Serum ferritin and vitamin D levels in premature hair graying of college student at the Universitas Sumatera Utara area

D R Anggraini1*, L Feriyawati1, and Hidayat2
1Department of Anatomy, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia
2Department of Biochemistry, Faculty of medicine, Universitas Sumatera Utara, Medan, Indonesia
*Email: dwirita@usu.ac.id

Abstract. Premature hair graying (PHG) is defined as a person has five gray hairs and < 25 years old in Asia. Although genetic factors associated with PHG, environmental factors and micronutrient deficiencies are risk factors of PHG. This study was designed to evaluate serum ferritin and vitamin D levels in PHG of young adult at the Universitas Sumatera Utara (USU) area. We conducted a cross-sectional study recruited 100 respondents with the inclusion criteria: male sex, < 25 years old, have PHG and does not have skin pigmentation disorders. The data were collected by questionnaires including age, location of graying, and number of gray hairs. The blood samples were collected to assess serum ferritin and vitamin D levels by Elisa methods. The mean age was 20.09 ± 2.01 years (mean ± SD). Distribution pattern of gray reported diffuse or undefined (35%), followed by the parietal regions (31%), frontal, occipital and temporal was 6%, 5% and 2% respectively. The majority of cases decreased of vitamin D level was 77% and normal status was 23% of cases, whereas serum ferritin level showed 91% was normal status, 6% was low and 3% was high of cases. There was not significant difference between number of graying with serum ferritin and vitamin D levels were p=0.633 and p=0.191 respectively. Limitation of the study female sex not evaluated. The vitamin D deficiency associated with PHG was found of college student at USU area.

1. Introduction
Hair colour contribute in visual appearance and self-perception [1,2]. Gray hair is one of the prominent signs of aging, usually occurring in the fourth decade of life regardless of sex, but the age at onset varies from one person to the next varies in different races; age 43.9 ± 10.3 years in Africans, 34.2 ± 9.6 years in Whites and between the ages of 30-39 years in the Japanese population [3]. Premature hair graying (PHG) is defined if graying begins before the usual age of onset, varies with race and ethnicity. In Asia, the hair has been considered to gray prematurely if occurs before 25 years old [4].

Although the genetic factor is primary cause of PHG, many factors contribute such as environmental and nutritional deficiencies. Micronutrient deficiencies such as ferritin, calcium and vitamin D may also be associated with PHG. Deficiency states of micronutrient lead to a broad spectrum of the clinical manifestations especially in skin and hair caused pigmented changes and hair loss [5,6].

Previously, the studies about the association of PHG with micronutrient deficiencies had been done by another researchers. Shontalia et al reported low level of vitamin B12 and hypothyroidism...
significant association with PHG of North India [3]. Another study in India have found decreased of serum ferritin levels in male (P=0.001) and female (P = 0.014), vitamin B12, and HDL-C in young adult associated with PHG [5]. Bath, et al reported ferritin and vitamin D3 levels were low in adolescent of the semi-urban area in India patients with PHG [4], while as other studies showed deficiency of serum iron, ferritin and calcium levels affected with graying [7].

The information about the studies of epidemiology and investigated of PHG reported in Indonesia, especially in the Universitas Sumatera Utara (USU), Medan is still less or unidentified. The present study was designed to evaluate the status of serum ferritin and vitamin D of college student at the USU area with premature hair graying.

2. Materials and methods
We conducted a cross-sectional study recruited 100 participants of the college student at the USU area such as Faculty of Medicine, Dentistry, Engineering, Public Health, Mathematics and Natural Science, Agriculture and Politeknik Negeri Medan. The sample in this study should the inclusion criteria of male, the age less than 25 years, have premature hair graying and does not have skin pigmentation disorders. The protocol of this study has been approved by Medical Ethics Committee Universitas Sumatera Utara.

The data were collected by self-reports using questionnaires consist of characteristic sample including age, location of graying, and number of gray hairs. The number of gray hairs was classified less than 10 and more than 100 hairs. The blood samples were collected from antecubital vein as much as 3 ml to assess serum ferritin and vitamin D levels.

2.1. Measurement of serum ferritin
Ferritin level from the blood sample is determined by ELISA with Ferritin kit manufacturing by DBC (Diagnostics Biochem Canada Inc.). Ferritin level of healthy normal males and females range 25-283ng/mL.

2.2. Measurement of vitamin D
The 25-hydroxyvitamin D Elisa for the quantitative determination of 25-hydroxyvitamin D in human serum and plasma by enzyme immunoassay. The 25(OH)D kit manufacturing by DBC (Diagnostics Biochem Canada Inc.). Another source reports the following threshold level (ng/mL):

- <19 : deficiency state
- 20-50 : normal in the healthy
- 51-80 : increased risk of hypercalciuria
- >80 : toxicity

2.3. Statistical Analysis
The mean, standard deviation (SD), number and percentage of samples were tabulated. We analyzed with Chi-Square Tests, *P < 0.05 were considered significant.

3. Results and discussions
3.1. Characteristic samples
This study included 100 participants of PHG with age was 20.09±2.01 (mean ± SD). The earliest age onset of graying was 9 years. The distribution of age with range 20-22 years (44%) was similar to that of the 17-19 years age group (43%) (Fig.1).
In this study, the first strands of graying reported diffuse or undefined (35%), followed by the parietal regions (31%), the frontal, occipital and temporal was 6%, 5% and 2% respectively. The majority number of gray hairs ≤ 100 was 84% and > 100 hairs was 16% of cases (table 1).

| Location of PHG | Number (n=100) | Percentage (%) |
|-----------------|----------------|----------------|
| Frontal         | 6              | 6              |
| Parietal        | 31             | 31             |
| Temporal        | 2              | 2              |
| Occipital       | 5              | 5              |
| > one location   | 21             | 21             |
| Diffuse         | 35             | 35             |

| The number of gray hairs | Number (n=100) | Percentage (%) |
|--------------------------|----------------|----------------|
| ≤ 100                    | 84             | 84             |
| > 100                    | 16             | 16             |

Even physiological are different distribution pattern of graying hair based on sex. In male tends to begin from the temporal and sideburn areas, while in female from the scalp margins. Daulatabad et al. reported that frontal involvement more than temporal and hypothesized that premature hair graying may represent an entity distinct from chronological graying [8]. However, another study reported the racial variation may be an important role in the different pattern.

We found that some clinical features of PHG in USU were parietal areas more commonly involved than another areas. This study accordance with study Jo et al showed initially involved scalp regions were also different depending on onset-age; in early-onset group (<40 years) the parietal or occipital area was more involved whereas in late-onset group (>40 years) initially the frontal area was more involved. Early onset did not mean faster progress. In contrast, the level of grayness streakly increased after the fifth decade regardless of age at onset [9].

### 3.2. Level of serum ferritin and vitamin D

The mean serum ferritin and vitamin D levels are summarized in Table 2. The majority of sample have found decreased vitamin D level were 77% of cases and 23% of cases in normal status, whereas serum ferritin level showed 91% was normal status, 6% was low and 3% was high of cases. There was not significant difference between number of graying hairs with serum ferritin and vitamin D levels were $p=0.633$ and $p=0.191$ respectively.
The level of serum ferritin reflects iron stores in the body since ferrous iron combined with apoferritin is stored by ferritin in many organisms. Deficiency levels of serum ferritin are associated with several disorders such as telogen effluvium, iron deficiency anemia (IDA), and bone mineral density [10]. Pigmentation abnormality may also affected with iron deficiency and manifestation of pernicious anemia [7]. In the literature, main function of vitamin D contributed to be controlling the calcium levels and bone metabolism, but it also plays a role in the proliferation and differentiation of keratinocytes has been extensively studied and well reviewed in the previous studies [11].

The melanin pigment was essential substance to color of hair and skin produced by melanocytes in the organella cytoplasm called melanosomes. It is of a complex biochemical pathway (melanogenesis) with tyrosinase being the rate-limiting enzyme. The resultant pigment loss in graying hair depends on the presence or absence activity and number of anagen hair follicles in hair bulbs [12].

Kruglugeret et al. reported that iron and vitamin B12 contribute hair growth and pigmentation [13] whereas another study reported that premature graying associated with vitamin D3 and calcium deficiencies [14]. Deficiency in trace metal ions may also caused hypopigmentation. Tyrosinase enzyme in melanocytes requires copper ion to maintain normal color of hair [7]. Bath et al. reported a significant low concentration of serum iron, ferritin and calcium with premature graying [7]. Other study have also shown decreased level of serum ferritin and calcium were significant [4]. This study showed low concentration of vitamin D in premature graying suggested that intake the source of vitamin D is still less in this population. Our study had some limitations, the young female not evaluated in this study.

4. Conclusion

This study showed low level of vitamin D but normal status serum ferritin in premature hair graying of the Universitas Sumatera Utara area. However, further studies large scale and female sex are needed to substantiate these observations.

Acknowledgement

The authors gratefully acknowledge to the Universitas Sumatera Utara for supporting this study.

References

[1] Trueb RM. 2005 Aging of hair J Cosmet Dermatol 4 60-72
[2] Tobin DJ, Paus R 2001 Graying: Gerontobiology of the hair follicle pigmentary unit Exp Gerontol 36 29–54
[3] Sonthalia S, Priya A, Tobin DJ 2017 Demographic Characteristics and Association of Serum Vitamin B12, Ferritin and Thyroid Function with Premature Canities in Indian Patients from an Urban Skin Clinic of North India: A Retrospective Analysis of 71 Cases Indian J Dermatol 62(3) 304-308
[4] Bhat RM, Sharma R, Pinto AC, Dandekeri S, Martis J 2013 Epidemiological and investigative study of premature graying of hair in higher secondary and pre-university school children. Int J Trichology 5 17–21
[5] Chakrabarty S, Krishnappa PG, Gowda DG and Hiremath J 2016 Factors Associated with Premature Hair Graying in a Young Indian Population Int J Trichology 8 (1) 11–14
[6] Heath ML, Sidbury R. 2006. Cutaneous manifestations of nutritional deficiency Curr Opin Pediatr 18 417–22
[7] Bhat YJ, Hassan I, Sajad P, Malik R, Majid S, Mubashir S and Latief I 2013 Serum Iron,

| Table 2. Serum ferritin and vitamin D levels |
|---------------------------------------------|
| Category | Hypo (%) | Normal (%) | Hyper (%) | Mean ± SD |
|------------|-----------|-------------|-----------|-----------|
| Ferritin   | 6         | 91          | 3         | 71.26 ± 66.99 |
| 25(OH)D    | 77        | 23          | 0         | 16.16 ± 6.77 |
Ferritin and Calcium Levels in Premature Canities *Hair Ther Transplant* 6 (1) 1-3

[8] Daulatabad D, Singal A, Grover C, Chhillar N 2016 Profile of Indian patients with premature canities *Indian J Dermatol Venereol Leprol* 82 169–72

[9] Jo SJ, Paik SH, Choi JW, Lee JH, Cho S, Kim KH, et al. 2012 Hair graying pattern depends on gender, onset age and smoking habits *Acta Derm Venereol* 92 160–1. [PubMed]

[10] Cook JD, Flowers CH, Skikne BS 2003 The quantitative assessment of body iron *Blood* 101 3359–3364.

[11] Lehmann B 2009 Role of vitamin D3 pathway in healthy and diseased skin-facts, contradictions, and hypotheses *Exp Dermatol* 18 97-108 [PubMed]

[12] Commo S, Gaillard O, Bernard BA 2004 Human hair graying is linked to a specific depletion of hair follicle melanocytes affecting both the bulb and the outer root sheath *Br J Dermatol* 150 435-43.

[13] Krugluger W, Stiefsohn K, Laciak K 2011 Vit B 12 activates wnt pathway in human hair follicle by induction of β catenin and inhibition of glycogen synthase kinase 3 transcription. *J Cosmet, Dermatol Sci Appl* 1 25-29

[14] Rosen CJ, Holick MF, Millard PS 1994 Premature graying of hair is a risk marker for osteopenia. *J Clin Endocrinol Metab* 79 854-857