Brief Report

Auditory System Abnormalities in Early Graying of Hair: A Cross-Sectional Study

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Abstract

Background: Melanocytes in the hair and melanocytes in the stria vascularis of the inner ear have common origins. Many congenital and acquired disorders of cutaneous pigmentation have auditory abnormalities. There is a paucity of studies on the auditory associations of early graying. **Aim and Objectives:** The aim of the study was to determine the association between early graying and auditory system abnormalities. **Materials and Methods:** A cross-sectional analytical study was done on 100 patients with early graying and 100 controls. Pure tone audiometry was done at 0.25 to 4 kHz for bone conduction, conventional and high frequencies from 0.25 to 8 kHz for air conduction, and extended high frequencies from 9 kHz to 20 kHz for air conduction in both ears. **Results:** Bilateral hearing loss >25 dB was present in three patients with early graying based on the four-frequency average of 0.5, 1, 2, and 4 kHz. Patients with early graying had significantly higher thresholds for hearing except at 0.25 kHz in the right ears and 0.25, 2, 10, and 11 kHz in the left ears. **Limitations:** We did not assess cochlear function with otoacoustic emissions, and our study design did not allow us to assess causality and temporal association. **Conclusion:** Our study found that early graying may be a visible marker of changes in auditory thresholds. Patients with early graying need periodic auditory evaluations and health education to prevent further hearing loss.

Keywords: *Graying, hearing loss, premature canities*

Introduction

Cutaneous, ocular, and inner ear melanocytes have shared origins in the neural crest.[1] Inner ear melanocytes play a crucial role in generating endo-cochlear potential.[2] Genetic auditory-ocular-pigmentary disorders such as Waardenburg syndrome and Tietze syndrome have sensorineural hearing loss and depigmentation as common features.[3] Acquired autoimmune pigmentary disorders such as Vogt-Koyanagi-Harada syndrome, Alezzandrini syndrome, and sympathetic ophthalmia also have ocular and auditory abnormalities.[4] Vitiligo has been associated with significant high-frequency hearing loss. Melanin pigmentation in the cochlea has been suggested as a protective factor for hearing.[5] However, the systemic implications of early graying of the hair have not been sufficiently explored. Ozbay *et al*.[6] reported significant hearing loss at extended high frequency in patients with premature canities compared to controls. However, the study included individuals aged under 40 who recalled graying in their twenties. Thus, studies need to examine the association between hair pigmentation and auditory function.

Aim and Objectives

The aim of the study was to determine the association between early graying and auditory system abnormalities.

Materials and Methods

The Institutional Ethics Committee approved the study. The cross-sectional analytical study was done with 100 cases and 100 controls after informed consent. The study was done in a tertiary care institute's outpatient department of dermatology and otorhinolaryngology. The study duration was two months.

Inclusion criteria for cases

Patients above seven years and under 30 years of age with a minimum of 50 gray hairs were included. A dermatologist diagnosed the cases. There are no

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evidence-based age criteria for defining early graying in the Indian population. Although some definitions mention 25 years, the age cut-off is arbitrary. After 30 years, chronological aging is associated with a 10–20% reduction in pigment-producing melanocytes per decade. The average age of graying is in the late 30s for Asians.[7] Thus, we included patients under 30 years of age.

Exclusion criteria for cases

Participants with medical or neurological conditions that can cause auditory abnormalities, tinnitus, diseases of the external or middle ear, diabetes mellitus, family history of hearing loss, history of acoustic trauma, barotrauma, otologic diseases, otologic surgery, conductive hearing loss, exposure to ototoxic drugs, exposure to medication implicated in hair depigmentation, occupational noise exposure, history of autoimmune diseases, history of smoking, chronic inflammatory conditions and systemic infections, use of hair dyes, and cutaneous disorders associated with depigmentation such as piebaldism and vitiligo were excluded.

Inclusion criteria for controls

Patients above seven and under 30 years of age without graying and with minor unrelated conditions (e.g., cutaneous warts, abrasions, etc.).

Exclusion criteria for controls

Canities and medical or neurological conditions that can cause auditory abnormalities, tinnitus, diseases of the external or middle ear, diabetes mellitus, family history of hearing loss, history of acoustic trauma, barotrauma, otological diseases, otological surgery, conductive hearing loss, exposure to ototoxic drugs, exposure to drugs implicated in hair depigmentation, occupational noise exposure, history of autoimmune diseases, history of smoking, chronic inflammatory conditions and systemic infections, use of hair dyes, and cutaneous disorders associated with depigmentation such as piebaldism and vitiligo.

Procedure

The dermatologist and otorhinolaryngologist collected a detailed history and examined the participants. Patients with clinically normal external and middle ear function were included. Immittance audiometry was done to assess middle ear function and exclude tympanic perforation. The cases and controls wore a surgical cap for blinding during pure tone audiometry (PTA). The participants were briefed about the procedure and assessed by the same personnel. PTA was done at 250 Hz, 500 Hz, 1000 Hz, 2000 Hz, and 4000 Hz for bone conduction, conventional and high frequencies at 250 Hz, 500 Hz, 1000 Hz, 2000 Hz, 4000 Hz, and 8000 Hz for air conduction, and extended high frequencies at 9000 Hz, 10000 Hz, 11000 Hz, 12500 Hz, 14000 Hz, 16000 Hz, 18000 Hz, and 20000 Hz for air conduction in both ears using a Grason-Stadler Audiostar audiometer. The test was performed in a soundproof room, and patients were presented with sounds of different intensities and frequencies.

Sample size

The sample size was calculated for a 5% alpha error and 90% power using OpenEpi software version 3.01. The number required was 63 in each group, as per the study by Ozbay *et al*.[6] The hearing threshold at a frequency of 20 kHz among patients with early canities and controls was 107.2 ± 5.4 standard deviation (SD) and 103.8 ± 6.3 SD, respectively. However, because of racial influence on pigmentation, hearing, and differences in methods, we increased the sample size to 100.

Data analysis

The continuous variables were summarized as mean and SD or median and interquartile range. The normality of variables was assessed with the Shapiro-Wilk test. The comparison of continuous variables between the study groups was done using the independent *t*-test or Mann-Whitney U test. The comparison of categorical variables between the study groups was done using the Chi-square test. Pearson correlation test was done to assess the correlation between the duration of graying and PTA parameters. A *P* value less than 0.05 was considered statistically significant. The data analysis was done using IBM Statistical Package for Social Sciences (SPSS) version 26.

Results

One hundred patients with early graying and 100 controls were included in the analysis. The baseline characteristics of the study participants are shown in Table 1. The mean (SD) age of the participants in both study groups was 22.8 (4.1) and 21.8 (3.2) years. The difference was not statistically significant. Family history of early graying in first-degree relatives was present in 24% of the cases and none in controls. The mean (SD) duration of graying was 2.8 (1.7) years in patients with early graying.

Table 1: Baseline characteristics of patients with early graying and controls

Characteristics	Early graying	Controls	*P*
Age, mean (SD), years	22.8 (4.1)	21.8 (3.2)	0.063*
Gender			
Male, *n* (%)	81 (81.0)	91 (91.0)	0.171**
Female, *n* (%)	19 (19.0)	12 (12.0)	
Family history of early graying			
Present, *n* (%)	24 (24.0)	0 (0.0)	<0.001**
Absent, *n* (%)	76 (76.0)	100 (100.0)	

*Independent *t*-test. **Chi-square test

Table 2 compares PTA threshold values in patients with early graying and controls. The mean PTA values of participants with premature canities at all frequencies were higher than controls in both ears. Bilateral hearing loss >25 dB was present in three patients with early graying based on the four-frequency average of 0.5, 1, 2, and 4 kHz. No participant in the control group had a hearing loss >25 dB. The highest mean deficit in hearing was seen at 16000 Hz in the right ears (23.4) dB and left ears (22.5) dB of the patients with early graying. Figure 1 shows the mean difference of PTA between the study groups in the right and left ears at different frequencies. The PTA significantly differed between the study groups except at 0.25 kHz in the right ears and 0.25, 2, 10, and 11 kHz in the left ears.

Table 3 shows the bone conduction results of the two groups. The differences were not statistically significant except in the right ear at 1 kHz.

Discussion

Our study found a significant association between hearing loss and early graying of hair. Conventional frequencies, high frequencies, and extended high-frequency audiometry were used in our study to identify hearing abnormalities. Early hearing loss at high frequencies often goes unnoticed as patients can comprehend speech. Extended high-frequency audiometry is helpful in the early detection of populations at risk of hearing loss. It is reportedly more sensitive than conventional audiometry and distortion-product otoacoustic emission.[8] Three patients (3%) with early graying had mild hearing loss. Hearing loss is mild when the PTA average of air conduction thresholds at 0.5, 1, 2, and 4 kHz in the better-hearing ear is 25–40 dB.[2] Significantly higher hearing thresholds in air-conduction were seen in patients in early graying except at 0.25 kHz in the right ears and 0.25, 2, 10, and 11 kHz in the left ears. The duration of hair graying correlated with hearing loss at frequencies above 1 kHz. The differences in bone conduction were not clinically relevant. Family history of early graying first-degree relatives was common (24%) in patients with early graying. This may reflect the autosomal dominant inherence pattern in some patients with early graying.[7] More male patients had early graying in our study. Male patients tend to have a higher prevalence and severe graying.[9] The lower proportion of females in our study may be due to the exclusion of patients who used hair colors. Hair coloring interferes with the accurate assessment of gray hairs and thus we excluded patients who used any hair colors.

Ozbay *et al*.[6] reported significantly higher hearing thresholds at higher frequencies (8–20 kHz) in patients with premature canities compared to controls. However, they only included patients up to the age of 40 years with almost complete graying of their hair. Factors leading to early graying may also affect the inner ear's function. Genetic and environmental factors affect hair follicles, melanocyte stem cells, and melanocytes. Premature aging

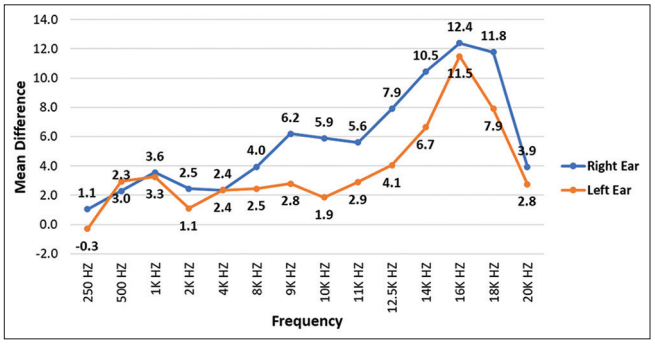

Figure 1: Trend of the mean difference of PTA between the early graying group and control group at different frequencies

Table 2: Comparison of pure tone audiometry (PTA) threshold values in patients with early graying and controls

Frequency	Right ear			Left ear		
	Early graying (*n*=100) Mean±SD	Control (*n*=100) Mean±SD	*P**	Premature canities Mean±SD	Control Mean±SD	*P**
250 HZ	11.6±5.9	10.5±3.5	0.569	10.9±6.4	11.2±4.1	0.121
500 HZ	14.4±5.3	12.1±3.7	<0.001	14.3±5.9	11.3±3.8	<0.001
1 kHZ	17.2±5.4	13.6±4.2	<0.001	16.1±5.7	12.9±4.7	<0.001
2 kHZ	13.5±5.5	11.0±4.2	<0.001	12.7±5.6	11.6±4.1	0.243
4 kHZ	15.6±9.1	13.3±7.4	0.017	15.0±7.7	12.6±6.1	0.033
8 kHZ	14.6±10.7	10.7±7.5	0.002	12.7±8.1	10.3±5.4	0.044
9 kHZ	15.8±17.7	9.5±7.9	0.002	12.8±10.8	10.0±9.1	0.033
10 kHZ	13.7±13.7	7.8±10.7	0.001	10.1±12.3	8.25±9.3	0.516
11 kHZ	13.7±13.8	8.1±12.0	0.003	10.0±11.5	7.1±10.5	0.067
12.5 kHZ	16.6±15.5	8.7±13.6	<0.001	12.4±13.3	8.3±14.4	0.003
14 kHZ	20.3±19.2	9.9±17.1	<0.001	16.1±18.7	9.4±17.6	0.001
16 kHZ	23.4±21.9	11.0±19.2	<0.001	22.5±21.2	11.0±19.1	<0.001
18 kHZ	19.4±13.9	7.6±13.5	<0.001	17.2±13.1	9.3±14.1	<0.001
20 kHZ	9.4±7.4	5.5±7.3	<0.001	8.2±7.9	5.5±8.6	0.015

*Mann-Whitney U test

Table 3: Comparison of bone conduction threshold in patients with early graying and controls

Frequency	Right ear			Left ear		
	Premature canities Mean (SD)	Control Mean (SD)	*P*	Premature canities Mean (SD)	Control Mean (SD)	*P**
250 HZ	2.7±5.4	2.8±3.4	0.814	2.5±5.6	3.7±3.6	0.072
500 HZ	5.5±5.1	4.5±2.9	0.094	4.9±5.1	3.9±3.5	0.109
1 kHZ	7.2±5.0	5.4±3.0	0.003	6.3±4.9	5.5±3.5	0.185
2 kHZ	4.5±5.2	3.8±3.5	0.266	4.5±5.5	4.4±3.5	0.939
4 kHZ	5.1±6.3	4.0±5.2	0.163	4.3±6.5	5.0±4.1	0.402

*Mann-Whitney U test

syndromes such as progeria and pangeria cause early graying.[10] Arck *et al*.[11] reported that reductions in hair follicle melanocytes and melanocyte apoptosis in graying are related to oxidative stress. Melanocytes in the hair are highly susceptible to exogenous oxidative stress; thus, graying hairs have been suggested as models for oxidative stress and aging. Psycho-emotional and inflammatory disease-induced stress can enhance oxidative stress on melanocytes. Autoimmune damage, drugs, nutritional deficiencies, smoking, and thyroid dysfunction are other implicated factors.[10] Free radical-related oxidative stress and inflammation also have a causal role in hearing loss.[12] Melanin in the inner ear may scavenge free radicals and protect against oxidative stress. A reduction in antioxidant enzymes and melanin and an increase in free radical levels have been reported in melanocytes cultured with ototoxic drugs. Thus, inner ear melanin and melanocytes have an integral role in hearing.[5] The auditory abnormalities seen in our study suggest that gray hairs may reflect systemic disturbances. It may also reflect other age-related changes in the middle or inner ear. Patients at risk of hearing loss need preventive strategies such as avoiding ototoxic drugs, noise avoidance, and noise reduction.[7] The ideal treatment for this subset of patients with both auditory abnormalities and early graying of hair requires further studies on the pathophysiological links between the two conditions. Antioxidants may have a role if oxidative stress is identified as a causal link.

Limitations

Our study evaluated peripheral hearing with PTA. We did not assess cochlear function with transient evoked otoacoustic emissions. We did not use the objective graying severity score to evaluate the number of gray hairs. We avoided it as the procedure is time-consuming and requires participants to crop their hair. Causality and temporal association could not be assessed in the cross-sectional study design.

Conclusion

Early graying may be an easily visible clinical marker of changes in auditory thresholds. Patients with early graying need periodic auditory evaluations and health education on preventing further hearing loss. Melanocyte dysfunction may be a widespread phenomenon. Further preclinical studies on melanocyte biology and clinical studies with larger sample sizes are needed to evaluate this association.

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Conflicts of interest

There are no conflicts of interest.

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