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Clinical Study of Deep Vein Thrombosis of Lower Limbs

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Abstract

Background and Aim: Understanding the natural history of venous thrombosis is important for optimal management of this condition. Once risk factors are recognized it is possible to avoid these risk factors or to use active prophylaxis to reduce the morbidity and mortality. This study is targeted at identifying the risk factors of deep vein thrombosis in our set up, the role of Heparin in prophylaxis and to do a comparative study of low molecular weight Heparin with unfractionated Heparin in treatment of deep vein thrombosis of lower limb in Guru Gobind Singh Government hospital, Jamnagar.

Material and Methods: Study population consisted of 50 consecutive patients with deep vein thrombosis, admitted to Guru Gobind Singh hospital, Jamnagar. We have studied 50 patients above 18 years of age with proven deep venous thrombosis by Doppler ultrasound. A complete clinical history was taken to assess risk factors, level of immobility if present and thorough physical examination was done. Routine investigations such as hemogram, haematocrit, blood indices, and liver and renal function tests were done. Diagnosis of deep vein thrombosis was detected by radiographic imaging like Doppler ultrasonography.

Results: In our study, most of patients presented with complaints of swelling (70%) and pain (48%) of the affected lower limb. Few patients (4%) had symptoms of breathlessness (SOB), chest pain and orthopnea suggestive of pulmonary embolism. 34 patients in our study were having reasonably good level of haemoglobin while rests of all were having anaemia of different degree[4] patients had haemoglobin below 8gm/dl and that needed separate treatment also. Leukocytosis was present in 16 patients. 16 patients had smoking as associated risk factor along with other acquired risk factors and 5 patients had obesity along with other risk factors. The most common complication of DVT is pulmonary embolism which occurs due to dislodgement of thrombus.

Conclusion: Even though it is grievous, DVT can be prevented and treatable. Better and regular availability of drugs like LMWH and safer oral anticoagulants in the smallest possible region of the country can do wonders to save lives. Larger studies focusing more on coagulation cascade, molecular biology and genetics will be even bigger help to mankind.

Keywords: Doppler ultrasound; Hemoglobin; Pulmonaryembolism; Venous thrombosis.

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Introduction

Deep vein thrombosis is formation of semisolid

coagulum within the venous system involving deep veins. Most commonly affects the deep veins of lower limb in legs, thighs or pelvis. The initial thrombus formation usually takes place in the paired calf veins, if not recognized and treated may result in continuous clotting and more proximal extension of the clot. DVT is the most common type of venous thrombosis. It is an important cause of morbidity and mortality worldwide.[1,2]

In the past decade, deep vein thrombosis has increasingly been recognized as an important and possibly preventable cause of morbidity and mortality in hospitalized patients. According to American heart association, more people suffer from deep vein thrombosis annually than heart attack or stroke. DVT affects approximately 0.1% of person per year that signifies estimated incidence of acute DVT is approximately 1/1000 per year.3,4 The life time prevalence of DVT is 3.1% and tends to rise in older age group. The incidence of venous thromboembolism is low in children. A study by Keenan and White revealed that African-American patients are the highest risk group for first time venous thromboembolism. The risk of recurrence in Caucasians is lower than that of African–American.

Understanding the natural history of venous thrombosis is important for optimal management of this condition. Once risk factors are recognized it is possible to avoid these risk factors or to use active prophylaxis to reduce the morbidity and mortality.[5] Deep vein thrombosis is generally related to factors included under the classical triad of stasis, vessel wall damage and hypercoagulability. In particular, the association of hypercoagulability with venous stasis, which allows accumulation of activated coagulation factors invenous valve sinuses of the calf, is presently regarded as the primary triggering mechanism in development of most venous thrombi.[6]

The primary (inherited) abnormalities in some of the natural inhibitors of coagulation are associated with an increased risk of venous thromboembolism. Deficiencies of Protein C, Protein S and Antithrombin-III in patients with venous thrombosis are higher as compared with normal population in the western study. Approximately 50% of cases of deep vein thrombosis were considered to be secondary (acquired) to major risk factors like immobilization, trauma, and recent surgery.[7,8] Among additional risk factors, increased age (over 60years), male gender, malignant neoplasm, heart failure, Systemic Lupus Erythematosus and arteriopathy were independently associated with the risk of acute deep vein thrombosis.[9,10] This study is targeted at identifying the risk factors of deep vein thrombosis in our set up, the role of Heparin in prophylaxis and to do a comparative study of low molecular weight Heparin with unfractionated Heparin in treatment of deep vein thrombosis of lower limb in Guru Gobind Singh Government hospital, Jamnagar.

Objectives of the studies are

- To study risk factors of deep vein thrombosis of lower limb.
- To study role of Heparin in prophylaxis of deep vein thrombosis.
- To do a comparative study of low molecular weight Heparin and unfractionated Heparin in treatment of deep vein thrombosis.

Material and Methods

Study population consisted of 50 consecutive patients with deep vein thrombosis, admitted to Guru Gobind Singh hospital, Jamnagar. We have studied 50 patients above 18 years of age with proven deep venous thrombosis by Doppler ultrasound. A complete clinical history was taken to assess risk factors, level of immobility if present and thorough physical examination was done. Routine investigations such as hemogram, haematocrit, blood indices, and liver and renal function tests were done.

All these patients of DVT were treated according to standard treatment guidelines with low molecular weight Heparin or unfractionated Heparin and simultaneous overlapping with tablet warfarin from 4th day of Heparin with monitoring of PT-INR (Prothrombin Time and International Normalised Ratio). Ambulation, as tolerated, was advised along with elastic compression stockings. The patients were examined daily in ward and clinical features recorded regularly.

Systemic antibiotics, analgesics along with limb elevation were advised in treatment. Average hospital stay was 7-10 days. The patients were discharged with advice of continuing oral anticoagulants and regular follow up with serial measurement of PT-INR.

Inclusion Criteria

- Patients with a radiographically (Doppler ultrasound) proven deep vein thrombosis.
- Age above 18 years.

Exclusion Criteria

- Age below 18 years.
- Colour Doppler did not confirm DVT.
- Patients who had superficial thrombophlebitis.

The detailed case history was taken and physical examination was done according to the enclosed proforma. Diagnosis of deep vein thrombosis was detected by radiographic imaging like Doppler ultrasonography.

Blood sample: With informed consent, blood samples were collected from patients suffering from deep vein thrombosis. This was done at the time of presentation before starting anticoagulants and then regularly during the treatment for monitoring.

The venous blood samples from all subjects were collected into one- tenth volume (1:9) of 3.2%trisodium citrate. Plasma was prepared by centrifugation at 2500x g for 15 minutes and kept at –70 degree Celsius until use. An EDTA blood sample was collected for complete hemogram study.

The investigations done in all the patients include blood count, peripheral blood smear, liver and renal function tests, platelet count, Prothrombin time (PT), activated Partial Thromboplastin Time (APTT), renal and liver function test assay were performed.

Results

We enrolled 50 patients admitted in Shree Guru Gobind Singh Hospital, Jamnagar and fulfilling the inclusion criteria. Our study period was of 2 years from 2019 to 2021. We studied demography, clinical presentation, comorbidities, acquired risk factors, site of thrombosis, treatment and outcome of all these patients.

Table 1: Age Distribution of Study Participants.

Age Distribution (Years)	Total
21-30	4
31-40	11
41-50	15
51-60	12
61-70	8

We enrolled patients from 21 years to 70 years of age. The highest incidence was seen between 41 to 50 years of age and that was followed by 51 years to 60 years.

Graph 1: Age distribution of study participants.

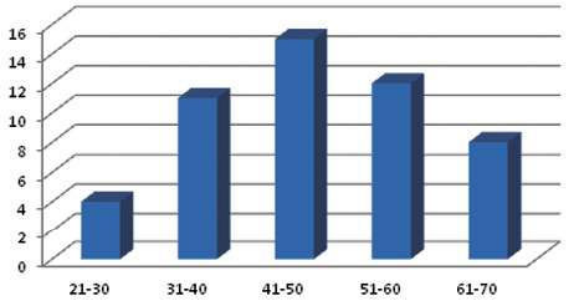


Table 2: Gender wise Distribution of Study Participants.

Sex	Number of Patients	Percentage
Total	50	100%
Male	27	54%
Female	23	46%

In our study, 27 were males and 23 were females. Male to female ratio was 1.08:1.

Graph 2: Gender wise distribution of study participants.

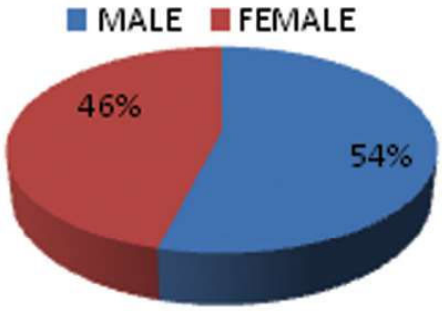
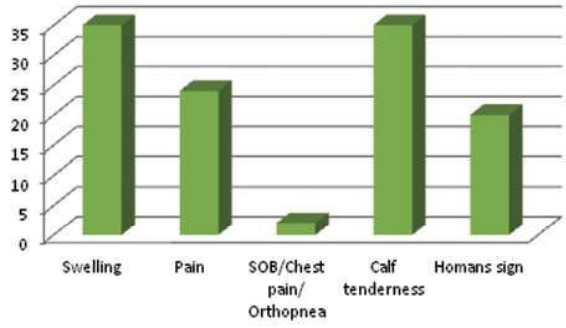


Table 3: Analysis of Symptoms and Signs of LimbDVT.

Symptoms and Signs	No. of Patients (N=50)	Percentage (%)
Swelling	35	70
Pain	24	48
SOB/Chest pain/Orthopnea	2	4
Calf tenderness	35	70
Homans sign	20	40

Graph 3: Analysis of symptoms and signs of Limb DVT.



In our study, most of patients presented with complaints of swelling (70%) and pain (48%) of the affected lower limb. Few patients (4%) had symptoms of breathlessness (SOB), chest pain and orthopnea suggestive of pulmonary embolism.

In our study, over 15% of the patients had type-2 diabetes mellitus and over 25% of the patients were suffering from various cholesterol related cardiac diseases like hypertension, coronary artery disease & ischemic heart disease and congestive cardiac failure. Others like cerebrovascular accident, chronic kidney disease and seizure were next to follow. In our study, proximal deep veins of lower limb like external iliac veins, femoral veins and popliteal veins were affected more than distal veins like anterior tibial veins and posterior veins.

Table 4: Color Doppler Findings.

Veins	Right Lower Limb		Left Lower Limb		Bilateral Lower Limb	
	Complete DVT	Partial DVT	Complete DVT	Partial DVT	Complete DVT	Partial DVT
External iliacvein	1	-	2	-	2	-
Femoral vein	5	1	12	3	-	-
Popliteal vein	2	2	4	4	-	-
Anterior tibial	1	1	6	-	-	-
Posterior tibial vein	1	-	2	1	-	-

Graph 5: Type of DVT and Limp Affected.

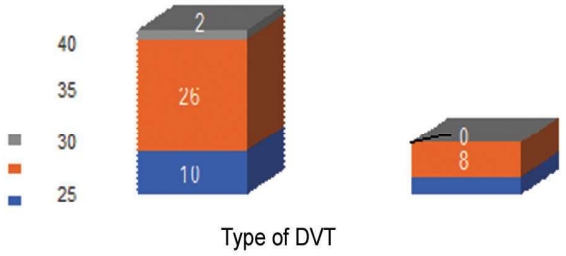


Table 5: Investigation Profile.

HB [GM/DL]	No. of Patients	WBC [Microl/ Cumm]	No. of Patients
<6.5	1	<5000	4
6.6-8.0	3	5000-10000	30
8.1-10.0	7	10000-150000	8
10.1-12	34	150000-20000	5
>12	5	>20000	3

PT (Sec)	No. of Patients	APTT (Sec)	No. of Patients	INR	No. of Patients
<11.0	3	<21.0	0	<0.80	1
11.1-12.5	8	21.1-26.0	3	0.81-0.90	20
12.6-13.0	25	26.1-31	8	0.91-1.0	5
13.1-13.5	10	31.1-35	32	>1.1	24
>13.5	4	>35	7		

34 patients in our study were having reasonably good level of haemoglobin while rests of all were having anaemia of different degree. 4 patients had haemoglobin below 8gm/dl and that needed separate treatment also.Leukocytosis was present in 16 patients. But rests of all patients were having total leukocyte count within normal limits. This might be due to early presentation of the patients.4 patients had altered prothrombin time, 7 patients had altered aptt and 5 patients had INR > 1.1.1 patient had altered renal function test. 10 patients had hypoalbuminemia.

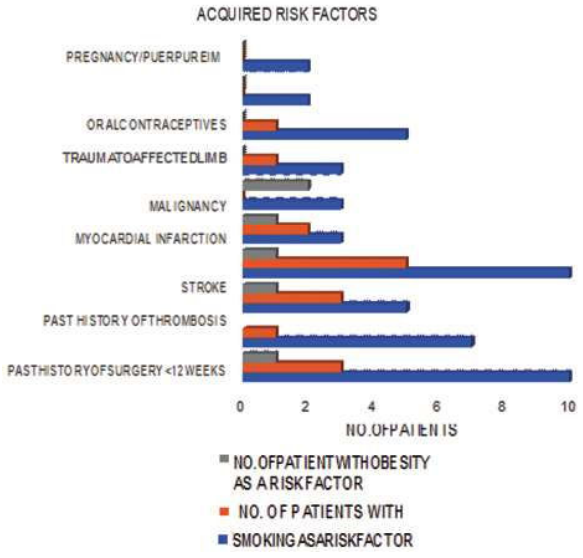
Table 6: Acquired risk factors.

Risk Factors	No. of patients having Smoking as Associated Risk Factor	No. of Patients Having Obesity as Associated Risk Factor	Total
Non-specific	3	1	10
Bed rest >3 days (immobilization)	1	0	7
History of Surgery <12 week	3	1	5
Past history of thrombosis	5	1	10
Stroke	2	1	3
Malignancy	1	0	3
Myocardial infarction	0	2	3
Trauma to the affected limb	1	0	5
Oral Contraceptive pills	0	0	2
Pregnancy/puerpuriem	0	0	2

16 patients had smoking as associated risk factor along with other acquired risk factors and 5 patients had obesity along with other risk factors. 5 patients were covid positive during the covid pandemic most common acquired risk factor is past history of thrombosis (20%) followed by immobilization (14%). Most common associated risk factor is smoking which is present in 32% of patients. 20% of the patient had no acquired risk factors. 10% patients had history of surgery in less than 12 weeks, 6% patients had acquired risk factor of stroke, malignancy and myocardial infarction

respectively. 10% patients had risk factor of trauma to the affected limb, 4% patients had risk factors of pregnancy and oral contraceptive pills use respectively.

Graph 6:



Out of 50 patients, 22 patients were given unfractionated Heparin and 28 patients were given low molecular weight Heparin. After 3 days oral anticoagulants were started. Low molecular weight Heparin is costlier, but due to better tolerability, better bioavailability and easy administration, it is preferred anticoagulant over unfractionated Heparin. 10 Patients were given Tab. Rivaroxaban (10 mg) and 40 patients were given Tab. Warfarin (5mg) started on fourth day depending upon the availability of the drugs.

Table 7: Outcome of the treatment.

Outcome	UFH (Out of 22)	LMWH (Out of 28)
Resolution of Pain	17	24
Resolution of Swelling	18	25
Reduction of Limb Girth	19	25
Prolonged APTT	6	0
Recanalization	17	22
Bleeding	3	-
Thromboembolism	2	-
Recurrence	2	1

In our study, we have compared two groups of patients each having lower limb DVT, first group of 22 patients who were administered unfractionated Heparin; second group of 28 patients, who were administered low molecular weight Heparin. We have compared the outcome of both anti-coagulants by clinical parameters, blood investigations and doppler ultrasound. The results of our study after one week are as follows:

77.27% of patients had resolution of pain after treatment with UFH & in 85.71% patients had resolution of pain after treatment with LMWH. 81.82% of patients had resolution of swelling after treatment with UFH & in 89.28% patients had resolution of swelling after treatment with LMWH. 86.36% of patients had reduction of limb girth after treatment with UFH & in 89.28% patients had reduction of limb girth after treatment with LMWH. 27.27% of patients had prolonged APTT after treatment with UFH & no patients had prolonged APTT after treatment with LMWH. 77.27% of patients had recanalization after treatment with UFH & in 78.57% patients had recanalization after treatment with LMWH. 13.6% of patients had bleeding after treatment with UFH & no patients had bleeding after treatment with LMWH. 9% of patients had thromboembolism after treatment with UFH & no patients had thromboembolism after treatment with LMWH. 9% of patients had recurrence after treatment with UFH & in 3% patients had recurrence after treatment with LMWH.

Table 8: Resolution of Clinical Signs.

Resolution of Clinical Sign	No. of Patient	%
Yes	44	88%
No	6	12%

In our study, carried out in 50 patients who developed DVT, 44 patients (88%) had complete resolution of clinical signs including cellulitis and reduction of limb girth. And 6 patients (12%) did not have resolution of clinical signs over duration of 6 weeks.Complications of DVT are inevitable if not properly treated with anticoagulants. The most common complication of DVT is pulmonary embolism which occurs due to dislodgement of thrombus. In our study, out of 50 patients, 4 patients (8%) developed pulmonary embolism, out of which 2patients died (4%), 2 patient (4%) developed varicose veins and 2 patient (4%) developed venous ulcer.

Out of 50 patients, minor bleeding in the form of hematuria occurred in 3 patients (6%). 28 Patients were on low molecular weight Heparin and 22 patients who were on unfractionated Heparin developed hematuria. Other complications like major bleeding – hematemesis, bleeding per rectal, conjunctival hemorrhage, petechiae or intra cranial bleeding were not noted.

Discussion

50 patients admitted with a diagnosis of deep vein thrombosis in lower limb, to Guru Gobind Singh hospital, Jamnagar were analyzed with respect to the demographic profile, clinical spectrum, presence of acquired/inherited risk factors for development of venous thrombosis, management and outcome of treatment.

In our study mean age of patients was 46.26 years with a most commonly affected age group is middle age group. According to Pal Naresh et al[11] study, maximum number of patients in male were in age group of 21-30 years as well as in females also and most common age group in both sexes were 21-30 years. According to Kasabe PS et al[12] study, most common age group affected were in 50–59-year age group.

Out of 50 patients, 27 patients were male (54%) and 23 patients were female (46%). The ratio of males to females is 1.08:1.According to a clinical study in Kasabe PS et al12 male to female ratio was 1:078.According to a clinical study in Pal Naresh et al[11] male to female ratio was 1:1.7.According to a clinical study in Anderson and Colleagues 13, 70% were males and 30% were females. The male to female ratio was 1.4:1.

In the 50 patients who presented with lower limb deep vein thrombosis, the most common presenting features were swelling of limb in patients (70%) and pain in patients (48%). On examination patients (60%) had pedal edema and calf tenderness was present in patients (70%).

O'Donnell et al[14] and Molly et al[15] study showed that pain (78%) and swelling (85%) were the most common symptoms; Homan sign (60s%) and tenderness (76%) were the common clinical signs. Kasabe PS et al[12] study showed that pain (100%) and swelling (100%) were the most common symptoms; Homan's sign (76%) and tenderness (94%) were the common clinical signs. breathlessness and chest pain suggesting pulmonary embolism.

In our study, 6 patients had hypertension, 8 patients had diabetes mellitus type-2, 4 patients had congestive cardiac failure/coronary artery disease, 3 patients had ischemic heart disease, 3 patients had history of CVA and one patient had history of chronic kidney disease and one patient had seizure. 3 patients had malignancy. And there were no comorbidities in 24 patients. Kniffins large study of venous thromboembolic disease in elderly patients found congestive heart failure in 265 of 7174 patients with pulmonary embolism and 14% of 8923 patients with DVT.

Deep venous thrombosis was diagnosed in 50 patients in our setup by Doppler study. 38 patients (76%) had proximal venous thrombosis and 12 patients (24%) had lower distal venous thrombosis in lower limb. According to western studies, Huisman MV et al16, multisegmented involvement of the proximal veins is most common, proximal veins like superficial femoral and popliteal veins being involved in 74% and 73% of patients respectively. However, isolated involvement of the iliac veins may occur in 2 to 5% of cases, 20 and 12 to 35% remain confined to the distal limb (calf) veins.17.2 patients (8%) had pulmonary embolism which was diagnosed by CT chest and echocardiography.

In our study 34 patients (68%) had DVT in left lower limb and 14 patients (28%) had DVT in right lower limb and bilateral lower limb were affected in 2(4%) patients. In a study by Pal Naresh and et al[11], 40.7% in right lower limb, 57.4% in left limb and 1.85% in bilateral lower limb. In a study by Kasabe PS1236% patients had right sided lower limb DVT, 64% patients had left sided lower limb DVT and 0 patients had bilateral lower limb DVT. According to Stamatakis & et al[18] study, major thrombi more frequently occurred in left lower limb.

10 patients (28%) had history of previous episode of venous thrombosis. In the population study by Anderson and colleagues, one third of episodes of acute VTE were recurrent.[13] In a larger series of patients followed up over a mean of 9.3 months period, new thrombotic events were observed in 52%.[19]

5 Patients had been hospitalized and underwent surgery within the past 12 weeks. The incidence of deep vein thrombosis following general or gynecologic surgical procedures is approximately 20% to 25%, and clinically significant pulmonary embolism occurs in 1% to 2% of these patients. There is 6% risk of developing lower limb DVT in patients undergoing major surgeries if prophylactic Heparin was not given in our setup, while there is 6.5% chance according to Eric J. Rydberg & et al[20] study and 20% chance according to Alexander CG Turpie et al[21] study to develop lower limb DVT postoperatively, if prophylaxis of Heparin was not given. According to Alexander CG Turpie et al[21] study, the chances of postoperative lower limb DVT reduces to 4% if prophylaxis with LMWH was given.

Out of 23 female patients with lower limb venous thrombosis, 2 patients (4%) were pregnant /puerperium. Western studies have proven that pregnancy is associated with an approximately sixfold increased risk of venous thromboembolism

although the incidence of deep vein thrombosis and pulmonary embolism has been estimated to be as high as 1%. 5 patients had BMI more than 29 kg/m2 who developed lower limb venous thrombosis.[22,23] Obesity was found to be an independent risk factor (relative risk 3.0) for symptomatic pulmonary embolism in the nurse's health study. Most common acquired risk factor is past history of thrombosis (20%) followed by immobilization (14%).

Most common associated risk factor is smoking which is present in 32% of patients. 20% of the patient had no acquired risk factors. 10% patients had history of surgery in less than 12 weeks, 6% patients had acquired risk factor of stroke, malignancy and myocardial infarction respectively. 10% patients had risk factor of trauma to the affected limb , 4% patients had risk factors of pregnancy and oral contraceptive pills use respectively.

All patients with venous thrombosis received LMWH and oral anticoagulants initially and later oral anticoagulants were continued. Out of 50 patients, 22 patients were given unfractionated Heparin and 28 patients were given low molecular weight Heparin.

Our study showed resolution of symptoms of DVT with LMWH were better than UFH while Rubina Naz & et al both studies show that complications with LMWH are lesser than UFH. 24 Low molecular weight Heparin has advantage over unfractionated Heparin, with benefit of lesser hospital stay, convenient subcutaneous mode of administration, and lesser complications like bleeding. LMWH has better outcome than UFH.

In our study, carried out in 50 patients who developed DVT, 44 patients (88%) had complete resolution of clinical signs including cellulitis and reduction of limb girth. And 6 patients (12%) did not have resolution of clinical signs.After treatment with anticoagulants, there is visible resolution in clinical features like swelling, pain and reduction in limb girth in most of the patients.

In our study, out of 50 patients, 4 patients (8%) developed pulmonary embolism, out of which 2 patients died (4%), 2 patient (4%) developed varicose veins and 2 patient (4%) developed venous ulcer. Complications of DVT are inevitable if not properly treated with anticoagulants. The most common complication post DVT is pulmonary embolism due to dislodgement of thrombus.

28 Patients were on low molecular weight Heparin and 22 patients who were on unfractionated Heparin developed hematuria. Other complications like major bleeding–hematemesis, bleeding per rectal, conjunctival hemorrhage, petechiae or intra cranial bleeding were not noted. Comparing our study with other studies, UFH had more complications than LMWH. Hence LMWH is comparatively safer with lesser complications.[22,23]

Conclusion

The ultimate aim of treatment of DVT is to prevent further extension of thrombus from deep veins, development of acute PE, recurrence and prevention of later complications such as post-thrombotic syndrome. So high index of suspicion should be kept in patients even if classical clinical signs are not present and prophylactic treatment should be given to these patients. Though costlier but better tolerable LMWH gives comparable success with UFH by its better bioavailability, easy dosage schedule, better treatment outcome and lesser complication. It is also worth for prophylaxis. At the end of this small study, we can conclude that even though it is grievous, DVT can be prevented and treatable. Better and regular availability of drugs like LMWH and safer oral anticoagulants in the smallest possible region of the country can do wonders to save lives. Larger studies focusing more on coagulation cascade, molecular biology and genetics will be even bigger help to mankind.

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