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An Investigation of Hearing Levels, Tinnitus and Vertigo Symptoms in Children with Cardiac Disorders

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Abstract

Objective: Comorbidities accompanying to cardiac disorders might be as detrimental as the diseases themselves. While it is not common, comorbidities associated with inner ear functions may also be seen. This study was planned to investigate evaluation of hearing which also includes high frequencies, and the presence of vestibular and tinnitus symptoms in children with acute rheumatic fever (ARF), Kawasaki disease (KD) or who underwent open heart surgery (due to atrial septal defect and/or ventricular septal defect, Tetralogy of Fallot).

Methods: This study included a patient group including 214 children patients diagnosed with cardiac disorders (116 males, 98 females; mean age 9.70 [range 6-16]) and a control group including 44 healthy children who do not have any kind of chronic disease (21 males, 23 females; mean age 9.38 [range 6-16]). The subjects underwent hearing test with frequencies between 250-20000 Hz, vestibular and tinnitus symptoms were evaluated by Symptom Questionnaire Forms. Results: Out of 214 patients in the patient group, 6 (2.8%) had hearing loss in pure tones, 25 (11.7%) had in high frequencies, 35 (16.4%) had tinnitus symptoms, and 21 (9.8%) had vertigo symptoms. Hearing loss in high frequencies was detected in 11.7% of patients with ARF, in 22.7% of patients with KD, and in 7.8% of patients who underwent open heart surgery. The difference between KD patients and the control group in terms of hearing loss was statistically significant (p=0.014). Out of 214 patients in the patient group, 4 (1.9%) had hearing loss in pure tones and high frequencies, vertigo and tinnitus symptoms.

Conclusions: Our results suggest that some childhood cardiac disorders can cause some changes in the inner ear, although the exact cause is unknown. Perhaps, a detailed hearing and balance examination should be a routine in a child diagnosed with a cardiac disorders. We think it is necessary to work on more comprehensive patient groups and tests in the future.

Keywords: Cardiology, pediatric, hearing level, tinnitus, vertigo, child

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Introduction

Despite many developments today, cardiac diseases remain to be an important cause of morbidity and mortality in general population. Comorbidities accompanying to these diseases might be as detrimental as the diseases themselves. While it is not common, comorbidities associated with inner ear functions may also be seen. Acute rheumatic fever (ARF) is an autoimmune response to pharyngitis caused by group A Streptococcus and Streptococcus pyogenes. ARF is an illness which may cause pain and swelling in joints, heart valve regurgitation, chorea, skin and subcutaneous tissue involvement, and fever.[1,2] Though the etiology or pathophysiology remains to be completely illuminated, Kawasaki disease (KD) is one of the causes of systemic vasculitis characterized with acute inflammation, and it is mostly seen in early childhood.[3] First defined by Louis Arthur Etienne Fallot in 1888, Tetralogy of Fallot (TOF) is a disease consisting of ventricular septal defect (VSD), pulmonary artery stenosis, overriding aorta shifting to right side and right ventricular hypertrophy.[4,5] VSD is known as the most common congenital cardiac anomaly. While it can be isolated, it can also accompany other cardiac anomalies such as TOF.[6] Being one of the common cardiac anomalies, atrial septal defect (ASD) is the condition of the link between atria being permanent.[7] In ASD, VSD and TOF anomalies, repair by open heart surgery might be necessary based on the clinical condition.[8] There are several studies indicating that sensorineural hearing loss in KD and after open heart surgeries in the literature, however, there is still no clear information about the mechanism of occurrence and the effect on the vestibular system. This study was planned to investigate evaluation of hearing which also includes high frequencies, and the presence of vestibular and tinnitus symptoms in children with cardiac disorders (ARF, KD or who underwent open heart surgery (due to ASD and/or VSD, TOF).

Methods

This study included a patient group including 214 children patients (116 males, 98 females; mean age 9.70 [range 6-16]) who were diagnosed with ARF or KD in pediatric cardiology clinic or who underwent open heart surgery (due to VSD and/or ASD, TOF) and a control group including 44 healthy children who do not have any kind of chronic disease (21 males, 23 females; mean age 9.38 [range 6-16]). The study was prepared in accordance with Helsinki Declaration. The study was approved by the Institutional Review Board. Patients who did not meet study inclusion criteria were excluded to avoid bias.

Inclusion criteria for the patient group;

- Age between 6 and 16,
- Being diagnosed with ARF or KD, or history of open heart surgery (due to VSD and/or ASD, TOF) within the last year.

Exclusion criteria for the patient group;

- Mental retardation,
- A syndrome affecting the vestibulo-cochlear system,
- Current upper respiratory tract infection,
- Current otitis media and otitis media with effusion,
- Presence of wax in the ear to an extent which can affect the results of the audiological tests,
- History of ear surgery or adeno-tonsillectomy,
- Known diagnosis of a chronic disease other than the cardiac condition.

After written informed consent form was taken from the subjects' parents, these children underwent a complete otolaryngologic examination and their ears were checked using otoscope. Tympanometry was performed by an audiologist using MAICO m40 (Minneapolis, USA). Subjects in the study and the control groups underwent air conduction hearing tests, acoustic reflex recording and bone conduction audiometry (500-1000-2000-4000Hz), by the same audiologist in anechoic in IAC (Industrial Acoustics Company) standards using MAICO m42 (Berlin, Germany) audiometry device between the frequencies of 250 and 20000 Hz, and pure tone average (PTA) consisting of frequencies of 500-1000-2000-4000 Hz and high frequency average (HFA) consisting of frequencies of 8000-16000-20000 Hz were recorded. Subjects with conductive hearing loss detected in the audiometry tests and ears with a tympanogram result of Type B or Type C were excluded study. Tests were performed for both ears, and since the difference between two ears was less than 10 dB for almost all frequencies, the results were treated as single. 0-20 dB was considered as the normal hearing level.[9] Since there is no "vestibular symptom questionnaire form in Turkish language" in pediatric patient group with international validity, "Turkish-translated version" of the internationally accepted Pediatric Vestibular Symptom Questionnaire (PVSQ) form was used.[10] Consisting of 10 questions, this questionnaire form included responses of "mostly=3", "sometimes=2", "hardly ever=1", "never=0",

"I don't know", the patients chose the option that is relevant for them. The total score of 10 responses was calculated, and if the PVSQS was 0 to 15, it was considered to be normal, and a score of 16 to 30 was considered to be vertigo symptom (PVSQS+). Furthermore, for tinnitus assessment, the patients were asked the question of "Do you have complaints of buzzing, ringing and noise in your ears?" and requested to choose from one of the options; "mostly=3", "sometimes=2", "hardly ever=1", "never=0", "I don't know", patients who answered 2 or 3 were considered to have tinnitus symptom (TIN+). Patients with missing answers in the form or answering "I don't know" were excluded from the study.

All statistical analyses were performed using IBM SPSS ver. 23.0 (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.). Shapiro Wilk test was used as normality test. For non-normally distributed data, continuous variables were compared using Mann-Whitney U test. Categorical variables were compared using Pearson's chi-squared test and Fisher's exact test. A p-value of <0.05 was considered as significant.

Results

When the study group consisting of 214 patients and the control group consisting of 44 healthy children were compared in terms of age and sex, there was no statistically significant difference (p=0.956, 0.992, respectively). Table 1 shows the age and sex distribution, and PTA and HFA values of the study and the control groups. Out of 214 patients in the study group, 128 (59.8%) had ARF, 22 (10.3%) had KD, 64 (29.9%) had the history of open heart surgery (out of 64, 35 underwent operation due to ASD and/or VSD, and 29 due to TOF). Table 2 shows in pure tones and high frequencies, mean, minimum and maximum hearing values. Patients with a PTA, HFA or PTA&HFA (both PTA and HFA values) value above 20 dB were considered to have hearing loss. Out of 214 patients in the study group, 6 (2.8%) had a PTA value above 20 dB, 25 (11.7%) had a HFA value above 20 dB, 6 (2.8%) had a PTA&HFA value above 20 dB. No statistically significant difference was detected between the whole study and the control group in terms of PTA, HFA and PTA&HFA values being above 20 (p=0.594, 0.094, 0.594, respectively). When ARF patients, post-operative ASD and/or VSD+TOF patients were compared with the control group in terms of PTA, HFA and PTA&HFA values being above 20 dB, the difference was not statistically significant (p>0.05). Statistically significant difference was detected between Kawasaki patients and the control group in terms of PTA, HFA and PTA&HFA values being above 20 (p=0.010, 0.014, 0.010, respectively). Table 3 shows the Number/Percentage/p value of the subjects with a PTA, HFA, PTA&HFA value above 20 dB in the study and the control groups.

When evaluated individually for each studied frequency (250-20000Hz), various numbers of hearing loss (>20dB) were detected in the whole study group and the subgroups, though the statistically significant difference was only detected between Kawasaki patients and the control group for the frequencies of 1000-2000-4000-8000-16000 and 20000 (p=0.034, p=0.039, p=0.014). Table 4 shows the number/percentage (%)/p value of the individuals with a hearing level of >20 dB at each studied frequency.

Out of 214 patients in the whole study group, 35 (16.4%) had tinnitus and 21 (9.8%) had vertigo symptoms. Tinnitus and vertigo symptoms were detected in various rates in the study subgroups, however, no statistically significant difference was detected when the whole study group and the subgroups were compared with the control group. Table 5 shows tinnitus symptoms and PVSQS values of the study and the control groups.

Out of 214 patients in the study group, 4 (1.9%) had PTA of >20dB + Vertigo symptoms (Pure tone average above 20 dB together with PVSQS+), 9 (4.2%) had HFA of >20dB + Vertigo symptoms (High frequency average above 20 dB together with PVSQS+), 4 (1.9%) had PTA&HFA of >20dB + Vertigo symptoms (Both pure tone average and high frequency average above 20 dB together with PVSQS+), 4 (1.9%) had PTA of >20dB + Vertigo + Tinnitus symptoms (Pure tone average above 20 dB together with PVSQS+ and TIN+), 8 (3.7%) had HFA of >20dB + Vertigo + Tinnitus symptoms (High frequency average above 20 dB together with PVSQS+ and TIN+), 4 (1.9%) had PTA&HFA of >20dB + Vertigo + Tinnitus symptoms (Both pure tone average and high frequency average above 20 dB together with PVSQS+ and TIN+), however, the difference compared to the control group was not statistically significant (Table 6).

Discussion

This study was planned to investigate evaluation of hearing which also includes high frequencies, and the presence of vestibular and tinnitus symptoms in children with the age between 6 and 16 who were diagnosed with ARF or KD, or who underwent open heart surgery (due to ASD and/or VSD, TOF).

Table 1. Age and sex distribution of study and control groups, PTA, HFA values

	Control Group	ARF	Kawasaki	ASD-VSD	TOF	ASD-VSD +TOF	Study Group
Number Rate (%)	44 (100%)	128 (59.8%)	22 (10.3%)	35 (16.4%)	29 (13.6%)	64 (29.9%)	214 (100%)
Boy/Girl (Number)	21/23	60/68	11/11	18/17	14/15	32/32	116/98
Boy/Girl Rate (%)	47.7/52.3	46.9/53.1	50/50	51.4/48.6	48.3/51.7	50/50	54.2/45.8
Age Average	9.3864	9.6719	9.9545	9.7143	9.6552	9.6875	9.7056
Pure Tone Average (PTA)	5,9091	5.9082	9.2614	4.9643	4.0086	4.2354	5.1765
High Frequency Average (HFA)	5.6818	8.3984	14.4697	7.2857	6.0345	6.7522	8.6532

Table 2. In pure tones and high frequencies, mean, minimum and maximum hearing values.

		Pure Tones 250-500-1000-2000-4000 Hz	High Frequencies 8000-16000-20000 Hz
	N	44	44
Control Group	Mean±SD	5.9±3.83	5.68±5.24
	Minimum- Maximum	0.00-18.75	0.00-33.33
	N	128	128
ARF	Mean±SD	5.9±5.38	8.39±11.15
	Minimum- Maximum	0.00-20.00	0.00-50.00
	N	22	22
KAWASAKİ	Mean±SD	9.26±10.37	14.46±10.37
	Minimum- Maximum	0.00-36.25	0.00-58.33
	N	35	35
ASD-VSD	Mean±SD	4.96±5.75	7.28±12.00
	Minimum- Maximum	0,00-25.00	0,00-56.67
	N	29	29
TOF	Mean±SD	4.00±5.24	6.03±9.27
	Minimum- Maximum	0.00-25.00	0.00-41.67

Table 3. Number, Rate, %, pValue of PTA, HFA, PTA&HFA values of more than 20 dB in the study and control groups

	Control Group n=44	ARF n=128	Kawasaki n=22	ASD-VSD n=35	TOF n=29	ASD-VSD +TOF n=64	Study Group n=214
PTA >20dB	0/0%	0/0% No p value	**4/18.2% p=0.010**	1/2.9% p=0.443	1/3.4% p=0.397	2/3.1% p=0.513	6/2.8% p=0.594
HFA>20dB	0/2.3%	15/11.7% p=0.074	5/22.7% **p=0.014**	3/8.6% p=0.317	2/6.9% p=0.559	5/7.8% p=0.398	25/11.7% p=0.094
PTA&HFA >20dB	0/0%	0/0% No p value	**4/18.2% p=0.010**	1/2.9% p=0.443	1/3.4% p=0.397	2/3.1% p=0.513	6/2.8% p=0.594

*A p-value <0.05 was considered as significant.

Table 4. Number, Rate%, pValue of children with hearing level> 20 dB at viewed frequencies.

	Control Group n=44	ARF n=128	Kawasaki n=22	ASD-VSD n=35	TOF n=29	ASD-VSD +TOF n=64	Study Group n=214
250 Hz	0 (0%)	0 (0%) No p value	0 (0%) No p value	0 (0%) No p value	0 (0%) No p value	0 (0%) No p value	0 (0%) No p value
500 Hz	0 (0%)	0 (0%) No p value	1 (4.5%) p=0.333	0 (0%) No p value	0 (0%) No p value	0 (0%) No p value	1 (0.5%) p=1.000
1000 Hz	0 (0%)	0 (0%) No p value	3 (13.6%) **p=0.034**	1 (2.9%) p=0.443	1 (3.4%) p=0.397	2 (3.1%) p=0.513	5 (2.3%) p=0.592
2000 Hz	1 (2.3%)	2 (1.6%) p=0.971	4 (18.2%) **p=0.039**	2 (5.7%) p=0.581	1 (3.4%) p=1.000	3 (4.7%) p=0.644	9 (4.2%) p=1.000
4000 Hz	1 (2.3%)	12 (9.4%) p=0.188	4 (18.2%) **p=0.039**	2 (5.7%) p=0.581	1 (3.4%) p=1.000	3 (4.7%) p=0.644	19 (8.9%) p=0.214
8000 Hz	1 (2.3%)	11 (8.6%) p=0.301	4 (18.2%) **p=0.039**	2 (5.7%) p=0.581	1 (3.4%) p=1.000	3 (4.7%) p=0.644	18 (8.4%) p=0.213
16000 Hz	1 (2.3%)	15 (11.7%) p=0.074	5 (22.7%) **p=0.014**	3 (8.6%) p=0.317	2 (6.9%) p=0.559	5 (7.8%) p=0.398	25 (11.7%) p=0.094
20000 Hz	1 (2.3%)	15 (11.7%) p=0.074	5 (22.7%) **p=0.014**	3 (8.6%) p=0.317	2 (6.9%) p=0.559	5 (7.8%) p=0.398	25 (11.7%) p=0.094

*A p-value <0.05 was considered as significant.

Table 5. Demonstration of Tinnitus and PVSQS values/Rate%/p value in study and control groups.

		Control Group n=44	ARF n=128	Kawasaki n=22	ASD-VSD n=35	TOF n=29	ASD-VSD +TOF n=64	Study Group n=214
Tinnitus scores	**0 or 1**	38 (86.4%)	109 (85.2%)	15 (77.3%)	27 (77.1%)	26 (89.7%)	53 (82.8%)	179 (83.6%)
	2 or 3 **(Tinnitus symptom+)**	6 (14.6%)	19 (14.8%) p=0.845	5 (22.7%) p=0.485	8 (22.9%) p=0.286	3 (10.3%) p=0.676	11 (17.2%) p=0.619	35 (16.4%) p=0.653
PVSQS	**0-15**	42 (95.5%)	117 (91.4%)	18 (81.2%)	31 (88.6%)	27 (93.1%)	58 (90.6%)	193 (90.2%)
	16-30 (Vertigo symptom+)	2 (4.5%)	11 (8.6%) p=0.519	4 (18.2%) p=0.09	4 (11.4%) p=0.398	2 (6.9%) p=0.666	6 (9.4%) p=0.09	21 (9.8%) p=0.387

*A p-value <0.05 was considered as significant

Table 6. Demonstration of hearing loss and/or vertigo and/or tinnitus symptom in control and study groups as patient number/percentage%/p value.

	Control Group n=44	ARF n=128	Kawasaki n=22	ASD-VSD n=35	TOF n=29	ASD-VSD +TOF n=64	Study Group n=214
PTA>20dB +Vertigo symptom	0 (0%)	0 (0%)	2 (9.1%) p=0.108	1 (2.9%) p=0.443	1 (3.4%) p=0.397	2 (3.1%) p=0.513	4 (1.9%) p=0.361
HFA>20dB +Vertigo symptom	0 (0%)	4 (3.1%) p=0.573	2 (9.1%) p=0.108	2 (5.7%) p=0.443	1 (3.4%) p=0.397	3 (4.7%) p=0.269	9 (4.2%) p=0.365
PTA&HFA>20dB +Vertigo symptom	0 (0%)	0 (0%)	2 (9.1%) p=0.108	1 (2.9%) p=0.443	1 (3.4%) p=0.397	2 (3.1%) p=0.513	4 (1.9%) p=0.361
PTA>20dB +Vertigo +Tinnitus symptom	0 (0%)	0 (0%)	2 (9.1%) p=0.108	1 (2.9%) p=0.443	1 (3.4%) p=0.397	2 (3.1%) p=0.513	4 (1.9%) p=0.361
HFA>20dB +Vertigo +Tinnitus symptom	0 (0%)	4 (3.1%) p=0.573	2 (9.1%) p=0.108	2 (5.7%) p=0.443	1 (3.4%) p=0.397	3 (4.7%) p=0.269	8 (3.7%) p=0.358
PTA&HFA>20dB +Vertigo +Tinnitus symptom	0 (0%)	0 (0%)	2 (9.1%) p=0.108	1 (2.9%) p=0.443	1 (3.4%) p=0.397	2 (3.1%) p=0.513	4 (1.9%) p=0.361

*A p-value <0.05 was considered as significant.

While a medical therapy given for a short hospitalization period is mostly sufficient for the treatment of ARF, due to permanent and chronic damage in cardiac valves, it may lead to rheumatic heart disease which is an important cause of morbidity and mortality, though this is not common.[1,2,11,12] Out of 128 ARF patients in our study, 15 (11.7%) had hearing loss in high frequencies, 19 (14.8%) had tinnitus symptoms, 11 (8.6%) had vertigo symptoms, 4 (3.1%) had hearing loss in high frequencies, tinnitus and vertigo symptoms together. While these values were not statistically significant, they are very high. There is a possibility that these audio-vestibular changes are seen due to autoimmune causes. The most important antigen in the pathogenesis of autoimmune hearing loss is collagen.[13] In their study, Yoo and Yazawa [14] showed increased levels of serum antibodies against bovine type-2 collagen antigen in 5 of 12 patients with otosclerosis. In the following years, many authors have reported an association between type-2 collagen antibodies and different inner ear conditions including sudden hearing loss, idiopathic progressive sensorineural hearing loss, otosclerosis and Meniere's disease.

Clinically, KD is characterized with erythema on lips and mucosae, cervical lymphadenopathy, polymorphous exanthema, erythema and edema on hands and feet, and fever lasting for 5 days or more.[3] Out of 22 Kawasaki patients in our study, 4 (18.2%) had hearing loss in pure tones, 5 (22.7%) had in high frequencies, 4 (18.2%) had both in pure tones and high frequencies. When these patients were compared with the control group, the difference was statistically significant (p=0.010, 0.014, 0.010, respectively). Four patients (18.2%) had hearing loss at frequencies of 2000-4000-8000 Hz and 5 patients (22.7%) at frequencies of 16000-20000 Hz. At these frequencies, the difference compared to the control group was statistically significant (p=0.034, p=0.039, p=0.014). Sundel et al. [17] have reported sensorineural hearing loss in 7 of 23 Kawasaki patients (30.4%), Knott et al [18] in 19 of 62 patients (30.6%), Magalhaes et al [19] in 22 of 40 patients (55%), and Alves et al. [20] in 38 of 115 patients (33%). Out of 22 Kawasaki patients in our study, 15 (22.7%) had tinnitus symptoms, 4 (18.2%) had vertigo symptoms, 2 (9.1%) had hearing loss, tinnitus and vertigo symptoms together. The mechanism via which KD affects the inner ear is yet to be proven, however, there are various theories. High-dose acetylsalicylic acid (ASA) is used for the treatment of KD, and while there are studies suggesting that this may cause hearing loss, there also studies suggesting vice versa. [18,21] While some authors that inflammation-associated thrombocytosis, prolonged anemia and increased sedimentation rate are involved, others state that hearing loss is caused by the direct cytopathic effect on cochlea or labyrinth via a mechanism of action similar to viral diseases. Other theories include immune system activation, presence of increased circulatory immune complexes, and vasculitis.[17,18,20-22]

VSD is known as the most common congenital cardiac anomaly. While it can be isolated, it can also accompany other cardiac anomalies such as TOF.[6] Being one of the common cardiac anomalies, ASD is the condition of the link between atria being permanent [7]. In ASD, VSD and TOF anomalies, repair by open heart surgery might be necessary based on the clinical condition.[8,9] In this study, out of 64 patients who underwent open heart surgery within the last year (35 of 65 patients due to ASD and/or VSD, 29 due to TOF), 2 (3.1%) had hearing loss in pure tones, 5 (7.8%) had in high frequencies, 11 (17.2%) had tinnitus symptoms, 6 (9.4%) had vertigo symptoms, 2 (3.1%) had hearing loss, tinnitus and vertigo symptoms together. While these values were not statistically significant, they are very high. The first case of sensorineural hearing loss after open heart surgeries was reported by Arenberg et al. [8] in 1972, and in 1975 Wright and Saunders [23] and later Plasse et al [24] assessed 7000 cases retrospectively and reported the rates of hearing loss. The hearing loss rates were reported to be between 0.01 and 0.14%, and the described cases were mostly reported to be in high frequencies.[24-26] There are various theories for the development of these audio-vestibular changes. Possible sensorineural hearing loss following open heart surgeries has been reported due to various reasons including thromboembolic event, hypotension or perfusion insufficiency, hypothermia, hypercoagulability and ototoxic medication use.[8,9,25-27] Some animal studies have demonstrated that hearing loss may develop as labyrinthine artery may be affected as a result of thrombosis, embolism or spasm.[28,29]

In the pediatric cardiac study group consisting of 214 patients, 6 (2.8%) had hearing loss in pure tone frequencies, 25 (11.7%) had in high frequencies, though, the difference compared to the control group was not statistically significant. Thirty-five (16.4%) patients had tinnitus symptoms and 21 (9.8%) had vertigo symptoms, though, the difference compared to the control group was not statistically significant. Eight (3.7%) patients had hearing loss in high frequencies, vertigo and tinnitus symptoms, 4 (1.9%) had hearing loss both in pure tone and high frequencies, vertigo

Study Limitations

Our aim was to evaluate hearing in pediatric patients diagnosed with cardiac disorders such as ARF, KD or who underwent open heart surgery. Hearing is one of the functions of the inner ear, and tinnitus symptoms may also occur when the hearing is affected. Vertigo symptoms can be seen in pathologies affecting the inner ear. We evaluated tinnitus and vertigo only with a symptom questionnaire and determined the presence and degree of symptoms. We know that we did not performed advanced objectif tests such as Videonystagmography, Head Impulse Test, and Vestibular Evoked Myogenic Potential for vertigo. If we had done these objective tests, the study might have been more specific, but we believe that it would be valuable in pediatric patients with different cardiac disorders, due to lack of such a study. However, our study may be valuable as it is the first study to evaluate the hearing functions of pediatric patients with different cardiac disorders as well as both vertigo and tinnitus symptoms. We believe that our work may be the beginning of future studies in this field and the study contributes to the literature.

Conclusion

Our results suggest that some childhood cardiac disorders can cause some changes in the inner ear, although the exact cause is unknown. Perhaps, a detailed hearing and balance examination should be a routine in a child diagnosed with an cardiac disorder. We think it is necessary to work on more comprehensive patient groups and tests in the future.

COMPLIANCE WITH ETHICAL STANDARDS

Ethics Committee Approval: The study was approved by the Institutional Review Board. **Informed Consent:** Informed written consent was obtained from the parents of the children studied after explanation of the research purpose.

Research involving Human Participants and/or Animals: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards

Authorship Contributions: Concept: Murat Koçyiğit, Helen Bornaun, Safiye G. Örtekin, Design: Murat Koçyiğit, Helen Bornaun, Safiye G. Örtekin, Taliye Çakabay, Selin Üstün Bezgin, Data Collection or Processing: Taliye Çakabay, Safiye G. Örtekin, Helen Bornaun, Selin Üstün Bezgin, Guven Ozkaya, Ebru Sahan, Analysis or Interpretation: Taliye Çakabay, Ebru Sahan, Güven Özkaya, Literature Search: Murat Koçyiğit, Writing: Murat Koçyiğit. Helen Bornaun

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