

# Premature Greying: Role of Vit D3, Vit B12 and S.Ferritin

B.K. Brar<sup>1</sup>, Nidhi Kamra<sup>2</sup>, Aanchal Singla<sup>4</sup>

<sup>1</sup>Professor, GGSMCH, Faridkot, India

<sup>2</sup>Assistant Professor, KCGMC, Karnal, India

<sup>3</sup>Senior Resident, GMCH, Chandigarh, India (corresponding author)

**Abstract:** Background: Canities or greying of hairs is a physiologic process that occurs with age in both men and women. A role of various nutritional deficiencies has been postulated. Aim: To determine the levels of Vit D3, Vit B12 and S. ferritin in patients with premature graying of scalp hairs. Materials and methods: A total of 60 patients with age less than 30 years and greater than 30% graying of scalp hairs were enrolled for the study. They were investigated for various parameters like S.vit D3, S.vit B12 and S. ferritin after taking informed consent. Result: The mean S.ferritin, S.Vit B12 and S.ferritin levels were significantly low in study group as compared to the control group. There was significant Vit D3 insufficiency in the study group as compared to the control group (60% versus 36.67%). Combined Vit D3 and Vit B12 deficiency was present in 13.33% of patients and triple deficiency was present in 8.33%. Conclusion: Our study suggests significant association between nutritional deficiency and canities. Due to smaller study group and observed pandemic with Vit D3 deficiency larger trials are required to validate the results.

**Keywords:** canities, ferritin levels, vit B12, vit D3

## 1. Introduction

Canities or greying of hairs is a physiologic process that occurs with age in both men and women. The average age of onset of hair graying is 34 to 44 years depending on race, with an estimated 50% of men and women being 50% gray by 50 years of age, known as '50' rule of thumb, while 50% grey hair coverage at age 50 years leads to a global range of 6-23%, according to ethnic/geographical origin and natural hair colour. However 50 rule of thumb is challenged in several studies showing at least 50% gray hair coverage at age 50 years lead to a global range of 6%–23%, according to ethnic/geographical origin and natural hair color<sup>[1]</sup>. Hairs are said to gray prematurely only if graying occurs before the age of 20 years in Whites, 25 years in Asians and 30 years in Africans<sup>[2]</sup>. Considering the important role played by hair in social communication, canities has significant adverse effects on the appearance, self-esteem, and social acceptance of the affected individual. As emphasized by the above quote, it is viewed as a sign of old age and loss of health and vigor. Hair cell pigmentation occurs due to bulbar melanocytes and from the reservoir in the outer root sheet, individual hair follicle will experience fewer than 15 melanocyte seeding, suggesting limited capacity of pigmentary reservoir. Premature canities may appear alone without any underlying pathology as an autosomal dominant condition occurring before 20 years of age<sup>[3]</sup>. It may also occur in association with certain organ-specific autoimmune disorders and environmental factors like pernicious anemia, hyper/hypothyroidism, as a part of various premature ageing syndromes (e.g. progeria and pangeria) and atopic diathesis<sup>[4]</sup><sup>[5]</sup>. The evidence for hair graying from oxidative stress has led to the investigation of premature graying as a risk factor for age related pathologies such as coronary artery disease<sup>[6]</sup>. Trace element deficiencies lead to a spectrum of the clinical manifestations especially in the skin and hair. Studies provided evidence for the role of iron in the modulation of the activity of tyrosinase. Premature graying of hair may be

a manifestation of pernicious anemia. Proliferation of cells of hair follicle are dependent on synthesis of DNA and therefore, on sufficient supply with vitamin B12.<sup>[7]</sup> Premature hair graying has also been linked to osteopenia/low bone mineral density. Calcium has also been involved in some steps of melanogenesis. In view of the above mentioned hypotheses, we conducted an investigative study to determine the levels of Serum ferritin, serum vitamin B12 and Serum vitamin D3 in patients and controls attending the out-patient department.

## 2. Materials and methods

60 patients with premature graying of hairs and 30 age and sex matched controls attending the dermatology OPD from March to September 2104 were enrolled for the study. Patients with more than 30% graying of hairs and age group less than 30 years were included in the study group. An exhaustive history and detailed examination were carried out in every patient enrolled after taking informed consent from the patients and the parents. Patients who refused to give consent to undergo investigations were excluded from the study. Blood investigations including Serum ferritin levels, Serum vitamin B12 and Serum Vitamin D3 levels were carried out in all the enrolled patients. The data was analysed by using ANOVA test and p-value was calculated between two groups. Approval from the institutional ethical committee was obtained prior to the study.

## 3. Observation and Results

The mean age of patients enrolled in our study was 17.62 years and the youngest patient was 4 years old male child. Most of the patients belonged to the age group of 11-20 years followed by 21-30 years (Table 1). Male to female ratio was 1:1 indicating no sex predilection. One of the

patient was a diagnosed case of celiac disease and one other suffered from renal carcinoma.

**Table 1:** Age distribution of patients

Age group	Percentage
<= 10 years	13.33%
11-20 years	50%
21-30 years	36.67%

The investigative characteristics of 90 patients are summarized in Table 2 and normal range has been mentioned in Table 3.

The mean S.ferritin, S.vit B12 and S.vit D3 levels were significantly low in study group as compared to the control group.( S.ferritin 13.06±9.45 versus 82.95±47.25 mg/dl, P=0.001, S.Vit B12 169.25±74.85 versus 529.533±370.469 , P=0.001, S.Vit D3 13.94±5.22 versus 37.07±11.30 , P=0.001). There was significant higher number of Vit D3 insufficient in the study group as compared to the control group (60% versus 36.67%). Combined Vit D3 and Vit B12 was present in 13.33% of patients and triple deficiency ( Vit D3+Vit B12+S.Ferritin) was present in 8.33% of patients.

**Table 2:** Comparison of S.ferritin, S.vit B12 and S.vit D3 in cases and control

	Study group	Control group	P value
S.ferritin (mg/dl)	13.06±9.45	82.95±47.25	0.001 (HS)
S. vitamin B12 (pg/ml)	169.25±74.85	529.533±370.469	0.001 (HS)
S.vit D3 (ng/ml)	13.94±5.22	37.07±11.30	0.001 (HS)

**Table 3:** Normal range of parameters

S.Vit D3		
Insufficient = 10-30ng/ml	Deficient <10ng/ml	Sufficient= 30-70ng/ml
S.Vit B12= 180-914pg/ml		
S.Ferritin		
Females=6-159ng/ml		Males=28-397ng/ml

## 4. Discussion

Premature greying of hairs is considered as a sign of old age and loss of health and vigour. As of now etiology of graying is not completely understood. Currently, it is considered to be genetic with interplay of various environmental factors.

Premature canities may appear alone without any underlying pathology as an autosomal dominant condition occurring before 20 years of age [3]. It may also occur in association with auto-immune disorders like pernicious anemia, vitiligo, hyper/hypothyroidism, and as part of various premature ageing syndromes and atopic diathesis [4].

Reversible hypopigmentation of hair has also been noticed in association with nutritional deficiencies like chronic protein loss, celiac disease and copper deficiency. [8] Serum copper levels were significantly lower in 66 patients with premature canities, as compared to normal controls in one study [4]. Binding of copper ions is essential for the activity of tyrosinase and thus the process of melanogenesis. Menkes disease, caused by mutation in the adenosine triphosphate ATP 7A and ATP 7B genes has defective copper transport, leading to usually the low level of copper in tissues [9].

Other causes implicated in causation include stress, and administration of drugs like chloroquine, phenylthiourea, the epidermal growth factor receptor inhibitor imatinib and interferon-alpha, and topically applied agents like dithranol, resorcin, prostaglandin F2 alpha analogs [10].

Oxidative stress generated outside hair follicle melanocytes, for example, by pollution, UV light, psycho-emotional or inflammatory stress, may add to this endogenous oxidative stress and overwhelm the hair follicle melanocyte antioxidant capacity resulting in enhanced terminal damage in the hair follicle [11]. Apart from oxidative stress, other factors implicated include insufficient neuroendocrine stimulation of hair follicle melanogenesis by locally synthesized agents, such as ACTH,  $\alpha$ -MSH, and  $\beta$ -endorphin [12].

Iron deficiency has also been implicated in causation of premature greying of hairs. It has been shown that iron affects melanogenesis, for example, in the rearrangement of dopachrome to 5, 6 – dihydroxyindoles and the oxidative polymerization of 5, 6 – dihydroxyindoles to melanin pigments [13]. Moreover, studies provided evidence for the role of iron in the modulation of the activity of tyrosinase (new ref). It is reported that in a tautomerization reaction by dopachrome tautomerase, which is one of the later stages of melanin biosynthesis, the isomerization of dopachrome to dihydroxyindole-2-carboxylic acid DHICA occurs. As informed by them, this enzyme is a metalloenzyme with ferrous at its active site. A case report by Sato et al of canities segmenta sideropaenica suggests the role of iron deficiency in premature greying of hairs [14].

Premature greying of hairs has been associated with pernicious anemia while B12 deficiency paradoxically causes hyper-pigmentation of skin. Possible mechanism underlying this fact is that cells of the hair follicle are rapidly dividing cells, and proliferation of the cells is dependent upon synthesis of DNA and therefore, on sufficient supply with vitamin B12 and Folic acid. Vitamin B12 stabilizes the initial anagen phase of the hair follicle and might decrease post transplantational effluvium in hair restoration surgery [15]. A study by Sonthalia et al showed association of deficiency of vitamin B12 as our study but did not show any association with ferritin levels and canities [16].

Premature hair graying is considered analogous to aging and thought to reflect the internal aging. Few studies showed premature hair graying to be an important predictor of low bone density and osteopenia [17]. Alternatively, premature hair graying has been shown to be less frequent in racial groups with higher bone density. [18] The actual pathophysiology of melanin depletion in hair follicles is unknown, although it has been shown that this trait is genetically determined, as is acquisition of bone mass. Morton *et al.* found no association between premature graying of hair and low bone mineral density. [19]. Therefore, it is reasonable to hypothesize that premature greying might be a marker for a variety of genetic and non-genetic conditions.

## 5. Conclusion

Despite the plethora of research on hair pigmentation and graying, its etiology, treatment and prevention still remains elusive. Our study suggests significant association between nutritional deficiency and canities. But due to smaller study group and observed pandemic with VitD3 deficiency larger trials are required to validate the results. Thus our study serves as a lightning bolt to constitute such trials and thence restore the hair color and lost vigere of such patients.

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