

# Effect of vitiligo on the cochlea

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## Background

Vitiligo is the disappearance of functional melanocytes (MCs) from the involved skin by a mechanism(s) that has not yet been identified.

## Objective

The aim was to study the effects of different types of vitiligo on cochlear function.

## Patients and methods

This study involved 30 vitiligo patients who constituted the study group and 30 matched healthy individuals who served as the control group. Cochlear function was studied using pure-tone audiometry and transient-evoked otoacoustic emission.

## Results

Normal pure-tone thresholds were found in vitiligo patients with no statistically significant difference between the control and vitiligo groups on both ears. There was a statistically significant difference between control and vitiligo groups as regards the signal-to-noise ratio at a frequency band of 4 kHz on both ears. Cochlear function is affected equally in both generalized and localized vitiligo subgroups. The duration of vitiligo does not have an effect on cochlear function.

## Keywords:

otoacoustic emission, pure-tone audiometry, signal-to-noise ratio, vitiligo

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## Introduction

Vitiligo is an idiopathic, acquired, circumscribed hypomelanotic skin disorder resulting from loss of pigment-forming melanocytes (MCs). Many possible causes of vitiligo have been proposed, including stress, infections, mutations, neural factors, melatonin receptor dysfunction, and impaired MC migration and/or proliferation by Kemp *et al.* [1].

MCs are found not only in the skin but also in the leptomeninges, retinal pigment epithelium, uveal tract, and in the inner ear. The role of MCs in the inner ear is not completely understood. It is known that they are necessary for the normal development and function of the stria vascularis Steel and Barkway [2], Cable *et al.* [3], Tachibana [4], and Araki *et al.* [5].

Franz *et al.* [6] and Ardic *et al.* [7] have suggested a direct relation between cochlear dysfunction and decreased amounts of melanin. It is thus thought that melanin has a protective role against harmful agents in the inner ear. Loss of MCs, resulting in decreased melanin production as occurs in vitiligo, could decrease cochlear health.

Evaluation of auditory functions in patients with vitiligo has been the subject of only a few studies and a variety of abnormalities have been reported. In

this regard, the present study was designed to detect the effect of vitiligo on the cochlea.

## Patients and methods

### Patients

The study group included 30 vitiligo patients (eight men and 22 women). The duration of the disease ranged from 6 months to 30 years. They were divided as follows: (a) according to the type of vitiligo into generalized (15 patients) and localized (15 patients) and (b) according to the duration of vitiligo into: less than 10 years and greater than or equal to 10 years. They were selected from the Dermatology Clinic at Al Zhraa University Hospital. Thirty healthy participants served as a control group (six men and 24 women). The age of the control and study groups ranged from 6 to 40 years with a mean of 20.4±8.1 and 21.2±10.2, respectively.

Exclusion criteria for the control and study groups included any middle ear disease, previous ear surgery, familial hearing loss, ototoxic drug intake,

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chronic noise exposure, head trauma, and presence of any systemic disease such as diabetes or hypertension. Patients with other autoimmune disorders and skin manifestations were also excluded.

### Methods

All participants included were subjected to the following: otological examination, audiometric testing using Interacoustics AC40 (Interacoustics, Danish) pure-tone audiometry (PTA) was done (air conduction and bone conduction threshold). Immittanceometry were performed using Miaco 44 (MI44) (Miaco, German) to insure normal middle ear function. Transient-evoked otoacoustic emissions (TEOAEs) using Madsen Capella (Otometrics, Danish) (cochlear emission analyzer) were elicited by nonlinear click stimuli at stimulus intensity ranges from 80 dB peak equivalent sound pressure level, 80  $\mu$ s duration, at a rate of 50 clicks per second, within a time window of 20 ms. TEOAEs were analyzed by recording 260 sweeps in one session and averaged within five frequency bands centered at (1, 1.5, 2, 3, and 4 kHz). According to Kemp [8], those who showed an overall reproducibility of 70% were described to have a pass result and those with less than 70% but still had greater than 50% were considered to have a present TEOAE and were described to have a partial pass result.

### Statistical analysis

Data were analyzed with SPSS version 21 (SPSS Inc., Chicago, Illinois, USA). The normality of data was first tested with one-sample Kolmogorov–Smirnov test. Qualitative data were described using number and percent. The association between categorical variables was tested using  $\chi^2$ -test. Continuous variables were presented as mean $\pm$ SD. The two groups were compared with Student's *t*-test. Analysis of variance test was used for comparison of means of more than two groups.

### Results

No statistically significant difference was found between control and study groups as regard age and gender. No statistically significant difference between control and study groups in PTA threshold at all frequencies. TEOAE (SNR) shows highly statistically significant difference between control and study groups at high frequency. All of the control show pass response. In the study group, most of the ears show pass response (39/60) 65%, about one third of the ears(21/60) 35% show partial pass response. Neither the control nor the study group showed failed response. No statistically significant difference was found in the pure tone threshold between control group and type of vitiligo subgroups at any frequency in right and left ears ( $P>0.05$ ). TEOAE (SNR) shows highly statistically significant difference between control group and different type of vitiligo subgroups at frequency band 4 kHz in right and left ears. No statistically significant difference was found in the pure tone threshold of the control group and vitiligo subgroups according to vitiligo duration. TEOAE (SNR) showed highly statistically significant difference between control group and different duration of vitiligo subgroups at frequency band 4 kHz in the right and left ears. But no statistically significant difference was found between the two vitiligo subgroups with different vitiligo duration.

### Discussion

The present study was designed to examine cochlear function in generalized and localized vitiligo patients and to detect the effect of duration of vitiligo on cochlear function. There is no statistically significant difference in results between control and study groups as regards age and gender (Tables 1 and 2).

In the current study, audiological assessment using PTA shows that there is no hearing loss in the control and study groups and no statistically

**Table 1 Age distribution of the control group and the study group**

Control (n=30)		Study group (n=30)		Test of significance	P
Mean $\pm$ SD	Minimum–maximum	Mean $\pm$ SD	Minimum–maximum		
20.4 $\pm$ 8.1	6–40	21.2 $\pm$ 10.2	6–40	1.184	0.236

No statistically significant difference was found between control and study groups as regards age.

**Table 2 Gender distribution of the control group and the study group**

Gender	Control (n=30) [n (%)]	Study (n=30) [n (%)]	Test of significance	P
Male	6 (20.0)	8 (26.7)	$\chi^2=0.373$	0.542
Female	24 (80.0)	22 (73.3)		

No statistically significant difference between control and study groups as regards gender.

**Table 3 Comparison of pure-tone thresholds (mean±SD) in control and study groups**

Frequency in Hz	Side	Control (n=30)	Study (n=30)	t-test	P
250	Right	10.00±5.25	11.00±4.24	0.812	0.420
	Left	10.00±4.55	10.17±4.45	0.143	0.886
500	Right	10.33±4.72	11.33±4.90	0.805	0.424
	Left	10.00±4.15	12.17±4.09	2.037	0.062
1000	Right	10.67±4.50	10.50±4.80	0.139	0.890
	Left	10.67±4.10	10.83±3.73	0.165	0.870
2000	Right	9.00±4.62	9.83±4.25	0.727	0.470
	Left	12.00±3.62	11.33±4.72	0.614	0.542
4000	Right	11.33±4.72	11.17±4.68	0.137	0.891
	Left	11.67±4.80	11.83±5.94	0.120	0.905
8000	Right	11.67±4.01	13.17±6.36	1.092	0.279
	Left	11.00±3.81	13.17±6.76	1.530	0.131

No statistically significant difference between control and study groups in pure-tone audiometry threshold at all frequencies.

**Table 4 Comparison of TEOAE SNR (mean±SD) in control and study groups**

Frequency band	Side	Control (n=30)	Study (n=30)	t-test	P
1000	Right	8.33±5.25	8.33±5.30	0.097	0.923
	Left	9.73±7.67	8.00±5.36	1.015	0.314
1500	Right	12.07±6.22	12.77±5.31	0.469	0.641
	Left	11.13±4.44	12.03±4.32	0.796	0.429
2000	Right	13.13±7.72	14.10±5.80	0.549	0.585
	Left	13.13±5.26	14.03±6.60	0.584	0.561
3000	Right	12.13±8.17	12.63±6.38	0.264	0.793
	Left	11.27±4.48	12.57±6.15	0.936	0.353
4000	Right	16.87±4.67	10.33±6.57	4.442	≤0.001**
	Left	15.73±5.76	9.53±5.60	4.230	≤0.001**

TEOAE (SNR) shows highly statistically significant difference between control and study groups at high frequencies. \*\*Means highly statistically significant difference.

significant difference of PTA threshold between control and vitiligo groups at any frequency from 250 to 8000 Hz (Table 3).

These results are in agreement with Anbar *et al.* [9], Shalaby *et al.* [10], Ozuer *et al.* [11], Escalante-Ugalde *et al.* [12], and Orecchia *et al.* [13], who found that vitiligo patients had near-normal pure-tone thresholds and no statistically significant difference between the control and vitiligo groups in PTA on both ears.

The current study disagrees with the results of Mohamed *et al.* [14], Fleissig *et al.* [15], Mahdi *et al.* [16], Akay *et al.* [17], Hong *et al.* [18], who found different degrees of SNHL in vitiligo patients as

**Table 5 Number and percent of pass, partial pass, and failed responses of TEOAE in control and study groups**

TEOAE	Side	Control [n (%)]	Study [n (%)]
Pass	Right	30 (100)	20 (66.6)
	Left	30 (100)	19 (63.3)
Partial pass	Right	0 (0)	10 (33.4)
	Left	0 (0)	11 (36.7)
Failed	Right	0 (0)	0 (0)
	Left	0 (0)	0 (0)

All of the control show pass response. In the study group, most of the ears show pass response [(39/60) 65%], about one-third of the ears [(21/60) 35%] show partial pass response. Neither the control nor the study group showed a failed response.

compared with controls. This difference was statistically significant ( $P<0.001$ ). This disagreement may be due to different sample sizes and different ages of the study group.

Comparing the cochlear function of both ears in patients with vitiligo with the cochlear function of the control group using TEOAEs was done. Cochlear dysfunction was evident in patients with vitiligo in the form of smaller S/N ratio at 4000 Hz band (Table 4) and higher percentage of abnormal TEOAE findings in the form of partial pass response (35%) (Table 5). This supports previous studies that demonstrated subclinical abnormalities of melanin-containing cellular elements of the auditory system in patients with vitiligo Tosti *et al.* [19] and Aydogan *et al.* [20]. Also Mohamed *et al.* [14] reported that TEOAEs had the advantages of detecting minimal cochlear dysfunction in vitiligo patients.

This result agrees with Aslan *et al.* [21], who found a significant reduction in the amplitude of TEOAEs only at 4 kHz in the vitiligo group. The current study agrees also with Anbar *et al.* [9], who found that 64 ears (60%) of patients with vitiligo had cochlear dysfunction while the control group exhibited no abnormalities using DPOAEs.

The lost cochlear emission in the vitiligo group was previously explained by Schrott *et al.* [22]. They stated that hypopigmentation disorders may lead to degeneration of the outer hair cells beginning from the basal turn of the cochlea. The MCs in the inner ear have multiple roles critical for hair cell survival, including maintenance of the normal function of the stria vascularis Tachibana [4]. Inner ear melanin functions as an intracellular calcium buffer and as a depot of essential metal ions that control the activity of various enzymes and metabolic processes Barrenas and Lindgren [23], and Barrenas and Axelsson [24]. MCs in the inner

**Table 6 Comparison of pure-tone thresholds (mean±SD) in the control group and study subgroups according to the vitiligo type**

Frequency in Hz	Side	Control (n=30)	Types of vitiligo		F	P
			Generalized (n=15)	Localized (n=15)		
250	Right	10.00±5.25	10.40±4.31	14.00±2.24	1.553	0.220
	Left	10.00±4.55	10.20±4.20	10.00±6.12	0.014	0.986
500	Right	10.33±4.72	10.80±5.14	14.00±2.24	1.264	0.290
	Left	10.00±4.15	12.40±4.11	11.00±4.18	2.045	0.139
1000	Right	10.67±4.50	10.40±4.55	11.00±6.52	0.044	0.957
	Left	10.67±4.10	10.80±4.00	11.00±2.24	0.019	0.982
2000	Right	9.00±4.62	10.00±4.33	9.00±4.18	0.365	0.696
	Left	12.00±3.62	11.80±4.76	9.00±4.18	1.128	0.331
4000	Right	11.33±4.72	10.80±4.93	13.00±2.74	0.465	0.630
	Left	11.67±4.80	11.20±6.00	15.00±5.00	1.059	0.354
8000	Right	11.67±4.01	12.80±6.31	15.00±7.07	0.948	0.393
	Left	11.00±3.81	12.40±6.63	17.00±6.71	2.729	0.074

No statistically significant difference was found in the pure-tone threshold between the control group and type of vitiligo subgroups at any frequency in right and left ears ( $P>0.05$ ).

**Table 7 Comparison between mean and SD of TEOAE (SNR) of the control group and study subgroups according to the vitiligo type**

Frequency band	Side	Control (n=30)	Types of vitiligo		F	P	Post-hoc test
			Generalized (n=15)	Localized (n=15)			
1000	Right	8.33±5.25	7.80±5.28	11.80±4.82	1.222	0.302	–
	Left	9.73±7.67	7.44±5.01	10.80±6.76	1.054	0.355	–
1500	Right	12.07±6.22	13.52±5.17	9.00±4.74	1.421	0.250	–
	Left	11.13±4.44	11.52±4.22	14.60±4.28	1.373	0.262	–
2000	Right	13.13±7.72	14.64±5.54	11.40±6.95	0.619	0.542	–
	Left	13.13±5.26	13.88±6.57	14.80±7.46	0.457	0.636	–
3000	Right	12.13±8.17	13±6.081	10.80±8.29	0.220	0.803	–
	Left	11.27±4.48	12.96±6.25	10.60±5.77	1.862	0.165	–
4000	Right	16.87 ±4.67 <sup>a,b</sup>	11.08±6.23 <sup>a</sup>	6.60±7.67 <sup>b</sup>	11.471	≤0.001**	Control vs. generalized vitiligo, control vs. localized vitiligo
	Left	15.73 ±5.76 <sup>a,b</sup>	9.68±5.46 <sup>a</sup>	8.80±6.87 <sup>b</sup>	8.855	≤0.001**	Control vs. generalized vitiligo, Control vs. localized

Groups with similar superscript letters are statistically significantly different according to post-hoc tests. TEOAE (SNR) shows highly statistically significant difference between control group and different types of vitiligo subgroups at a frequency band of 4 kHz in right and left ears. \*\*Means highly statistically significant difference.

**Table 8 Comparison of pure-tone thresholds (mean±SD) in the control group and study subgroups according to vitiligo duration**

Frequency in Hz	Side	Control (n=30)	Duration of vitiligo		F	P
			<10 years (n=19)	≥10 years (n=11)		
250	Right	10.00±5.25	10.79±4.49	11.36±3.93	0.374	0.690
	Left	10.00±4.55	9.74±4.24	10.91±4.91	0.244	0.784
500	Right	10.33±4.72	10.80±5.07	12.27±4.67	0.651	0.525
	Left	10.00±4.15	11.84±4.15	12.73±4.10	1.958	0.151
1000	Right	10.67±4.50	10.26±4.24	10.91±5.84	0.076	0.927
	Left	10.67±4.10	10.53±4.05	11.36±3.23	0.171	0.844
2000	Right	9.00±4.62	10.26±3.90	9.09±4.91	0.502	0.608
	Left	12.00±3.62	11.84±5.58	10.45±2.70	0.565	0.572
4000	Right	11.33±4.72	12.11±4.81	9.55±4.16	1.063	0.352
	Left	11.67±4.80	12.11±6.08	11.36±5.95	0.072	0.931
8000	Right	11.67±4.01	13.16±5.82	13.18±7.51	0.586	0.560
	Left	11.00±3.81	12.63±6.32	14.09±7.69	1.405	0.254

No statistically significant difference was found in the pure-tone threshold of the control group and vitiligo subgroups at any frequency.

**Table 9 Comparison of TEOAE (SNR) mean±SD in the control group and study subgroups according to vitiligo duration**

Frequency band	Side	Control (n=30)	Duration of vitiligo		F	P	Post-hoc test
			<10 years (n=19)	≥10 years (n=11)			
1000	Right	8.33±5.25	8.53±5.36	8.36±5.60	0.008	0.992	–
	Left	9.73±7.67	8.26±5.10	7.55±6.01	0.547	0.582	–
1500	Right	12.07±6.22	13.68±5.31	11.18±5.15	0.766	0.469	–
	Left	11.13±4.44	12.58±4.05	11.09±4.80	0.716	0.493	–
2000	Right	13.13±7.72	14.89±5.57	12.73±6.20	0.499	0.610	–
	Left	13.13±5.26	15.37±6.066	11.73±7.12	1.070	0.350	–
3000	Right	12.13±8.17	13.11±6.84	11.82±5.72	0.140	0.869	–
	Left	11.27±4.48	13.53±6.30	10.91±5.77	1.887	0.161	–
4000	Right	16.87±4.67 <sup>a,b</sup>	11±6.77 <sup>a</sup>	9.18±6.35 <sup>b</sup>	10.168	≤0.001**	Control vs. <10 years, control vs. ≥10 years
	Left	15.73±5.76 <sup>a,b</sup>	9.47±5.87 <sup>a</sup>	9.64±5.35 <sup>b</sup>	8.795	≤0.001**	Control vs. <10 years, control vs. ≥10 years

Groups with similar superscript letters are statistically significantly different according to post-hoc tests. TEOAE (SNR) showed a highly statistically significant difference between the control group and different duration of vitiligo subgroups at a frequency band of 4 kHz in the right and left ears. But no statistically significant difference was found between the two vitiligo subgroups with different vitiligo duration.

ear are required for the development of endocochlear potentials, control of ions and fluid gradient between the endolymph and the perilymph Halaban *et al.* [25].

In the current study, the cochlear function of the ears of patients with generalized vitiligo and the cochlear function of the ears of patients with localized vitiligo were compared. No statistically significant difference in the PTA threshold and the TEOAE S/N ratio were found (Tables 6 and 7). This suggests that there is no significant effect of vitiligo subtype on cochlear function.

These results are in agreement with Fleissig *et al.* [15] and Anbar *et al.* [9], who found that hearing losses in the groups with different types of vitiligo were not significantly different from each other. On the other hand, Sharma *et al.* [26] and Hong *et al.* [18] found generalized vitiligo and nonsegmental vitiligo to be a risk factor for SNHL.

PTA and TEOAE results showed no statistically significant difference between patients with a duration of less than and more than 10 years (Tables 8 and 9). It is concluded that the duration of vitiligo does not have an effect on cochlear function. This could be explained by the possibility that otic MCs are affected at the start of the vitiligo and then stabilized afterwards Mahdi *et al.* [16].

Fleissig *et al.* [15], Shalaby *et al.* [10], and Sharma *et al.* [26] found that the duration of vitiligo does not affect hearing. They postulated that there is no correlation between the duration of vitiligo and hearing loss.

The current study contradicts Aslan *et al.* [21], who concluded that the duration of vitiligo affects hearing. They found a statistically significant positive correlation between the duration of vitiligo and hearing loss.

## Conclusion

Vitiligo has an effect on cochlear function and the affection is usually asymptomatic for a long time. Cochlear function is affected equally in both generalized and localized vitiligo subgroups. There is no correlation between the duration of vitiligo and hearing loss. TEOAE is a sensitive test for detecting cochlear dysfunction before symptoms become manifested as the TEOAE was impaired in 35% of the ears with normal hearing.

## Recommendation

Vitiligo patients required routine monitoring by specialists for early identification of auditory changes. Further study should be done to assess the effect of vitiligo on the central auditory nervous system.

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## Conflicts of interest

There are no conflicts of interest.

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