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CORRELATION OF HEMATOLOGIC PARAMETERS WITH SERUM ALBUMIN AND CHOLESTEROL LEVELS IN CHILDREN WITH NEPHROTIC SYNDROME

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ABSTRACT

Background: Pediatric nephrotic syndrome (NS) is the most common kidney disorder in children. The diagnosis of NS is established by clinical abnormalities, characterized by proteinuria, hypoalbuminemia, edema, and as well as hypercholesterolemia. Regarding the examination of hematologic parameters in patients with NS, one can recognize the risk of infection, and thromboembolism.

Objective: To assess the correlation between hematologic parameters with serum albumin and cholesterol levels in patients with NS.

Method: This was a cross-sectional study conducted at Haji Adam Malik Hospital, Medan, North Sumatera. The study was conducted on February 1st, 2017 until December 1st, 2017 with total sample of 65 children with NS. Inclusion criteria was all patient SN whose age 2 until 18 years with hypoalbuminemia and hypercholesterolemia, did not have severe malnutrition, liver function was normal, remission NS was excluded. There were 49 children who included. Pearson and Spearman correlation test were used to evaluate which one was required.

Results: There were 31 boys and 18 girls. 43% of children were well-nourished and 6% of children were moderate malnourished. Patients with relapsing NS were 37.7% and patients with SN steroid resistance NS were 63.26%. There were 3 types of hematologic parameters that correlates with serum albumin levels; it were leukocytes ($r = -0.29$; $P = 0.044$), platelets ($r = -0.23$; $P = 0.047$), ESR ($r = -0.29$; $P = 0.039$). The hematologic parameter that correlates with cholesterol levels was platelets ($r = 0.44$; $P = 0.001$).

Conclusion: There was a weak negative-correlation between leukocytes, platelets, and erythrocytes sedimentation rate with albumin. There was a moderate negative-correlation between platelets and cholesterol. There were means with examination of hematologic paramaters we can recognize the risk of infection, and thromboembolism in patient with NS.

KEYWORDS : nephrotic syndrome, hematologic parameters, hypoalbuminemia, hypercholesterolemia, children.

Background

Nephrotic syndrome (SN) in children is the most common kidney disease of children. The incidence of SN in children in the literature in the United States and the United Kingdom is 2 to 7 new cases per 100,000 children per year, with prevalence ranging from 12 to 16 cases per 100,000 children. SN that occurs in children in developing countries is higher incidence. In Indonesia reported 6 per 100,000 per year in children aged less than 14 years , with comparison of boys and girls 2: 1.[1,2]

Diagnosis is established with clinical abnormalities characterized by symptoms of proteinuria, hypoalbuminemia, edema, and accompanied by hypercholesterolaemia.[1] In a long-term study the response to steroid treatment is more often used to determine prognosis than with anatomical pathology. Therefore, at present SN classification is based more on the clinical response of steroid sensitive nephrotic syndrome (SNSS) and steroid-resistant nephrotic syndrome (SNRS).[2]

Kidney is one organ that produces erythropoetin which is a glycoprotein with a molecular weight of 30,400 dalton produced by peritubular cells of the kidney. Erythropoetin works primarily in the proliferation and maturation of erythroid cells in the bone marrow functioning in the maturation of red blood cells.[2] Studies in Bangladesh are mentioned about the occurrence of anemia in SN patients, a significant association between hemoglobin with hypoalbumin ($P = 0.001$) and hypercholesterolemia ($P = 0.005$).[3,4] Other studies conducted in Austria also mentioned a significant association between hemoglobin and hypoalbumin values ($P = 0.001$).[5,6] Research conducted on 37 children in China mentioned that serum transferrin was positively correlated with serum albumin, and negative with urinary transferrin ($r = -0.586$, $P < 0.05$). Serum erythropoietin (EPO) was positively correlated not only with serum albumin, but also with Hb ($r = 0.554$, $P < 0.05$). Subsequently urinary EPO levels were positively correlated with proteinuria levels within 24 h ($r = 0.618$, $P < 0.01$) .[7]

SN patients with long-term steroid treatment have a risk of infection caused by their own disease or due to steroid drugs.[8] The risk of infection can occur due to decreased concentration of immunoglonulin G, factor B and factor I, suppressed T cell function. The most frequent infection is peritonitis , occurred 2 to 6%, followed by cellulitis, pneumonia and upper respiratory tract infections.[8] Research conducted in Brawijaya University states that patients with SN have pneumonia infection as much as 5%, and urinary tract infection as much as 28.6% .[9] Frequency of infection incidence more often in patients with SNRS.[10] Research conducted in Iran mentioned that in patients with SN there was an increase in the number of leukocytes associated with the occurrence of infection in patients SN ($P = 0.001$) .[11]

One of the risks to be aware of in patients with SN is a decrease in blood viscosity resulting in an increase in Erythrocyte sendimentation rate (ESR) rate. The increase of ESR and the presence of thrombocytosis in SN patients may increase the risk of thromboembolism especially patients with SN relaps and steroid-resistant.[8,12] ESR examination in SN patients has been done by several researchers, a recent study conducted in Bangladesh which mentions there is a weak and insignificant correlation between serum albumin and LED values with ($P = 0.083$) .[13]

The risk of complications of SN if not realized treatment quickly then it will have a bad prognosis. It is important to assess the hematologic parameters and their relation to albumin and cholesterol levels.

METHODS

The study was Cross sectional Study, conducted in Outpatient Installation and Inpatient Installation of Nephrology of H.Adam Malik Hospital, from February 2017 to December 2017. Target population was pediatric patients with those diagnosed with nephrotic syndrome. Populations are children with nephrotic syndrome who seek treatment in an outpatient installation and are

hospitalized in the hospital ward of H.Adam Malik Hospital Medan.
Inclusion criteria:

1. All patients of Idiopathic SN with the age of 2 years to 18 2.
2. Criteria of children with SN that there are proteinuria, edema, hipoalbuminemia and hiperkolesterolemia. The serum albumin value under less than 2.5 g / dl, serum cholesterol value greater than 200 mg / dl and there is proteinuria (+2).
3. The patient's parents have signed the research approval sheets.

Exclusion Criteria

1. Patients with liver disease
2. Patients with severe malnutrition.
3. Patients with SN remission
4. Parents of patients do not agree to follow the study.

All subjects were requested approval from parents after the first explanation. The explanatory form is attached to this research proposal. This research was conducted after the approval by the Ethics Committee of the Faculty of Medicine, University of Sumatera Utara

Data analysis

Data processing by using computer software with significance P value <0,05. Correlation test used to see the relationship between hematology parameter measurement results with serum albumin and cholesterol value. Both test will be stated significant if P value <0,05. The value of r is interpreted as weak (0.1-0.29), moderate (0.30-0.49), strong (0.50-0.69), very strong (0.70-0.89), perfect (> 0.9) .35

Result

A total of 65 children with SN, and who meet the criteria of inclusion and exclusion were 49 samples. The mean age of children was 10.16 years (121.97 months) with male gender as many as 31 people (63.3%), and women as many as 18 people (36.7%). Mean value of consecutive parameters of hemoglobin 12,43 mg / dl, erythrocyte 4,63 million / µL, leukocyte 14.677 / µL, hematocrit 37,49%, platelet 428.916 / µL, LED 24,27 mm / hour, mean value of albumin 1 , 89 g / dl and cholesterol value 425.31 g / dl. All samples had SN criteria of edema, proteinuria, hypoalbuminemia, and hypercholesterolemia. Characteristics of sample values can be seen in Table 4.1.

Tabel 4.1 Characteristic data sample

Variabel	SN N=49 orang	
Ages (years), Average (SD)	10,16	(3,67)
Gender, n(%)		
Boys	31	(63,26)
Girls	18	(36,74)
Nutritional status,n (%)		
Well nourish	43	(87,7)
Moderate malnutrition	6	(12,2)
Parameter hematologi		
Hemoglobin (g/dl), average (SD)	12,43	(2,28)
Erythrocyte (juta/µL), average (SD)	4,63	(0,89)
Hematocrit (%), average (SD)	37,49	(6,82)
Leukocytes/µL, mean (SD)	14.677,10	(5.641,68)
Platelets/µL, mean (SD)	439.816	(127.305,27)
MCV (fl), average (SD)	80,53	(5,36)
MCH (pg), average (SD)	27.04	(2,42)
MCHC (g/dl), average (SD)	33,40	(1,67)
ESR (mm/jam), average (SD)	24,27	(19,57)
Albumin (g/dl), average (SD) g/dl	1,89	(0,71)
Cholesterol (mg/dl), average (SD) mg/dl	425,31	(167,12)
Criteria SN		
Edema , n (%)	49	100
Proteinuria, n (%)	49	100
Hypoalbuminemia, n (%)	49	100
Hypercholesterolemia, n (%)	49	100
SN Relaps, n (%)	18	(37,74)
SN Resistent steroid, n (%)	31	(63,26)

Tabel 4.2 Correlation of hematological parameters with serum albumin values

No	Variabel	Correlation test	
		r	P*
1	Hemoglobin	-0,19	0,185
2	Erythrocyte	0,24	0,085
3	Hematocrit	-0,29	0,044
4	Leucocytes	-0,01	0,915
5	Platelets	-0,23	0,047
6	MCV	-0,23	0,107
7	MCH	-0,03	0,789
8	MCHC	-0,14	0,318
9	ESR	-0,29	0,039

*P<0,05 ; Pearson Correlation test

There are 3 types of hematology parameter profile on the table 4.2 , that has a weakly patterned negative correlation with serum albumin value, namely leukocytes (r = - 0.29, P = 0.044), platelets (r = - 0.23, P = 0.047) , and ESR (r = - 0.29; P = 0.039), which means that the decrease in albumin value wil increase platelets value, leucocytes, and ESR. There was no correlation relationship between blood albumin value and other hematological profile, ie hemoglobin, erythrocytes, hematocrit, MCV, MCH, MCHC.

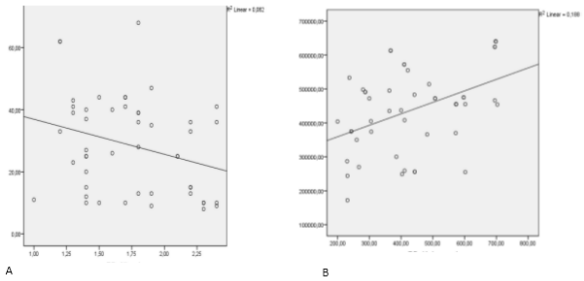
Tabel 4.3 Correlation of hematologic parameters of serum choletesterol values

No	Variabel	Correlation test	
		r	P
1	Hemoglobin	-0,01	0,421*
2	Erythrocyte	-0,09	0,524*
3	Hematocrit	0,06	0,720**
4	Leucocytes	-0,03	0,791*
5	Platelets	0,44	0,001*
6	MCV	0,06	0,651*
7	MCH	-0,02	0,847*
8	MCHC	0,04	0,741*
9	ESR	0,09	0,512**

*P <0,05 ; Uji korelasi Pearson
**P<0,05; Uji korelasi Spearman

In Table 4.3, hematology parameter that correlates with cholesterol was platelets. Platelets have a moderately positive correlation with cholesterol levels (r = 0.44; P = 0.001), which means the higher the cholesterol value can be the higher the platelets.

Scatter Plot diagram is found in figures A, there is a line diagram inversely between platelets and with albumin values. While in figure B, obtained Scatter plot with a line diagram that is directly prohibited between platelets with cholesterol value.



A B

Gambar 4.3 (A) Correlation platelets and albumin , (B) Correlation platelets and cholesterol

DISCUSSION

Nephrotic syndrome (SN) is a clinical condition characterized by symptoms of edema, proteinuria, hypoalbuminemia and hypercholesterolemia. Based on the response to steroid reactions, SN was classified into the SN sensitive steroids, and SN resistant

steroids. Proteinuria is a major symptom in SN patients, whereas other symptoms such as edema, hypoalbuminemia and hypercholestrolemia are secondary. In a long-term study response to steroid treatment is more commonly used to determine prognosis than with anatomical pathology treatment. Therefore, the classification of SN is based more on the clinical response, namely: steroid sensitive nephrotic syndrome and steroid-resistant nephrotic syndrome.[1,2,3] Hematologic parameters can be used to determine the risk of anemia, infection and thromboembolism in patients with SN. Parameters examined included hemoglobin, erythrocytes, hematocrit, leucocytes, platelets, MCV, MCH and MCHC.[3,4,5]

Research conducted in Brawijaya University mentioned that from 91 children with SN, 16% of them are SN relaps.[9] Similarly, research conducted in Bali from 2001 to 2007, new patient recorded 68 cases, with the age range of 6 months to 11 years. Male sufferers 73.5% and women 26.3% [.34] In laboratory tests found the presence of hypoalbuminemia, hypercholesterolemia and proteinuria. A study conducted in Bangladesh in 2016 revealed that of the 100 children with SN, 24% were SN relaps and 48% were steroid-resistant S. The serum albumin ratio in patients with SN relaps was lower in the steroid-resistant SN than the relapse of SN test Anova P <0.01. Hypercholesterolemia occurs in relapse and steroid-resistant SN with elevated serum cholesterol levels higher in steroid-resistant S. (P <0.001) .[11]

Anemia is a chronic feature of nephrotic syndrome in adults and children, which can be partly explained by erythropoietin deficiency. [18]Research conducted in 37 children in China who studied levels of transferrin and hemoglobin found that normal hemoglobin values in children with SN, but the value of tranferin decreased.[19,20] Nephrotic syndrome can alter the metabolism of EPO and transferrin which can cause EPO and tranferin deficiency. The metabolism of EPO and trasferrin remains to be studied further.[7,21,22] There was no correlation between hemoglobin with albumin and cholesterol values. This may be explained because erythropoietin deficiency has not affected erythropoiesis.[20,21,22] Further investigation is the length of illness that has been suffered in the patient and the duration of steroid therapy given.

The incidence of infection in the study conducted in UB states that 92.3% of children suffering from ARI, 28.6% suffer from urinary tract infection and the rest is pneumonia[9] Some factors that make SN children easier to get infection are low IgG levels due to synthesis imperfection, loss of factor B in urine, and imperfect T lymphocytes. In addition, corticosteroid or immunosuppressive treatment increases the risk of infection.[15]

Infection is the most common cause of increased leukocytes. An increase in leukocytes between about 10,000 and 20,000 / mm3 generally points to an infection / reactive process.[20] Data associated with increased leukocytes in SN patients are still very small, other studies are more focused on the occurrence of diseases, such as pneumonia, bacterial peritonitis and urinary tract infections . A study conducted to assess the association between leukocytes and SN patients was a study conducted in India and found a significant association between leukocytes and nephrotic syndrome with P <0.001.[3,15,20]

Although the incidence of thromboembolism is more common in adults, the risk of thromboembolism is a serious complication. Renal Vein Thrombosis occurs in 37% of patients with membranous gromerulonephritis.[31] The pathogenesis of thromboembolism is highly multifactorial, associated with hypoalbuminemia, hypercholesterolaemia and hyperfibrinogenemia.[31,33] Hipoalbuminemia increases the binding of arachidonic acid albumin, which increases thromboxan A2 formation in platelets, a stimulus for thrombocyte aggregation.[32,33] Increased platelet aggregation and decreased blood viscosity may increase the rate of blood sedimentation.[33] Studies have been conducted to suggest that there is a negative weak correlation between the ESR and albumin.[13]

In this study we found a negative correlation between leukocytes, platelets and ESR and hypoalbuminemia and positive correlation between platelets and hypercholesterolemia was found. This is in accordance with the above study where there is a negative correlation between blood sedimentation rate and serum albumin value. Other studies suggest that the ESR increases in patients with SN relaps and steroid-resistant.[13] In a study conducted by the authors, the sample of the study consisted of SN relaps and steroid-resistant SN.

The limitation of the study is that the sample still varies between SN relaps and SN resistant steroids, preferably done on one sample type only to minimize bias. Research should also be performed with longer monitoring example with cohort study to see therapeutic effects as well as complications in SN patients in terms of hematologic parameters.

Conclusion

We found a weak correlation with a negative pattern between platelet value, leukocyte and sedimentation rate of blood with serum albumin value. There was a moderately positive correlation between platelets and serum cholesterol values. By examination of hematologic parameters can be known earlier risk of infection and thromboemboembolism in patients SN.

Suggestion

Further research is needed to see the relationship between hematological parameters and serum albumin and cholesterol values with larger and equal samples, and the length of treatment time is considered.

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