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EVALUATION OF THE ROLE OF D- DIMER TEST IN THE PREDICTION AND EXCLUSION OF VENOUS THROMBOEMBOLISM IN COMBINATION WITH PRETEST PROBABILITY SCORE AT A TERTIARY CARE CENTRE.

Pathology

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ABSTRACT

Background: Clinical suspicion of venous thromboembolism requires objective testing to predict and exclude the diagnosis. Plasma D-dimer is sensitive marker for thrombosis but lack specificity. The combined use of pretest probability score and D-dimer can be used for exclusion of VTE and safely avoid costly imaging tests.
Material and Methods: In this prospective observational study, we used Wells PTP score and D-dimer test to evaluate 50 patients who presented with sign and symptoms of VTE. Radiological imaging studies were taken as confirmatory test.
Result: The sensitivity, specificity and NPV of D-dimer test were 100%, 83.7% and 100% respectively. The sensitivity, specificity and NPV of D-dimer test in combination with low PTP score were 100%, 72.1% and 100% respectively. The agreement between radiologically confirmed cases and D-dimer test was significant.
Conclusion: D-dimer test can be safely used in low or moderate PTP score patients to exclude VTE and costly invasive radiological imaging studies can be obviated in a significant proportion of patients.

KEYWORDS

D-dimer, PTP score, Venous thromboembolism

INTRODUCTION

Venous thromboembolism (VTE) commonly present as Deep vein thrombosis (DVT) and pulmonary embolism (PE) that require urgent recognition, diagnosis, and treatment to prevent or minimize the risk of thromboembolic complications.[1]

Although the clinical symptoms and signs such as dyspnea, pleuritic chest pain, tachypnea, and tachycardia can raise suspicion of PE, and symptoms and signs of swollen, red, tender, and hot lower limbs can raise suspicion of DVT, these are nonspecific and need to be confirmed by further diagnostic and costly imaging techniques[2].

A diagnostic tool, that is noninvasive and highly accurate is needed for VTE, allowing immediate treatment decisions to be made in most cases. These criteria partially fulfilled by cross-linked fibrin derivatives called Plasma D-dimer because they are sensitive markers for thrombosis but lack specificity.

A simple but reliable noninvasive test for VTE is highly desirable and should ideally have a sensitivity and negative predictive value of 100% as the consequences of nondiagnosis are potentially life threatening.[3][4] Plasma D-dimers have proved to be the most useful blood marker of intravascular fibrinolysis[5] and are of interest as an adjunctive exclusionary test in suspected VTE. To use this test preferentially in place of diagnostic imaging, a combination of D-dimer assay and pretest probability (PTP) score should give a negative predicative value (NPV) of >98%, which is equivalent to that of compression ultrasonography for proximal DVT as recommended by The Haemostasis and Thrombosis Task Force of the British Committee for Standards in Haematology [6],[7].

The D-dimer test has low specificity and high sensitivity (more than 95%), making it effective at excluding, but not confirming, a diagnosis[8]. Therefore, in patients with low or intermediate probability, a negative (below 0.5 µg/ml) D-dimer test can safely rule out a VTE diagnosis[9].

MATERIAL AND METHODS

We conducted a prospective study in Gwalior region during 18 months period (January 2019 to June 2020)

INCLUSION CRITERIA:

We enrolled 50 consenting adults (18 years old or above) who required D-dimer test in suspected cases of venous thromboembolism (VTE), that is, deep venous thrombosis (DVT) and pulmonary embolism (PE).

EXCLUSION CRITERIA:

Patients were excluded if they

1. Refused to participate in the study,
2. If they were less than 18 years of age,
3. If they were pregnant, or
4. If they were lost to follow-up.

All patients clinically evaluated at the time of presentation. A data collection form including exclusion criteria, signs and symptoms included by Wells Pretest Probability Score was used. Regardless of the PTP score, patients underwent the appropriate imaging technique and a sample was collected for D-dimer testing.

Venous blood was collected by aseptic venipuncture into 3.2% sodium citrate to a final ratio of 9:1 using vacutainer tubes. Each sample was centrifuged for 15 minutes at 2500rpm.

Plasma was drawn into clean plastic tube and stored at 4℃ until testing done within 24 hrs from collection.

D-dimer testing was carried out in laboratory on plasma sample using STA-LIA TEST D-DI PLUS kit on STA satellite analyser (Diagnostic ca stage). According to the manufacturer's instructions STA-LIA TEST D-DI is a rapid, automated, quantitative immune-turbidimetric assay.

Table 1 : Clinical model for predicting the pretest probability score (PTP score) of DVT

(adapted from Wells et all)

Clinical Characteristics	Score
1. Active cancer (ongoing treatment or within past 6 months or palliative)	1
2. Paralysis, paresis, or recent plaster immobilization of lower Extremities	1
3. Recently bedridden for >3 days or major surgery within 4 wks	1
4. Local tenderness	1
5. Calf swelling atleast 3 cm larger than asymptomatic side	1
6. Pitting edema	1

7. Collateral superficial veins	1
8. Previous documented DVT	1
9. Alternative diagnosis atleast as likely as DVT	-2

Low probability = 0-1 , Moderate = 1-2 , High = >2

* In patient with symptoms in both legs , the more symptomatic leg is assessed.

Table 2 : Clinical model for predicting the probability score for pulmonary embolism

(adapted from *Wells et al*)

Clinical characteristics	Score
1. Clinical signs and symptoms of DVT	3
2. An alternative diagnosis deemed less likely than PE	3
3. Heart rate >100 bpm	1.5
4. Immobilization of surgery in previous 4 weeks	1.5
5. Previous DVT or PE	1.5
6. Hemoptysis	1
7. Cancer (receiving treatment, treated in past 6 months or palliative care)	1

RESULTS

50 patients fulfilled the inclusion criteria and were included in the study. There were 56% (28) female and 44% (22) male with a mean age 50.38.

The prevalence of VTE in this study cohort was 14% (4) DVT and (3) PE.

Based on PTP score 29 patients were clinically suspected for DVT. The most common presenting complaint was swollen limb (75.9%).

21 patients were clinically suspected for PE and most common clinical presentation was dyspnea (95.2%) and chest pain in 42.9%.

The PTP score of suspected DVT was found to be low in 60% and moderate to high in 40%.

The PTP score in suspected PE was low in 67% and moderate to high in 33%. The agreement between PTP score and radiology results for VTE was significant ($p<0.01$).

We evaluated diagnostic value cutoff reference of D-dimer (<0.5 µg/ml FEV) against radiology result in patients clinically suspected for VTE. There were (14) cases with positive D-dimer but only (07) was confirmed on radiology. The calculated sensitivity, specificity, PPV and NPV was 100%, 83.7%, 50%, 100% respectively.

Table 3 : Distribution of the Participants in terms of Gender

Gender	Frequency	Percentage
Male	22	44%
Female	28	56%
Total	50	100%

Table 4 : Distribution of the Participants in terms of D-dimer cut-off

D-dimer	Frequency	Percentage
Positive	14	28%
Negative	36	72%
Total	50	100%

Table 5 : Distribution of the Participants in terms of Radiologically confirmed VTE

VTE (Radiology)	Frequency	Percentage
Present	7	14%
Absent	43	86%
Total	50	100%

Table 6 : Performance of study parameters for excluding VTE

Variable	Sensitivity	Specificity	NPV
D-Dimer	100%	83.7%	100%
PTP Score	100%	72.1%	100%
D-Dimer+ PTP Score	100%	72.1%	100%

DISCUSSION:

- The sensitivity of D-dimer test in suspected cases of VTE was 100% and this is comparable with sensitivity obtained in the study carried out by Wells et al[10], Anoop et al[12] where the sensitivity was also 100%. Similar observations were also obtained in the studies conducted by Knecht et al[11] and Legnani et al[13].
- The Negative predictive value of D-dimer test in this study to rule out VTE in suspected cases was 100% and this is comparable with Negative predictive value observed in other studies carried out by Knecht et al, Legnani et al and Anoop et al.
- The specificity of D-dimer test in this study was 83.7% which was comparable with specificity observed in other studies done by Wells et al and Legnani et al.
- The sensitivity of D-dimer test combined with PTP score in the present study was 100% and this is comparable to the study done by Van der Graaf et al[14] and Anderson et al[15].

CONCLUSION:

- D-dimer test has evolved as a simple, relatively non invasive and cost effective test in workup of suspected cases of venous thromboembolism.
- D-dimer test can be safely used in low or moderate PTP score patients to rule out venous thromboembolism.
- Negative D-dimer test with low PTP score makes the diagnosis of venous thromboembolism unlikely, so costly and invasive radiological imaging test can be obviated in a significant proportion of patients.
- Radiological imaging test should be done only in patients with positive D-dimer test with moderate or high PTP score.
- Evidences collected from our study confirms the cost effectiveness and accuracy of D-dimer test in combination with pretest probability score and it can be safely be incorporated into diagnostic algorithm of suspected VTE due to its high NPV and sensitivity.

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