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DEEP VENOUS THROMBOSIS– A RETROSPECTIVE STUDY IN A TERTIARY CARE CENTER- SOUTH INDIA

Internal Medicine

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ABSTRACT

Background: Venous thrombosis is a condition of abnormal thrombus formation in the deep veins. It mainly manifests as Deep venous thrombosis and pulmonary embolism. DVT is the commonest. If not treated promptly it can cause significant mortality and morbidity.
Aims: The study is undertaken to find out :1) The proportion of unprovoked and provoked DVT 2) the precipitating factors if provoked, 3) types, duration and complications of treatment 4) the follow up of patients.
Methods: Our study population included 100 patients with radiological evidence of lower limb DVT from January 1, 2019 to December 31, 2019. It is a cross sectional observational study where clinical data were taken using Electronic Medical Records. Further data regarding compliance, and development of complications while on anticoagulation was taken using OAT clinic data of the hospital. The results obtained were analyzed and compared by statistical methods and conclusions drawn.
Results: The majority of DVT belonged to the age group 51- 70 (49%). 54% were women and 46%men. The major risk factor was malignancy. Majority showed no complications of DVT . Majority were treated with warfarin than NOACS. Majority who were treated for <6 months had good follow up while a significant number on indefinite treatment showed poor follow up. Majority who developed clinically significant bleeding while on treatment were on warfarin.
Conclusion: Some of our findings differ from the published reports. While majority of patients are still being treated with warfarin in spite of better compliance with NOACS a rising trend of NOACS usage is seen. An increased risk of bleeding with warfarin than NOACS needs special attention especially when a significant proportion of patients on indefinite treatment were lost to follow up. A stringent clinical and laboratory monitoring of treatment and patient education is a need of the hour. Some of our findings differ from the published reports.

KEYWORDS

KIMS - Kerala Institute Of Medical Sciences, VTE- Venous Thrombo Embolism, DVT- Deep Vein Thrombosis, Pe- PULMONARY EMBOLISM, VKA- Vitamin K Antagonists, NOACS- Newer Oral Anticoagulants, OAC- Oral Anti Coagulant, TTR - Time In Therapeutic Range, INR- International Normalised Ratio.

INTRODUCTION

Venous thrombosis is a condition of abnormal thrombus formation in the deep veins of the body. Venous thromboembolism mainly manifests as lower extremity Deep venous thrombosis (DVT)and pulmonary embolism (PE). Venous thrombosis also affects other areas of the body which are upper limb venous thrombosis, Cerebral venous thrombosis (thrombosis of cerebral veins) abdominal vein thrombosis (thrombosis of portal vein and its branches), retinal vein thrombosis[1].Deep venous thrombosis is the commonest among venous thrombosis[2]. In western world incidence of DVT is 50 -80 per 100,000 per year and the incidence increases with age (more than 60-65) and in females.[2]

DVT of the lower limbs can be proximal (above knee) and distal (below knee). Proximal DVT is more serious and requires more caution as pulmonary embolism occurs more as a consequence of proximal DVT than distal. DVT can occur in a provoked or a unprovoked setting. Provoking factors include prolonged immobilization as in fracture of long bones of legs, pelvis, hips, hip and knee arthroplasty, major general surgery, major trauma, spinal cord injury, chronic medical illness, central venous catheters, malignancy, pregnancy , postpartum, estrogen therapy, varicose veins. Unprovoked DVT without any obvious causes may have occurred due to underlying genetic causes including anticoagulants proteins C and S deficiency, antithrombin III deficiency, factor V Leiden mutation or systemic rheumatic diseases like Antiphospholipid Antibody Syndrome (APLA)[10]. The genetic causes are not very common in India and expensive investigations are avoided in case of a DVT. Investigations are usually undertaken in a provoked DVT occurring at a younger age (45 years) without any precipitating factors.

Since DVT and oral anticoagulants usage is common in everyday clinical practice[11], the study is undertaken to find out the prevalence of DVT in a tertiary center. In addition to the prevalence, the study aims to find out the proportion of unprovoked and provoked DVT, the precipitating factors if provoked, types, durations and complications of treatment and the follow up of patients undergoing anticoagulation. It aims to give a better understanding about the real clinical scenario prevailing in the current setting in order to enable us to make recommendations to improve the anticoagulation treatment in developing countries[12].

It is important to diagnose and manage the patients with DVT without delay before developing complications to reduce the patient mortality and morbidity[13]. It is also important to ensure adequate follow up in order to avoid the drug complications which can also be life threatening at times [14].

MATERIALS AND METHODS

The institute is a tertiary care institute with Department of Internal Medicine being a primary and referral center for DVT and its complications. Our study population included 100 patients who attended the Department of Internal Medicine with radiological evidence of lower limb DVT from January 1, 2019 to December 31, 2019. It is a retrospective study where data is obtained and analysed based on the past medical records.

AIM

To determine the etiological factors of DVT in a tertiary hospital.

Objective Sprimary Objective

To describe the etiological factors of Deep Vein Thrombosis

Secondary Objectives

1To describe the proportion of provoked and unprovoked DVT 2To describe proximal and distal DVT.
3To describe the treatment profile of provoked and unprovoked DVT.
4To find out the prevalence of patients on good follow up.
5To study the complications and to compare between the different anticoagulant therapies.

Study Site

This study was conducted at Kerala Institute Of Medical Sciences, Thiruvananthapuram, Kerala.

Study Population

Patients with radiological confirmation of Deep Venous Thrombosis in

KIMS, Thiruvananthapuram (Out Patient and In Patient Department) .

Study Design
Cross sectional observational study

Primary Outcome
In this study we find out the prevalence of patients with Deep Venous Thrombosis with radiological confirmation using Venous Doppler Ultrasound.

Sample Size
The total number of patients with radiological confirmation of Deep Venous Thrombosis was 100.

Inclusion Criteria
1 Patients with radiological confirmation of diagnosis of Deep Venous Thrombosis in KIMS, Thiruvananthapuram.

Exclusion Criteria
1 Patients (<13 years of age) diagnosed to have Deep Venous Thrombosis in KIMS, Thiruvananthapuram.
2 Patients with clinical suspicion of Deep Venous Thrombosis but with no radiological evidence in KIMS, Thiruvananthapuram.

Method Of Measurement Of Outcome Of Interest
The past medical records were retrieved and meticulously analyzed to determine the prevalence of DVT. The prevalence is estimated with the help of the data including the total number of patients (outpatient and inpatient) attending the hospital in the study period. The diagnosis of DVT is made with the help of radiological evidence.

Data regarding the clinical history including the history of risk factors of DVT like prolonged immobilization, surgery, trauma, varicose veins, malignancy, systemic rheumatic disease; relevant lab values and radiological data available regarding DVT, type and duration of the anticoagulant treatment used and development of complications was taken with the help of Electronic Medical Records.

Further data regarding the follow up, compliance, and development of complications in patients on while on anticoagulation was taken with the help of the OAT clinic of the hospital.

The results obtained were meticulously analyzed and compared by statistical methods and conclusions were drawn.

Data Collection Methods
Relevant clinical, laboratory and radiological data will be collected using Electronic Medical Records.

Statistical Methods
Prevalence of DVT was calculated from the proportion of patients with documented radiological evidence of thrombosis in the deep veins of upper and lower limbs. The personal data and the risk factors were summarized by frequencies and percentages. Categorical variables were compared using the Pearson chi square test. A p value < 0.05 was considered statistically significant. The data was entered into MS Excel and analyzed using the software SPSS version 16.0.

ETHICAL CONSIDERATION
Approval from Institutional Human Ethics Committee was obtained.

RESULTS

AGE GROUP	PATIENTS AFFECTED WITH DVT(%)
<30	14 (14%)
30-50	16 (16%)
50-70	49 (49%)
>70	21(21%)

46 % were males and 54% were females.

51% were right sided DVT, 47% were left sided DVT and 2 % affected both sides 30% of patients showed recurrence of DVT mad 70% did not show any recurrence.64% of DVT affected distal extremity and 12% of patients affected proximal extremity while 24% of patients had distal extending to proximal DVT 69% were provoked DVT and 31 % were unprovoked DVT Out of the 69 cases of provoked DVT,

Out of 31% of unprovoked cases, 18 (58%) patients had systemic rheumatic diseaseand 13 (42%) cases were idiopathic.

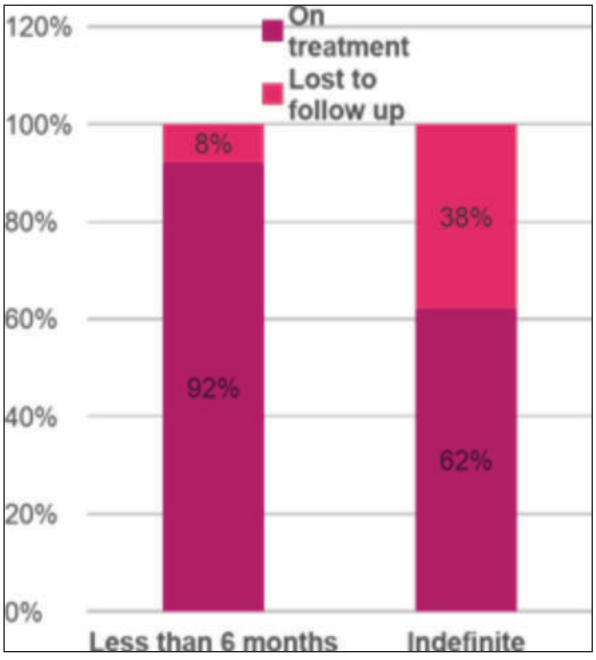
PROVOKING FACTORS	NUMBER (PERCENTAGE(%))
MALIGNANCY	30(43.4%)
TRAUMA AND SURGERY	22 (36%)
IMMOBILISATION DUE TO CHRONIC MEDICAL CONDITIONS	10(14.6%)
PREGNANCY	3(4%)
VARICOSE VEIN	2(3%)
LONG FLIGHT	2(3%)

TYPES OF MALIGNANCY	NUMBER (PERCENTAGE(%))
PANCREATIC CANCER	30(30%)
PROSTATE CANCER	25(25%)
URINARY BLADDER CANCER	10(10%)
PAPILLARY CARCINOMA THYROID	20(20%)
BREAST	7(7%)
CERVIX	2(2%)
COLON	2(2%)
CNS TUMORS	2(2%)
RENAL	1(1%)
ADVANCED METASTASIS WITH UNKNOWN PRIMARY	1(1%)

Among surgeries, hip surgeries accounted for 97% of DVT cases. 68% were treated with warfarin and 32% were treated with NOACS 92% of patients on anticoagulation treatment did not develop any complications to treatment. 8% developed bleeding as a complication of anticoagulant therapy and there was found to be an association with the use of bleeding and use of warfarin with statistical significance of 0.02 (p value 0.05).

DURATION OF TREATMENT	PATIENTS ON TREATMENT(%)	PATIENTS LOST TO FOLLOW UP(%)
LESS THAN 6MONTHS	92(92%)	8 (8%)
INDEFINITE	62(62%)	38(38%)

Death occurred was found to be due to pulmonary embolism.



DISCUSSION
DVT is becoming a very common clinical problem for practicing physicians in India. The awareness and the investigatory facility have improved in India, which might be the reason behind it. In our institution, all patients who are admitted and requiring immobilisation (>5 days, due to various causes) are getting DVT prophylaxis with LMWH. This practice has led to the decrease in the incidence of DVT and pulmonary embolism in our institution. Institutional policy is to give oral anticoagulation to all patients with provoked DVT for a duration of 3 months.

In the retrospective studies, we have made some important observations regarding the various aspects of DVT, The mean age of DVT in our study was found to be 54.29; whereas a study by Mayo clinic was (61.7)(decade late) [3]and a study in India by Pranay Pawar et.al (43.9) (decade earlier)[4].In our study we found that the DVT affects majority of females (54%) compared to a clinical review of Deep Venous Thrombosis by Emekia Kesieme, Chinenye Kesieme and Andrew Dongo[5]where DVT predominantly affected elderly males.

In our study, 69% of DVT was provoked and 31% was unprovoked which was found to be statistically significant 0.03 (p value:<0.05).

Cancer (30%)was found to be the most common cause accounting for DVT. It may be biased as the hospital is a oncological reference center;The results was contrary to the study by Pranay Pawar et.al (48.8%) where medical conditions were found to be the most common cause.

In our study, we have included malignancy under special category due to its nature of being a persistent risk factor[6].In most of the patients with active cancer and DVT, the anticoagulant treatment is continued beyond 3 months. This is because DVT can recur in a state of active malignancy.

Among provoked factors, most common provoking factor was trauma and surgery. Among surgeries, orthopedic surgery constitutes as an important factor in our study.

Among unprovoked DVT 42% were idiopathic even after most of the common investigations for thrombophilia. As a policy, we do not investigate these patients for rare genetic causes like Factor V Leiden mutation, Prothrombin gene mutation, antithrombin III , Protein C, S deficiency because of the very low incidence of these conditions in India in previous studies conducted in India[6]. Other causes of unprovoked DVT was Systemic Lupus Erythematosus and AntiPhospholipid Antibody Syndrome.

In our study the distal extremity was affected more than the proximal while in a study conducted by M J Stubbs,Maria Mouyis, Mari Thomas[7], majority of the DVT affected the proximal extremity(40%).

In our study, majority did not develop any complications, which confirms with the study done by Waheed SM , Kudaravalli P, Hotwagner DT[8]. In our study majority of the DVT cases affected the distal extremity which may be the reason for less number of complications like pulmonary embolism as proximal DVT (above knee) accounts for more cases of pulmonary embolism than distal(below the knee) whereas it was proximal in theirs.

In a study done by Jonathan Stone, Patricck Hangge and Rahmi Oklu[9] the majority of DVT was treated with warfarin with LMWH as bridging in concordance with our study. In our study, 32% of DVT patients were treated with NOACS. In our study we were not able to find any DVT cases requiring IVC filters. All the patients were treated with compression stockings and elevation of bed along with treatment with anticoagulants.

In our study, the use of Warfarin was 68% and NOACS was 32%. A rising trend of NOACS use was seen compared to the previous studies in India.

Most of the patients on anticoagulation didnot develop any complications due to anticoagulation. Risk of clinical bleeding was more with warfarin (92%) than NOACS which was found to be statistically significant 0.01 (p value <0.05).

Majority of patients on anticoagulation were on follow up but a significant number of patients on indefinite anticoagulation were lost to follow up compared to the patients on anticoagulation for<6 months.

Lacunae In Literature

From the resume of literature, it is revealed that a studies regarding the etiologies of Deep Vein Thrombosis, different types of anticoagulation treatments and its comparison, patient compliance and follow up have not been done much in India. This study is to fill up the said lacunae.

CONCLUSION

This retrospective study we were able to find out that the majority of DVT were found to be provoked. Malignancy (persistent risk factor) was the predominant cause. Among the provoked causes surgery and trauma was the most common cause unprovoked, and among the unprovoked systemic inflammatory disease was found to be the most common. Patients treated with warfarin were found to develop more tendency towards bleeding as compared to those on NOACS.. A rising trend of usage of NOACS were seen in our study compared to the previous Indian studies. It might be due to the lack of need of monitoring despite of high cost, according to our best search this is an important finding regarding anticoagulation treatment in India. Majority of the patients with DVT did not develop any complications. Patients with unprovoked DVT were on indefinite anticoagulant treatment in most of the cases and most of the provoked DVT cases were treated for 6 months or less. No significant number of patients treated with IVC filters were found out. A s ignificant number of patients on indefinite anticoagulation were lost to follow up compared to the patients on anticoagulation for<6 months.

Our patients are being followed up in a OAT clinic which is managed by the nursing staff and consultants to give then adequate advice. The clinic has a register in which all the patients taking OAC are registered and monitored every month.The patients are encouraged to do the monthly laboratory investigations like the INR and keep in touch with the team of health care workers at the OAT clinic. Even with this great effort patients lost to follow up was remarkable especially those on indefinite anticoagulation therapy.

TTR is a concept in which patients on anticoagulation are closely monitored to find out the number of patients on therapeutic range of INR . The target range of INR on patients with warfarin is 2-3. It is found that the complications of DVT are reduced when more number of patients are under TTR. In our study majority of patients on anticoagulation did not develop any complication.

RECOMMENDATIONS

The recommendations for giving a maximum benefit for patients on oral anticoagulation especially warfarin in India will be:

1) Every hospital with venous thrombosis load of more than 75 cases per year should have a well managed oral anticoagulation clinic where the health care staff should be given charged with complete details of all patients diagnosed with DVT including their contact information.

2) Patients on warfarin should have once a month INR check up (NABHL accredited).

3) Provision of better health care education and training of the medical staff in keeping the target INR of the patients under warfarin treatment in the normal range by appropriately adjusting the drug dose. This will definitely help to prevent the complication of anticoagulation therapy like recurrent thrombosis or excessive bleeding leading to more efficient patient care.

Ethical Consideration

Approval from Institutional Human Ethics Committee was obtained

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