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SIGNIFICANT OF D-DIMER AND PROTEIN C TESTING IN PREDICTING AND EVALUATION OF VENOUS THROMBOSIS AND PULMONARY EMBOLISM AMONG SUDANESE ADULT: 40 YEAR OF AGE OR LESS THAN 40 YEAR POPULATION STUDY

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ABSTRACT

Background: Deep venous thrombosis (DVT) and pulmonary embolism (PE) in young people can occur at any age, but the first month of life (especially in premature and other hospitalized infants) and the teenage years appear to be times of increased risk for blood clots. This study aimed to investigate and evaluate the significant of D-dimer and protein C testing in predicting and evaluation of venous thrombosis and pulmonary embolism among across age categories. **Methodology:** A total of eighty (80) adult individuals were recruited to participate in this study their age were 40 year old with their mean 36 year old with thrombosis or pulmonary embolism first diagnosed between Marches 2017 to September 2018. The protein C and D-dimer were measured using ELISA and manually respectively. **Results:** The individuals with thromboembolism (deep-vein thrombosis, pulmonary embolism) had significantly higher D-dimer levels (572±12.8), when compared with the control group (237.8±4.3) (P. value = 0.024). A total of 19 (23.7%) of 80 patients had VTE (deep-vein thrombosis [n = 12] and pulmonary embolism [n = 7). Patients with recurrent VTE had significantly higher D-dimer levels (49(61.3%) of 80) than those without (mean: 553 ng/mL vs 240 ng/mL, respectively, P. value = 0.01). In the individuals with thromboembolism (deep-vein thrombosis, pulmonary

embolism) protein C was decreased significantly. Protein C was decreased in about 77.5% of the cases (62 patients) and the mean was (55.8±20.1%) versus the control the mean (110.3±25.1%) (P. Value = 0.001). **Conclusions:** The D-dimer test has great sensitivity (> 95%) and specificity (> 92.0%) in predictive deep venous thrombosis or pulmonary embolism in those young adult patients. While decreased in protein C values have predictive indicator for significantly increased risk of venous thrombosis and pulmonary embolism in those patients.

KEYWORDS: D-dimer, venous thrombosis, pulmonary embolism, protein C.

INTRODUCTION

Pulmonary embolism (PE) is the third most common cause of cardiovascular death among Americans, behind myocardial infarction and stroke.[1] Mortality varies greatly, depending on various factors including age, comorbid conditions, and stability on presentation. Patients with low-risk PE have a 1-year survival rate over 95%. In contrast, patients presenting with high risk PE and hemodynamic instability have an approximately 40.0% mortality rate within 90-days.[2]

The main determinants of PE severity are: presence of right heart strain either on echocardiography or computed tomography, myocardial damage based on troponin elevation, and overall clot burden. Although the overall clot burden appears to have only a variable relationship to outcomes, large PE are typically associated with worse outcomes than smaller or segmental PE.[3] One must also consider the general overall health of the patient and take into account age and presence of comorbid illness that may affect prognosis. While there is variability in the classifications systems used to define short-term risks from PE, for the purposes of this discussion we will categorize patients as low-risk, intermediate-risk, and high-risk.[4,5]

Pulmonary embolism spans a broad spectrum of illness, ranging from asymptomatic, incidentally discovered subsegmental thrombus detected on chest CT scan[6] to pressor-dependent PE complicated by cardiogenic shock and multisystem organ failure.[7,8] Between these two extremes are patients with symptomatic low-risk or intermediate-risk disease.[9,10]

MATERIALS AND METHODS

This is a descriptive Cross sectional study done during the period of March 2017 to September 2018 in Omdurman teaching hospital in Khartoum state to measure the D-dimer and protein C values among Sudanese patients affected with venous thrombosis and pulmonary embolism. Eighty (80) patients with thromboembolism and 80 healthy individuals control group.

Preparation of platelet poor plasma (PPP): The blood samples were collected from patients and controls in tri-sodium citrate (3.2%) anticoagulant (ratio1:9). platelet poor plasma sample were prepared by centrifugation at 2000g for 15 min. The plasma samples were divided into two plane tubes; the first tube was stored at -70^{O}C and tested within one month for protein C estimation. The second tube was stored at 20 ± 5^{O}C and tested within three hours for D-Dimer measurement. The samples were being kept at room temperature manually D-dimer measurement and for protein C measurement using the Elisa technique.

Data analysis: All data are presented as mean ± SD using Statistical Package for the Social Sciences, unless otherwise noted. Statistical comparisons were performed using unpaired student's t-test with $p<0.05$ considered as significant.

RESULTS

The Patients with thromboembolism (deep-vein thrombosis, pulmonary embolism) had significantly higher D-dimer levels (572±12.8), when compared with the control group (237.8±4.3) (P. value = 0.024).

A total of 19 (23.7%) of 80 patients had VTE (deep-vein thrombosis [n = 12] and pulmonary embolism [n = 7]) (Table: 1). Patients with recurrent VTE had significantly higher D-dimer levels (49(61.3%) of 80) than those without (mean: 553 ng/mL vs 240 ng/mL, respectively, P = 0.01) (Table: 2).

In patients with thromboembolism (deep-vein thrombosis, pulmonary embolism) protein C was decreased significantly. Protein C was decreased in about 77.5% of the cases (62 patients) and the mean was (51.8±15.1%) versus the control the mean (110.3±25.1%) (P. value = 0.001).

(Table: 1): The distribution of the study population by the Frequency of deep-vein thrombosis and pulmonary embolism.

Case	Number of patients	Percent %
Deep-vein thrombosis	12	15%
Pulmonary embolism	7	8.7%

(Table: 2): Positive D-dimer level according to grade (+) and grade (++) among the patients.

Case	Number of cases	Percent %
Number of grade (+) D-dimer	32	65.3%
Number of grade (++) D-dimer	17	34.7%

P. value: 0.01

DISCUSSION

The diagnostic yield of D-dimer is affected not only by the choice of assay, but also by patient characteristics. Certain factors influence the sensitivity and specificity in D-dimer testing, such as the extent of thrombosis and fibrinolytic activity, duration of symptoms, age, surgical procedures, anticoagulants, and comorbid conditions such as inflammatory states, cancer, pregnancy and the postpartum period, and previous VTE.[11] Venous thromboembolism is a common condition that cannot be diagnosed solely on the basis of clinical presentation due to the lack of sensitivity and specificity of signs and symptoms. PE is a common yet potentially fatal disease, which results in >250,000 hospitalizations in the United States each year.[12] The prevalence of DVT and PE is 20% or less among clinically suspected individuals.[13]

The risk factors for VTE are increasing age, cancer and its treatment, paralysis, prolonged immobility, long air travel, congestive heart failure, acute infection, pregnancy or puerperium, hormonal treatment, varicose veins, dehydration, previous VTE, inflammatory bowel disease, rheumatologic disease, nephrotic syndrome, persistent elevation of D-dimer, and atherosclerotic disease.[14] Protein C is a vitamin K-dependent protein synthesized primarily by hepatocytes in the liver and plays an important physiologic role in the Protein C anticoagulant System.[15,16]

The protein C pathways are the specific chemical reactions that control the level of expression of activated protein C (APC) and its activity in the body. Protein C is pleiotropic,

with two main classes of functions: anticoagulation and cytoprotection (its direct effect on cells).[17]

Protein C deficiency, either congenital or acquired, may lead to serious thrombotic events such as thrombophlebitis, deep vein thrombosis, or pulmonary embolism.[18] Patients with a congenital heterozygous deficiency may present with venous thrombosis in young adulthood, while patients with the rare homozygous deficiency present with massive thrombosis (purpura fulminans) during the neonatal period.[19] this is very severe and usually fatal.[20]

CONCLUSIONS

The D-dimer test has great sensitivity (> 91.0%) in predictive deep venous thrombosis or pulmonary embolism in those adult individuals, While decreased in protein C values have predictive indicator for significantly increased risk of venous thrombosis and pulmonary embolism in those patients.

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