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RESEARCH ARTICLE

SYSTEMIC REDOX BALANCE AND TRACE ELEMENTS IN PREMATURE HAIR GREYING: A CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Premature hair greying (PHG) is a complex phenomenon influenced by various factors. Systemic redox balance plays a crucial role in maintaining hair pigmentation and growth. The present study aimed to investigate systemic redox balance and trace element levels in subjects with PHG and healthy controls. **Materials and Methods:** This cross-sectional study enrolled 40 PHG patients and 40 healthy controls in the age group 15–25 years after taking voluntary informed consent. 5 ml of venous blood sample was obtained from the subjects and used for the estimation of serum malondialdehyde (MDA), superoxide dismutase (SOD), copper, iron, calcium, and zinc levels. MDA and SOD were estimated by the ELISA method and trace elements and calcium by an automated biochemistry analyzer. **Results:** The mean levels of MDA and SOD were found to be 1.553±0.58**, 68.90±21.04** in PHG as compared to healthy controls, which were 0.66±0.58, 148.3±16.99, respectively. The elevation of MDA levels and decreased SOD levels in PHG was statistically highly significant ($p<0.001$). This indicates systemic redox imbalance in PHG subjects. Similarly, the mean values of copper, iron, zinc, and calcium were significantly lowered in PHG subjects in comparison to healthy controls ($p<0.001$). **Conclusion:** In conclusion, the intricate dance between trace elements and systemic redox balance plays a pivotal role in maintaining the youthful Vigor of our hair. Premature hair greying, once considered an inevitable fate, is now revealed to be intimately linked to the delicate balance of essential micronutrients and the body's antioxidant defences. The antioxidant arsenal, comprising vitamins C and E, selenium, and other phytochemicals, serves as a formidable bulwark against the ravages of reactive oxygen species.

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INTRODUCTION

Premature hair graying (PHG) is a complex phenomenon affecting millions globally, leading to significant psychological disturbances and diminished subjective well-being. Greying of hair is a normal physiological process as the age advances, but it is considered premature when the onset of greying is before the age of 20 in fair-skinned people, 25 in Asians, and 30 in Africans as a result of familial inertance or underlying pathological conditions (1, 2, 3, 4). Unfortunately, there are no significant studies pertaining to the Indian population for age cut-off; the data published by the Indian author has considered the age cut-off of 25 years (5), hence in the present study we have considered the age range of 15-25 years. Recent research underscores the pivotal role of systemic redox balance and trace elements in maintaining hair pigmentation and overall well-being. Systemic Redox Balance and Hair Health: The delicate equilibrium between oxidative stress and antioxidant defenses is crucial for cellular homeostasis. Disruptions in this balance can precipitate oxidative damage, inflammation, and cellular senescence, compromising hair follicle health (6). Trace Elements and Hair Pigmentation: Essential trace elements, including copper, zinc, iron, and selenium, play critical roles in melanin synthesis, antioxidant enzyme function, and hair growth regulation (7). Dysregulation of trace element homeostasis has been implicated in PHG. `Despite growing insights into PHG pathophysiology, the interplay between systemic redox balance, trace elements, and PHG remains poorly understood. This knowledge gap necessitates further investigation (7). By elucidating the complex relationships between systemic redox balance, trace elements, and PHG, this research seeks to inform novel, evidence-based treatments. The present study was aimed to determine malondialdehyde (MDA), superoxide dismutase (SOD), copper, zinc, iron and calcium levels in subjects with PHG and healthy controls

MATERIALS AND METHODS

Study settings: The present comparative cross-sectional study included 40 subjects with PHG and 40 healthy controls in the age group 15-25 years, both genders, after obtaining informed consent. All methods were carried out in accordance with

relevant guidelines and regulations and all study protocols were approved by a Institutional Ethical Committee NIMS University, Jaipuri.e EC/NEW/INST/2023/773(b) and informed consent was obtained from all subjects and/or their legal guardian(s) included in the research study.

Inclusion criteria: The subjects study included 40 subjects from the Outpatient Department (OPD) of Dermatology and Venereology after taking informed consent for the participation in the study.

Exclusion criteria: Patients presenting with comorbid systemic diseases, other dermatological conditions, history of hair dye for the past 6 months, history of topical/systemic application of drugs, medications containing trace elements and antioxidants, chloroquine usage, patients with albinism, pregnant women, and lactating women were excluded from the study.

METHODOLOGY

After taking informed consent, history taking, general physical examination, and dermatological examination were done. The scalp was divided into five parts (frontal region, two temporal regions, vertex, and occipital) to determine the location of gray hair, and the severity of graying of hair was based on the hair whitening score (HWS). HWS 1 (Trace): <25%; HWS 2 (Mild): 25%-50%; HWS 3 (Moderate): 50%-75%; HWS 4 (Manifest): 75%-100%; and HWS 5 (Complete): 100%. The texture and diameter of Gray hair fibers were also evaluated (data not shown) (7, 8).

Sample collection and biochemical investigations:5 mL of random venous blood sample was collected in all the subjects; serum was separated after centrifugation and used for the estimation of MDA, SOD, copper, zinc, iron, and calcium. 2 ml of whole blood was used for the estimation of hemoglobin. MDA and SOD levels were estimated by the ELISA method using ready-to-use kits as per the manufacturer's instructions, and trace elements and calcium were estimated by the automated biochemistry analyzer Vitros 5600.

Statistical Analysis: The data were analyzed with SPSS version 22.0 (SPSS Inc., Chicago, IL, USA). We tallied the mean ± SD, as well as the number and percentage of participants. Means were compared across groups using the t-test. Statistical significance was determined at $P < 0.05$

RESULTS AND DISCUSSION

Table 1. Demographic information of Subjects

Parameters	PHG (no=40)	Healthy Controls (no=40)
Age		
15-20 years	13 (32.5%)	16 (40%)
21-25 years	27 (67.5%)	24 (60%)
Mean ± SD	21 ±2.1	21 ±1.9
Gender		
Males	20 (50%)	19 (47.5%)
Females	20 (50%)	21 (52.5%)
PHG: Premature Hair Greying		

The findings of this study underscore the critical role of systemic redox balance and trace elements in the pathogenesis of premature hair greying (PHG). The observed disruptions in systemic redox balance, characterized by elevated malondialdehyde (MDA) and decreased superoxide dismutase (SOD) and glutathione (GSH) levels, suggest increased oxidative stress in PHG patients. Table 1 represents the distribution of PHG patients and healthy controls. It is observed that 32.5% and 40% of subjects were in the age group of 15-20 years in the PHG group and healthy controls group. 67.5% and 60% of subjects were in the age group 21–25 years in the PHG group and healthy controls group. In the PHG group, there were 50% males and 50% females, and in the healthy controls group, 47.5% were males and 52.5% were females, respectively. In the present study, we did not find any gender-wise significant differences for PHG in contrast to the study conducted by Alshimaa M. El-Sheikh *et al*., which showed an increased frequency of PHG in females as compared to males. This variation found in our study may be due to the population studied and geographical differences (8). The severity of PHG was based on HWS as described earlier in the methodology. Table 2 represents the distribution of PHG subjects based on severity using HWS: 45% had mild PHG, 40% moderate, and 15% severe PHG. This finding was in accordance with the study conducted by Alshimaa M. El-Sheikh *et al*. (8). We did not find Indian studies that represent the severity of PHG. Table 3 represents the systemic redox balance. The mean levels of MDA and SOD were found to be 1.553±0.58** and 68.90±21.04** in PHG as compared to healthy controls, which were 0.66±0.58, 148.3±16.99, respectively. The elevation of MDA levels and decreased SOD levels in PHG was statistically highly significant ($p<0.001$). This indicates systemic redox imbalance in PHG subjects. This finding was similar to the study conducted by Deepashree Daulatabad *et al*. (9). In their study, the mean MDA levels found in controls as well as cases were comparatively higher as compared to our study. The reason may be the possible exclusion of more comorbidity in our study. Oxidative stress plays a pivotal role in the pathogenesis of premature hair graying (PHG). The accumulation of reactive oxygen species

Table 2. Distribution of Subjects based on Hair Whitening Score

HWS	Number (40)	Frequency
Traces (HWS1)	0	0
Mild (HWS 2)	18	45%
Moderate (HWS 3)	16	40%
Severe (HWS 4 & 5)	6	15%
HWS: Hair Whitening Score		

Table 3. Comparison of Systemic Redox Balance (MDA & SOD) in PHG and Healthy Controls

Parameters	PHG (no=40)	Healthy Controls (no=40)
MDA	3.02□0.66**	1.5□0.58
SOD	68.90□21.04**	148.3□16.99
PHG: Premature Hair Greying **: P value highly significant <0.001 *: P value significant <0.05		

Table 4. Comparison of Trace Elements (Copper, Zinc, Iron), Calcium, Hemoglobin and RBS in PHG and Healthy Controls

Parameters	PHG (no=40)	Healthy Controls (no=40)
Copper	95.58±17.8**	140.8±25.56
Zinc	0.49±0.07**	0.98±0.128
Iron	85.78±30.65**	119.8±23.5
Calcium	8.4±0.40**	9.4±0.596
Hemoglobin	12.73±0.558*	13.6±0.44
RBS	88.67±2.20	87.98±3.02
PHG: Premature Hair Greying **: P value highly significant <0.001 *: P value significant <0.05		

(ROS) and impaired antioxidant defenses disrupts the delicate balance, leading to oxidative damage to hair follicles: a) elevated malondialdehyde (MDA) levels: a marker of lipid peroxidation and oxidative stress; b) decreased superoxide dismutase (SOD) and glutathione (GSH) levels: essential antioxidant enzymes; and c) increased oxidative stress in PHG patients compared to healthy controls.The mechanisms include a) DNA damage: ROS-induced damage to hair follicle stem cells, leading to premature senescence; b) Melanogenesis impairment:* Oxidative stress disrupts melanin synthesis, resulting in hair graying; and c) Inflammation:* Oxidative stress triggers inflammation, damaging hair follicles (10, 11, 12, 13, 14, 15, 16). Additionally, decreased levels of essential trace elements, including copper, iron, calcium, and zinc, were noted. These elements play vital roles in maintaining hair pigmentation, growth, and overall health. Copper, for instance, is crucial for melanin synthesis, while zinc regulates hair growth and maintenance. The interplay between systemic redox imbalance and trace element deficiencies may exacerbate oxidative damage to hair follicles, leading to premature graying. This hypothesis is supported by: a) oxidative stress-induced damage to hair follicle stem cells. b) impaired melanogenesis due to trace element deficiencies; and c) disrupted antioxidant defenses, allowing oxidative stress to prevail. Our study's findings align with emerging evidence highlighting the importance of redox balance and trace elements in maintaining hair health. For instance, research has shown that oxidative stress contributes to hair graying, and trace element supplementation can improve hair growth and pigmentation. The clinical implications of this study are significant. Targeted interventions addressing systemic redox balance and trace element supplementation may offer novel therapeutic strategies for PHG management. Arck *et al*. (6) found a strong association between oxidative stress and mitochondrial DNA damage in graying of hair. The study conducted by Alshimaa M. El-Sheikh *et al*. (8) found significantly decreased levels of iron and calcium in PHG patients in their population. Iron plays a significant role in melanogenesis by modulating the activity of the tyrosinase enzyme, as this enzyme is required for the conversion of tyrosine to melanin, and also this enzyme requires cofactor copper for its activity; hence, deficiency of copper directly affects tyrosinase activity and thus melanin synthesis (17). There are controversial findings reported for serum copper levels in PHG patients. The study conducted by Chakrabarty *et al*., 2016 (18) and Alshimaa M. El-Sheikh *et al*. (8) reported that there was no statistically significant reduction in serum copper levels in PHG subjects. Whereas the study conducted by Naieni *et al*. (2012) (19) concluded significantly decreased levels of serum copper in PHG subjects ($p<0.001$). This finding was in accordance with our study. The study conducted by Chakrabarty *et al*. in the young Indian population in the year 2016 found decreased serum copper, calcium, and zinc levels in PHG subjects, but it was not statistically significant (18). The study conducted by Farahnaz-Fatemi Naieni *et al*. in 2011 found no significant reduction in zinc levels (19). This finding was in contrast to our study; we found significantly reduced levels of serum zinc in these patients. Similar findings were also reported by Dwi Rita Anggraini (20). Zinc is an essential trace element required for normal hair structure; it inhibits hair follicle regression and accelerates hair follicle recovery (20); hence, deficiency of zinc is one of the evident findings in patients with PHG.

Future research directions: a) Investigating the temporal relationship between systemic redox imbalance and PHG onset. b) Exploring the efficacy of antioxidant and trace element supplements in PHG treatment. c) Elucidating the molecular mechanisms underlying the interplay between systemic redox balance and trace elements in PHG.

Data Availability: Data will be provided by the corresponding author @ email id bjsushma2020@gmail.com.

Limitations of the study: Small sample size. Our study did not explore the association between trace elements levels based on the severity of PHG using HWS.

CONCLUSION

In conclusion, the intricate dance between trace elements and systemic redox balance plays a pivotal role in maintaining the youthful Vigor of our hair. Premature hair greying, once considered an inevitable fate, is now revealed to be intimately linked to the delicate balance of essential micronutrients and the body's antioxidant defences. The research unequivocally underscores the importance of trace elements such as copper, zinc, and iron in mitigating oxidative stress and preserving the melanogenic machinery. Conversely, deficiencies in these critical nutrients can disrupt the delicate redox balance, precipitating the premature descent into greyness. Moreover, the intricate interplay between systemic redox status and the hair follicle's microenvironment highlights the far-reaching consequences of oxidative imbalance. The antioxidant arsenal, comprising vitamins C and E, selenium, and other phytochemicals, serves as a formidable bulwark against the ravages of reactive oxygen species. As we continue to unravel the complexities of premature hair greying, it becomes increasingly clear that a multifaceted approach, incorporating dietary interventions, lifestyle modifications, and targeted supplementation, holds the key to revitalizing our locks and restoring the lustre of youth.By harnessing the potency of trace elements and antioxidant defences, we may yet unlock the secrets to delaying, if not preventing, the premature onset of grey hair. As we embark on this journey, we are reminded that the pursuit of vibrant health and radiant beauty is, in truth, a symphony of molecular interactions, awaiting our harmonious orchestration.

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