ORL, DOI: 323181 Gelen Kutusu | x

Reber, Christoph Kime: drhayriye, bana ayrıntıları görüntüle 30 Kas Yanıtla

<<Document as attachment>>

ORL
AUDIOLOGICAL FINDINGS IN CELIAC DISEASE
KARABULUT et al.
DOI: 10.1159/000323181

Dear Dr. Karabulut

I am pleased to inform you that the above-mentioned paper has been accepted for publication and handed over to the production editing department for copyediting and typesetting. From now on, I will be your contact person for the further processing of your manuscript. Should you have any questions or need more detailed information, please do not hesitate to contact me. Please always quote journal name and DOI number (323181) of your article in the subject line of any correspondence.

Please find attached our Estimation for PAGE CHARGES . Save this document on your PC and complete it. Please send it back by email.

Yours sincerely,

Christoph Reber

S. Karger AG - Medical and Scientific Publishers
Christoph Reber
Production Editor
Allschwilerstrasse 10
CH-4009 Basel (Switzerland)
fax +41 61 306 1234
email: c.reber@karger.ch
www.karger.com

AUDIOLOGICAL FINDINGS IN CELIAC DISEASE

Running tittle: Celiac Disease and Hearing

Category of Manuscript: Original Manuscript

(1)Hayriye KARABULUT MD, MSc, (2)Şamil HIZLI MD, (3)Muharrem DAGLI MD, (4)Ismail KARABULUT MD, PhD, (1)Baran ACAR, MD, (1)Emrah CELIK MD, (5)Ayhan ABACI MD, (5)Osman OZDEMIR, MD, (1)R.Murat KARASEN MD.

(1) MH Kecioren Training and Research Hospital, Department of Otorhinolaryngology

(2) Gaziantep University Faculty of Medicine Department of Pediatric Gastroenterology

(3) MH Kecioren Training and Research Hospital, Department of Pediatrics

(4) Hacettepe University Faculty of Medicine Department of Physiology

(5) MH Diskapi Yildirim Beyazit Training and Research Hospital, Department of Otorhinolaryngology

Corresponding Author:

Dr. Hayriye KARABULUT

Kecioren Training and Research Hospital

Department of Otorhinolaryngology and Audiology

Pinarbasi mahallesi sanatoryum caddesi Ardahan sok. no:1

Keciören

06310, Ankara, TURKEY

Tel: +90 312 356 90 00

Fax: +90 312 356 90 22

E-mail: hayriyekarabulut@gmail.com

Abstract

Objective: Celiac disease (CD) is a gluten-triggered immune enteropathy caused by a genetic predisposition. Recent papers suggest that atypical CD is increasingly recognized which is defined with wide range of extraintestinal findings. The aim of this study was to investigate the effect of CD on hearing pathway including olivocochlear efferent system in children.

Methods: Forty one children who had CD, normal otoscopic findings and who had type A tympanogram, and 31 age and sex-matched healthy controls were included into the study. Both groups were evaluated with the tests of audiometry, tympanometry, transiently evoked otoacoustic emission (TEOAE), distortion product otoacoustic emission (DPOAE), and contralateral suppression of the TEOAE.

Results: Air conduction threshold at 250 Hz of the patients with CD were significantly higher than controls ($p<0.05$). Speech discrimination score were lower in CD than control group ($p<0.0001$). The SNR (signal to noise ratio) amplitudes were significantly lower at 1000 Hz in the CD than control group on DPOAE testing ($p<0.05$). There was no significant difference between CD and control group regarding contralateral suppression amplitudes. The SNR amplitudes at 1000 Hz with and without contralateral acoustic stimulus (CAS) in TEOAE testing were significantly lower in the CD than control group ($p<0.05$).

Conclusion: CD seems to have an important impact on the auditory system, and results in elevation of the thresholds at low frequencies on audiometry, and a decrease in the amplitudes of linear TEOAE and DPOAE at low frequencies in children.

Keywords: Celiac disease, contralateral suppression, TEOAE, DPOAE, hearing

Introduction

CD is an inherited autoimmune chronic disease caused by gluten intolerance grouped as typical and atypical. Chronic diarrhea, failure to thrive and abdominal complaints are among findings of typical CD. Atypical CD was found to be predominantly presented with extraintestinal features such as anemia, osteoporosis, short stature, pubertal delay, infertility, liver dysfunction, dermatitis herpetiformis, malignancies, neurological disturbances with few or no gastrointestinal symptoms. Hypotonia, peripheral neuropathy, developmental delay, learning disorders, cerebellar ataxia, epilepsy, migraine, attention deficit hyperactivity, headache and night blindness are among the neurologic findings of atypical CD [1-4].

Sensorineural hearing loss (SNHL) is a neurological condition that may result in negative effects on speech and language acquisition, social, emotional and academic development deficits [5,6]. The inner ear can be subject of the target of an autoimmune attack, and SNHL can occur in various non-organ-specific autoimmune diseases. Many studies have been published about hearing in various autoimmune diseases such as rheumatoid arthritis, ankylosing spondilitis, Behçet's disease, Sjögren's syndrome, polyarteritis nodosa and systemic lupus erytematosus after the first description of autoimmune SNHL in 1979 by McCabe [7,8,9].

We hypothesized that the inner ear could be the target of an autoimmune attack, and SNHL may occur in children with CD. There is no pediatric data related with this topic and there are only two adult audiometric studies searching the presence of hearing impairment in CD patients with contradictory results [10,11]. In this study, we aimed to assess the hearing of the children with CD.

Materials and Methods

This research was performed in accordance with the principles of the Declaration of Helsinki, and approval for this study was granted by the local ethics committee. Written informed consents were obtained from the patients and controls tested in this study.

Patients and Controls

Forty one patients with CD patients (82 ears) who were diagnosed and treated in the department of pediatric gastroenterology and 31 healthy age and gender matched controls (62 ears) were included in the study.

None of the participants had a history of ototoxic drug use, noise exposure, ear surgery, chronic middle ear disease, secretory otitis media, cranial trauma and metabolic diseases except CD, otoscopic evidence of a perforated tympanic membrane or other middle ear pathology, presence of a flat tympanogram or absence of acoustic reflexes at 1 kHz with contralateral stimulation.

Audiometry and middle ear evaluation

The initial hearing examination included otoscopy, tympanometry, pure-tone air and bone conduction threshold measurement, and speech audiometry. Pure-tone audiometry was performed at the frequencies 250, 500, 1000, 2000, 4000, 8000 Hz using the diagnostic audiometer (Madsen orbiter 922-2 Clinical Audiometer, Denmark) in a sound-treated cabin. Normal middle-ear function was defined as proper if the hearing threshold for both air and bone conduction was equal. Tympanometric measurements were done using a TDH- 39 headset and Middle Ear Analyzer (TympStar GSI, Grason-Stadler Inc., Milford, USA). On immitance, all participants had a normal peak compliance, peak pressure, gradient and ear canal volume, and acoustic reflex, as defined by American Speech Language and Hearing Association. Audiometric examination was performed in children who were cooperated in the audiomety. Audiometric evaluations were performed in 33 children of CD group, and in 26 children in the control group. Otoacoustic emission tests were performed in all children.

Otoacoustic emission (OAE) testing

All OAE measurements were performed bilaterally, and recorded using the ILO 292 USB II OAE analyzer, version 6 (Otodynamics Ltd., London, UK), with two ILO UGD TE+ DPOAE probes (insert phone) in the sound-proof room.

The test parameters for TEOAE were as follows; test at the frequencies of 1000- 1500- 2000- 3000- 4000 Hz , stimulus rate of 84 ± 3 dB, TE-nonlinear -bilateral test type, time out: 260 sweeps, noise rejection level of 49.5 dB SPL, wave reproducibility > %70, and the stimulus stability > %80.

Distortion product otoacoustic emission (DPOAE) testing was performed bilaterally using the ILO device. The emission at 2f1-f2 was the distortion product measured. Distortion product response amplitude and noise floor across the range of frequencies corresponding to the following frequency values for f2: 1000, 1500, 2000, 3000, 4000, 5000, and 6000 Hz were recorded. The test parameters for DPOAEs were the followings; stimulus, f1=65 dB, f2=55 dB and 2f2/f1=1.22; time out (NLo), 500 sweeps or 100 second; noise rejection level, 49.5 dB SPL; and point / octave was 2.

Testing contralateral suppression of TEOAEs

The TEOAEs were registered on the linear click channel. The data set from the test with contralateral acoustic stimulation (CAS) was designated memory store 1, and that from the test without CAS was designated memory store 2. The CAS consisted of continuous broad band white noise at 60 dB SPL, delivered through channel B of the ILO and presented by an ILO General Purpose UGD TE+ DPOAE probes. All subjects were tested bilaterally in a randomized fashion. After the two probes were in place, TEOAE were recorded in alternating blocks (with and without CAS) for the linear mode, always in the same order. TEOAE contralateral suppression was calculated by subtracting the with CAS TEOAE SNR level from the without CAS TEOAE level.

In all patients, with CAS TEOAE and without CAS TEOAE was recorded in linear mode. Under all conditions, an intensity of the clicks was 80 dB SPL, and total of 260 sweeps were recorded for each ear. The measurements were averaged after 260 responses and were only accepted when stimulus stability was better than 80%. The linear TEOAE recording mode is most sensitive to contralateral suppression.

Statistical analyses

The Statistical analyses were performed using SPSS 15.0 for Windows. Chi-square test was used to compare CD and control groups regarding gender. The normality of the variables was analyzed by Kolmogorov-Smirnov test. The Independent Sample T test was used to compare the ages and all of the audiologic parameters of patients and controls. Chi-square testing was used to compare the number of hearing loss and the gender of patients and controls. Mann-Whitney U Test was used to compare the age and all of the audiologic parameters of the CD and controls. Criterion for statistically significant difference was accepted for two-tailed p values of less than 0.05.

Results:

The mean age of subjects in CD and control groups were 10.5 ± 3.9 years (range 3-16 years) and 9.8 ± 2.3 years (range 6-14 years) respectively. There were 29 (70.7%) female and 12 (29.3%) male in CD and 21 (67.7%) female and 10 (32.3%) male subjects in control group. The ages and genders of the CD and control groups were similar ($p > 0.05$).

Normal peak compliance, peak pressure, gradient, ear canal volume and acoustic reflexes obtained by immitance measures in the patients and the controls. As there was no air-bone gap in the participants, only air conduction thresholds were taken into consideration.

The air conduction thresholds of the CD and the control groups are shown in Table 1. There was significant difference between the pure-tone thresholds of the CD and the control groups at 250 Hz ($p = 0.005$).

Pure tone averages (PTA) of air conduction thresholds at 250 and 500 Hz (PTA1), 500, 1000 and 2000 Hz (PTA2), 4000 and 8000 Hz (PTA3) were measured separately for

each ear. The mean PTA value were PTA1 11± 6, PTA2 7.6±4, PTA3 8.2±5.7 for CD group. The mean PTA value were PTA1 8.5±4, PTA2 7.1±2.8, PTA3 8±5 for control group. The PTA results over 15 dB was described as hearing loss. The PTA1 of the CD and the control groups were significantly different ($p<0.05$). According to the PTA test, the number of subjects with hearing loss were significantly higher in the CD than in the control group ($p <0.001$, Table 2).

The mean speech disrimination scores (SDS) of the CD and the control groups were 96.9 ± 4 dB (range 84-100 dB) and 99.4 ± 1.7 dB (range 92-100 dB) respectively ($p<0.0001$).

The TEOAE, DPOAE SNR findings of the patients and the controls are shown in figure I and II. With and without CAS, TEOAE SNR findings of the CD and control groups are shown in figure III and IV. There was statistically significant difference between the levels of SNR of the CD and the control groups at 1000 Hz results on DPOAE testing. On TEOAE testing with nonlinear stimulus, there was no difference between the levels of SNR of the CD and the control groups at all frequencies ($p>0.05$). There was no difference between the contralateral suppression amplitudes and the number of suppression positive frequencies on TEOAE test of the CD and the control groups, either ($p>0.05$). The SNR amplitudes at 1000 Hz with and without CAS TEOAE testing with linear stimulus were significantly lower in the CD than the control group ($p<0.05$).

Discussion

The nature of the connection between CD and neurologic involvement remains unknown. However, recent reports point to the involvement of immune-mediated mechanisms, including lymphocytic infiltration and anti-gliadin antibodies (Abs) in the central and peripheral nervous system of the affected individuals, as well as the associated cerebellar ataxia and peripheral neuropathy have been reported to respond to gluten-free diet in some of the cases [12-14]. In other studies, patient serum and anti-gliadin Abs have been shown to bind neural tissue, implying that the Abs may be cross-reacting with the

autoantigens and point to an immune-mediated mechanism of pathogenesis in at least some of the associated neurologic symptoms [15,16].

Medial olivocochlear (MOC) efferent fibers originate from the medial part of the superior olivary complex on both sides, and project trough the vestibular nerve, and terminate on the outer hair cells of the cochlea [17]. Activation of MOC efferents results in a decrease in the amplitudes of OAE's [18]. MOC acoustic reflex can increase the response to transient sounds by reducing the response to the noisy background, and this helps to detect speech in a noisy background. When the MOC reflex is absent or reduced, this can be associated with difficulties in sound localization and lateralization and difficulty in understanding speech in a noisy background. Lack or reduction of MOC reflex, implicating auditory neuropathy or dyssynchrony, is a pathologic state [19]. In our study we did not find difference between contralateral suppression amplitudes of CD and control groups but mean SDS in CD patients was lower than control group.

Autoimmune inner ear disease is a result of direct immune attack against an endogeneous antigen or a cross-reacting exogeneous epitope such as food, drug or viral components [20] Clinical presentation of inner ear disease is extremely variable and dependent on the type of immune reaction as well as the site of tissue injury within inner ear.

Otoacoustic emissions are sounds in the external auditory canal that originate from mechanical activity of the cochlea transmitted in a reversed direction through the middle ear and the tympanic membrane. These emissions arise from the vibratory motion of the outer hair cells of the cochlea [21]. The function of outer hair cells is integral to the overall sensitivity and frequency-selectivity of the auditory system. The most useful clinically evoked otoacoustic emissions are the TEOAEs and the DPOAEs. Specifically, measurements of DPOAEs correspond closely to the physiological state of outer hair cells of the cochlea. Their main applications are the assessment of cochlear function to determine the site of pathological conditions associated with SNHL. DPOAEs, if normal, provide extremely strong evidence of normal cochlear function, regardless of audiometric data [22].

In our study we found that there was statistically significant difference between the levels of SNR of the patients and controls at 1000 Hz results on DPOAE testing. Although there were no difference between the levels of SNR of groups at all frequencies on TEOAE testing with nonlinear stimulus, the SNR amplitudes at 1000 Hz with and without CAS TEOAE testing using linear stimulus were significantly lower in CD than control group. Linear mode stimulation is more sensitive in detecting shifts in the TEOAE recorded in the presence of competitive noise than in those recorded without competitive environmental noise [23].

The results of present study depict a relation of the SNHL and CD in children. Previous adult reports were mentioning about the relation of SNHL with CD with contradictory results. Although we could not measure lower than 1000 Hz frequencies on OAE testing, because of our procedural limitation of OAE testing, we evaluated hearing at low frequencies by audiometric measurement. This study confirms that cochlear function is affected at low frequencies region in CD patients.

In previous reports the SNHL was defined as a finding of HLA related autoimmune diseases such as Behçet's dissease, ankylosing spondilitis etc. But the mechanism of this involvement was not clear. In this study we describe a relation of SNHL with CD and also clarify the mechanism of impact of CD on hearing in children.

Our study results are parallel to findings of a cohort of 100 children with a diagnosis of autism spectrum disorder, those with a history of language regression had more gastrointestinal symptoms and were more likely to have a family history of an autoimmune disorder, and possibly of gastrointestinal disorders such as celiac disease or inflammatory bowel disease. SNHL may be an explaining link between CD and language regression might be due to a common HLA related autoimmune etiology.

Conclusion: CD seems to have an important impact on the auditory system, and results in elevation of the thresholds at low frequencies on audiometry, and a decrease in the amplitudes of linear TEOAE and DPOAE at low frequencies in children.

References:

1. Zelnik N, Pacht A, Obeid R, Lerner A: Range of neurologic disorders in patients with celiac disease. Pediatrics 2004;113:1672–6
2. Kinney HC, Burger PC, Hurwitz BJ, Hijmans JC, Grant JP: Degeneration of the central nervous system associated with celiac disease. J Neurol Sci.1982;53:9-22
3. Gobbi G, Bouquet F, Greco L: Celiac disease, epilepsy, and cerebral calcifications. Lancet. 1992; 340:439–443
4. Pellecchia MT, Scala R, Perretti A: Cerebellar ataxia associated with subclinical celiac disease responding to gluten- free diet. Neurology.1999; 53:1606–1608
5. Wake M, Hughes EK, Poulakis Z, Collins C, Rickards FW: Outcomes of children with mild-profound congenital hearing loss at 7 to 8 years: a population study. Ear Hear 2004; 25:1-8.
6. Wake M, Tobin S, Cone-Wesson B, Dahl HH, Gillam L, Mc Cormick L: Slight/mild sensorineural hearing loss in children. Pediatrics 2006; 118:1842-51.
7. Karabulut H, Dagli M, Ates A, Karaaslan Y: Results for audiology and distortion product and transient evoked otoacoustic emissions in patients with systemic lupus erythematosus. J Laryngol Otol. 2010;124(2):137-40.
8. Eryilmaz A, Dagli M, Karabulut H, Sivas FA, Erkol EI, Gocer C: Evaluation of hearing loss in patients with ankylosing spondylitis. J Laryngol Otol. 2007;121(9) :845-9.
9. McCabe BF: Autoimmune sensorineural hearing loss. Ann Otol Rhinol Laryngol 1979; 88: 585-9
10. Leggio L**,** Cadoni G**,** D'Angelo C**,** Mirijello A**,** Scipione S**,** Ferrulli A**,** et al. : Coeliac disease and hearing loss: preliminary data on a new possible association. Scand J Gastroenterol 2007;42:1209—13.
11. Volta U**,** Ferri GG**,** De Giorgio R**,** Fabbri A**,** Parisi C**,** Sciajno L**,** Castellari A**,** Fiorini E**,** Piscaglia M**,** Barbara G**,** Granito A**,** Pirodda A**:** Sensorineural hearing loss and celiac disease: a coincidental finding. Can J Gastroenterol. **2**009;23:531—5.

12. Hadjivassiliou M, Davies-Jones GA, Sanders DS, Grunewald RA: Dietary treatment of gluten ataxia. J. Neurol. Neurosurg. Psychiatry 200; 74: 1221–1224.

13. Sander HW, Magda P, Chin RL, Wu A, 3rd Brannagan TH, Gren PH, Latov N: Cerebellar ataxia and coeliac disease. Lancet. 2003;8;362(9395):1548.

14. Hadjivassiliou M, Kandler RH, Chattopadhyay AK, Davies-Jones AG, Jarratt JA, Sanders DS, Sharrack B, and Grunewald RA: Dietary treatment of gluten neuropathy. Muscle Nevre 2006; 34: 762-766.

15. Hadjivassiliou M, Boscolo S, Davies-Jones GA, Grunewald RA, Sanders DS, Simpson JE, Tongiorgi E, Williamson CA, and Woodroofe NM: The humoral response in the pathogenesis of gluten ataxia. Neurology. 2002;58: 1221-1226.

16. Briani C, Zara G, Toffanin E , Ruggero S, Ferrarini A, DeLazzari F, Luca M, Faggian D, Grassivaro F, Ermani M: Neurological complications of celiac disease and autoimmune mechanisms: preliminary data of a prospective study in adult patients. Ann. N.Y Acad. Sci. 2005;1051: 148-155.

17. Guinan JJ. Olivocochlear efferents: Anatomy, physiology, function and the measurement of efferent effects in humans. Ear Hearing 2006; 27: 589- 607

18. Kemp DT: Otoacoustic emissions, traveling waves and cochlear mechanisms. Hear Res 1986; 22: 95-104

19. Hood LH, Berlin CI, Bordelon J and Rose K. Patients with auditory neuropathy/dys-synchrony lack efferent suppression of transient evoked otoacoustic emissions. Journal of the Acoustical Society of America 2003;302–313.

20. Dornhoffer JL, Arenberg JG, Arenberg IK, Shambaugh GE: Pathophysiological mechanisms in immune inner ear disease. Acta Otolaryngol Suppl. 1997; 526:30-6.

21. Boyman O, Hefti HP, Conrad C, Nickoloff BJ, Suter M, Nestle FO: Spontaneous development of psoriasis in a new animal model shows an essential role for resident T cells and tumor necrosis factor-alpha. J Exp Med. 2000;5:731-6.

22. Korres S, Balatsouras D, Economou C , Ferekidis E , Kandiloros D, Adamopoulos G:The effect of the number of averaged responses intransiently evoke do to acoustic emissions on the results of neonatal hearing screening, Audiology. 2000;39: 293-299.

23. Berlin CI, Hood LJ, Hurley AE: Binaural noise suppresses linear click-evoked otoacoustic emissions more than ipsilateral or contralateral noise. Hear Res. 1995; 87: 96-103.

Table I. Air conduction thresholds of CD and control groups

Group	Frequency	N	Minimum (dB HL)	Maximum (dB HL)	Mean (dB HL)	Std. Deviation
CD	250 Hz	66	0	30	13.0	7.0
	500 Hz	66	0	30	9.5	5.8
	1000 Hz	66	0	30	6.4	4.5
	2000 Hz	66	0	25	7.1	4.8
	4000 Hz	66	0	25	6.0	5.0
	8000 Hz	66	0	25	10.3	7.7
Control	250 Hz	52	0	20	9.1	5.4
	500 Hz	52	0	15	7.8	3.8
	1000 Hz	52	0	10	6.2	3.1
	2000 Hz	52	0	15	7.4	4.4
	4000 Hz	52	0	25	7.1	5.8
	8000 Hz	52	0	20	8.8	6.2

dB (Decibel), HL (Hearing Level), Hz (Hertz),

Table II. Number of hearing loss in CD and control groups

Freq(Hz)	CD Group (n=66) n(%)	Control Group (n=52) n(%)	P value
250	17 (25.8)	3 (5.8)	0.006
500	2 (3%)	0	0.51
1000	1 (1.5%)	0	1
2000	1 (1.5%)	0	1
4000	1 (1.5%)	3 (5.8%)	0.31
8000	12 (18.2%)	6 (11.5%)	0.44
PTA 1	19 (28.8%)	2 (3.8%)	0.001
PTA 2	1 (1.5%)	0	1
PTA 3	10 (15.2%)	3 (5.8%)	0,142

Figure I. TEOAE SNR findings of CD and control groups

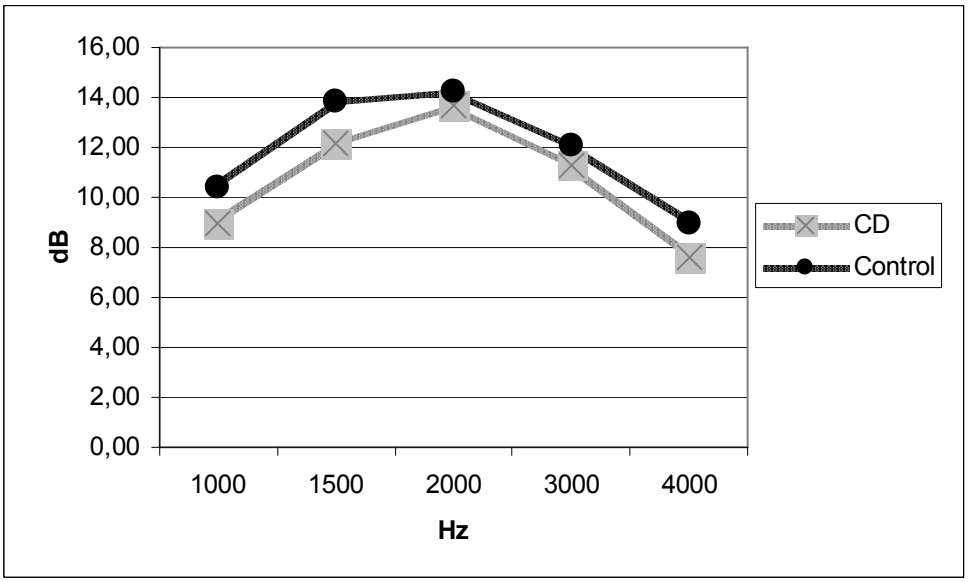

Figure II. DPOAE SNR findings of CD and control groups

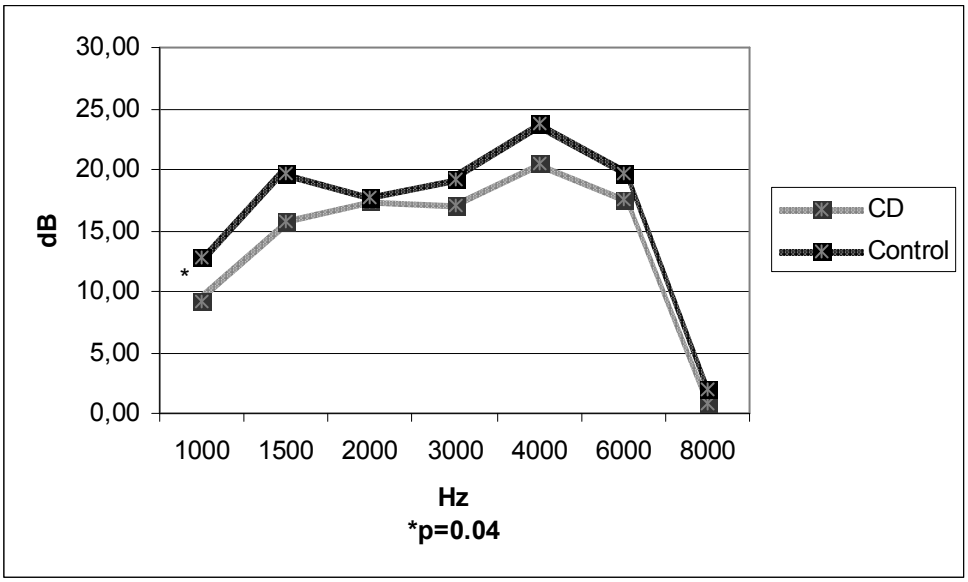

Figure III. CAS (+) TEOAE SNR findings of CD and control groups

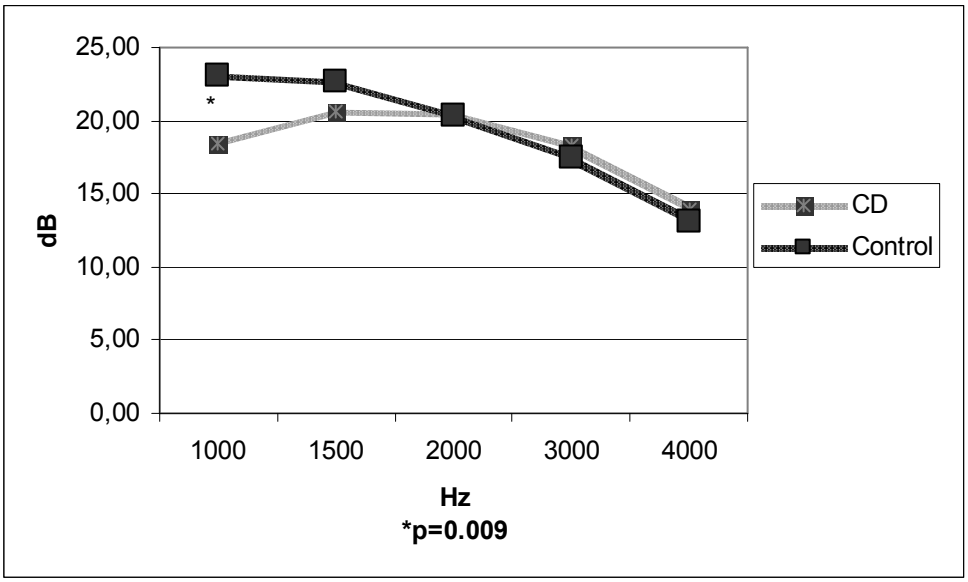

Figure IV. CAS (-) TEOAE SNR findings of CD and control groups.