

Relationship between ionized calcium and serum albumin level in children with idiopathic nephrotic syndrome

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Abstract

Background Nephrotic syndrome (NS) patients frequently have abnormalities in calcium metabolism that manifest as hypocalcemia and reduced intestinal absorption of calcium. Hypocalcemia is initially attributed to hypoalbuminemia but it may also relate to a low level of ionized calcium. The ionized calcium level depends on the severity and duration of proteinuria.

Objective To assess the relationship between ionized calcium and serum albumin level in idiopathic NS children.

Methods An analytical study with cross-sectional design was applied to NS and healthy children between 1-14 years old in the Child Health Department of Hasan Sadikin Hospital, Bandung from December 2009 to April 2010. Ionized calcium was examined by Ca²⁺ analyzer AVL 980 with ion-selective electrodes (ISE) methods.

Results A total of 34 subjects were recruited, consist of 17 NS and 17 healthy children. The mean ionized calcium and serum albumin level in NS children was 4.56 (SD 0.23) mg/dL and 1.45 (SD 0.24) g/dL, respectively. Statistical difference between ionized calcium level in NS and in healthy children was significant ($P < 0.05$). Pearson correlation test between ionized calcium and serum albumin was significant ($P < 0.05$) with correlation coefficient (r) 0.53. We found the following equation to estimate ionized calcium (\hat{y}) based on the serum albumin level (x): $\hat{y} = 3.84 + 0.49x$.

Conclusion There is a moderately positive linear relationship between ionized calcium and serum albumin level in NS children. [Paediatr Indones. 2010;50:361-4].

Keywords: nephrotic syndrome, ionized calcium, serum albumin

Nephrotic syndrome (NS) is a pathological entity characterized by massive proteinuria and hypoalbuminemia. It is a chronic disease indicated by remission and relapse. Its prognostic varies according to histopathology and the clinical symptoms.^{1,2} Ponco³ reported 129 NS cases during 4.5 years in the Child Health Department of Hasan Sadikin General Hospital, Bandung with an average age of 6 years 2 months.

One of the proteins that lost from the body into urine along with albumin is vitamin D binding protein. Calcium absorption in intestine depends on vitamin D.² Hypocalcemia in NS is initially attributed to hypoalbuminemia but many also have low ionized calcium levels.⁴ Total calcium in human body is in three forms, which is ionized, bound to protein, and complexed with anions. They are in equilibrium each other. Only the ionized calcium has been reported to be physiologically active. If the ionized calcium level declines below normal, nervous system progressively becomes more sensitive and provokes clinical

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symptoms.⁵

A previous study showed that there was a negative and weak relationship between ionized calcium and serum albumin level in NS children.⁶ The purpose of this study is to evaluate that relationship in children with idiopathic NS.

Methods

An analytical study with cross-sectional design had been conducted between December 2009 and April 2010 in the Child Health Department of Hasan Sadikin General Hospital Bandung. Subjects consisted of NS children and healthy children. Inclusion criteria for NS children were active NS (first diagnose or relapse), aged between 1-14 years. Healthy children with the same age and sex as NS children were recruited as a control group. The criteria of healthy was based on to the Indonesian law, which is state of health including the body (physical), spiritual (mental), and social, and not limited to a state free from disease, disability, and weakness. Exclusion criteria for NS and healthy children were those who had taken calcium supplements 8-12 hours before the study, were receiving blood transfusion, had liver abnormalities and acid-base disorder, or had history of severe malnutrition.

History taking and physical examination were performed by the doctor to all eligible subjects. Blood was taken from both healthy and NS children. Ionized calcium level, serum albumin level, serum glutamic oxaloacetic transaminase (SGOT), and serum glutamic

pyruvic transaminase (SGPT) were measured in NS children. The healthy children were only performed ionized calcium level. Ionized calcium was examined by Ca^{2+} analyzer AVL 980 models⁷ in the laboratory of Clinical Pathology of the Hasan Sadikin Hospital. Laboratory method used for measuring the concentration of ionized calcium was ISE.⁷

Written informed consents were obtained from the parent of each patient before participating in this study. This study had been approved by the Ethical Committee of Medical Faculty of Padjadjaran University, Hasan Sadikin General Hospital, Bandung.

Statistical analysis using Pearson correlation

and linear regression was performed to evaluate the relationship between ionized calcium and serum albumin level in NS children. Unpaired T-test was used to compare the mean difference between ionized calcium level in NS children and in healthy children. The statistical analysis was performed using the Statistical Product and Service Solutions (SPSS) version 16.0 for Windows.

Results

A total of 34 children (17 NS children and 17 healthy children) were recruited to this study. The characteristics of the subjects are shown in **Table 1**.

The mean ionized calcium in NS children (4.56, SD 0.23) mg/dL was lower than that in healthy children (5.50, SD 0.24) mg/dL, with a mean difference of 0.94 mg/dL (95% CI 0.78 to 1.09)

The mean ionized calcium and serum albumin level in NS children were 4.56 (SD 0.227) mg/dL and 1.45 (SD 0.242) g/dL, respectively. There was significant positive correlation ($r=0.528$; $P=0.03$) between ionized calcium and serum albumin level in NS children. Based on the calculation of linear regression, we found an equation to estimate ionized calcium level (\hat{y}) based on the serum albumin level (x), that was $\hat{y}=3.84+0.49x$ with adjusted r square 0.23 as shown in **Figure 1**.

Table 1. Characteristics of subjects

	NS children n=17	Healthy children n=17
Sex		
Male (%)	11(64.7)	11 (64.7)
Weight (kg)		
Mean (SD)	16.84 (5.09)	20.59 (8.124)
Median	17	18
Range	10-27	12-44
Height (cm)		
Mean (SD)	103.29 (15.6)	107.53 (17.745)
Median	102	104
Range	79-133	83-146
Nutritional status		
Good (%)	11 (64.7)	17 (100)
Mild malnutrition (%)	6 (35.5)	0

SD= standard deviation

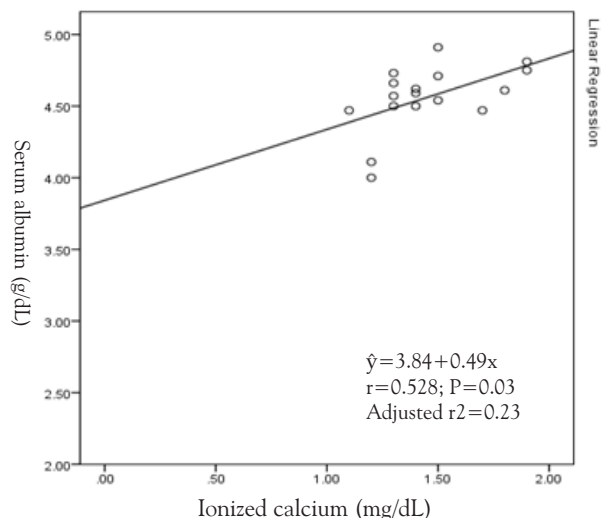


Figure 1. Relationship between ionized calcium level and serum albumin level in nephrotic syndrome children

Discussion

The serum albumin concentration in NS children in this study was low, ranged from 1.1. to 1.9 g/dL with a mean of 1.45 (SD 0.24) g/dL. The decreased albumin level in NS children is due to a damaged glomerular filtration membrane in the renal cortex. Consequently, the negative charge on the glomerular capillary endothelial is lost. Furthermore, the nature of size-selectivity in the glomerular capillary epithelium becomes disrupted.⁹ Sekarwana¹⁰ showed the importance of hyperlipidemia in atherosclerosis incidence in NS relapse children. He also showed that the value of total cholesterol and sVCAM-1 could be used as basic to predict long term prognosis in patients with NS relapse.

This study also showed that the ionized calcium level of NS children was lower than that in healthy children. However, in this study some children with NS have a normal value of ionized calcium according to Fischbach's range for children aged 1-18 years (4.8-5.52 mg/dL)¹¹. This may be due to the decrease of ionized calcium in NS children occurs subsequently during the course of the disease associated with timing of proteinuria.¹² Hooft et al¹² observed that the ionized calcium in NS children decrease after having proteinuria for more than two months. In this

study, the duration of proteinuria before being treated varied from 7 days until 2 months. On the other hand, Choi et al⁶ found a weak positive relationship between duration of NS and ionized calcium level.

Amballi et al¹³ reported that in a state of hypoalbuminemia (in chronic renal failure, nephrotic syndrome, and malnutrition), only the total calcium and not the ionized calcium was affected, and thus, clinical manifestations were rare. Garniasih¹⁴ found an association between serum albumin level and total serum calcium in children. The total serum calcium would decline in NS children. There was 50% of ionized calcium in total serum calcium, so when the total serum calcium level decreased then the ionized calcium level also decreased.^{2,4,15,16} In this study, we found a positive relationship between ionized calcium level and serum albumin. This means that the lower the albumin level, the lower ionized calcium levels will be. Previous research conducted by Choi et al⁶ showed a weak negative correlation between serum albumin and ionized calcium level. Choi et al⁶ also found a very weak positive relationship between the duration of disease and ionized calcium level from their 14 NS samples. So, it is reasonable to assume in this study that the ionized calcium level is determined by the severity of proteinuria. Other factors that may affect ionized calcium level are the duration of proteinuria before being treated and the patients' diagnosis (first diagnose or relapse NS) but there were no significant statistical correlation with ionized calcium level in this study.

Ionized calcium is an important physiological component and its levels are not influenced by protein. Thus, measurement of ionized calcium level from total serum calcium is important for optimal clinical decision making.⁵ When the concentration of ionized calcium in extra-cellular fluid falls below normal, the nervous system progressively becomes more sensitive and easily generates an action potential, which includes muscle spasms and leg cramps (tetani), numbness around the lips, tongue, fingers and toes, and muscle cramps (tetani) in the face, back and legs.^{8,16,11} Ionized calcium level less than 2 mg/dL can cause life-threatening complication.¹¹

Based on the linear regression analysis, we found an equation to estimate the concentration of ionized calcium (\hat{y}) as the dependent variable based on serum albumin (x) as the independent variable. The resulting

regression equation was $\hat{y} = 3.84 + 0.49x$ with adjusted r square 0.23. This means that the equation may be used to estimate ionized calcium level for only 23% while the remaining 77% involves variables outside the scope of this study.

The limitation of this study is that the examination of the ionized calcium level was done only once upon the first diagnose of NS or relapse. In addition, we did not examine the quantitative levels of proteinuria to determine its severity.

In conclusion, there is a moderately positive linear relationship between ionized calcium and serum albumin level of idiopathic NS children.

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