

## **Auditory Function In Vitiligo Patients**

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### **Abstract**

**Background:** Vitiligo is a systemic disorder influencing the whole pigmentary system including melanocytes in the inner ear. Many possible causes of vitiligo have been proposed, including stress, infection, mutations, neural factors, melatonin receptor dysfunction and impaired melanocyte migration or proliferation. Cochlear melanocytes may be affected in vitiligo and interfere with the conduction of action potentials in the auditory pathway.

**Aim:** Evaluation of the effect of melanin deficiency in vitiligo patients on cochlear and brain stem auditory function.

**Material and Methods:** 30 patients affected by vitiligo of various durations and distributions 10 normal subjects were evaluated. Pure tone audiometry, with extended high frequency, auditory brain stem response audiometry, and transient otoacoustic emission were done for both groups.

**Conclusion:** vitiligo, which is a type of pigment disorder had a definite effect on cochlear function. Melanin containing cells in the inner ear had a protective function, and melanin was reported to play a role in  $Ca^{2+}$  homeostasis of endolymph.

### **Introduction**

Vitiligo is an acquired hypomelanotic disorder characterized by circumscribed depigmented macules or patches resulting from the loss of functional melanocytes and of melanin from the epidermis [6]. Vitiligo is

not transmitted by of simple Mendelian mechanism and its inheritance patters is more consistent with that of a polygenic trait [7].

Many possible causes of vitiligo have been proposed, including stress, infections, mutations, neural factors, melatonin receptor dysfunction, and impaired melanocyte migration and/or proliferation. In addition, the accumulation of toxic intermediate products of melanin synthesis [8], the breakdown of free radical defence [10] and the build up of excessive quantities of hydrogen peroxide [12] have all been suggested to result in the self-destruction of pigment cells.

Although loss of melanocytes from the skin is almost always the primary and initial symptom in vitiligo, other pigment cells in the body can be affected. Melanocytes are located in the inner ear [4] and vitiligo associated auditory problems have been reported is some patients [15] and [1].

Damage can also occur to melanocytes within the eye. The affection of extracutaneous melanocytes in some vitiligo patients suggests that systemic immunological reactions directed at pigment cells might play a role in the development of the disease [6].

The purpose of this study was to investigate how much the auditory function is affected in patients with vitiligo of different distributions and durations.

## **Materials And Methods**

### **I. Subjects:**

1- Study group: It consisted of 30 vitiligo patients, 13 males and 17 females. Their age ranged from 6-63 years with a mean of  $(22.2 \pm 12.6)$ . They had different durations of disease ranging from 6 months to 15 years  $(4.7 \pm 3.5)$ , and variable distributions. They were referred to the Audiology Clinic from Dermatology Clinic, El Hussein Hospital. All patients who were exposed to factors known to be responsible for sensorinural hearing loss were excluded from the start e.g. ototoxic drug intake, noise exposure or systemic diseases.

2- Control group: It consisted of 10 normal subjects, 4 males and 6 females. Their age ranged from 6-53 years  $(27.6 \pm 17.04)$ . They were chosen from those accompanying patients attending the Audiology Clinic, El Hussein Hospital.

### **II. Equipment:**

1- Pure tone and speech audiometer (Interacoustics Ac40).

2- Sound treated room (IAC locally made).

- 3- Cochlear Emission Analyzer Madsen (Celesta, 503).
- 4- Immittancemeter (Interacoustics Az7).
- 5- Evoked Response Audiometer Nickolet Compact four (CA2000).

### **III. Method:**

All subjects in this study were submitted to a full history taking, general medical and skin examination, otological history and otological examination. Hearing assessment was conducted in the Audiology Clinic of El Hussein Hospital. It included conventional pure-tone, speech audiometry as well as extended high frequency audiometry at (12, 16 KHz) using head phone (koss HV/PRO digital). Immittancemetry and Transient Evoked Otoacoustic Emission (TEOAE) using condensation click stimulus at intensity equal to 70 dB SPL. The software determined the amplitude of TEOAE in three frequency bands (1, 2, 3 KHz). The analysis was also performed for the amplitude and reproducibility percent. Auditory Brain stem Evoked Response (ABR) was performed also with the following parameters was made:

Stimulus: rarefaction click with a duration of 100 msec.

Filter: 150-3000 Hz.

Time window: 10 msec.

Intensity: 90 dB n HL

Number of sweeps: 1000.

Rate: regular repetition rate at 21.4 pulse/second and high repetition rate at 71.4 pulse/second.

Silver chloride electrodes were used at CZ, CPZ, M1 and M2 sites, then the following measurements were calculated: Absolute latencies of wave I-III and V and interpeak latencies I-III, III-V and I-V at regular repetition rate. Also, absolute latency of wave V (-V) at high repetition rate was recorded.

### **Statistical Analysis**

Mean, standard deviation were used for data description. Student's t test was used to compare between two sample means. The chi square test was used to find significant relation between qualitative data. Pearson's correlation was used to find significant relation between two numeric variables was conducted. Results were considered significant if  $P < 0.05$ .

### **Results**

**Table 1:** Mean ( $\bar{X}$ ) and Standard Deviation (SD) of PTA (dB) of both control and study group.

There was no statistically significant difference between control and study groups in PTA threshold on both sides.

**Table 1:** Mean ( $\bar{X}$ ) and Standard Deviation (SD) of PTA (dB) of both control and study group.

Frequency KHz	Ear	Control $\bar{X}$ S.D	Study $\bar{X}$ S.D	t	P
0.25	Rt	12.8 $\pm$ 2.4	13.7 $\pm$ 3.4	0.47	> 0.05
	Lt	13.2 $\pm$ 2.1	12.9 $\pm$ 3.7	0.51	
0.5	Rt	13.3 $\pm$ 2.1	13.5 $\pm$ 2.3	0.39	> 0.05
	Lt	14.1 $\pm$ 1.9	13.9 $\pm$ 3.4	0.28	
1	Rt	18.7 $\pm$ 3.0	21.2 $\pm$ 4.3	0.61	> 0.05
	Lt	18.0 $\pm$ 2.5	20.8 $\pm$ 4.7	0.57	
2	Rt	20.4 $\pm$ 3.6	21.7 $\pm$ 3.6	0.42	> 0.05
	Lt	20.8 $\pm$ 4.7	22.9 $\pm$ 5.8	0.56	
4	Rt	22.3 $\pm$ 3.5	23.3 $\pm$ 3.8	0.32	> 0.05
	Lt	21.2 $\pm$ 2.8	23.4 $\pm$ 2.9	0.45	
8	Rt	20.8 $\pm$ 4.5	23.3 $\pm$ 3.5	0.70	> 0.05
	Lt	19.9 $\pm$ 5.1	22.8 $\pm$ 4.1	0.51	
12	Rt	19.0 $\pm$ 6.1	21.2 $\pm$ 11.35	0.57	> 0.05
	Lt	18.0 $\pm$ 4.8	21.0 $\pm$ 10.5	0.87	
16	Rt	22.5 $\pm$ 7.2	32.3 $\pm$ 19.6	1.5	> 0.05
	Lt	22.5 $\pm$ 7.1	29.5 $\pm$ 19.5	1.1	

There was no statistically significant difference between control and study groups in PTA threshold on both sides

**Table 2:** Reproducibility Percent and the mean of TEOAE at different frequencies in both groups.

There was significant decrease in reproducibility % of TEOAE in the study group. Also significant differences in TEOAE at different frequencies were detected between control and study groups.

<b>P</b>	<b>t</b>	<b>Study -X S.D</b>	<b>Control -X S.D</b>		<b>TEOAE</b>
> 0.05 < 0.01*	1.14 3.05	0.2 ± 7.0 2.2 ± 5.4	2.8 ± 1.9 3.2 ± 1.35	Rt Lt	1 KHz
< 0.05* < 0.001*	2.3 4.1	-2.13 ± 5.4 -6.0 ± 5.8	1.9 ± 2.4 1.8 ± 2.4	Rt Lt	2 KHz
< 0.01* < 0.01*	3.7 5.2	-5.4 ± 4.4 -7.4 ± 4.4	-0.13 ± 1.8 0.08 ± 1.9	Rt Lt	3 KHz
< 0.001*	4.1	33.3%	98%		Reproducibility %

There was significant decrease in reproducibility % of TEOAE in the study group. Also significant differences in TEOAE at different frequencies were detected between control and study groups.

\* Significant value.

**Table 3:** Mean (-X) and Standard Deviation (S.D) of ABR parameters in both control and study groups.

There was no statistically significant difference between cases and control in all ABR parameters measured.

<b>ABR (msec)</b>	<b>Side</b>	<b>Control (10) -X S.D</b>	<b>Control (30) -X S.D</b>	<b>t</b>	<b>P</b>
Wave I	Rt	1.59 ± 0.09	1.55 ± 0.1	0.97	> 0.05
	Lt	1.63 ± 0.11	1.57 ± 0.12	1.33	
III	Rt	3.7 ± 0.07	3.74 ± 0.42	0.63	> 0.05
	Lt	3.7 ± 0.07	3.73 ± 0.39	0.32	
V	Rt	5.7 ± 0.08	5.58 ± 0.19	1.92	> 0.05
	Lt	5.73 ± 0.09	5.6 ± 0.21	1.85	
Interpeak I-III	Rt	2.08 ± 0.06	2.08 ± 0.11	Zero	> 0.05
	Lt	2.07 ± 0.07	2.06 ± 0.14	0.22	
Interpeak III-V	Rt	2.06 ± 0.05	2.09 ± 0.11	1.09	> 0.05
	Lt	2.03 ± 0.07	2.1 ± 0.14	1.8	
Interpeak I-V	Rt	4.1 ± 0.09	3.93 ± 0.37	1.53	> 0.05
	Lt	4.09 ± 0.07	3.95 ± 0.41	1.1	
-V	Rt	5.87 ± 0.12	5.83 ± 0.24	0.51	> 0.05
	Lt	5.88 ± 0.11	5.84 ± 0.23	0.48	

There was no statistically significant difference between cases and control in all ABR parameters measured

**Table 4:** Correlation between duration, severity of the disease (no. of affected sites) and PTA among cases

No significant correlation between duration, distribution sites of vitiligo and PTA in the study group was found.

Frequency KHz	Duration r-value	Severity r-value	P
0.25	0.06	0.12	> 0.05
0.5	0.14	0.07	> 0.05
1	0.18	0.13	> 0.05
2	0.09	0.01	> 0.05
4	0.11	0.06	> 0.05
8	0.17	0.18	> 0.05
12	0.15	-0.11	> 0.05
16	0.21	0.12	> 0.05

No significant correlation between duration, distribution sites of vitiligo and PTA in the study group was found

**Table 5:** Correlation between duration, severity of the disease Con. of affected sites and ABR, TEOAE

No significant correlation between duration, distribution of vitiligo and ABR, TEOAE parameters was found.

ABR (msec)	Duration r-value	Severity r-value	P
I	-0.01	0.25	> 0.05
III	-0.06	0.25	> 0.05
V	-0.03	0.12	> 0.05
I-III	-0.29	0.09	> 0.05
III-V	-0.03	0.31	> 0.05
I-V	-0.08	0.04	> 0.05
~V	-0.07	0.22	> 0.05
TEOAE 1 KHz	0.07	0.07	> 0.05
2 KHz	-0.02	0.04	
3 KHz	0.16	0.22	

No significant correlation between duration, distribution of vitiligo and ABR, TEOAE parameters was found.

## Discussion:

The role of the melanocytes within the inner ear is not well understood. Congenital and acquired deafness have been associated with vitiligo in certain kindreds [14] and [16]. In this study 30 patients with vitiligo of different durations and distributions were compared to a matching control subjects in terms of the following audiologic tests:

### 1. Pure Tone Audiometry (PTA) with extended high frequency (12, 16 KHz):

The mean of pure tone threshold in the frequencies 0.25-16 KHz was elevated in the study group than control group ([Table 1](#)), but this difference is not statistically significant. 15% of patients with vitiligo who demonstrated audiologic changes were symptomatically free regarding hearing sensitivity. It seems logic to assume that the affection of hearing organ is minimal and usually not detected by the patient, and although vitiligo patients had near normal pure tone thresholds in conventional audiometry, some subjects in the study group showed hearing affection at extended high frequency. These results reflect the importance of extended high frequency audiometry in detecting minute affection of hearing sensitivity prior to its appearance in conventional audiometry. The above result was in agreement with other investigators, [15] examined 50 patients with vitiligo and auditory abnormalities were detected in 16% of cases. All had sensorineural hearing loss and they were affected by generalized vitiligo. They attributed their findings to the involvement of the inner ear melanocytes which are thought to prevent damage to hair cells of the inner ear due to environmental ototoxic agents. This hypothesis is also supported by the finding that black-skinned persons are less commonly affected by noise-induced hypoacusis than are white skinned persons who live in the same habitat [5].

In another more recent study, [1] found that the pure tone thresholds of the vitiligo group were significantly lower than the control group starting from 4 KHz up to 16 KHz.

### 2. Transient Evoked Otoacoustic Emission (TEOAE):

Using another audiologic test for evaluation of cochlear function (TEOAE, [Table 2](#)) revealed a significant decrease in reproducibility percent of TEOAE in the vitiligo group. The reproducibility percent was 33.3 in the study group compared to 98% in the control group. Significant differences in TEOAE at different frequencies were also detected. In a study by [2] the mean of the whole reproducibility percentage was 49% for vitiligo group with more than 10 years duration. The lost cochlear emission in vitiligo group was explained previously by [13]. They stated that hypopigmentation disorders for a long duration may lead to degeneration of the outer hair cells beginning from the basal turn of the

cochlea while inner ear hair cells remain structurally and functionally intact. Another explanation was related to endolymph  $\text{Ca}^{2+}$  levels, [3] found that in pigmented animals the endolymph  $\text{Ca}^{2+}$  tended to increase from base to apex of the cochlea, while endocochlear potential systematically decreased towards the apex. In contrast, no significant  $\text{Ca}^{2+}$  gradient was found in albinos and the endocochlear potential decline was far less. Their results confirm the involvement of melanin in the active transport of  $\text{Ca}^{2+}$  into endolymph.

### 3. Auditory Brainstem Response (ABR):

Studying the ABR absolute and interpeak latencies revealed no statistically significant difference ( $P > 0.05$ ) between cases and control (Table 3). This agreed with [11], who studied 50 patients affected by vitiligo and compared the results with 50 healthy controls. No statistically significant difference was noted between both groups as regards latencies, interpeak latencies and amplitudes. They recommended postmortem histopathological studies of the inner ear and brainstem to provide more accurate knowledge in vitiligo patients.

On the other side, [9] studied 30 patients with active vitiligo and found a statistically significant ( $P < 0.01$ ) decrease of the peak I latency and increase of the I-III interpeak latency in the patients as compared to the controls. They explained the decrease of first peak latency to be due to numerical decrease of active melanocytes in the inner ear resulting in an impairment of the ion exchange between the endolymph and perilymph with disturbance of the transduction of the auditory stimuli in the inner ear. The increased I-III interpeak latency was explained to be due to abnormal synaptic activity and transmission of the action potential from the auditory nerve to the superior olive. Similarly, [2] found a statistically significant decrease of wave I latency due to slight cochlear lesion present in all melanin deficient patients. They put another explanation for increase I-III interpeak latency; they proposed that the shorter latency of wave I is responsible for the delayed I-III interpeak latency as the absolute latency of wave III in their study and in the study of [9] was within normal range.

No relation was found between duration, severity of the disease (number of affected sites) and any audiological parameters (table 4, 5).

## Conclusions

1- Vitiligo has an effect on cochlear function and the affection is usually asymptomatic for long time.

2- Extended high frequency audiometry has an advantage in detecting early minute affection in the auditory sensitivity.



3- TEOAE is a valuable tool in detection of minimal cochlear lesion.

4- Some patients with vitiligo will have a certain amount of auditory defect irrespective of the duration or distribution of the disease. The mechanism is most probably multi factorial and may be related to individual susceptibility, residual number of melanocytes in the inner ear and the nature of immunologic abnormalities in patients with vitiligo.

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