

## Serum Iron, Ferritin and Calcium Levels in Premature Canities

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### Abstract

**Background:** Premature canities is defined as a minimum of five gray hairs present in a person less than 20 years of age. Etiologically, it is genetically mediated or may be associated with autoimmune syndromes. Few studies have found an association of decreased levels of trace elements with early canities, however the scientific evidence for the same is lacking.

**Aims and objectives:** of this study were to evaluate the relationship of serum iron, ferritin and calcium concentrations with premature canities.

**Material and methods:** This was a hospital based case-control cross-sectional study in which 50 patients aged less than 20 years with premature canities were studied. Age and sex matched 50 subjects with other mild skin ailments but no canities were taken as controls. A detailed history, thorough examination and lab investigations were carried out in all the patients and controls after taking informed consent. The severity of canities was graded as: mild (up to 50), moderate (50-100) and severe (more than 100 gray hairs).

**Results:** Seventeen patients (34%) had mild disease, 30 patients (60%) had moderate disease and 3 patients (6%) had severe disease. The mean age of onset was about 2 years earlier than mean age of presentation. Female-male ratio was 1.38:1. Positive family history was present in 31 patients (62%). The mean levels of serum iron, ferritin and calcium were statistically significantly low in patients when compared to controls.

**Conclusion:** The significantly low levels of these trace elements in our patients with premature canities support the fact that their supplementation might prevent the progression of canities. However, large scale studies are needed to substantiate these observations.

**Keywords:** Canities; Gray hair; Serum iron; Ferritin; Calcium

### Introduction

Canities or graying of hair is a regular feature of chronological ageing that occurs in all regions and races. Genetic constitution of an individual determines the rate at which the hair turns gray. In men, graying usually begins at the sides, while as in women it starts at the perimeter of the hairline. It then progresses through the vertex, sides, and back of the hair [1,2]. Premature graying of hair is defined as having a minimum of five gray hairs in a person less than 20 years of age. Premature canities may occur without any underlying cause with autosomal dominant inheritance. Canities has also been associated with a number of autoimmune disorders such as vitiligo, pernicious anemia, and autoimmune thyroid disease and some premature ageing syndromes such as Werner's syndrome [3]. Environmental factors and nutritional deficiencies also play a role. Few studies have found a decreased level of serum copper to be associated with premature canities, while as other studies have found a deficiency of serum calcium, ferritin and vitamin D3 to be associated with premature canities [4,5]. In this study we have made an attempt to study the relationship of serum iron, ferritin and calcium with premature canities.

### Material and Methods

This cross-sectional study was undertaken in the department of dermatology and biochemistry, from Jan 2014 to Dec 2015 after taking institutional ethical clearance. A total of 50 ethnic Kashmiri patients with more than 5 gray hairs under the age of 20 years of either sex were enrolled for study. Age and sex matched 50 controls with other mild skin ailments but no canities were taken as controls. Informed consent was taken from both cases and controls. Patients as well as controls on dietary supplements in the past three months and those with comorbid conditions like thyroid disease, vitiligo, atopy and malabsorption were excluded. The severity of canities was graded as: mild (up to 50), moderate (50-100), and severe (more than 100 gray hairs).

An elaborate history was taken from the patients on a proforma including age of presentation and age of onset of canities, sex, socio-economic status, residence, family history, comorbid disease, hair care practices, diet, smoking and medication use. It was followed by thorough systemic and cutaneous examination.

### Procedure for trace element estimation

Blood samples were taken from both cases as well as controls and samples were immediately processed by centrifugation (4000 rpm) at room temperature.

**Iron estimation:** Plasma iron was measured by Ferene-S kit/method (Abbot laboratories Inc.USA), and analyzed on Automatic Analyzer (ARCHITECTc 4000). The iron forms with Ferene-S, a stable colored complex of which the color intensity is proportional to the amount of iron in the sample.

**Ferritin estimation:** Serum ferritin levels were measured by Chemiluminescent Microparticle Immunoassay kit/method (Abbot laboratories Inc.USA) and analyzed on Automatic Analyzer (ARCHITECTi 1000). The ARCHITECT Ferritin assay is a two-step immunoassay. The sample and anti-ferritin coated paramagnetic microparticles are combined in the first step. After washing, anti-ferritin

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acridinium labelled conjugate is added in the second step. Pre-trigger and trigger solutions are then added, the resulting Chemiluminescent reaction is measured as relative light units (RLU).

**Calcium estimation:** Plasma calcium was measured by ArsenazoIII kit/ method (Abbot Laboratories Inc.USA), and analyzed on Automatic Analyzer (ARCHITECTc 4000). ArsenazoIII dye reacts with calcium in an acidic solution to form blue-purple complex. The color developed is measured at 660 nm and is proportional to the concentration of calcium in the sample. The mean of the levels of the above trace elements of cases and controls were calculated. After tabulation of the data, the results were analysed for statistical significance by using unpaired t- test.

## Results

The age of the patients ranged from 3-19 years. The mean age of onset was about 2 years earlier than mean age of presentation. The female-male ratio was 1.38:1 (Table 1). Thirty one patients had positive family history with 18 having it in both first and second degree relation whereas 13 had it in first degree relatives only. The socio-economic and demographic profile of patients is given in (Table 2). The control group didn't differ much from patients in these parameters. Majority of the patients and controls were of average build with BMI in the normal range. Only two patients were smokers. Thirty patients had the history of oil application and two patients used hair dye.

Seventeen patients (34%) had mild disease, 30 (60%) had moderate disease and 3 (6%) had severe disease. Sixty four percent patients belonged to the age group of 16-20 years. The mean level of serum iron was  $78.42 \pm 30.16$  mcg/dl as compared to  $106.32 \pm 32.53$  mcg/dl in controls which is significant; serum ferritin in cases was  $63.290 \pm 28.13$  ng/dl ( $117.00 \pm 43.21$  ng/dl in controls), hence a significant difference. The mean serum calcium level was low in cases ( $9 \pm 0.50$  mg/dl) as compared to controls ( $9.52 \pm 0.68$ ) (Table 3). However, no correlation of mean trace element levels was seen with the severity of canities in our patients.

## Discussion

The biochemical aspect of human hair pigmentation was reviewed by Ortonne and Prota [6]. Premature graying of hair or canities occurs more commonly without any underlying cause but is said to be inherited as autosomal dominant trait. Premature graying has been shown to be associated with various autoimmune disorders with environmental

Age group (years)	Males	Females	Total
1-5	1	-	1
6-10	1	2	3
11-15	6	8	14
16-20	13	19	32

Table 1: Age and Sex distribution of patients.

Socio-economic status	Rural	Urban	Total
Below average	12	6	18
Average	9	11	20
Good	4	8	12
Total	19	31	50

Table 2: Demographic profile of patients.

Trace element	Cases	Controls	p value
Sr Iron (mcg/dl)	$78.42 \pm 30.16$	$106.32 \pm 32.53$	<0.001
SrFerritin (ng/dl)	$63.29 \pm 28.13$	$97.08 \pm 33.21$	<0.005
SrCalcium (mg/dl)	$9.0 \pm 0.50$	$9.52 \pm 0.68$	<0.001

Table 3: Mean level of trace elements in cases and controls with significance.

factors and nutritional deficiencies also playing a role [7]. The color of hair depends on the presence or absence of melanin pigment. Skin and hair melanins are formed in cytoplasmic organelles called melanosomes, produced by the melanocytes, and are the product of a complex biochemical pathway (melanogenesis) with tyrosinase being the rate-limiting enzyme. The activity and number of active in the hair bulb of anagen hair follicles are reduced with resultant pigment loss in canities. Defective melanosomal transfer to cortical keratinocytes and melanin incontinence due to melanocyte degeneration also contribute [4]. The graying of hair is usually progressive and permanent, but there are occasional reports of spontaneous repigmentation of grey hair [8,9]. Cytokines in the hair bulb area may also be involved in the development of premature canities [10]. Environmental factors such as ultraviolet light, climate, smoking, drugs, trace elements, and nutritional deficiencies all play a role in the pathogenesis of canities [11]. Trace element deficiencies lead to a spectrum of the clinical manifestations especially in skin and hair. Kruglugeret et al. hypothesized that iron and vitamin B12 affect hair growth and pigmentation [12] whereas Rosen et al. hypothesized that premature graying is associated with osteopenia indicating a probable role for vitamin D3 and calcium deficiencies in the pathogenesis of premature graying [13]. Deficiency in trace metal ions may also lead to hypopigmentation. Tyrosinase enzyme in melanocytes requires copper ion to maintain normal color [14]. Iron deficiency may also result in pigmentation abnormality. Premature graying of hair may be a manifestation of pernicious anemia [15]. Calcium is also involved in some steps of melanogenesis. Fatemi et al. in their study of serum iron, zinc and copper concentrations in premature canities observed a low serum copper concentration and normal levels of serum iron and zinc [16]. In our study we observed a significantly low concentration of serum iron, ferritin and calcium in patients with premature canities. Other studies have also shown significantly lower concentrations of serum ferritin and calcium in premature canities [17]. Our study had some limitations in the form of less number of patients and lack of supplementation with the trace elements in these patients to see the therapeutic response.

## Conclusion

Since the serum levels of iron, ferritin and calcium have been found to be significantly low in our patients with premature canities, supplementation with these trace elements might reverse and is expected to prevent the progression of canities in which the treatment options are limited. However, large scale studies are needed to substantiate these observations.

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