The Vestibulospinal Reflex in Vitiligo Patients

Original Article

Mariam Magdy Medhat[a], Abeir Osman Dabbous[b], Marwa Salah El-Din El-Mesidy[c]

Department of [a,b]Otolaryngology, [c]Dermatology, Kasr-Al-Ainy Faculty of Medicine, Cairo University, Egypt.

ABSTRACT

Background: The otic melanocytes are located in the stria vascularis, the modiolus of the cochlea, the semi-circular ducts, and the vestibular organs, which are structures involved in vestibular and cochlear function, could be lost in vitiligo. The aim of this study was to assess the saculo-colic and vestibulospinal reflexes in patients with different severity and activity of vitiligo.

Patients and Methods: This study included 50 adult vitiligo patients and 25 healthy adults as controls. They were subjected to cervical vestibular evoked myogenic potentials (cVEMP) and sensory organization test (SOT) of the computerized dynamic posturography (CDP).

Results: There was a statistically significant difference between the cases and controls regarding latency and amplitude of the VEMP in the right ear and N23 latency and amplitude in the left ear and interaural amplitude difference ratio (IAADR). Although there was no statistically significant difference between the cases and controls regarding CDP parameters, sensory analyses ratios or the composite score, individual analyses of data showed abnormal findings in SOT conditions and the sensory analysis of the patients. There was no statistically significant correlation between either age of patients, disease duration, VASI, VIDA and both VEMP and CDP parameters.

Conclusion: Vitiligo can cause vestibular dysfunction anywhere in the vestibulospinal reflex pathway, and the vestibular dysfunction is not related to the severity of vitiligo or disease duration or patient's age. We recommend using both cVEMP and SOT test for early detection of vestibulospinal reflex affection in vitiligo patients.

Key Words: (cVEMP), computerized dynamic posturography, (SOT), vestibulospinal reflex, vitiligo.

Received: 18 November 2022, **Accepted:** 6 January 2023

Corresponding Author: Mariam Magdy Medhat, MD, Department of Otolaryngology, Kasr-Al-Ainy Faculty of Medicine, Cairo University, Egypt. **Tel.:** 01061237972, **E-mail**: mariammedhat83@gmail.com

ISSN: 2090-0740, 2024

INTRODUCTION

Vitiligo is a frequent acquired depigmentation condition, which affects 1% of the general population, is defined by a gradual loss of functioning melanocytes in the epidermis and hair follicles[1]. As a result of migration during embryonic development, melanocytes can be found not only in the interfollicular epidermis and hair follicles but also in the eyes, ears, brain, and leptomeninges. The stria vascularis, the modiolus of the cochlea, the semi-circular ducts, and the vestibular organs-structures involved in vestibular and cochlear function-are where the otic melanocytes are situated and may be lost in vitiligo[2]. The function stria vascularis, the cochlea, the generation of endo-cochlear potentials, and the ion and fluid gradient between the endolymph and the perilymph all depend on the presence of melanocytes in the inner ear[3]. Melanocytes are also found in the leptomeninges, especially in the areas surrounding the ventral and lateral sides of the spinal cord, the medulla oblongata, the locus coeruleus, and the subtancia nigra[4,5]. Neuromelanin chelates redox-active metals and toxic metals, binds neurotoxins in vivo, and prevents their capacity to cause neurodegeneration[5]. Parkinson's disease is linked to pigment loss in the subtancia nigra[6]. Vitiligo patients have not been directly shown to have melanocyte degeneration in the inner ear or brainstem, according to reports[7-12].

Wright and Lee[14] demonstrated in their animal study that melanin lines the posterior-superior section of the saccule's membranous wall, and that these pigmented cells actively regulate the endolymph composition, which is a crucial factor in modulating vestibular inputs. One of the most used clinical tests for otolith function is the vestibular-evoked myogenic potential (VEMP) test. The sound-evoked cervical vestibular-evoked myogenic potential (cVEMP), which measures saccular function, is arguably the most extensively used test[15].

 DOI: 10.21608/ejentas.2023.175178.1578

The only test that can evaluate the overall function of balance by isolating the relative contributions of visual, somatosensory, and vestibular feedback is the Sensory Organization Test (SOT). It is not a specific pathology test[16,17]. It employs both visual and proprioceptive cues to trigger postural responses to changes in the centre of gravity. The computer examines compensatory postural responses and body sway[18].

Rationale:

So, affection of otic melanin could affect the saccule and thus, the sacculo-colic reflex resulting in cVEMP abnormalities. Many studies evaluated the auditory function in patients with vitiligo, but to the best of our knowledge, there is paucity of studies on vestibular evaluation in vitiligo patients especially using the sensory organization test of dynamic posturography.

Aim:

The aim of this work was to assess the sacculo-colic and vestibulospinal reflexes in patients with different severity and activity of vitiligo.

PATIENTS AND METHODS:

The study was carried out during the period between October 2016 and June 2017 at the Audiology Unit outpatient clinic, Otorhinolaryngology department, and the dermatology department in Kasr Al-Ainy hospital, Cairo University. The study was approved by the Research Ethical Committee and Otolaryngology department council of Faculty of Medicine, Cairo University. An informed consent was signed by all subjects for participation in the study.

Participants were divided into two groups:

• **A study group (cases)**, which included 50 adults suffering from vitiligo, aged 18–45 years. They were recruited from those attending the dermatology outpatient clinic.

• **A control group**, which included 25 healthy adults not complaining of vitiligo aged 18–45 years, well matched to the cases with respect to age and sex. Controls were recruited from those performing the preoccupation assessment at the audiology clinic.

- Exclusion criteria:

Middle ear diseases, neurological diseases, muscular disorders, Previous ear surgery, or any disease or condition affecting hearing or balance.

Patients in this study will be subjected to Vitiligo diagnosis and scoring:

I. Clinical diagnosis of Vitiligo by the dermatologist.

II. Scoring of severity and activity by the dermatologist.

• Vitiligo area scoring index (VASI):

Quantitative parametric score calculated using a formula to measure disease severity[19]. The percentage of vitiligo involvement is calculated in terms of hand units. One hand unit is approximately equivalent to 1% of the total body surface area. The degree of pigmentation is estimated to the nearest of one of the following percentages: 100% - complete depigmentation, No. pigment is present; 90% - specks of pigment present; 75% - depigmented area exceeds the pigmented area; 50% - pigmented and depigmented areas are equal; 25% - pigmented area exceeds depigmented area; and 10% - only specks of depigmentation present. The VASI for each body region is determined by the product of the area of vitiligo in hand units and the extent of depigmentation within each hand unit measured patch. Total body VASI = S All body sites (Hand Units) x (Residual depigmentation). The VASI is then derived by multiplying the values assessed for the vitiligo involvement by the percentage of affected skin for each body site and summing the values of all body sites together: VASI= $\sum$ [HAND UNITS] × [RESIDUAL DEPIGMENTATION][20,21].

• Vitiligo disease activity score (VIDA):

Six-point scale to determine the activity of vitiligo[22]. VIDA score is a six-point scale for evaluating vitiligo activity. Individuals own opinion is the base in VIDA score. VIDA score based on patients' opinion divided in 6 stages: Grading is as follows. VIDA Score: +4: Activity of 6 weeks or less period; +3: Activity of 6 weeks to 3 months; +2: Activity of 3 to 6 months; +1: Activity of 6 to12 months; 0: Stable at least for 1 year and; −1: Stable at least for 1 year with spontaneous re-pigmentation[20].

Each participant included in this study will be subjected to:

1. Detailed history taking.

2. Otologic Examination including otoscopy and tuning fork tests.

3. Basic Audiological evaluation included Pure tone audiometry (PTA): and Tympanometry.

4. Cervical Vestibular Evoked Myogenic Potentials (cVEMP): Using Neuro – Audio. Net, Neurosoft Ltd, Russia. Ivanovo. First, the skin was cleansed before application of

the electrodes to ensure that the impedance is less than 5 k Ω. The active (positive) electrode (first right, then left) was placed on the middle of the sternocleidomastoid muscle, the inverting (negative) on the upper sternum (suprasternal notch), and the ground electrode on the forehead. Two repeatable recordings were obtained for each condition. Patients were given 60 s to relax between each recording to avoid fatigue. They were asked to flex the neck against resistance. The stimulus type used was 500 Hz tone burst, of a rarefaction polarity, 1 ms rise/fall time and 2 ms plateau, Blackman ramp, and an intensity of 100 dB nHL band pass filtered 30 to 2000 Hz presented through EAR-3A10Ω insert phones. The stimulus rate was 5/s. At least 100 sweeps were averaged. Two trials were obtained to ensure reproducibility. VEMP responses were judged as either present or absent according to the presence or the absence of a P13-N23 biphasic response. Parameters analyzed in the preserved VEMP responses were wave latencies and amplitude, P13 and N23 latencies (in 'ms' is the time from the onset of the stimulus to the peak), and the peak-to-peak amplitude (in μV) of the first positive-negative peak (P13-N23). The instrument calculated the rectified amplitude, and corrected asymmetry amplitude Ratio or the inter-aural amplitude difference ratio (IAAD) of is the P13-N23 peak to peak amplitude difference between the 2 ears divided by the total amplitude of both ears (i.e amplitude asymmetry): IAAD = Rt – Lt / Rt + Lt.. An IAD > 0.36 is considered abnormal. P13 and N 23 latencies were considered delayed when the latency was more than mean +2 SD of latency of the control group (Rt P13: 16.48 ms; Rt N 23: 25.98ms; Lt P13: 16.8 ms; Lt N23: 25.53).

5. Sensory Organization test (SOT) of the Computerized dynamic posturography (CDP) using the Neurocom Smart balance master version 4.01 (Neurocom International Inc., Clackamas, Oregon, USA). Each test comprises three trials for each of the six conditions: 1) eyes open, platform, surface and visual surround steady. 2) eyes closed, platform, surface and visual surround steady. 3) platform steady, visual surround rotated, eyes open. 4) visual surround steady, eyes open and platform rotated. 5) visual surround steady, eyes closed, and platform rotated. 6) eyes open, platform and visual surround rotated. For each condition, an equilibrium score (ES1-6) is calculated that quantifies the center of gravity sway or postural stability under each of the three trials of the six sensory conditions. A score of 100 represents perfect balance (No. sway) and a score of 0 represents a potential fall (sway exceeds limits of stability). The composite score is the mean overall score. Composite scores were compared to normal values, matched for age and weight, provided by the software. The sensory analysis shows the relative contribution of the different sensory afferents and is calculated from the Equilibrium scores obtained under the different test conditions: Somatosensory ratio (SOM) [condition 2 score / condition 1 score], is a measure of the patient's ability to use somatosensory information for maintenance of balance. Visual ratio (VIS) [condition 4 score / condition 1 score], is a measure of the patient's ability to use visual information for maintenance of balance. Vestibular ratio (VEST) [condition 5 score / condition 1 score], is a measure of the patient's ability to use vestibular information for maintenance of balance. Preference ratio (PREF) [condition 2 + condition 5 score / condition 3 + condition 6 score], is a measure of the patient's reliance of visual information, even when that information is incorrect[23,24].

Statistical Analysis:

Data was coded and entered using the statistical package SPSS (Statistical Package for the Social Sciences) version 24. Data was summarized using mean, standard deviation, median, interquartile range, minimum and maximum in quantitative data; and using frequency (count) and relative frequency (percentage) for categorical data. Comparisons between 2 groups were done using unpaired t test. Comparisons between more than 2 groups were done using ANOVA test and using Kruskal Wallis Test for non-parametric data. For comparing categorical data, Chi square ($\chi 2$) test was performed. Exact test was used instead when the expected frequency is less than 5. Correlations between quantitative variables were done using Pearson correlation coefficient. *P-values* less than 0.05 were consider as statistically significant.

RESULTS:

This study included 75 subjects with a mean age of 29.71 ± (8.56) ranging from 18-45 years, 24 Males and 51 Females: 50 Cases and 25 Controls. There was no statistically significant difference between cases and controls regarding age or gender (Table 1). The mean duration of vitiligo in the cases: 5.65 ± 5.52 years, ranging from 0.04-30 years. The mean VASI score in the cases: = 6.26 ±10.02.

Table 1: Comparison between cases and controls regarding age and gender.

	Cases (n=50)	Control (n=25)	*P value*
Age Median (IQR)	30 (22-36)	28 (22-38)	*0.9*
Gender Male/Female	15/35	9/16	*0.6*

cVEMP Results (Figure 1):

VEMPs were present in 47/50 (94%) of cases. VEMPs were lost bilaterally in 3 patients (6%). VEMPs were lost unilaterally in the right ear only of one patient. IAAD ratio was abnormal i.e. amplitude asymmetry in 6 patients (12%). Three of them had decreased amplitude in the left ear. Two of them had decreased amplitude in the right ear. VEMP was lost in the right ear only of one patient (100% asymmetry). Latency was delayed in 18 patients (36%). P13 and N23 of the right ear was delayed in 11 (22%), 7 (14%) patients respectively. The left ear response was delayed in 7 (14%), 6 (12%). Combined amplitude asymmetry and delayed latency were found in 2 patients (4%) (Figure 1). There was a statistically significant difference between the cases and controls regarding latency and amplitude of the VEMP in the right ear and N23 latency and amplitude in the left ear and IAADR (Asymmetry %) (Table 2).

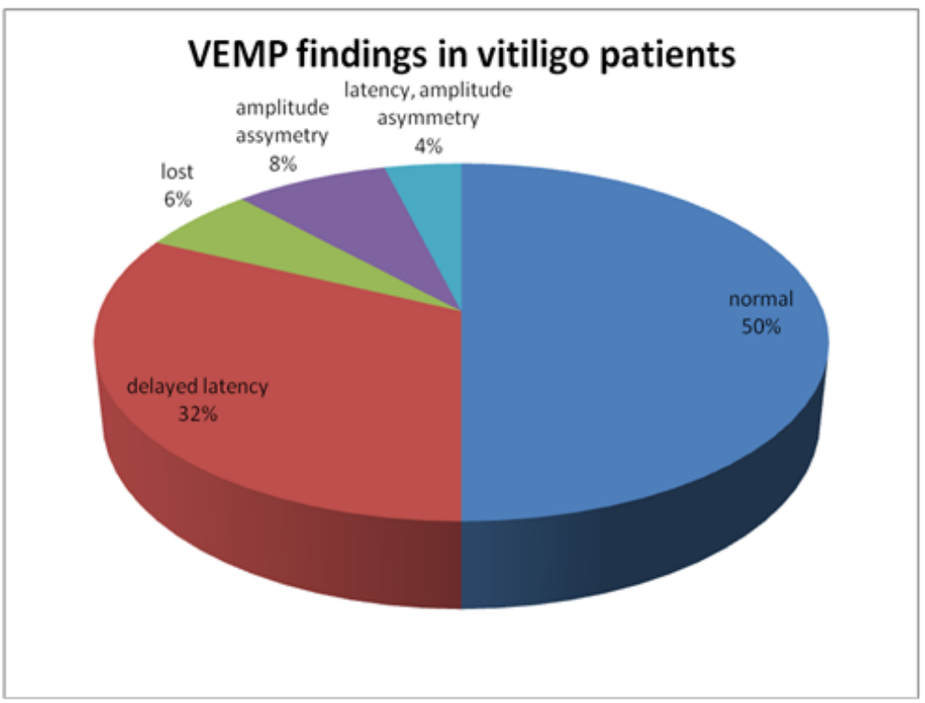

Fig. 1: cVEMP Results in vitiligo patients.

Table 2: Comparison between cases and controls regarding VEMP parameters.

VEMP	Cases		Controls (n=25)		*t value*	*P value*
	mean	SD	mean	SD		
Right (n=46)						
P13	15.22	1.82	14.18	1.15	2.575	*0.012*
N23	23.57	2.23	22.18	1.90	2.649	*0.010*
P13-N23 Amplitude	0.82	0.34	1.03	0.41	-2.317	*0.023*
Left (n=47)						
P13	15.01	1.81	14.36	1.22	1.599	*0.114*
N23	23.62	2.16	22.27	1.63	2.742	*0.008*
P13-N23 Amplitude	0.87	0.33	1.08	0.44	-2.253	*0.027*
Asymmetry (IAADR)	0.15	0.14	0.06	0.04	3.014	*0.004*

SOT of CDP:

Although test results revealed abnormalities in 10 patients (20%), composite score was abnormal in 5 patients (10%). Sensory analysis showed abnormal sensory ratios as following; visual ratio in 5 patients (10%), vestibular ratio in 4 patients (8%), Preference ratio in 4 patients (8%). Visual ratio was the only abnormal ratio in 3 patients (6%). While, the vestibular ratio was the only abnormal ratio in 2 patients (4%). Three patients (6%) had low visual preference ratio. One patient (2%) had Combined low visual and vestibular ratios. Combined visual, vestibular and preference ratios abnormalities

was found in 1 patient (2%) (Figure 2). SOT conditions showed abnormal results as the following; Condition 4 in 6 patients (12%), Condition 5 in 5 patients (10%), and Condition 6 in 7 patients (14%). Condition 4 was the only abnormal condition in 3 patients (6%). Condition 6 was the only abnormal condition in 2 patients (4%). Combined conditions 5 and 6 abnormalities were found in 2 patients (4%). Combined conditions 4, 5 and 6 abnormalities were found in 3 patients (6%). There was no statistically significant difference between the cases and controls regarding CDP parameters sensory analyses ratios or the composite score (Table 3).

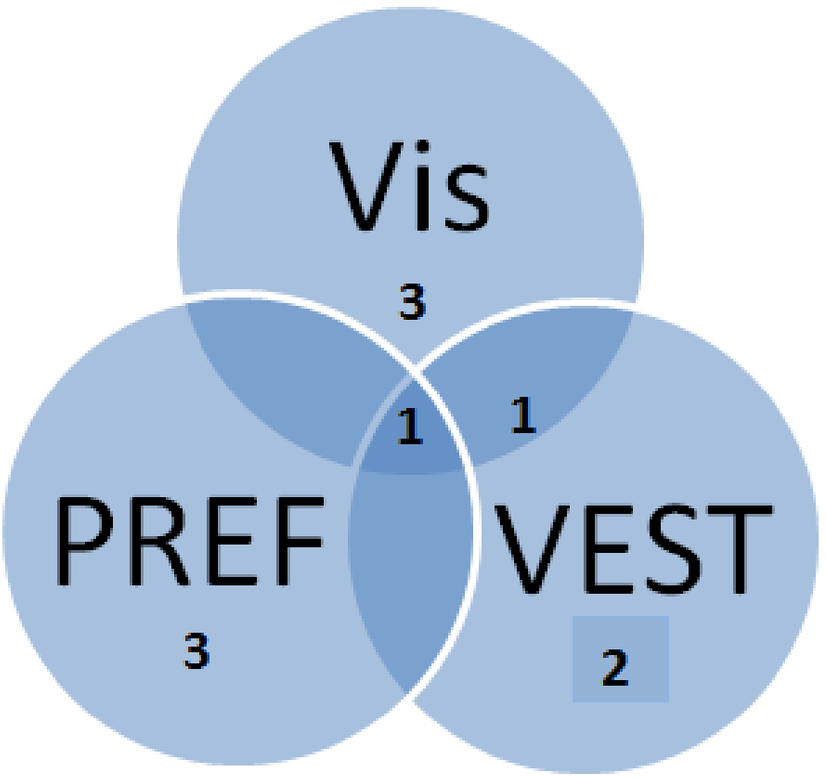

Fig. 2: Sensory analysis of SOT findings in vitiligo patients

Table 3: Comparison between cases and controls regarding CDP parameters.

VEMP	Cases (n=50)		Controls (n=25)		t value	*P value*
	Mean	SD	mean	SD		
EQ score C1	93.04	1.86	94.00	2.12	-2.009	*0.048*
EQ score C2	90.80	2.91	91.40	2.86	-0.847	*0.400*
EQ score C3	90.86	2.81	90.72	2.42	0.213	*0.832*
EQ score C4	78.32	8.98	81.68	5.79	-1.700	*0.093*
EQ score C5	62.92	9.12	67.04	6.91	-1.988	*0.051*
EQ score C6	59.44	17.46	63.44	8.67	-1.078	*0.285*
Composite score	75.14	6.30	77.68	3.73	-1.856	*0.067*
Somatosensory ratio	0.98	0.03	0.97	0.02	0.510	*0.611*
Visual ratio	0.84	0.09	0.87	0.06	-1.687	*0.096*
Vestibular ratio	0.68	0.10	0.71	0.07	-1.781	*0.079*
Visual Preference ratio	0.98	0.10	0.98	0.06	-0.055	*0.956*

Correlation between cVEMP parameters with age, vitiligo duration and severity:

There was no statistically significant correlation between either age of the patients, disease duration, VASI and VEMP parameters (Table 4).

Table 4: Correlation between age, duration and VASI with VEMP parameters.

		AGE	DURATION	VASI
Right (n-=46)				
P13	R	-0.215	-0.107	0.266
	P	0.151	0.477	0.074
N23	R	-0.100	-0.035	0.113
	P	0.508	0.818	0.455
P1-N23 Amplitude	R	-0.073	0.087	-0.020
	P	0.628	0.565	0.897
Left (n-=46)				
P13	R	-0.010	0.226	0.156
	P	0.947	0.126	0.295
N23	R	-0.179	-0.058	-0.118
	P	0.227	0.698	0.429
P1-N23 Amplitude	R	-0.169	0.130	0.054
	P	0.256	0.385	0.719
Asymmetry (IAADR)	R	-0.038	0.125	0.259
	P	0.804	0.406	0.083

Correlation between CDP parameters with age, vitiligo duration and severity:

There was no statistically significant correlation between either age of patients, disease duration, VASI and CDP parameters: equilibrium (EQ) scores in the 6 SOT conditions or the sensory analyses ratios or the composite score (Table 5).

Table 5: Correlation between age, duration and VASI with CDP parameters.

		AGE	DURATION	VASI
EQC1 score	R	-0.143	-0.140	-0.189
	P	0.323	0.332	0.188
EQC2 score	R	-0.134	0.055	-0.030
	P	0.354	0.707	0.835
EQC3 score	R	-0.022	0.073	-0.027
	P	0.882	0.614	0.852
EQ4 score	R	-0.035	-0.275	-0.194
	P	0.807	0.053	0.178
EQ5 score	R	-0.006	0.001	-0.145
	P	0.965	0.995	0.315
EQC6 score	R	-0.080	0.048	-0.135
	P	0.580	0.740	0.351
Composite score	R	-0.073	-0.041	-0.195
	P	0.613	0.778	0.176
Somatosensory ratio	R	-0.096	0.112	0.084
	P	0.508	0.438	0.564
Visual ratio	R	-0.014	-0.275	-0.183
	P	0.922	0.053	0.204
Vestibular ratio	R	0.018	0.015	-0.121
	P	0.904	0.919	0.404
Preference ratio	R	-0.079	0.082	-0.085
	P	0.584	0.571	0.557

Comparison between cVEMPs Asymmetry and Grades of vitiligo activity:

There were no statistically significant differences among the different Grades of vitiligo activity in the cases, assessed by VIDA scale, regarding the distribution of the VEMP IAAD ratio abnormality (Amplitude asymmetry) (Table 6).

Comparison between SOT Abnormalities and Grades of vitiligo activity:

There were no statistically significant differences among the different Grades of vitiligo activity in the cases, assessed by VIDA scale, regarding the distribution of the CDP composite score abnormality (Table 7).

Table 6: Comparison between cVEMPs Asymmetry and Grades of vitiligo activity

			VIDA						Total
			-1	0	1	2	3	4	
VEMP IAAD ratio	Abnormal (Asymmetry)	No.	0	1	0	0	2	3	6
		%	0.0%	33.3%	0.0%	0.0%	20.0%	12.5%	12.8%
	Normal	No.	2	2	1	7	8	21	41
		%	100.0%	66.7%	100.0%	100.0%	80.0%	87.5%	87.2%
	Total	No.	2	3	1	7	10	24	47
		%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

X^2= 3.074
p value = 0.689

Table 7: Comparison between composite score Abnormalities and Grades of vitiligo activity

			VIDA						Total
			-1	0	1	2	3	4	
Composite score	Abnormal	No.	1	0	0	0	2	2	5
		%	50.0%	0.0%	0.0%	0.0%	20.0%	8.3%	10.6%
	Normal	No.	1	3	1	7	8	22	42
		%	50.0%	100.0%	100.0%	100.0%	80.0%	91.7%	89.4%
	Total	No.	2	3	1	7	10	24	47
		100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

X^2= 5.625
p value = 0.380

Abnormal cVEMPs vs abnormal SOT findings:

Twenty-eight patients (56%) showed abnormal findings either in cVEMPs or SOT. Twenty-five patients of them (89.3%) had cVEMPs abnormalities. Ten patients (35.71%) had SOT abnormalities. Seven patients (25%) showed combined cVEMPs and SOT abnormalities. These seven patients: 5 had delayed latency, one showed asymmetry, and one with unilateral lost cVEMPs response.

Four of the six patients (66.7%) with VEMP amplitude asymmetry, had normal equilibrium scores in conditions 4, 5 and 6, composite score and normal SA analyses, and this was not statistically significant (data not shown). The patient with unilaterally lost cVEMPs (100% VEMP amplitude asymmetry) showed abnormal SOT results. i.e., only 2/6 (33.3%) with VEMP amplitude asymmetry, showed abnormal SOT results. Those with bilaterally lost VEMP had normal equilibrium scores in all SOT conditions and normal SA analyses. Five patients of those with delayed VEMP latencies 5/18 (27.8%) showed abnormal SOT findings.

DISCUSSION

Vitiligo is more common in females than males. Shoenfeld *et al*.[25] suggested that hormones could be the cause of this predominance as estrogens stimulate autoimmune conditions. Another cause is the cosmetic concern of females. In the current study, the majority of patients with vitiligo were females 35/ 50 (70%). Similarly, Abd El Mageed *et al*.[26] results showed

higher prevalence of female gender in cases with vitiligo (60.3%). Also, Koura *et al*.[27] reported that 24/30 (80%) of the patients were females.

cVEMP:

In the current study, cVEMPs were lost bilaterally in 3/50 (6%) of patients, unilaterally in the right in 1/50 (2%) of patients. Similarly, Abd El Mageed *et al*.[26] found that cVEMPs were absent bilaterally in 2 patients (3.2%). While 4 patients (6.3%) showed unilateral absent waves. Manno *et al*.[28] found that 1/35 (3%) had no cVEMPs response. In comparison, Koura *et al*.[27] found that cVEMP was absent bilaterally in 8 of 30 (26.6%) and absent unilaterally in 6 of 30 (20%) in the left ear. Mahdi *et al*.[29] cVEMPs findings revealed an absent response in the left ear of 1(4.76%) patient.

In the current study, P13 and N23 latencies of cVEMPs were delayed in 18 (36%) patients. Similarly, Abd El Mageed *et al*.[26] reported that 27 (42.9%) patients had delayed latency. In contrast, Manno *et al*.[28] cVEMPs findings revealed abnormal latency of P13 in 5 patients: One of them with a unilateral absent response. Latency of n23 was affected in only 2 patients, 1 with an absent response.

The current study showed a statistically significant delayed cVEMPs latency in the cases compared to the controls regarding cVEMPs latency in the right ear and N23 latency in the left ear. In accordance with our results, Mahdi *et al*.[29] findings showed a statistically significant prolongation of p13 on the left ears. Also, Koura *et al*.[27] P13 and N23 mean latencies were statistically significantly delayed in patients with vitiligo compared with controls. Abd El Mageed *et al*.[26] reported that latency of P and N waves showed a significant difference between cases and controls.

In the current study, amplitude asymmetry ratio was abnormal in 6/50 (12%) of patients: (4% had decreased amplitude in the right ear and 6% had decreased amplitude in the left ear and 2% had 100 % asymmetry in the right ear). There was a statistically significant difference between the cases and controls regarding the corrected cVEMP amplitude in both ears and the corrected IAAD (asymmetry %). In contrast, Mahdi *et al*.[29] did not find any amplitude abnormalities of VEMP. One patient (4.76%) had abnormal amplitude ratio; however, it was not statistically meaningful. Koura *et al*.[27] found that IAAD ratio was abnormal (prolonged) in 1 and normal in 9 of patients. In 46.6%, IAAD could not be calculated. But they did not find statistically significant difference regarding the mean P13–N23 amplitudes between controls and patients with vitiligo. Abd El Mageed *et al*.[26] reported that the amplitude measured in both ears and amplitude ratio showed no significant difference between the two groups.

Mahdi *et al*.[29] explained that due to the connection between the dark cells and the nearby blood vessels, melanocytes have a role in vestibular metabolism. These cells have also been observed to produce more melanin in response to certain stressful situations. Wright and Lee,[14] discovered in their animal study that melanocytes line the posterior superior region of the saccule's membranous wall, and that these cells are highly effective at regulating the endolymph composition, which is in charge of modulating vestibular impulses. It makes sense that vitiligo could be linked to the breakdown of the epithelium and abnormalities of the inner ear because skin pigmentation is thought to be an indication of melanocyte function (which contains melanocytes)[30]. Delays in latencies may result from problems with inputs being transmitted through the inferior vestibular nerve[29]. Another explanation for the function of melanin in the inner ear can be found in Gill and Salt's[31] confirmation that melanin participates in the active transport of calcium into the endolymph.

According to Colucci *et al*.[32] vitiligo is an autoimmune dermatosis and is a complex illness that involves autoimmunity. A case of vitiligo with classic Meniere's disease was described by Gwak *et al*.[2] in a 15-year-old male patient who had depigmented maculo-patches on his left pre-auricular, forehead, and lower cheek areas. Although the potential that the two diseases developed accidentally cannot be ruled out, they claimed that the two diseases may share autoimmunity as a common mechanism of pathogeneses. Both disorders are bilateral diseases that can first manifest unilaterally. Melanocytes are crucial to the inner ear's fluid and ion hemostasis. It is anticipated that vitiligo may have an impact on VEMP amplitude, similar to the typical findings with Meniere's illness[26].

Only 2 patients (4%) showed combined amplitude asymmetry and delayed latency. The current study findings are in consistence with the other studies regarding cVEMP latency. However, regarding cVEMP amplitude, the current study is the only study that showed a statistically significant difference between the cases and controls regarding amplitude of the VEMP in both ears and IAADR (Asymmetry %). This could be attributed to the use rectified VEMP amplitude in this study and monitoring of the sternocleidomastoid muscle (SCM) contraction throughout the recording time to increase the accuracy and decrease the variability of cVEMPs amplitude measurements. The fact that the SCM EMG is highly variable and can create false-positive or false

negative cVEMP findings is the primary motivation for incorporating amplitude normalization techniques into the data analysis[33]. Mahdi *et al*.[29] stated that the failure to evidence any amplitude abnormalities of VEMP in their study might be due to marked inter-individual variability of amplitude in normal.

SOT of CDP:

By systematically altering the three sensory channels during standing balance, SOT measures deficiencies in the integration of visual, vestibular, and somatosensory inputs in maintaining balance[34]. To the best of our knowledge, there is no studies explore the SOT findings in vitiligo patients. The neural crest gives rise to melanocytes, which are found in the skin's epidermis, hair bulbs, uveal tract, retinal pigment epithelium, inner ear, and leptomeninges[3]. Visual and vestibular affection are the results of their affection.

Although there was no statistically significant difference between the cases and controls regarding CDP parameters, sensory analyses ratios or the composite score, individual analyses of data showed that there were abnormal findings in SOT conditions and the sensory analysis of the patients. SOT abnormalities were found in 10 patients (20%). However, composite score was abnormal in only 5 patients (10%). Sensory analysis showed abnormal visual ratio in 5 patients (10%), abnormal vestibular ratio in 4 patients (8%), abnormal Preference ratio in 4 patients (8%). Visual ratio was the only abnormal ratio in 3 patients (6%). Vestibular ratio was the only abnormal ratio in 2 patients (4%). Three patients (6%) had low visual preference ratio. One patient (2%) had Combined low visual and vestibular ratios. Combined visual, vestibular and preference ratios abnormalities in 1 patient (2%).

All of the patients showed within normal results in conditions 1, 2, and 3. Condition 4 was abnormal in 6 patients (12%). Condition 5 was abnormal in 5 patients (10%). Condition 6 was abnormal in 7 patients (14%). Condition 4 was the only abnormal condition in 3 patients (6%). Condition 6 was the only abnormal condition in 2 patients (4%). Combined conditions 5 and 6 abnormalities were found in 2 patients (2%). Combined conditions 4, 5 and 6 abnormalities were found in 3 patients (6%). Vestibular ratio is abnormal in only 4 patients (8%) in the present study. This could be due to the ability of the vestibular system to compensate for deficit. According to Manno *et al*.[28] their findings demonstrated that hearing loss predominated over vestibular deficiency. The vestibular system's capacity to carry out a central compensation that enables patients to be asymptomatic even when there is a hidden vestibular loss forms the basis of a theory.

Correlation between VEMP and SOT parameters and abnormalities with Severity and activity of vitiligo:

In the current study, there was no statistically significant correlation between either age of the patients, disease duration, VASI with VEMP parameters (Table 4). There were no statistically significant differences among the different Grades of vitiligo activity in the cases, assessed by VIDA scale, regarding the distribution of the VEMP amplitude asymmetry or the other measured VEMP parameters. Segmental and non-segmental vitiligo did not significantly affect VEMP parameters according to Abd El Mageed *et al*.[26] analysis. Additionally, there was a substantial difference between cVEMP and disease duration. According to Dawoud *et al*.[35] there was no statistically significant relationship between the auditory or vestibular functions and the type of vitiligo (mixed-acrofacial), percentage of surface area involved, or duration of vitiligo. These findings led researchers to the hypothesis that the process may be connected to individual vulnerability, the presence of remaining melanocytes in the inner ear, and the type of immunologic abnormalities seen in vitiligo patients. According to Koura *et al*.[27] there was no statistically significant relationship between age, disease activity, vitiligo severity, and cVEMP results. However, a statistically significant negative correlation between disease duration and latency of N 23 of cVEMP was reported.

In the current study, there was no statistically significant correlation between either age of patients, disease duration, VASI with CDP parameters sensory analyses ratios or the composite score (Table 5). There were no statistically significant differences among the different Grades of vitiligo activity in the cases, assessed by VIDA scale, regarding the distribution of the CDP composite score abnormality or the other measured CDP parameters.

Thus, results of the current study suggests that vestibular affection is not related to the severity of vitiligo. It seems that once the disease process occurs, there is an abnormality in melanocytes functions. The presence of vestibular abnormalities depends on the extent of inner ear damage which is not related to extent of skin affection.

Abnormal cVEMPs vs abnormal SOT findings:

Only 33.3% with VEMP amplitude asymmetry, showed abnormal SOT results. And only 27.8% with delayed VEMP latencies, showed abnormal

SOT findings. There were no statistically significant differences regarding the VEMP IAAD abnormality (asymmetry) distribution and the CDP composite score abnormality or sensory analyses abnormalities.

CONCLUSION

Vitiligo can cause vestibular dysfunction anywhere in the vestibulospinal reflex pathway, and the vestibular dysfunction is not related to the severity of vitiligo or disease duration or patient's age. The effect could be shown in either abnormal VEMP or SOT test results: either VEMP only without affection of SOT or to lesser extent this affects SOT without affecting VEMP. So, we recommend using both tests for early detection of vestibulospinal reflex pathway affection in vitiligo patients.

CONFLICT OF INTEREST

There are no conflicts of interest.

REFERENCES

1. Kovacs SO. Vitiligo. J Am Acad Dermatol. 1998; 38: 647-666.

2. Gwak MJ, Shin EJ, Shin MK, Jung KH, Lee MH. A Case of Vitiligo Associated with Meniere's Disease. Pigmentary Disorders. 2015; 2(215): 2376-0427.

3. Aydogan K, Turan OF, Onart S, Karadogan SK, Tunali S. Audiological abnormalities in patients with vitiligo. Clin Exp Dermatol. 2006; 31(1): 110-113.

4. Goldgeier MH, Klein LE, Klein-Angerer S, Moellmann G, Nordlund JJ. The distribution of melanocytes in the leptomeninges of the human brain. J invest dermatol. 1984; 82(3): 235-238.

5. Zecca L, Shima T, Stroppolo A, Goj C, Battiston GA, Gerbasi R, Sarna T, Swartz HM. Interaction of neuromelanin and iron in substantia nigra and other areas of human brain. Neurosci. 1996; 73(2): 407-415.

6. Fedorow H, Tribl F, Halliday G, Gerlach M, Riederer P, Double KL. Neuromelanin in human dopamine neurons: comparison with peripheral melanins and relevance to Parkinson's disease. Prog neurobiol. 2005; 75(2): 109-124.

7. Tosti A, Bardazzi F, Tosti G, Monti L. Audiologic abnormalities in cases of vitiligo. J Am Acad Dermatol. 1987; 17(2): 230-233.

8. Steel KP, Barkway CHRIS. Another role for melanocytes: their importance for normal stria vascularis development in the mammalian inner ear. Development. 1989; 107(3): 453-463.

9. Nikiforidis GC, Tsambaos DG, Karamitsos DS, Koutsojannis CC, Georgiou SV. Abnormalities of the auditory brainstem response in vitiligo. Scand Audiol. 1993; 22(2): 97-100.

10. Ardiç FN, Aktan Ş, Kara CO, Şanli B. (1998). High-frequency hearing and reflex latency in patients with pigment disorder. Am j otolaryngol. 1998; 19(6): 365-369.

11. Özüer MZ, Şahiner T, Aktan Ş, Şanli B, Bayramoğlu İ . Auditory evoked potentials in vitiligo patients. Scand Audiol. 1998; 27(4): 255-258.

12. Tachibana M. Sound needs sound melanocytes to be heard. Pigment cell res. 1999; 12(6): 344-354.

13. Sharma L, Bhawan R, Jain RK. Hypoacusis in vitiligo. Indian J Dermatol Venereol Leprol. 2004; 70: 162-164.

14. Wright CG, Lee DH. Pigmented epithelial cells of the membranous saccular wall of the chinchilla. Acta oto-laryngologica. 1986; 102(5-6): 438-449.

15. Welgampola MS, Colebatch JG. Characteristics and clinical applications of vestibular-evoked myogenic potentials. Neurology. 2005; 64(10): 1682-1688.

16. Mirka A, Black F. Clinical application of dynamic posturography for evaluating sensory integration and vestibular dysfunction. Neurol clin. 1990; 8(2): 351-359.

17. Bittar R. How Can Dynamic Computerized Posturography Help in Cases of Dizziness? Int Arch Otorhinolaryngol São Paulo. 2007; 11(3): 330-333.

18. Eviatar L. Management of dizziness in children. In: Bernard LM, ed. Current Management of Child Neurology, third edition. Decker BC Inc; 370-376.

19. Hamzavi I, Jain H, McLean D, Shapiro J, Zeng H, Lui H. Parametric modeling of narrowband UV-B phototherapy for vitiligo using a novel quantitative tool: the Vitiligo Area Scoring Index. Arch Dermatol. 2004; 140(6): 677-683.

20. Feily A. Vitiligo Extent Tensity Index (VETI) score: a new definition, assessment and treatment evaluation criteria in vitiligo. Dermatol pract concept. 2014; 4(4): 81-84.

21. Dicle O Z L E M. Assessment methods in vitiligo. J Pigment Dis. 2015; 2(1): 160.

22. Bhor U, Pande S. Scoring systems in dermatology. Indian J Dermatol Venereol Leprol. 2006; 72(4): 315–21.

23. Zammit G, Wang-Weigand S, Peng X. Use of computerized dynamic posturography to assess balance in older adults after nighttime awakenings using zolpidem as a reference. BMC geriatrics. 2008; 8(1): 1-7.

24. Farid AS, Shabana M, El khousht M, El fouly H, Hamdi M. Difficulties encountered during vestibular testing of pediatric patients (Aged 6-12 years). Med. J. Cairo Univ. 2012; 80(2): 17-24.

25. Shoenfeld Y, Tincani A, Gershwin ME. Sex gender and autoimmunity. J autoimmun. 2012; 38(2-3): J71-J73.

26. 26- Abd El Mageed HK, El-Abedein AMZ, Hassan RA, Madian AA. Audio-vestibular evaluation in vitiligo patients. Menoufia Med J. 2022; 35(2): 919.

27. Koura RA, Basiouny IM, Doss RW, Mostafa AMA, Arafa AE. (2017). Assessment of audiovestibular system in patients with vitiligo: a case–control study. The Egypt J Otolaryngol. 2017; 34(1): 60-67.

28. Manno A, Pace A, Iannella G, Rossetti V, Polimeni R, Milani A, Cocuzza S, Maniaci A, Magliulo G. Audiological and vestibular evaluations in vitiligo patients. Bosn J Basic Med Sci. 2022; 22(1): 140.

29. Mahdi P, Amali A, Ruzbahani M, Pourbakht A, Mahdavi A. The effect of otic melanocyte destruction on auditory and vestibular function: a study on vitiligo patients. Acta Medica Iranic. 2016; 54 (2): 96-101.

30. Cernea P, Damien C. Retinitis pigmentosa, vitiligo and deaf-mutism. Apropos of a case. J Fr ophtalmol. 1994; 17(8-9): 501-503.

31. Gill SS, Salt AN. Quantitative differences in endolymphatic calcium and endocochlear potential between pigmented and albino guinea pigs. Hear res. 1997; 113(1-2): 191-197.

32. Colucci R, Dragoni F, Moretti S. Oxidative stress and immune system in vitiligo and thyroid diseases. Oxidative medicine and cellular longevity, 2015.

33. McCaslin DL, Fowler A, Jacobson GP. Amplitude normalization reduces cervical vestibular evoked myogenic potential (cVEMP) amplitude asymmetries in normal subjects: proof of concept. J Am Acad Audiol. 2014; 25(3): 268-77.

34. Nashner LM, Peters JF. Dynamic posturography in the diagnosis and management of dizziness and balance disorders. Neurol clin.1990.

35. Dawoud EAE, Ismail EI, Eltoukhy SAG, El-Sharabasy AES. Assessment of auditory and vestibular functions in vitiligo patients. J otol. 2017; 12(3): 143-149.