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Original Research Article

An Observational Study of Correlation of Plasma D-Dimer Level with Severity of Cerebral Venous Thrombosis

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Abstract

Introduction: Cerebral venous thrombosis (CVT) is an uncommon but clinically significant cause of stroke, characterized by the formation of thrombi within the cortical veins and/or the draining dural venous sinuses. Plasma D-Dimer (fibrin degradation product) is a biological marker of endogenous fibrinolysis. It is easy to carry out and affordable investigation to reliably rule out CVT. D-Dimer has a very high negative predictive value of ruling out venous thromboembolism. Early diagnosis of this condition will prevent mortality and morbidity. Several studies been done for analyzing the value of D-Dimer in excluding cerebral venous thrombosis. Hence this study is to correlate the plasma D-Dimer level in subjects with cerebral venous thrombosis.

Material and Methods: This is an Observation study was conducted in the Department of General Medicine at Tertiary Care Teaching Hospital patients >18 years presented with headache and other symptoms suggestive of cerebral venous thrombosis. In all subjects with symptoms suggestive of CVT and diagnosed to have cerebral venous sinus thrombosis by means of MRI brain and MR venogram, detailed history was taken and clinical examination was done after taking informed consent. After confirming the diagnosis of CVT blood samples were drawn, plasma separated and sent to laboratory. Plasma D-dimer level was measured by ELISA method.

Results: In the present study of 40 subjects, 25 subjects (62.5%) had positive D-dimer level (>500ng/ml) and 15subjects (37.5%) had negative D-dimer level (0-500ng/ml). D-dimer was positive in 25 subjects out of which 19 subjects (76%) presented with acute onset of symptoms and 6 subjects (24%) presented with subacute onset of symptoms. D-dimer was negative in 15 subjects out of which 9 subjects (60%) presented with acute onset of symptoms and 6 subjects (40%) presented with chronic onset of symptoms. In subjects with subacute and chronic onset of symptoms mean D-dimer was low 401.53± 191.84 and 191 ± 151.12 respectively. The p-value is 0.00001 which is statistically significant at $p<0.05$.

Conclusion: The diagnostic value of D-dimer is particularly pronounced in the acute phase due to active fibrinolysis, with mean levels decreasing substantially in subacute and chronic cases. While common symptoms such as headache, focal neurological deficits, or altered consciousness are frequently present, they do not consistently correlate with D-dimer elevation, underscoring the need for comprehensive clinical and radiological evaluation.

Keywords: D-dimer, MR venography, Acute CVT.

Introduction

Cerebral venous thrombosis (CVT) is an uncommon but clinically significant cause of stroke, characterized by the formation of thrombi within the cortical veins and/or the draining dural venous sinuses. [1] It may occur in isolation or in combination, affecting approximately 5 individuals per million annually and accounting for 0.5–1% of all strokes worldwide. [2] The condition exhibits a marked female predominance, with about 75% of adult patients being women, a trend often attributed to hormonal influences, pregnancy, and the puerperium. [3] In the Indian context, CVT is particularly noteworthy, contributing to 10–20% of stroke cases in young adults**.** [4] More than 100 etiological factors have been reported in the literature, encompassing infectious processes, systemic prothrombotic states, autoimmune disorders, malignancies, and local cranial pathologies. [5] Despite comprehensive diagnostic evaluation, no definitive cause is identified in 20–25% of patients, leaving a substantial proportion classified as idiopathic CVT. [6] The clinical

presentation of CVT is highly variable, posing significant diagnostic challenges. The onset can be acute**,** subacute, or chronic, with symptoms ranging from mild headaches to life-threatening neurological deficits. [7] Headache is the most common presenting symptom, reported in 70–90% of cases, followed by seizures (approximately 40%), and focal neurological deficits such as monoparesis, hemiparesis, paraparesis, or hemisensory disturbances. [8] Alterations in consciousness occur in 15–20% of patients, and papilledema is observed in 20–30%**.** This broad symptom spectrum often leads to delayed recognition and misdiagnosis. [9]

The pathogenesis and clinical impact of CVT depend on multiple factors, including the location of thrombosis, its extent, the duration of the occlusion, and the rate of thrombus formation. [10] The disease may present de novo or occur in conjunction with other systemic or neurological disorders. Given its heterogeneity and nonspecific clinical profile, a high index of suspicion is essential for early diagnosis and prompt management. [11]

Neuroimaging plays a central role in confirming the diagnosis. While CT brain remains a useful initial modality, it detects abnormalities in only about 70% of cases**.** [12] MRI brain combined with MR venography is considered the gold standard, offering superior visualization of venous sinus occlusion, collateral venous flow, and associated parenchymal changes. [13]

Material and Methods

This is an Observation study was conducted in the Department of General Medicine at Tertiary Care Teaching Hospital patients >18 years presented with headache and other symptoms suggestive of cerebral venous thrombosis.

Inclusion Criteria

Age above 18 yrs Subjects presented with severe headache & other symptoms suggestive of CVT, who are diagnosed to have CVT by means of MRI & MRV in Tertiary Care Teaching Hospital.

Exclusion Criteria

- Pregnancy
- Pulmonary embolism or Deep vein thrombosis
- Arterial stroke within past 3 months
- Head injury within past 3 months
- Septicemia

Method of Collection: In all subjects with symptoms suggestive of CVT and diagnosed to have cerebral venous sinus thrombosis by means of MRI brain and MR venogram, detailed history was taken and clinical examination was done after taking informed consent. After confirming the diagnosis of CVT blood samples were drawn, plasma separated and sent to laboratory. Plasma D-dimer level was measured by ELISA method.

Statistical Analysis: All the data were entered in a data collection sheet in an Excel format and analysed using SPSS Software. Numerical values were reported using mean and standard deviation. Categorical values were reported using number and percentages.

Statistical significance will be shown by Chi-square test. Probability (p) value less than 0.05 was considered a statistically significant.

Results

Table 1: Plasma D-dimer level distribution in CVT

D – dimer (ng/ml)	Number of subjects	Percentage %
Positive (>500)	25	62.5
Negative (0-500)	15	37.5
Total	40	100

In the present study of 40 subjects, 25subjects (62.5%) had positive D-dimer level (>500ng/ml) and 15subjects (37.5%) had negative D-dimer level (0-500ng/ml).

Table 2: Correlation of plasma D-dimer with mode of onset

Onset of symptoms	D – dimer ng/ml		
	Positive (>500)	Negative (0-500)	Total
Acute	19 (76%)	0	19
Subacute	6 (24%)	9 (60%)	15
Chronic	0	6 (40%)	6
Total	25 (100%)	15 (100%)	40

D-dimer was positive in 25 subjects out of which 19 subjects (76%) presented with acute onset of symptoms and 6 subjects (24%) presented with subacute onset of symptoms. D-dimer was negative in 15 subjects out of which 9 subjects (60%) presented with acute onset of symptoms and 6 subjects (40%) presented with chronic onset of symptoms. The p-value is 0.000199 which is statistically significant at $p<0.05$.

Table 3: Correlation of mean D-dimer with mode of onset

Onset of symptoms	D-Dimer in ng/ml Mean	Standard deviation ±SD
Acute	1986.68	±1048.10
Subacute	401.53	±191.84
Chronic	191	±151.12

Among subjects with acute onset of symptoms mean D-dimer was high 1988.68±1048.10.

In subjects with subacute and chronic onset of symptoms mean D-dimer was low 401.53± 191.84 and 191 ± 151.12 respectively. The p-value is 0.00001 which is statistically significant at $p<0.05$.

Table 4: Correlation of plasma D-dimer with headache

Headache	D-dimer (ng/ml)		Total
	Positive (>500)	Negative (0-500)	
Yes	22 (88%)	10 (66.66%)	32
No	3 (12%)	5 (33.33%)	8
Total	25 (100%)	15 (100%)	40

25 subjects were D-dimer positive of which 22 subjects (88%) were having headache and 3 subjects (12%) were not having headache 15 subjects were D-dimer negative of which 10 subjects (66.66%) were having headache and 5 subjects (33.33%) were not having headache. The p-value is 0.010247 which is statistically not significant at $p<0.05$.

Table 5: Correlation of plasma D-dimer with level of consciousness

	D dimer ng/ml		
	Positive (>500)	Negative (0-500)	
Altered sensorium	8 (32%)	6 (40%)	14
Conscious	17 (68%)	9 (60%)	26
Total	25 (100%)	15 (100%)	40

25 subjects were D-dimer positive of which altered sensorium was present in 8 subjects (32%) and 17 subjects (68%) were conscious. 15 subjects were D-dimer negative of which altered sensorium was present in 6 subjects (40%) and 9 subjects (60%) were conscious. The p-value is 0.607565 which is statistically not significant at $p<0.05$.

Table 6: Correlation of plasma D-dimer with focal deficits

Focal deficits	D-dimer (ng/ml)		Total
	Positive (>500)	Negative (0-500)	
Yes	12(48%)	8(53.33%)	20
No	13(52%)	7(46.6%)	20
Total	25 (100%)	15 (100%)	40

25 subjects were D-dimer positive of which 12 subjects (48%) were having focal deficits and 13 subjects (52%) did not have focal deficit 8 subjects (53.3%) with D-dimer negative were having focal deficit and 7 subjects (46.6%) did not have focal deficits. The p-value is 0.182422 which is statistically not significant at $p<0.05$.

Table 7: Correlation of plasma D-dimer with CT brain plain

	D – dimer ng/ml		
CT Brain	Positive (>500)	Negative (0-500)	Total
Normal	7(28%)	9(60%)	16
Abnormal	18(72%)	6(40%)	24
Total	25(100%)	15(100%)	40

In this study of 40 subjects with CVT, 7 subjects (28%) with D-dimer positive were having normal CT brain and 18 subjects (72%) with positive D-dimer were having abnormal CT brain. The p-value is 0.022796 which is statistically significant at $p<0.05$.

Table 8: Correlation of mean plasma D-dimer with sinus involvement (MRV)

MRV Number of sinus involved	Mean D-dimer (ng/ml)	Standard deviation ±SD
1	296.75	±157.9
2	1558	±1059.65
3	2433.33	±1582.19

Mean plasma D-dimer was less (296.75±157.9 ng/ml) in subjects with 1 sinus involvement. In subjects with 3 sinuses and 2 sinuses involvement mean D-dimer was positive 2433.33±1582.19 and 1558 ± 1059.65 ng/ml respectively. The p-value is 0.00004 which is statistically significant at $p<0.05$.

Discussion

The present study evaluated the relationship between plasma D-dimer levels and various clinical as well as radiological parameters in patients diagnosed with cerebral venous thrombosis (CVT). Out of 40 subjects, 62.5% demonstrated elevated plasma D-dimer levels (>500 ng/ml), while 37.5% had normal levels. This proportion of D-dimer positivity aligns with previous research, such as Kosinski et al. (2004), [13] who reported D-dimer elevation in approximately 60–80% of acute CVT cases, emphasizing its diagnostic utility, particularly in early disease stages.

In our study, elevated D-dimer levels were significantly associated with acute onset of symptoms (p=0.000199). Mean D-dimer levels were highest in the acute group (1986.68 ± 1048.10 ng/ml), followed by subacute (401.53 ± 191.84 ng/ml) and chronic (191 ± 151.12 ng/ml) presentations. This is consistent with Coutinho et al. (2012), who observed that D-dimer levels peak during the acute phase due to active fibrinolysis and decline with chronicity as the thrombus stabilizes. [15] Our findings reinforce the concept that D-dimer is most valuable as a diagnostic marker in acute CVT, whereas normal levels do not exclude subacute or chronic cases. Although headache was the most common presenting symptom (80% of subjects), its correlation with D-dimer positivity was not statistically significant (p=0.10247). This is similar to findings by Linn et al. (2003), who noted that headache, though frequent, is nonspecific and may be present in patients with both elevated and normal D-dimer levels. [16] Therefore, headache alone cannot be considered a predictor of D-dimer elevation. [17]

No statistically significant association was found between altered sensorium and D-dimer positivity (p=0.607565). This parallels the observations of Ferro et al. (2004), who suggested that clinical severity markers such as decreased consciousness are more related to the extent and location of thrombosis rather than to fibrin degradation activity. [18]

Similarly, focal neurological deficits did not show significant correlation with D-dimer levels (p=0.182422). Prior studies, including those by Guenther et al. (2005), have also demonstrated that focal deficits in CVT reflect local venous congestion and parenchymal injury, which may occur independently of ongoing thrombus formation or fibrinolytic activity. [19]

We found a significant association between abnormal CT findings and elevated D-dimer levels (p=0.022796). This agrees with Linn et al. (2006), who reported higher D-dimer values in patients with radiologically evident parenchymal lesions, suggesting that more extensive thrombus burden and secondary venous infarction trigger greater fibrin degradation. [20]

A significant positive correlation was observed between the number of sinuses involved and mean plasma D-dimer levels (p=0.00004). Patients with three sinuses affected had the highest mean levels (2433.33 ± 1582.19 ng/ml), followed by two sinuses (1558 ± 1059.65 ng/ml) and one sinus (296.75 ± 157.9 ng/ml). These findings are consistent with Meng et al. (2018), who concluded that the extent of thrombosis directly influences fibrin turnover and thus D-dimer concentration. [21]

Plasma D-DIMER and ONSET of CVT Compared to Other Studies

- In our study there is strong relationship between D-dimer and duration of presentation, plasma D-dimer was positive in acute 76% and subacute 24% of subjects. These results are comparable with studies conducted by DR. A Akila et al and Misra et al.
- In study conducted by DR. A Akila et al plasma D-dimer was positive in 80% subjects with onset upto7 days and negative in 20% subjects with >7days duration of symptoms.
- In study conducted by Misra et al subjects with positive D-dimer results had shorter duration of illness (mean=12 days) compared with those with negative D-dimer results (mean= 76 days)

Plasma D-DIMER and MRI / MRV

- D-dimer has a strong relationship with the MRV findings. In our study, all the subjects with D-dimer positive test had features of CVT in MRI. The association between D-dimer and MRI is statistically significant in our study.
- In the correlation between MRV and mean D-dimer if there is a single sinus involvement the positivity of D-dimer is less. When the number of sinus involvement is more, the positivity of D-dimer is high.
- It is comparable with other study conducted by DR. A Akila et al which shows similar results.

Our study supports the utility of plasma D-dimer measurement as a useful adjunctive diagnostic tool in suspected acute CVT, especially in cases with extensive sinus involvement and radiological

abnormalities. However, normal D-dimer values should not exclude the diagnosis, particularly in subacute or chronic cases where the thrombotic process is less active.

Conclusion

This study demonstrates that plasma D-dimer levels are significantly elevated in patients with acute onset cerebral venous thrombosis (CVT), in those with multiple sinus involvement, and in cases with abnormal CT brain findings. The diagnostic value of D-dimer is particularly pronounced in the acute phase due to active fibrinolysis, with mean levels decreasing substantially in subacute and chronic cases. While common symptoms such as headache, focal neurological deficits, or altered consciousness are frequently present, they do not consistently correlate with D-dimer elevation, underscoring the need for comprehensive clinical and radiological evaluation. MR venography remains the gold standard for diagnosis, and D-dimer measurement serves best as an adjunctive tool, particularly in excluding acute CVT when levels are normal.

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