ORIGINAL ARTICLE

Correlation between Mean Plasma Fibrinogen Level and Mean Lesion Volume on CT Scan in Acute Ischemic Stroke

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ABSTRACT

Background: Stroke remains the leading cause of death and severe disability in young and elderly people. In Pakistan health care facilities are limited with neuroimaging inaccessible in certain areas; plasma fibrinogen is an easily available and cost effective parameter.
Aim: To determine correlation between mean plasma fibrinogen level and mean lesion volume on CT scan in acute ischemic stroke.
Methods: This cross Sectional Study was conducted from 23 Mar 2013 to 15 Aug 2013 at Neurology and General Medicine Departments of Military Hospital Rawalpindi (MH). We included 40 cases between 35 to 65 years of both genders with acute ischemic stroke confirmed on CT scan.
Results: In our study, mean age was calculated as 53.45+7.03 years, 29(72.5%) were male and 11(27.5%) were females, mean infarct volume in our study was calculated as 64.32+1.15 cm^3 while mean plasma fibrinogen level was calculated as 4.78+1.43 g/L, correlation coefficient r value was calculated as 0.5 while p value was calculated as 0.02.
Conclusion: We concluded a positive correlation between mean plasma fibrinogen level and mean lesion volume on CT scan in acute ischemic stroke.
Keywords: Acute ischemic stroke, mean plasma fibrinogen level, mean lesion volume, correlation.

INTRODUCTION

Stroke is a dreadful disease, has devastating consequences for individual and the community. It has recently become the second leading cause of death and disability worldwide[1]. In Pakistan as compared to existing worldwide literature, the prevalence of stroke is almost twice the highest and is reported to be 4.8%[2-4].

Almost 85% of all strokes are ischemic and remaining 15% are hemorrhagic[5]. Prompt diagnosis and an estimation of size of infarct improve the clinical outcome and minimize disability. Research and studies are going on worldwide to establish methods for early diagnosis and improve the clinical outcome.

Computerized axial tomography (CT) brain is the standard initial imaging study. CT scan may appear normal in early stages of ischemic stroke but for intracerebral hemorrhage (ICH) it is the fastest and most robust technique[6]. A number of biological markers such as leptin, high sensitivity C-reactive protein (hs-CRP), insulin, cortisol, fibrinogen, protein C, protein S, vonWillebrand factor, D-dimer, Antithrombin III and MMP-9 have been evaluated for their prognostic values and their relationship with lesion volume in stroke patients[7].

Fibrinogen is a plasma glycoprotein that is converted by thrombin into fibrin during blood clot formation. Fibrinogen circulates in the plasma at a concentration of approximately 200 to 400mg/dL, with a half-life of four days and a catabolic rate of approximately 25 percent per day[8]. The mean Fibrinogen levels was higher in patients with ischemic infarct (381±126 mg/dl) as compared to intracerebral hemorrhage (348±96 mg/dl)[9,10]. The acute phase response can elevate plasma fibrinogen by two- to 20-fold. The peak elevation in fibrinogen during the acute phase occurs by three to five days, with a gradual return to baseline following resolution of the inflammation[11,12]. Epidemiologic studies indicate that high fibrinogen levels are associated with stroke severity in almost all studied populations[13]. Plasma fibrinogen levels increase after ischemic stroke and are also associated with stroke prognosis, they along with other markers like IL-6 and miR-210 have a prognostic sensitivity of 95.2%[14]. In another study increase in fibrinogen level positively correlated in patients with cerebral infarction of different sizes[15].A detail review of literature showed positive correlation between mean plasma fibrinogen level and mean lesion volume in acute ischemic stroke with r=0.5 and p=0.005[3].

Some animal studies suggest that fibrinogen has an intrinsic CNS toxicity, promoting apoptosis, neurodegeneration and an inhibition of functional recovery after injury[16].

In a developing country like Pakistan where health care facilities are limited with neuroimaging inaccessible in certain areas, plasma fibrinogen is an

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easily available and cost effective parameter. The purpose of this study is to determine the correlation between mean plasma fibrinogen level and infarct volume on CT scan among local patients with acute ischemic stroke. On the basis of fibrinogen levels, it can be recommended as a screening tool for estimation of infarct volume.

MATERIALS AND METHODS

This cross Sectional Study was conducted from 23 Mar 2013 to 15 Aug 2013 at Neurology and General Medicine Departments of Military Hospital Rawalpindi (MH). We included 40 cases between 35 to 65 yrs of both genders with acute ischemic stroke confirmed on CT scan. Patients excluded from study were those with history of recurrent strokes, known bleeding disorder like ITP, chronic liver disease and on anticoagulants, antiplatelet drugs or chemotherapy. Moreover Suspicion of any disease as pulmonary embolism, deep vein thrombosis, malignancy, sepsis or concurrent severe systemic illness that may cause raised fibrinogen level. The above mentioned conditions act as confounders and if included will introduce bias in the study results.

Informed consent was taken after explaining purpose and benefits of study from those patients fulfilling the inclusion criteria regarding the study enrolment. This study was conducted after approval from the hospital's ethical and research committee. All indoor patients meeting the inclusion criteria were included in the study. The diagnosis of acute stroke was based on symptoms of focal neurologic deficit and CT scan brain evidence of infarct.

All patients were subjected to detailed history and examination. Mean Lesion volume on CT scan was calculated by the following formula: A×B×C/2, where A is the largest diameter and B is the perpendicular diameter of the infarct lesion, as measured, and C is the sum of the thicknesses of the slices where the lesion was visible.

From all patients 5 cc of blood was taken under strict aseptic technique and sent to specified laboratory of the hospital on the same day. Plasma fibrinogen level was measured under the supervision of an experienced pathologist. The mean plasma fibrinogen value was measured in terms of g/L (Normal Value: 1.5 - 4.0 g/L).

Strict exclusion criteria were followed to control confounders and bias in study results.

Data collected was entered in SPSS 16. Mean ± SD was calculated for continuous variables like age, infarct volume on CT scan, Plasma fibrinogen level and categorical variable like gender were expressed as frequencies and percentages. Correlation coefficient in range of (+1,-1) was calculated to investigate the bivariate relationship between Plasma fibrinogen level and infarct volume on CT scan. P value less than 0.05 was significant. All Results were presented as tables and graphs.

RESULTS

A total of 40 cases fulfilling the inclusion/exclusion criteria were enrolled to determine correlation between mean plasma fibrinogen level and mean lesion volume on CT scan in acute ischemic stroke.

Age distribution of the patients was done which shows that 12(30%) were between 35-50 years and 28(70%) were between 51-65 years of age, mean+sd was calculated as 53.45+7.03 years (Table 1).

Gender distribution of the patients was done which shows that 29(72.5%) were male and 11(27.5%) were females (Table 2)

Correlation between Mean Infarct Volume on CT Scan and Mean Plasma Fibrinogen level: Mean infarct volume in our study was calculated as 64.32+1.15 cm^3 while mean plasma fibrinogen level was calculated as 4.78+1.43g/L, correlation coefficient r value was calculated as 0.5 while p value was calculated as 0.02 (Table 3).

Table 1: Age distribution (n=40)

Age (in years)	n	%age
35-50	12	30
51-65	28	70
Total	40	100
Mean+sd	**53.45+7.03**	

Table 2: Gender distribution (n=40)

Gender	n	%age
Male	29	72.5
Female	11	27.5
Total	40	100

Table 3: Correlation between mean infarct volume on CT scan and mean plasma fibrinogen level (n=40)

Mean infarct volume	Mean plasma fibrinogen level
64.32+1.15 cm^3	4.78+1.43 g/L

Correlation coefficient r=0.5 P value= 0.02

DISCUSSION

Stroke remains the third leading cause of death and the leading cause of severe disability in portions of Asia in young [17] and elderly people [18-20]. Actually, the successful therapy for acute stroke is thrombolysis and bleeding is often a complication that can also depend on the lesion size[21].

We considered that developing country like Pakistan where health care facilities are limited with neuroimaging inaccessible in certain areas; plasma fibrinogen is an easily available and cost effective parameter. However, we planned to determine the local correlation between mean plasma fibrinogen

level and infarct volume on CT scan among patients with acute ischemic stroke. On the basis of fibrinogen levels, it can be recommended as a routine screening tool for estimation of infarct volume.

In our study, 12(30%) were between 35-50 years and 28(70%) were between 51-65 years of age, mean+sd was calculated as 53.45+7.03 years, 29(72.5%) were male and 11(27.5%) were females, mean infarct volume in our study was calculated as 64.32+1.15cm^3 while mean plasma fibrinogen level was calculated as 4.78+1.43g/L, correlation coefficient r value was calculated as 0.5 while p value was calculated as 0.02.

Our findings are in agreement with Varoqlu AO[7] who recorded a positive correlation between mean plasma fibrinogen level and mean lesion volume in acute ischemic stroke with r = 0.5 and p = 0.005[3].

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[22].

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[23].

Our results indicate the association of inflammatory biomarkers with ischemic lesion size suggesting the contribution of inflammation as a prognostic indicator for the development of clinical complications following cerebral acute events. High fibrinogen concentrations provide additional information about risk, even if it is simply a bystander of the inflammatory response in ischemic stroke and transient ischemic attack[24] https://stroke.ahajournals.org/content/40/5/1549.full - ref-12https://stroke.ahajournals.org/content/40/5/1549.full - ref-25https://stroke.ahajournals.org/content/40/5/1549.full - ref-26. All of the studies are also consistent in showing that the effect of fibrinogen on stroke prognosis is somewhat attenuated with more thorough adjustment for confounding variables, because fibrinogen is correlated with many known prognostic factors. The contribution of fibrinogen to the improvement of any prognostic prediction model would depend on exactly which other variables are included in the model. It follows logically that measures of prediction such as area under the receiver-operating-characteristic curve would always be better with inclusion of fibrinogen than without it.

The primary goal of biomarker use in stroke patients should be the identification of high-risk individuals who can be targeted for aggressive acute treatment and improved secondary prevention measure. Because compliance with lifestyle recommendations is directly related to the absolute risk perceived by the patients, the fibrinogen addition in screening procedures provides an improved prediction tool.

Actually, there is a substantial interest in the use of biomarkers panel to identify subjects at higher risk for the development of complications following thrombolysis therapy. The present study examines the association between biomarkers, paying attention, in particular, to the hypothesis that different plasma levels of biomarkers assessed at baseline in subjects affected by AIS could be predictive for development of both size lesions and clinical outcome. These results further confirm our assumption that multivariate analyses of relevant biomarkers are necessary to reduce the risk of inaccurate prognosis. We highlight the importance of differentiation of normal interval levels of serum biomarkers to improve not only clinical decision making but also post acute clinical outcome.

CONCLUSION

We concluded a positive correlation between mean plasma fibrinogen level and mean lesion volume on CT scan in acute ischemic stroke and in country like Pakistan where health care facilities are limited with neuroimaging inaccessible in certain areas, plasma fibrinogen is an easily available and cost effective parameter which may be used as a routine screening tool for estimation of infarct volume.

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