

Correlation between HS-CRP in Serum with Neurological Deficit Measured by Nihss in Acute Ischemic Stroke

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Abstract

Background: CRP can increase the regulation of adhesion receptors on endothelial cells which can lead to infiltration of neutrophil and monocyte cells to endothelial cells. This causes endothelial cell damage and blood brain barrier dysfunction eventually leading to brain cell death. This brain cell death will result in impaired brain function and affect the severity of the stroke. The problem that arises is whether there is a correlation between CRP levels in serum and the severity of acute ischemic stroke as measured by NIHSS.

Method: Sixty patients with acute thrombotic stroke who were treated at the neurology ward of Dr. Soetomo General Hospital (a Teaching Hospital of Faculty of Medicine, Universitas Airlangga) during June-September 2019 had serum levels of CRP measured with sandwich ELISA method using high sensitivity CRP (hs-CRP) and neurological deficit was assessed using the NIHSS.

Result: Mean age of subjects was 57,45±8,89 years. The study subjects consisted of 37 male and 23 female. The median serum levels of hs-CRP is 0,4 mg/dL with a range of 0,1-15,1 mg/dL. Median NIHSS is 5 with a range of 2-15. There is a positive correlation with moderate correlation strength between serum levels of hs-CRP and the NIHSS value in patients with acute thrombotic stroke and statistically significant ($p=0.000$, $r=0.454$).

Conclusion: There is a moderate positive correlation between serum levels of hs-CRP and neurological deficit measured by NIHSS.

Keywords: CRP, hs-CRP, NIHSS, acute ischemic stroke.

Introduction

Stroke is a condition resulting from impaired blood flow to the brain characterized by a focal or global neurological deficit that occurs more than 24 hours or dies before 24 hours with other causes excluded.¹

Currently, stroke is the second leading cause of death worldwide. In the first 1 year after stroke, about 20% of

sufferers die. Stroke also causes the highest disability in the world. Stroke is the leading cause of serious long-term disability.² Stroke is a disease of critical public health with serious economic and social consequences.³

The number of ischemic stroke patients is more than the haemorrhagic stroke. In western countries, the number of ischemic stroke sufferers is around 80-85% of all stroke sufferers. Ischemic stroke is caused by a decrease in cerebral blood flow which results in brain cell death and dysfunction.⁴

Ischemia in the brain activates microglia releasing proinflammatory products such as IL-1 β , IL-6 and TNF- α .^{5,6} Several other inflammatory mediators such as

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lymphocytes and leukocytes also rise in acute ischemic stroke.⁷ These proinflammatory cytokines can induce hepatocyte and neuronal cells to synthesize CRP.^{8,9}

CRP increases the regulation of adhesion receptors on endothelial cells. The two main adhesion receptors, namely ICAM-1 and VCAM-1, cause infiltration of neutrophil and monocyte cells to endothelial cells.^{9,10} This causes endothelial cell damage and blood brain barrier dysfunction resulting in vasogenic oedema and ultimately leading to brain cell death.⁶ This brain cell death will result in impaired brain function and affect the severity of the stroke.

The problem that arises is whether there is a correlation between CRP levels in serum and the severity of acute ischemic stroke as measured by NIHSS.

Method

This research is an analytical study with a cross sectional design. Inclusion criteria included: onset <72 hours, first stroke of attack, NIHSS score 5-15 and willingness to attend the study (signed informed

consent). Exclusion criteria included: Infection on admission, acute heart disease, history of malignancy, and liver disease (hepatic failure). Based on the formula for calculating the sample size of the correlation research, the minimum sample size is 60 people.

All study subjects underwent the same clinical and laboratory examinations. The serum levels of hs-CRP measured with sandwich ELISA method using HS (High Sensitivity) CRP. The normality of the data distribution was checked by the Kolmogorov Smirnov test. The Spearman statistical test was used to determine the correlation between the two variables with an abnormal distribution.

Results

This study involved a total sample of 60 acute thrombotic ischemic stroke patients who came to the emergency department of Dr. Soetomo who met the inclusion criteria and did not meet the exclusion criteria. General characteristics and laboratory tests are shown in Table 1.

Table 1 General Characteristics

Variable	n (%)	Mean ± SD	Range
Gender			
Male	37 (61,7)		
Female	23 (36,3)		
Age (years)		57,45±8,89	32–74
Onset of attack (hours)		12±14,05	2-55

Serum hs-CRP levels in study subjects

The median value of serum hs-CRP levels in the study subjects was 0.4 mg / dL with a range of 0.1-15.1. This data can be seen in table 2.

Table 2 Median serum hs-CRP levels

Variable	Median	Range
hs-CRP	0,4 mg/dL	0,1–15,1

The results of the NIHSS examination on research subjects

The results of the NIHSS examination carried out when the research subjects had their blood samples taken at the Dr. Soetomo Hospital showed the median NIHSS value was 5 with a range of 2-15, this data can be seen in table 3.

Table 3 Average NIHSS values

Variable	Median	Range
NIHSS	5	2-15

CORRELATION BETWEEN Hs-CRP SERUM LEVELS WITH NIHSS VALUE

There was a positive correlation with moderate correlation strength between the hs-CRP level and the NIHSS value and statistically significant with $p < 0.05$ and a correlation coefficient of 0.454. This can be seen in table 3.

Table 5.5 Correlation between the hs-CRP level and the NIHSS value

Variable	Correlation coefficient	p
hs-CRP levels vs NIHSS value	0.454	0.000

Discussion

The research design was cross sectional. The selection of consecutive sampling as a method for selecting research subjects because this method is the best and easy non-probability sampling method.¹¹

For approximately 3 months of the study, it was found that 60 subjects met the research criteria. Of the 60 subjects, 37 subjects (61.7%) were male and 23 subjects (36.3%) were female. This study shows that male experience more acute thrombotic strokes than female. It is in accordance with stroke epidemiological data that male experience more strokes than female.¹² Another literature study states that the percentage of thrombotic strokes in female in India and Southeast Asia is 33% to 36%.¹³

Of the 60 samples, the mean age of the patients was 57.45 ± 8.89 years (table 1). In accordance with stroke epidemiological data, stroke affects many patients over 50 years of age.¹⁴ This is consistent with data from other studies that show stroke cases increase at over 55 years of age.¹⁵

The baseline data that has been collected are then tested for normality first with the Kolmogorov-Smirnov test (KS test). This test aims to determine the distribution of normal or abnormal data. Analysis using the KS test, it was found that the distribution of the research data was not normal. Therefore, the analysis to determine the correlation between CRP levels and NIHSS levels in acute ischemic stroke was performed using Spearman's correlation analysis.

It was seen that there was a positive correlation with moderate correlation strength of 0.454 between serum CRP levels and NIHSS values in acute ischemic stroke patients, which was statistically significant ($p < 0.05$). This means that the higher the serum CRP level, the greater the NIHSS value.

The results of this study are supported by other research which states that the increase in CRP in the serum fluid of patients in acute stroke has a worse prognosis measured by the BI modification (Barthel Index).¹⁶ In addition, there are other studies that show a correlation between CRP and stroke outcome using the SSS (Scandinavian stroke scale) in acute ischemic stroke.¹⁷ Other studies have also shown that an increase in crp is associated with stroke severity as measured by the Modified Rankin Scale (MRS) scale.¹⁸

Conclusions and Suggestions

There was a positive correlation with a correlation coefficient ($r = 0.454$) between CRP in serum and functional output as measured by NIHSS in acute ischemic stroke which was statistically significant ($p < 0.05$). Further research needs to be done, namely measuring CRP levels with the NIHSS 7 and 30 days after stroke. So that it can be seen the long-term neurologic outcome rate and with a larger sample size so as to provide more representative results.

Ethical Clearance: This study received an ethical test from Dr. Soetomo General Hospital

Source of Funding: This research was carried out through individual funding.

Conflict of Interest: There was no conflict of Interest from this study

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