

Association of Skin Pigmentation and Risk of Hearing Loss: A Homogenous Race Study

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ABSTRACT

Melanocytes are melanin-producing neural crest-derived cells located in many parts of human body including cochlea. Melanin is a dark pigment primarily responsible for skin color. Many studies on hearing impaired individuals across race/ethnicity found dark skinned individuals have lower risk of hearing loss. The present study investigated the association of skin pigmentation and risk of cochlear hearing loss for normal hearing adults within same racial population. Relevant cross-sectional data from the students of AWH special college, 2018 to 2019, for 60 participants 18 to 21 years of age was examined. Very fair skin and dark brown skin tone were classified based on Fitzpatrick scale (Grade I and grade IV). All the participants were having normal hearing with PTA \leq 15dB according to Goodman's classification. We demonstrate for the first time that lower skin pigmentation is associated with poor OAE amplitudes for individuals of same race/ethnicity and thus indicate the increase risk of having hearing loss in future. These results add to the growing literature of reduced melanocytes/melanin pigmentation related health disturbances and also add to the urgency in instituting public health measures to reduce it.

Key Words: Melanocytes, Melanin, cochlear hearing loss, Otoacoustic emission (OAE)

INTRODUCTION

The presence of pigment cells in the inner ear was first identified by Alphonse Corti. ^[1] In human cochlea, melanocytes are mainly present in the modiolus, osseous spiral lamina, Reissner's membrane and vascular stria, but they also exist in the vestibular organs. According to Wright and Lee melanin is present in the posterior superior portion of the membranous wall of the saccule and these pigmented cells are plays an active role in regulating endolymphatic composition and it has an important role in modulating the vestibular stimuli. ^[2] Melanocytes are found especially in highly vascularized areas of apparently important secretory or metabolic function. In the inner ear, melanin has a vasomotor function, although its exact role is unknown

(Gottesberge, 1988). ^[3] The presence of melanocytes is not only limited to peripheral auditory system, but also present in some parts of central nervous system (Goldgeier, Klein, Klein-Angerer, Moellmann, & Nordlund, J. J. 1984). ^[4] Melanin produced by strial melanocytes (intermediate cells) in the cochlea has been hypothesized to serve a protective role as a free radical scavenger, metal chelator, or regulator of calcium homeostasis in the stria vascularis, which is involved with generating and maintaining the endolymphatic potential necessary for normal hearing (Murillo-Cuesta, Contreras, Zurita, Cediell, Cantero, Varela-Nieto, & Montoliu (2010); Riley, 1997). ^[5,6] Deficiency in strial melanin is associated with marginal cell loss and decline in the endocochlear potential (Ohlemiller, Rice,

Lett & Gagnon (2009).^[7] Although not well specified, some studies have suggested that melanin is involved in the structural, metabolic and vascular health of the cochlea (Barrenas, 1997; Barrenas & Axelsson, 1992).^[8,9] Melanin also has been found to accentuate some antioxidant activities in the cochlea and as such, likely plays an otoprotective role (Wu, Sha, McLaren, Kawamoto, Raphael & Schacht 2001).^[10] Melanin is associated with increased ototoxicity because many toxins and pharmacologic agents bind with melanin, resulting in an accumulation of the chemicals in melanin-rich tissues and potentiation of their actions (Barr-Hamilton, Matheson, & Keay, 1991; Heijmen, Klis, de Groot, & Smoorenburg, 1999).^[11,12] Although not clear, melanin likely plays a complex role in the long term health of the cochlea. A different finding was observed by Price and Fisher in 2001.^[13] The inner ear function does not directly depend on melanocyte pigment instead melanocyte deficiency displayed a measurable alteration in the ionic composition of extracellular inner ear fluid endolymph with correspondingly low K⁺ composition in endolymph, suggesting that it may affect the capacity of hair cells response to a stimulus (Steel, 1995).^[14]

On the whole, it has been supported that melanin is otoprotective against excessive noise exposure although the mechanism has not been well established (Conlee, Abdul-Baqi, McCandless, & Creel, 1986; Gratton & Wright, 1992).^[15,16] Other epidemiologic studies using a case-control approach recruiting individuals with similar occupational exposures have also demonstrated a reduced risk of hearing loss in black subjects (Ishii, & Talbott, 1998; Jerger, Jerger, Pepe & Miller, 1986).^[17,18] Contradictory findings were reported by Ward (1995),^[19] found that cochlear susceptibility to damage from noise has not been dependent on gender, skin color, any known diseases, mental attitude toward the noise, exposure history, and pre exposure hearing loss.

Lin, Li, Curhan, Stankovic, Qureshi and Curhan (2017)^[20] investigated the relation between skin pigmentation and risk of hearing loss in women. They used Fitzpatrick skin phototype (for type IV vs. type I) and found black individuals have a lower risk of hearing loss. Similar findings were found by Lin, Maas, Chien, Carey, Ferrucci and Thorpe (2012)^[21] on race/ethnicity and its association with hearing thresholds. They concluded that skin pigmentation as a marker of melanocytic functioning and mediate the strong association observed between race/ethnicity and hearing loss. Study on different racial specimens observed that melanin pigmentation is significantly more abundant in African American cochleae than in Caucasian cochleae (Sun, Zhou, Lin, Francis, Carey and Chien 2014).^[22] Studies on skin disorders also have similar supporting outcomes. Angrisani, Azevedo, Pereira Lopes and Garcia (2009)^[23] found that patients with vitiligo, particularly males, have a greater predisposition to cochlear dysfunction, especially in the right ear. As far as the OAE suppression effect was concerned, there was a greater alteration in the female efferent system, particularly in the left ear. It was found that even after accounting for years of occupational noise exposure; race/ethnicity had a substantive influence on the magnitude of noise-induced hearing loss. The white soldiers exhibited less hearing sensitivity than black soldiers, and soldiers of other races, even after accounting for noise exposure and age (Henselman, Shadoan, Subramaniam, Saunders & Ohlin 1995).^[24] The Black soldiers also demonstrated the best retention of hearing sensitivity across years of military service. Previous observational studies investigating the role of race and hearing loss have consistently demonstrated that black race is associated with a 60–70% lower odd of noise-induced hearing loss and age related hearing loss when compared to white subjects (Agrawal, Platz & Niparko, 2008; Cooper, 1994).^[25,26] In a study done from

1999–2004 by National Health and Nutrition Examination Survey, hearing thresholds were obtained and data examined by age-group, gender, race and hearing loss configuration showed that the prevalence of hearing loss was higher for the White and Mexican American men than the Black men (Pratt, Kuller, Talbott, McHugh-Pemu, Buhari & Xu, 2009).^[27] In addition, other risk factors such as smoking, noise exposure, and cardiovascular risk increased the likelihood of hearing loss, especially in white men. Therefore, the results indicate that there is a link to the melanocytes in our skin (Pugh and Crandell, 2002).^[28] In general, the literature suggests that racial differences may reflect differences in hardness or resistance to the permanent tissue damage (i.e., spiral ligament and stria vascularis) that commonly is associated with the aging cochlea (Lang, Schulte, & Schmiedt, 2003; Schuknecht & Gacek, 1993).^[29,30]

A number of human studies have suggested that darker skin and iris pigmentation is associated with resistance to noise-induced hearing loss. The density of melanin within the cochlea corresponds to general pigmentation as reflected in eye and skin color. In a review study conducted by Mujica-Mota, Schermbucker and Daniel (2015)^[31] on eye color and SNHL, Evidence suggests that melanin can be protective against radiation-noise induced sensorineural hearing loss, but may predispose individuals to cisplatin ototoxicity. Also pigmentation, as reflected by iris and skin color, was found to have a negative correlation with susceptibility to noise, i.e. the more pigment the less PTS developed (Attias & Pratt, 1985).^[32]

Lower skin pigmentation may correspond to factors relevant to hearing loss. Earlier studies have either conducted on across ethnicity / race or in hearing impaired individuals. None of them have assessed the hearing impairment susceptibility in relation to the individuals particularly from same ethnicity or race based on skin pigmentation. Assessment on

homogeneous race could minimize extraneous variables. Thus this study has carried out on normal hearing individuals from same race/ethnicity by use of OAE testing. Otoacoustic emission parameters have been chosen since it has advantageous to reveal early cochlear damage, even before it can be diagnosed by standard audiometric techniques.

In this study, we sought to evaluate the association between skin tone and hearing impairments within same race/ethnicity. Early identification of HL vulnerability would serve awareness among hearing professionals and also to include as one of the extraneous factor for OAE testing.

MATERIALS AND METHODS

2.1 Participants. Data from 60 adults, (18 - 21 years of age), from students of the AWH special college (2018 to 2019) were examined. All participants were taken from same ethnicity/race and were divided into 2 groups (30 each) based on their skin tones on Fitzpatrick scale grade 1 (very fair) and VI (dark brown). Participants were evaluated after a questionnaire interview to determine family history, medical history, medication use, noise exposure, history of any drug abuse, and socioeconomic status.

2.2 Audiometric measures. Normal-hearing young adults were recruited for this study. Prior to testing, a standard consent form was read and signed by each participant. Subjects were instructed to avoid loud sounds for 8 hours prior to testing. Otoscopic examination carried out using Welch- Allyn otoscope, 226 Hz tympanometry, and 1 kHz ipsilateral reflex measurements were obtained using GSI TYMPSTAR impedance module to confirm normal middle ear status. Audiometric thresholds to pure-tone air conduction audiometry were measured using the MAICO MA42 at 0.25, 0.5, 1, 2, 4, and 8 kHz using the modified Hughson-Westlake protocol. Hearing was categorized as normal where thresholds were better than or equal to 15 dB HL.

Following confirmation of normal hearing thresholds and middle ear status, DPOAEs were recorded using the IHS DUET instrument. DPOAEs were measured using primary tones labelled f1 and f2, with a ratio (f2/f1) equal to 1.22. The Fdp frequencies measured covered the range of 996, 1416, 1992, 2827, 3994 and 5645 Hz, and primary tone intensity levels used for f1=65 dB SPL, and f2=55 dB SPL). Artifact-free averaging was conducted at each f2 frequency for 20 seconds to allow the noise at each frequency to reach sufficiently low levels. Testing was conducted for 5 minutes per ear across the frequency range and results were continuously displayed and stored in a DP-Gram for further analysis. All testing was conducted in a quiet test room, consistent with (ANSI S3.1, 1991). The DPOAE parameters i.e. Distortion product (DP) amplitude (dB SPL) and SNR (dB SPL) are analysed. Only DP amplitudes those with minimum 6dB SNR were estimated and considered for the analysis (Abdala and Visser-Dumont, 2001) [33]

2.3 Statistical Analysis. One sample t test was used to find out the mean and standard deviation of DP amplitudes across frequencies within each ears of grade I and grade IV group. Further, one sample two tailed test was carried out to find out the significant frequencies. Also, Independent two-tailed test were performed to investigate the significance between the normal weight and lower weight group. P value < 0.05 was considered as statistically significant. All analyses were performed using SPSS version 15.

Simple mean analysis were also used, based on the corresponding normality and homogeneity of variance at each frequency, to measure the differences in DPOAE amplitudes among the between two groups at the 6 tested frequencies (996, 1416, 1992, 2887, 3994 & 5645Hz) in both ears.

RESULTS

One sample t test was done separately for right ear and left ear of both dark brown (grade IV) and very fair group (grade 1) to identify the mean and standard deviation and is shown in [Table. 1]. Dark brown group showed mean amplitude of 3.0333 and 3.0222 for both right and left ear which is higher while compared against 2.7000 and 0.3000 for fair skin group respectively. Further, one sample 2 tailed test showed a significance (p<0.05) across frequencies within each group ear from both category group. Figure 1 revealed Mean DPOAE amplitudes of all six frequencies. The table shows highest distortion product amplitude mean value obtained for 996 Hz (Fdp) followed by 1416 Hz irrespective of ears and groups. However, the least mean value was found for 2827 Hz for right ear of both groups and 3994 Hz for left ear of both groups. Amplitudes of all six frequencies were averaged in order to compare between ears from each BMI groups and independent two tailed statistics were administered on the data. Comparison was made between right ear of “dark skin” with right ear of “fair skin” and left of “dark skin” with left of “fair skin” groups. The result showed significance, and was given in [Table 2]. Additional, mean analysis were done between frequency bands and found “fair skin” category has better DPOAEs amplitude while compared with DPOAEs of dark skin category, irrespective of ears [Table 3]. Moreover, when averaged the DPOAEs regardless of frequencies overall mean was better identified for fair skin group [Figure 2]

Table 1:-Mean and standard deviation				
	N	Mean	Std. Deviation	Std. Error Mean
Dark brown right	6	3.0333	4.82784	1.97096
Very fair right	6	2.7000	3.92139	1.60090
Dark brown left	6	3.0222	6.26846	2.55909
Very fair left	6	.3000	5.32462	2.17377



Figure 1:- Mean DPOAE amplitudes of frequencies
Table 2:- Independent Sample Test: comparison between the ears

	Group Differences					t	df	Sig.(2-tailed)
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
				Lower	Upper			
Darkbrown right Very fair right	.33333	1.67915	0.68551	-1.42883	2.09550	7.991	5	0.03113
Dark brown left Very fair left	2.72222	1.51638	0.61906	1.3088	4.0147	8.397	5	0.0271

Table 3:- mean analysis between frequency bands

RIGHT	RIGHT		LEFT	
	Dark skin	Very fair skin	Dark skin	Very fair skin
996	10.93333	7.8	12.06667	7.733333
1416	6.4	7.2	8	5.333333
1992	2.2	1.533333333	5	0.666667
2827	-2.4	-1.266666667	-2.33333	-4.6
3994	0.733333	1.8	-2.86667	-5.33333
5645	0.3333333	-0.86666667	-1.73333	-2

DISCUSSION

In this study, lower skin pigmentation was found to be associated with reduced DPOAE amplitude when compared between individuals with fair skin when compared against dark brown skin. These changes in DPOAE amplitude noted for all frequencies in both ears. The reduction in DPOAEs amplitude in among grade 1 individuals indicates a possible reduction in outer hair cell (OHC) function. These findings were similar to the other studies which were done on hearing impaired population. Pratt et.al found white skinned individuals had a high prevalence of hearing loss while tested with standard audiometric tests.

Earlier studies done on across races have shown that substantial number of hearing impaired individuals seen among

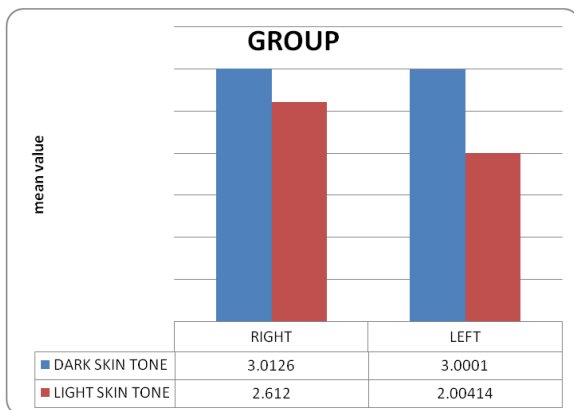


Figure 2:- averaged DPOAEs regardless of frequencies

white skinned population. But while considering across race, other factors such as head circumference, length of ear canal, type of diets, and amount of sun light exposure may influence inner ear mechanism and therefore the results too. In addition, we chose the participants only with normal hearing in order to find hearing loss susceptibility. In any case, outer hair cell dysfunction can be easily noticed in sensitive OAE testing even before its being observed in standard pure tone audiometry. The results of the present study show that there is a significant difference in OAE amplitude across the groups (grade I and grade IV). The grade I group had lower OAE amplitude which might due to their lower melanocytes/melanin distribution which is responsible for their deprived OHC function. Melanocytes and its influence on outer hair cell function have been clearly documented in earlier studies. Though, the present study is just a preliminary evaluation of the difference in OAEs in individuals with two different skin tones, the findings indicates OAE can be used as a timely tool for identifying hearing loss susceptibility among fair skin population. Moreover, in future, for any experimental studies with OAE, while considering other parameters that affect amplitude of emissions such as poverty status, gender, and race/ethnicity noise exposure and any pathological conditions, the skin pigmentation also should be included. However, further studies are essential to explore and find direct possible relationship between melanocytes and its effect on the level of cochlear physiology.

CONCLUSION

The present study attempted to determine the relationship between skin pigmentation and risk of having hearing impairment by using DPOAE measures. The results of the study showed that there was a significant reduction in DPOAE amplitude for individuals with lower skin tone compared to dark skin tone groups. The entire study was carried out in individuals

with normal OHC function and was confirmed with DPOAE evaluation. Though both groups have passed the DPOAE test, while data analysed there was significant better DPOAE amplitude found for dark brown (Fitzpatrick grade IV) skin individuals compared to fair skin (grade I). This reduction in OHC response might due to reduced melanocytes distribution on skin which has major role in cochlear OHC development and transduction as well. This study suggests the researchers to include skin pigmentation as one of the extraneous factor for OAE testing. Further evaluations on larger groups of individuals are essential to generalize the results.

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