Original Article

Hemostatic Abnormalities in Ischaemic Stroke Patients

Abnormalities in Ischaemic Stroke

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ABSTRACT

Objective: To evaluate hemostatic markers, D. Dimers, PT and APTT in ischaemic stroke patients.
Study Design: Observational study.
Place and Duration of Study: This study was conducted at the Medical Department of Mardan Medical Complex (Medical Teaching Institute) and Pathology Department of Bacha Khan Medical College, Mardan, from November, 2018 to July, 2019.
Materials and Methods: Hundred patients of stroke and fifty healthy individuals were included in this study. All patients and healthy individuals were subjected to hemostatic markers i.e. D. Dimers, PT and APTT.
Results: In this study total of 65 patients with stroke showed elevated D. Dimers levels. Eighteen out of 100 i.e. 18% had D. Dimers level in the range of 199-500 ng/ml. Fifteen patients had D. Dimers in the range of 501-1000 ng/ml and 32 out of 100 i.e 32% of the stroke patients showed D. Dimers levels In the range of 1001-2000 ng/ml. Thirty five patients had D. dimers in the normal range. Activated partial prothrombin time (APTT) in 8 patients was found to be shortened. Mean APTT was 33 +.562 seconds. Similarly prothrombin time (PT) in 6 patients was found to be shortened than normal. Mean PT value was 11 + .265 seconds. This study showed that D. Dimers were significantly elevated and PT and APTT were significantly shortened in stroke patients. P value for D. Dimer was P<.00265 and for PT and APTT, P value was < .00326.
Conclusion: This study concluded that stroke patients with infarction are associated with significant hemostatic abnormalities which reflect changes in hemostasis and thrombosis. Findings of elevated D. Dimers and shortened PT and APTT in patients with infarction will reduce morbidity and mortality in such patients if properly identified and managed in time.
Key Words: D. Dimer, PT, APTT, Stroke Patients.

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INTRODUCTION

Stroke is a syndrome characterized by the initiation of acute neurological disorder lasting for at least 24 hours. It reflects the focal disturbance in brain circulation[1, 7, 8]. If the disorder lasts for less than 24 hours, it is referred as Transient Ischemic Attack (TIA)[2]. The neurons of the affected area die due to obstruction of the arteries and so there is no supply of oxygen and neutrients to the involved area[3]. There are two main types of stroke, ischemic and hemorrhagic, accounting for approximately 85% and 15% respectively[4].

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Stroke is the world's third leading cause of mortality and morbidity with high incidence in the population[5].
It has been reported by the American Heart Association that on average, every 40 seconds someone in the United States has a stroke [(6)]. Various studies have been conducted which demonstrated that hemostatic disturbances are common in stroke patients[7] and that stroke is a thrombo inflammatory disease[8]. The pathophysiological mechanism of this phenomenon is multifactorial. Stroke is associated with significant coagulation abnormalities. There is evidence of increased thrombin generation and fibrin turn over, altered fibrinolytic activity and disturbed endothelial dysfunction[9,10].
D. dimer is a useful marker and elevated level easily identify thrombus formation in such patients before going into expensive, time consuming investigations. Elevated level can give immediate information to the clinician regarding thrombolic status of the patient. Similarly shortened PT and APTT also help in the prediction of ischaemic stroke.

MATERIALS AND METHODS

This study was conducted in Pathology Department of Bacha Khan Medical College, Mardan and Medical

Department at Mardan Medical Complex (MTI), Mardan, from November, 2018 to July, 2019.

A total 100 patients of ischaemic stroke were included in the study and 50 patients were taken as a control group. Sixty patients (60%) were males and 40% were females. Age was from 50-70 years. Patients with history of venous thrombosis, septicemia, malignancy and infection were excluded from the study. For D. Dimer 1.8 cc of blood was taken in a tube containing 0.2 cc of sodium citrate. The same procedure was adopted for PT and APTT. These samples were then centrifuged. For D. dimers plasma was analyzed by Hi-tech machine Architect C 400 using Quantia D. Dimer reagent.

For PT 200 ul of soluplastin (PT reagent) was added to 100 ul of patients serum white 100 ul of APTT reagent along with 100 ul of calcium chloride was added to 100 ul of patients serum for measurement of APTT. The tests were performed on K.C 4 (Anelung) machine.

D. dimer is formed as plasmin mediated proteolytic degradation product of cross linked fibrin clots. D. dimer fragments increase in any condition where clot formation and subsequent fibrinolysis occurs. Measurement of D. dimer identify both clot formation and degradation and also determine the severity of hypercoagulable state as hypercogulable state is more prone to thrombosis. The normal value of D. dimers in our study was 140-198 ng/ml.

Prothrombin Time and APTT are also hemostatic investigations which determine the activity of both the extrinsic and intrinsic pathways. Normal value of PT and APTT in our study was 12 second and less than 35 seconds respectively. These investigations were also performed according to standard procedure. Its high level identify that there is coagulation factor deficiency or there is consumption of the coagulation factors. Its low level signify a hypercoagulate state and activated hemostatic mechanism.

All the data was subjected to statistical analysis by using Chi.square Test and T. Test. Level of significance was set at P value less than .002.

RESULTS

In our study hundred cases of stroke with infarction were included. In all these patients infarction was confirmed by C.T or MRI. They were both adult males and females. Age range was 50 to 70 years. All patients were subjected to hemostatic markers i.e. D. Dimers, PT and APTT. Fifty healthy individuals were taken as control group. Their D. dimers, PT and APTT were also performed.

Sixty five patients of ischaemic stroke showed elevated D. dimer levels. Eighteen of them i.e 18% had D. dimers level in the range of 199-500 ng/ml. Fifteen percent had D. dimers level in the range of 501-1000 ng/ml while in 32% of the patients it was in the range of 1001-2000 ng/ml. This study of stroke patients with infarction showed that D. dimers are significantly elevated in such patients as compared to control group. P. value is less than .00265.

Similarly PT and APTT of these patients were also performed. In eight patients out of hundred mean value of APTT was 33+.562 seconds which was significantly shortened than control group. Six patients showed shortened PT with mean value of 11 + .265 seconds, significantly lower than control group. P value of APTT and PT was less than 0.00326.

Prothrombin time (PT) and APTT were performed by manual and coagulation analyzer method for accurate results.

Table No.1: Frequency of Hemostatic Markers in Stroke Patients.

S.No.	Hemostatic Marker	
1.	Raised D. dimer	65%
2.	Shortened PT	5%
3.	Shortened APTT	8%

Mean Values of Hemostatic Markers in Stroke Patients.

Table No.2: Hemostatic marker observations in patients with mean value of control subjects

Hemostatic Marker	No. of Patients	Observed Value	Mean Value of Control Subjects
D. dimer level	18 15 32 35	199 – 500 ng/ml 501 – 1000 ng/ml 1001– 2000 ng/ml 140 – 198 ng/ml	140-198 ng/ml
APTT	8	33 + .562	33.5–35 seconds
PT	6	11 + .265	11.3 – 12 seconds

P value for D. dimer P< .00265

P value for APTT & PT P< .00326

DISCUSSION

Stroke is a major health problem worldwide resulting in high rates of morbidity and mortality[11]. Thrombosis is a key mechanism for many acute strokes and is associated with severe coagulation and fibrinolysis[12]. D. dimer is a frinogen degradation product that reflects thrombus formation and breakdown and its elevated level shows prothrombotic tendency in the patient and is an independent risk factor for ischemic stroke[13,14].

In the present study we evaluated hemostatic marker, D. dimer, PT and APTT in stroke patients as stroke patients are associated with coagulation abnormalities. In the present study 65% of the stroke patients showed elevated D. dimer levels. Eighteen patients had D. dimer level in the range of 199-500 ng/ml. Fifteen patients had D. dimer level in the range of 501-1000 ng/ml and 32 patients had D. dimer level in the range 1001-2000 ng/ml. Thirty five patients had D. dimer level in the normal range.

Similar studies have been conducted which have shown positive association of D. dimer levels in stroke patients. Usman et al in his study identified that stroke patients are associated with elevated D. dimer level[15]. The study of Sazonova et al also shows similar correlation to our study. They have also reported that raised D. dimer level are found in stroke patients[16]. A lot of other studies have been conducted on this issue, the results showed that elevated D. Dimer levels are found in stroke patients which strongly signify thrombotic tendency[17,18].

In the present study PT and APTT of the stroke patietns were also performed. Eight patients showed shortened APTT while Six patients presented with shortened PT. Mean PT and APTT was 11+. 265 seconds and 33+. 562 seconds respectively as compared to control group. Different authors have studied PT and APTT in stroke patients. Some reported shortened PT and APTT while others reported the results to be prolonged. Some authors have reported no change in the results. Sari Kaya et al reported in their study that no change in PT and APTT occurs in patients with ischaemic stroke[19]. Similarly Selyopranoto et al concluded no change in PT and APTT in ischaemic stroke patient as compared to control group[20]. However Gaston et al in their study reported shortened PT and APTT in ischaemic stroke[21]. Similarly Kuowy et al reported in their study that shortened APTT occurs in stroke patients[22].

A large number of studies have demonstrated that hemostatic disturbances play major role in the pathogenesis of stroke but the exact mechanism is unknown or multifactorial[23]. Fiirstly elevated D. dimer levels may reflect the ongoing thrombus formation within cerebral vessels and hence act as a marker of systemic hypercoagulability[24]. Secondly thrombi formed in hypercoagulable state and D. dimer levels may be resistant to fibrinolytic system[25]. Thirdly D. Dimer levels act as marker of acute phase reactants as there is evidence that D. dimer may stimulate the inflammatory response D. dimer stimulate monocyte synthesis and release pro-inflammatory cytokines IL-6[26,27]. This increase inflammatory response further contribute to ischaemic stroke and as progression.

D. dimer is a circulating peptide degradation product of cross linked fibrin so higher levels of D. dimer indicate more systemic fibrin formation and degradation of fibrin clot [(28)] and so elevated D. dimer is a marker of coagulation and fibrinolytic system[29].

The present study revealed that stroke is associated with hemostatic abnormalities as indicated by elevated D. dimer levels and shortened APTT and PT. This hemostatic activation may be an important contributor to progressing ischemic stroke[9].

CONCLUSION

The study concluded that hemostatic markers are significantly elevated in ischaemic stroke. Patients elevated D. dimer is a useful marker for the clinician to identify stroke patients at risk of thrombosis. Its low level excludes thrombus formation while elevated level immediately guides the clinician that stroke patient has thrombo-embolic phenomenon which can be further confirmed by other supportive investigations like C.T or MRI brain. Shortened PT and APTT are also associated with ischaemic infarction.

Author's Contribution:

Concept & Design of Study:	Naveed Khan
Drafting:	Murad Ali, Subhan-ud-Din
Data Analysis:	Shah Zeb, Muhammad Amjad
Revisiting Critically:	Naveed Khan, Murad Ali
Final Approval of version:	Naveed Khan

Conflict of Interest: The study has no conflict of interest to declare by any author.

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