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RESEARCH ARTICLE

SERUM D – DIMER LEVELS AS A SCREENING TEST IN ACUTE HEMORRHAGIC STROKE

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ABSTRACT

Background: Stroke is sudden reduction in blood supply to the brain resulting in loss of its functions. Hemorrhagic stroke, though a less common type of stroke, is associated with greater morbidity and mortality, and its rapid diagnosis requires early neuroimaging techniques like CT scan brain or MRI brain. Since in Pakistan health care facilities are limited with neuroimaging inaccessible in certain areas, therefore, the main objective of this study was to find out the frequency of raised serum D-dimer levels in patients of hemorrhagic stroke, as plasma d-dimer level is an easily available and cost effective parameter, and may be used to as a screening tool.

Methods: By nonprobability convenience sampling, all patients with hemorrhagic stroke admitted in the medical unit of Ayub teaching hospitals were included in the study. The study was conducted from 13th March 2015 to 12th March 2016. The diagnosis of hemorrhagic stroke was done on CT scan brain and plasma D-Dimer levels were send. Data was collected on specific proforma and was put to SPSS version 20.

Results: The study group comprised of 243 patients with hemorrhagic stroke as per operational definition. The mean age of the patients was 56.27 ± 8.85. Minimum age was 40 years and maximum age was 78 years. There were 147 (60.5%) males and 96 (39.5%) females. D-dimer levels were found high in 50 (61.7%) patients in the entire study groups.

Conclusion: The Frequency of serum D-dimer levels was found to be 61.7%. Therefore, even though a positive correlation was found, D-dimer assay alone is inadequate for screening of patients with suspected hemorrhagic stroke.

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INTRODUCTION

Hemorrhagic stroke is a neurological emergency with a very high mortality rate. It is divided into two types on the basis of whether the bleed is into the brain parenchyma or into the subarachnoid space (Hemorrhagic strokes, 2013). Patients with acute hemorrhagic stroke present with a very wide range of signs and symptoms. These include sudden loss of consciousness, sudden onset of severe headache, nausea, vomiting, unilateral hemiplegia or hemiparaesis, altered consciousness (Connolly *et al.,* 2012). Most of these patients are currently diagnosed by computerized tomography (CT) scan brain in most parts of the world, with other radiological techniques like angiography CT (CTA) and cranial magnetic resonance imaging (MRI) also sometimes used. However, most of the diagnostic tests are expensive, time consuming and not readily available (Connolly *et al.,* 2012; Morgenstern *et al.,* 2010). Hemorrhagic stroke is associated with a very high mortality and morbidity (Gregson *et al.,* 2012). According to one study, the in-hospital mortality rates were 31.9% and 25.6% for Subarachnoid Hemorrhage (SAH) and intracranial hemorrhage (ICH) respectively with estimated median survival through 4 years was 256 days for subarachnoid hemorrhage and 353 days for intracranial hemorrhage (Lee *et al.,* 2007). D-dimer is a fibrinogen degradation product. Raised D – dimer levels have been seen in a wide variety of disorders, and therefore can help in their diagnosis or treatment. Some of these disorders include malignancy, trauma, pulmonary embolism, deep venous thrombosis, postsurgical managements, liver and heart disease (Cervellin *et al.,* 2014). Hospitalized patients have also been found to have elevated D - dimer levels in high frequency (Spring *et al.,* 2014). Circulating D-dimer level has also been shown to be elevated in patients with spontaneous intracranial hemorrhage (SICH) (Fujii *et al.,* 2001). In one study, the prevalence of raised D-dimer in patients of acute hemorrhagic stroke was found to be 70% (Cheng Ting Hsiao *et al.,* 2012), however no local data on prevalence of raised D-dimer in acute hemorrhagic stroke was found to be available. The main purpose of this study was to find out the frequency of raised serum D- dimer levels in acute hemorrhagic stroke. If the frequency is found high, then it can be used as a screening test for hemorrhagic stroke as the above mentioned radiologic

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detections are time consuming, expensive and not available at every medical facility. Serum D-dimer levels monitoring is cheap and easily available.

MATERIALS AND METHODS

This descriptive cross sectional study was conducted in the department of Medicine, Ayub Teaching Hospital from 13th March 2015 to 12th March 2016. A sample of 243 patients aged between 40 and 90, and diagnosed within 48hrs of development of symptoms on the basis of CT scan was selected. All previously diagnosed hemorrhagic stroke patients were excluded and strict exclusion criteria was followed to control bias. After approval from the hospital ethics committee, details was taken from the patient or his attendant and complete physical examination was done. Then a 3ml of venous blood was taken from the patient and was sent to the laboratory for serum D-dimer levels. All investigations were done in the same lab and by the same biochemist. Data was collected on a specific pro forma and then put to SPSS version 20.

RESULTS

The study group comprised of 243 patients with hemorrhagic stroke as per operational definition. Minimum age was 40 years and maximum age was 78 years, with mean ± SD being 56.27 ± 8.85. There were 147 (60.5%) males and 96 (39.5%) females. D-dimer levels were found high in 150 (61.7%) patients in the entire study groups of which 93 (63.2%) were males and 57 (59.3%) were females, showing a slightly increase levels in male gender.

Table 1. Patients with raised D-Dimer levels (n=243)

Test	No of Patients	Percentage
Raised D-dimer levels	150	61.7%
Normal D-dimer levels	93	38.2%
Total	243	100%

Table 2. Gender wise stratification of raised d-dimer levels

Gender	No of Patients	D-Dimers Positive	Percentage	Pearson Chi Square test	Significance Level
Male	147	93	63.2%	3.48	0.05
Female	96	57	59.3%	1.73	0.1
Total	243	150	61.7%	5.21	0.01

DISCUSSION

We studied 243 non-traumatic patients with signs and symptoms suggestive of SICH confirmed on CT scan brain to find out the frequency of raised D-dimer levels and it was only 61.7%. Therefore, our results indicate that D-dimer assay alone is not adequate as a screening tool for determining patients with suspected SICH. Previous studies have evaluated hemostasis and fibrinolysis activation after SAH (Peltonen *et al.,* 1997). Some of these studies established an association between coagulopathy at admission and poor neurological outcome (Juvela and Siironen, 2006; Delgado *et al.,* 2006; Parra, 2006). One study concluded that the D-dimer assay was inadequately sensitive to be used for the purpose of screening in traumatic or spontaneous ICH (Hoffmann *et al.,* 2001). This was a prospective study of 319 patients with suspected ICH who had a serum D-dimer assay obtained before undergoing CT. Twenty-five of the patients has a positive CT scan for ICH. The D-dimer assay had four false-negative results and the sensitivity was therefore 84.0%. However another study, Antovic J and colleagues, while investigating the association between D- dimer and stroke found that D-dimer levels were significantly raised in hemorrhagic stroke (Antovic *et al.,* 2012). Delgado *et al.* (2013) reported that poor neurologic outcome was associated with increased plasma D- dimer levels in patients with acute hemorrhagic stroke. They measured initial and followup (24 hours, 48 hours, 7th day, and 3rd month) D-dimer levels in 21 patients after reaching the conclusion. This was also reported by Juvela *et al.* 2006 who demonstrated that increased D-dimer levels might predict poor prognosis in patients with hemorrhagic stroke. Contrary to the studies mentioned, Squizzato *et al.,* 2006 suggested that D-dimer levels in acute stroke had low specificity and sensitivity, and therefore would not be useful in determining long term prognosis. Similarly, in their study on 143 patients, Ebihara and colleagues (Ebihara *et al.,* 2006) suggested that patients with subarachnoid hemorrhage had higher D- dimer levels than the patients with hypertensive intracerebral hemorrhage. Thus they concluded that coagulative/fibrinolytic cascade might have been activated via different mechanisms in different types of stroke. Acute hemorrhagic stroke is associated with high mortality and morbidity and therefore requires early diagnosis and treatment. However, in addition to brain damage, it affects coagulopathy. Due to this phenomenon, coagulation markers such as D-dimer and fibrinogen levels might help early diagnosis. In our study, though a positive correlation has been found, however, further studies are necessary to assess the clinical value of these markers in early screening of hemorrhagic strokes.

Conclusion

The frequency of raised d-dimer levels in patients of hemorrhagic stroke was found to be 61.7%. Therefore, although raised d-dimer levels in acute hemorrhagic stroke patients are still reported from many parts of the world, our findings indicate that initial screening with D-dimer assay alone of non-traumatic patients who present with symptoms and signs suggestive of acute hemorrhagic stroke is not adequate and hence cannot be used alone as a screening test. However we conclude our study with recommendations of further research work over in raised d-dimer levels in acute hemorrhagic stroke and finding out the basic pathophysiology involved into it before moving on to recommendations in current management principles for the investigations of patients presenting with sign and symptoms of hemorrhagic fever.

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