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"Study of D-dimer levels as short term prognostic marker in patients with acuteischemic stroke.

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Abstract

Background: Elevated levels of plasma D-dimer increase the risk of ischemic stroke, stroke severity, and the prognosis of stroke patient. The plasma D-dimer level increases during blood thrombosis and degradation of fibrin, hence it is a biological marker of haemostatic abnormalities and thrombosis. Association between plasma D-dimer level and functional outcome of acute ischemic stroke is unclear hence we have undertaken study to investigate whether plasma D-dimer level is a determinant of short-term poor functional outcome in patients with acute ischemic stroke (AIS). **Methods:** Present study was cross sectional in nature conducted on 100 AIS patients. All patients fulfilling inclusion criteria and exclusion criteria were taken up for the study. **Results:** In the present study, there was strong positive correlation of Modified Rankin Scale scores in patients with AIS with D dimer level (r=0.6; p=0.04) which means patients with poor short-term outcomes had significantly raised D dimer levels.

Conclusion: Plasma D dimer level is determinant of short-term poor outcome & prognosis inpatient with acute ischemic stroke.

Key words: Plasma D dimer, Ischemic stroke, short term outcome, prognosis.

Introduction:

Elevated levels of plasma D-dimer increase the risk of ischemic stroke, stroke severity, and the prognosis of stroke patient.[1,2] The plasma D-dimer level increases during blood thrombosis and degradation of fibrin, hence it is a biological marker of haemostatic abnormalities and thrombosis.[3] D-dimer is a soluble fibrin degradation final product and derived from the cross-linked fibrin network as it undergoes plasmin-mediated degradation.

Elevated D-dimer concentrations could be associated with cerebral venous sinus thrombosis, acute pulmonary embolism, spontaneous intracerebral hemorrhage, long-term neurologic outcomes in arterial ischemic stroke.[4] Markers of fibrin formation were found to be significantly increased after acute ischemic stroke and transient ischemic attack (TIA); their levels significantly differed according to stroke subtype.[5]

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As only few studies have been carried out, the association between plasma D-dimer level and functional outcome of acute ischemic stroke is unclear. The aim of this study is to investigate whether plasma D-dimer level is a determinant of short-term poor functional outcome in patients with acute ischemic stroke (AIS).

Objectives

To estimate levels of D-dimer in patients of acute ischemic stroke and to determine the association of elevated levels of D-dimer with short-term outcomes.

Materials and Methods

This was a longitudinal follow up study conducted over a period of six months from December 2022 to May 2023. We have taken approval from the Institutional Ethical committee of the medical college and this study is consistent with all the ethical standards. Written informed consent was taken from all study subjects.

All patients fulfilling inclusion criteria and exclusion criteria admitted in ICU of Dr. PDMMC and tertiary care hospital were taken up for the study until fulfilling the required sample size.

A total of 100 male and female patient with acute ischemic stroke (AIS) >18 years age admitted in our tertiary care hospital were recruited in the study. AIS was diagnosed according to the World Health Organization criteria combined with brain CT or MRI confirmation within 48 hours. Patients with acute hemorrhagic stroke and venous stroke, preexisting significant disability & those who did not willing to participate were excluded from study. Pre-validated, pretested, semi structured questionnaire was used as data collection tool.

Thorough systemic and general examination was done for clinical evaluation.

All participants were subjected to detailed neurological history taking (with stressing on the vascular, cardiac risk factors) and full general and neurological examination. Blood investigation (CBC, ESR, CRP, KFT, LFT, lipid profile & D-dimer), Radiological investigation (CT brain, MRI brain) were carried out. The normal range of morning plasma D-dimer concentration considered in our study was 0–0.5 mg/L. Each participant was followed up after 3 months i.e. 90 days via telephone and face to face for the assessment of short term outcomes. outcome was assessed with modified Rankin Scale (mRS). A good functional outcome was defined as an mRS score of 0–2 points, whereas a poor outcome was mRS score of3–6 points.

1-α/2 Sample size was calculated with n = [DEFF*Np(1-p)]/ [(d^2/Z^2*(N-1) + p*(1- p)] usingOPENEPI software version 3. Tao Yao et al[6] in their study of Elevated plasma D-dimer levels are associated with short-term poor outcome in patients with acute ischemic stroke, found that sensitivity of D-dimer level for detection of poor outcome was 83.8%. Considering this, with 95% confidence interval and absolute precision of 8%, sample size came out to be 82 which was rounded to 100 for convenience of calculations.

Data was entered in Microsoft Excel and analyzed using SPSS Software. Means were compared by using student t test while qualitative variables compared by using Chi square test ofsignificance.

Results:

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The present study was prospective in nature conducted on 100 acute ischemic stroke patients, on follow up assessment of outcome at 90th day by Modified Rankin Scale we have found that 42 (42%) patient was having good outcome while 58 (58%) was having poor outcome. Mean age of the patient in good outcome group was 59.3 ± 11.4 years vs 61.8 ± 10.8 years in poor outcome group & there was no significant difference between the two (p=0.2).

Significantly more no. of males (61.9%) had good outcome while significant no. of females (62.1%) had poor outcome (p=0.01). Comorbidities seen in our study were coronary artery disease, diabetes, hypertension, previous stroke, dyslipidemia. Patients with good & poor outcome did not differ significantly according to comorbidities (p.0.05). Two groups also did not differ as per addictions (p>0.05). Mean D dimer level of patients with poor outcome (1.88 ± 0.98 mg/l) was significantly raised than the patients with good outcome (0.44 ± 0.22 mg/l) (p<0.0001). (Table 1)

In the present study, there was strong positive correlation of Modified Rankin Scale scores in patients with AIS with D dimer level (r=0.6; p=0.04) which means patients with poor short-term outcomes had significantly raised D dimer levels. (Table 2)

Discussion:

In our study, higher plasma D-dimer level on admission was a significant independent determinant of short-term outcome at 90th day as measured by mRS (Modified Rankin Scale). 42% patient was having good outcome while 58% was having poor outcome.

Mean age of the patient in these two groups did not differ significantly (p=0.2). Significantly more no. of males (61.9%) had good outcome while significant no. of females (62.1%) had poor outcome (p=0.01). Comorbidities seen were coronary artery disease, diabetes, hypertension, previous stroke, dyslipidemia. Patients with good & poor outcome did not differ significantly according to comorbidities (p>0.05). Two groups also did not differ as per addictions (p>0.05). Mean D dimer level of patients with poor outcome (1.88 ± 0.98 mg/l) was significantly raised than the patients with good outcome (0.44 ± 0.22 mg/l) (p<0.0001). Potential confounders: age, comorbidities, addictions fortunately equally distributed between the two groups. These findings are in line with Tao Yao et al and Yosria[6] and Al Hameed AlTaweel etal.[7]

In the present study, there was strong positive correlation of Modified Rankin Scale scores in patients with AIS with D dimer level (r=0.6; p=0.04) which means patients with poorshort-term outcomes had significantly raised D dimer levels. Many of the epidemiological studies have revealed that there is a positive association between plasma D-dimer levels and stroke,[8-10] stroke severity,[11,12] infarct volume,[13-15] and progression.[16,17] This is consistent with Tao Yao et al[6] who reported that after adjustment for potential confounding variables, higher plasma D-dimer level on admission was associated with poor outcome and Jing Zhang et al[18] who noted elevated D dimer level associated with poor functional outcome at

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both 30 days and90 days.

Conclusion:

As the raised plasma D dimer levels are strongly correlated with short term poor outcomemeasured by Modified Rankin Scale, we can conclude that plasma D dimer level is determinant of short-term poor outcome & prognosis in patient with acute ischemic stroke.

Declaration:

There was no source of funding in our study and there was no any conflict of interest inthis study.

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Table 1Association of short-term outcomes with baseline characteristics.

Baseline characteristic		**Good Outcome (n=42)** **N0. (%)**	**Poor Outcome (n=58)** **N0. (%)**	**P**
Age (years)	Mean ± SD	59.3 ± 11.4	61.8 ± 10.8	0.2
Gender	Male	26 (61.9)	22 (37.9)	**0.01**
	Female	16 (38.1)	36 (62.1)	
Comorbidities	CAD	11 (26.2)	13 (22.4)	0.6
	DM	19 (45.2)	28 (48.3)	0.7
	HTN	32 (76.2)	42 (72.4)	0.6
	Previous stroke	06 (14.3)	08 (13.8)	0.9
	Dyslipidemia	27 (64.3)	41 (70.7)	0.5
	Obesity	17 (40.5)	24 (41.4)	0.9
	Alcohol	09 (21.4)	15 (25.9)	0.6

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Addictions	Smoking	18 (42.9)	24 (41.4)	0.8
D dimer (mg/l)	Mean ± SD	0.44 ± 0.22	1.88 ± 0.98	**<0.0001**

Table 2. Correlation of D dimer level with Modified Rankin Scale scores in patients with AIS.

D dimer level	**mRS score**	**Pearson correlation**	
Mean ± SD	**Mean ± SD**	**R**	**P**
1.16 ± 0.7	4.3 ± 2.89	0.6	**0.04**