



Assessment of auditory and vestibular functions in vitiligo patients

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Abstract

Objectives: To evaluate audiological and vestibular functions via basic audiological evaluation, otoacoustic emissions and videonystagmography (VNG) in vitiligo patients.

Material and methods: 30 vitiligo patients (8 acrofacial and 22 mixed types) as the study group and 30 normal healthy adults as the control group were included in the study. All participants were submitted to basic audiological evaluation, transient and distortion product otoacoustic emissions (TEOAEs and DPOAEs), vestibular assessment including history taking, office tests and videonystagmography (VNG) and dermatological assessment to determine type, percent of body surface area involvement and duration of vitiligo.

Results: This study showed statistically significant difference between control and study groups in pure tone audiometry (PTA) and otoacoustic emissions results. Fifty percent of vitiligo patients had peripheral vestibular disorders (10 vestibular neuritis and 5 posterior canal benign paroxysmal positional vertigo).

Conclusion: The results in this study showed that 50% of vitiligo patients suffered from peripheral vestibular disorders in addition to auditory affection. Vitiligo patients require routine monitoring for auditory and vestibular functions for early identification and monitoring of changes as the disease progress.

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Keywords: Vitiligo; Otoacoustic emissions; Videonystagmography

1. Introduction

Vitiligo (leukoderma) is an acquired, sometimes familial, depigmentary disorder resulting from selective destruction of melanocytes (Mahdi et al., 2012). Vitiligo occurs worldwide with a prevalence of 0.06–2.28 percent (Krüger and

Schallreuter, 2012). Vitiligo commonly occurs in childhood or young adulthood, with peak onset of 10–30 years, but it may occur at any age (Liu et al., 2005). All races are affected and both sexes are equally vulnerable. Female preponderance has been reported and has been attributed to the cosmetics use in female (Alkhateeb et al., 2003). Positive family history affects the onset of vitiligo and in those patients the disease appears earlier than in sporadic cases (Laberge et al., 2005).

Many possible causes of vitiligo have been assumed, including stress, autoimmune, mutations, neural factors, melatonin receptor dysfunction and impaired melanocyte migration and/or proliferation, in addition to the accumulation of toxic intermediate products of melanin synthesis (Moellmann et al., 1982). The melanocytes arise from the neural crest, and they

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are located in the epidermis, hair bulbs of the skin, the uveal tract and retinal pigment epithelium of the eye, the inner ear, and the leptomeninges (Ortonne and Bose, 1993).

Corti (1831) was the first researcher to mention the presence of pigment cells in the inner ear (Angrisani et al., 2009). There are many melanocytes in the human cochlea, particularly in the modiolus, osseous spiral lamina, Reissner's membrane and in the vascular stria; melanocytes are present especially in highly vascularized areas of apparently important secretory or metabolic function (Savin, 1965). In the vestibular labyrinth, melanocytes present in the utricle, saccule, pars commune, ampulla, endolymphatic duct and sac. Although its exact role – and that of melanin remains unknown, it is probable that they have a vasomotor function in the inner ear (Gill and salt, 1997). According to Savin (1965) cells containing pigments are partially or fully adhered to blood vessel walls, which are sites of intense metabolite exchanges.

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 (Tosti et al., 1987). Vitiligo associated auditory problems have been reported in some patients (Aydogan et al., 2006). Few studies had studied the audiological manifestations in vitiligo such as Aslan et al. (2010); Mahdi et al. (2012). There are discrepancies in the literature about the specific influence of vitiligo on auditory threshold. Some authors reported hearing affection (Angrisani et al., 2009), while others reported no hearing affection (Escalante-Ugalde et al., 1991; Elsaied et al., 2008).

To our best knowledge no study discussed the vestibular manifestations in vitiligo patient except Mahdi et al. (2016) who studied cervical vestibular evoked myogenic potential (cVEMP) on these patients. Accordingly, this study is designed to evaluate the audiological & vestibular functions in vitiligo patients. Aims of this study are (1) to evaluate audiological functions via basic audiological evaluation and otoacoustic emissions in vitiligo patients. (2) to evaluate vestibular function in vitiligo patients via videonystagmography

2. Material and methods

This study was performed after fulfilling the requirements of Mansoura ORL Department Ethical Committee and approved by the Institutional Research Board of Faculty of Medicine, Mansoura University. All participants filled an informed consent.

This is a prospective cohort study conducted at Audiology Unit, Otolaryngology Department, Mansoura University, Egypt. This study included: 1) study group: 30 vitiligo patients with different pathologies (type, site & duration) were collected from the Dermatology department and 2) control group: 30 healthy volunteers with matched age and sex to the study group. The study was carried out between August 2014 and December 2016.

3. Exclusion criteria

Subjects of both groups (study and control) who had one or more of the following conditions: medical or neurological

problems known to affect audiovestibular system, family history of hearing impairment, neck or visual problems, ototoxic drug intake and noise exposure were excluded from this study. Also, subjects with abnormal middle ear function were excluded from the study.

All participants in this study were subjected to the following procedures: (1) Full medical and otological history taking. (2) Clinical and otoscopic examination. (3) Basic audiological evaluation including (a) pure tone audiometry at 250, 500, 1000, 2000, 4000, 8000 Hz and speech audiometry including speech reception threshold and speech discrimination using two channels diagnostic audiometer, Orbiter 922, Madsen Electronic, version 2 (Denmark) and (b) immittance including tympanometry and acoustic reflex using GSI, tymptstar, middle ear analyser version 2 with 226 Hz probe tone frequency (USA). (4) Otoacoustic Emissions including (a) transient-evoked otoacoustic emissions (TEOAEs) were collected at 1, 1.5, 2, 3, 4 kHz in a 20-ms window. The level of click stimulus was 80 dB peSPL and (b) distortion product otoacoustic emissions (DPOAEs). DP-Gram at 750, 984, 1500, 2016, 3000, 3984, 6000, 7969 Hz using L1 at 65 dB SPL, L2 at 55 dB SPL and with f2/f1 equal to 1.22 were used in recording. All DPOAE responses were recorded in f2, but are equal to 2f1-f2. TEOAEs were considered present if response (signal to noise ratio (SNR)) ≥ 6 dB with reproducibility $\geq 70\%$ at least in three frequencies with overall SNR ≥ 6 dB and overall reproducibility $\geq 70\%$. DPOAEs were considered present if SNR ≥ 6 dB at least in four frequencies. Otoacoustic emissions were measured using Bio-logic Scout OAE, Natus hearing diagnostic version 4.0. (5) Vestibular evaluation including: (a) history of vestibular symptoms with emphasis on their onset, course, duration, severity of attacks and precipitating factors; (b) office tests including inspection for spontaneous nystagmus and assessment of gaze holding, alternate cover test for skew deviation, head shaking nystagmus, head impulse test, Romberg test, tandem gait test and Fukuda stepping test and (c) VNG test battery including recording of spontaneous nystagmus, Gaze, positional and positioning tests (Dix-Hallpike maneuver, supine roll maneuver and straight head hanging maneuver), oculomotor testing (saccade, pursuit and optokinetic tests) and alternate binaural bithermal caloric testing (Water irrigation was done with 250 mL of water irrigated for 30 s at 30 °C for the cool irrigation and 44 °C for the warm irrigation. Unilateral weakness $>20\%$ are considered significant). VNG done using Micro medical, spectrum, visual eye, version 6.1. (USA). (4) Dermatological assessment including: (a) type of vitiligo (b) extent of area affected according to rule of nine Fig. 1. (c) duration of vitiligo: duration less than or equal 18 months or with duration more than 18 months.

Statistical analysis of the data used IBM SPSS software package version 20. Parametric quantitative data were described as mean and standard deviation while non-parametric data were described as median and interquartile range (IQR). Significance of the obtained results was judged at the 5% level. The used tests were: 1 – Student *t*-test: For normally quantitative variables, to compare between vitiligo

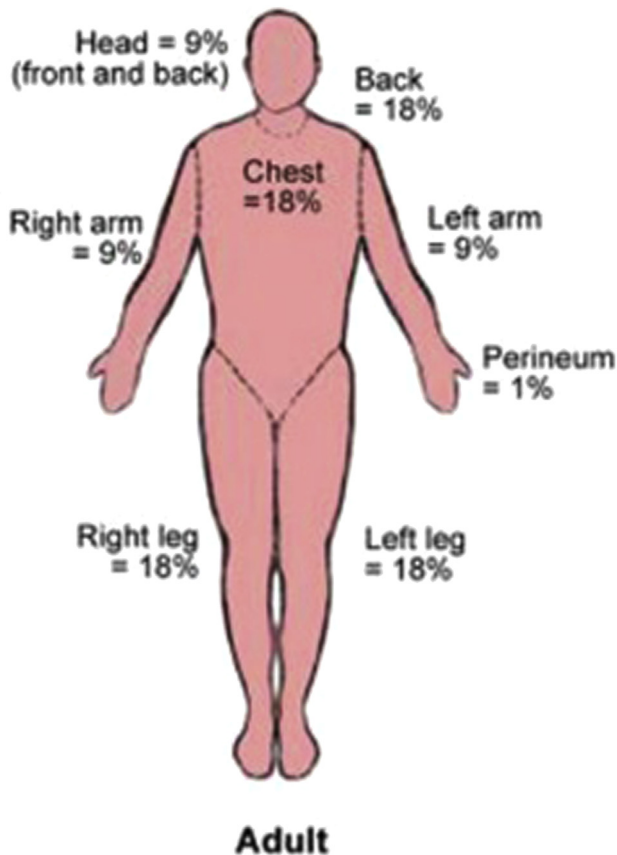


Fig. 1. Rule of nine (Lloyd and Rodgers, 2012).

study and control groups; 2 – Mann Whitney test: For abnormally quantitative variables, to compare between vitiligo study and control groups; 3 – F-test (ANOVA) was done to compare between PTA, TOAEs and DPOAEs results in the different patient categories of the study group including those with vestibular neuritis, BPPV and those with normal vestibular function and 4 – Pearson's correlation was used to find relationships between 2 type of vitiligo, percent of body surface area involved and duration of vitiligo on auditory and vestibular functions, the criterion for statistical significance was defined as $P \leq 0.05$.

4. Results

This study included 60 subjects. They were divided into two groups. The first group (control) consisted of 30 normal subjects (12 males and 18 females), while the second group (study) consisted of 30 patients (14 males and 16 females). The mean age for control group was (29.77 years \pm 11.16 with range 16–49 years), and for study group was (31.27 years \pm 12.13 with range 14–47 years). There were no statistical difference between groups regarding gender or age ($p = 0.60$).

Table 1 showed the demographic data of the study group. While Table 2 showed pure tone audiometry and speech discrimination scores in the study and control groups with significant differences at some frequencies in pure tone audiometry.

Table 1

Dermatological results of study group as regards type of vitiligo, percent of body surface area involved and duration of vitiligo.

	No.	%
Type of vitiligo		
Acrofacial	8	26.7
Mixed	22	73.3
Percent of body surface area involved		
Less than 25%	20	66.7
25-50%	10	33.3
Duration of vitiligo		
Less or equal 18 months	13	43.33
More than 18 months	17	56.66

The study group had 23 (76.7%) patients with normal pure tone threshold and 7 (23.3%) patients with mild to moderate SNHL (1 patient at frequencies 2–8 kHz, 2 patients at 4 kHz, 3 patients at 4–8 kHz and 1 patient at 8 kHz).

Results of TEOAEs and DPOAEs showed in Tables 3 and 4 respectively. There was statistically significant difference in TEOAEs at 1000 and 1500 Hz. While, statistically significant difference of DPOAEs were present at 750, 984, 1500, 6000, 7969 Hz between study and control groups.

TEOAEs and DPOAEs were present in all ears of control subjects (SNR \geq 6 dB nearly in all tested frequencies). However, in vitiligo patients, TEOAEs were absent in 10 ears (10/60 ears) while the DPOAEs were absent in 9 ears (9/60 ears).

As regards vestibular finding in control group all measurements were in the normal range. The results of vestibular assessment in the study group showed normal oculomotor testing, 10 (33%) superior vestibular neuritis (VN) patients (2 cases diagnosed in first week from attack, 3 cases in second week, 3 cases after about one month and 2 cases after about two months), 5 (17%) posterior canals canalolithiasis benign paroxysmal positional vertigo (BPPV) and remaining 15 (50%) vitiligo patients had normal vestibular function (Fig. 2). Caloric testing showed caloric weakness in control (14.03 \pm 3.32) and study (19.53 \pm 13.32) (Fig. 3). It was

Table 2

Comparison between the study and control groups as regard to pure tone audiometry and speech discrimination scores.

Frequency Hz	Ear	Study (n = 30 patients)	Control (n = 30 subjects)	T	P
250	Right	16.67 \pm 5.92	13.33 \pm 3.56	2.643*	0.011*
	Left	16.0 \pm 4.98	12.33 \pm 2.54	3.592*	0.001*
500	Right	14.33 \pm 4.69	13.50 \pm 3.51	0.780	0.439
	Left	16.0 \pm 4.43	13.0 \pm 2.82	3.128*	0.003*
1000	Right	15.0 \pm 4.91	13.17 \pm 3.59	1.650	0.104
	Left	13.83 \pm 4.49	14.0 \pm 3.57	0.159	0.874
2000	Right	17.33 \pm 5.53	13.83 \pm 3.13	3.017*	0.004*
	Left	15.67 \pm 5.37	15.50 \pm 4.22	0.134	0.894
4000	Right	21.17 \pm 9.62	14.67 \pm 3.70	3.454*	0.001*
	Left	20.0 \pm 10.42	16.67 \pm 4.61	1.602	0.117
8000	Right	22.33 \pm 10.65	14.83 \pm 4.45	3.560*	0.001*
	Left	19.67 \pm 11.59	16.33 \pm 4.14	1.483	0.147
DS%	Right	99.73 \pm 1.01	99.60 \pm 1.61	0.384	0.703
	Left	99.87 \pm 0.73	99.20 \pm 2.20	1.573	0.125

*Statistically significant at $p \leq 0.05$. There were statistically significant differences at some frequencies in pure tone audiometry.

Table 3
Comparison of transient otoacoustic emissions signal to noise ratio (SNR) in study and control groups.

Frequency Hz	Study (60 ears)		Control (60 ears)		P
	Median	IQR	Median	IQR	
1000	3.05	0.85–6.40	8.05	5.75–10.05	<0.001*
1500	6.00	3.20–11.80	9.45	6.00–12.90	0.007*
2000	8.50	4.55–12.40	9.10	5.85–11.10	0.7
3000	8.10	2.30–11.00	9.40	5.60–11.50	0.085
4000	8.15	6.10–11.35	7.9820	5.45–11.25	0.99

Test used: Mann–Whitney *statistically significant. There were statistically significant differences at 1000 and 1500 Hz between study and control groups.

statistically significant in two groups ($p = 0.032$). ANOVA test was done to compare between PTA, TOAEs and DPOAEs results in the different patient categories of the study group including those with vestibular neuritis, BPPV and those with normal vestibular function and showed no significant difference ($p > 0.05$).

Diagnosis of VN was based on the presence of (1) a single episode of rotational vertigo lasting days with no auditory symptoms; (2) office tests were suggestive of unilateral peripheral vestibular lesions; (3) normal audiogram and (4) VNG finding including spontaneous nystagmus in some cases with fast phase beating towards healthy ear suppressed by visual fixation and unilateral caloric weakness more than 20%.

As regards posterior canal canalolithiasis BPPV diagnosis based on history of rotatory vertigo that lasts less than 1 min, precipitated by head movements with Positive Dix-Hallpike maneuver with presence of the following criteria (1) 1–20 s latency before the onset of vertigo and nystagmus; (2) torsional upbeating nystagmus on hyperextended head position; (3) vertigo and nystagmus less than 1 min and (4) reversal of nystagmus directions on setting.

There were no significant effects for type, body affection surface area and duration of vitiligo on the auditory and vestibular functions.

5. Discussion

Vitiligo is an acquired, sometimes familial, depigmentary disorder which is a result of selective destruction of

melanocytes and characterized by milky-white patches of diverse shapes and sizes, in the midst of normally pigmented skin (Mahdi et al., 2016). Although melanocytes loss in vitiligo is predominately confined to patient's skin, alteration in the extracutaneous sites have been reported and implied sometimes for inner ear with an associated function compromise in this sensory organ (Aslan et al., 2010).

Melanocytes are primarily localized throughout the stria vascularis and modiolus of cochlea, they also present in the vestibular organs (Aslan et al., 2010). Destruction of melanocytes in the inner ear which have multiple roles critical for hair cells survival, including maintenance of the normal function of stria vascularis and the cochlea, the development of endocochlear potentials and ion and fluid gradient between the endolymph and perilymph (Arya et al., 2015).

This study was designed to assess effects of vitiligo on audiological and vestibular function.

Sixty adult individuals involved; thirty vitiligo patients, (16 female patients and 14 males) and thirty matched persons in control group. The study was applied on vitiligo patient with age range, 14–57 years, which is matched with control group. There was no statistically significance between control and study groups as regards sex and age.

All vitiligo patients had elevated hearing threshold than control at almost frequencies in the range of 250–8000 Hz. The mean pure tone threshold showed statistically significant difference in right and left ears of patients with vitiligo. In addition, Speech recognition was statistically insignificant in vitiligo patients in comparison to the control group.

This result can be explained by the concept that melanocytes in the inner ear is thought to have crucial rule in normal stria vascularis development modulating the transduction of auditory stimuli through maintenance endocochlear potential preventing damage to the hair cells due to environmental ototoxic agents. The current results are in accordance with Mahdi et al. (2012) who stated that, the mean pure tone threshold was found to be statistically greater in the right and left ears of patients with vitiligo. Their findings strengthen the hypothesis that an alteration of inner ear pigment cells might favor the occurrence of hypoacusis. There are discrepancies in the literature about the specific influence of vitiligo on auditory threshold. Some authors state that vitiligo affects hearing

Table 4
Comparison of distortion otoacoustic emissions SNR in study and control groups.

F2 frequency Hz	Study (60 ears)			Control (60 ears)			P
	Median	Percentile 25	Percentile 75	Median	Percentile 25	Percentile 75	
750							
1.80	–3.35	8.45	9.50	7.90	11.60		<0.001*
984							
6.60	–1.05	10.55	9.70	8.10	13.50		<0.001*
1500	9.00	–0.30	15.80	11.05	8.70	14.60	0.01*
2016	10.15	5.10	16.95	10.75	8.70	16.80	0.16
3000	13.40	9.15	18.80	12.00	9.00	17.80	0.98
3984	11.45	7.10	18.70	11.55	9.00	18.70	0.4
6000	8.35	0.25	12.60	11.40	8.30	15.40	0.001*
7969	6.80	3.10	10.20	9.90	7.70	12.90	<0.001*

Test used: Mann Whitney test. *statistically significant. There were statistically significant differences at most frequencies between study and control groups.

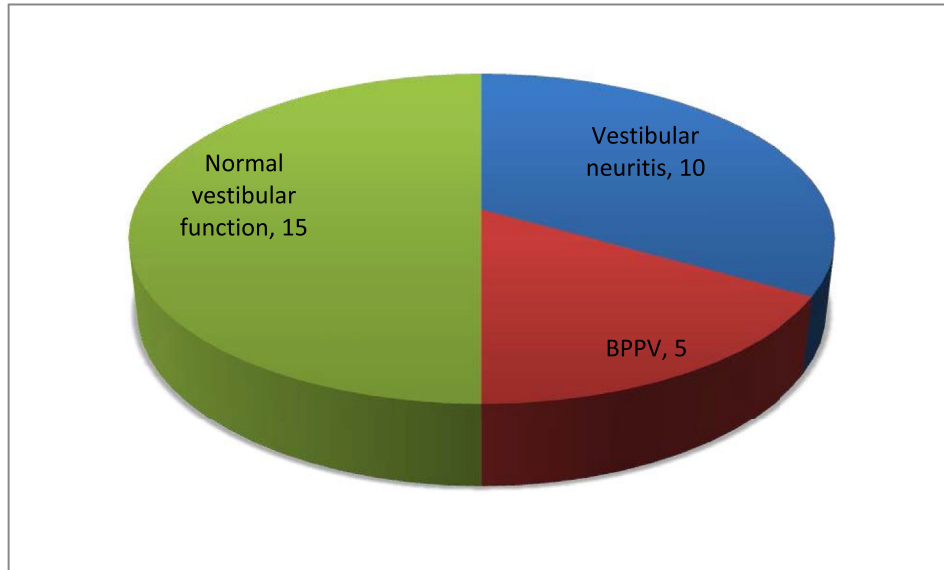


Fig. 2. Vestibular test results in study group. Fig. 2 showed 10 (33%) patients VN, 5 (17%) pcBPPV and 15 (50%) with normal vestibular function in vitiligo patients.

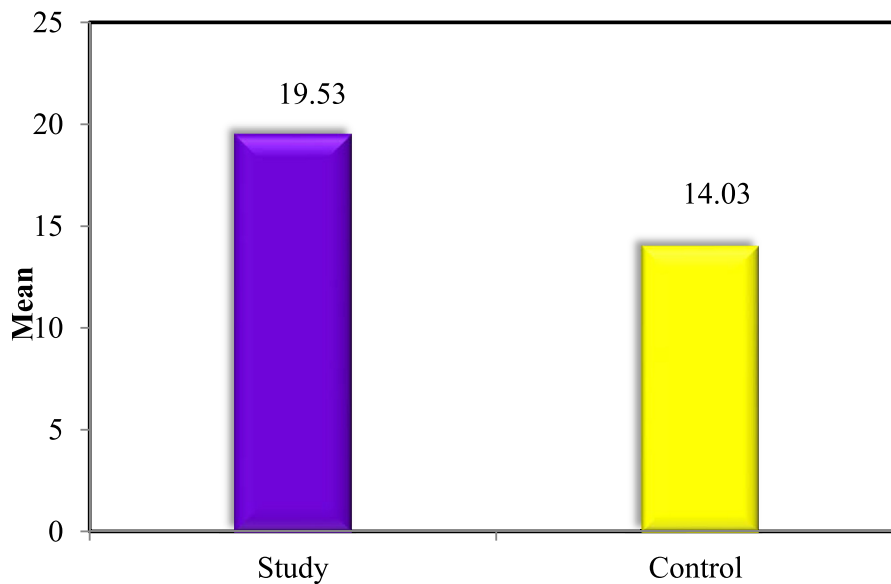


Fig. 3. Comparison of caloric test in study and control groups. Fig. 3 showed caloric weakness in study and control groups.

threshold (Angrisani et al., 2009). Whereas other authors against such affection (Escalante-Ugalde et al., 1991; Elsaied et al., 2008). This controversy may be attributed to difference in selection criteria among studies.

Ardiç et al. (1998) concluded that pure tone thresholds of the vitiligo patients were significantly poorer than the control group at 4,000, 6,000, 8000 and 10,000 Hz. Also, Aslan et al. (2010) stated that 59% of the ears of their vitiligo group had extended high frequency affection (10–12.5 kHz). While, Fleissig et al. (2013) studied pure tone audiometry (250–12000 Hz) and showed that hearing impairment in vitiligo patients was more frequent in (4000–8000 Hz). The extended high frequencies were not evaluated in this study to discuss these results. We plan to be evaluated in another study.

Otoacoustic emissions are low intensity acoustic signal emitted by healthy cochlea. Otoacoustic emission recording is a reliable method to check the functionality of the outer hair cells in cochlea (Arya et al., 2015).

The present study showed that patients with vitiligo had marked reduction in amplitude of DPOAEs as compared to the control group at most frequencies; also the results of TEOAEs amplitude were statistically reduced in vitiligo patients when compared to the control group at 1000, 1500 Hz. This result strengthens the hypothesis that vitiligo is a significant factor for altered cochlear function, and that melanin as assumed could have an important role in cell metabolism, facilitating substance exchange and maintain endolymph, perilymph and ionic balance. Similar results obtained by Arya et al. (2015)

who studied the audiological and electrophysiological changes in patients with vitiligo and to compare the finding with otologically and audiological normal controls. Also, these results were confirmed by [Shalaby et al. \(2006\)](#) studied the auditory function in vitiligo patients. They concluded that hypopigmentation disorder may lead to degeneration of outer hair cells beginning from basal turn of the cochlea, and that the inner hair cells remain structurally and functionally intact. [Gill and Salt \(1997\)](#) found that in pigmented animals the endolymph Ca^{+} tended to increase from base to apex of cochlea, while endocochlear systemically decreases towards the apex. In contrast, no significant Ca^{+} gradient was found in albinos and endocochlear potential decline was far less. Their results confirm the involvement of melanin in active transport of Ca^{+} into endolymph, which can be considered as another explanation for the melanin role in the inner ear.

[Angrisani et al. \(2009\)](#) stated that conventional audiometry with TOAE testing are reliable tests for early detection of cochlear dysfunction in vitiligo patients, which agree with results obtained in this study.

To our best knowledge no study discussed vestibular manifestations in vitiligo patient except [Mahdi et al. \(2016\)](#) who studied cervical VEMP on these patients. They stated that, abnormality was the statistically significant prolongation of p13 on the left ear and 33% of their patient had abnormal VEMP and attributed this prolongation in latency to disturbance of stimuli transduction through inferior vestibular nerve.

In concern to vestibular function, there was statistically significant difference in caloric results between study and control groups. The vestibular assessment revealed 10 patients had superior vestibular neuritis, 5 patients had posterior canal canalolithiasis benign paroxysmal positional vertigo and 15 patients had normal vestibular function. There was no significant correlation between auditory and vestibular functions.

[Mahdi et al. \(2016\)](#) explained that melanocytes take part in vestibular metabolism through an apparent relationship between the dark cells and adjacent blood vessels and in response to various stressful conditions, these cells have been reported to show increased melanin synthesis.

In the present study, vestibular assessment revealed 50% of patients had peripheral vestibular disorders. Although, exact pathogenesis of vestibular affection in vitiligo is unknown; one can assume that melanocytes could be responsible based on the following: 1. It arise from the neural crest; 2. are located in cochlea and in vestibular labyrinth; 3. are present in leptomeninges covering the vestibular nerve and vestibular ganglion; 4. are adherent to blood vessels wall.

There was no statistically correlation between type of vitiligo (mixed -acrofacial), percent of surface area involvement, duration of vitiligo and between the auditory or vestibular functions. Based on these results, one may concluded that, the mechanism might be related to individual susceptibility, residual number of melanocytes in the inner ear and nature of immunologic abnormalities in patients with vitiligo. Our results are in agreement with [Mahdi et al. \(2016\)](#). On the other hand, the result of the study disagree with [Arya et al. \(2015\)](#) who found statistical difference in average

amplitude of TOAEs in two groups (localized and generalized) in left ear at 2, 3 & 4 KHz. This may be attributed to difference in selected groups in their study.

In conclusion, the results in this study showed that 50% of vitiligo patients suffered from peripheral vestibular disorders in addition to auditory affection. Vitiligo patients require routine monitoring for auditory and vestibular functions for early identification and monitoring of changes as the disease progress. Further studies are needed to assess vestibular functions in larger group and discover the possible mechanisms of vestibular affection.

Conflict of interest

All the authors declare that they have not any conflict of interest.

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