

The Relationship between Vitiligo and Hearing Loss: A Case-Control Study

Sahar Binesh¹ , Raheb Ghorbani² , Kamyar Mansori³ , Ramin Taheri^{1*} 

1. Development of Internal Medicine, School of Medicine Semnan University of Medical Sciences, Semnan, Iran

2. Social Determinants of Health Research Center, Semnan University of Medical Sciences, Semnan, Iran

3. Clinical Research Development Unit, Valiasr Hospital, Zanjan University of Medical Sciences, Zanjan, Iran

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Corresponding Information:

Ramin Taheri,

Dept. of Internal Medicine, Semnan University of Medical Sciences, Semnan, Iran

E-Mail:

ramintaheri2010@gmail.com

ABSTRACT

Background & Objective: Vitiligo as an acquired disorder is caused by the gradual loss of functional melanocytes. Aiming to assess whether vitiligo is associated with hearing loss.

Materials & Methods: A population-based case-control study (case, n=50; control, n=51). The case group included all vitiligo patients referred to public and private clinics in Semnan in March 2021 to October 2021. Then, for each case, one control was selected from the people who did not have any skin disease and had only visited the same center for cosmetic procedures. Audiometric tests including pure tone audiometry (PTA), speech discrimination score (SDS), speech reception threshold (SRT), acoustic reflex (AR) and tympanometry were performed for both case and control groups.

Results: The mean of age ($\pm$ SD) was 31.3 (8.5) and 33.5 (7.9) in two groups. The numbers (%) of women were 32 (64%) and 27 (52.9%); respectively. The result of AR test was normal in 80% of the patients and 92% of the control group; respectively. PTA test result was abnormal in 18 and 2% of cases and controls, respectively. SDS, SRT and Tympanometry Tests were normal in all people of the two groups under investigation. However, the odds of having an abnormal PTA test in vitiligo patients was 10.97 times that of healthy people (OR=10.97; 95% CI: 1.39 – 15.38) (P=0.007).

Conclusion: A relationship was observed between vitiligo and hearing loss, so regular hearing checks are recommended in these patients.

Keywords: Vitiligo, Hearing loss, Melanocyte, Case-control study



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Introduction

Vitiligo as an acquired disorder is caused by the gradual loss of functional melanocytes (1). In vitiligo, the melanocytes in part of the skin are destroyed, and in this way, milky white spots appear on the skin (2). Vitiligo can occur in both sexes and all races and at any age, but its peak 10-30 years. The global prevalence of the disease is estimated to be approximately 0.5- 2%. However, studies have reported higher prevalence rates in Africa and female gender (3, 4,5). In Iran, there is no accurate information about the prevalence of this skin disease.

Which are often located in the form of carina (6, 7). Different theories have been mentioned about the causes of loss of skin pigments in vitiligo, which can be referred

However, it is estimated that 0.9 -1.2% of the total population of Iran suffer from the disorder (4).

The types of vitiligo are divided based on the distribution of depigmented lesions (5). The most specific types of vitiligo include focal, segmental, generalized and universal vitiligo. Generalized vitiligo is the most common type of vitiligo and it is determined by the presence of several macules or a large number of macules scattered in different areas of the body,

as autoimmunity, cytotoxicity, neurochemical mediators and free radicals (8, 9).

In the final stages of vitiligo, the melanocytes are decomposed, which can happen in any organ with melanocytes, such as the retinal pigment epithelium, uveal apparatus, leptomeninges and inner ear (10, 11). Studies have shown that inner ear melanocytes have a protective role when exposed to loud noises. Hence, vitiligo may affect hearing and cause disruption in melanin production, interference in endolymph calcium homeostasis and cochlear function (12, 13).

However, results of studies conducted about hearing loss and this disorder are contradictory. On the other hands, due to the fact that Vitiligo is mainly seen in visible areas and in young people, it may lead to a decrease in self-confidence, problems in social and sexual relations, depression, and finally a decrease in the quality of life in affected people (14). Therefore, given that the main effect of hearing loss is communication impairment and can negatively affect family and friend relationships, cause problems in the workplace, and ultimately lead to social isolation and reduced quality of life (15, 16). This research was conducted to evaluate the relationship between vitiligo and hearing loss.

Materials and Methods

Study Design and Subjects

A population-based case-control study (case, n= 50; control, n=51). The case group included all vitiligo patients referred to public and private clinics in Semnan in March 2021 to October 2021.

The case group included all vitiligo patients referred to public and private clinics in Semnan in 2021. Then, for each case, one control was selected from the people who did not have any skin disease and had only visited the same center for cosmetic procedures. A total of 50 vitiligo patients (case group) were compared with 51 healthy individuals (control group). Inclusion criteria for cases consisted of suffering from vitiligo, and willingness to attend the research. Inclusion criteria for controls were consisted of absence of any skin disease and informed consent to participate in the research. In the present study, people with a history of ear disease (such as chronic otitis media or tympanic perforation), metabolic diseases affecting hearing (Hashimoto's thyroiditis, diabetes mellitus), chronic exposure to noise, family history of hearing loss (Meniere's disease, acoustic neuroma and otosclerosis), taking ototoxic drugs, metabolic disorder, neurological, autoimmune and vascular disorders were ignored.

In tympanometry, which was performed to check the condition of the eardrum, a flexible probe was placed inside the ear, which changed the air pressure in the ear at the same time as the sound was presented.

The AR test was performed after tympanometry and the contraction reflex of the stapedius muscle was investigated after the presentation of loud sounds.

Patients with vitiligo were diagnosed by a dermatologist. Disease diagnosis was based on clinical criteria and its severity was determined based on Vitiligo Area Scoring Index (VASI). Whole-body VASI is calculated using the following formula, which includes contributions from all body regions and ranges from 0-100:

$$\text{VASI} = \sum_{\text{All Body Sites}} [\text{Hand Units}] \times [\text{Residual Depigmentation}]$$

A hand unit, which includes the palm plus the volar surface, is considered approximately 1% of the total body surface area and is used as a guide to estimate the percentage of vitiligo involvement in each body area. The whole body is divided into five distinct regions: 1- hands 2- upper extremities (excluding hands) 3- trunk 4 - lower extremities (excluding feet) 5- feet. The axillary region of the upper body and buttocks and inguinal areas are considered as part of the lower body. Finally, the severity of vitiligo is classified according to VASI as follows: mild = 1-25 - moderate = 26-50 - severe = 51-75 and very severe = 76-100% (17).

Then, in order to perform audiometric tests including PTA, SRT, SDS, AR and tympanometry, the participant entered the soundproof room and sat on a chair. Pejvak ava clinical audiometer CA81 and Pejvak ava clinical impedance audiometer ZA84 devices were used for audiometric tests. To perform the PTA test, headphones was placed on the ears and was connecting to the audiometer. Voices were sent to each ear separately. After hearing the sound, the person had to press the answer button. The audiologist plotted the lowest intensity of sound heard at each frequency on the audiogram. Finally, the degrees of hearing loss were described as follows: mild loss: 25-40 decibels (dB), moderate loss: 40-55 dB, moderate to severe loss: 55-70 dB, severe loss: 70-90 dB and profound loss: more than 90 dB.

In the SDS and STS tests, which were conducted to determine the level of a person's understanding of speech, words were presented to the person through headphones and the person had to repeat these words. In SRT, specific two-syllable words were presented to people in different intensities, and the lowest intensity level where the person repeated 50% of the received words correctly was considered as SRT. In SDS, using monosyllabic words and the maximum level of 30 dB above the speech understanding threshold (hearing comfort level), the person's ability to understand words was calculated.

Simultaneously with the change of air pressure, the movement of the tympanic membrane was recorded. Finally, the tympanometry results were drawn as a graph on the tympanogram sheet.

Finally, by measuring the threshold of this reflex, the type of hearing loss was diagnosed. In this test, the probe was placed inside the ear and the sounds were

presented to the same ear or the opposite ear, and the corresponding response was recorded as a threshold. This reflex was tested at a pressure and had the highest energy transmission in tympanometry using a 226 Hz tone probe.

Results

A total of 101 people were investigated in two groups (case, n= 50; control, n=51). The mean of age ($\pm$ SD) was 31.3 (8.5) and 33.5 (7.9) in case and control groups; respectively. As can be seen, the numbers (%) of women were 32 (64%) and 27 (52.9%) in case and control groups. The result of the acoustic reflex test was normal in 80% of the patients and 92% of the control group; respectively. PTA test result was not normal in 18 and 2% of cases and controls, respectively. However, SDS, SRT and Tympanometry Tests were normal in all individuals of the case and control groups (Table 1).

In the present study, the mean ($\pm$ SD) age of onset and duration of vitiligo were 18.9 ($\pm$ 8.9) and 12.4 ($\pm$ 7.7) years; respectively. In terms of severity, 32 (64%)

Data was analyzed by Stata14 and Logistic regression model was used for their analysis.

patients were suffering from moderate to severe form of vitiligo (Table 2).

Then, in order to eliminate potential confounding variables, P-Value ≤ 0.20 were entered the multivariable logistic, simultaneously. The odds of having an abnormal PTA test in vitiligo patients was 10.97 times that of healthy people (OR=10.97; 95% CI: 1.39 – 15.38) (P=0.007) (Table 3).

The area under the ROC curve was 0.7595, for the multivariable model which demonstrates the high discriminative power. (Figure 1).

Table 1. Demographic and clinical characteristics of participants in groups

	Qualitative Variables	Case group	Control group
		Number (%)	Number (%)
Sex	Female	32 (64)	27 (52.9)
	Male	18 (36)	24 (47.1)
	Total	50 (100)	51 (100)
Age (year)	<30	20 (40)	17 (33.1)
	30-39	17 (34)	17 (33.1)
	≥ 40	13 (26)	17 (33.1)
	Total	50 (100)	51 (100)
History of hearing loss in family	Yes	1 (2)	0 (0)
	No	48 (98)	51 (100)
	Total	50 (100)	51 (100)
History of vitiligo in family	Yes	2 (4)	0 (0)
	No	48 (94)	51 (100)
	Total	50 (100)	51 (100)
Acoustic reflex	Normal	40 (80)	47 (92.2)
	Abnormal	10 (20)	4 (7.8)
	Total	50 (100)	51 (100)
Pure -Tone Average (PTA)	Normal	41 (82)	50 (98)
	Mild	7 (14)	-
	Moderate/ Severe	2 (4)	1 (2)
	Total	50 (100)	51 (100)
Speech Discrimination Score (SDS)	Normal	50 (100)	51 (100)
	Abnormal	0 (0)	0 (0)
	Total	50 (100)	51 (100)
Speech Reception Threshold (SRT)	Normal	50 (100)	51 (100)
	Abnormal	0 (0)	0 (0)
	Total	50 (100)	51 (100)
Tympanometry Test	Normal	50 (100)	51 (100)
	Abnormal	0 (0)	0 (0)
	Total	50 (100)	51 (100)

Table 2. Characteristics of patients with vitiligo

Qualitative Variables	Case group				
	Number (%)				
The duration of the disease (year)	<5	5 (10)			
	5-9	14 (28)			
	10-14	15 (30)			
	≥ 15	16 (32)			
	Total	50 (100)			
The severity of vitiligo	Mild	18 (36)			
	Moderate	27 (54)			
	Severe	5 (10)			
	Total	50 (100)			
Quantitative variables	Mean	S.D	Median	Min	Max
Age of onset of vitiligo (year)	18.9	8.9	17	4	38
The duration of vitiligo (year)	12.4	7.7	10.5	1	33

Table 3. Predictive factors of vitiligo by multivariate model

Qualitative Variables	Adjusted OR (95% CI)		P-Value
Sex	Female	Reference	0.260
	Male	1.58 (0.66 – 3.89)	
Age (year)	<30	Reference	-
	30-39	1.17 (0.42 – 3.31)	0.733
	≥40	1.53 (0.52 – 4.54)	0.383
Acoustic reflex	Normal	Reference	0.077
	Abnormal	2.94 (0.76 – 13.69)	
Pure -Tone Average (PTA)	Normal	Reference	0.007
	Moderate/ Severe	10.97(1.39 – 15.38)	
Speech Discrimination Score (SDS)	Normal	-	1.000
	Abnormal	1	
Speech Reception Threshold (SRT)	Normal	-	1.000
	Abnormal	1	
Tympanometry Test	Normal	-	1.000
	Abnormal	1	

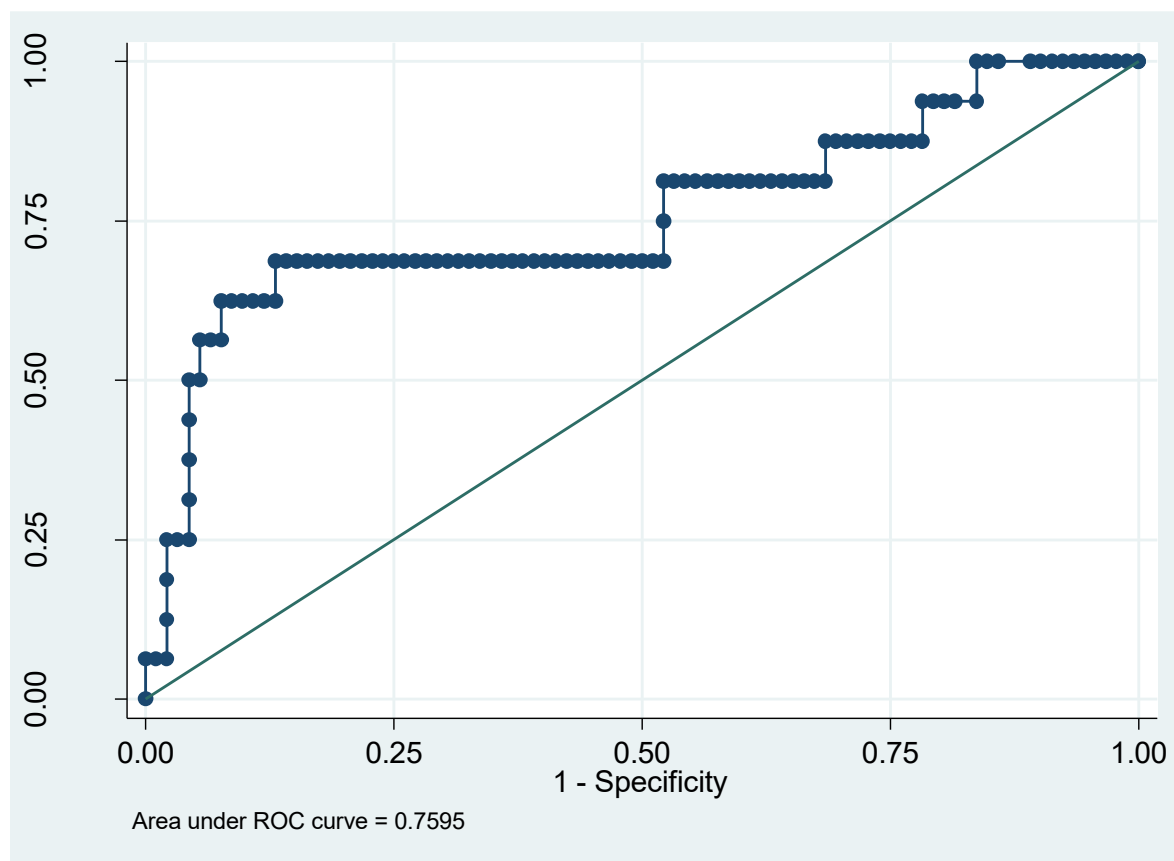


Figure 1. The area under the ROC curve of the multivariable logistic regression model

Discussion

The study was conducted to assess the relationship between vitiligo and hearing loss. The results showed the mean of age ($\pm$ SD) was 31.3 (8.5) and 33.5 (7.9) in case and control groups; respectively. The numbers (%) of women were 32 (64%) and 27 (52.9%) in case and control groups. The result of AR test in 80% of the cases and 92% of the controls was normal. PTA test result was abnormal in 18 and 2% of cases and controls, respectively. However, SDS, SRT and Tympanometry Tests were normal in all individuals of the case and control groups. Also, the odds of having an abnormal PTA test in vitiligo patients was 10.97 times that of healthy people (OR=10.97; 95% CI: 1.39 – 15.38) ($P=0.007$).

In our study, PTA test result was abnormal in 18% and 2% of cases and controls, respectively and in people with vitiligo odds of having an abnormal PTA test was 10.97 times that of healthy people. This finding was inconsistent with some other studies. (12, 18). In the study by Rahimi *et al.*, the results of none of the PTA

and DPOAE tests in vitiligo patients and normal healthy subjects were not statistically significant. Finally, it was reported that the hearing status of vitiligo patients is normal (19). Another study by Al-Mutairi *et al.*, vitiligo did not show a significant relationship between hearing loss and this disorder (20). In the case-control study conducted by Nawaf Al-Mutairi *et al.* with the aim of comparing hearing loss with PTA test in 197 patients with vitiligo and 106 healthy people, no significant difference was observed between healthy subjects and patients (20). Likewise, Escalante-Ugalde *et al.* did not observe hearing loss in patients with vitiligo. They even suggested that the combination of dark skin in vitiligo patients is associated with better hearing (21). Conversely, other studies reported a significant association between vitiligo and hearing loss. In a meta-analysis study by K.-H. Lien *et al.* aimed to determine the relationship between vitiligo and hearing threshold at different frequencies, 9 case-control studies with 371 vitiligo

patients and 349 control subjects were included in the meta-analysis. Finally, it was found that vitiligo patients had higher pure hearing thresholds at frequencies of 2000, 4000 and 8000 than healthy people. Therefore, these patients are more prone to hearing loss in high frequencies (22). In another meta-analysis study that was conducted on 14 case-control studies with 938 patients with vitiligo. A statistically significant relationship was observed between this disorder and hearing loss (OR: 6.02, 95% CI: 3.41-10.62). This relationship was still maintained even after adjusting for study quality and publication bias (23). Regarding the role of cellular melanocytes in animal samples, we can refer to the study of Murillo-Cuesta. In this study, mice suffering from depigmentation, hearing loss caused by increasing age had a higher prevalence and the possibility of hearing threshold improvement following intentional exposure to harmful noises was less in comparison with pigmented rats (24). In general, it can be said that the results of the PTA test in the present study strengthen the assumption that changes in ear melanocytes increase the probability of hearing loss.

Various factors are involved in the inconsistency of the results of these studies. Perhaps one of the most important factors is their very diverse methodology, such as the different definition of hearing loss. Another factor is the variety of ethnicities and different characteristics of the participants of these studies. Also, some researches have not excluded patients with systemic diseases, which may be associated with these co-morbidities.

In general, the loss of skin melanocytes is the most obvious clinical finding in vitiligo patients, but due to

the widespread presence of melanocytes in other organs such as the inner ear, there is a possibility of involvement in other systems with functional defects in them (25). Based on the structural and physiochemical characteristics of otic melanocytes, a series of special functions such as antioxidant properties have been attributed to them. Most of the pathological processes occurring on the level of the cochlea, such as age-related hearing loss (ARHL) or noise-induced hearing loss (NIHL) are biologically oxidative. The existence of an antioxidant agent such as melanocytes can slow down the occurrence of these destructive processes and delay the damage to the auditory system (24, 26).

The general consensus is that the damage of melanocytes in the vitiligo disease leads to an increase in the latency of sensory evoked potentials by causing defects in the conduction of nerve impulses (27). The cause of the defect in the conduction of nerve signals can be related to the semi-conductive property of melanocytes. Melanocytes play the role of storing and retrieving some effective metal ions in controlling the enzyme activity required for the release of chemical neurotransmitters. The defects in synaptic activity and as a result defects in conduction of action potentials along the auditory nerve to the auditory nuclei of the brainstem is the main cause of the increase in latency observed as a result of ABR (auditory brainstem response) in vitiligo patients (10, 28).

This study, like other studies, has limitations that need to be mentioned: 1- no thyroid test in the subjects under investigation 2- low sample size 3- uncertainty of insulation of the sound room.

Conclusion

There was a significant relationship between vitiligo and hearing loss so regular hearing checks are recommended in these patients. However, it is

suggested to conduct cohort studies with a larger sample size and comprehensive tests.

Ethics approval and consent to participate

This study was performed according to the principles expressed in the Declaration of Helsinki and was approved by the Deputy of Research and Ethics Committee of Semnan University of Medical Sciences (Iran) (ID: IR.SEMUMS.REC.1400.084).

Conflict of Interest

The authors declare that they have no competing interests.

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Authors' Contribution

Conceptualization, supervision, funding acquisition and resources: Ramin Taheri and Sahar Binesh; Methodology: Raheb Ghorbani; Data collection:

Sahar Binesh; Data analysis: Kamyar Mansori; Investigation and writing: All authors

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