CORRELATION BETWEEN PLASMA D-DIMER LEVEL AND LESION VOLUME IN ACUTE ISCHEMIC STROKE

Amina Noor[1], Hassan Mustafa[2], Syed Affan Ali[3], Sumera kazmi[4], Nasma Noor[5], Saqib Malik[6]

[1,3,4] Department of Medicine, Abbottabad International Medical Institute, Abbottabad - Pakistan.
[2,5] Department of Medicine, Ayub Teaching Hospital, Abbottabad - Pakistan.
[6] Department of Meidicne, Lady Reading Hospital, Peshawar - Pakistan.
Address for correspondence:
Dr. Amina Noor
Senior Registrar, Department of Medicine, Abbottabad International Medical Institute, Abbottabad - Pakistan.
E-mail: noor.amna@gmail.com
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ABSTRACT

Objective: To find out correlation between serum D-dimer and lesion volume in acute ischemic stroke.

Methodology: This cross-sectional study was conducted in Ayub Teaching Hospital, Abbottabad from April 2018 to December 2018. A total of 83 patients with ischemic stroke were enrolled in this study using non-probability consecutive sampling. Diagnosis was made on history, examination and computerized tomography (CT) brain findings. A pre-designed proforma was used to collect data, which was analyzed using SPSS version 20. Descriptive and inferential statistics were applied where needed.

Results: Out of 83 patients, the mean age was 52.78 ± 10.37 years with range from 35 to 65 years. In total, 64 (77.11%) were males. Infarct volume on CT ranged from 18.00 to 192.00 cc with mean of 74.10 ± 35.02 cc. Plasma D-dimer level ranged from 10 to 200 µg/l with mean of 80.23 ± 54.65. Gender stratification of age, infarct volume and plasma D-dimer in male revealed means of 53.41 ± 10.30, 74.01 ± 34.98, and 82.20 ± 55.64 respectively, while in females means were recorded as 50.68 ± 10.58, 74.42 ± 36.11, and 73.58 ± 52.08 respectively. The correlation statistics, between infarct volume and plasma D-dimer level revealed significant positive correlation (r=0.537; p=<0.001). Correlation was further stratified based on gender and a significatly positively corelation coefficient was found.

Conclusion: Significant positive correlation was found between plasma D-dimer and lesion volume in acute ischemic stroke.

Key Words: Acute ischemic stroke, Plasma D-dimer, Lesion volume

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INTRODUCTION

Acute stroke is one of the most common causes of morbidity and mortality in the world, particularly in the developed countries[1]. Acute stroke is divided into two types; ischemic and hemorrhagic stroke. Worldwide, ischemic stroke accounts for 73% to 83% of cases while hemorrhagic stroke is found in 8% to 18%[2] patients. Diagnosis of ischemic stroke begins with history and examination, which can also help in localizing the lesion site. Computerized tomography (CT) of the brain is the standard initial imaging study but it may appear normal in early stages of ischemic stroke especially if done within 24 hours of the onset of symptoms. Though magnetic resonance imaging (MRI) of the brain is more sensitive than CT scan in picking early lesions but it is not always physically accessible or economically affordable. A number of biologic markers such as C reactive protein (CRP), D-dimer, and Matrix metalloproteinase-9 (MMP-9) are also found to be raised or changed especially in acute phase[3], which might not only help in diagnoses, but can aid in judging stroke progression and prognosis[4].

D-dimer is a fibrinogen degradation product and is one of basic laboratory markers of fibrinolysis system activity. D–dimer levels are found to rise in the initial 6 hours of onset of stroke. Its level is also found high in patients with large artery infarct and in those with more severe disease[3,5]. Review of literature has shown positive correlation between D-dimer and lesion volume in acute stroke on CT scan. In one study, D–dimer levels were found to be increased from 566.2 µg/L to 844.0 µg/L as infarct volume increased from 1cc to 200 cc[6]. Similarly, in another study, results showed a spearman's correlation coefficient of r=0.27 and p=0.001, indicating positive correlation between D-dimer and infarct volume size[7].

The present study was designed to determine the correlation between plasma D-dimer and infarct volume in patients with acute ischemic stroke. This study will add local data to the literature. The results of this study can be utilized in making future recommendations with regards to monitoring of the patients for increasing the infarct volume.

METHODOLOGY

This cross sectional study was conducted in department of Medicine, Ayub Teaching Hospital, Abbottabad from April 2018 to December 2018. A sample of 83 patients was enrolled through non probability consecutive sampling. The sample was calculated using correlation coefficient of 0.4498 between plasma D-dimer levels and infarct volume with power of 99% and level of significance as 5% using the formula mentioned below[8,9].

$$n \geq \left[\frac{Z_{1-\alpha/2} + Z_{1-\beta}}{\frac{1}{2}\log_e \frac{1+r}{1-r}}\right]^2 + 3$$

Patients aged 35-65 years, diagnosed with ischemic stroke in last 48 hours confirmed by computerized tomography (CT) scan of the brain were included in the study. Patients already on anticoagulants or with any other known bleeding disorder, with history of recurrent stroke, or having any other disease that increases D-dimer levels like pulmonary embolism, deep vein thrombosis (DVT), sepsis etc. were excluded from the study. Patients were said to have acute ischemic stroke if they had developed any focal neurological deficit within last 48 hours and showing hypodense lesion on CT brain.

After getting the approval from hospital ethical committee, informed consent was taken from the patient or from next of kin. The purpose of the study was explained to the participants followed by a detailed history and complete physical examination. Mean Lesion volume on CT scan was calculated by the following formula:

$$\frac{A \times B \times C}{2}$$

Where A was greatest infarct diameter, B was perpendicular diameter of the infarct lesion and C was number of CT slices multiplied by CT slice thickness. About 5 cc of blood was drawn from all patients, which was then sent to hospital laboratory for plasma D-dimer levels. All tests were performed in the same laboratory and by the same pathologist and information was recorded on a pre-designed proforma. SPSS version 20 was used to analyze the data, where mean ± SD was calculated for continuous variables like age, infract volume on CT and plasma D-dimer level, while categorical variables like gender was described as frequency and percentages. To know the relationship between D – dimer and infarct volume on CT scan, Pearson's correlation coefficient was used to find correlation between D-dimer level and lesion volume of stroke.

RESULTS

The mean age of the patients was 52.78 ± 10.37 years ranging from 35 to 65 years. In total, 64 (77.11%) were males, while 19 (22.89%) were females. Infarct volume on CT scan ranged from 18.0 to 192 cc with mean of 74.10 ± 35.02 cc. Plasma D-dimer level ranged from 10 to 200 µg/l with the mean of 80.23 ± 54.65 as given in table 1. The correlation statistics, between infarct volume and plasma D-dimer level revealed significant positive correlation (r=0.537; p=<0.001) as shown in table 2. Correlation was stratified based on gender. In male patients, correlation co-efficient was r=0.537 with a significance level of p=<0.001 while in females correlation co-efficient was recorded to be r=0.548 and significance level was p=0.015.

Table 1: Descriptive Statistics of age, infarct volume and plasma D-dimer level

	N	Min	Max	Mean	Std. Deviation
Age in years	83	35	65	52.78	10.371
Infarct Volume on CT (cc)	83	18.0	192.0	74.108	35.0215
Plasma D-Dimer level(µg/l)	83	10	200	80.23	54.658

Table 2: Correlation between Infarct Volume and Plasma D-dimer level

		Infarct Volume on CT (cc)
Plasma D-Dimer level(µg/l)	Pearson Correlation	0.537**
	Sig. (2-tailed)	0.000
	N	83
**. Correlation is significant at the 0.01 level (2-tailed).		

Table 3: Stratification with respect to gender, age, infarct volume, and D-dimer level

Gender	Age (Years)	Infarct Volume (cc)	D-dimer level µg/l
Male (n = 64)	53.41 ± 10.30	74.01 ± 34.980	82.20 ± 55.64
Female (n = 19)	50.68 ± 10.58	74.42 ± 36.11	73.58 ± 52.08

DISCUSSION

Stroke remains a major cause of disability in both young and old patients in Asia, with its mortality rates on the rise[10-12]. Its management includes timely thrombolysis which is, however, associated with increased risk of intracerebral bleed[13]. In a developing country like Pakistan, where Computerized Tomography (CT) scan is not readily available in every city and as most of the patients are poor, so serum D-dimer, being cost effective and easily available test, can prove to be productive. We found a significant positive correlation between infarct volume and D-dimer levels. Our results are in agreement with Matsumoto, et al[14]. and Young-woo, et al[6]. who reported that serum D-dimer levels and infarct volume in ischemic stroke were positively correlated.

Zi and his colleagues[15] also studied the correlation of serum D-dimer levels and infarct size on CT scan. They observed that D-dimer levels were significantly high in acute ischemic stroke. In addition, they also reported that patients with more severe ischemic stroke tend to have higher D–dimer levels. Similar results were also observed by Yousry, et al[16]. who reported that high D–dimer level in ischemic stroke is a poor prognostic marker. The results of both Zi, et al[15]. and Yousry, et al[16]. are in concordance with our results.

Hamatani, et al[17]. found that the incidence of ischemic stroke is significantly high among patients with high D-dimer levels admitted with acute heart failure[17]. In another study conducted by Skoloudík[18] it was observed that patients with larger infarct sizes have higher serum D-dimer values in their initial 6 hours of onset of stroke. Barber et al[19]. noted that D - dimer levels can provide useful information regarding early worsening after acute ischemic stroke. However, others do not recommend D-dimer levels usage as an assessment tool in ischemic stroke, except in cardioembolic stroke[18,20].

Lövblad, et al[21]. postulated that severity of the stroke can be predicted from infarct size. In addition, they observed that infarct size also correlates with National Institutes of Health (NIH) Stroke Scale and other severity scores[22-23]. Koch, et al. found that cardioembolic strokes have higher D-dimer levels compared to the non-cardioembolic subtype[24].

In literature, numerous mechanisms have been proposed that link D-dimer levels to acute ischemic stroke and poor outcomes. Hypercoagulable states have strong association with ischemic stroke, and in these patients D-dimer levels are usually high. In addition, D-dimer is also an acute phase reactant, therefore its level increases whenever there is inflammation. Since larger strokes are associated with inflammation, this explains why D-dimer levels may be high in patients with larger strokes[19,25-27].

LIMITATIONS

It was a single center study and the sample size was small. Moreover, no serial D-dimer levels were measured to see the relationship between D-dimer levels and prognosis of the patient.

CONCLUSION

There is a positive correlation between mean plasma D-dimer level and mean lesion volume on CT scan in acute ischemic stroke.

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CONTRIBUTORS

AN conceived the idea, wrote initial manuscript, carried out literature search and organized bibliography. HM and SA executed the project, helped acquisition and interpretation of data and corrected references. SK, NN and SM went through the manuscript, did corrections, interpreted the data in the light of objectives and wrote final manuscript. All authors contributed significantly to the submitted article.