

Association between the Levels of Ferrum, Zinc and Copper Serum and Premature Canities

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Abstract: Graying hair that occurs at earlier age is referred as premature canities and it thought caused by genetics with the interaction of any various factors. Premature canities also associated with a variety of pathological conditions such as mineral deficiencies. Few studies have reported the association of premature canities and trace elements serum such as ferrum (Fe), zinc (Zn) and copper (Cu) level. To assessed the association of Fe, Zn and Cu serum level and premature canities. This is an analytic study to assess the association between the levels of Fe, Zn and Cu serum and premature canities with cross-sectional designed in 31 case subjects and 31 controls. Diagnosis based on anamnesis and clinical examination and the blood samples were collected. The Mann Whitney test used to assess the difference between Fe serum level. The t-independent test used to assessed the difference between Zn and Cu serum level. There was a significant correlation between Zn serum and premature canities ($p < 0.05$), there was no significant correlation between Fe and Cu serum with premature canities ($p > 0.05$). There was a significant difference between Zn and Cu serum levels of the premature canities group compared to controls group ($p < 0.05$), there was no significant difference between Fe serum premature canities group compared to controls group ($p < 0.05$). There was a significant association between zinc serum level and premature canities, there was no association between ferrum and copper serum levels and premature canities.

1 INTRODUCTION

Hair is a complex structure of keratinized epithelial cells and acts as the most effective protector of scalp from sunlight exposure.(Mistry et al., 2010) The appearance of hair plays an important role in social communication, where premature gray hair has a significant impact on appearance.(Trüeb, 2006) Graying hair that occurs at an earlier age is referred to as premature canities. It is primarily thought to be caused by genetic with interactions of various environmental factors.(Trueb, 2005; Tobin, 2008; Pandhi and Khanna, 2013) Premature canities may also appear alone without underlying pathology as an autosomal dominant condition.(Slominski et al., 2005) Premature canities is diagnosed if graying hair appears before the age of 20 in Caucasians, 25 in Asians, and 30 in Africans. Although graying hair is understood as a loss of pigment in the hair shaft, to date, the exact cause of premature canities is not fully understood.(Wasitaatmadja, 2014; Sonthalia and Sarkar, 2018)

Premature canities is also associated with a variety of pathological conditions including vitamin and mineral deficiencies.(Pandhi and Khanna, 2013) Trace elements deficiency causes a spectrum of clinical manifestations especially on the skin and hair. From several studies it is known that there is a associations between the levels of ferrum, zinc and cuprum serum with premature canities where trace elements play a role in the process of melanogenesis.(Fatemi Naieni et al., 2012) Although extensive molecular research continues to be undertaken to understand the pathogenesis of premature canities, treatment options remain far from satisfactory and no effective therapy is available. Some oral therapies have been tried with inconsistent results so that despite recent studies have been published, therapy and prevention remain elusive.(Wasitaatmadja, 2014; Pandhi and Khanna, 2013; Sonthalia and Sarkar, 2018)

2 METHODS

This study is a analytic study to assessed the association between the levels of trace elements iron, zinc and copper serum and premature canities with cross-sectional designed in 31 subjects of premature canities and 31 controls. Diagnosis of premature canities based on anamnesis and clinical examination. The target population was male and female subjects who had premature canities and non-premature canities between the ages of 15-39 years at Faculty of Medicine, University of Sumatera Utara Medan and Adam Malik General Hospital Medan, were examined in March 2017 to August 2017 involved 62 participants, with the total sample are 31 subjects of canities premature and 31 controls. Samples were taken using consecutive sampling method. Exclusion criteria were subjects with premature aging syndrome, subjects with hipomelanosis hair disorder, subjects with poliosis, and subjects who had premature canities with psychiatric disorders (anxiety and depression).

Diagnosis of premature canities was made based on clinical examination of hair and calculation the number of gray hairs. Severity degree of premature canities defined in the form of mild canities (≤ 50 sheets of gray hair), medium canities (51-100 sheets of gray hair) and severe canities (>100 sheets of gray hair) with a minimum of 5 gray hairs. Blood sample was collected to examine the levels of ferrum, zinc and ferrum serum subjects of premature canities and controls group.

The characteristic of subjects were analyzed descriptively and presented in the form of frequency distribution. The Mann Whitney test used to assess the difference between trace elements of ferrum serum level. The t-independent test used to assessed the difference between trace elements of zinc and copper serum level and the results were significant at level $P < 0.05$.

3 RESULTS

Characteristics of premature canities group and controls group were assessed by age, sex, duration of illness and severity degree of premature canities. Based on subject characteristics, the mean age of 62 subjects (31 subjects with premature canities and 31 controls) was 27 years. The predominant age distribution in premature canities group was found over 27 years (57.6%) whereas the predominant in the controls group were less than 27 years (58.6%). Based on gender, the majority of subjects premature canities mostly were men (59.3%) whereas in the controls group the majority of subjects were women (57.1%). Classification based on duration of premature canities, subjects of premature canities group were mostly in the range 5-10 years (51.6%), >10 years (35.5%) and the lowest percentage in the range < 5 years (12.9%). Based on the severity degree of premature canities, the most commonly found with mild canities (64.5%) moderate premature canities (19.4%) and severe premature canities (16.1%) is the lowest from total of 31 subjects of premature canities.

Based on the correlations between the levels of trace elements ferrum, zinc and cuprum serum with premature canities, the levels of Ferrum (Fe) serum in premature canities group was at normal range (51.9%) while in the controls group the levels of Fe serum were under normal limits (60.0%). Zinc (Zn) serum levels in premature canities group were under normal limits (90.0%) while in the controls group the levels of Zn serum were at normal range (57.7%). Copper (Cu) serum levels in premature canities group at normal range (53.4%) while in the controls group the levels of Cu were under normal limits (46.6%). It was found that there was a significant correlations between Zn serum and premature canities ($p < 0.05$) but there was no significant correlation between Fe and Cu serum levels with incidence of premature canities ($p > 0.05$). (Table 1).

Table 1. The association between the levels of trace elements serum and premature canities

Serum Levels	Premature canities		Controls		Total		P-value
	n	%	n	%	n	%	
Ferrum (Fe)							
Normal	2	51.9%	25	48.1%	5	100.0%	
Abnormal	7				2		
	4	40.0%	6	60.0%	1	100.0%	0.366
Total	3	50.0%	31	50.0%	6	100.0%	
	1				2		

Zinc (Zn)							
Normal	2	42.3%	30	57.7%	5	100.0%	
	2				2		
Abnormal	9	90.0%	1	10.0%	1	100.0%	0.006
	0				0		
Total	3	50.0%	31	50.0%	6	100.0%	
	1				2		
Copper (Cu)							
Normal	3	53.4%	27	46.6%	5	100.0%	
	1				8		
Abnormal	0	00.0%	4	100.0%	4	100.0%	0.056
	0				0		
Total	3	50.0%	31	50.0%	6	100.0%	
	1				2		

Table 2. Comparison the levels of trace elements serum of premature canities and controls

Trace elements	Mean	Median	SD	p-value
Ferrum (Fe)				
Premature canities	115.35	105.00	± 49.61	0,499
Controls	121.23	118.00	± 55.84	
Zinc (Zn)				
Premature canities	65.16	65.00	± 11.16	0.000
Controls	78.23	75.00	± 14.23	
Copper (Cu)				
Premature canities	1,029.26	1,030.00	± 120.89	0,006
Controls	1,191.19	1,158.00	+ 290.93	

Comparison of the levels of trace elements ferrum (Fe) serum between of premature canities groups and controls group, it was found that the mean levels Fe serum are lower (115.35 ± 49.61) compared to the controls group (121.23 ± 55.84). However, in hypothesis test using Mann Whitney test, there was no significant correlation between Fe serum of premature canities group compared to controls group ($P > 0.05$). Meanwhile levels of trace elements zinc (Zn) serum (65.16 ± 11.6) and copper (Cu) serum ($1,029.26 \pm 120.89$) between of premature canities groups are lower compared to the controls group. Based on the hypothesis test by using independent t test, it showed that there was a significant difference between the concentration of zinc and cuprum serum levels between of the premature canities group compared to the controls group ($P < 0.05$). (Table 2)

4 DISCUSSION

In this study, it was found that the characteristics of subjects with premature canities based on age range were found that the majority within the age group are more than 27 years (57.6%). Based on the

research of the sample data, in this study the earliest onset subject of premature canities is 9 years. The results of this study different from the results of previous studies conducted by Chakrabarty et al where the age subject of premature canities were 22 years.(Chakrabarty et al., 2016) Based on gender, in this study the majority of subjects with premature canities were men (59.3%). This results is different from study conducted by Bhat et al assessed the characteristics profile of subjects with premature canities shows ratio between male and female is 1: 1 indicating no sex predilection.(Bhat et al., 2013) Another study by Hyoseung et al in Korea who assessed the association between premature canities with family history and lifestyle also give the same results where there is no sex predilection.(Shin et al., 2015)

Based on duration of illness, subjects had premature canities in this study were mostly within duration 5-10 years (51.6%), this results is different from previous studies conducted by Bhat et al shows that the average duration of premature canities were less than 5 years.(Bhat et al., 2013) Meanwhile, the results of previous studies by Deepasheree et al where the duration of premature canities were more

than 10 years where the earliest age onset of premature canities in this study was 3 years. (Deepasree and Aschana, 2016) Based on the severity degree of premature canities, in this study the most commonly found was with mild canities (64.5%). The results of this study different from the results of previous studies by Bhat et al, where the most common severity degree of premature canities was moderate canities.(Bhat et al., 2013)

Few studies have reported the association of premature canities and trace elements serum such as iron, zinc and copper level. From several studies it is also known that there is a relationship between Fe, Zn and Cu concentration with premature canitis where trace elements play a role in melanogenesis process.¹⁰ There are two types of pigments that plays a role in melanogenesis namely as eumelanin and pheomelanin. In the oxidative reaction, tyrosine is converted to 3,4- dihydroxyphenylalanine (DOPA), where both pigments originate. One of the most important enzymes in oxidative reactions is tyrosinase in which copper ions are required for the activity of tyrosinase enzymes. Ferrum and zinc ions also play a role in melanogenesis, as in the preparation of dopachrome to 5,6-dihydroxyindoles and oxidative polymerization of 5,6-dihydroxyindoles to melanin pigments. Trace elements deficiencies causes a spectrum of clinical manifestations especially on the skin and hair. Low levels of trace elements in serum have been demonstrated in several studies related to premature canities conditions.(Slominski et al., 2005; Fatemi Naieni et al., 2012; Pandhi and Khanna, 2013)

In this study, based on the the association between of trace elements ferrum, zinc and cuprum serum with premature canities, the mean level of Zn serum were significantly lower in the premature canitis group than in the controls group, indicated that there was an association between low zinc serum level and premature canities. Meanwhile there was no statistically significant associated between trace elements ferrum and cuprum serum with premature canities.

The results in this study were different from a study conducted by Fatemi et al assessed the association between Fe, Zn and Cu serum concentrations with premature canities, where the mean level of Fe serum were significantly higher in the case group than in the control group.¹⁰In another study by Chakrabarty et al found that low ferritin serum levels were significantly associated with premature canities, and no significant differences in serum Zn and Cu concentrations were found in both case and control groups.(Chakrabarty et al., 2016)

Comparison of levels of trace elements ferrum, zinc and copper serum between the group of premature canitis and controls, the mean levels of Zn and Cu serum in the premature canities group was lower than in the controls group. The results of this study different from the results of a study conducted by Fatemi et al, assessed the association between Fe, Zn and Cu serum levels with premature canitis which found no difference in mean levels of Zn levels either in the case group or in the controls group.(Fatemi Naieni et al., 2012)

5 CONCLUSIONS

There was a significant association between trace elements zinc serum level and premature canities, but there was no association were found between trace elements ferrum and copper serum levels and premature canities.

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