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ORIGINAL ARTICLE

Hearing loss can also be seen in patients with nonradiographic axial spondyloarthropathies as well as radiographic axial spondyloarthropathies

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ABSTRACT

Objectives: Hearing loss has been described in patients with radiographic axial spondyloarthropathies (R-AxSpA) but has not been studied in patients with non-radiographic axial spondyloarthropathies (NR-AxSpA); accordingly, the aim of the study was to compare hearing loss in patients with NR-AxSpA, R-AxSpA, and healthy individuals.

Patients and methods: This cross-sectional observational study was conducted with 68 participants (30 males, 38 females; mean age: 39.8±7.4 years) between March 2021 and March 2022. Of the participants, 16 were patients with NR-AxSpA, 15 were patients with R-AxSpA, and 37 were healthy controls. Disease activity and radiological and audiological features were analyzed. The audiological assessment included pure-tone audiometric tests at octave frequencies of 250 to 8000 Hz and transient evoked otoacoustic emissions.

Results: Hearing loss was found in three (8%) in the healthy group, five (31.3%) in the NR-AxSpA group, and 10 (66.7%) in the R-AxSpA group. The chi-square analysis showed a statistical significance (p=0.001). Values of audiometric tests yielded significant differences between the control and R-AxSpA group and also the control and NR-AxSpA group. For the air conduction studies, the statistical significance began at 1000 Hz in the R-AxSpA group. It was found that in the NR-AxSpA group, the statistical difference started in higher frequencies. The bone conduction audiometric studies were similar to air conduction studies. Transient evoked otoacoustic emission studies showed that the R-AxSpA group was significantly affected compared to the control and NR-AxSpA groups. There was no statistical difference between the control and NR-AxSpA groups.

Conclusion: Both NR-AxSpA and R-AxSpA patients had hearing loss; however, in pure-tone audiometric tests, the abnormalities began in lower frequencies in the R-AxSpA group than in the NR-AxSpA group.

Keywords: Axial spondylarthritis, hearing loss, pure tone audiometry.

Spondyloarthropathies (SpA) are a group of chronic inflammatory rheumatoid diseases involving peripheral joints, entheses, digits, and the axial spine. Ankylosing spondylitis (AS) is a type of this group of diseases. In the past, the New York Criteria published in 1984 was used for the classification of AS. However, many patients could not be classified as SpA since the detection of radiological damage on plain radiographs was one of the main items in the New York Criteria.[1] Assessment of Spondyloarthritis International Society (ASAS) published a new classification

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criteria for SpA in 2009. SpA was classified into axial SpA (AxSpA) and peripheral SpA according to the most pronounced symptoms. Later, the AxSpA was classified as radiographic AxSpA (R-AxSpA) and nonradiographic AxSpA (NR-AxSpA). The term R-AxSpA was accepted as the alternative diagnostic label for AS.[2] Rheumatologists have widely accepted the new criteria and the related terminology, and several studies were done to compare the clinical, laboratory, and radiological features of NR-AxSpA and R-AxSpA. In summary, higher radiographic damage, C-reactive protein (CRP) levels, and incidence of acute anterior uveitis are more commonly observed in patients with R-AxSpA. The prevalence of psoriasis and inflammatory seems to be similar in R-AxSpA in comparison with NR-AxSpA. Both clinical situations lead to similar disease activity, and treatment responses are also similar.[3]

The prevalence and characterization of audiological dysfunction in patients with AS have been well-studied. Both conductive hearing loss (CHL) and sensorineural hearing loss (SNHL) have been reported in the literature in patients with AS.[4,5] Ankylosing of joints and ossicular fixation lead to CHL.[6] Alternatively, immune-mediated inner ear problems could result in SNHL.[7] It was speculated that hearing loss was one of the extraarticular involvements of AS.[8] However, according to our best knowledge, there were no studies after the ASAS classification criteria. The literature seemed quite old before the constitution of new criteria and did not reflect the current clinical practice. In this study, we aimed to compare hearing loss in patients with NR-AxSpA, R-AxSpA, and healthy individuals. The secondary aim of the study was to determine the factors affecting hearing loss in patients with axSPpA.

PATIENTS AND METHODS

This cross-sectional observational study was conducted with 68 participants (30 males, 38 females; mean age: 39.8±7.4 years) between March 2021 and March 2022. Initially, 40 patients with AxSpA and 40 healthy controls were enrolled in the study. Nine patients from the AxSpA group and three participants from the control group were excluded according to exclusion criteria. The first researcher performed the clinical assessment of the patients. The classification of NR-AxSpA and R-AxSpA was based on the 2009 ASAS criteria.[2] The disease duration, number of tender and swollen joints, erythrocyte sedimentation rate (ESR), CRP levels, radiographic findings, history of drug use, and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Bath Ankylosing Spondylitis Metrology Index (BASMI) scores were recorded in all patients. All patients and healthy controls were referred to an experienced otologist for otoscopic examinations of both ears. Detailed information was obtained about possible etiological factors leading to hearing loss (ototoxic drugs, noise exposure, ear surgery, perforated tympanic membrane, Meniere's disease, cranial trauma, metabolic diseases, and systemic disease). Participants with diabetes, hypertension, cardiovascular disease, infectious diseases, neurological deficits, autoimmune diseases, pulmonary diseases, endocrine disorders, malignancies, ototoxic drug use, prior ear surgery or head or ear trauma, eardrum perforation or acquired hearing loss and congenital ear disorder were excluded. After the assessment by the otologist, the patients and healthy controls underwent pure-tone audiometric tests in the same center by experienced audiologists. Additionally, transient evoked otoacoustic emissions (TEOE), and tympanometry tests were also performed on both groups. The data was collected and analyzed by an independent researcher.

Rheumatologic assessment

Bath Ankylosing Spondylitis Disease Activity Index is a self-administered instrument used to measure disease activity. It includes six features: fatigue, swelling, spine pain, enthesitis, morning stiffness severity, and morning stiffness duration. Each of these six features is rated from 0 to 10 on a numerical rating scale. The overall score ranges from 0 to 10, whereby a higher score reflects a more active disease.[8]

Bath Ankylosing Spondylitis Metrology Index is a five-item index to quantify the mobility of the axial skeleton in AS patients. Cervical rotation, tragus-to-wall distance, lumbar flexion, lumbar side flexion, and intermalleolar distance is measured by an experienced clinician. Each item

is scored from 0 to 10 based on previously defined cut-off points. A higher score reflects a more significant impairment of spinal mobility.[9]

For CRP evaluation, the erythrocytes of the capillary or venous blood sample were separated from the plasma by centrifugation. Then, the plasma sample was diluted with HEPES buffer and transferred into a reaction chamber where it was mixed with CRP antibody-latex reagent. The CRP in the diluted plasma binds with the CRP antibody on the latex particle. The concentration of CRP was calculated as a function of the changed absorbance measured at 525 nm and 625 nm, which is in relation to the amount of agglutination. The concentration of CRP was displayed in mg/L. The ESR was measured by Westergren method in the same laboratory. The first clinician evaluated plain anteroposterior hip graphs and sacroiliac magnetic resonance imaging according to recent guidelines.[9,10]

Standardized otorhinolaryngology assessment

An experienced otorhinolaryngologist performed a physical examination of the ear, nose, and throat and audiological tests. An otoscopic examination had done to prove a healthy tympanic membrane. All subjects were questioned for tinnitus, vertigo, facial nerve function, and family history of hearing loss. The audiological assessments include pure-tone audiometry at conventional and extended high frequencies and impedance audiometry.

Pure-tone audiometry measurements were performed with airway and bone conduction measurements in an Industrial Acoustic Company standard double-walled soundproof audiology booth by the same audiologist. Audiometry measurements were performed using Madsen Astera (Madsen Astera, Copenhagen, Denmark) test battery for the frequencies of 250, 500-1000, 2000, 4000, 6000, and 8000 Hz. High-frequency test measurements included 9000, 10000, 11200, 12500, 14000, 16000, 18000, and 20000 Hz frequencies and were carried out by Sennheiser HDA 300 circumaural headphones (Sennheiser electronic GmbH & Co. KG, Wedemark, Germany). Hearing loss was defined as being present when the audiometric tests disclosed pure-tone thresholds ≥25 dB HL in two frequencies of the audiogram.[6]

Transient evoked otoacoustic emission measurements were performed with the Echoport ILO292 (Otodynamics, UK) instrument. Measurements were made in a quiet room in the Industrial Acoustic Company standard, and the patient was in a sitting position during the

Table 1. Baseline qualitative demographic characteristics of the three groups

	Control (n=37)		AxSpA (n=31)			
	n	%	n	%	χ^2	*p*
Sex					0.421	0.625
Female	22	59.5	16	51.6		
Male	15	40.5	15	48.4		
Education					5.442	0.06
Primary school	9	24.3	10	32.3		
High school	11	29.7	15	48.4		
University	17	45.9	6	19.4		
Occupation					2.641	0.267
None	6	16.2	7	22.6		
Body	5	13.5	8	25.8		
Office worker	26	70.3	16	51.6		
Comorbid diseases					13.99	0.001
None	37	100	21	67.7		
One	0	0	9	29		
More than one	0	0	1	3.2		
Smoking					3.28	0.06
–	27	73	28	90.3		
+	10	27	3	9.7		

Table 2. Baseline quantitative demographic characteristics of the three groups

	n	Mean±SD	*p*
Age (year)			0.203
R-AxSpa	15	42.9±8.3	
NR-AxSpa	16	39±7.0	
Control	37	38.8±7.7	
Body mass index (kg/m^2)			0.397
R-AxSpa	40	27.2±2.9	
NR-AxSpa	58	27.4±4.9	
Control		26.1±3.2	

R-AxSpA: Radiographic axial spondyloarthritis; NR-AxSpA: Nonradiographic axial spondyloarthritis; SD: Standard deviation.

test. A stimulus intensity of 84 dB was used during tests. The resulting transient impulses were averaged 260 times, and the results were recorded.

Statistical analysis

Sample size was estimated for primary outcome measures with the G*Power version 3.1.7 program (Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany). According to the literature, mean values were determined as 23.9±18.1 in patient groups and 16.8±9.3 in healthy controls.[6] The sample size was calculated for a significance level of 0.2 and 80% power. The resulting sample size was 13 per group. Assuming a dropout of 5%, the target sample size was 15 for each group.

Data were analyzed using IBM SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Percentage, mean, median, and standard deviation values were obtained using descriptive statistical methods. The conformity of the data to the normal distribution was evaluated with the Shapiro-Wilk test. The Pearson chi-square test was used to compare categorical data. For the quantitative data, analysis of variance was used according to normality tests. A p-value <0.05 was considered statistically significant.

RESULTS

NR-AxSpA, R-AxSpA patients, and the control group had mean ages of 39±7.0, 42.9±8.3, and

Table 3. Comparison of R-AxSpA and NR-AxSpA

	Group	n	n		Mean±SD	*p*	
Age (year)	R-AxSpa	15			42.9±8.3	0.163*	
	NR-AxSpa	16			39±7.0		
Sex	R-AxSpa	15	4 Female	11 Male		7.42**	0.007*
	NR-AxSpa	16	12 Female	4 Male			
Pharmacological treatment	R-AxSpa	15	14 Biologics	1 NSAID		8.71**	0.004*
	NR-AxSpa	16	7 Biologics	9 NSAID			
BASDAI	R-AxSpa	15			3.21±0.83	0.04*	
	NR-AxSpa	16			3.96±1.14		
BASMI	R-AxSpa	15			3.56±1.06	0.001*	
	NR-AxSpa	16			0.8±0.3		
CRP (mg/L)	R-AxSpa	15			10.33±4.03	0.001*	
	NR-AxSpa	16			4.63±2.37		
Disease duration (months)	R-AxSpa	15			76.26±24.49	0.001*	
	NR-AxSpa	16			43.62±14.10		
Eritrosit sedimentation rate (mm/h)	R-AxSpa	15			45.2±21.05	0.002*	
	NR-AxSpa	16			24.37±9.37		

R-AxSpA: Radiographic axial spondyloarthritis; NR-AxSpA: Nonradiographic axial spondyloarthritis; SD: Standard deviation; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; CRP: C-reactive protein; * T test; ** Chi-Square test.

Table 4. Pure-tone audiogram air conduction results

	Control (37)	NR-AxSpA (n=16)	R-AxSpA (n=15)	ANOVA	
	Mean±SD	Mean±SD	Mean±SD	*p*	Multiple comparisons (Tukey HSD)
Right ear 250 Hz	6.08±5.42	8.75±7.19	11.00±11.37	0.092	Control-NR-AxSpA: 0.462 Control-R-AxSpA: 0.08 NR-AxSpA -R-AxSpA: 0.682
Right ear 500 Hz	9.19±6.51	11.56±6.51	14.00±11.83	0.138	Control-NR-AxSpA: 0.582 Control-R-AxSpA: 0.127 NR-AxSpA -R-AxSpA: 0.672
Right ear 1000 Hz	8.65±5.61	11.56±7.47	17.00±11.46	0.003	Control-NR-AxSpA: 0.416 Control-R-AxSpA: 0.002 NR-AxSpA - R-AxSpA: 0.126
Right ear 2000 Hz	5.54±4.83	9.06±6.12	16.33±14.70	0.001	Control-NR-AxSpA: 0.333 Control-R-AxSpA: 0.001 NR-AxSpA - R-AxSpA: 0.04
Right ear 4000 Hz	7.57±5.22	16.88±8.54	31.67±23.50	0.001	Control-NR-AxSpA: 0.036 Control-R-AxSpA: 0.001 NR-AxSpA - R-AxSpA: 0.004
Right ear 6000 Hz	9.32±7.65	16.56±8.11	32.67±25.20	0.001	Control-NR-AxSpA: 0.184 Control-R-AxSpA: 0.001 NR-AxSpA - R-AxSpA: 0.004
Right ear 8000 Hz	5.95±7.62	17.81±9.48	31.00±26.94	0.001	Control-NR-AxSpA: 0.02 Control-R-AxSpA: 0.001 NR-AxSpA - R-AxSpA: 0.03
Right ear high frequency	17.15±11.07	29.93±11.15	42.21±22.05	0.001	Control-NR-AxSpA: 0.01 Control-R-AxSpA: 0.001 NR-AxSpA - R-AxSpA: 0.06
Right ear pure tone mean	7.76±4.55	11.06±4.67	15.87±12.21	0.001	Control-NR-AxSpA: 0.259 Control-R-AxSpA: 0.001 NR-AxSpA - R-AxSpA: 0.142
Left ear 250 Hz	6.08±6.02	12.19±16.93	8.67±8.96	0.138	Control-NR-AxSpA: 0.11 Control-R-AxSpA: 0.68 NR-AxSpA - R-AxSpA: 0.6
Left ear 500 Hz	8.11±6.91	14.69±17.93	12.67±10.33	0.112	Control-NR-AxSpA: 0.12 Control-R-AxSpA: 0.37 NR-AxSpA - R-AxSpA: 0.86
Left ear 1000 Hz	7.70±5.48	13.75±15.97	15.00±14.39	0.049	Control-NR-AxSpA: 0.163 Control-R-AxSpA: 0.08 NR-AxSpA - R-AxSpA: 0.94
Left ear 2000 Hz	6.08±5.54	12.81±9.99	19.33±18.60	0.001	Control-NR-AxSpA: 0.09 Control-R-AxSpA: 0.001 NR-AxSpA - R-AxSpA: 0.21
Left ear 4000 Hz	8.51±6.65	15.63±11.67	31.00±24.22	0.001	Control-NR-AxSpA: 0.191 Control-R-AxSpA: 0.001 NR-AxSpA - R-AxSpA: 0.007
Left ear 6000 Hz	10.95±8.40	18.44±10.91	36.67±25.26	0.001	Control-NR-AxSpA: 0.194 Control-R-AxSpA: 0.001 NR-AxSpA - R-AxSpA: 0.002
Left ear 8000 Hz	9.59±11.45	21.88±12.63	32.00±26.10	0.001	Control-NR-AxSpA: 0.033 Control-R-AxSpA: 0.001 NR-AxSpA - R-AxSpA: 0.191
Left ear high frequency	17.45±13.76	30.20±14.62	42.79±23.55	0.001	Control-NR-AxSpA: 0.043 Control-R-AxSpA: 0.001 NR-AxSpA - R-AxSpA: 0.112
Left ear pure tone mean	7.00±4.37	13.75±14.02	15.80±13.53	0.006	Control-NR-AxSpA: 0.061 Control-R-AxSpA:0.012 NR-AxSpA - R-AxSpA: 0.829

NR-AxSpA: Nonradiographic axial spondyloarthritis; R-AxSpA: Radiographic axial spondyloarthritis; SD: Standard deviation.

Table 5. Pure-tone audiogram bone conduction results

	Control (37)	NR-AxSpA (n=16)	R-AxSpA (n=15)	ANOVA	
	Mean±SD	Mean±SD	Mean±SD	*p*	Multiple comparisons (Tukey HSD)
Right ear 250 Hz	5.81±5.59	8.75±7.19	11.00±11.37	0.072	Control-NR-AxSpA: 0.4 Control-R-AxSpA: 0.07 NR-AxSpA - R-AxSpA: 0.687
Right ear 500 Hz	4.05±5.51	5.00±6.06	7.00±10.49	0.393	Control-NR-AxSpA: 0.894 Control-R-AxSpA: 0.360 NR-AxSpA - R-AxSpA: 0.707
Right ear 1000 Hz	4.19±4.00	6.56±5.39	10.33±12.17	0.018	Control-NR-AxSpA: 0.486 Control-R-AxSpA: 0.01 NR-AxSpA - R-AxSpA: 0.287
Right ear 2000 Hz	2.57±4.02	5.31±4.64	12.33±15.10	0.001	Control-NR-AxSpA: 0.484 Control-R-AxSpA: 0.001 NR-AxSpA - R-AxSpA: 0.043
Right ear 4000 Hz	4.19±4.64	10.94±8.00	24.00±22.69	0.001	Control-NR-AxSpA: 0.141 Control-R-AxSpA: 0.001 NR-AxSpA - R-AxSpA: 0.008
Right ear 6000 Hz	9.73±7.54	16.56±8.11	32.67±25.20	0.001	Control-NR-AxSpA: 0.218 Control-R-AxSpA: 0.001 NR-AxSpA - R-AxSpA: 0.004
Right ear 8000 Hz	6.35±7.61	17.81±9.48	31.00±26.94	0.001	Control-NR-AxSpA: 0.027 Control-R-AxSpA: 0.001 NR-AxSpA - R-AxSpA: 0.36
Right ear high frequency	17.15±11.07	29.93±11.15	42.21±22.05	0.001	Control-NR-AxSpA: 0.015 Control-R-AxSpA: 0.001 NR-AxSpA - R-AxSpA: 0.061
Right ear pure tone mean	3.57±3.72	5.63±4.84	10.20±11.60	0.006	Control-NR-AxSpA: 0.542 Control-R-AxSpA: 0.04 NR-AxSpA - R-AxSpA: 0.13
Left ear 250 Hz	5.81±6.18	10.94±17.05	8.33±9.00	0.244	Control-NR-AxSpA: 0.226 Control-R-AxSpA: 0.703 NR-AxSpA - R-AxSpA: 0.762
Left ear 500 Hz	3.38±5.53	5.63±6.55	6.67±10.47	0.267	Control-NR-AxSpA: 0.544 Control-R-AxSpA: 0.292 NR-AxSpA - R-AxSpA: 0.912
Left ear 1000 Hz	3.38±4.26	6.88±6.55	11.00±14.17	0.009	Control-NR-AxSpA: 0.312 Control-R-AxSpA: 0.007 NR-AxSpA - R-AxSpA: 0.325
Left ear 2000 Hz	2.97±4.63	6.25±6.45	15.00±17.93	0.001	Control-NR-AxSpA: 0.487 Control-R-AxSpA: 0.001 NR-AxSpA - R-AxSpA: 0.034
Left ear 4000 Hz	3.92±5.79	9.38±7.50	24.33±22.90	0.001	Control-NR-AxSpA: 0.290 Control-R-AxSpA: 0.001 NR-AxSpA - R-AxSpA: 0.003
Left ear 6000 Hz	11.62±8.42	18.44±10.91	35.33±25.60	0.001	Control-NR-AxSpA: 0.262 Control-R-AxSpA: 0.001 NR-AxSpA - R-AxSpA: 0.005
Left ear 8000 Hz	10.95±11.36	21.88±12.63	33.00±25.69	0.001	Control-NR-AxSpA: 0.062 Control-R-AxSpA: 0.001 NR-AxSpA - R-AxSpA: 0.131
Left ear high frequency	17.45±13.76	30.20±14.62	42.77±24.52	0.001	Control-NR-AxSpA: 0.046 Control-R-AxSpA: 0.001 NR-AxSpA - R-AxSpA: 0.126
Left ear pure tone mean	3.54±4.31	6.13±5.80	11.00±13.19	0.007	Control-NR-AxSpA: 0.481 Control-R-AxSpA: 0.005 NR-AxSpA - R-AxSpA: 0.171

NR-AxSpA: Nonradiographic axial spondyloarthritis; R-AxSpA: Radiographic axial spondyloarthritis; SD: Standard deviation.

Table 6. TEOE results

	Control (37)	NR-AxSpA (n=16)	R-AxSpA (n=15)	ANOVA	
	Mean±SD	Mean±SD	Mean±SD	*p*	Multiple comparisons (Tukey HSD)
Right 1000 Hz	9.12±4.76	7.99±4.97	7.39±5.30	0.471	Control-NR-AxSpA: 0.725 Control-R-AxSpA: 0.487 NR-AxSpA - R-AxSpA: 0.937
Right 1500 Hz	12.66±5.60	13.04±6.12	10.34±6.90	0.381	Control-NR-AxSpA: 0.977 Control-R-AxSpA: 0.422 NR-AxSpA - R-AxSpA: 0.431
Right 2000 Hz	10.25±5.20	11.60±6.31	5.77±5.59	0.011	Control-NR-AxSpA: 0.696 Control-R-AxSpA: 0.028 NR-AxSpA - R-AxSpA: 0.01
Right 3000 Hz	7.59±5.73	6.28±5.01	3.69±4.94	0.069	Control-NR-AxSpA: 0.696 Control-R-AxSpA: 0.05 NR-AxSpA - R-AxSpA: 0.383
Right 4000 Hz	6.37±4.84	3.81±3.57	3.39±5.00	0.05	Control-NR-AxSpA: 0.159 Control-R-AxSpA: 0.095 NR-AxSpA - R-AxSpA: 0.965
Left 1000 Hz	10.93±6.17	6.95±5.75	5.03±6.03	0.004	Control-NR-AxSpA: 0.079 Control-R-AxSpA: 0.006 NR-AxSpA - R-AxSpA: 0.651
Left 1500 Hz	12.95±5.25	10.95±6.31	7.15±4.29	0.003	Control-NR-AxSpA: 0.428 Control-R-AxSpA: 0.002 NR-AxSpA - R-AxSpA: 0.125
Left 2000 Hz	10.05±4.68	7.26±5.84	5.01±5.05	0.005	Control-NR-AxSpA: 0.163 Control-R-AxSpA: 0.005 NR-AxSpA - R-AxSpA: 0.434
Left 3000 Hz	7.22±5.15	5.17±4.34	2.31±2.68	0.003	Control-NR-AxSpA: 0.291 Control-R-AxSpA: 0.002 NR-AxSpA - R-AxSpA: 0.194
Left 4000 Hz	5.98±4.60	3.94±3.86	2.65±3.45	0.029	Control-NR-AxSpA: 0.244 Control-R-AxSpA: 0.032 NR-AxSpA - R-AxSpA: 0.671

NR-AxSpA: Nonradiographic axial spondyloarthritis; R-AxSpA: Radiographic axial spondyloarthritis; SD: Standard deviation.

38.8±7.7, respectively. There was no clinical significance between AxSpA and control group regarding sex, education, occupation, smoking, age, and body mass index (p=0.625, p=0.06, p=0.267, p=0.06, p=0.203, and p=0.397, respectively). The AxSpA group had significantly more extraarticular involvement than the control group (p=0.001). Five patients had previous acute anterior uveitis flare, three patients had inflammatory bowel disease, and one patient had psoriasis. Four patients with NR-AxSpA and five patients with R-AxSpA had extraarticular involvement, and no statistical significance was found between two patient subgroups (Tables 1 and 2).

The subgroup analysis revealed that the NR-AxSpA group had higher BASDAI scores than the R-AxSpA group (p=0.04). R-AxSpA group had more male patients, received more biological treatments, higher CRP and ESR levels, higher BASMI scores, and longer disease duration than the NR-AxSpA group (p=0.007, p=0.004, p=0.001, p=0.002, p=0.001, and p=0.001, respectively). The subgroup analysis is demonstrated in Table 3.

Hearing loss was found in three (8%) in the healthy group, five (31.3%) in the NR-AxSpA group, and 10 (66.7%) in the R-AxSpA group. The chi-square analysis showed a statistical significance between patient subgroups and the control group (p=0.001).

All audiometric results are summarized in Tables 4 to 7 and illustrated in Figures 1 and 2. Values of audiometric tests yielded significant differences between the control and R-AxSpA group and also the control and NR-AxSpA group.

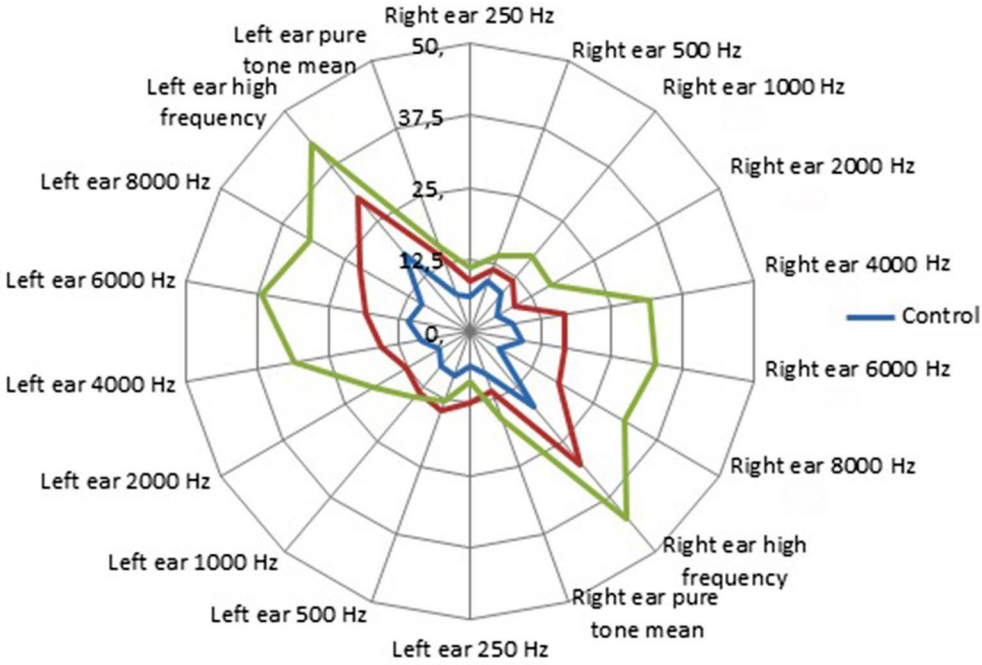

Figure 1. Pure-tone audiogram air conduction.

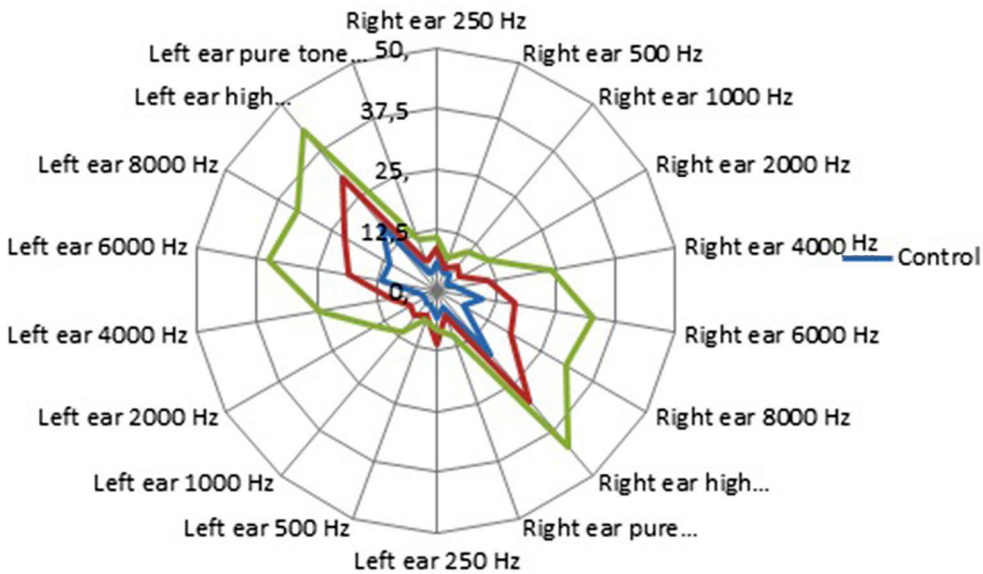

Figure 2. Pure-tone audiogram bone conduction.

For the air conduction studies, the statistical significance began at 1000 Hz in the R-AxSpA group. It was found that in the NR-AxSpA group, the statistical difference started in higher frequencies. The bone conduction audiometric studies were similar to air conduction studies. The statistical significance was found in 1000 Hz and higher frequencies in the R-AxSpA group and 2000 Hz and higher frequencies in the NR-AxSpA group.

TEOE studies showed that the R-AxSpA group was significantly affected compared to the

control and NR-AxSpA groups. There was no difference between the control and NR-AxSpA group (Table 6).

DISCUSSION

This study confirms that patients with R-AxSpA have a high rate of hearing loss. The new finding of the study was that hearing loss can be seen in patients with NR-AxSpA. Previous studies in patients with AS reported impaired audiological functions compared to the healthy controls.[6-8] Both CHL and SNHL can be seen in patients with AS. SHNL is more common than CHL, according to previous studies.[11] The ankylosis of the joints and bone fixation in the joints was said to be the cause of CHL.[6] SNHL can occur due to an immune-mediated mechanism like in other autoimmune disorders or might be caused by ototoxic drugs.[12] In a meta-analysis conducted on patients with AS, the rate of hearing loss was found to be 42.4%. In our study, this rate was found to be 66.7% in R-AxSpA patients and 31.1% in NR-AxSpA patients. By subtype, the rate of SNHL in patients with AS was 37.2%; the rate of CHL was 13.5%. In our study, the definition of hearing loss was accepted as a value above 25 dB in at least two frequencies. Most of the hearing loss subtype was SNHL, as in previous studies. Previous studies in the literature demonstrated that audiologic abnormality is prominent in high frequencies.[6,12-15] Our study also confirmed this finding, but in the R-AxSpA group, hearing loss was seen at lower frequencies and more advanced than in the NR-AxSpA group. In the NR-AxSpA group, all of the patients with hearing loss were SNHL. This was an expected finding because of the low probability of bony ankylosis in the NR-AxSpA group. In the R-AxSpA group, 20% of the hearing loss seen was the CHL type, and the hearing loss was more severe.

A controversial issue is whether drugs can cause hearing loss. The main drugs used in the medical treatment of SpA patients are nonsteroidal anti-inflammatory drugs (NSAIDs) and biological agents. The ototoxic profile of these drugs is not clear. While Savastano et al.[16] mentioned the ototoxic potential of tumor necrosis factor (TNF) inhibitors, other studies emphasized the protective effect of TNF inhibitors on cochlear functions.[17] Niwano et al.[18] showed improvement in a patient with SNHL after TNF treatment in a case report. In our study, the vast majority of patients were using TNF inhibitors, and we could not comment on this possible effect. Prospective studies that assess audiologic studies before and after using the drug will provide more accurate information. The overuse of NSAIDs may also induce ototoxicity according to literature. NSAIDs generally cause transient hearing loss and tinnitus. In our study, all of the patients had used NSAIDs. This was also an important issue that might influence the study results.[19] One of the important results in our study is the findings obtained with TEOE. Only the R-AxSpA group was negatively affected in these studies. This might be associated with a higher disease duration, higher inflammation level, and worse BASMI value. It should be noted that another condition that impairs this test was the use of ototoxic drugs. However, the fact that there were also patients in the NR-AxSpA group using biological agents and the values of this group were similar to the control group suggested that the cause was the amount of inflammation rather than using drugs.

This study has limitations. Although the sample size is sufficient to compare the audiological tests of only three groups, it was insufficient to perform a subgroup analysis. Since it was a cross-sectional study, it was not possible to establish a cause-effect relationship, particularly in terms of drug toxicity.

In conclusion, this was the first study to compare audiological tests in patients with NR-AxSpA and R-AxSpA. Hearing loss can also be seen in NR-AxSpA patients, although not as much as in R-AxSpA. TEOE was the main audiological test that differentiated the two groups.

Ethics Committee Approval: The study protocol was approved by the SB Istanbul Medeniyet University Ethics Committee (date: 24.02.2021, no: 2021/0156). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Concept: H.C.Y., O.I.O.; Design: I.Y.; Data collection: C.T.S., O.E.; Analysis and/or interpretation: I.Y.; Literature review: I.Y., H.C.Y., O.I.O.; Writing: H.C.Y., I.Y.; Critical review: O.I.O.

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