

PREVALENCE, DETERMINANTS AND BIOMARKERS OF DEEP VEIN THROMBOSIS AMONG PATIENTS IN TERTIARY CARE CENTRE IN SOUTH KERALA

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Abstract

Background: Deep vein thrombosis is an obstructive disease with hindering venous reflux mechanism usually involving the lower limb venous system. Diagnosis of DVT only based on clinical signs and symptoms might be inaccurate. Early detection of deep vein thrombosis by venous ultrasound Doppler can prevent its catastrophic complications. The objective is to estimate the proportion of deep vein thrombosis among patients presenting with cellulitis of lower limb in a tertiary care centre. To identify the determinants of deep vein thrombosis among these patients. To identify the biomarkers of deep vein thrombosis among these patients. **Materials and Methods:** Hospital based cross sectional study done in surgery department of a medical college in south Kerala for a period of 18 months, after obtaining institutional ethical committee clearance. All patients diagnosed as cases of lower limb cellulitis who are subjected to Doppler study by the treating clinical team were included in the study. A semi-structured proforma containing 3 sections: socio demographic details of the patient, Symptoms and Contributory factors, Clinical, Laboratory and Radiological Assessment were used to collect the relevant information. Chi-square test was used to find out the association between DVT and explanatory variables. **Result:** Prevalence of deep vein thrombosis among the study subjects was 3.1%. Determinants of DVT include old age, female gender, history of immobility, trauma, Diabetes mellitus, systemic Hypertension, calf swelling more than 3cm of affected limb, severe pain, Random Blood Sugar more than 180mg/dl, total WBC count more than 10000/mm³. **Conclusion:** The determinants which will be more favouring to a diagnosis of DVT are old age, female gender, history of immobility, trauma, Diabetes mellitus, systemic Hypertension, calf swelling more than 3cm of affected limb, severe pain, Random Blood Sugar more than 180mg/dl, total WBC count more than 10000/mm³. And minor risk factors are previous history of DVT, history of smoking, active malignancy, collateral superficial veins of affected limb, Haemoglobin less than 11g/dl and platelet count more than 400000/mm³.

INTRODUCTION

Deep vein thrombosis is an obstructive disease with hindering venous reflux mechanism DVT usually involves the lower limb venous system,^[1] with clot

formation originating in a deep calf vein and propagating proximally. This is a common venous thromboembolic disorder affecting 1.6 per 1000 annually.

Deep-vein thrombosis is a blood clot which forms within the deep veins usually of the leg but can also occur in the arms and the mesenteric veins and cerebral veins. Deep-vein thrombosis is a common yet important disease. It is part of the venous thromboembolism disorders and it is the third most common cause of death from cardiovascular disease next to heart attacks and stroke. Even in patients who do not get pulmonary emboli, recurrent thrombosis and "post-thrombotic syndrome" were found to be major causes of morbidity.^[2]

Diagnosis of DVT only based on clinical signs and symptoms might be inaccurate as the signs and symptoms of DVT are generally non-specific. They could be associated and misdiagnosed with other lower extremity disorders. Accordingly, lymphedema, superficial venous thrombosis, and cellulitis should also be excluded. However, the most common presenting symptoms with inconsistent sensitivity and specificity are calf pain and swelling. The former index has a sensitivity of 75% to 91% and a specificity of 3% to 87%, and the latter might have a sensitivity of up to 97% and a specificity of up to 88%.^[3] None of the signs or symptoms is sufficiently sensitive or specific, either alone or in combination, to accurately diagnose or exclude thrombosis.^[4]

Hence early detection of deep vein thrombosis by venous ultrasound doppler can prevent its catastrophic complications rather than treating it clinically as cellulitis by administering antibiotics and waiting. Treatment with anticoagulation must be started at appropriate time to prevent its dreadful complications.

Modified Well's criteria help estimate the clinical likelihood of DVT. Patients with risks of developing DVT should undergo initial evaluation with d-dimer testing and radiological imaging tests.^[5]

Low probability (5%) of DVT (score -2 to 0), moderate probability (17%) of DVT (score 1-2), high probability (17-53%) of DVT (score >2).

Investigations

Blood tests the quantitative plasma d-dimer enzyme-linked immunosorbent assay (ELISA) rises in the presence of DVT because of the breakdown of fibrin by plasmin.^[6]

The sensitivity is >80% for DVT.^[7]

Ultrasound Venous Doppler:

Ultra-sound of deep venous system reveals loss of vein compressibility.^[8]

When imaged in cross-section, a normal vein readily collapses with gentle pressure from the ultrasound transducer. With acute DVT, the deep vein will lose its compressibility nature because of the passive distention of vein by an acute thrombus. Acute DVT is even easily diagnosed on direct visualisation of the thrombus. It appears as homogeneous and it has low echogenicity. The vein usually appears mildly dilated and also collateral channels will be absent.^[9]

Objectives

1. To estimate the proportion of deep vein thrombosis among patients presenting with

cellulitis of lower limb in Dr. SMCSI Medical College and Hospital, Karakonam.

2. To identify the determinants of deep vein thrombosis among these patients.

3. To identify the biomarkers of deep vein thrombosis among these patients.

MATERIALS AND METHODS

Study Design: Hospital based Cross sectional study

Study Setting: The study was conducted in the Surgery Department of Dr. Somervell Memorial CSI Medical College, Karakonam, Trivandrum.

Study Period: October 2019 to November 2021(18 months) after obtaining Institutional Ethics Committee Clearance.

Study Population: All the patients admitted in Dr. Somervell Memorial CSI Medical College, Karakonam, Trivandrum, clinically diagnosed as cellulitis of lower limb were the study subjects.

Inclusion Criteria

All patients diagnosed as cases of lower limb cellulitis in Dr. Somervell Memorial CSI Medical College, Karakonam, Trivandrum, who are subjected to Doppler study by the treating clinical team. The patients in the age group of 18-80 years are selected for this study. (Older age group selected due to increased incidence of cellulitis in the age group)

Exclusion Criteria

1. Those who do not consent for the study.

2. Filarial lower limb

Sample Size: Sample size is calculated using a previous study done by Afzal et al,^[10] in July 2015. According to the study, prevalence (p) of DVT is 5.9%.

$p = 5.9\%$ (p- Proportion or prevalence of interest)

$q = (100-p) = 94.1\%$

$d = 20\%$ of p (d = clinically expected variation i.e., 20% of p)

Sample size is calculated as

The formula used is: $n = 4pq / d^2$

$= 4 \times 5.9 \times 94.1 / (20/100 \times 5.9)^2$

$= 2220.76 / 1.3924$

$= 1594.91$

$= 1595$

Sampling technique: Consecutive patients with cellulitis presenting to Dr. SMCSI Medical College and Hospital, Karakonam fulfilling the inclusion criteria were selected and assessed for possible inclusion into the study.

Study Variables: Age, sex, Blood pressure, temperature, symptoms of the patient, risk factors, co morbidities, history of trauma, immobility, smoking history, clinical examination findings, random blood sugar, haemoglobin value, total WBC count, platelet count, Doppler Ultrasound of lower limb venous system.

Operational Definition: Deep Venous Thrombosis was diagnosed if lower limb Doppler Ultrasound showed presence of thrombus, non compressible venous segment.

Data Collection Tools: A semi-structured proforma containing 3 sections

Section A – Patient details

Section B – Symptoms, Contributory factors

Section C – Clinical, Laboratory and Radiological Assessment

Data collection technique: Consecutive patients presenting with lower limb cellulitis satisfying the inclusion and exclusion criteria were enrolled into the study. All the patients included were clinically assessed after eliciting a proper history and routine investigations was done. A semi-structured proforma was used to collect patient’s details and history relevant to the study and Ultrasound Doppler of the lower limb venous system was done according to treating clinical team’s order. Each patient was examined in a systematic manner. The blood pressure was measured at the time of admission in the right upper arm using a mercury sphygmomanometer; Temperature was measured at the time of admission in the right axilla using a clinical thermometer, heart rate was also recorded. The blood samples were collected under aseptic precautions and the levels of Random blood sugar was recorded. Routine blood investigation reports were also recorded.

Data entry and analysis: After entering the data into Microsoft excel sheet the data was analysed using the statistical package for social sciences [SPSS] software (trial version). All contributory factors were expressed as frequency and percentages and age, duration of stay, duration of symptoms, heart rate, blood pressure, Random Blood Sugars as mean and standard deviation. The association between the presence of deep venous thrombosis and the independent variables were assessed using chi square test.

Ethical consideration: Institutional ethics committee clearance was obtained before the commencement of the study. Written informed consent in English and local languages (Malayalam and Tamil) from all the study participants was obtained. Privacy and confidentiality of the data and study subjects was maintained during all stages of study. It was assured that this study will not cause any risk to the patient. Through this study the patient will be benefited as diagnosis of DVT can be assessed early and treatment protocol can be modified accordingly and the severe morbidity and mortality of DVT can be reduced.

RESULTS

In the present study, 49 patients have DVT among the 1595 patients who presented with lower limb cellulitis giving a prevalence of 3.1%

Variable	Score
Lower limb trauma or surgery or immobilisation in a plaster cast	1
Bedridden for >3 days or surgery in last 4 weeks	1
Tenderness along the line of femoral or popliteal veins	1
Entire limb swollen	1
Calf >3cm larger circumference than the other side	
10cm below the tibial tuberosity	1
Pitting oedema	1
Dilated collateral superficial veins (not varicose veins)	1
Previous DVT	1
Malignancy (including treatment up to 6 months ago)	1
Intravenous drug abuse	3
Alternative diagnosis more likely than DVT	-2

Figure 1: Modified Well’s Criteria for predicting DVT

Table 1: Age and sex distribution of the study participants

Age	Non-Doppler ultrasound	%
<35 Years	1	2.00%
35-45 Years	2	4.10%
45-55 Years	6	12.20%
>55 Years	40	81.60%
Chi-square value:10.794	p value 0.013*	
Gender		
Male	30	61.20%
Female	19	38.80%
Chi-square value:5.154	p value 0.023*	

Table 2: Symptoms and contributory factors in DVT

Local rise in Temperature	Frequency (n)	Percentage (%)
No	0	0.00%
Yes	49	100.00%
Chi-square value:0.577	p value 0.447	
Tenderness		
Mild	15	30.60%
Moderate	15	30.60%
Severe	19	38.80%
Chi-square value:8.446	p value 0.038*	
Lower Limb Swelling		
No	0	0.00%
Yes	49	100.00%
Chi-square value:0.512	p value 0.474	
History of Smoking		

No	39	79.60%
Yes	10	20.40%
Chi-square value:26.710		p value 0.000*
History of Trauma		
No	11	22.40%
Yes	38	77.60%
Chi-square value:36.973		p value 0.000*
History of Previous DVT		
No	42	85.70%
Yes	7	14.30%
Chi-square value:73.644		p value 0.000*
History of Immobility		
No	6	12.20%
Yes	43	87.80%
Chi-square value:625.191		p value 0.000*
Active Malignancy		
No	33	67.30%
Yes	16	32.70%
Chi-square value:121.468		p value 0.000*

Table 3: Clinical, laboratory and radiological investigations

Calf Swelling>=3cm of affected Limb	Frequency (n)	Percentage (%)
No	3	6.10%
Yes	46	93.90%
Chi-square value:5.154		p value 0.995
Pitting Edema of affected Limb		
No	0	0.00%
Yes	49	100.00%
Chi-square value:0.512		p value 0.474
Collateral Superficial Veins of affected Limb		
No	32	65.30%
Yes	17	34.70%
Chi-square value:90.534		p value 0.000*
Haemoglobin		
11-13.5 g/dl	32	65.30%
<11 g/dl	17	34.70%
Chi-square value:69.256		p value 0.000*
Platelet count		
150000-400000/mm ³	27	55.10%
>400000/mm ³	22	44.90%
Chi-square value:212.273		p value 0.000*
Blood glucose values		
Less than 180 mg/dl	22	45
More than 180mg/dl	27	55
Chi-square value:35.845		p value 0.000*
Systemic hypertension		
Present	30	61.22%
Absent	19	38.78%
Chi-square value:77.481		p value 0.000*

DISCUSSION

Deep Vein Thrombosis is a severe condition in which thrombus is formed inside the deep venous system. It has the potential to embolize and cause pulmonary embolism. Other morbidity causing problems are chronic venous insufficiency, post thrombotic leg. DVT share clinical features with lower limb cellulitis. So in some cases of lower limb cellulitis there is a clinical dilemma, and if we are treating a DVT patient with just antibiotics and waiting, it would be a catastrophe to the patient. So timely investigations and treatment modality changes must be done. Mainstay of treatment is anticoagulation for DVT.

The age group varied from a minimum of 18 years to maximum of 80 years. The incidence of DVT is more in older age group in our study, age more than 55. In a similar study conducted by Paneesha et al it was

found that incidence of DVT is found to be more in older age group.^[11]

Female gender preponderance for DVT was noted in our study. Similar incidence was also found in a study conducted by Lee et al. in Korea.^[12] But many studies also showed that male gender is more at risk for developing DVT. This change may be due to the local, socio economic and occupational factors of the study population in our study.

32.7% of DVT patients were suffering from active malignancy. In a similar study conducted by Cook et al active malignancy was found be a risk factor for developing DVT.^[13]

Majority of DVT patients have history of immobility, history of trauma, corresponds with the studies conducted by Kahn et al.^[14]

Majority of DVT patients have Diabetes mellitus, Random Blood Sugar more than 180mg/dl, Systemic Hypertension. Chung et al conducted a similar study

and found to have similar increased incidence of DVT in Diabetic population.^[15]

In our study, majority (93.9%) are having calf swelling more than 3cm of affected limb and pain, with majority (38.8%) having severe pain. Also majority of DVT patients have total WBC count more than 10000/mm³. And only 14.3% of DVT patients had previous history of DVT, which was found to be similar in incidence in a study done by Sandoval et al.^[16]

CONCLUSION

The determinants which will be more favouring to a diagnosis of DVT are old age, female gender, history of immobility, trauma, Diabetes mellitus, systemic Hypertension, calf swelling more than 3cm of affected limb, severe pain, Random Blood Sugar more than 180mg/dl, total WBC count more than 10000/mm³. And minor risk factors are previous history of DVT, history of smoking, active malignancy, collateral superficial veins of affected limb, Haemoglobin less than 11g/dl and platelet count more than 400000/mm³.

If these major risk factors are present in the patient, it is advisable to do Ultrasound Venous Doppler, so that early detection of DVT can be done which otherwise if not treated at appropriate time with anticoagulation can cause severe morbidity and mortality to the patient. But regular Ultrasound venous Doppler for all cellulitis patients is not warranted because majority of the patients' diagnosis remains the same, that is cellulitis, which can be managed by antibiotics.

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