdisciplininę kochlearinės implantacijos sistemą, kuri koordinuotų skirtingų institucijų bendradarbiavimą ir užtikrintų kochlearinius implantus naudojančių vaikų ilgalaikę stebėseną.

PUBLICATIONS AND PRESENTATIONS

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Education

2013–2018. PhD studies at Vilnius University, Faculty of Medicine.
2002–2006. Residency in Otorhinolaryngology at Vilnius University, Faculty of Medicine.
2001–2002. Medical residency at Vilnius University, Faculty of Medicine.
1997–2001. Vilnius University, Faculty of Medicine.
1995–1997. Kaunas Medical University, Faculty of Medicine.
1984–1995. Secondary school in Vilnius.

Work experience

2006–present: Otorhinolaryngologist and audiologist at the Children‘s ENT Department of the Children’s Hospital, Affiliate of Vilnius University Hospital Santaros Klinikos.
2017–present: Otorhinolaryngologist in the Children‘s Clinic “Pagalba Mažyliui.”
2017–present: junior scientific worker in the project “Social Integration Challenges of Children with Cochlear Implants in Lithuania,” funded by a grant from the Research Council of Lithuania.

Memberships

Since 2009 – a member of International Society of Audiology.
Since 2006 – a member of the Lithuanian Otorhinolaryngologic Society, board member and secretary during 2010–2018.
Since 2006 – a member of the Vilnius Association of Otorhinolaryngologists.

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