

## Audiological Profile of Patients with Vitiligo

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### Abstract

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

**Aim of the work:** Evaluation of the cochlea and the auditory nerve in vitiligo patients.

**Patients and Methods:** Cross sectional clinical study included total number of 60 subjects were examined. All subjects included were subjected to the following procedures: Full history taking, clinical examination, Basic audiologic evaluation, Transient Evoked otoacoustic emissions (TEOAEs), Distortion Product Otoacoustic Emission (DPOAE), Auditory Brainstem Response test (ABR).

**Results:** The ABR finding concluded that melanin play a significant role in establishment and maintenance of structure and function of the auditory system and may modulate the transduction of auditory stimuli by the inner ear.

**Conclusion:** TEOAE and DPOAE are sensitive tests for detecting cochlear dysfunction before symptoms become manifested as the TEOAE and DPOAE were impaired in 35% and 35% of the ears with normal hearing.

**Key words:** Audiological profile, vitiligo.

### Introduction

Vitiligo is an acquired hypomelanotic disorder characterized by circumscribed depigmented macules or patches resulting from loss of functional melanocytes and of melanin from the epidermis<sup>(1)</sup>. Vitiligo is not transmitted by simple Mendelian mechanism and its inheritance pattern is more consistent with that of a polygenic trait<sup>(2)</sup>.

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<sup>(3)</sup>, the breakdown of free radical defense<sup>(4)</sup> and the build up of excessive quantities of hydrogen peroxide have all been suggested to result in the self-destruction of pigment cells<sup>(4)</sup>.

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 and vitiligo associated auditory problems have been reported in some patients<sup>(5)</sup>.

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<sup>(1)</sup>.

### **Aim of the work:**

Evaluation of the cochlea and the auditory nerve in vitiligo patients.

### **Patients and Methods:**

#### **Procedure:**

First Informed written consent was taken from the parents before entrance of the operating room and study was approved by ethics committee in Sohag medical university.

**Design:** Cross sectional study.

### Patients:

A total number of 60 subjects were examined in this study.

They were divided into two main groups:-

#### 1- Control group:

It composed of 30 persons who had no vitiligo, no complaints of hearing loss and no history of ear infections, trauma, use of ototoxic drugs or history of familial hearing loss were selected for the study. They were 6 males and 24 females. Their age ranged from 16- 40 years. They were chosen from those accompanying patients attending Audiology unit sohag university.

#### 2. Study group:

It composed of 30 vitiligo patients. They were 8 males and 22 females. Their age ranged from 17-46 years. The duration of the disease ranged from 4 months to 35 years. The age of onset ranged from 4-44 years. They were selected from dermatology clinic, sohag university. Audiological evaluation were done at Audiology unit, sohag universty.

The study group was divided as the following;

According to type of vitiligo into:

- Generalized vitiligo: they were 17 patients.
- Localized vitiligo: they were 13 patients

According to family history of vitiligo into:

- Patients with positive family history they were 11 patients  
○ (36.7%).
- Patients with negative family history they were 19 patients  
○ (63.3%).

According to age of onset into:

- Patients with age of onset of vitiligo <20 years old (subgroup A).
- Patients with age of onset of vitiligo 20-30 years old (subgroup B).
- Patients with age of onset of vitiligo ≥30 years old (subgroup C).

According to duration of vitiligo into:

- Patients with duration of vitiligo <10 years.
- Patients with duration of vitiligo ≥10 years.

According to Skin type into :

- Patients with skin type III: They were 19 patients (63.3%).
- Patients with skin type IV: They were 11 patients (36.7)

### Methods:

All subjects included were subjected to the following procedures:

#### 1. Full history taking:

including personal history, history of hearing loss,,tinnitus, vertigo, history to exclude any otological or neuro - otological diseases

#### 2. Clinical examination:

including otologic examination, and skin examination.

#### 3. Basic audiologic evaluation: including:

- a) Pure tone audiometry; in the form of: Air conduction in the frequency range of 250 - 8000 Hz. Bone conduction in the frequency range of 500 - 4000 Hz.
- b) Speech audiometry; including: Speech reception threshold (SRT), using Arabic spondaic words. word discrimination score (WDS), using Arabic phonetically balanced (PB) words.
- c) Immittancemetry: including single-component, single- frequency tympanometry with a probe tone of 226 Hz and testing of the acoustic reflex threshold for the ipsilateral and the contralateral elicited reflexes, using pure tones at frequencies 500, 1000, 2000 and 4000 Hz.

The measurements following those were made after acoustic immittance assessments, which were used to demonstrate that middle-ear function was normal at the time of the TEOAE test.

#### 4) **Transient Evoked otoacoustic emissions (TEOAEs).**

TEOAEs were elicited using non-linear click stimuli at stimulus intensity ranges from 80 dB peak equivalent sound pressure level (SPL), 80 us duration, at a rate of 50 clicks per second, within a time window of 20 msec. TEOAEs were analyzed by recording 260 sweeps in one session and averaged within 5 frequency bands centered at (1, 1.5, 2, 3 and 4 KHz). The differential non-linear test paradigm was used. The stimulus was characterized by a train of four clicks, three with the same amplitude and polarity, followed by a fourth one with 3-fold greater amplitude and an opposite polarity. Responses were represented by an average of a maximum of 260 click stimuli trains (1040) stored into two different buffers averaged separately (A and B) for a total of 2080 clicks. The averaged amplitude in dB, of these two waveforms presented the overall echo level in dB SPL. In addition the reproducibility of TEOAEs was tested by the correlation between signals from the two buffers. All responses were stored for analyses.

#### 5) **Distortion Product Otoacoustic Emission (DPOAE).**

DPOAEs occur in response to two simultaneous tones of different frequencies presented to the ear. The lower frequency tone is called F1 and the higher frequency tone is called F2. F2 is frequently, but not always, 1.21 times the frequency of F1. In response to F1 and F2 presentation, the ear generates other tones of different frequencies but with a clear frequency relationship to F1 and F2. These

generated tones are called distortion products. The largest distortion product is usually at the frequency that is two times the frequency of F1 minus the frequency of F2 or (2F1-F2). Although 2F1-F2 is of a much lower frequency than either F1 or F2, the presence/absence and/or amplitude of the 2F1-F2 component correlates most closely with hearing thresholds at either the F2 frequency or approximately the midpoint between the F1 and F2 frequencies called geometric mean.

#### 6) **Auditory Brainstem Response test (ABR).**

■ Skin preparation and electrode montage:

The skin over the forehead and mastoids was prepared and cleaned by alcohol to reduce electrode impedance. Four disposable electrodes were fixed according to the Smart EP manual specification as follows: one high frontal Fz (positive electrode), one low frontal Fpz (ground electrode). The last two electrodes were placed on the left and right mastoids (as negative electrode or reference electrode) depending on the recording side. All electrodes were connected to the pre-amplifier of the Smart EP equipment.

#### **Exclusion criteria:**

- A history of any middle ear disease, previous ear surgery, familial hearing loss, ototoxic drug intake, chronic noise exposure and head trauma.
- The presence of any systemic disease such as diabetes or hypertension.
- Patient with age more than 70 years.

**Results**

**Table ( 1 ) Age and gender distribution of the control group and the study group.**

	Control No = 30	Study group No = 30	t-test	P Value
	Mean ± SD	Mean ± SD		
Age	21.40±10.10	25.26 ± 12.58	1.184	.236
Gender	M 20.0	26.7	0.373	.542
	F 80.0	73.3		

**Table ( 2 ): Comparison between pure tone threshold of control group and family history of vitiligo subgroups .**

Freq. Bands	Side	Control ( 30 )	Family history		F	P value
			Positive ( 11 )	Negative (19)		
250	R	10.00±5.25	13.18±3.37	9.74±4.24	2.250	0.115
	L	10.00±4.55	10.46±4.16	10.00±4.71	0.045	0.956
500	R	10.33±4.72	13.64±3.23	10.00±5.27	2.440	0.096
	L	10.00±4.15	13.18±4.62	11.58±3.75	2.605	0.083
1000	R	10.67±4.50	10.91±5.39	10.26±4.56	0.076	0.927
	L	10.67±4.10	10.91±3.75	10.79±3.82	0.017	0.984
2000	R	9.00±4.62	10.91±4.91	9.21±3.82	0.774	0.466
	L	12.00±3.62	13.18±4.05	10.26±4.85	1.945	0.152
4000	R	11.33±4.72	10.91±4.37	11.32±4.96	0.035	0.966
	L	11.67±4.80	13.64±6.74	10.79±5.34	0.992	0.377
8000	R	11.67±4.01	15.46±6.88	11.84±5.82	2.292	0.110
	L	11.00±3.81 <sup>a</sup>	16.36±7.10 <sup>a</sup> b	11.32±5.97 <sup>b</sup>	4.510	0.015*

**Table (3) : Comparison between TEOAE -SNR of control group and age of onset of vitiligo subgroups.**

Freq . bands	Side	Control ( 30 )	Age of onset			F	P value
			<20y ( A)	20-30y ( B)	≥30y ( C)		
1000	R	8.33±5.25	8.24±5.86	9.60±2.61	8.25±5.92	0.092	0.964
	L	9.73±7.67	8.12±5.97	8.20±4.32	7.63±5.15	0.343	0.794
1500	R	12.07±6.22	13.53±4.12	12.40±8.26	11.38±5.95	0.326	0.807
	L	11.13±4.44	11.76±4.44	9.40±2.07	14.25±4.37	0.498	0.685
2000	R	13.13±7.72	14.94±5.15	13.40±5.32	12.75±7.63	0.301	0.825
	L	13.13±5.26	14±6.18	15.40±7.89	13.25±7.42	0.241	0.868
3000	R	12.13±8.17	13.29±6.62	14.80±4.55	9.88±6.60	0.589	0.624
	L	11.27±4.48	12.71±5.50	14.80±5.45	10.88±7.97	1.139	0.341
4000	R	16.87±4.67 <sup>ab</sup>	10.24±7.0 <sup>a</sup> <sub>c</sub>	16.20±3.57 <sup>cd</sup>	6.88±4.49 <sup>b</sup> <sub>d</sub>	10.502	≤0.001* *
	L	15.73±5.76 <sup>ab</sup>	8.76±5.27 <sup>a</sup>	13.40±5.41	8.75±6.04 <sup>b</sup>	6.989	≤0.001* *

**Table (4) Measurement of central tendency, dispersion and position, by frequency to the value of amplitude of the distortion otoacoustic emission Product in the study group .**

Freq . bands	Side	Mean	SD	Minimum	Maximum
1000	R	8.58	6.71	-3.2	18.6
	L	10.07	4.58	3.9	22
1500	R	15.41	7.63	1.6	26.7
	L	13.78	6.01	2.3	23.1
2000	R	14.63	5.61	3.2	22.3
	L	15.24	6.11	6.2	29.1
3000	R	12.43	9.71	-17.2	24.1
	L	14.17	6.04	6.3	23.6
4000	R	19.56	6.04	6	31.4
	L	19.49	5.94	6.6	30.5
8000	R	17.92	8.10	-1	33.9
	L	15.8	10.4	-1.6	32.7

**Table ( 5 ) Mean and SD of auditory brainstem response ( ABR ) latencies in milliseconds of both control and study group .**

ABR waves at 90 dB nHL	side	Control group	Study group	t-test	P value
		Mean ± SD	Mean ± SD		
Wave I	Rt	1.52 ±0.0276	1.48 ± 0.0234	3.314	0.002**
	Lt	1.53 ± 0.025	1.49 ± 0.027	4.120	0.001***
Wave III	Rt	3.56 ± 0.0887	3.54 ± 0.0688	0.935	0.012*
	Lt	3.36 ± 0.084	3.35 ± 0.071	1.550	0.011*
Wave V	Rt	5.636 ± 0.110	5.643 ± 0.128	1.563	0.011*
	Lt	5.62 ± 0.105	5.60 ± 0.086	0.883	0.013*

No statistically significant difference was found between control and study groups as regard age and gender in **table 1**.

Groups with similar superscript letters are statistically significantly different according to post-hoc LSD test ( $p \leq 0.05$ ). Statistically significant difference in pure tone threshold between control group & positive family history subgroup and between positive & negative family history subgroups at 8 kHz in the left ears ( $p < 0.05$ ) in **table 2**.

Groups with similar superscript letters are statistically significantly different according to post-hoc LSD test ( $p \leq 0.05$ ). TEOAE SNR showed highly statistically significant difference in SNR between control group & subgroups (<20y) & ( $\geq 30y$ ) at frequency band 4 kHz in right and left ears, and between (20-30y) & (<20y) & ( $\geq 30y$ ) subgroups at frequency band 4 kHz in the right ears as shown in **table 3**.

The amplitude of the otoacoustic emissions distortion products in study group was major in the frequency of 4 KHz, in both ear. The mean of the values of amplitude of frequency 4 KHz was 19.56 in the right ear, 19.49 in the left ear in **table 4**.

The latency of waves I, III, and V, in all ears, lied within the normal range for our normative data for latency-intensity functions. When the control group results are compared with study group result, significant differences are explicit especially for wave I in **table 5**.

## Discussion

In the current study the mean age is  $21.40 \pm 10.10$  years in the control group and  $25.26 \pm 12.58$  years in the study group without statistical significant difference between the two groups. Hence, both the groups did not fall into geriatric age group to exclude the degenerative factor of age. In this study 73.3% of study are females and 26.6% are males. In controls 80% are females and 20% are males. This difference in gender composition of the study group and control, which may be due to greater awareness and concern about cosmetic defect among females than among males, is statistically

insignificant due to the match of control to the study group.

### Effects of vitiligo on hearing:

#### PTA results

In this study, audiological assessment showed that there is no statistical significant difference of hearing threshold between control group and vitiligo group at all frequencies from 250 to 8000 Hz.

Our results disagree with the results of Fleissig et al. <sup>(5)</sup>, Mahdi et al., <sup>(6)</sup>, Akay et al., <sup>(7)</sup>, Ardic et al., <sup>(8)</sup>, Aslan et al., <sup>(9)</sup>.

Mahdi et al., <sup>(6)</sup> found that audiometric thresholds were

statistically greater in both ears of the patients with vitiligo at 2, 4 and 8 kHz compared with control subjects ( $P \leq 0.05$ ). This findings strengthen the hypothesis that an alteration of the inner ear pigment cells might favor the occurrence of hypoacusis.

### Results of TEOAE

In our study all controls showed bilateral pass response at all frequency bands. But in the study group 17/30(56.66%) showed bilateral pass response and 5/30 (16,66 %) of the cases showed unilateral pass (unilateral partial pass); The remaining 8/30 (26.66%) had bilateral partial pass response. The percentage of Pass response was 65% of ears [39/60 ears (34 ears of bilateral pass) and (5 ears of unilateral pass)]. Percentage of Partial pass response was 35% of ears [21/60 ears (5 ears of partial pass) in addition to (16 ears of bilateral partial pass)]. When comparing the TEOAE findings in control and vitiligo groups in a frequency-specific way we found that SNR of TEOAEs were lower at the frequency band 4 KHz in the study group than in the control group, which yield a highly statistically significant difference.

In the present study, the difference between control and study groups in TEOAE at frequency band 4 KHz is due to outer hair cell dysfunction towards the base of cochlea which not apparent in PTA. This means that TEOAE is more sensitive in detecting the cochlear dysfunction than PTA. The same concept represented by Angrisani et al. <sup>(10)</sup> who found that TEOAE were absent in 66.7% of subjects with normal hearing so they concluded that TEOAE are sensitive test for detecting cochlear function before symptoms become manifest. Our result agree with Aslan et al. <sup>(9)</sup> who found a significant reduction in the amplitudes of TEOAEs only at 4 KHz in vitiligo group. When the values

for reproducibility, stimulus intensity, stability and average TEOAE amplitude of patients and control groups, were compared no statistically significant difference was found.

The lost cochlear emission in the vitiligo group was previously explained by Schrott & Spoendlin <sup>(11)</sup> 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.

In our study the OHCs dysfunction which was detected by TEOAE can be explained by affection of the melanocytes in the inner ear which have multiple roles critical for hair cell survival, Including maintenance of the normal function of the stria vascularis and cochlea, the development of endocochlear potentials, and the ion and fluid gradient between the endolymph and the perilymph <sup>(12-14)</sup>.

In this study the decrease in the TEOAE occurred at high frequency (at frequency band 4 KHz), which means that OHC affection occurred at the base of the cochlea. OHCs at the base of the cochlea seems be more susceptible to damage than those preset in the apex. This is supported by the finding of Steel et al. <sup>(15)</sup> in their study of Wv/Wv mutant mice, observed that inner ear hair cells were preserved, but outer hair cells in the basal half of cochlea were degenerating, possibly as a result of primary strial dysfunction. They also found that the organ of Corti looked reasonably normal in the apical turns, but there was degeneration of the hair cells towards the base.

### Results of DPOAE

In this study all control subjects showed bilateral pass response. In the study group 19/30(63.33%) showed bilateral pass response and 3/30 (10.00%) of the cases showed

unilateral pass response (unilateral partial pass), the remaining 8/30 (26.66%) had bilateral partial pass response. The percentage of Pass response was 68% of ears [41/60 ears (38 ears of bilateral pass) and (3 ears of unilateral pass)]. Percentage of Partial pass response was 32% of ears [19/60 ears (3 ears of partial pass) in addition to (16 ears of bilateral partial pass) ]. When comparing the DPOAE findings in control and vitiligo groups in a frequency-specific way we found that SNR of DPOAEs were lower at the frequency band 4 &8 KHz in the study group than in the control group, which yield a highly statistically significant difference. Also there was a significant difference between value of amplitude of distortion otoacoustic emission in the frequency bands 4 &8 KHz in the study group.

In the present study, the difference between control and study groups in DPOAE at frequency band 4&8 KHz is due to outer hair cell dysfunction towards the base of cochlea which not apparent in PTA. This means that DPOAE is more sensitive in detecting the cochlear dysfunction than PTA. Our result agree with Tosti et al. <sup>(16)</sup> and Aydogan et al. <sup>(17)</sup> who found a significant reduction in amplitude and high percentage of abnormal DPOAE findings in vitiligo patients and there no significant effect of vitiligo subtype on cochlear function.

#### **Results of ABR**

In our study, ABR assessment to latency of component peak showed a significant difference in the latency of waves I, III, and V specially for wave I between control group and vitiligo group, wave I decrease more remarkably in vitiligo patients.

This results are in agreement with Hong et al., <sup>(18)</sup> and Aydogan et al., <sup>(17)</sup>.

#### **Effect of the type of vitiligo on hearing:**

In our study, vitiligo patients were classified according to the type, of vitiligo into, generalized and localized type, Patients with generalized type were 25 (83.3 %) and those with localized type were 5 (16.7%). As regard to TEOAE there was statistically significant difference in SNR between control group and generalized vitiligo and between control group and localized vitiligo at frequency band 4 KHz in right and left ears.

Our results was in agreement with Fleissig et al. <sup>(5)</sup> and Ardic et al. <sup>(8)</sup>.

#### **Effect of age of onset of vitiligo.**

In our study vitiligo patients were divided according to the age of onset of the disease into 3 groups (A, B and C). Patients with age of onset less than 20 years old (group A) they were 17 (56.6%), those between 20 to 30 (group B) were 5 (16.6%) and those more that and equal to 30 years old (group C) were 8 (26.6%).

Comparing the results of TEOAE, SNR showed a statistically significant difference among the control and the three subgroups of age of onset of vitiligo at 4 KHz frequency band. This statistically significant difference was found between control & subgroup A, control group & subgroup C on the right and left ears. While the right ears show also statistically significant difference between subgroups B &A and between subgroups B &C. The reproducibility % of TEOAE showed the same differences in SNR in addition to statistically significant difference between subgroup B and C. This means that patients with age of onset more than 30 have higher risk of developing auditory affection as they may be more vulnerable to oxidative damage caused by sever noise, ototoxic medication and even age -related hearing loss.

Our results was in agreement with Fleissig et al. <sup>(5)</sup> who founded a

tendency towards increased severity of SNHL in older vitiligo patients and late onset of vitiligo.

#### **Effect of the duration of vitiligo on hearing:**

In our study vitiligo patients were classified according to duration of the disease into 2 categories less and more than 10 years. Patients with duration less than 10 were 19 (63.33%) and those with the duration more than 10 years were 11 (36.66%). The results were in agreement with Fleissig et al.<sup>(5)</sup> and Sharma et al.<sup>(20)</sup> who concluded that the duration of vitiligo does not affect hearing, they found that no correlation between duration of vitiligo and hearing loss.

#### **Conclusion**

- Vitiligo has an effect on cochlear function and the affection is usually asymptomatic for long time.
- TEOAE&DPOAE are sensitive tests for detecting cochlear dysfunction before symptoms become manifested as the TEOAE and DPOAE were impaired in 35% and 35% of the ears with normal hearing.
- The ABR finding concluded that melanin play a significant role in establishment and maintenance of structure and function of the auditory system and may modulate the transduction of auditory stimuli by the inner ear.

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