

Correlation between serum albumin and creatinine levels in children with nephrotic syndrome

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Abstract

Background Nephrotic syndrome is a glomerular disorder characterized by massive proteinuria, hypoalbuminemia, edema, and hyperlipidemia. Hypoalbuminemia in nephrotic syndrome leads to hypovolemia, a decrease in renal perfusion and glomerular filtration rate. Serum creatinine level reflects the glomerular filtration rate.

Objective The aim of this study was to determine the correlation between serum albumin and creatinine levels in children with nephrotic syndrome.

Methods A cross-sectional study was carried out on children with idiopathic nephrotic syndrome, aged between 1 to 14 years old, admitted to Pediatric Department in Hasan Sadikin Hospital from January 2001 to September 2007. We used data from patients' medical records to obtain serum albumin and creatinine levels during nephrotic stage. Statistical analysis using Pearson correlation test was performed to establish the correlation between serum albumin and creatinine levels. The type of correlation was determined by regression analysis.

Results Subjects were 113 children, consisted of 81 boys (72%) with mean of age 6.8 (SD 3.3) years. Mean of serum albumin and creatinine levels were 1.4 (SD 0.4) g/dL and 0.7 (SD 0.4) mg/dL, respectively. Analysis using Pearson correlation test showed a moderate ($r = -0.478$) significant correlation ($P < 0.01$) between serum albumin and creatinine levels in children with nephrotic syndrome. Regression analysis suggested a negative linear relationship between serum albumin level as the independent variable (X) and serum creatinine level as the dependent variable (Y) by using equation $\hat{Y} = 1.328 - 0.460X$.

Conclusion In patients with nephrotic syndrome there is a moderate negative correlation between serum albumin and creatinine levels. [Paediatr Indones. 2008;48:354-7].

Keywords: idiopathic nephrotic syndrome, hypoalbuminemia, serum creatinine, glomerular filtration rate

Nephrotic syndrome (NS) remains a major cause for referral to pediatric nephrologists because of the chronicity of the disorder and the complexities of its evaluation and management.¹ The characteristic features of NS are heavy proteinuria (>40 mg/m²/hr), hypoalbuminemia (<2.5 g/dL), edema, and hyperlipidemia. The underlying abnormality in NS is an increase in permeability of the glomerular capillary wall, which leads to massive proteinuria and hypoalbuminemia. Hypoalbuminemia leads to a decrease in the plasma oncotic pressure and transudation of fluid from the intravascular compartment to the interstitial space.² The reduction in intravascular volume decreases renal perfusion, leading to a decreased glomerular filtration rate (GFR). A decreased GFR is one of the etiologies of acute renal failure (ARF) in children with NS.^{3,4}

Berg and Bohlin found a decreased GFR which was directly correlated with serum albumin concentration during nephrotic stage in children with minimal change NS (MCNS).⁵ Lowenberg and

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Berg also found a positive correlation between serum albumin concentration and GFR in MCNS children, lower serum albumin level in MCNS children was related to lower GFR, thus the opposite remained the same.⁶ Guasch and Myers reported that hypofiltration was associated with higher serum creatinine level,⁷ but there hasn't been studied yet in children.

Estimation of GFR provides an indication of overall level of renal function, which is important to be done in children with NS due to its progression to ARF.⁸ Inulin clearance is a gold standard for GFR estimation, but it's invasive and not a practical method. The alternative method which is more simple and economical is serum creatinine level. Serum creatinine level examination reflects the GFR.^{8,9} The purpose of this study was to determine the correlation between serum albumin and creatinine levels in children with NS.

Methods

A cross-sectional study was carried out on children with Idiopathic Nephrotic Syndrome (INS), aged between 1 and 14 years old, admitted to Pediatric Department in Hasan Sadikin Hospital from January 2001 to September 2007. The inclusion criteria were children with INS during nephrotic stage (initial attack or relapse), and aged between 1 and 14 years old. We excluded patients with severe malnutrition and liver cirrhosis.

Data of the subjects including name, age, birth date, sex, history of current and previous illness, body weight, dry weight, height, nutrition, and status serum albumin and creatinine levels during nephrotic stage were collected from patient's medical record. To determine serum albumin level, we used brom cresol green (BCG) method, and Jaffe method was used to determine serum creatinine level.

If the significance level was $\alpha = 0.01$, one-tailed test, and power of the test was 0.80, then the minimal size of the sample needed was 59 subjects.¹⁰ INS was defined as NS with unknown etiology.^{2,11} Hypoalbuminemia was defined as serum albumin level < 2.5 g/dL.^{1,2,11} Normal serum creatinine levels based on age were used according to Kher.¹²

Statistical analysis using Pearson correlation test was performed to establish the intensity of correlation

between serum albumin and creatinine levels. The type of correlation was determined by regression analysis.¹³ Data were analyzed using SPSS version 13.0 for Windows.

Results

During January 2001 until September 2007, there were 113 children who met the inclusion criteria, consisted of 81 (72%) boys and 32 (28%) girls. The youngest subjects was 15 months old and the oldest one was 13 years old with mean of age 6.8 (SD 3.3) years and average onset was 5.8 (SD 3.3) years. Mean of weight was 19.4 (SD 7.7) kg and mean of height was 110.1 (19.4) cm. Other characteristics are shown in **Table 1**.

Table 1. Characteristics of subjects

Variables	n	Mean (SD)	Median
Age (years old)	113	6.8 (3.3)	7
Body weight (kg)	113	19.4 (7.7)	17.9
Height (cm)	113	110.1 (19.4)	110
Sex			
Male	81 (72%)		
Female	32 (28%)		
Onset (years old)	113	5.8 (3.3)	5

Table 2 shows the distribution of serum albumin and creatinine levels of the subjects. Mean of serum albumin level was 1.4 (SD 0.4) g/dL with the lowest level was 0.3 g/dL and the highest level was 2.3 g/dL. Mean of serum creatinine level was 0.7 (SD 0.4)/dL with the lowest level of 0.4 mg/dL and the highest level of 2 mg/dL.

Table 2. Distribution of serum albumin and creatinine levels

Variables	n	Mean (SD)	Median
Serum albumin (g/dL)	113	1.4 (0.4)	1.4
Serum creatinine (mg/dL)	113	0.7 (0.4)	0.6

From 113 subjects, there were 34 subjects who had elevation in serum creatinine level above upper normal limit based on age (**Table 3**).

Table 3 shows that mean of serum creatinine level elevation was 58.4 (SD 52.8%) or 1.6 (SD 0.5) times above upper normal limit based on age. The lowest percentage of serum creatinine level elevation

Table 3. Elevated serum creatinine level during nephrotic stage

Variables	n	Mean (SD)	Median
Percentage of serum creatinine level elevation (%)	34	58.4 (52.8)	50
Multiplication rate of serum creatinine level elevation (times)	34	1.6 (0.5)	1.5

was 1.4% and the highest was 188%. The lowest multiplication rate of serum creatinine level elevation was 1.01 times and the highest was 2.9 times above upper normal limit of the serum creatinine level based on age. These elevations of serum creatinine level occurred in the range of serum albumin level between 0.25 g/dL and 1.8 g/ dL.

Figure 1 shows the correlation between serum albumin and creatinine levels in children with NS.

Figure 1 describes a negative linear relationship between serum albumin and creatinine levels in children with NS. Pearson correlation test was used to determine the intensity of this correlation. Based on that analysis, there was a significant negative correlation between serum albumin and creatinine levels ($P < 0.01$) with correlation coefficient or $r = 0.478$.

Regression analysis was used to determine the decrease of serum albumin level that influenced the elevation of serum creatinine level, with serum

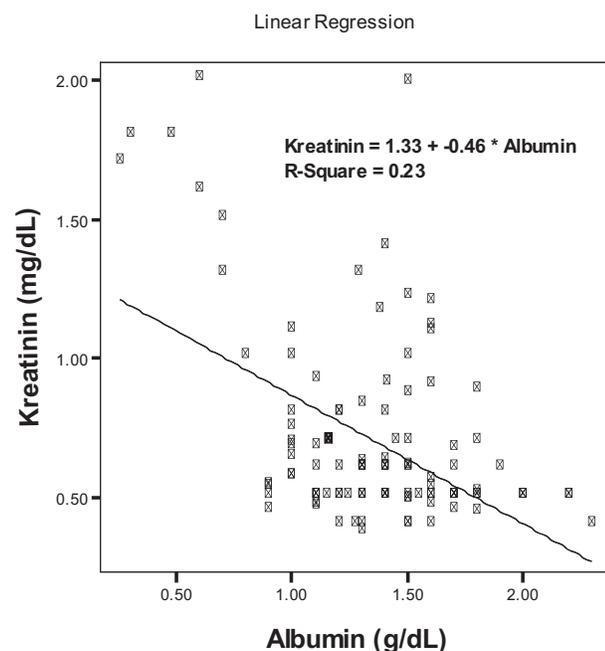


Figure 1. The correlation between serum albumin and creatinine levels in children with NS

albumin level as the independent variable and serum creatinine level as the dependent variable. Figure 1, the regression shows that equation was: $Y = 1,328 - 0,460X$, with Y as the mean estimation of serum creatinine level (mg/dL); X as serum albumin level (g/dL), 1.328 as constanta, and 0.460 as intercept (the regression coefficient), confirmed that the lower serum albumin level was related to the higher serum creatinine level.

Discussion

This study showed that mean of age of the subjects was 6.8 (SD 3.3) years and average onset was 5.8 (SD 3.3) years, with the youngest subject was 15 months old and the oldest one was 13 years old. Nash *et al* stated that two-third of NS cases occurred at the age less than five years, with 95% at the age of 1-4 years and almost 50% at the age less than 4 years,¹⁴ while Vogt and Avner stated that INS occurred at the age of 2-6 years.² According to Haycock, the highest incidence of idiopathic NS occurred at 2-5 years of age.¹¹

Most of the subjects in this study were male, i.e., 81 (72%) boys with the ratio of male : female was 2.5:1. This was comparable with that stated in literature that INS was found more frequent in boys than in girls.^{2,11,14} The ratio of male : female in this study was similar with that found by Nash (2:1 to 2.6:1),¹⁴ but this ratio was higher than that observed by Haycock (1.5-2:1).¹¹

Based on the International Study of Kidney Disease in Children (ISKDC), the decrease of serum albumin level (hypoalbuminemia) is the mandatory laboratory criteria to diagnose NS, with the level less than 2.5 g/dL.¹⁵ In this study, all of the subjects had a decreased of serum albumin level, with 1.4 (SD 0.4) g/dL as a mean level, the lowest level was 0.25 g/dL and 2.3 g/dL as the highest. The decrease of the serum albumin level in NS patients occurs due to elevation of glomerular filtration of serum albumin, causing a massive proteinuria. Although the synthesis of serum albumin in the liver increases up to 3-4 times, it is not enough to compensate the lost of albumin.¹

Hypoalbuminemia leads to hypovolemia, decreased oncotic plasma pressure that leads to plasma leakage to interstitial, diminished effective

blood volume circulation and renal blood flow.² Hypovolemia is the main cause of the decline of GFR. Hypovolemia generally occurred when serum albumin level less than 1.5 g/dL.^{3,4}

In this study, the renal function is estimated by measuring the level of serum creatinine. We found that 79 (70%) subjects had normal level of serum creatinine, and 34 (30%) subjects had an elevation of the serum creatinine level. The elevation of the serum creatinine level was occurred in the range of 0.25-1.8 g/dL of the serum albumin level. This result was similar to Vogt and the level of serum creatinine of INS patients that found by Avner usually within normal limit, but it can increase due to the decrease in renal perfusion caused by a decrease in intravascular volume.²

Haycock stated that serum ureum and creatinine levels during the onset of NS is usually normal, but in some cases it could be elevated from mild to moderate degree due to hypovolemia that lead to a decreased renal perfusion (prerenal azotemia).¹¹ This study showed that the mean percentage of serum creatinine level elevation was 58.4 (SD 52.8) percent or 1.6 (SD 0.5) times above the upper normal limit of serum creatinine level based on age.⁷ The intensity of correlation between serum albumin and creatinine levels in this study was moderate, with $r = -0,478$, and statistically significant ($P < 0.01$), because hypoalbuminemia is not the only factor that reduce the GFR but there are other factors that influence it such as glomerular hydrostatic pressure, Bowman's hydrostatic and oncotic pressure. This study could not be compared with other studies because there were no similar studies before.

In conclusion, there is a moderate negative correlation between serum albumin and creatinine levels in children with NS, confirmed that the lower serum albumin level is related to the higher serum creatinine level.

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