


## Correlation between Serum Fibrinogen Level and Acute Ischemic Stroke Severity

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### ARTICLE INFO

#### Article history:

Received  
30 June 2023

Revised  
12 August 2023

Accepted  
31 August 2023

Manuscript ID:  
JSOCMED-300623-28-3

Checked for Plagiarism: Yes

Language Editor:  
Rebecca

Editor-Chief:  
Prof. Aznan Lelo, PhD

### Keywords

### ABSTRACT

**Introduction:** Indonesia still has a high burden for stroke, and stroke became the number one cause of mortality, in which the condition caused 328,5 thousand deaths (21,2% of death from all cause) in 2012 according to WHO. Until now, there are multiple parameters that can be used to determine the severity of an acute ischemic stroke event, one of the laboratory parameters being serum fibrinogen level. The aim of this study was to find the relationship between serum fibrinogen level and the severity of acute ischemic stroke.

**Method:** The study used a cross-sectional design from acute ischemic stroke patients in the inpatient wards of H. Adam Malik Medan Hospital and network hospital. We used contingency coefficient correlation analysis test to determine the relationship between serum fibrinogen level and the severity of acute ischemic stroke. This study involved 40 acute ischemic stroke patients.

**Results:** The results of statistical analysis found a significant positive correlation between serum fibrinogen level and acute ischemic stroke severity with weak correlation strength ( $p=0.028$ ;  $r=0.328$ ) with the median NIHSS score of the subject 6,5 and median serum fibrinogen level being 320,9mg/dL (87 – 881 mg/dL).

**Conclusion:** There was a significant relation between serum fibrinogen level and acute ischemic stroke severity. The result of this study proved that a higher serum fibrinogen level is associated with increased stroke severity.

Acute ischemic stroke, Fibrinogen, Severity

**How to cite:** Rambe AHD, Batubara CA, Nasution IK. Correlation between Serum Fibrinogen Level and Acute Ischemic Stroke Severity. *Journal of Society Medicine*. 2023; 2(8): 271-275. DOI: <https://doi.org/10.47353/jsocmed.v2i8.79>

## INTRODUCTION

From all neurological diseases arising in the adulthood, stroke comes first in the level of frequency. Ischemic stroke itself is defined as an episode of neurological dysfunction caused by cerebral focal infarction, spinal cord, or retinal caused by an ischemia, which is based on pathological imaging or other objective evidence of a cerebral focal ischemic disorder, spinal cord, or retinal at a particular location of vascular distribution; or the presence of clinical evidence of a cerebral focal ischemic, spinal cord, or retinal disorder based on symptoms 2 that persist for more than 24 hours or cause death, and other etiologies have been excluded.[1]

Many scales are available to measure stroke severity, including the National Institutes of Health Stroke Scale (NIHSS). The NIHSS is the most widely used deficit assessment scale in modern neurology.[2] Fibrinogen is a coagulation factor, the main determinant of plasma viscosity and a key factor for platelet activation. In patients with acute ischemic stroke, higher plasma fibrinogen levels are associated with an increased risk of unfavorable functional outcomes and death.[3]

## METHOD

This research is descriptive-analytic with cross-sectional data collection. The study was conducted in an integrated inpatient room, Stroke Corner, and Intensive Care Unit of H. Adam Malik Medan Hospital and

network hospital. The inclusion criteria for this study included patients with acute ischemic stroke who were established based on history, physical examination, neurological examination and head CT scan, patients aged  $\geq 18$  years and gave consent to participate in the study, by signing informed consent.

A total of 40 patients have been selected using the nonrandom sampling method consecutively. The severity of stroke was determined using a NIHSS score with a total score of 42. The severity is divided into 2, the moderate-severe stroke is defined with a score of  $>4$  and mild with a score of  $\leq 3$ . Serum fibrinogen is divided into 2 groups, namely the group with increased fibrinogen levels  $> 360$  mg/dL and normal. To determine the relationship between laboratory parameters and the severity of acute ischemic stroke, a contingency coefficient correlation analysis test was carried out to assess the strength of the relationship and the direction of the relationship.

## RESULT

Based on the characteristics of 40 research subjects, it was found that the age of all research subjects had an average of  $56.6 \pm 15.1$  years with the most age group aged 51-60 years (32.5%). The gender of the study subjects was mostly male (60%). Based on educational background, the most are high school education (40%) with self-employment as the most jobs (30%). (Table 1)

Table 1. Description of demographic characteristics of the subject of study

Demographic Characteristics	n=40
Age, year	
Average (SD)	55.6 ( $\pm 15.1$ )
Age, n (%)	
21-30	4 (10,0)
31-40	2 (5,0)
41-50	6 (15,0)
51-60	13 (32,5)
61-70	8 (20,0)
71-80	5 (12,5)
$>80$	2 (5,0)
Gender, n (%)	
Man	24 (60,0)
Woman	16 (40,0)
Education, n (%)	
No School	1 (2,5)
SD	3 (7,5)
JUNIOR	6 (15,0)
SMA	16 (40,0)
College	14 (35,0)
Occupation, n (%)	
IRT	10 (25,0)
Farmer	9 (22,5)
Civil Servants	6 (15,0)
Self employed	12 (30,0)
Private Employees	1 (2,5)
Not Working	2 (5,0)

The severity of stroke at admission was divided into mild (NIHSS score 1 – 3) and moderate-severe (NIHSS score 4 – 42), this study found most of the subjects had moderate-severe stroke (55%), with a median NIHSS score of 6.5. Serum fibrinogen levels were divided into normal (fibrinogen levels 150 – 360 mg / dL) and elevated (fibrinogen levels  $> 360$  mg / dL), and in this study found normal serum fibrinogen levels (65%) with a median value of 320.9mg / dL. (Table 2)

Table 2. Characteristics of severity and serum fibrinogen of the study subject

Characteristics of severity and serum fibrinogen	
Severity of acute ischemic stroke	
Median (Min – Max)	6,5 (1 – 29)
Severity of Acute Ischemic Stroke, n (%)	
Mild	18 (45,0)
Moderate-Severe	22 (55,0)
Serum Fibrinogen Levels, mg/dL	
Median (Min – Max)	320,9 (87 – 881)
Serum Fibrinogen Levels, n (%)	
Normal	26 (65,0)
Elevated	14 (35,0)

The relationship between serum fibrinogen levels and the severity of acute phase ischemic stroke is shown in table 3. Based on the continental coefficient test, it is known that there is a relationship between serum fibrinogen levels and the level of acute phase ischemic stroke with a significance value of  $p = 0.028$  and correlation  $r = 0.328$  So it can be said that there is an influence of serum fibrinogen levels on the severity of acute phase ischemic stroke with a weak correlation level.

Table 3. Relationship between serum fibrinogen levels and severity of acute phase ischemic stroke

Severity of acute ischemic stroke	Fibrinogen		Total (%)	p	r
	Normal	Elevated			
Mild	15	3	18(45%)	0,028*	0,328*
Moderate-Severe	11	11	22(55%)		

\*Contingency coefficient correlation test

## DISCUSSION

This study was done with 40 research subjects who had met the criteria for inclusion and exclusion, the largest age group of research subjects was in the age range of 51-60 years, followed by the 61-70 years group, with a median value of 56.5 years, the youngest age was 21 years and the oldest age was 83 years. This result is in line with research by Torana, et al (2020) which states that there is an increase in the incidence of stroke at the age of  $\geq 55$  years.[4] The results of RISKESDAS 2018 also show an increase in the incidence of stroke with increasing the age of a person.[5] Research by Metipranolol, et al (2019) shows that the highest prevalence risk of stroke cases is 62 in the age range of 50-59 years.[6] In this study, the most subjects were men (60%) compared to women (40%), RISKESDAS 2018 explained that the prevalence of stroke occurred in 11% of the male population and 10.9% female population.[5]

In the population of subjects studied, the highest level of education was found to be high school (40%) with the most jobs in the form of self-employed (30%). RISKESDAS in 2018, found the highest level of education in stroke patients, namely in patients who never attended school as much as 21.2%.[5] The differences in education level distribution results seen in this study may be influenced by education level and its relationship to medical literacy, where previous studies have been shows that low health literacy leads to delays in diagnosis. Other research suggests that high health literacy can promote health-seeking behavior.[7,8]

This study found a significant association between serum fibrinogen levels and the severity of acute ischemic stroke. This is in line with previous research which said that as an acute phase reactant, increased fibrinogen levels can be associated with the severity of an ischemic event. The study found that patients with fibrinogen levels of  $>360$  mg/dL had worse outcomes based on NIHSS scores. They speculate that this may be due to more stable fibrin clots formed under conditions of higher serum fibrinogen levels.[9]

The effect of fibrinogen on blood viscosity has been widely studied before, the relationship between fibrinogen and blood viscosity has been found significantly. Increased blood viscosity in acute stroke is responsible for low cerebral blood flow and impaired perfusion, which can lead to ischemia and infarction. This process affects the severity of neurological disorders which can be observed through NIHSS scores.[10]

Elevated fibrinogen levels result in changes in the rheological properties of the blood that exacerbate complications in peripheral blood circulation during stroke.[11] The difference in yield at higher fibrinogen levels may be related to clot structure. Clumps formed in the presence of high concentrations of fibrinogen can be made of thinner, denser fibers that are more resistant to fibrinolysis than clots formed at lower concentrations. The structure of the clot also depends on the conditions during the polymerization of fibrinogen.[9] Fibrinogen levels after acute ischemic stroke are associated with poorer neurological outcomes and efficacy for thrombolysis because they independently and directly shorten the time for occlusion and increases thrombus resistance to thrombolysis.[12]

## CONCLUSION

This study concluded that there was a significant association between serum fibrinogen levels and the severity of acute phase ischemic stroke based on NIHSS scores. This relationship may be explained by changes in clot structure arising in high levels of fibrinogen.

## DECLARATIONS

Ethics approval and consent to participate. Permission for this study was obtained from the Ethics Committee of Universitas Sumatera Utara and Haji Adam Malik General Hospital.

## CONSENT FOR PUBLICATION

The Authors agree to publication in Journal of Society Medicine.

## FUNDING

None

## COMPETING INTERESTS

The authors declare that there is no conflict of interest.

## AUTHORS' CONTRIBUTIONS

All authors significantly contribute to the work reported, whether in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas. Contribute to drafting, revising, or critically reviewing the article. Approved the final version to be published, agreed on the journal to be submitted, and agreed to be accountable for all aspects of the work.

## ACKNOWLEDGMENTS

None

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