



# Evaluation of hearing with pure-tone audiometry in alopecia areata patients

*Alopesia areata hastalarında saf ses odyometri ile işitmenin değerlendirilmesi*

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## Abstract

**Background and Design:** We aimed to evaluate whether alopecia areata (AA) patients had hearing loss with pure-tone audiometry.

**Materials and Methods:** In the study, 48 patients with AA and 39 healthy volunteers were included. All the patients were examined by the otorhinolaryngologist and audiometric examinations were performed using a pure-tone audiometer. Pure-tone thresholds for both ears were evaluated at frequencies of 250-8000 Hz for air conduction.

**Results:** Sensorineural hypoacusis was found in 18.8% of AA patients and 10.3% of control subjects. There was no statistically significant difference between the two groups ( $p=0.422$ ). The pure-tone average for the right ear and the left ear in AA patients was  $10.89\pm 5.45$  and  $10.50\pm 5.98$ , respectively. In control subjects, it was  $10.25\pm 3.43$  for the right ear and  $10.23\pm 5.46$  for the left ear. Pure-tone averages for both ears in AA patients were higher than controls; but the differences were not statistically significant ( $p=0.829$  and  $p=0.526$ , respectively). When we compared hearing thresholds for both ear for frequencies, there were not any significant differences between AA patients and controls ( $p>0.05$ ).

**Conclusion:** There was no difference in terms of hearing loss between AA patients and healthy controls.

**Keywords:** Hearing loss, audiometry, alopecia areata, autoimmune, pure tone, hypoacusis

## Öz

**Amaç:** Alopesia areata (AA) hastalarında işitme kaybı olup olmadığını saf ses odyometri ile değerlendirmeyi amaçladık.

**Gereç ve Yöntem:** Çalışmaya 48 AA hastası ve 39 sağlıklı gönüllü dahil edildi. Hastaların kulak burun boğaz hastalıkları uzmanı tarafından muayeneleri yapıldı. Odyometrik değerlendirme saf ses odyometrisi ile yapıldı. Her iki kulak için 250-8000 Hz frekanslarında hava yolu işitme düzeylerine bakıldı.

**Bulgular:** AA hastalarının %18,8'inde, kontrol grubunun ise %10,3'ünde sensorinöral hipoakuzi saptandı. İki grup arasındaki fark istatistiksel olarak anlamlı değildi ( $p=0,422$ ). Saf ses ortalaması AA hastalarında sağ kulak için  $10,89\pm 5,45$ , sol kulak için  $10,50\pm 5,98$  idi. Kontrol grubunda ise sağ kulak için  $10,25\pm 3,43$ , sol kulak için ise  $10,23\pm 5,46$  olarak bulundu. AA hastalarının saf ses ortalaması her iki kulak için de kontrol grubundan daha yüksek olmasına rağmen bu fark istatistiksel açıdan anlamlı değildi (sırasıyla  $p=0,829$ ,  $p=0,526$ ). Her iki kulak için AA ve kontrol grubunun frekanslara göre işitme eşiği değerleri karşılaştırıldığında iki grup arasında istatistiksel olarak anlamlı fark görülmedi ( $p>0,05$ ).

**Sonuç:** AA hastalarında işitme kaybı yönünden kontrol grubuna göre fark saptanmadı.

**Anahtar Kelimeler:** İşitme kaybı, odyometri, alopesia areata, otoimmün, saf ses, hipoakuzi

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## Introduction

Alopecia areata (AA) is a common inflammatory disease characterized by sudden-onset hair loss<sup>1</sup>. Its pathogenesis is not clear, however, it is thought that AA is a T cell-mediated autoimmune disease targeting anagen phase hair follicles<sup>2</sup>. Besides, AA have been reported to be accompanied by vitiligo, systemic lupus erythematosus, psoriasis, atopic dermatitis, allergic rhinitis, autoimmune thyroid diseases, anxiety, major depression, and obsessive compulsive disorder<sup>1,3</sup>.

Sensorineural hearing loss can develop as a result of dysfunction of the inner ear, auditory nerve or auditory center. It can occur due to different etiologies, and autoimmunity is one of the possible etiologies. While the inner ear was considered to be an immune-privileged area in the past, the relationship of lymphocyte and macrophages in endolymphatic sac was suggested later, and a new era has begun for the immunology of the ear. Inflammation caused by macrophages, T lymphocytes and macrophage-like melanocytes was determined to cause damage to the inner ear and result in hearing loss<sup>4</sup>.

There are many studies investigating hearing loss in various inflammatory dermatoses such as vitiligo, psoriasis, and Behçet's disease<sup>5-12</sup>. However, there has been only one study investigating the audiologic anomalies in AA patients in the literature<sup>13</sup>. In our study, we aimed to evaluate whether AA patients had hearing loss with pure-tone audiometry.

## Materials and Methods

Forty-eight AA patients without hearing loss complaint were included in the study. Control group was composed of 39 sex- and age-matched healthy subjects.

Kırıkkale University Local Ethics Committee approved the study (approval number: 20/05, date: 18.08.2014). The patients were informed about the study and informed consents were taken.

Patients with diabetes mellitus, hypertension, history of head trauma, recurrent otitis media, those exposed to noise, and patients using systemic steroids, immunosuppressants and ototoxic drugs were excluded from the study. Socio-demographic characteristics of the patients, age of onset of the disease, disease duration, location, type, family history, presence of accompanying nevus flammeus, nail involvement, pre-existing stress, and accompanying diseases (autoimmune and psychiatric) were questioned.

Before audiologic examination, the patients were examined by an otorhinolaryngologist. Audiometric assessment was performed in a sound-proof cabin with a pure-tone audiometer. Pure-tone audiometry is a test that determines the hearing thresholds by giving pure-tone voices. The measurements were performed with a Resonance R37A audiometer (Italy). Air-conduction hearing thresholds were examined for both ears with 250-8000 Hz frequencies. After determining hearing thresholds, pure-tone averages were calculated by adding up the hearing thresholds obtained at 500-1000 and 2000 Hz and determining the arithmetic average. Hearing loss at 26 dB or above was determined as hypoacusis.

Continuous data were presented as average  $\pm$  standard deviation, while categorical data were presented in percentage (%).

## Statistical Analysis

The Shapiro-Wilk test was used for studying the compliance of data with normal distribution. The independent sample t-test was used for cases

with two group numbers in the comparison of groups demonstrating normal distribution; while the Mann-Whitney U test was used in cases with two group numbers in the comparison of groups that do not comply with normal distribution. Furthermore, Yates' chi-square and Fisher's exact tests were used in the analysis of the cross-tables. IBM SPSS Statistics 21.0 program was used in the analyses and a p value of less than 0.05 was considered statistically significant.

## Results

A total of 48 AA patients, 27 (56.3%) men and 21 (43.8%) women, were included in the study. The average age of the patients was  $30.93 \pm 8.72$  (18-53) years. Control group consisted of 20 women (51.3%) and 19 men (48.7%) with ages varying between 18-60 years (average:  $27.94 \pm 11.99$ ). Both groups were similar in terms of age and gender ( $p=0.198$ ,  $p=0.628$ ).

When clinical characteristics of the patients were examined, the most common alopecia involvements were on the scalp (60.4%) and beard (22.9%) areas. Family history was positive in 20.8% of the patients. Six patients (12.5%) had nail involvement, and only 1 patient (2.1%) had nevus flammeus. Six patients had an accompanying autoimmune disease (autoimmune thyroiditis) (12.5%), and 9 patients had an accompanying psychiatric disease (18.8%) (8 patients had major depression and 1 patient had common anxiety disorder). Twenty-eight (58.3%) patients described emotional stress before the development of lesions. The mean age of onset was  $30.41 \pm 8.93$  (18-53) years and disease duration was  $8.25 \pm 26.60$  (1-180) months (Table 1).

Autoscopic examination was normal in all the patients. Sensorineural hypoacusis was determined in 9 AA patients (18.8%) and 4 controls (10.3%). However, the difference between the two groups was not statistically significant ( $p=0.422$ ) (Table 2).

When the presence of hypoacusis in both ears was compared between patient and control groups, hypoacusis was determined in the right ear in 7 AA patients (14.6%), and 3 controls (7.7%). For the left ear, hypoacusis was determined in 7 AA patients (14.6%) as well and 2 subjects (5.1%) in control group. The difference between the ears was not statistically significant either ( $p=0.501$ ,  $p=0.178$ ) (Table 3).

In order to determine the degree of the hearing loss, we examined pure-tone averages (250-8000 Hz). It was  $10.89 \pm 5.45$  for the right ear and  $10.50 \pm 5.98$  for the left ear in AA patients. In control group, it was  $10.25 \pm 3.43$  for the right ear, and  $10.23 \pm 5.46$  for the left ear. Although pure-tone average in AA patients was higher than in control group for both ears, the differences were not statistically significant ( $p=0.829$  and  $p=0.526$ , respectively). When hearing threshold values in AA and control groups were compared for both ears according to frequency, no statistically significant differences were observed between the two groups ( $p>0.05$ ) (Tables 4, 5).

In AA patients, statistically significant differences were not determined when the presence of hypoacusis and audiological values of the right and left ears were compared ( $p>0.05$ ) (Table 6).

Since there were a small number of patients in each group, audiological statistical comparisons could not be performed in AA patients with regard to clinical characteristics of patients such as involvement area, nail involvement, accompanying autoimmune/psychiatric diseases.

**Table 1. Clinical characteristics of alopecia areata patients**

		Frequency (n)	Percentage (%)
Localization	Scalp	29	60.4
	Beard	11	22.9
	Scalp + beard	5	10.4
	Eyebrow + eyelash + scalp	2	4.2
	Eyebrow + eyelash	1	2.1
Family history	Yes	10	20.8
	None	38	79.2
Nevus flammeus	Yes	1	2.1
	None	47	97.9
Nail involvement	Yes	6	12.5
	None	42	87.5
Type of nail involvement	Longitudinal striations	2	4.2
	Onychophagy	1	2.1
	Pitting	1	2.1
	Trachyonychia	1	2.1
	Transverse striations	1	2.1
Accompanying autoimmune disease	Yes	6	12.5
	None	42	87.5
Past emotional stress	Yes	28	58.3
	None	20	41.7
Accompanying psychiatric disease	Yes	9	18.8
	None	39	81.3
		<b>Minimum-maximum</b>	<b>Mean ± standard deviation</b>
Age (years)		18-53	30.93±8.72
Age of onset (years)		18-53	30.41±8.93
Disease duration (months)		1-180	8.25±26.60

**Table 2. Comparison of the presence of hypoacusis in patient and control groups**

		Group n (%)		$\chi^2$ ; p*
		Patient	Control	
Hypoacusis	None	39 (81.3%)	35 (89.7%)	0.644
	Yes	9 (18.8%)	4 (10.3%)	0.422

\*Yate's chi-Square test

**Table 3. Comparison of the presence of hypoacusis between both ears in patient and control groups**

Right ear	n (%)		p*
	Patient	Control	
Hypoacusis	None	41 (85.4%)	0.501
	Yes	7 (14.6%)	
Left ear	n (%)		p*
	Patient	Control	
Hypoacusis	None	41 (85.4%)	0.178
	Yes	7 (14.6%)	

\*Fisher's exact test, chi-square test

**Table 4. Comparison of air conduction hearing thresholds according to frequencies for right ear between patient and control group**

Right ear	Mean ± standard deviation Median (Q1 - Q3)		p*
	Group		
Frequency	Control (dB ± SD)	Patient (dB ± SD)	
250	12.44±4.42 10.00 (10.00-15.00)	12.81±4.48 10.00 (10.00-15.00)	0.761
500	13.46±14.74 10.00 (10.00-15.00)	10.94±5.02 10.00 (6.25-15.00)	0.508
1000	8.85±3.71 10.00 (5.00-10.00)	9.38±4.57 10.00 (5.00-10.00)	0.877
2000	9.49±4.26 10.00 (5.00-10.00)	9.79±6.18 10.00 (5.00-10.00)	0.577
4000	13.46±9.47 10.00 (10.00-15.00)	14.58±12.24 10.00 (6.25-18.75)	0.853
8000	14.23±10.91 10.00 (10.00-15.00)	17.29±15.23 10.00 (10.00-20.00)	0.367

\*Mann-Whitney U test, SD: standard deviation

**Table 5. Comparison of air conduction hearing thresholds according to frequencies for left ear between patient and control group**

Left Ear	Mean ± standard deviation Median (Q1 - Q3)		p*
	Group		
Frequency	Control (dB ± SD)	Patient (dB ± SD)	
250	11.92±3.56 10.00 (10.00-15.00)	12.60±4.37 10.00 (10.00-15.00)	0.626
500	10.51±2.76 10.00 (10.00-10.00)	10.31±4.05 10.00 (10.00-10.00)	0.602
1000	8.85±4.21 10.00 (5.00-10.00)	9.38±3.94 10.00 (5.00-10.00)	0.785
2000	9.62±5.18 10.00 (5.00-10.00)	9.90±5.88 10.00 (5.00-10.00)	0.833
4000	13.59±10.94 10.00 (10.00-15.00)	13.54±11.11 10.00 (5.00-15.00)	0.504
8000	13.21±9.35 10.00 (10.00-15.00)	14.79±15.47 10.00 (6.25-15.00)	0.586

\*Mann-Whitney U test

## Discussion

Although AA is generally regarded as a benign disease, studies have shown that it affects the quality of life of patients as much as chronic skin diseases such as psoriasis and atopic dermatitis<sup>14</sup>. It is also known that both psychiatric and autoimmune diseases are observed more commonly in AA patients<sup>1,3</sup>.

The hair follicle is an immune-privileged mini organ with its own immune and hormonal microenvironment. Due to this immune privilege, it is protected against immunologic attacks. This protection is provided by the absence of MHC class I expression in anagen hair follicle<sup>15,16</sup>. This immune privilege in the hair follicle is disturbed in AA. MHC I and II expression and abnormal HLA-DR antigen expression in hair follicle keratinocytes are suggested to play a key role in AA pathogenesis. In AA patients, CD4+T and CD8+T cells infiltrate the hair follicle and cause disturbances in its structure and function. Changes in the sub-groups of CD4+T cells (T<sub>h</sub>1, T<sub>h</sub>2, T<sub>h</sub>17) and regulatory T cells, and secretion of various cytokine and chemokines are blamed in the development of AA<sup>2,17</sup>.

Multisystem, autoimmune diseases such as Wegener granulomatosis, lupus erythematosus and polyarteritis nodosa have been demonstrated to cause sensorineural hearing loss by affecting the inner ear<sup>4</sup>. Also, there are studies in the literature on hearing abnormalities in autoimmune/ autoinflammatory dermatologic diseases such as vitiligo<sup>5,6</sup>, psoriasis<sup>7-10</sup> and Behçet's disease<sup>11,12</sup>.

**Table 6. Comparison of pure tone averages and presence of hypoacusis in right and left ear in alopecia areata patients**

Frequency	Mean ± standard deviation median (Q1-Q3)		p*
	Group		
	Right ear (dB ± SD)	Left ear (dB ± SD)	
250	12.81±4.48 10.00 (10.00-15.00)	12.60±4.37 10.00 (10.00-15.00)	0.785
500	10.94±5.02 10.00 (6.25-15.00)	10.31±4.05 10.00 (10.00-10.00)	0.647
1000	9.38±4.57 10.00 (5.00-10.00)	9.38±3.94 10.00 (5.00-10.00)	0.780
2000	9.79±6.18 10.00 (5.00-10.00)	9.90±5.88 10.00 (5.00-10.00)	0.767
4000	14.58±12.24 10.00 (6.25-18.75)	13.54±11.11 10.00 (5.00-15.00)	0.534
8000	17.29±15.23 10.00 (10.00-20.00)	14.79±15.47 10.00 (6.25-15.00)	0.211
500-4000	11.92±5.57 10.00 (10.00-10.00)	11.60±4.57 10.00 (10.00-10.00)	0.967
250-1000	11.25±3.30 10.00 (10.00-11.50)	11.23±2.73 10.00 (10.00-12.00)	0.604
2000-8000	14.25±9.29 10.00 (10.00-13.00)	13.56±8.61 10.00 (10.00-10.00)	0.698
	<b>n (%)</b>	<b>n (%)</b>	<b>p**</b>
Hypoacusis	None	41 (85.4%)	1.000
	Yes	7 (14.65%)	

\*Mann-Whitney U test \*\*Yate's chi-square test (Q1: 25% Quartile; Q3: 75% Quartile)

Vitiligo is an autoimmune disease characterized by the destruction of melanocytes. Aydoğan et al.<sup>5</sup> found that sensorineural hypoacusis was more common in vitiligo patients; and they suggested that melanocytes in the inner ear were important for stria vascularis and cochlea function, formation of endocochlear potentials, and ion and liquid balance between endolymph and perilymph. Likewise, in AA patients, histological and ultrastructural abnormalities in melanocytes have been shown<sup>18</sup>. Consequently, melanin may play a key role in the regulation and maintenance of the structure and function of the hearing system. The levels of proinflammatory cytokines, such as tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), interleukin-1 (IL-1), IL-6 and IL-8, increase in psoriasis<sup>7,9</sup>. Wang et al.<sup>19</sup> showed that cochlear inflammation and hearing loss decrease with TNF- $\alpha$  inhibitor etanercept. Hearing loss that can be observed in psoriasis is suggested to be related with increased levels of cytokines that may cause cochlear degeneration<sup>7,8,10</sup>.

There is only one study in the literature investigating the audiologic anomalies in AA patients. Ucak et al.<sup>13</sup> found sensorineural hypoacusis in 54.9% of AA patients, and it was more frequent than in control group in a statistically significant level. They have suggested that autoimmune process may cause hearing anomalies by targeting follicular melanocytes. We found sensorineural hypoacusis in 18.8% of AA patients; there was no statistically significant difference with control group. The difference between the study of Ucak et al.<sup>13</sup> and our study can be explained by the patients with severe disease, long disease duration, more patients with positive family history and nail involvement in the first study.

The exact mechanism of hearing loss that is observed in AA patients is not known. Audiologic abnormalities in AA patients might originate from the autoimmune nature of AA or the increased levels of various proinflammatory cytokines, mainly TNF- $\alpha$ . On the other hand, the pathologies in melanocytes in the inner ear like in vitiligo patients may be one of the reasons.

### Study Limitations

It is not uncommon that sensorineural hearing loss starts from high frequencies above 8000 Hz. Although the inner ear is affected, in early period, this effect may not reflect on pure-tone values. Limitations of our study consist of being unable to examine high frequency thresholds in patient and control groups, and being unable to perform autoacoustic emission test, that can show the effects on the inner ear in early period and can measure the outer hair cell function, due to technical insufficiencies. For these reasons, the difference between AA patients and control subjects in terms of hearing loss might not be detected exactly in our study.

### Conclusion

In our study, there was no difference in terms of hearing loss between AA patients and healthy controls. In order to determine whether AA is associated with hearing loss or not; further larger-scale studies examining the relationship of AA severity and clinical characteristics with hearing loss by using high frequency audiometry, autoacoustic emission test and autoimmune-inflammatory markers are required.

### Ethics

**Ethics Committee Approval:** Kırıkkale University Local Ethics Committee approved the study (approval number: 20/05, date: 18.08.2014).

**Informed Consent:** The patients were informed about the study and informed consents were taken.

**Peer-review:** Externally peer-reviewed.

### Authorship Contributions

Surgical and Medical Practices: H.K.E., E.A., A.H., Concept: H.K.E., E.A., A.H., I.B., Design: H.K.E., E.A., A.H., I.B., Data Collection or Processing: H.K.E., E.A., A.H., Analysis or Interpretation: H.K.E., M.B., E.A., A.H., I.B., A.İ., Ö.P., Literature Search: H.K.E., E.A., Writing: H.K.E., E.A.

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