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Deep Venous Thrombosis Recurrence and Its Predictors at Selected Tertiary Hospitals in Ethiopia: A Prospective Cohort Study

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Abstract

Deep venous thrombosis (DVT) is a common clinical problem associated with substantial morbidity and mortality. Knowledge of the global burden of DVT recurrence is deficient in Africa, including Ethiopia. The objective of the study was to assess deep venous thrombosis recurrence and its predictors at selected tertiary hospitals in Ethiopia. Prospective cohort study was conducted among hospitalized DVT patients. Data were analyzed using SPSS version 21.0. To identify the independent predictors of DVT-recurrence, multiple stepwise-backward Cox-regression analysis was done. Statistical significance was considered at P value < .05. A total of 129 participants were included (65.1% females) with mean $\pm$ SD age of 38.63 $\pm$ 17.67 years. About 26.4% of patients developed recurrent venous thromboembolism. Pulmonary embolism accounted for 17.60% of recurrent event. The overall incidence density of DVT recurrence was 2.99 per 1000 person-days. The mean $\pm$ SD survival time to DVT recurrence was 42.03 $\pm$ 22.371 days. Age $\geq$ 50 years (adjusted hazard ratio [AHR]: 5.566; 95% CI: 1.587-19.518; $P = .007$), occasional alcohol consumption (AHR: 2.011; 95% CI: 1.307-6.314; $P = .019$), surgical history (AHR: 6.218; 95% CI: 1.540-25.104; $P = .010$), pregnancy (AHR: 2.0911; 95% CI: 1.046-4.179; $P = .037$), diabetes mellitus (AHR: 8.048; 95% CI: 2.494-25.966; $P < .001$), unmet activated partial thromboplastin time target after 24 hours of heparin (AHR: 1.129; 95% CI: 0.120-10.600; $P = .011$), proximal site involvement (AHR: 5.937; 95% CI: 1.300-27.110; $P = .022$), and previous history of DVT (AHR: 2.48; 95% CI: 1.085-11.20; $P = .0002$) were independent predictors of DVT recurrence. The DVT recurrence rate was high in the study area, which is even complicated with pulmonary embolism as well as death. Efforts are needed to prevent and reduce the development of DVT recurrence.

Keywords

deep vein thrombosis, recurrence, pulmonary embolism, bleeding

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Introduction

Venous thromboembolism (VTE) is the formation of a blood clot in a deep vein that can lead to complications including deep vein thrombus (DVT), a pulmonary embolism (PE), or postthrombotic syndrome (PTS). Venous thromboembolism is a serious condition with an incidence of 10% to 30% of people dying within 1 month of diagnosis and half of those diagnosed with a DVT have long-term complications. Deep venous thrombosis is considered the third most common cardiovascular condition after myocardial infarction and stroke, and it is a growing public health problem due to an increase in the aging population.[1] The development of single or multiple blood clots within the deep veins of the extremities or pelvis, usually accompanied by inflammation of the vessel wall and which is commonly affects the leg veins (such as the femoral vein or the popliteal vein) or the deep veins of the pelvis which made them common sources of serious complications.[2,3]

Deep venous thrombosis is a major and common preventable cause of death worldwide; it affects approximately 0.1% of persons per year. Both sexes are equally afflicted by a first DVT, men having a higher risk of recurrent thrombosis. Deep venous thrombosis is predominantly a disease of the elderly with an incidence that rises markedly with age.[3] Data from the United States show that DVT and PE are a major disease burden, it affects an estimated population of approximately 1 million each year and results in several hundred thousand hospitalizations that can be contributing an about 33% of death

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from the disease. The estimated 66% nonfatal cases of DVT result in several hundred thousand primary hospitalizations or extended hospital stays in patients who develop both DVT and PE while hospitalized.[4]

In Western countries, population studies have reported incidence rates of VTE was estimated to be between 80 and 180 per 100 000 person-years. Autopsy studies have suggested that the incidence of the most serious complication of VTE, fatal PE, could be underestimated in population studies. For almost a quarter of PE patients, the initial clinical presentation is sudden death.[5,6] The outlook after an episode of symptomatic VTE can be blighted by long-term sequelae including recurrence of VTE. A mortality rate of 6% has been reported in the first 6 months after the disease onset. Recent studies found a high incidence of recurrent DVT with half of DVT incidences in the United States. A relapse after a 5-year disease-free interval is observed in 20% to 30% of the patients.[7] While some studies reported the annual incidence rate of the first recurrent attack to be 3% to 5%, which is generally most probable to happen during the first 2 years after the discontinuation of anticoagulation treatment, others claimed a higher rate of 5% to 10%.[8]

The incidence of disease recurrence, as a condition with multifactorial pathogenesis, is related to the number and severity of the risk factors.[9,10] Patients with an initial episode of symptomatic DVT are at high risk of recurrent DVT. Recurrence rates are higher if there is residual thrombus in the vessel.[11,12] A recent report found that 60% of higher recurrence risk among men compared to women. A study suggested that this increase in risk could be explained by a lower recurrence risk among women who were using exogenous hormones at the time of their first event. The risk appears to be highest in the 6 to 12 months following cessation of anticoagulation, regardless of the initial duration of anticoagulation.[13]

One prospective cohort study from Ethiopia conducted in 1998 G.C among admitted DVT patients revealed a relatively common disease associated with severe complications and mortality.[14] A similar recent study at a tertiary hospital showed malignancy, prolonged immobilization, pregnancy-related problems, and major trauma were the most common risk factors noted for DVT occurrence.[15] Due to a lack of evidence on the DVT recurrence in Ethiopian hospitals, we focused to assess the recurrence rate of DVT over 3-months period among patients on anticoagulation at 2 selected tertiary care setting in Ethiopia.

Methods and Materials

Study Setting and Period

This study was conducted among hospitalized DVT patients at 2 tertiary hospitals available in the country; Jimma University Medical Center (JUMC) and St. Paul's Hospital Millennium Medical College (SPHMMC). Jimma University Medical Centre found in Southwest Ethiopia about 352 km far away from the capital, Finfinnee (Addis Ababa) and St. Paul's Hospital Millennium Medical College is located in Finfinnee (Addis Ababa) city. We enrolled participants at these 2 selected tertiary teaching hospitals concurrently from March 2018 to August 2018.

Study Design and Population

Three-months prospective open cohort study was conducted among adult patients diagnosed with DVT, who was admitted to inpatients wards of JUMC and SPHMMC.

Participants Enrollment and Inclusion

We included adults with age $\geq$18 years old patients with proven DVT by Doppler ultrasonography and patient willing to give consent. Participation in study was offered to all consecutive patients with DVT. Each patient included for the final analysis was followed within the cohort at least for 90 days for the outcome. Patients who were unable to follow their monthly follow-up and who started anticoagulants for the prophylaxis purpose were excluded from the study. A total of 146 patients, who initially had confirmed DVT by Doppler ultrasound at JUMC and SPHMMC were recruited to participate in the study. Eight patients dropped out/lost to follow-up during the study period. All loss to follow-ups were from SPHMMC. Nine patients also self-discharged (left against medical advice) by themselves. Finally, a total of 129 patients, whose outcome within 90 days was known, were included in the final analysis (Figure 1).

Data Collection Procedure and Quality Assurance

A structured data collection questionnaire was developed by researchers from relevant kinds of literature. Patient chart review and self-report were used to determine the various variables. Patient information, sociodemographic and clinical characteristics, and diagnostic test results were collected from patient medical charts, medication order sheets, and laboratory orders at the time of clinical diagnosis during the patient's hospital stay. Patients were enrolled in the cohort starting from the anticoagulation initiation date. Then, those patients were followed for the outcome using laboratory investigations, periodic reviews of medical charts of the patients, and face-to-face and/or a telephone interview by using a structured questionnaire at first, second, and the third month of anticoagulant initiation. The training was given for data collectors on the data collection procedure, objectives and collection of follow-up data. Four pharmacists and 2 medical residents were involved in the data collection and patient evaluation. The investigators were involved in a supervision role, data daily quality management, and following each patient at follow-up clinic and/or by telephone.

Data Processing and Analysis

All collected patient's data were entered into EpiData version 4.2 for data cleaning and then exported to Statistical Package for Social Science (SPSS) version 21.0 for analysis. Categorical and continuous data were expressed as percentages and

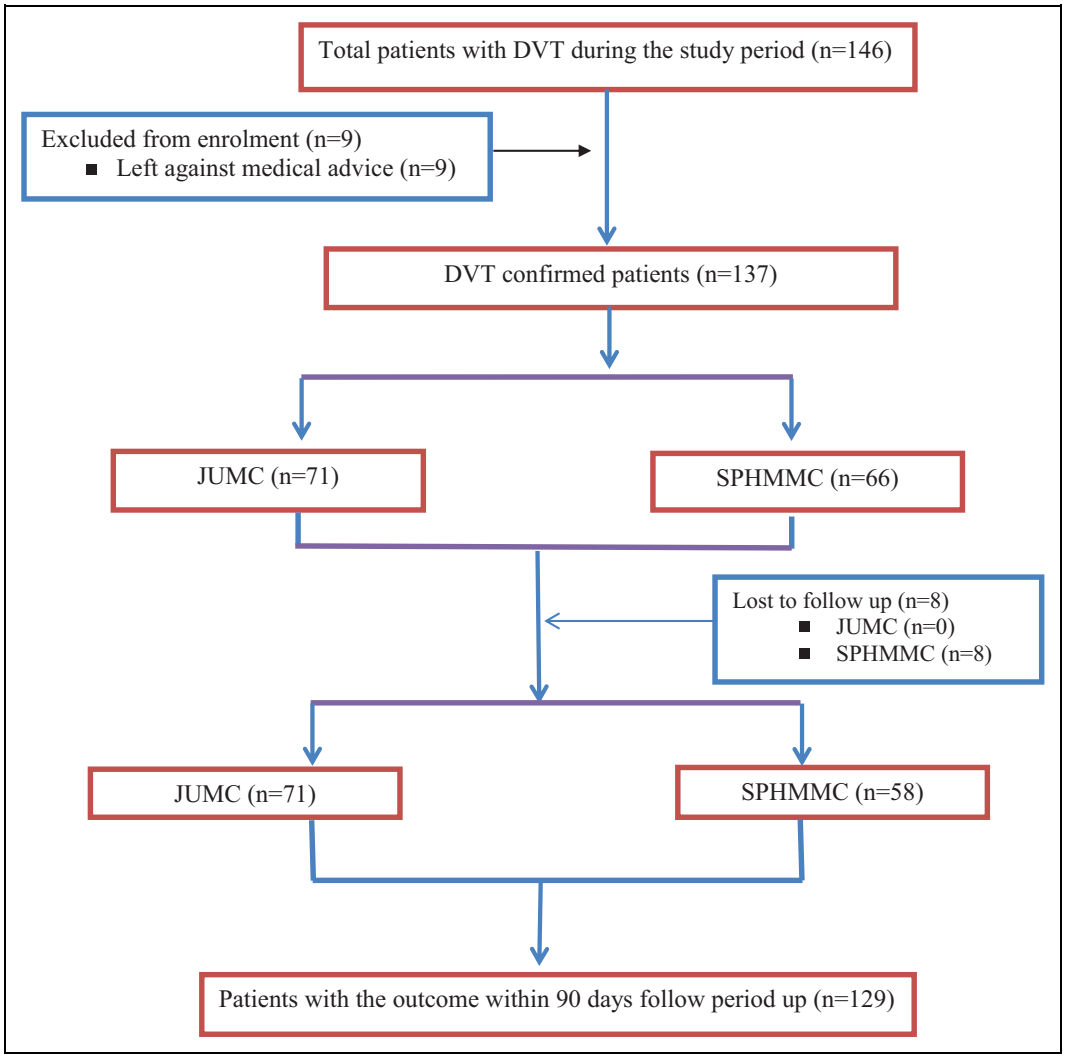

Figure 1. Study participant recruitment flow diagram.

mean ± SD, respectively. Descriptive statistics were applied for the analysis of patient characteristics, including means, SD, medians, and percentiles and categorical variables were analyzed by using the χ^2 test. Using Cox proportional hazards (PHs) modeling, we tested relevant variables as potential associated factors for DVT recurrence from anticoagulation date to 90 days. All variables were initially tested for an association with the rate of DVT recurrence in bivariate Cox PH models. Those variables demonstrating a univariate association with at least marginal significance ($P < .25$) were included in a multivariable model. Multivariable Cox-regression analyses were used to assess the crude and adjusted effect of seemingly significant predictors of DVT recurrence. The adjusted hazard ratio was used as a measured strength of association. A P value of $< .05$ was considered to be statistically significant.

Outcome and Validating Methods

Deep venous thrombosis management in Ethiopia depends on the national Standard Treatment Guidelines for General Hospital[16] and international clinical practice guideline such as American college chest physicians DVT treatment guideline.[17] The protocol for management and case definition is similar. In Ethiopian hospital, acute DVT is treated in inpatient setting for 5 to 7 days. Initially, a weight-based parenteral anticoagulant is initiated. Usually, unfractionated heparin (UFH) is preferable to low-molecular-weight heparin–like enoxaparin (except in selected patients) due to cost and availability. After 24 to 48 hours, warfarin, the only routinely available oral anticoagulant, will be added to the parenteral regimen. The parenteral regimen will be continued until 5 to 7 days and then after, it will be discontinued when international normalization ratio (INR) is between the recommended ranges of 2 to 3. Based on the risk factor(s), the patient is prescribed with warfarin for the recommended duration of anticoagulation. In case of pregnancy and oncology, enoxaparin is drug of choice in the setting. In our setting, there is not test of hereditary thrombophilia. The available medications in the setting were UFH and enoxaparin and warfarin. In this study, patients were enrolled and followed starting from patient hospital arrival and

date of anticoagulant initiation until 90 days. Recurrence ascertainment was made based on the following criteria; if the patient is readmitted to the hospital:

1. With a new case of DVT or its complication during 90 days of anticoagulant therapy and/or
2. Exacerbation of the current DVT, which was diagnosed on the preceding hospital admission.

Ethical Consideration

A letter of ethical clearance was obtained from the Ethical Review Board of the institute of health, Jimma University. A formal request letter was presented to JUMC and SPHMMC to get access permission to patient data. After relevant information was given on the research purpose and process, written informed consent was obtained from participants, and the patient's confidentiality was secured. The raw data were not made available to anyone and not used as the determinant of the participant. All steps in data collection and compilation were conducted and supervised by the investigators. Strict confidentiality was assured through anonymous recording and coding of questionnaires and placed in a safe place.

Definitions of Terms

- **Bleeding** is defined as clinical status, laboratory, and/or imaging evidence of bleeding from the internal or external body as a result of anticoagulant therapy.[18]
- **Comorbidity** is the presence of one or more additional diseases or disorders co-occurring with (ie, concomitant or concurrent with) a primary disease DVT.
- **Recurrence** is an objectively verified hospital discharge diagnosis of DVT or as a fatal complication of DVT confirmed at ultrasonography, or occurrence of thrombosis on previously uninvolved site or had interval documentation of incident DVT (it is a worsened DVT) after anticoagulation initiation.

Results

Sociodemographic Characteristics of Study Participants

From a total of 129 study participants included in the final analysis, about 84 (65.1%) were females, with male to female ratio of 1:1.86. The mean ± SD age of participants was 38.63 ± 17.67 years. The majority of the patients 76 (58.9%) were within the age-group between 18 and 35 years. About 57.4% of participants were residing in a rural area. A large number (111 [86.0%]) of study participants were living with their immediate family. About three-fourth of patients were married. Nearly, 5% of study participants had a smoking history (Table 1**)**.

Clinical Characteristics and Laboratory Test Data of Study Participants

As to the anatomic site of DVT, the majority of patients (124/96.1%) had the thrombosis of the lower extremities extending from the common iliac vein to the popliteal veins. About 115 (89.1%) of participants were found to have unilateral and only 14 (10.1%) patients have combined involvement of bilateral DVT, whereas approximately two-third of participants had left lower extremity involvement. On the Doppler ultrasonography examination, the majority of 103 (79.8%) of DVT cases were proximal and only 21 (16.3%) cases were located distal area for the lower extremity. The mean ± SD length of hospital stay (LOS) was 22.03 ± 16.719 days and 21.33 ± 14.104 days at JUMC and SPHMMC, respectively, with an overall range of 2 to 90 days. From a total of 129 DVT patients, 127 (98.4%) of participants had received UFH, with a mean ± SD duration of UFH-warfarin overlap of 15.792 ± 9.2454 days (range of 1-44 days). The mean ± SD result of aPTT was 34.164 ± 12.024 seconds within 24 hours and 38.81 ± 18.07 seconds in the fifth days; it was 45.628 ± 21.06 seconds immediately before discontinuing heparin. The mean ± SD of INR was 1.822 ± 1.061 and 2.136 ± 1.455 on fifth day and immediately before stopping heparin, respectively. About 34 (26.4%) had a higher risk of major bleeding, with a Hypertension, Abnormal renal and liver function, Stroke Bleeding, Labile INR, Elderly, Drugs or alcohol (HAS-BLED) score of ≥3 points (Table 2).

Deep Venous Thrombosis Risk Factors Among Study Participants

The major risk factors related to DVT occurrence among the study participant at the 2 clinical care settings were prolonged immobilization 113 (87.6%), prior surgical history 35 (27.1%), and pregnancy 32 (24.8%). Left side DVT 23 (71.9%) was the predominant location in pregnant women. It was found that 74 (57.4%) of the patients were presented with a combined significant medical condition (ie, metabolic, endocrine or respiratory pathologies, acute infectious disease, inflammatory conditions [arthritis]). Other risk factors included chronic lung disease (17.8%), active cancer (10.9%), oral contraceptive pills use (18.6%), and congestive heart failure (15.5%; Table 3).

The prevalence of comorbidity among study participants showed that about 77.5% of them had current comorbid conditions. Thus, 15 (11.6%) of them had active cancer. Renal failure and heart failure accounted for 19 (14.7%) and 20 (15.5%), respectively (Table 4).

The majority of study participants, 127 (98.4%) received UFH on their admission. About 89.1% of patients' warfarin was prescribed with parenteral anticoagulant therapy. Majority of the participant was on ancillary medication, of which one-third of participants were on antibiotics, 16 (12.4%) were on cardiovascular drugs, and 26 (20.2%) of participants were on vitamin and minerals (Figure 2).

Table 1. Baseline Socio-Demographic and Behavioral Characteristics of Study Participants.

Variables		Settings			*P* value
		JUMC (n [%])	St. Paul (n [%])	Total (n [%])	
Gender	Male	29 (40.8)	16 (27.6)	45 (34.9)	.116
	Female	42 (59.2)	42 (72.4)	84 (65.1)	
Age (years)	18-35	40 (56.3)	36 (62.1)	76 (58.9)	.384
	35-50	12 (16.9)	5 (8.6)	17 (13.2)	
	>50	19 (26.8)	17 (29.3)	36 (27.9)	
Marital status	Single	17 (23.9)	9 (15.5)	26 (20.1)	.237
	Married	49 (69.0)	47 (81.0)	96 (74.4)	
	Divorced	2 (2.8)	2 (3.4)	4 (3.1)	
	Widowed	3 (4.2)	0	3 (2.3)	
Occupation	Office worker	3 (4.2)	12 (20.7)	15 (11.6)	<.001
	Farmer	33 (46.5)	4 (6.9)	37 (28.7)	
	Merchant	9 (12.7)	13 (22.4)	22 (17.1)	
	Student	5 (7.0)	5 (8.6)	10 (7.8)	
	Daily labourer	6 (8.4)	4 (6.9)	10 (7.8)	
	Others[a]	15 (21.1)	20 (34.5)	35 (27.1)	
Residence location	Rural	48 (67.6)	26 (44.8)	74 (57.4)	.009
	Urban	23 (32.4)	32 (55.2)	55 (42.6)	
Educational status	Cannot read and write	36 (50.7)	16 (27.6)	52 (40.3)	.001
	Primary school	25 (35.2)	16 (27.6)	41 (31.8)	
	Secondary school	7 (9.9)	20 (34.5)	27 (20.9)	
	College and above	3 (4.2)	6 (10.3)	9 (7.0)	
Living condition	With immediate family	54 (76.1)	57 (98.3)	111 (86.0)	.004
	With extended family	6 (8.5)	1 (1.7)	7 (5.4)	
	Living alone	5 (7.0)	0	5 (3.9)	
	Others[b]	6 (8.5)	0	6 (4.6)	
Alcohol consumption	Never	50 (70.4)	37 (63.8)	87 (67.4)	.491
	Occasionally	11 (15.5)	15 (25.9)	26 (20.2)	
	Regularly	9 (12.7)	5 (8.6)	14 (10.8)	
	Ex-consumer	1 (1.4)	1 (1.7)	2 (1.5)	
Smoking behavior	Current Smoker	8 (12.3)	0	8 (6.2)	.018
	Nonsmoker	63 (88.7)	57 (98.3)	120 (95.2)	
	Ex-smoker	0	1 (1.7)	1 (0.8)	
Khat chewing behavior	Yes	11 (15.5)	0	11 (8.5)	.002
	No	60 (84.5)	58 (100)	118 (91.5)	
Herbal medicine use	Yes	10 (14.1)	0	10 (7.8)	.003
	No	61 (85.9)	58 (100)	119 (92.2)	

Abbreviation: JUMC, Jimma University Medical Center.
[a]House wife.
[b]Live in prison.

Deep Venous Thrombosis Follow-Up Outcome of Participants

A cohort of 129 patients was followed up for a total of 11 348 person-days. More than three-fourth of study participants developed DVT for the first time. During the 90-day follow-up period of each participant from a cohort of DVT, 34 (26.4%) recurrent VTE was observed. The type of event was DVT in 28 (82.40%) patients and the rest were admitted with PE, which was confirmed by computed tomography scan. During the study period, none of the patients with recurrent VTE event were within the therapeutic range. Their INR was below 2. The overall incidence rate was 2.99 per 1000 patient-days. A few numbers of patients, 6 (4.7%), had confirmed complete DVT resolution within 3 months of treatment. The overall mean $\pm$ SD duration of DVT recurrence was 42.03 $\pm$ 22.371 with a range of 26 to 90 days (Table 5).

Kaplan Meier Survival Outcome Analysis

The mean $\pm$ SD survival time to DVT recurrence was 42.03 $\pm$ 22.371 days. On the Kaplan Meier survival outcome analysis, variables such as LOS, anatomical location of DVT, HAS-BLED score, age of the patients, diabetes mellitus (DM) comorbidity, gender, early initiation of warfarin, achieving target aPTT within 24 hours of heparin were done. From the result, the survival time to DVT recurrence were not statistically significant between gender (log-rank $P = .120$), early initiation of warfarin (log-rank $P = .174$), and LOS (log-rank $P = .303$). However, there were differences in survival time to

Table 2. Baseline Clinical Characteristics and Laboratory Test Data of Study Participants.

Variables		Settings			
		JUMC (n [%])	St. Paul (n [%])	Total (n [%])	*P* value
Baseline clinical data					
Types of DVT	Unilateral	61 (85.9)	54 (93.1)	115 (89.1)	.192
	Bilateral	10 (14.1)	4 (6.9)	14 (10.9)	
Sites of DVT	Upper extremity[a]	1 (1.4)	4 (6.9)	5 (3.9)	.108
	Lower extremity	70 (98.6)	54 (93.1)	124 (96.1)	
Lower extremity DVT	Right leg	15 (21.1)	18 (31.0)	33 (25.6)	.234
	Left leg	52 (73.2)	33 (56.9)	85 (65.9)	
	Both legs	3 (4.2)	3 (5.2)	6 (4.7)	
Anatomic location of DVT[b]	Proximal DVT	61 (85.9)	42 (72.4)	103 (79.8)	.168
	Distal DVT	9 (12.7)	12 (20.7)	21 (16.3)	
Pain	Yes	70 (98.6)	58 (100)	128 (99.2)	.550
	No	1 (1.4)	0	1 (0.8)	
Swelling	Yes	68 (95.8)	58 (100)	126 (97.7)	.164
	No	3 (4.2)	0	3 (2.3)	
Local tenderness	Yes	49 (69.0)	26 (44.8)	75 (58.1)	.006
	No	22 (31.0)	32 (77.6)	54 (51.9)	
Pitting edema	Yes	41 (57.7)	27 (46.6)	68 (52.7)	.138
	No	30 (42.3)	31 (53.4)	61 (47.3)	
Skin discoloration	Yes	20 (28.2)	12 (20.7)	32 (24.8)	.328
	No	51 (71.8)	46 (79.3)	97 (75.2)	
Baseline laboratory tests and others data during hospital stay (mean $\pm$ SD)					
Hemoglobin (g/L)		10.685 $\pm$ 3.0484	12.656 $\pm$ 3.0517	11.604 $\pm$ 3.1917	.001
Hematocrit (percentage)		31.494 $\pm$ 8.4922	38.951 $\pm$ 8.4922	34.951 $\pm$ 9.3860	<.001
Platelet, $\times 10^9$/L		317.2 $\pm$ 146.53	340.3 $\pm$ 165.5	327.3 $\pm$ 154.84	.440
aPTT (seconds) at 24 hours		33.34 $\pm$ 5.713	35.973 $\pm$ 19.90	34.164 $\pm$ 12.024	.358
aPTT (seconds) at 48 hours		34.3 $\pm$ 16.76	38.030 $\pm$ 17.657	36.41 $\pm$ 17.156	.500
aPTT (seconds) at fifth days		32.059 $\pm$ 8.46	43.587 $\pm$ 21.47	38.81 $\pm$ 18.07	.043
aPTT (seconds) at immediately before DC heparin		35.625 $\pm$ 4.95	48.591 $\pm$ 23.093	45.628 $\pm$ 21.06	.128
INR at 24 hours		1.441 $\pm$ 0.603	1.747 $\pm$ 1.268	1.5612 $\pm$ 0.93	.101
INR at 48 hours		1.521 $\pm$ 0.783	1.854 $\pm$ 1.3235	1.7242 $\pm$ 1.147	.260
INR at fifth days		1.666 $\pm$ 0.6891	1.9411 $\pm$ 1.269	1.822 $\pm$ 1.061	.244
INR on discharge days		2.046 $\pm$ 1.1658	2.204 $\pm$ 1.649	2.136 $\pm$ 1.455	.661
Serum creatinine (mmol/L)		0.0851 $\pm$ 0.0815	0.0845 $\pm$ 0.0781	0.0848 $\pm$ 0.0795	.969
Duration of heparin–warfarin overlap (days)		16.394 $\pm$ 9.276	14.918 $\pm$ 9.2259	15.792 $\pm$ 9.2454	.392
Length of hospital stay (days)		22.03 $\pm$ 16.719	21.33 $\pm$ 14.104	21.71 $\pm$ 15.542	.800
Antithrombotic use prior to admission		9 (12.9)	16 (27.6)	25 (19.4)	.033
Base line HAS-BLED score	$\geq$3 points (high risk)	11 (15.5)	23 (39.7)	34 (26.4)	.02
	<3 points (low risk)	60 (84.5)	35 (60.3)	95 (73.6)	

Abbreviations: aPTT, activated partial thromboplastin time; DC, discontinue; DVT, deep venous thrombosis; HAS-BLED, Hypertension, Abnormal renal and liver function, Stroke Bleeding, Labile INR, Elderly, Drugs or alcohol; INR, international normalization ratio; US, ultrasonography.
[a]Two were right hand and 3 were on the left hand, all occurred at proximal sites.
[b]For lower extremity only.

DVT recurrence concerning HAS-BLED score (Log rank $P = .05$; Figure 3).

Factors Associated With DVT Recurrence Among Study Participants

The association of independent variables with the dependent variable was investigated using both univariate and multivariate Cox regression techniques. On univariate Cox regression analysis, female gender (crude hazard ratio [CHR]: 1.799; 95% CI: 0.828-3.905; $P = .038$), age $\geq$ 50 years (CHR: 3.438; 95% CI: 1.091-10.838; $P = .035$), occasional alcohol consumption (CHR: 2.460; 95% CI: 0.694-8.723; $P = .031$), regular alcohol consumption (CHR: 1.110; 95% CI: 0.494-2.656; $P = .054$), pregnancy (CHR: 1.091; 95% CI: 1.46-11.179; $P = .057$), hypertension (CHR: 0.077; 95% CI: 0.017-0.358; $P = .001$), DM (CHR: 3.869; 95% CI: 1.295-11.558; $P = .015$), uninitiated warfarin within 24 hours of heparin initiation (CHR: 2.797; 95% CI: 1.087-7.213; $P = .051$), not achieving aPTT target within 24 hours (CHR: 1.108; 95% CI: 0.020-0.600; $P = .032$), and (CHR: 2.130; 95% CI: 1.201-11.472; $P \leq .001$) showed statistically significant association with DVT recurrence. The result of the multivariate Cox regression analysis showed that, age between 30 and 50 years, age $\geq$ 50

Table 3. Distribution of Risk Factors of Deep Venous Thrombosis Among Study Participants.

S.no	Risk factors	Settings		Total [n (%)]	*P* value
		JUMC (n [%])	SPHMMC (n [%])		
1.	Pregnancy	10 (14.1)	22 (37.9)	32 (24.8)	.002
2.	Active cancer	8 (11.3)	6 (10.3)	14 (10.9)	.549
3.	Prior history of surgery	13 (18.3)	22 (37.9)	35 (27.1)	.013
4.	Obesity	3 (4.2)	2 (3.4)	5 (3.9)	.603
5.	Chronic lung disease	8 (11.3)	15 (25.9)	23 (17.8)	.027
6.	Prolonged immobilization	69 (97.2)	44 (75.9)	113 (87.6)	<.001
7.	Heart failure	6 (8.4)	14 (24.1)	20 (15.5)	.014
8.	Prior history of Trauma	9 (12.7)	6 (10.3)	15 (11.6)	.681
9.	Neurologic disease	3 (4.2)	6 (10.3)	9 (7.0)	.175
10.	History of major bleeding	19 (26.8)	13 (22.4)	32 (24.8)	.059
11.	OCP use	16 (22.5)	8 (13.8)	24 (18.6)	.204
12.	HRT	2 (2.8)	0	2 (1.6)	.198
13.	Previous VTE history	8 (11.3)	10 (17.2)	18 (14.0)	.330
14.	More significant medical conditions[a]	48 (67.6)	26 (44.8)	74 (57.4)	.561

Abbreviation: HRT, hormone replacement therapy, JUMC, Jimma University Medical Centre; OCP, Oral contraceptive pills; SPHMMC, St, Paul's Hospital Millennium Medical College; VTE, venous thromboembolism.
[a]Metabolic, endocrine, or respiratory pathologies, acute infectious disease, inflammatory conditions (arthritis).

Table 4. Distribution of Comorbidity Presenting With DVT in Study Participants.

S.no	Types of comorbidities		Settings		Total (n [%])	*P* value
			JUMC (n [%])	SPHMMC (n [%])		
1.	Presence of comorbidity	Yes	53 (74.60)	47 (81)	100 (77.5)	.387
		No	18 (25.40)	11 (19)	29 (24.5)	
2.	Types of comorbidity					
	a. Atrial fibrillation		0	2 (3.4)	2 (1.5)	.115
	b. Diabetes mellitus		1 (1.4)	6 (10.3)	7 (5.4)	.026
	c. Hypertension		5 (7.0)	7 (12.1)	12 (8.6)	.328
	d. Previous stroke		1 (1.4)	1 (1.7)	2 (1.5)	.885
	e. Heart failure		6 (8.4)	14 (24.1)	20 (15.5)	.014
	f. Chronic liver disease		3 (4.2)	4 (6.9)	7 (5.4)	.505
	g. Renal failure		5 (7.0)	14 (24.1)	19 (14.7)	.006
	h. Coronary artery disease		2 (2.8)	3 (5.2)	5 (3.9)	.491
	i. HIV/AIDS		2 (2.8)	4 (6.9)	6 (4.6)	.274
	j. Others[a]		41 (57.7)	20 (34.5)	61 (47.3)	.904
	k. Cancer		8 (11.3)	7 (12.1)	15 (11.6)	.888
	l. Type of cancer	CRC	0	1 (1.7)	1 (0.8)	.461
		Rectal	0	1 (1.7)	1 (0.8)	
		Brain	0	1 (1.7)	1 (0.8)	
		Lung	0	1 (1.7)	1 (0.8)	
		Other[b]	5 (7.0)	4 (6.9)	9 (7.0)	

Abbreviations: CRC, colorectal cancer, DVT, deep venous thrombosis; MDD, major depressive disorder.
[a]combined comorbidity (anemia, TB, epilepsy, MDD).
[b]Ovarian cancer, non-Hodgkin lymphoma.

years, alcohol consumption, prior history of surgery, pregnancy, DM comorbidity, inability to achieve target aPTT within 24 hours of heparin and proximal site involvement were statistically associated with DVT recurrence. On adjusted model, there was statistically significant hazard (more than twice) of DVT recurrence for patients with previous history of DVT (adjusted hazard ratio [AHR]: 2.48; 95% CI: 1.085-11.20; $P = .0002$).

The likelihood of DVT recurrence was about 8 times among diabetic comorbid patients (AHR: 8.048; 95% CI: 2.494-25.966; $P < .001$) when compared with nondiabetics. And also the relative risk of DVT recurrence was about 6 times among patients with prior history of surgery (AHR: 6.218; 95% CI: 1.540-25.104; $P = .010$). The relative risk of DVT recurrence was also higher among patients who didn't achieve target aPTT within 24 hours (AHR: 1.129; 95% CI: 0.120-10.600;

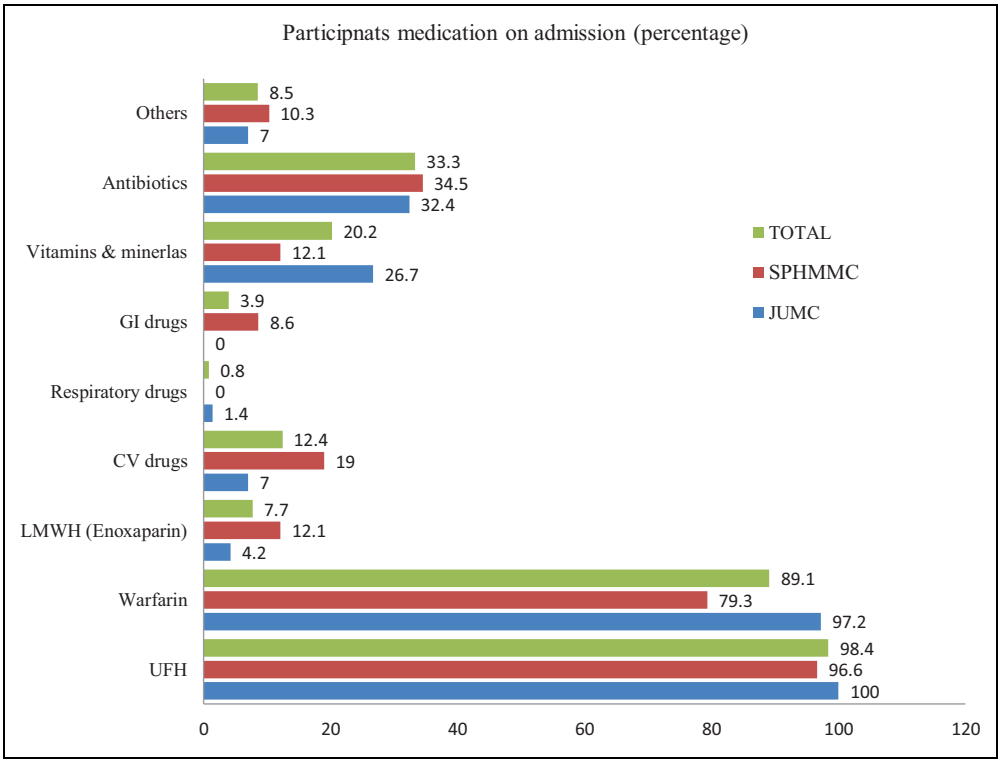

Figure 2. In-hospital medications used by study participants from March to August, 2018. CV indicates cardiovascular; GI, gastrointestinal; JUMC, Jimma University Medical Center, SPHMMMC, St Paul Hospital Millennium Medical College; LMWH, low molecular weight heparin; UFH, unfractionated heparin.

Table 5. Distribution of DVT Outcome Measures Among Study Participants.

Variables		Setting			*P* value
		JUMC (n [%])	SPHMMC (n [%])	Total (n [%])	
DVT admission status	First episode	60 (84.5)	38 (65.5)	98 (76.0)	.035
	Second times	9 (12.7)	18 (31.0)	27 (20.9)	
	> 2 times	2 (2.8)	2 (3.6)	4 (3.1)	
90 days follow-up DVT status	Recurrence	12 (16.9)	22 (37.9)	34 (26.4)	.007
	No recurrence	59 (83.1)	36 (62.1)	95 (73.6)	
Recurrence diagnosis	DVT + PE	0	6 (27.3)	6 (17.6)	.046
	DVT only	12 (100.0)	16 (72.7)	28 (82.4)	
90 days of DVT status	Worsened	12 (16.9)	22 (37.9)	34 (26.3)	.147
	No change	19 (26.8)	11 (19.0)	30 (23.3)	
	Improved	36 (50.7)	23 (39.7)	59 (45.7)	
	Complete resolution	4 (5.6)	2 (3.4)	6 (4.7)	
All-cause mortality	Yes	0	4 (6.9)	4 (3.1)	.025
	No	71 (100)	54 (93.1)	125 (96.9)	
Platelet less than 150 000 cells/mm^3	Yes	3 (4.2)	8 (13.8)	11 (8.5)	.053
	No	68 (95.8)	50 (86.2)	118 (91.5)	
Drop in platelet count >50% from baseline	Yes	4 (5.6)	7 (12.1)	11 (8.5)	.193
	No	67 (94.4)	51 (87.9)	118 (91.5)	
Time to DVT recurrence in days (mean ± SD)		41.42 ± 18.595	42.03 ± 22.37	42.03 ± 22.371	.908
INR (2-3) achievement in days (mean ± SD)		10.73 ± 17.232	15.70 ± 21.086	13.22 ± 19.286	.270
aPTT ≥ 2 to 2.5 above baseline in days (mean ± SD)		7.50 ± 6.364	7.74 ± 8.812	7.71 ± 8.480	.971

Abbreviations: aPTT, activated partial thromboplastin time; DVT, deep venous thrombosis; INR, international normalization ratio; JUMC, Jimma University Medical Centre; PE, pulmonary embolism; SPHMMC, St, Paul's Hospital Millennium Medical College.

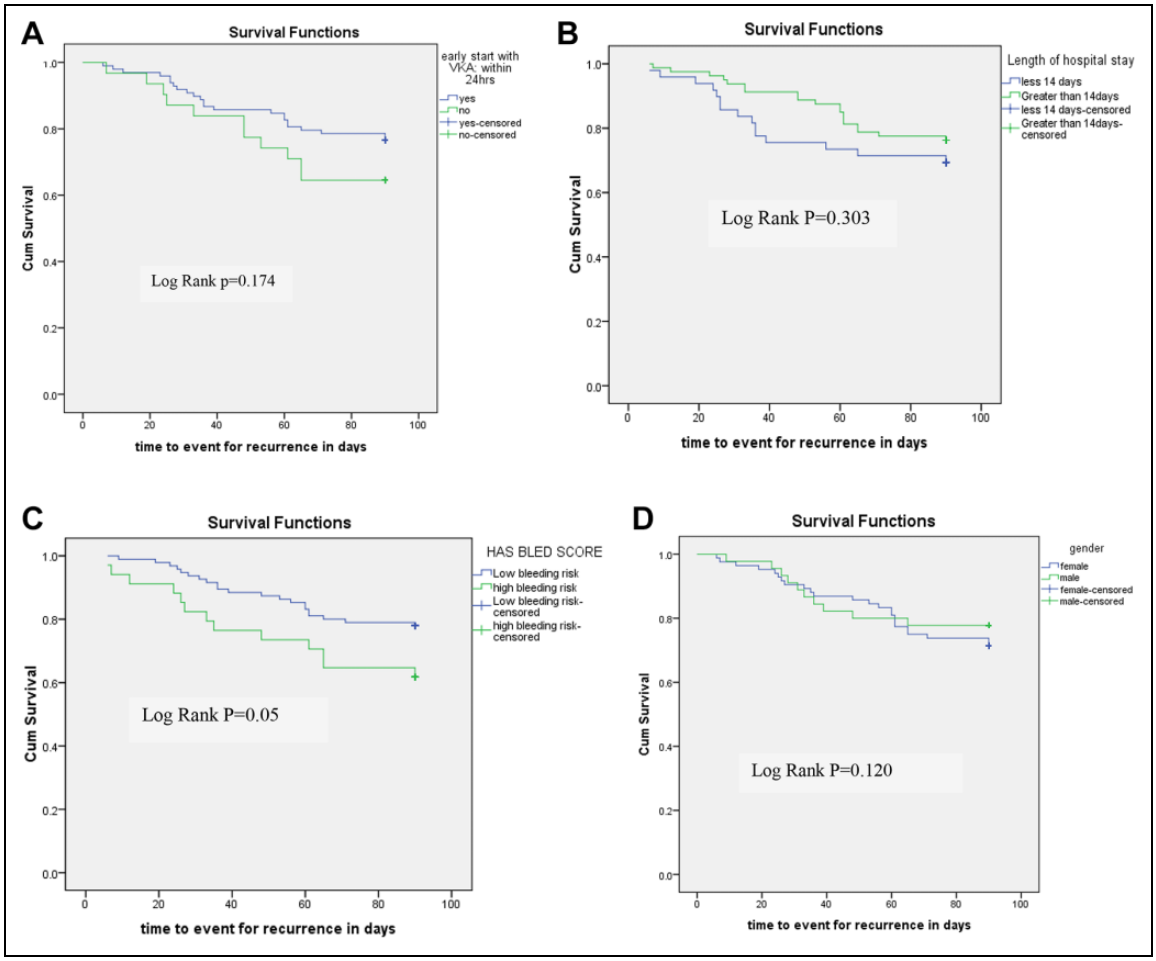

Figure 3. Survival function estimates of cumulative incidence of DVT recurrence event derived from Log rank Kaplan Meier; early warfarin therapy (A), length of hospital stay (B), HAS BLED score (C), and gender of patients (D).

$P = .011$) of in-hospital heparin administration. The relative risk of DVT recurrence was also seen among alcoholics. For example, regular consuming of alcohol (AHR: 1.947, 95% CI: 0.448-8.468; $P = .074$) and occasional users (AHR: 2.011; 95% CI: 0.701-5.768; $P = .019$) doubled the risk of DVT recurrence. The relative risk of DVT recurrence among pregnant women was about 2 times (AHR: 2.0911; 95% CI: 1.046-4.179; $P = .037$). The likelihood of DVT recurrence was also associated with the age of the patients. For example, age $\geq$50 years carries a risk of DVT recurrence more than 5 times for patients (AHR: 5.566; 95% CI: 1.587-19.518; $P = .007$). Proximal site involvement (AHR: 5.937; 95% CI: 1.300-27.110; $P = .022$) showed higher hazards of DVT recurrence (Tables 6 and 7).

Discussions

The risk of recurrence following an episode of VTE is highest during the first 3 months and declines rapidly to about 5% per year. We conducted this current study at 2 tertiary teaching hospitals setting using a prospective open cohort study design to determine the burden of DVT recurrence and associated factors. Hospitalized confirmed DVT patients were carefully assessed for valuable information, and the study participants were strictly followed for about 3 months for the outcome.

During the study period, about 713 medical cases at JUMC and 893 at SPHMMC were admitted; with a total of 1606 patients. It was found that the incidence of DVT was 9.96% and 6.5% at JUMC and SPHMMC, respectively, with the overall incidence of 8.1%. This DVT incidence burden was comparable with the study done in Thailand,[19] which was 10.5%, and in Uganda,[20] which was 9.1%. The recurrence rate of DVT was 16.9% and 32.3% from JUMC and SPHMMC, respectively, with an overall recurrence rate of 26.4%. The result was comparable with the study done in the United States,[21] which showed a DVT recurrence rate of 22%. But, the study done in France[22] showed a lower recurrence rate (5.5%). This variation may be related to a larger sample size (n = 1804) and the retrospective study design in the settings.

In our study, the highest DVT incidents were found in the age greater than 35 years. A similar result was found in Addis Ababa.[15,23,24] The highest incidence of DVT was varied from different studies. In most of the studies, DVT occurrence was high at a mean $\pm$ SD age of 63 $\pm$ 19.4 and 66 $\pm$ 17.[21,25] And

Table 6. Socio-Demographic and Behavioral Factors Associated With DVT Recurrence Among Study Participants.

Variables		Recurrent event					
		Yes (n [%])	No (n [%])	CHR (95% CI)	*P* value	AHR (95% CI)	*P* value
Gender	Male	10 (7.8)	35 (27.1)	1		1	
	Female	24 (18.6)	60 (46.5)	1.799 (0.828-3.905)	.038	1.116 (0.516-2.411)	.138
Age (years)	18-35	22 (17.1)	54 (41.8)	1		1	
	35-50	7 (5.4)	10 (7.8)	2.287 (0866-6.041)	.095	3.545 (1.216-10.338)	.056
	≥50	5 (3.9)	31 (24)	3.438 (1.091-10.838)	.035	5.566 (1.587-19.518)	.007
Marital status	Single	7 (5.4)	19 (14.7)	1			
	Married	27 (20.9)	69 (53.5)	0.591 (0.249-1.439)	.903		
	Divorced	0	4 (3.2)	0.947 (0.118-11.468)	.999		
	Widowed	0	3 (2.3)	0.471 (0.713-6.408)	.731		
Educational status	Cannot read and write	9 (7)	43 (33.3)	1.776 (0.658-4.790)	.257		
	Primary school	10 (7.8)	31 (24)	1.477 (0.559-3.905)	.431		
	Secondary school	11 (8.4)	16 (12.4)	1.842 (0.536-6.330)	.332		
	College and above	4 (3.2)	5 (3.9)	1			
Residence location	Rural	13 (10.7)	61 (47.3)	1			
	Urban	21 (16.3)	34 (26.4)	0.759 (0.373-1.547)	.448		
Occupational status	Office worker	7 (5.4)	8 (6.2)	1		1	
	Farmer	6 (4.7)	31 (24)	1.516 (0.486-4.735)	.474	1.376 (0.354-5.348)	.645
	Merchant	8 (6.2)	14 (10.8)	1.858 (0.659-5.240)	.241	3.249 (0.900-11.730)	.072
	Student	2 (1.6)	8 (6.2)	2.654 (0.508-13.858)	.247	1.651 (0.214-12.715)	.630
	Daily laborer	4 (3.2)	6 (4.6)	0.492 (0.137-1.767)	.277	0.236 (0.054-1.044)	.057
	Others[a]	7 (5.4)	28 (21.7)	0.660 (0.244-1.944)	.451	0.500 (0.155-1.619)	.245
Living condition	With immediate family	30 (23.3)	81 (62.8)	1			
	With extended family	2 (1.6)	5 (3.9)	1.594 (0.368-6.916)	.533		
	Living alone	1 (0.8)	4 (3.2)	1.922 (0.250-14.769)	.530		
	Others	1 (0.8)	5 (3.9)	1.361 (0.180-10.310)	.766		
Alcohol consumption	Never	22 (17.1)	65 (50.4)	1		1	
	Occasionally	7 (5.4)	19 (14.7)	2.460 (0.694-8.723)	.031	2.011 (0.701-5.768)	.019
	Regularly	3 (2.3)	11 (8.4)	1.110 (0.494-2.656)	.054	1.947 (0.448-8.468)	.074
	Ex-alcohol consumer	2 (1.6)	0	0.723 (0.168-3.121)	.664	0.098 (0.11-0.870)	.037
Smoking behavior	Current smoker	1 (0.8)	6 (4.6)	1.392 (0.185-10.485)	.748		
	Nonsmoker	33 (25.6)	89 (69)	1			
Khat chewing behavior	Yes	3 (2.3)	8 (6.2)	1.517 (0.445, 5.164)	.505		
Herbal medicine use	No	31 (24)	87 (67.4)	1			
Herbal medicine use	Yes	2 (1.6)	8 (6.2)	1.877 (0.436-8.034)	.398		
	No	32 (24.8)	87 (67.4)	1			

Abbreviations: AHR, adjusted hazard ratio; CHR, crude hazard ratio; DVT, deep venous thrombosis.
[a]House wife.

also on the Cox regression analysis, older age increased the risk of DVT recurrence. Patients aged between 35 and 50 years old had greater than 3 times relative risk of DVT recurrence and older than 50 years had significantly higher hazards (more than 5 times) of DVT recurrence. This report is incomparable with 2 studies from Spain,[21,26] which showed increased risk per additional decade. In addition to increased exposure to DVT risk factors, older age linked with a sedentary lifestyle, restricted movement, and biology of aging on vascular patency.

About two-thirds of participants had left lower extremity involvement. On multivariate Cox regression analysis, a proximal extension of DVT had strong risk predictors of DVT recurrence. This is strongly supported by different studies.[25,27-29] This is maybe explained by the anatomy of DVT of the lower extremity, showing highly involved site for DVT cases. And also multiple studies showed as if a resolution of proximal DVT is slow and less than half have complete lysis after 6 months of anticoagulation.

In our study, we found that previous history of thromboembolism to be independent risk factors for the DVT recurrence. The risk of DVT recurrence doubled among patient with previous history of DVT. This study was similar to a report from Iran,[28] United States,[30] Canada,[31] and Sweden.[32] May be this is related to the presence of a residual thrombus which is associated with an increased risk of thrombotic recurrence. In our setting, there is a poor monitoring for anticoagulation adequacy during the course of treatment. Therefore, residual vein thrombosis (RVT) assessment, which is not available in our setting, is useful for evaluating the features of a DVT of the affected limb. In fact, RVT assessment not only identifies a subset of patients at lower risk of recurrence but also allows us to gauge the individual risk of recurrence after a first DVT episode.

Table 7. Clinical and Laboratory Data Related Factors Associated With DVT Recurrence Among Study Participants.

Variables		Recurrent event		CHR (95% CI)	*P* value	AHR (95% CI)	*P* value
		Yes (n [%])	No (n [%])				
Pregnancy	Yes	13 (10.7)	19 (14.7)	1.091 (1.46-11.179)	.057	2.091 (1.046-4.179)	.037
	No	21 (16.3)	76 (58.9)	1		1	
Prior history of surgery	Yes	11 (8.5)	24 (18.6)	1.242 (0.275-1.185)	.132	6.218 (1.540-25.104)	.010
	No	23 (18.3)	71 (55)	1		1	
Chronic lung disease	Yes	5 (3.9)	18 (13.9)	2.000 (0.758-5.278)	.162	0.922 (0.341-2.495)	.874
	No	29 (22.5)	77 (59.7)				
Prolonged immobilization	yes	27 (20.9)	86 (66.7)	1.834 (0.771-4.360)	.170	2.392 (0.818-7.00)	.111
	No	7 (5.4)	9 (7)	1		1	
Heart failure	Yes	5 (3.9)	15 (11.6)	2.162 (0.808-5.786)	.125	0.440 (0.081-2.379)	.340
	No	29 (22.5)	80 (62)	1		1	
Prior history of Trauma	Yes	3 (2.3)	12 (9.3)	1.109 (0.328-3.746)	.868		
	No	31 (24)	83 (64.3)	1			
Neurologic disease	Yes	3 (2.3)	6 (4.6)	0.432 (0.127-1.465)	.178	2.504 (0.515-48.504)	.255
	No	31 (24)	89 (69)	1		1	
History of major bleeding	Yes	13 (10.7)	19 (14.7)	1.884 (0.440-1.776)	.729		
	No	21 (16.3)	76 (58.9)	1		1	
OCP use	Yes	8 (6.2)	16 (12.4)	1.965 (0.874-4.416)	.102	0.493 (0.177-1.375)	.176
	No	26 (20.2)	79 (61.2)	1			
HRT[a]	Yes	1 (0.8)	1 (0.8)	3.152 (0.399-24.899)	.276		
	No	33 (25.6)	94 (72.9)	1			
Previous DVT history	Yes	18 (13.9)	0	2.130 (1.201-11.472)	<.001	2.48 (1.085-11.20)	.0002
	No	16 (12.4)	95 (73.6)	1		1	
Other comorbidity[b]	Yes	16 (12.4)	58 (45)	1.054 (0.534-2.079)	.880		
	No	18 (13.9)	37 (28.7)	1			
Antithrombotic drug prior to admission	Yes	14 (11.1)	11 (8.5)	1.374 (0.684-2.758)	.372		
	No	20 (15.5)	84 (65.1)	1			
Diabetes mellitus	Yes	4 (3.1)	3 (2.3)	3.869 (1.295-11.558)	.015	8.048 (2.494-25.966)	<.001
	No	30 (23.3)	92 (71.3)	1		1	
Hypertension	Yes	3 (2.3)	9 (7)	0.077 (0.017-0.358)	.001	0.518 (0.046-5.782)	.593
	No	31 (24)	86 (66.7)	1		1	
Chronic liver disease	Yes	2 (1.6)	5 (3.9)	3.236 (0.733-14.294)	.121	3.33 (0.371-29.930)	.283
	No	32 (24.8)	90 (69.8)	1		1	
Lower extremity DVT	Proximal DVT	31 (25)	73 (58.9)	2.258 (0.670-7.614)	.189	5.937 (1.300-27.110)	.022
	Distal DVT	3 (2.4)	18 (14.5)	1		1	
Patient received UFH	Yes	32 (24.8)	95 (73.6)	1		1	
	No	2 (1.6)	0	2.207 (0.720-14.281)	.106	0.521 (0.096-2.833)	.451
Don't received warfarin within 24 hours of heparin	Yes	28 (21.7)	87 (64.4)	2.797 (1.087-7.213)	.051	1.453 (0.187-1.100)	.080
	No	6 (4.6)	8 (6.2)				
Risk factors for DVT	Single risk factor	2 (1.6)	15 (11.6)	1	.312	1	
	Two risk factors	8 (6.2)	38 (29.5)	2.188 (0.488. 10.680)	.130	1.658 (0.322-8.543)	.546
	Multiple risk factors	24 (18.6)	42 (32.6)	1.169 (0.272-5.020)	.312	1.026 (0.230-4.582)	.973
Parenteral anticoagulant for ≥5 days	Yes	29 (22.5)	86 (66.6)	1			
	No	5 (3.9)	9 (7)	0.895 (0.334-2.398)	.824		
INR ≥2.0 for ≥24 hours before	Yes	2 (1.6)	16 (12.4)	1			
	No	32 (24.8)	79 (61.2)	0.852 (0.201-3.618)	.832		
Early start of VKA (within 24 hours)	Yes	23 (17.8)	75 (58.2)	1			
	No	11 (8.5)	20 (15.5)	1.167 (0.558-2.441)	.682		
Initial with SC heparin	Yes	32 (24.8)	95 (73.6)	1		1	
	No	2 (1.6)	0	3.207 (0.720-14.281)	.184	1.918 (0.353-10.424)	.451
Reach aPTT target within 24 hours	Yes	2 (1.6)	7 (5.4)	1		1	
	No	32 (24.8)	88 (68.2)	1.108 (0.020-0.600)	.032	1.129 (0.120-10.600)	.011

Abbreviations: AHR, adjusted hazard ratio; aPTT, activated partial thromboplastin time; CHR, crude hazard ratio; DVT, deep venous thrombosis; HRT, hormonal replacement therapy; INR, international normalization ratio; OCP, oral contraceptive pills; VKA, vitamin K dependent anticoagulant; SC, subcutaneous; UFH, unfractionated heparin.

[a]Denominator female gender.

[b]Active infection, metabolic, endocrine or respiratory pathologies, inflammatory conditions, and varicose veins with phlebitis.

Among the study participants, pregnancy accounted for 32 (47.8%) of associated risk factors with DVT from a female of childbearing age. Pregnancy was significantly associated with the development of DVT recurrence, which is similar to reports from Arizona hospital,[21,33] where pregnancy is a common risk of DVT occurrence and rate of DVT recurrence. This is related to venous stasis (due to pregnancy-associated changes in venous capacitance and compression of large veins by the gravid uterus), endothelial injury (due to changes at the uteroplacental surface and vascular injury during delivery), and a hypercoagulable state (pregnancy is associated with progressive increases in several coagulation factors, a decrease in protein S, and a progressive increase in resistance to activated protein C).[34]

Regarding gender, our study finding showed that being female was statistically associated with DVT recurrence (CHR, 1.799; 95% CI: 0.828-3.905; $P = .038$). This finding was in line with the study from Minnesota.[21] But, other prospective studies failed to support this observation,[26,35] and male sex increased the risk of DVT recurrence. This difference might be related to long-term follow-up (up to 2 years) observational cohort with a large sample, and also a few numbers of male participants were included in our study. Besides, in this current study, more female within childbearing age was included, as females at a productive age are more susceptible, due to the hormonal influences.

In this study, we found that prior history of surgery as an independent predictor of increased risk of DVT recurrence. This finding was in line with the data from Minnesota.[26,35] This probably due to poor thromboprophylaxis practice in our set up and also endothelial damage exposes blood to collagen and tissue factor, which will then activate the coagulation cascade leading to DVT and as well general anesthesia has been documented to induce hypoxic endothelial activation and a prothrombotic state through reduction of blood flow to the lower limbs.[36]

Diabetes mellitus comorbidity was an independent predictor of DVT recurrence. Hazards on developing recurrent DVT was 8 times more among patients living with DM (AHR, 8.048; 95% CI: 2.494-25.966; $P < .001$). This finding was supported by a study from Canada[37] and also similar data from the previous study found that DM was associated with a 3-fold increase in the likelihood of developing DVT recurrence.[1] Theoretically, hyperglycemia contributes to elevated coagulation factors, impaired fibrinolysis, and increased likelihood of thrombosis. And also high plasma glucose level increase oxidative stress, which in turn increases gene transcription of coagulation factors; degrade the glycocalyx layer of the endothelial wall, which releases coagulation factors and stimulates the coagulation cascade; and increase glycation of proteins involved in coagulation and fibrinolysis, shifting their activity toward a procoagulant state.[38] Besides due to vascular complications from diabetes, decreased peripheral circulation will result in distal ischemia, which affects DVT occurrence and recurrence.

Another remarkable finding in this present study was the inability to achieve target aPTT within 24 hours of parenteral anticoagulant medications was 93%. In this study, it was an independent predictor for the development of recurrent DVT. Failure to rapidly achieve a target APTT appears to reflect heparin dosing, which will affect the inpatient anticoagulation adequacy.

Furthermore, we found that the unspecified amount of regular alcohol consumption was linked with increases in the development of DVT recurrence. Similar results were found from San Diego, California, United States,[39] where high maximum alcohol use is the behavior most linked to increasing the risk of DVT recurrence. This may be related to oxidative stress and mitochondrial toxicity from alcohol, which will cause tissue injury and cell death. This lead to triggers coagulation activation, via exposure at the cell surface of phosphatidylserine.[40]

Strengths and Limitations of the Study

The present study was the first original research reporting the recurrence of DVT in Ethiopia. The study also uses a more robust study design, prospective cohort study, which will control some of the confounders. However, the study has several limitations; small sample size due to short enrollment period, only 2 studies set in the country so cannot represent all of the countries. It will be better to research with long-term follow-up and large sample sizes across the country.

Conclusions

In general, the DVT recurrence rate was higher than most previously reported results. The recurrent DVT also complicated with PE as well as death during the follow-up period. The overall incidence recurrence rate was 2.99 in 1000 patient-days. Complete resolution of DVT was seen for a small number of patients within the currently recommended duration of anticoagulation, indicating poor inpatient treatment adequacy. Older age, prior history of surgery, pregnancy, DM, comorbidity, inability to achieve target aPTT within 24 hours of heparin initiation, proximal site involvement, previous history of DVT, and unquantified alcohol consumption were independent predictors of DVT recurrence. It is a high time that patient with these risk factors should be evaluated and followed to prevent the occurrence of DVT recurrence.

Authors' Note

The analysis was conceptualized by AM & TM. Data collection was managed by AM and data analysis was conducted by AM, TM, and LC. TM drafted the manuscript. All authors (AM, TM, and LC) participated in editing, feedback, and revisions. The data sets generated during and/or analyzed during the current study are available from the corresponding authors on reasonable request. Ethical clearance approval was obtained from the institution review board (IRB) of Jimma University. Before the start of the survey, informed consent was requested and received from the patient.

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Declaration of Conflicting Interests

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