Correlation between Prolactin Serum with Neutrophil Lymphocyte Ratio (NLR) in Systemic Inflammatory Response Syndrome

by Meita Hendrianingtyas

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ABSTRACT

Background: Systemic inflammatory response syndrome (SIRS) is a state of systemic inflammatory activation by various causes. SIRS have a high mortality rate. Prolactin is known to regulate cellular function of immune system. Neutrophil-lymphocyte ratio (NLR) is simple, cost effective and easy parameter that currently used as inflammation marker.

Objective: The aims of this study is to determine the correlation between prolactin serum with NLR in SIRS patients.

Methods: A cross sectional study was conducted on 50 clinically SIRS patients. Prolactin serum was measured by enzyme linked immunosorbent assay (ELISA) and NLR was calculated manually from absolute neutrophil and lymphocyte count measured by automatic hematology analyzer. Non-parametric Spearman test was used to analyze the correlation between prolactin with NLR

Results: Median value of serum prolactin level was 11.32 ng/mL (2.76-194.81), whereas the mean value NLR was 16.36 ± 11.58. The correlation between prolactin levels with NLR was r = 0.345, p = 0.014.

Conclusion: There is a weak positive significant correlation between prolactin with neutrophil lymphocyte ratio in SIRS

1. Introduction

Systemic inflammatory response syndrome (SIRS) state is systemic activation with multiple underlying causes. It has a high risk of sepsis and death[1]. Septic patients are generally admitted to the ICU for long periods of up to 2-3 weeks. Antimicrobial agents and advanced life support have been used, but the case fatality rate of septic patients has been between 20-30% over the past two decades.[2] The incidence of sepsis in Europe is estimated to be 54-116 cases in 100,000 populations per year.[3] Systemic inflammatory response syndrome (SIRS) is characterized by two or more symptoms: body temperature >38 °C or <36 °C; tachycardia >90 beats/minute; respiratory rate >20 breaths/ minute or PaCO2 <4.3 kPa (32mmHg); leukocyte count >12,000/mm3 or <4000/mm3 or >10% immature neutrophils (band).[1,2] The prevalence of SIRS is very high, covering one-third of total hospitalized patients and >50% of intensive care unit (ICU) patients. In surgical ICU, SIRS can cover > 80% of patients. The prevalence of infection increases with the number of SIRS criteria met and the severity of the symptoms of sepsis increases.[4]

The state of SIRS or sepsis can affect Hypothalamic-Pituitary-Adrenal (HPA) axis associated with inflammation. Early release of cytokines from immune cells plays a role in body homeostasis by acting as paracrine, autocrine and endocrine with increased release of ACTH hormone (adrenocorticotropic hormone), growth hormone and prolactin hormone at the onset of sepsis[5,6] Animal studies have shown that prolactin is associated with decreased survival and changes in the immune system.[7] Prolactin plays a role in stimulating phagocytosis in several infectious microorganisms.

In addition, prolactin also modulates leukocyte adhesion to the endothelium.[8]

The neutrophil-lymphocyte ratio (NLR) is an inexpensive and easy parameter of routine blood tests. Current use of NLR as a marker of inflammation has a good correlation with C-reactive protein (CRP).[9] Holub et al (2012) concluded that an NLR with a cut-off of 6.2 has a sensitivity of 91% and a specificity of 96% for bacteremia patients.[10] A study by Jager et al (2010) showed that NLR can be a predictor of bacteremia in emergency room patients.[11]

2. Method

The cross-sectional study was conducted in April-August 2016. The subjects were male, according to the SIRS criteria, age more than 18 years. Patients with autoimmune disease, domperidone and bromocriptine therapy were not included in this study. Serum prolactin hormone were examined by ELISA method. The reference value for male was 3-14.7 ng/mL, NLR value was obtained from the absolute number of neutrophils divided by absolute number of lymphocytes obtained from the automatic haematology analyzer. Data were presented in the form of mean ± standard deviation for numerical data with normal distribution, median (minimum-maximum) for abnormal distribution data. Data were analyzed using the Spearman correlation test to determine the correlation between serum prolactin level and NLR.

3. Results

Fifty (50) subjects were included in this study. The research characteristics can be seen in table 1. The data normality test results of NLR obtained normal distribution, but the prolactin result were not normal distribution so that the correlation test is done using Spearman Correlation test. The results of the Spearman correlation test analysis showed that there was a weak correlation between prolactin with NLR (r = 0.345, p = 0.014). (Fig.1)

Tabel 1. Baseline characteristics in subjects

| Parameter	Mean ±SD	Median (min-max)	p*
Age (years)	49.9 ± 13.9	55.5 (18-77)	0.00
Hemoglobin (mg/dL)	12.4 ± 2.3	12.8 (7.4 -16.3)	0.20
Leukocyte count (/μL)	16,965 ±6,749	16,150 (3,100-38,500)	0.01
Neutrophil (/μL)	14,635 ± 6,238	13,800 (2,490 – 35,000)	0.06
Lymphocyte (/μL)	1,287 ± 799	985 (200-3,300)	0.01
Platelet (/μL)	253,362 ± 109,280	239,500 (84,400-617,000)	0.20
NLR	16.37±11.58	14.8 (1.5-54.46)	0.11
Prolactin (ng/mL)	25.77 ± 38.6	11.32 (2.76-194.81)	0.00

p= Kolmogorov Smirnov
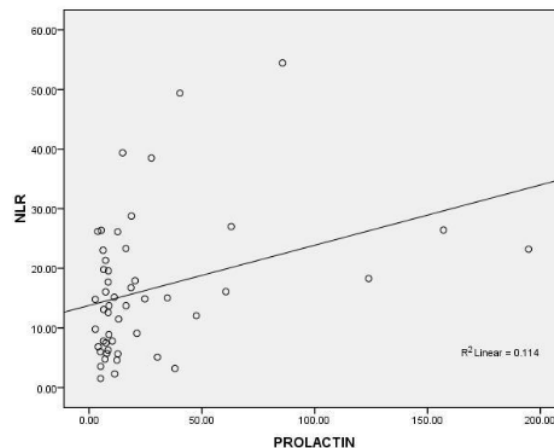
Figure 1. Scatter plot of the correlation between serum prolactin and NLR

4. Discussion

The mean age of the subjects of this study was 49.9 ± 13.85 years, with an age range between 18-77 years, median value of 55.5 years, these results are in accordance with the study of Kofoed et al. with median age was 56 year (range 20-94 years).[12] According to the study of Comstedt et al, SIRS occurred at the age of 15-96 years, whereas Lai et al, SIRS occurred at a mean age of 62 ± 17 years.[13,14] The results of the Spearman correlation test analysis showed that there was a weak correlation between serum prolactin levels and NLR (r = 0.345, p = 0.014). Study of Tuyan et al., reported a correlation between NLR and prolactin levels in infertility patients (r = 0.409, p = 0.043).[15]

The main biological function of prolactin hormone known so far is a lactation hormone. Some evidence suggests that the prolactin hormone is a growth factor for lymphocyte and stimulates an immune response. Prolactin is also produced by immune system cells, such as macrophages, NK cells, T lymphocytes and B lymphocytes. In addition, almost all hematopoietic cells have prolactin receptors on their cell surface.[16,17] Increased levels of the prolactin hormone can cause changes in the state of immunity in pathological conditions. Hyperprolactinemia has been reported to occur in several autoimmune diseases such as systemic lupus erythematosus (SLE), rheumatoid arthritis, and systemic sclerosis. The effect of the prolactin hormone on pancreatic beta cells, liver, T lymphocytes is to regulate cell proliferation, while in the prostate, lymphocytes, ovarian carcinoma cells, breast carcinoma cells and others, prolactin acts as an anti-apoptosis factor.[16,18,19] Prolactin regulates the functions of proliferation, differentiation, angiogenesis and protection from apoptosis and inflammation. The action of prolactin begins with binding to specific membrane receptors, where prolactin receptors are present in immune cells and are included in cytokine receptors such as IL-2, IL-3, IL-4, IL-6, IL-7 receptors, growth hormone and erythropoietin.[15] Prolactin acts as a pro-inflammatory cytokine by increasing the production of IFN-c, IL-12, and IL-1b in peritoneal macrophages.[20] Prolactin also increase the production of IFN-c and TNF-α in T cells and mononuclear cells.[21]

During inflammatory conditions prolactin has been described as inducing phagocytosis, although the mechanism by which prolactin regulates phagocytosis is unknown and induces release of pro-inflammatory cytokines. Immunomodulation of prolactin appears to be an increase in transcription factors such as IRF and NF-κB which play a role in immune function.[22] Brand et al (2004), have shown that prolactin increases the release of TNF-α and IL-2 from mononuclear cells by stimulation of LPS (lipopolysaccharide). TNF-α and IL-2 are important cytokines as mediators of inflammation, complications of sepsis and autoimmunity.[23]

There were several limitations of this study. This study did not exclude the presence of psychological stress that can increase prolactin levels. This study also did not measure the pro-inflammatory cytokines that play a role in the pathophysiology of SIRS.

5. Conclusion

There is a weak positive significant correlation between prolactin with neutrophil lymphocyte ratio in systemic inflammatory response syndrome.

Ethical Approval

This research was conducted upon approval from the Health Research Ethics Commission (KEPK) of the Faculty of Medicine of Diponegoro University/RSUP Dr. Kariadi Semarang with the number of 726/EC/FK-RSDK/VI/2016, issued on June 24, 2016.

Conflicts of Interest

The authors declare no conflict of interest.

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