

Comparison of changes in serum fibrinogen level in primary intracranial hemorrhage (ICH) and ischemic stroke

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Abstract

BACKGROUND: There is a growing body of evidence indicating that increase in fibrinogen is associated with increased risk of stroke. This study aimed to determine the type of stroke and the role of fibrinogen in stroke type.

METHODS: This case-control study comprised 58 hospitalized patients with intracranial hemorrhage (ICH) and ischemic stroke. Demographic and clinical characteristics, type of stroke and fibrinogen level were collected after starting the treatment.

RESULTS: The prevalence of ICH was higher in men than in women so that 60% of men and 39.3% of women in this study were diagnosed with this type of stroke. In contrast, the corresponding figures for ischemic stroke were 40% and 60.7%, respectively. Statistical analysis by chi-square test revealed significant difference in the type of stroke in terms of gender ($P = 0.026$). The mean fibrinogen levels was lower in patients with ICH (348 ± 96 mg/dl) than in patients with ischemic stroke (381 ± 126 mg/dl), however this difference was not statistically significant ($P = 0.12$). Fibrinogen levels were significantly higher in women than in men (390 ± 111 vs. 340 ± 110 mg/dl, respectively, $P = 0.017$).

CONCLUSION: Although the mean fibrinogen level was not significantly different in ICH and ischemic stroke patients, it is recommended to examine the serum fibrinogen and its related factors at least for those patients with non-modifiable risk factors and in particular for those with family history and genetic background.

Keywords: Cardiovascular Diseases, Ischemic Stroke, Fibrinogen.

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Introduction

Cerebrovascular diseases are among the main causes of disability and mortality in developed communities. Atherothrombotic syndromes of cerebral hemorrhage are among the pathogenesis of vascular diseases of the brain.¹ Although the role of coagulopathy, fibrinolytic systems have been studied in these trends and there are also available evidences that indicate that the increase in fibrinogen is associated with increased risk of stroke,² apparently increasing the fibrinogen and Willebrand factor are associated with increased bleeding in the brain.³ Therefore, it is important to determine the changes in coagulation and fibrinolytic activities in primary intracranial hemorrhage (ICH) patients compared with ischemic stroke. According to the literature search in Iran, we found that no previous study on the role of serum fibrinogen and the prevalence of the stroke. The purpose of this research was to study the possible role of fibrinogen in determining the type of stroke. The

secondary purpose of this study was to focus on the prevalence of stroke and the caused disabilities.

Materials and Methods

This study was a case-control study with two groups of 58 persons conducted in 2008-2009 in Al-Zahra teaching hospital in Isfahan, Iran. The study population included the patients who were admitted in this hospital and diagnosed with ICH and ischemic stroke. The study in general was approved by the Ethics Committee of Isfahan University of Medical Sciences and written informed consent was obtained from all participants before entering the study. The coagulation tests (PT, PTT and INR) were examined before the start of treatment for all the patients of this study and the patients who had coagulation disorders were excluded. The inclusion criteria were having ICH or ischemic stroke and the exclusion criteria were as follows: the patient who deceased before the

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measurement of fibrinogen, inability to take blood from the patient (lack of patient cooperation, known coagulation disorders, patients under treatment, patients with ICH due to an unknown etiology, using warfarin or having tumor). Demographic and clinical characteristics of patients were collected in the questionnaire after being recruited to the study. Patient's blood was sent to the laboratory to determine blood levels of fibrinogen and coagulation tests (PT, PTT and INR). After data entry to computer and data management, statistical analysis was conducted using SPSS software version 16. Mean and standard deviation was compared between the two groups by Student t-test, chi-Square and Mann-Whitney U tests, when applicable.

Results

In this study, 116 patients affected with stroke were studied. The mean age of patients was 65.4 ± 16.2 years, ranging 20 to 93 years. Overall, 60 patients (51.7%) were male and 56 (48.3%) were female. The mean age of men (65.2 ± 17.6 years) and women (65.8 ± 14.9 years) was not significantly different ($P = 0.83$). 58 patients were diagnosed to have ICH and 58 others were diagnosed with ischemic stroke. The mean age of these two types of stroke patients were 62.9 ± 15.5 and 67.8 ± 16.8 years, respectively ($P = 0.1$). Regarding gender distribution, the prevalence of ICH in men was higher than in women so that 60% of men and 39.3% of women diagnosed with this type of stroke. In contrast, the prevalence of

ischemic stroke in men and women were 40% and 60.7%, respectively. Chi-square test showed that the prevalence of stroke in both sexes were significantly different ($P = 0.026$, Table 1). Based on Magnetic Resonance Spectroscopy (MRS)⁴ criteria, 14 patients (12.1%) were diagnosed with mild disabilities, 64 (55.2%) with moderate disability, 34 (29.3%) with severe disability and 4 (3.4%) were completely disable.

The findings showed that mild disability in both ICH and ischemic groups was 13.8% and 10.3%, respectively. The moderate disability intensity was 56.9% and 53.4%, respectively. Prevalence of severe disability in both groups was equal and equivalent to 29.3% and finally, although there was no complete disability in the ICH group, it was 6.9% in studied ischemic stroke patients. Mann-Whitney U test also showed no significant differences between the two groups ($P = 0.28$, Table 2). The mean fibrinogen level was 364 ± 113 mg/dl, without significant difference between those with ICH (348 ± 96 mg/dl) and those with ischemic stroke (381 ± 126 mg/dl, Table 3). Serum fibrinogen levels in men and women were respectively 340 ± 110 and 390 ± 111 mg/dl. According to the t-test, serum fibrinogen level was significantly higher in women than in men ($P = 0.017$, Table 3). Comparison of mean serum fibrinogen levels in patients with the normal levels showed that the average difference was about 89 units and the difference was statistically significant after one sample t-test evaluation ($P < 0.001$, Figure 1).

Table 1. Frequency of stroke according to gender

Gender	Male		Female		Total	
	Number	Percentage	Number	Percentage	Number	Percentage
ICH	36	60	22	39.3	58	50
Ischemic	24	40	34	60.7	58	50
Total	60	100	56	100	116	100

$P = 0.026$

ICH: intracranial hemorrhage

Table 2. Distribution of severity of disabilities according to the type of stroke

Stroke	ICH		Ischemic		Total	
	Number	Percentage	Number	Percentage	Number	Percentage
Mild	8	13.8	6	10.3	14	12.1
Moderate	33	56.9	31	53.4	64	55.2
Severe	17	29.3	3	29.3	34	29.3
Impotent	0	0	4	6.9	4	3.4
Total	58	100	58	100	116	100

Table 3. Mean and SD of serum fibrinogen levels according to the type of stroke

Type	Fib Avg.	SD	P
ICH	348	96	
Ischemic	381	126	0.12
Total	364	113	
Male	340	110	
Female	390	111	0.017
Total	364	111	

It is noteworthy to mention that in both ischemic stroke and ICH patients, the mean fibrinogen levels showed significant differences with normal levels (P <0.001).

Discussion

In this study, a significant difference was found between fibrinogen levels in all kinds of strokes including ICH and ischemic stroke patients. Previous studies have shown that increase in fibrinogen is associated with increased risk of stroke.³ The increase in fibrinogen is considered a risk factor for ischemic stroke.⁵ So, the increase in serum fibrinogen accelerates the formation of atheroma in the arteries and thus, indirectly participates in the development of ischemic stroke.¹ It also seems that the race is another risk factor for creating ischemic stroke. For example, the serum fibrinogen level in blacks is more than that

in other races. In addition, there are relations between the increase in fibrinogen and other risk factors of stroke such as smoking, arterial pressure, diabetes and increases in blood hematocrit which can be caused by increases in fibrinogen levels and lead to stroke.¹ Another study on rats for determining the acute coagulation and fibrinolytic changes following the stroke-induced and starting thrombolytic medical treatment showed that animals that did not respond to the treatment had special coagulation situation, so the level of thrombin and antithrombin and TAT complexes were increased and consequently, the fibrinolytic effect of T-PA was reduced.⁶

Another study conducted in 2008 by Sturgeon and colleagues to determine haemostatic agents and inflammation risk factors in cerebral hemorrhage indicated that increasing the Willebrand factor and fibrinogen will increase the rate of bleeding.⁶ This study was performed on patients with a history of atherosclerosis and cardiovascular disease. The patients who had a history of atherosclerosis have been suffering from ICH more than those who had a history of severe heart disease ICH.⁷ Confirming the other results⁸⁻⁹, our study showed that average fibrinogen levels, especially in patients with ICH was lower than that in patients with ischemic stroke but there was no significant difference between the two types of strokes. This is probably related to the sampling, sample type and the sample size available for conducting the study.

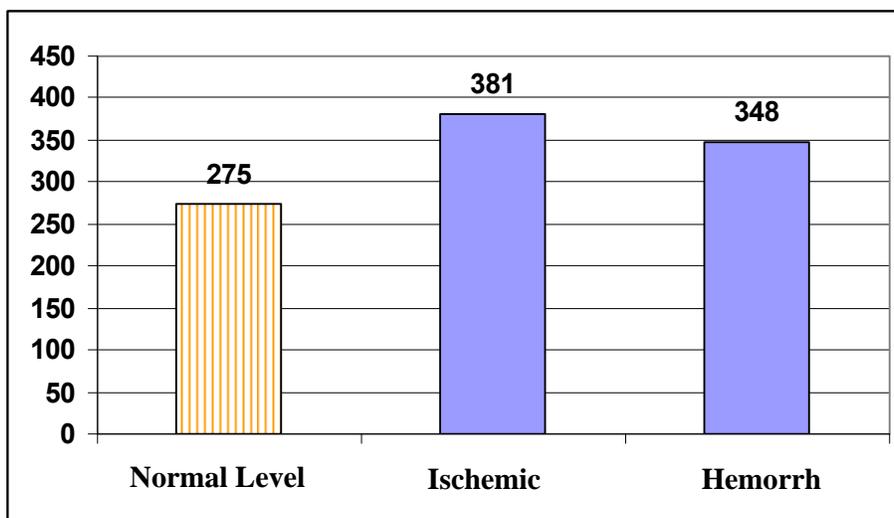


Figure 1: Compared with normal levels of fibrinogen in the two types of stroke

Another study conducted in the US showed the relationship between anchored treatment (an agent which is anti-fibrinogen) and the health of patients after the treatment. It was indicated that plasma concentrations were higher in ICH patients who were less symptomatic.⁹ Our study also showed that the age distribution regarding the two groups did not differ but regarding the type of stroke, the prevalence of ICH in men was higher than in women, so that 60% of men and 39.3% of women diagnosed with this type of stroke. In contrast, the prevalence of ischemic stroke in men and women were, respectively, 40% and 60.7% and the prevalence of the stroke was significantly different between the two genders. Cardiovascular disease is most common among men than in women and generally male gender is considered a risk factor for these diseases. But, the prevalence of stroke may be different between the two genders. A different study conducted on chronic ischemic heart patients who were without a history of stroke indicated that high plasma fibrinogen is associated with cerebrovascular accidents.¹⁰ Another study proved that the thrombin outside the vascular plays an important role in disturbances of and hemorrhagic and traumatic ischemic conditions so that its low concentration for neurons can be a protection factor against cell death caused by ischemia or cerebral hemorrhage and on the contrary, its high concentrations can lead to death of the brain cells and also the loss of blood-brain barrier causing seizures and cerebral edema.¹¹

Conflict of Interests

Authors have no conflict of interests.

References

- Bradley WG, Daroff RD. Principles of diagnosis and management. In: Bradley WG, Editor. Neurology in clinical practice: The neurological disorders. Philadelphia: Butterworth-Heinemann Elsevier; 2008. p. 1179-99.
- Adams RD, Victor M, Ropper AH. Principles of neurology. 7th ed. New York: McGraw-Hill, Health Professions Division; 2001.
- Catto AJ, Grant PJ. Risk factors for cerebrovascular disease and the role of coagulation and fibrinolysis. *Blood Coagul Fibrinolysis* 1995; 6(6): 497-510.
- Weber R, Ramos-Cabrer P, Hoehn M. Present status of magnetic resonance imaging and spectroscopy in animal stroke models. *J Cereb Blood Flow Metab.* 2006 May; 26(5): 591-604.
- Cudkowicz ME, Irizarry MC. Neurologic disorders in women. New York: Butterworth-Heinemann; 1997.
- Stehling F, Weber R, Ozcelik A, Brocker M, Volbracht L, Diener HC, et al. Acute changes of coagulation and fibrinolysis parameters after experimental thromboembolic stroke and thrombolytic therapy. *Neurosci Lett* 2008; 441(1): 39-43.
- Sturgeon JD, Folsom AR, Longstreth WT, Shahar E, Rosamond WD, Cushman M. Hemostatic and inflammatory risk factors for intracerebral hemorrhage in a pooled cohort. *Stroke* 2008; 39(8): 2268-73.
- Leira R, Davalos A, Silva Y, Gil-Peralta A, Tejada J, Garcia M, et al. Early neurologic deterioration in intracerebral hemorrhage: predictors and associated factors. *Neurology* 2004; 63(3): 461-7.
- Levy DE, Trammel J, Wasiewski WW. Ancrod for acute ischemic stroke: a new dosing regimen derived from analysis of prior ancrod stroke studies. *J Stroke Cerebrovasc Dis* 2009; 18(1): 23-7.
- Tanne D, Benderly M, Goldbourt U, Boyko V, Brunner D, Graff E, et al. A prospective study of plasma fibrinogen levels and the risk of stroke among participants in the bezafibrate infarction prevention study. *Am J Med* 2001; 111(6): 457-63.
- Xi G, Reiser G, Keep RF. The role of thrombin and thrombin receptors in ischemic, hemorrhagic and traumatic brain injury: deleterious or protective? *J Neurochem* 2003; 84(1): 3-9.