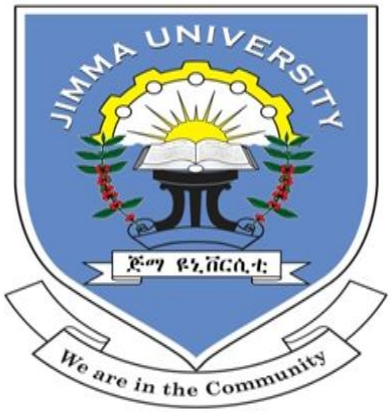
TREATMENT OUTCOME OF DEEP VEINOUS THROMBOSIS AND ITS PREDICTORS AMONG HOSPITALIZED PATIENTS AT SELECTED TERTIARY HOSPITALS IN ETHIOPIA: A PROSPECTIVE COHORT STUDY



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A RESEARCH PAPER SUBMITTED TO SCHOOL OF PHARMACY, INSTITUTE OF HEALTH, JIMMA UNIVERSITY, IN PARTIAL FULFILMENT FOR THE REQUIREMENTS FOR THE DEGREE OF MASTERS OF SCIENCE (MSC) IN CLINICAL PHARMACY

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Abstract

Background: *Deep Venous Thrombosis (DVT) is a common clinical problem that is associated with substantial morbidity and mortality. Knowledge on the global burden of DVT recurrence is deficient in Africa, including Ethiopia. Accurate data are needed to evaluate the burden of VTE in Africa to design effective preventive and treatment strategies.*

Objective: *To assess treatment outcome of deep venous thrombosis and its predictors among hospitalized patients at selected tertiary care setting in Ethiopia*

Methods: *A prospective cohort study was conducted among hospitalized DVT patients at Jimma University Medical Center and St. Paul's Hospital Millennium Medical College. Patient specific data was collected using structured data collection tool prepared from literatures. Data was entered using EpiData version 4.2 and analyzed using statistical software package, SPSS version 21.0. To identify independent predictors of DVT recurrence, multiple stepwise backward cox regression analysis was done. Data was presented in the form of charts, tables and graphs accordingly. Statistical significance was considered at p-value <0.05. Patient's written informed consent was obtained after explaining the purpose of the study. Patients were informed about confidentiality of the information obtained.*

Results: *A total of 129 participants included into study; of which 65.1% were females. The mean± SD age of patients was 38.63 ±17.67 years. About 34(26.4%) of patients developed recurrent VTE within 3 months of study. Type of recurrent event was DVT in 28 patients (82.40%) and the rest admitted with pulmonary embolism. The overall incidence density was 2.99 per 1000 person-days. The mean ± SD survival time to DVT recurrence was 42.03±22.371 days. Completes resolution was seen for about 4.7% of patients. Age between 30 to 50 years [AHR, 3.545; 95 % CI, 1.216, 10.338; p=0.020], age ≥ 50 years [AHR, 5.566; 95 % CI, 1.587, 19.518;p=0.007], alcohol use(AHR, 1.71; 95 % CI, 1.096, 2.662; p=0.018)], prior history of surgery [AHR, 6.218; 95% CI, 1.540, 25.104; p=0.010], pregnancy [AHR, 2.0911; 95% CI, 1.046, 4.179; p=0.037], diabetes mellitus comorbidity [AHR, 8.048; 95% CI, 2.494, 25.966; P<0.001], not achieve target aPTT within 24hrs of heparin initiation [AHR, 1.129; 95% CI, 1.020, 10.600; p=0.011], proximal site involvement [AHR, 5.937; 95% CI, 1.300, 27.110; p=0.022] were independent predictors of DVT recurrence.*

Conclusion and Recommendations: *In general, DVT recurrence rate was higher in the current study, which is even complicated with pulmonary embolism as well as death during the follow up period. Thus, efforts are needed to prevent DVT and reduce the development of recurrences.*

Key Words: *Deep Vein Thrombosis, Recurrence, Risk Factors, Jimma University Medical Center*

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Abbreviations and Acronyms

APTT	Activated Partial Prothrombin Time
ACCPs	American College of Chest Physicians
CBC	Complete Blood Count
CD4	T–lymphocyte cell bearing CD4 receptor
CI	Confidence Interval
COC	Combine Oral Contraceptive
DVT	Deep Vein Thrombosis
FMHACA	Food, Medicines and Health care Administration and Control Authority
HGB	Hemoglobin
HIV	Human Immunodeficiency Virus
JUMC	Jimma University Medical Center
LWMH	Low Weight Molecular Heparin
UFH	Unfractionated Heparin
PE	Pulmonary Embolism
VTE	Venous Thromboembolism
WHO	World Health Organization
INR	International Normalization Ratio
PT	Prothrombin Time
SPSS	Statistical Package for Social Sciences
SPHMMC	St. Paul's Millennium Medical College
PTS	Post-thrombotic Syndrome
VKA	Vitamin K- Antagonist
COC	Combined Oral Contraceptive
TASH	Tikur Anbessa Specialized Hospital
LOS	Length of Hospital Stay
G.C	Gregorian calendar
EPA	Ethiopian Pharmaceutical Association

1. Introduction

1.1. Background

The term thrombosis refers to the formation, from constituents of blood, of an abnormal mass within the vascular system. When this process occurs within the deep veins, it is referred to as deep vein thrombosis (DVT). It is considered as the third most common cardiovascular condition after myocardial infarction and stroke and it is a growing public health problem due to increase the ageing population (1). DVT is 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 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. An asymptomatic pulmonary embolism can be found in about half of patients presenting with symptomatic proximal DVT (2).

In Western countries population studies have reported incidence rates of VTE between 80–180 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(3). As out of hospital diagnosis and therapy is becoming more frequent, study populations need to include outpatients to assess the burden of VTE. The outlook after an episode of symptomatic VTE can be blighted by long-term sequelae including recurrence of VTE. VTE may be associated with risk factors and is classified as provoked (within three months following a recognized event), cancer-related and unprovoked (idiopathic) (4).

The most important side effects of anticoagulation medicines used for DVT could be death, disease recurrence, post-thrombotic syndrome, and severe bleedings (5). A mortality rate of 6% has been reported in the first six months after the disease onset. Recent studies found a high incidence of recurrent DVT with half of DVT incidences in the U.S being recurrent. A relapse after a five year disease free interval is observed in 20-30% of patients. While some studies reported the annual incidence rate of the first recurrent attack to be 3-5%, which is generally most probable to happen during the first two years after the discontinuation of anticoagulation

treatment, others claimed a higher rate of 5-10%. The incidence of disease recurrence, as a condition with a multifactorial pathogenesis, is related with the number and severity of the risk factors (6).

DVT risk factors include age over 40, obesity, immobilization especially after long journeys, history of hyper coagulation, genetic factors leading to thrombophilia, certain blood diseases, cancer, heart failure, bone fractures, smoking and recent surgeries. In women, however, oral contraceptive pills (OCPs) and hormone replacement therapy (HRT) are also among the main risk factors. In addition, idiopathic form of the disease is not uncommon (7).

DVT has been evident that these diseases develop in relation to invasive orthopedic surgeries of the lower extremities, such as total knee arthroplasty (TKA), total hip arthroplasty (THA), and hip fracture surgery (HFS) (8). Pregnant women have a much higher risk of DVT than non-pregnant women of similar age and the risk has been shown to be higher after caesarean section than after vaginal delivery. In a study conducted in an African population, the incidence appears to be highest in the postpartum period (9).

Various medical diseases confer a high risk of DVT, including malignant neoplasms with and without chemotherapy; prior superficial vein thrombosis; and neurological diseases with extremity paresis and the risk of DVT in women using combined oral contraceptives (COCs) is attributed to changes in homeostasis (10). HIV infection has been recognized as a hypercoagulable condition since the late 1980s and the current and other studies indicate that the prevalence in HIV positive patients is significantly increased with a two to tenfold increased risk in HIV infected patients compared to the general population (11).

Liver cirrhosis is accompanied by multiple changes in the hemostatic system due to the reduced levels of natural inhibitors of coagulation and coagulation factors because of the impaired hepatic synthetic activity. Thus, the global effect of liver disease on hemostasis is complex and therefore, patients with liver cirrhosis can experience bleeding or thrombotic complications (12).

The aim of treatment of VTE is to reduce morbidity and mortality. This is achieved by optimal therapy with anticoagulants to prevent thrombus extension and embolization. The major outcomes of venous thrombosis are death, recurrence, post-thrombotic syndrome and major bleeding due to anticoagulation therapy (13).

The mainstay of treatment involves bridging anticoagulation therapy from a parenteral heparin-type anticoagulant with 333 U/kg subcutaneously as a loading dose followed by 250 U/kg subcutaneously twice daily of UFH to a vitamin K antagonist such as warfarin (14), Low molecular weight heparin (LMWH) is the preferred parenteral anticoagulant during the initial treatment (1).

Furthermore, patients with an initial episode of symptomatic DVT are at high risk for recurrent DVT. Recurrence rates are higher if there is residual thrombus in the vessel (15). Recurrence, particularly of ipsilateral DVT, is a strong risk factor for post-thrombotic syndrome (PTS) (16).Weight adjusted fixed dose subcutaneous unfractionated heparin (UFH) is one of the options for the treatment of deep vein thrombosis (DVT), but the degree of its anticoagulant effect has not been assessing in our health care setting.

1.2. Statement of the Problem

DVT is the third most common cardiovascular disease after acute coronary syndromes and stroke, affecting 2 million individuals in the United States each year. DVT is mentioned as a major health problem and one of the most common preventable causes of hospital deaths in the western world where the incidence is one case of DVT per 1000 population per year (17, 18).

DVT is a major and a common preventable cause of death worldwide; it affects approximately 0.1% of persons per year. The overall average age and sex adjusted annual incidence of DVT, 48 per 100,000 subjects; with higher age-adjusted rates among males than females (130 vs. 110 per 100,000, respectively). Both sexes are equally afflicted by a first DVT, men having a higher risk of recurrent thrombosis. DVT is predominantly a disease of the elderly with an incidence that rises markedly with age (19). Data from U. S shows that DVT and PE are a major disease burden; affecting an estimated population of approximately one million each year's and result in several hundred thousand hospitalization that can be contributing to 33% of death. 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 (20).

The disease burden of DVT reported annual incidences ranging from 0.75 to 2.69 per 1,000 subjects, which increased to between 2.0 and 7.0 per 1,000 among subjects 70 years of age and DVT is a main cause of health care expenditure and hospitalization accounts for the majority of the health care costs. In the United States, the rate of hospitalization for DVT per 100,000 subject's age 60 years increased from 581 in 2001 to 739 in 2010 with an average length of stay in 2011 of 4.7 days for patients with deep venous thrombosis (4, 21, 22).

Recurrent DVTs after the acute period are surprisingly frequent, their cumulative incidence being 30% during an 8-year follow up (23).

The risk of DVT is highest among those whose initial episode was associated with cancer, and lowest among those whose initial episode was associated with a temporary risk factor such as surgery, older age and obesity were associated with higher recurrence risks. Recent report found that 60% of higher recurrence risk among men compared to women. 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 6–12 months following cessation of anticoagulation, regardless of the initial duration of anticoagulation (24).

The overall incidence rate for recurrent VTE was 4.9 per 100 person-years with a peak at 11.1 per 100 person-years in the first six months, falling to 8.1 between 6–12 months (25). The cumulative incidence rate of DVT recurrences at six months was 5% and 15% at 12 months (26).

The burden, risk factors and treatment outcomes of DVT in African region has not been well studied. While DVT incidence is increasing in the general population worldwide, there is very little evidence describing the incidence and determinants of DVT among hospitalized adult patients in this region. And there is no sufficient study done in our country too.

In Ethiopia, study done in 1998 G.C showed that DVT is a common medical and surgical problem associated with severe complications and mortality (27). And also, a recent report from Addis Ababa showed DVT was associated with malignancy, prolonged immobilization, pregnancy related problems and major trauma (28). The present study was conducted to assess the disease burden, short term treatment outcomes among hospitalised DVT patients of selected tertiary care setting. Significance of predisposing risk factors and ninety day treatment outcomes was studied.

1.3. Significant of the Study

Patients having different medical conditions are increasing the risk of development of deep venous thrombosis recurrence. Various studies conducted in worldwide showed that up to 70% of symptomatic DVT recurrence occur as a result of the presence of additional medical condition or unable to appropriately manage the disease. In the absence of thromboprophylaxis DVT is linked to an estimated 50% risk of DVT complication.

Disease patterns and life styles in Western countries are very not likely to be identical to those of our country particularly and African countries as well. Little evidence was reported on the prevalence of deep venous thrombosis but has not been investigating the burden of treatment outcomes and the likely hood of risk factors for disease recurrence in Ethiopia. Knowing the prevalence of DVT occurrence and its recurrence rate in both hospitals will not only highlight the magnitude of the problem but will be a basis to estimate the potential impact of thromboprophylaxis in patients at high risk and facilitate a future assessment of their long term burden and impact. In turn, this should enable valuable suggestions that may initiate interventions and appropriate community-based health promotion strategies to encourage healthy lifestyles among this groups and as well for whole population. It also provides base line information that may be helpful for further investigation on the topic, educational initiatives and helpful in the development of treatment guideline in the area of deep venous thrombosis.

2. Literatures Review

An understanding of the risk factors for DVT is necessary in order to maximize the prevention of this disease in high risk individuals and groups of patients, include endogenous patient characteristics such as obesity and genetic factors and triggering factors such as surgery, immobility or pregnancy. Some of the risk factors are modifiable, while others, like advancing age and genetic predispositions, are not (29).

Factor Affecting Treatment Outcomes

Approximately 30% to 50% of DVT are not completely resolved 6 to 12 months after diagnosis. Currently it is not possible to predict which patients will undergo complete resolution after an acute DVT or which patients will develop PTS (30, 31).

A one year period prospective cohort study done at American healthcare facility of North-western University showed that the rate of complete DVT resolution was 68%. The median INR values in patients with complete DVT resolution were significantly higher than those of patients with incomplete DVT resolution after 1, 3 and 6 months of treatment with warfarin (31).

A multicenter prospective cohort study identified that the cumulative incidence of recurrent VTE was 11.0% after 1 year, 19.6% after 3 years, 29.1% after 5 years, and 39.9% after 10 years. In this study unprovoked deep venous thrombosis, first episode DVT, shorter treatment period were found to be predictors of recurrence (32).

A two year prospective cohort study conducted at tertiary care hospital in South India, it was found that the mean starting and maintenance dose of heparin were 19360 IU (SD 3345) and 14490 IU (SD 2525) respectively. All patients had simultaneously received oral anticoagulation with warfarin (5 mg) from the first day onwards. The aPTT ratio was sub therapeutic in 15 of 55 patients (27.7 %), therapeutic in 37 (67 %) patients and supra therapeutic in three patients (33).

An article review done in Italy on unselected patients who started Vitamin-K Antagonist anticoagulation for the first time for whatever indication showed that the rate of bleeding (major and minor) was significantly higher during the first 3 months of treatment than thereafter (34, 35). The result of meta-analysis, suggested that available studies found a 2% risk of major bleeding during the first 3 months of treatment in patients treated for DVT, and a 2.7% patient

per years in the subsequent period. The rate of intracranial hemorrhage, the most feared complication during anticoagulation, was 1.48%. Patients were presenting with bleeding during the initial 3 months of therapy but decreased to 0.65% after stopping the drug (36).

Patient-Related and Behavioral Factors

Several studies across worldwide reported that, general anesthesia induces a reduction in blood flow to the lower extremities which is in turn increased by surgical procedures such as cross clamping of the aorta. As a result areas of endothelium in the calf veins become hypoxic and release inflammatory mediators that attract and activate platelets and endocytes. The subsequent clot propagates, particularly in the presence of reduction in fibrinolytic activity (37).

The study done in Swedish nationwide case-control study conduct on the assessment of the risk of VTE associated with use of combined oral contraceptives (COCs) in women with a family history of VTE identified that both among controls (14.6 % vs. 4.5 %; $p < 0.0001$) and cases (27.2 % vs. 8.8 %; $p < 0.0001$) COC use was more common in women without a family history of VTE compared with women with a family history of VTE. In a multivariate conditional logistic regression model the OR for VTE was 2.53 for COC users and 2.38 for individuals with a family history of VTE. The OR for VTE for COC users with a family history of VTE was 6.02. There was no significant interaction between family history of VTE and COC use (10).

DVTs were more common on the left side, with a left-to-right ratio of 1.32:1, calculated as the number of left- versus right-sided segments containing thrombus ($P < .001$). There was a preponderance of left-sided DVT in proximal compared with distal venous segments ($P < .001$), with the left-to-right ratio decreasing from 2.50:1 in the common iliac segment to 1.26:1 in the calf veins (38).

A study conducted in USA showed that female sex, lower educational attainment, failure to specify level of maximum alcohol consumption, history of immobility and family history of first degree relatives with varicose veins were significant independent risk predictor for recurrence of DVT (39).

An on-going prospective cohort study performed at the Department of Medicine in general Hospital Vienna, Austria for nearly consecutive sixteen years, the result was found that the risk of DVT recurrence in both sex among study participants were female proximal and male

proximal DVT with adjusted HR of 2.3(95CI: 1.1- 4.8) & 4.7(95%CI: 2.3-9.6)) increase the development of DVT recurrence, respectively (40).

Regarding pregnancy associated risk for the development of deep vein thrombosis, Previous studies reported that incidence rates ranging from 18 to 95 events per 100,000 woman per years during pregnancy and from 199 to greater than 1900 per 100 000 woman per years during the postpartum period (41).

A prospective cohort study to determine the prevalence of and risk factors for lower extremity deep vein thrombosis (DVT) among critically ill surgical patients in Thailand, the result was identified that among the 190 first-time admitted ICU patients with a mean APACHE II score of 9.2 ± 6.0 (range, 0–29), 20 patients had DVT (prevalence of 10.5%). Thromboprophylaxis was not given to any patient. The only independent and significant risk factor for DVT was a longer ICU stay. Age, sex, APACHE II score, presence of comorbidities and operative intervention were not associated with the presence of DVT (42).

A five-year prospective study done at Addis Ababa in a university teaching hospital, identify that 95% of the patients presented with lower and 5% with upper limb DVT with disease prevalence of 12%. So that DVT is common and it also may be associated with severe complications and mortality associated the disease (27).

The research conducted at Addis Ababa Tikur Anbessa Specialized Hospital found that malignancy was the most common identified risk factor (30.9% of the cases)followed by prolonged immobilization (19.8%), pregnancy related problems (6.2%) and severe trauma (6.2%) of the patients (28).

Disease-Related Factors

A study done in the population based Worcester on Venous Thromboembolism enrolled 2488 consecutive patients with diabetes were more likely than patients without diabetes to significantly suffer recurrent DVT (14.9% vs 10.7%) and long-term major bleeding complications (16.4% vs 11.7%). Diabetes was associated with a significant increase in the risk of recurrent deep vein thrombosis (AOR 1.74) (1, 43).

A study done in USA hospital cancer patients with DVT, reported that the median of DVT recurrence time was 92 days (IQR, 26-751; range, 1 day to 33 years). The cumulative DVT and PE recurrence rates at 1 week, 1 month, 3 months, 6 months, 1 year, 5 years, and 10 years were 1.6%, 10.3%, 18.0%, 21.4%, 26.7%, 45.0%, and 52.2%, respectively (44).

A cross-sectional study conducted in Uganda to determine the prevalence and sonographic features of lower limb DVT among HIV positive patients on anti-retroviral treatment found 9.1% among HIV patients on ART. Treatment with second line anti-retroviral therapy (ART) including protease inhibitors (PIs) was associated with higher odds of DVT occurrence compared with first line ART). The odds of DVT occurrence in patients with a lower CD4 count (< 200 cells/µl) were 5.36 times as high as in patients with CD4 counts above 500 cells/µl (4).

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2.1. Conceptual Framework

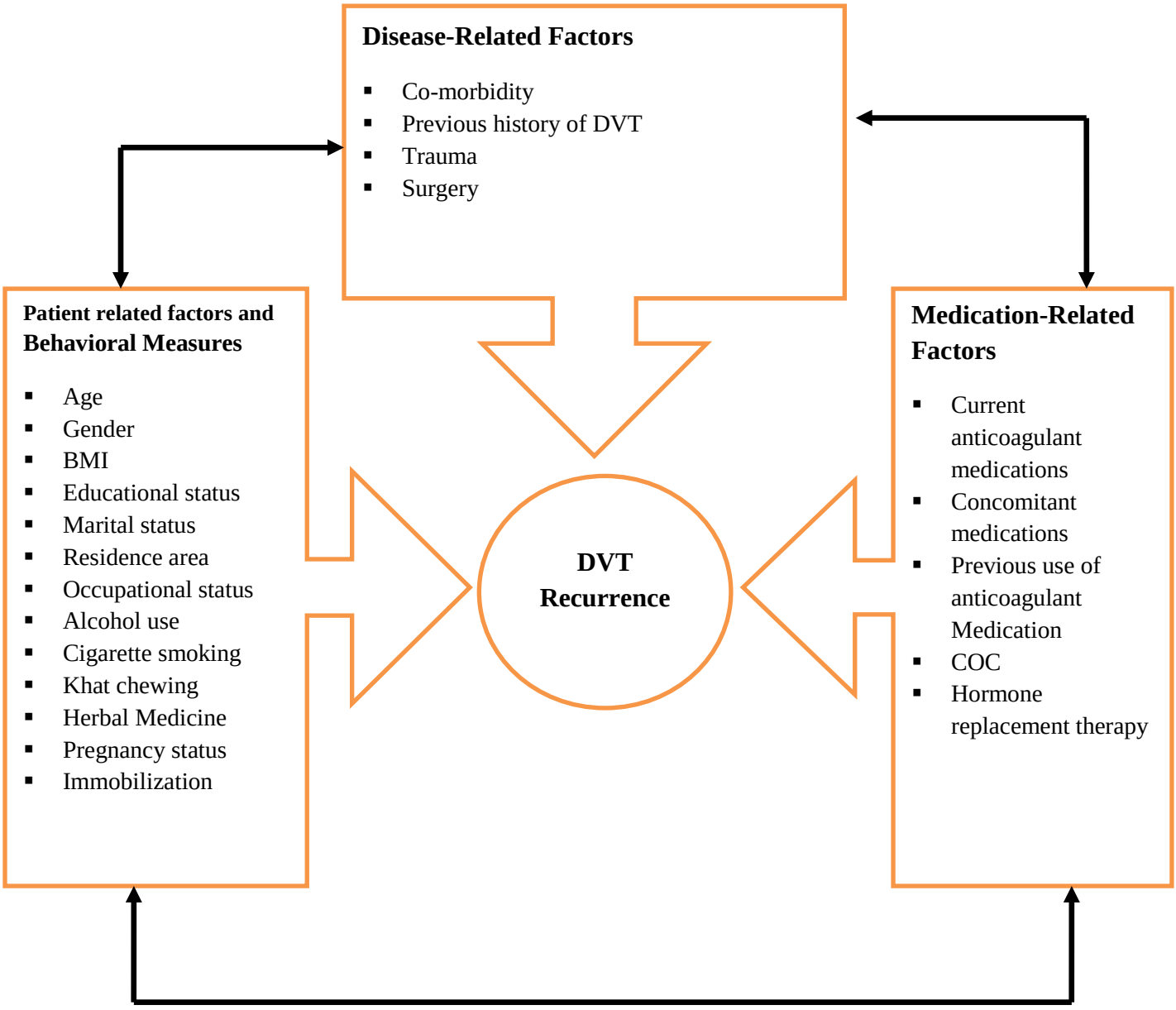


Figure 1: Conceptual frame work for factors associated with treatment outcome

Source: Developed after review of different literatures

3. Objectives

3.1.General objective

- To assess treatment outcome of deep vein thrombosis and its predictors among hospitalized adult patients at Jimma University Medical Center in Jimma and St. Paul's Hospital Millennium Medical College in Addis Ababa/Finfinnee.

3.2.Specific objectives

- To assess recurrence of DVT among patients on anticoagulant therapy within 3 months follow up in these two selected tertiary care settings.
- To assess the rate of DVT resolution, death and bleeding episodes among hospitalized patients.
- To identify factors associated with a higher likelihood of DVT recurrence among patients on anticoagulants in these two selected tertiary care settings.

4. Methods and Participants

4.1. Study Setting and Period

This study was conducted among hospitalized patients at two tertiary hospitals available in the country, Jimma University Medical Centre (JUMC), which is found in Jimma town; Southwest Ethiopia about 352km far away from the capital and St. Paul's Hospital Millennium Medical College located in Addis Ababa/"Finfinnee", the capital city of Ethiopia.

Jimma University Medical Centre (JUMC) is one of the oldest public hospitals found in the southwestern part of the country that runs under Jimma University. It is currently the only teaching and referral hospital in this part of the country; serving a total population of about 15million from the catchment area. The hospital has different departments, one of the departments inpatient ward service, which has about 632 beds for inpatient clients (from hospital source).

Second selected care setting was St. Paul's Hospital Millennium Medical College. The hospital was established through a decree of the council of Ministers in 2010G. C, although the medical college opened in 2007 G.C. And the hospital was established in 1968 by the late Emperor Haile Selassie. It is governed by a board under the federal Ministry of Health. The college initiated Ethiopia's first integrated modular and hybrid problem-based curriculum for its undergraduate medical education, and currently expanding to postgraduate programs. The college has more than 2800 clinical, academic and administrative and support staffs that provide medical specialty services to patients who are referred from all over the country. This teaching hospital has 700 beds for inpatient service; the hospital sees an average of 1200 emergency and outpatient clients daily (from hospital source). So, the study was conducted at this two selected tertiary teaching hospitals concurrently from March, 2018 to August, 2018.

4.2. Study Design

Prospective cohort study was conducted

4.3. Population

4.3.1. Source Population

- All adult patients, who were admitted to internal medicine, surgery and gynecology-obsterics wards of JUMC and SPHMMC.

4.3.2. Study population

- All adult patients with proven DVT by doppler ultrasonography during the study period from March to August, 2018 and fulfilling inclusion criteria.

4.4. Inclusion and Exclusion Criteria

4.4.1. Inclusion Criteria

- Proven DVT by doppler ultrasonography
- Age ≥18 years old
- Patient willing to give consent

4.4.2. Exclusion Criteria

- Inaccessible for follow-up

4.5. Sample Size Determination and Sampling Technique

4.5.1. Sample Size Determination

The sample is determined using Epi-Info 7 by single population proportion formula. Proportion of DVT recurrence was 22%, from six months prospective cohort study in USA (45).

The sample size can be determined as follows:

$$n = \frac{(Z\frac{\alpha}{2})^2 p(1-p)}{w^2}$$

Whereas: n – Sample size; Z – Confidence interval at 95% = 1.96; P – The prevalence of DVT recurrence; d – Margin of error = 5%. The size of the population is less than 10,000.Therefore; the sample size should be corrected using the following correction formula.

A total of, 264 participants were calculated from the above formula.

Since, a total of 270 DVT cases were admitted at the two hospitals in the last 6 months for health care need (JUMC=142; SPHMMC=128). So using correction formula, the sample can be corrected as follows,

Corrected sample size

$$n_f = \frac{n_i}{1 + \frac{n_i}{N}}$$

n_f = 134 study participants plus 10% of non-respondent or lost to follow-up was added to the final result. A total of 148 study participants were included in the study.

4.5.2. Sampling technique

Study participant were allocated proportionally into two selected tertiary care setting in the ratio of 1:1.2. Accordingly 80 DVT cases from JUMC and 68 DVT cases from SPHMMC were enrolled to the study. Data collection was undertaken from the first day of March to the last day of August for a total of consecutive six months and all admitted DVT cases was invited into the study based on the inclusion and exclusion criteria and a consecutive technique were used for the purpose of data collection.

4.6. Study variables

4.6.1. Dependent variable

- DVT recurrence

4.6.2. Independent variables

- Socio-demographics &behavioral characteristics of the patients
  - ✓ Age
  - ✓ Gender
  - ✓ BMI
  - ✓ Educational status
  - ✓ Marital status
  - ✓ Residence area
  - ✓ Occupational status
  - ✓ Religious
  - ✓ Income
  - ✓ Alcohol use
  - ✓ Cigarette smoking
  - ✓ Khat chewing
  - ✓ Herbal Medicine use
  - ✓ Pregnancy status
  - ✓ Immobilization
- Medication-related factors
  - ✓ Current anticoagulant medications
  - ✓ Concomitant medications
  - ✓ Previous use of medication
  - ✓ COC use
  - ✓ Coagulation Profile
  - ✓ Medication adherence
- Disease-related factors
  - ✓ Co-morbidity
  - ✓ Previous history of VTE
  - ✓ Recent history of DVT
  - ✓ Trauma
  - ✓ Surgery

4.7. Data Collection Instrument and Procedure

Patient information was collected from medical charts and medication order sheets and laboratory order papers about the socio-demographic, clinical characteristics, diagnostic test results during patients' hospital stay. Laboratory investigations and three month treatment outcomes were carefully followed at hospitalization durations, medical archives for periodic reviews of the hospital charts, participant information also gathered after at first, second, and third month of discharged from the hospital with face-to-face and/or a telephone interview by using validated questionnaire and risk of bleeding were searched for information on patient characteristics based on HAS-BLED score (uncontrolled hypertension, Abnormal liver or renal function, prior history of stroke, history of bleeding, Labile INR during follow-u, Elderly (age> 65years), and Drugs (use of platelet inhibitors or non-steroidal anti-inflammatory drugs)/alcohol use) each items has one point for the presence, patients were classified as non-high (<3points) or high-risk bleeding risk (≥3points). The English version check lists which contain several variables were used to evaluate treatment outcomes up on patients. Semi-structured questionnaire was developed after patient medical chart, laboratory order sheet, medication ordered sheet, and relevant literature were reviewed (28, 40, 46-50).

4.8. Data Quality Assurance

After data collection tool was carefully prepared to enable the data collectors to collect all necessary information to address study objectives, one day training on data collection tool and general procedures of data collection was given for three pharmacists (B. Pharm) and two medical residents at their clinical practice site. Medical residents act as supervisor at each hospital. Supervisor was responsible for supervising data collectors and facilitating daily activities. All filled data were checked for completeness of required information on daily basis by the principal investigator.

4.9. Data Processing and Analysis

All collected patient's data were entered into EpiData version4.2 and exported to SPSS version for cleaning and analysis, respectively. The data was analyzed by SPSS version 21.0. Frequency of risk factors distribution, treatment and average hospitalization duration (mean ± SD) were calculated. Student's t-test and chi-square test were used to determine the distribution of

demographic and clinical characteristics, risk factors, as well as utilized to check treatment outcome before performing Cox regression in risk factors in patients with recurrence of DVT compared with two settings. Kaplan-Meier rates for "survival" outcomes (cumulative incidence) such as DVT recurrence and major bleeding. Using Cox proportional hazards (PH) modeling, we tested demographic, baseline, and time-dependent characteristics as potential predictors of the rate of DVT recurrence from admission day to 90 days. All variables were initially tested for an association with rate of DVT recurrence in bivariate Cox PH models. Those variables demonstrating a bivariate association with at least marginal significance ($P<0.25$) were included in a multivariable model. Multivariable Cox regression was performed using backward LR method to identify independent predictors of treatment outcome. Adjusted hazard ratio was used as measure strength of association. The $P< 0.05$ was considered as statistically significant. Finally the result was presented by using narrative, tables, figures and charts.

4.10. Outcome and Validating Methods

Deep venous thrombosis recurrence, from hospital admission (0 day) to the minimum recommended duration of DVT management (90 days), was the clinical outcome of the study. Patients were enrolled and followed starting from their hospital arrival until 90 days. Recurrence ascertainment was made based on the following criteria; if the patient is readmitted to hospital:

1. With 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.

4.11. Ethical Consideration

Letter of ethical clearance was obtained from Ethical Review Board of Jimma University of institute of health, and then was send to Jimma University Medical Centre research committee and SPHMMC IRB to get permission to access patients' data. Patient socio-demographic data, clinical data and laboratory investigations were data collected as soon as consent was obtained. Name and address of the patient were not recorded in the data entry and analysis for maintain confidentiality. The raw data were not made available to anyone. All steps in data collection and compilation were conducted and supervised by the principal investigator. Strict confidentiality was assured through anonymous recording and coding of questionnaires and placed in safe place.

4.12. Dissemination Plan

The final result of the study will be disseminated to responsible bodies such as school of Pharmacy of Jimma University, JUMC,SPHMMC administrator's and Ethiopian federal ministry of health, Ethiopian food, medicines and health care administration and control authority (FMHACA), professional associations such as EPA, EPHA. Attempts will be made to present the finding on national and international scientific conferences. Finally, the study finding will be submitted to reputable professional journal for publication so as to serve as base line for further studies.

4.13. Definitions of Terms

Bleeding: is defined as clinical status, laboratory and/or imaging evidence of bleeding from internal or external body as result of anticoagulant therapy (51).

Comorbidity: is the presence of one or more additional concomitant diseases or disorders co-occurring with DVT.

Recurrence: is defined as an objectively verified hospital discharge diagnosis of DVT or as a fatal complication of DVT confirmed by ultrasonography, or site of thrombosis either previously uninvolved or had interval documentation of incident DVT.

5. Results

5.1. Study Participants Enrolment Information

A total of 148 patients, who initially had confirmed DVT by doppler ultrasound at JUMC and SPHMMC were recruited to participate in the study. Immediately after two days following enrolment, two patients were left because of normal doppler result finding after the initiation of parenteral and oral anticoagulation therapy. Eight patients dropped out/lost to follow up during the study period; all from SPHMMC. Nine patients also self-discharged (left against medical advice). A total of 129 patients, whose outcome within 90 days was known, were included into the final analysis (**Figure 2**).

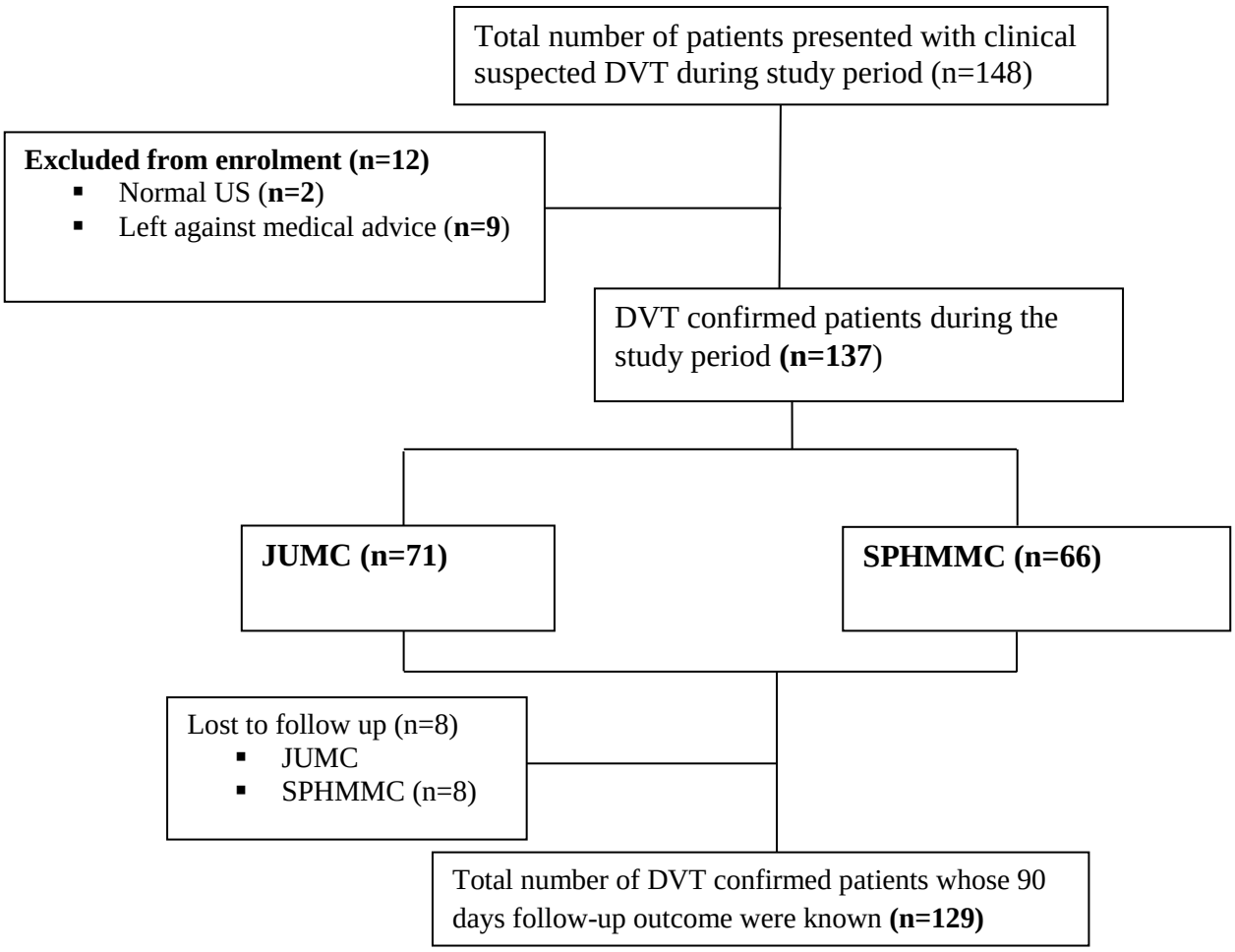


Figure 2: Study participant recruitment flow diagram

5.2. Socio demographic characteristics of study participants

During this six months study period, 713 medical cases at JUMC and 893 at SPHMMC were admitted; with a total of 1,606 patients at both settings. From the study, it was found that the prevalence of DVT was 9.96% and 6.5% at JUMC and SPHMMC, respectively; with the overall prevalence of 8.1%.

From a total of 129 study participants included into the final analysis, 84(65.1%) were females, with male to female ratio of 1:1.86. The age of study participants ranged from 18 to 85 years with the mean±SD of 38.63 ±17.67 years. Majority, 76(58.9%), of the patients were within the age group between 18-35 years.

About 74.4% of participants were married. About 57.4% of participants were residing in the rural area. Educational status of the participants revealed that, 52(40.3%) of them could not read and write; only 9(7.0%) patients had finished their college. Large number [111(86.0%)] of study participants were living with their immediate family. There were statistically significant differences were observed between the two study settings on different socio demographic variables; such as residence (P=0.009), educational status (P=0.001), living condition (p=0.004) and occupational status (P<0.001). All study participants were requested to respond for the behavioral measurements. It was found that the result from JUMC only eight patients were smokers, the chi-square test indicate that there was statistically significant difference (P<0.018) between the two study settings. Regarding khat chewing (P<0.002) and herbal medicine (P<0.003) use behavior, still there was statistical significant difference were noticed **(Table 1)**.

Table 1: Baseline socio-demographic & behavioral characteristics of study participants from March to August 2018

Variables		Settings		Total [n (%)]	P-Value
		JUMC [n (%)]	St. Paul [n (%)]		
Gender	Male	29(40.8)	16(27.6)	45(34.9)	0.116
	Female	42(59.2)	42(72.4)	84(65.1)	
	18-35	40(56.3)	36(62.1)	76(58.9)	
Age (years)	35-50	12(16.9)	5(8.6)	17(13.2)	0.384
	>50	19(26.8)	17(29.3)	36(27.9)	
	Single	17(23.9)	9(15.5)	26(20.1)	
Marital status	Married	49(69.0)	47(81.0)	96(74.4)	0.237
	Divorced	2(2.8)	2(3.4)	4(3.1)	
	Widowed	3(4.2)	0	3(2.3)	
	Office worker	3(4.2)	12(20.7)	15(11.6)	
	Farmer	33(46.5)	4(6.9)	37(28.7)	
Occupation	Merchant	9(12.7)	13(22.4)	22(17.1)	P<0.001
	Student	5(7.0)	5(8.6)	10(7.8)	
	Daily laborer	6(8.4)	4(6.9)	10(7.8)	
	Others*	15(21.1)	20(34.5)	35(27.1)	
Residence location	Rural	48(67.6)	26(44.8)	74(57.4)	0.009
	Urban	23(32.4)	32(55.2)	55(42.6)	
	Cannot read and write	36(50.7)	16((27.6)	52(40.3)	
Educational status	Primary school	25(35.2)	16(27.6)	41(31.8)	
	Secondary school	7(9.9)	2034.5)	27(20.9)	0.001
	College and above	3(4.2)	6(10.3)	9(7.0)	
	With immediate family	54(76.1)	57(98.3)	111(86.0)	0.004
Living condition	With extended family	6(8.5)	1(1.7)	7(5.4)	
	Living alone	5(7.0)	0	5(3.9)	
	Other***	6(8.5)	0	6(4.6)	
Alcohol consumption	Never	50(70.4)	37(63.8)	87(67.4)	0.491
	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)	0.018
	Non-smoker	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)	0.002
	No	60(84.5)	58(100)	118(91.5)	
Herbal medicine use	Yes	10(14.1)	0	10(7.8)	0.003
	No	61(85.9)	58(100)	119(92.2)	

*House wife, ***prison

5.3. Clinical characteristics and laboratory results of study participants

As to the anatomic site of deep venous thrombosis, majority of patients [124(96.1%)] had the thrombosis at the lower extremities extending from the common iliac vein to the popliteal veins. The study revealed that 115(89.1%) participants were found to have unilateral thrombosis and only 14(10.1%) patients have combined involvement of bilateral deep venous thrombosis. Approximately 2/3rd of participants had left lower extremity involvement. The upper extremities were affected in only five patients those have unilateral involvement. Majority 103(79.8%) of Doppler ultrasonography examination proven deep venous thrombosis cases were proximal and only 21(16.3%) cases were located at the distal area for the lower extremity.

With regard to clinical presentation, about 99.2% of patients presented with pain and 97.7% of them had swelling with the affected limbs on admission. The mean ±SD of hospital stay (LOS) was 22.03 ±16.719 and 21.33±14.104 at JUMC and SPHMMC days, respectively, with overall range of 2 to 90 days (LOS) without significant difference between the two settings (**Table 2**).

From a total of 129 DVT patients, 127(98.4%) have received UFH, with a Mean±SD duration of UFH with warfarin overlap of 15.792±9.2454 days. Mean ± SD result of aPTT was 34.164±12.024 seconds within 24hrs, 36.41±17.156 seconds within 72hrs, 38.81±18.07 seconds in the 5th days, and 45.628±21.06 seconds immediately before discontinuing heparin. Regarding INR result, a Mean±SD was 1.5612±0.93, 1.7242±1.147, 1.822±1.061, and 2.136±1.455 seconds within 24hrs, 72hrs, 5th days and immediately before stopping heparin, respectively. With regard to baseline blood count, it was found that the overall Mean±SD of hemoglobin (Hgb) was 11.604±3.191mg/dL, hematocrit (Hct) accounted for Mean±SD 34.951±9.3860 percentage, platelet accounted for mean ±SD327.3±154.84, X 10^9/L. At baseline, the participants were also assessed for bleeding risk while on anticoagulation by using standard HAS BLED score, which accurately predicts major bleeding events in patients with acute VTE. About 34 (26.4%) had higher risk of major bleeding, with HAS BLED score of ≥3points **(Table 2).**

Table 2: Baseline clinical characteristics and laboratory results of study participants from March to August 2018

Variables		Settings		Total [n (%)]	P-Value
		JUMC [n (%)]	St. Paul [n (%)]		
Baseline clinical data					
	Unilateral	61(85.9)	54(93.1)	115(89.1)	0.192
Types of DVT	Bilateral	10(14.1)	4(6.9)	14(10.9)	
	Upper extremity¥	1(1.4)	4(6.9)	5(3.9)	0.108
Sites of DVT	Lower extremity	70(98.6)	54(93.1)	124(96.1)	
	Right leg	15(21.1)	18(31.0)	33(25.6)	0.234
Lower extremity DVT	Left leg	52(73.2)	33(56.9)	85(65.9)	
	Both legs	3(4.2)	3(5.2)	6(4.7)	
	Proximal DVT	61(85.9)	42(72.4)	103(79.8)	0.168
Anatomic location of DVT	Distal DVT	9(12.7)	12(20.7)	21(16.3)	
Pain	Yes	70(98.6)	58(100)	128(99.2)	0.550
	No	1(1.4)	0	1(0.8)	
Swelling	Yes	68(95.8)	58(100)	126(97.7)	0.164
	No	3(4.2)	0	3(2.3)	
Local tenderness	Yes	49(69.0)	26(44.8)	75(58.1)	0.006
	No	22(31.0)	32(77.6)	54(51.9)	
Pitting edema	Yes	41(57.7)	27(46.6)	68(52.7)	0.138
	No	30(42.3)	31(53.4)	61(47.3)	
Skin discoloration	Yes	20(28.2)	12(20.7)	32(24.8)	0.328
	No	51(71.8)	46(79.3)	97(75.2)	
Baseline laboratory tests& others data during hospital stay [Mean±SD					
Hemoglobin (g/dl)		10.685±3.0484	12.656±3.0517	11.604±3.1917	0.001
Hematocrit (percentage)		31.494±8.4922	38.951±8.4922	34.951±9.3860	<0.001
Platelet , X 10^9/L		317.2±146.53	340.3±165.5	327.3±154.84	0.440
aPTT (seconds) at 24 hrs.		33.34±5.713	35.973±19.90	34.164±12.024	0.358
aPTT (seconds) at 48hrs		34.3±16.76	38.030±17.657	36.41±17.156	0.500
aPTT (seconds) at 5^{th} days		32.059±8.46	43.587±21.47	38.81±18.07	0.043
aPTT (seconds) at immediately before DC heparin		35.625±4.95	48.591±23.093	45.628±21.06	0.128
INR at 24 hrs.		1.441±0.603	1.747±1.268	1.5612±0.93	0.101
INR at 48hrs		1.521±0.783	1.854±1.3235	1.7242±1.147	0.260
INR at 5^{th} days		1.666±0.6891	1.9411±1.269	1.822±1.061	0.244
INR on discharge days		2.046±1.1658	2.204±1.649	2.136±1.455	0.661
Serum creatinine (mmol/L)		0.0851±0.0815	0.0845±0.0781	0.0848±0.0795	0.969
Duration of heparin-warfarin overlap (days)		16.394±9.276	14.918±9.2259	15.792±9.2454	0.392
Length of hospital stay (days)		22.03±16.719	21.33±14.104	21.71±15.542	0.800
Antithrombotic use prior to admission		9(12.9)	16(27.6)	25(19.4)	0.033
Base line HAS-BLED Score	≥ 3 points (High risk)	11(15.5)	23(39.7)	34(26.4)	
	<3 points (Low risk)	60(84.5)	35(60.3)	95(73.6)	0.002

DVT, Deep Venous Thrombosis; US, Ultrasonography; ¥ 2were right hand & 3 were on the left hand, all occurred at proximal sites. HAS BLED: **H**ypertension, **A**bnormal renal and liver function, **S**troke, **B**leeding, Labile INR, **E**lderly, **D**rugs or alcohol

5.4. Deep Venous thrombosis risk factors among study participants

The risk factors of DVT in the study population of the two care settings was presented as prolonged immobilization accounted for 113 (87.6%). About 35(27.1%) of patients had prior surgical history, and pregnancy accounted for 32(24.8%) of the risk factors. It was found that 74(57.4%) of the patients were presented with combined significant medical condition (i.e. metabolic, endocrine or respiratory pathologies, acute infectious disease, inflammatory conditions (arthritis)). Other risk factors included chronic lung disease (17.8%) active cancer (10.9%), OCP use (18.6%) & congestive heart failure (15.5%) **(Table 3**).

Table 3: Distribution of risk factors of deep venous thrombosis among study participants from March to August, 2018

S.No	Risk factors	Settings		Total [n (%)]	P-value
		JUMC [n (%)]	SPHMMC [n (%)]		
1.	Pregnancy	10(14.1)	22(37.9)	32(24.8)	0.002
2.	Active cancer	8(11.3)	6(10.3)	14(10.9)	0.549
3.	Prior history of surgery	13(18.3)	22(37.9)	35(27.1)	0.013
4.	Obesity	3(4.2)	2(3.4)	5(3.9)	0.603
5.	Chronic lung disease	8(11.3)	15(25.9)	23(17.8)	0.027
6.	Prolonged immobilization	69(97.2)	44(75.9)	113(87.6)	<0.001
7.	Heart failure	6(8.4)	14(24.1)	20(15.5)	0.014
8.	Prior history of trauma	9(12.7)	6(10.3)	15(11.6)	0.681
9.	Neurologic disease	3(4.2)	6(10.3)	9(7.0)	0.175
10.	History of major bleeding	19(26.8)	13(22.4)	32(24.8)	0.059
11.	OCP use	16(22.5)	8(13.8)	24(18.6)	0.204
12.	HRT	2(2.8)	0	2(1.6)	0.198
13.	Previous VTE history	8(11.3)	10(17.2)	18(14.0)	0.330
14.	More significant medical conditions~	48(67.6)	26(44.8)	74(57.4)	0.561

JUMC, Jimma University Medical Centre; SPHMMC, St, Paul's Hospital Millennium Medical College; HRT, Hormone replacement therapy, OCP, Oral contraceptive pills; ~, metabolic, endocrine or respiratory pathologies, acute infectious disease, inflammatory conditions (arthritis)

Regarding burden of risk factors among study participants, about 17(13.2%) of the cases had single risk factor for DVT, 46(35.7%) had two risk factor, and half of study participants were presented with three or greater risk factor for the development of DVT (**Figure 3**).

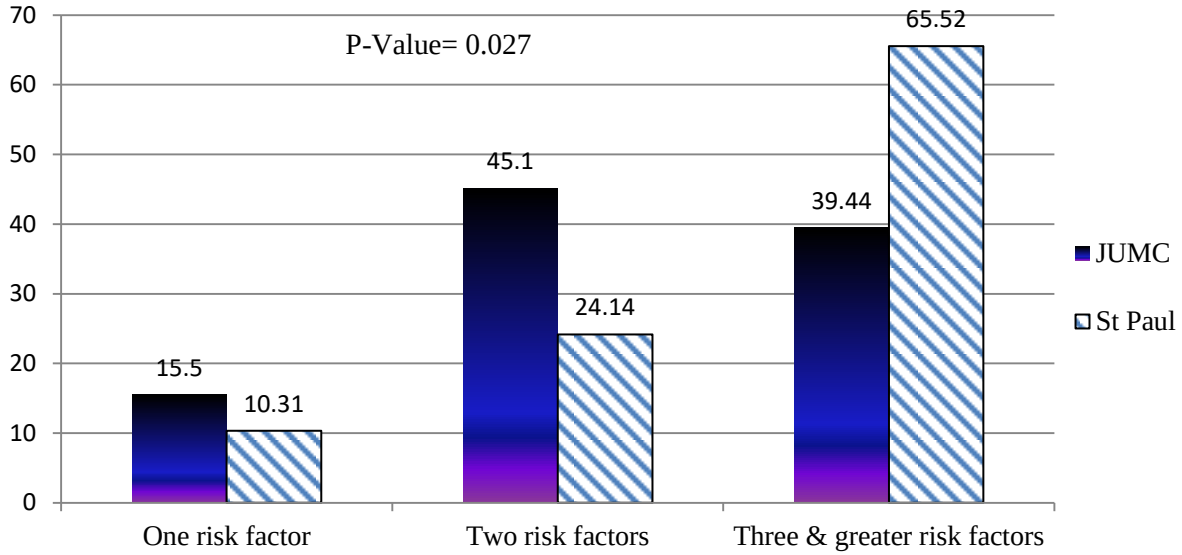


Figure 3: Burden of risk factors for DVT occurrence among study participants from March to August 2018

The prevalence of comorbidity among study participants showed that about 77.5% of them had current comorbid conditions. With regard to its distribution, about 15(11.6%) cases were presented with active cancer, 19(14.7%) cases were with renal failure, 20(15.5%) cases were with heart failure, and 61(47.3%) cases were with combined comorbidity disease. It was found that, statistically significant difference was observed in heart failure and renal failure between the two care settings, respectively (**Table 4**).

Table 4: Distribution of comorbidity presenting with DVT in study participants from March to August, 2018

S.No	Types of comorbidities		Settings		Total [n (%)]	P-value
			JUMC [n (%)]	SPHMMC [n (%)]		
1.	Presence of co-morbidity	Yes	53 (74.60)	47(81)	100(77.5)	0.387
		No	18 (25.40)	11(19)	29(24.5)	
2.	**Types of co-morbidity**					
	a. Atrial Fibrillation		0	2(3.4)	2(1.5)	0.115
	b. Diabetes Mellitus		1(1.4)	6(10.3)	7(5.4)	0.026
	c. Hypertension		5(7.0)	7(12.1)	12(8.6)	0.328
	d. Previous Stroke		1(1.4)	1(1.7)	2(1.5)	0.885
	e. Heart Failure		6(8.4)	14(24.1)	20(15.5)	0.014
	f. Chronic Liver Disease		3(4.2)	4(6.9)	7(5.4)	0.505
	g. Renal Failure		5(7.0)	14(24.1)	19(14.7)	0.006
	h. Coronary Artery Disease		2(2.8)	3(5.2)	5(3.9)	0.491
	i. HIV/AIDS		2(2.8)	4(6.9)	6(4.6)	0.274
	j. Others**		41(57.7)	20(34.5)	61(47.3)	0.904
	k. Cancer		8(11.3)	7(12.1)	15(11.6)	0.888
	l. Type of Cancer	CRC	0	1(1.7)	1(0.8)	
		Rectal	0	1(1.7)	1(0.8)	
		Brain	0	1(1.7)	1(0.8)	0.461
		Lung	0	1(1.7)	1(0.8)	
		Other***	5(7.0)	4(6.9)	9(7.0)	

CRC, Colorectal cancer, ***Ovarian, Non-Hodgkin's Lymphoma; MDD, Major depressive disorder

** combined comorbidity (Anemia, TB, epilepsy, MDD)

From the analysis, adherence level of the study participants from the two hospitals were assessed using 8-items modified Morisky Medication Adherence Scale-(MMAS-8) and categorized into three stages to explore adherence level of patients who was enrolled into this current study. Approached to 2/3rd of the participants were observed with high adherence level, 41(31.8%) patients had medium adherence level, and only 5(3.9%) patients were measured as low level adherence. On the chi-square tests, there were no statistically significant differences between the two care settings (**Figure 4**).

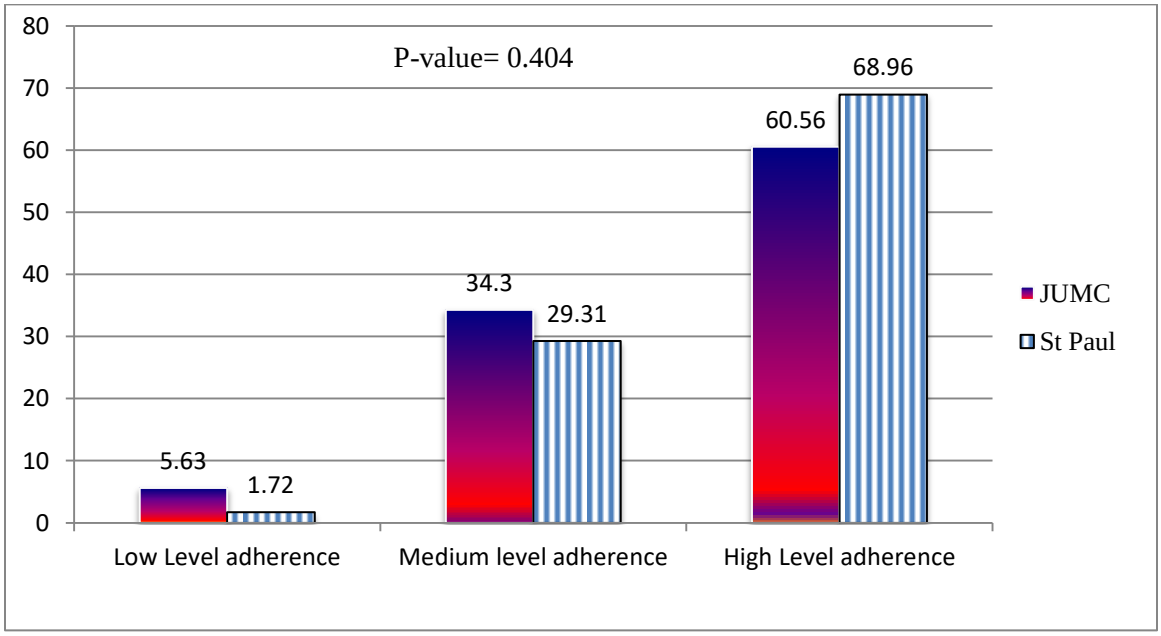


Figure 4: Percentage of adherence level of study participants from March to August, 2018

The aim of anticoagulant therapy and its dosing intensity in hospital care setting is to prevent extension of the clot formation and disease recurrence. Therefore, this current study assessed compliance to management protocol with the alignment of international guideline. It was found that 115(89.1%) patients had taken parenteral anticoagulation for greater than or equal to five days, only 18(14.0%) of study participants were achieved INR greater than 2 for 24hrs before stopping heparin, about 3/4th of the study participants were received early oral anticoagulant (Vitamin K-antagonist) within 24hrs of admission, all most all 127(98.4%) patients were treated with initial subcutaneous unfractionated heparin, and only few number [9(7.0%)] of participants were achieved aPTT target within admission of 24 hrs. **(Table 5)**.

Table 5: Compliance with in hospital DVT management core measures for study participants from March to August 2018

S.No	Core Measures		Settings		Total [n (%)]	P-Value
			JUMC [n (%)]	St. Paul [n (%)]		
1.	Administration of parenteral anticoagulation for ≥5 days	Yes	64(49.6)	51(87.9)	115(89.1)	0.688
		No	7(9.9)	7(12.9)	14(10.9)	
2.	Achievement of an INR >2.0 for 24hrs before stopping parenteral anticoagulants	Yes	10(14.1)	8(13.8)	18(14.0)	0.962
		No	61(85.9)	50(86.2)	111(86.0)	
3.	Early start with VKA within 24hrs of admission	Yes	59(83.1)	39(67.2)	98(76.0)	0.031
		No	12(16.9)	19(32.8)	31(24.1)	
4.	Initial treatment with SC heparin	Yes	71(100.0)	56(96.6)	127(98.4)	0.115
		No	0	2(3.4)	2(1.6)	
5.	Achieve target aPTT within 24hrs	Yes	4(5.6)	5(8.6)	9(7.0)	
		No	67(94.4)	53(91.4)	120(93.0)	0.508

VKA: Vitamin K-Antagonist

Majority [127(98.4%)] of study participants were taken unfractionated heparin during their admission, for 115(89.1%) patients warfarin was prescribed with parenteral anticoagulant therapy, of which 10(7.7%) patients were treated with LWMH (enoxaparin), majority 102(79.1%) of the participant was taken ancillary medication, of which 1/3rd of participants were taken antibiotics, 16(12.4%) were on cardiovascular drugs, and 26(20.2%) of participants were taken vitamin and minerals. From the analysis, it was statistically significance between the two settings in warfarin use (P<0.001) (**Table 6**).

Table 6: In hospital medications used by study participants from March to August, 2018.

Treatment		**Setting**		**Total [n (%)]**	**P-value**
		JUMC [n (%)]	**SPHMMC [n (%)]**		
Does the patient taking UFH	Yes	71(100.0)	56(96.6)	127(98.4)	0.115
	No	0	2(3.4)	2(1.6)	
Does warfarin prescribed	Yes	69(97.2)	46(79.3)	115(89.1)	0.001
	No	2(2.8)	12(20.7)	14(10.9)	
Enoxaparin	Yes	3(4.2)	7(12.1)	10(7.8)	
	No	68(95.8)	51(87.9)	119(92.2)	
Does the patient taking ancillary medications	Yes	53(74.6)	49(84.5)	102(79.1)	0.172
	No	18(25.4)	9(15.5)	27(20.9)	
Class of ancillary drugs	CVD	5(7.0)	11(19.0)	16(12.4)	0.016
	Respiratory Drugs	1(1.4)	0	1(0.8)	
	GI Drugs	0	5(8.6)	5(3.9)	
	Antibiotics	23(32.4)	20(34.5)	43(33.3)	
	Vitamins and Minerals	19(26.7)	7(12.1)	2(20.2)	
	Others (TCA, NSAIDS, non-opioids…)	5(7.0)	6(10.3)	11(8.5)	

CV, Cardiovascular; UFH, Unfractionated heparin; LMWH, Low molecular weight heparin ;GI, Gastrointestinal
JUMC, Jimma University Medical Center, SPHMMMC, St Paul Hospital Millennium Medical College

5.5. Deep venous thrombosis follow-up outcome of participants

5.3.1. DVT Recurrence

A cohort of 129 patients was followed up for a total of 11,348 person days. More than 3/4th of study participants developed deep venous thrombosis for first time, 27(20.9%) of participants had second deep venous thrombosis admission status, and only 4(3.1%) have multiple admission status. During the 90 days follow up period of each participants from a cohort of DVT, 34(26.4%) recurrent VTE were observed. Type of event was DVT in 28 patients (82.40%) and the rest admitted with pulmonary embolism as a result of DVT complication, which was confirmed by CT-scan. The overall incidence rate of DVT recurrence was 2.99 per 1000 patient-days. Little number [6(4.7%)] of patients had confirmed complete DVT resolution within three months of treatment. The overall mean± SD duration of DVT recurrence was 42.03±22.371 **(Table 7)**.

5.3.2. Bleeding

From a cohort of DVT on follow up, during 90 days, about 25(19.4%) of them presented with bleeding incidence. The mean ± SD time to the occurrence of bleeding in those 25 patients was 21.179±22.179 days; with range of five to thirty two days.

5.3.3. All-Cause Mortality

Four (3.1%) patients died during the observation period giving a mortality rate of 0.35 per 1000 person-days. The result revealed that statistically significant difference (P< 0.025) was observed between the hospitals, as all were reported from St. Paul's hospital (**Table 7**).

Table 7: Distribution of outcome measures for deep vein thrombosis among study participants from March to August, 2018.

Variables		Setting		Total [n (%)]	P-value
		JUMC [n (%)]	SPHMMC [n (%)]		
DVT admission status	First episode	60(84.5)	38(65.5)	98(76.0)	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)	0.007
	No recurrence	59(83.1)	36(62.1)	95(73.6)	
Recurrence diagnosis	DVT + PE	0	6(27.3)	6(17.6)	0.046
	DVT only	12(100.0)	16(72.7)	28(82.4)	
Current DVT status	Worsened	12(16.9)	22(37.9)	34(26.3)	
	No change	19(26.8)	11(19.0)	30(23.3)	0.147
	Improved	36(50.7)	23(39.7)	59(45.7)	
	Complete resolution	4(5.6)	2(3.4)	6(4.7)	
Bleeding episodes	Yes	13(18.3)	12(20.7)	25(19.4%)	0.734
	No	58(81.7)	46(79.3)	104(80.6)	
All-cause mortality	Yes	0	4(6.9)	4(3.1)	0.025
	No	71(100)	54(93.1)	125(96.9)	
Lost to Follow-up	Yes	0	8(12.1)	8(5.5)	0.002
	No	71(100)	58(87.9)	129(88.4)	
Platelet less than 150,000 cells/mm^3	Yes	3(4.2)	8(13.8)	11(8.5)	0.053
	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)	0.193
	No	67(94.4)	51(87.9)	118(91.5)	
Time to event for treatment outcomes[Mean ±SD]					
Time to bleeding occurrence in days		26.33±30.44	17.00±12.83	21.179±22.179	0.474
Time to DVT recurrence in days		41.42±18.595	42.03±22.37	42.03±22.371	0.908
INR target achievement in days		10.73±17.232	15.70±21.086	13.22±19.286	0.270
aPTT ≥2 to 2.5 above baseline in days		7.50±6.364	7.74±8.812	7.71±8.480	0.971

5.6. Kaplan Meier Survival Outcome analysis

The mean ±SD survival time to DVT recurrence was 42.03± 22.371 days. On the Kaplan Meier survival outcome analysis, variables such as length of hospital stay, anatomical location of DVT, HAS-BLED score, age of patients, comorbid DM, gender, early initiation of warfarin, achieving target aPTT within 24 hrs. of heparin were done. From the result, the survival time to DVT recurrence were not statistically significant between age group (Log rank p=0.503), gender (Log rank p=0.120), early initiation of warfarin (Log rank p=0.174), achieving target aPTT (Log rank p=0.887), length of hospital stay (Log rank p=0.303), anatomical location (Log rank p=0.157). However, there were differences in survival time to DVT recurrence with regard to HAS BLED score (Log rank p=0.052), and diabetes comorbidity (Log rank p=0.007). The cumulative survival time to DVT recurrence event were lower for patient with diabetes comorbidity (**Figure 5, 6**).

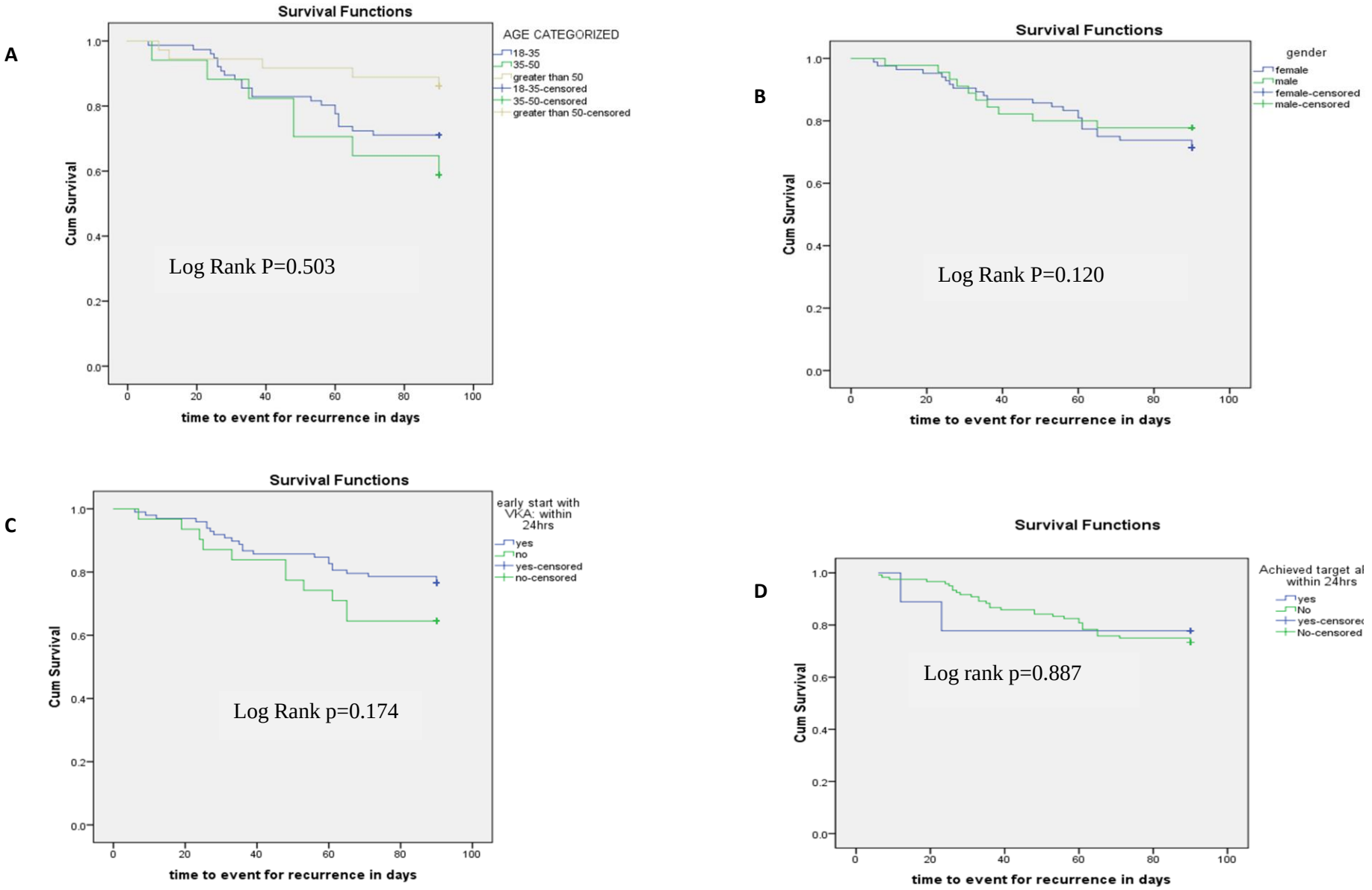
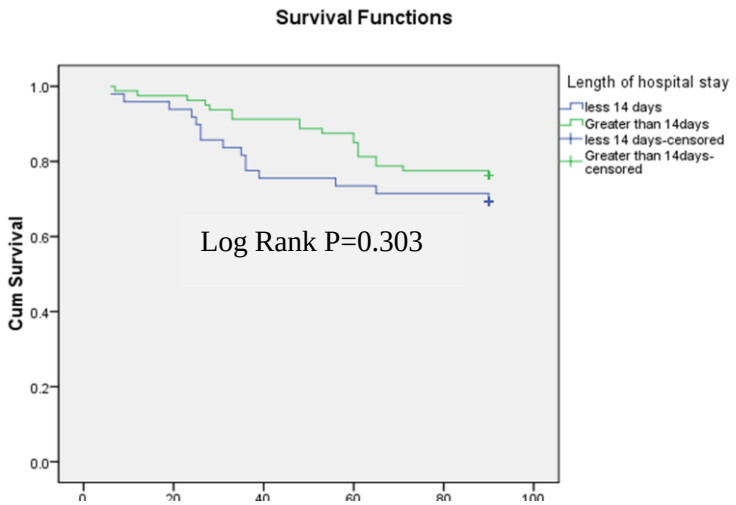
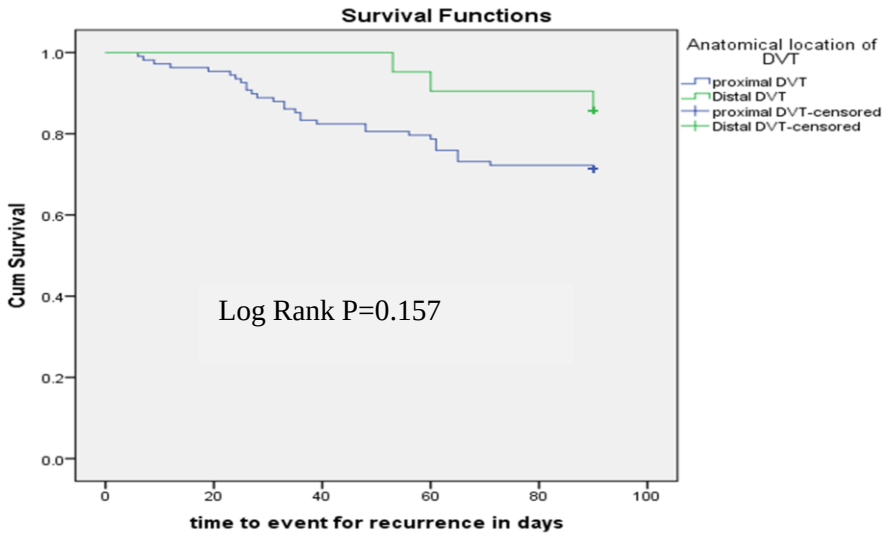


Figure 5: Survival function estimates of cumulative incidence of DVT recurrence event for age of patients (A), Gender of patients (B), Early Warfarin therapy (C), and Achieved target aPTT in 24 hrs. (D)

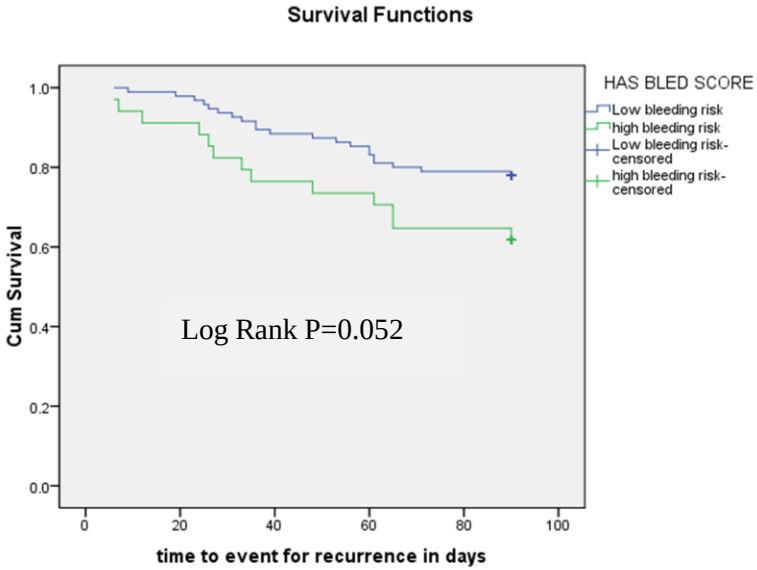
E



F



G



H

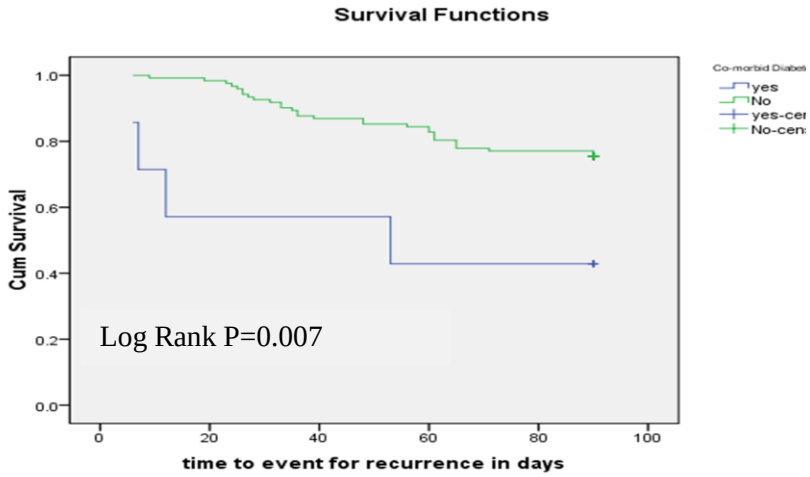


Figure 7: Survival function estimates of cumulative incidence of DVT recurrence event for LOS (E), Location of DVT (F), patients experienced bleedings (G); Comorbid DM (H) among study participants from March to August, 2018.

5.7. Factors associated with DVT recurrence among study participants

The association of independent variables with the dependent variable was investigated using both bivariate and multivariate cox regression techniques. On bivariate cox regression analysis, female gender [CHR; 1.799; 95 % CI, 0.828, 3.905; P=0.038], age ≥ 50 years [CHR, 3.438; 95% CI, 1.091, 10.838; p=0.035], regular alcohol consumption [CHR, 1.066; 95% CI, 0.510, 2.229; p=0.031] , regular alcohol consumption [CHR, 1.066; 95% CI, (0.510, 2.229); p=0.195], pregnancy [CHR, 1.091; 95 % CI, 1.46, 11.179; p=0.057], hypertension[CHR, 0.077; 95% CI 0.017, 0.358; p=0.001], diabetes mellitus [CHR, 3.869; 95 % CI, 1.295, 11.558;p=0.015], no warfarin within 24 hrs. of heparin initiation [CHR, 2.797; 95% CI, 1.087, 7.213; p=0.051], not achieving aPTT target within 24 hrs. [CHR, 1.108; 95 % CI, 0.020, 0.600; p=0.032] had statistically significant association with DVT recurrence

The result of the multivariate cox regression analysis showed that, age between 30 to 50 years, age ≥ 50 years, alcohol uses, prior history of surgery, pregnancy**,** diabetes mellitus comorbidity, inability to achieve target aPTT within 24 hrs. of heparin and proximal site involvement were statistically associated with DVT recurrence.

The likelihood of DVT recurrence were about eight times among patients with diabetic comorbidity [AHR, 8.048; 95% CI, 2.494, 25.966; P<0.001] when compared with non- diabetics. And also the relative risk of DVT recurrence were about six times among patients with prior history of surgery [AHR, 6.218; 95% CI, 1.540, 25.104; p=0.010]. The relative risk of DVT recurrence was also higher among patients who did not achieved target aPTT within 24 hrs. [AHR, 1.129; 95% CI, 01.020, 10.600; p=0.011] of in hospital heparin administration. The relative risk of DVT recurrence was also seen among alcohol use (AHR, 1.71; 95 % CI, 1.096, 2.662; p=0.019)]; approximately 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=0.037], compared to non-pregnant women. The likely hood of DVT recurrence was also associated with age of the patients. For example; age between 30 to 50 years carries risk of DVT recurrence more than 3 times [AHR, 3.545; 95 % CI, 1.216, 10.338; p=0.020], and more than 5 times for patients ≥ 50 years old [AHR, 5.566; 95 % CI, 1.587, 19.518; p=0.007]. Proximal site involvement [AHR, 5.937; 95% CI, 1.300, 27.110;p=0.022] showed higher hazards of DVT recurrence (**Table 8, 9).**

Table 8: Cox regression hazards results of socio-demographic and behavioral factors associated with DVT recurrence among study participants from March to August, 2018

Variables		Recurrent Event		CHR (95% CI)	P-Value	AHR (95% CI)	P-Value
		Yes [n (%)]	No [n (%)]				
Gender	Male	10(29.4)	35(36.8)	1		1	
	Female	24(70.6)	60(63.2)	1.799 (0.828, 3.905)	0.038	1.116 (0.516, 2.411)	0.138
	18-35	22(64.7)	54(56.8)	1		1	
Age (years)	35-50	7(20.6)	10(10.5)	2.287 (0866, 6.041)	0.095	3.545 (1.216, 10.338)	0.020
	≥50	5(14.7)	31(32.6)	3.438(1.091, 10.838)	0.035	5.566(1.587, 19.518)	0.007
Marital status	Single	7(20.6)	19(20.0)	1			
	Married	27(79.4)	69(72.6)	0.591 (0.249, 1.439)	0.903		
	Divorced	0	4(4.2)	0.947 (0.118, 11.468)	0.999		
	Widowed	0	3(3.2)	0.47 1(0.713, 6.408)	0.731		
Educational status	Cannot read & write	9(26.5)	43(45.3)	1.776 (0.658, 4.790)	0.257		
	Primary school	10(29.4)	31(32.6)	1.477 (0.559, 3.905)	0.431		
	Secondary school	11(32.4)	16(16.8)	1.842 (0.536, 6.330)	0.332		
	College & above	4(11.8)	5(5.3)	1			
Residence location	Rural	13(38.2)	61(64.2)	1			
	Urban	21(61.8)	34(35.8)	0.759 (0.373, 1.547)	0.448		
Occupational status	Office worker	7(20.6)	8(8.4)	1		1	
	Farmer	6(17.6)	31(32.6)	1.516 (0.486, 4.735)	0.474	1.376 (0.354, 5.348)	0.645
	Merchant	8(23.5)	14(14.7)	1.858 (0.659, 5.240)	0.241	3.249 (0.900, 11.730)	0.072
	Student	2(5.9)	8(8.4)	2.654 (0.508, 13.858)	0.247	1.651 (0.214, 12.715)	0.630
	daily labourer	4(11.8)	6(6.3)	0.492 (0.137, 1.767)	0.277	0.236 (0.054, 1.044)	0.057
	Others***	7(20.6)	28(29.5)	0.660 (0.244, 1.944)	0.451	0.500 (0.155, 1.619)	0.245
Living condition	With immediate family	30(88.2)	81(85.3)	1			
	With extended family	2(5.9)	5(5.3)	1.594 (0.368, 6.916)	0.533		
	Living alone	1(2.9)	4(4.2)	1.922 (0.250, 14.769)	0.530		
	Others	1(2.9)	5(5.3)	1.361 (0.180, 10.310)	0.766		
Alcohol Use	Yes	24(70.6)	65(68.4)	1.066 (0.510, 2.229)	0.195	1.71 (1.096, 2.266)	0.019
	No	10(29.4)	30(31.6)	1		1	
Smoking behaviour	Current smoker	1(2.9)	6(6.3)	1.392(0.185, 10.485)	0.748		
	Non-smoker	33(97.1)	89(93.7)	1			
Khat chewing behaviour	Yes	3(8.8)	8(8.3)	1.517 (0.445, 5.164)	0.505		
	No	31(91.2)	87(93.7)	1			

Herbal medicine use	Yes	2(5.9)	8(8.3)	1.877 (0.436, 8.034)	0.398
	No	32(94.1)	87(93.7)	1	
Adherence	Low	2(5.9)	3(3.2)	0.384 (0.083, 1.783)	0.222
	Medium	13(38.2)	28(29.4)	0.436 (0.095, 1.959)	0.279
	High	19(55.9)	64(67.4)	1	

***house wife,

Table 9: Cox regression hazards results of clinical and laboratory findings associated with DVT recurrence among study participants from March to August, 2018

Variables		Recurrent Event		CHR (95% CI)	P-Value	AHR (95% CI)	P-Value
		Yes [n (%)]	No [n (%)]				
Pregnancy	Yes	13(19.4)	19(28.4)	1.091 (1.46, 11.179)	0.057	2.091 (1.046, 4.179)	0.037
	No	17(25.4)	18(26.9)	1		1	
Prior history of surgery	Yes	11(32.4)	24(25.3)	1.242(0.275, 1.185)	0.132	6.218 (1.540, 25.104)	0.010
	No	23(67.6)	71(74.7)	1		1	
Chronic lung disease	Yes	5(14.7)	18(19.0)	2.000 (0.758, 5.278)	0.162	0.922 (0.341, 2.495)	0.874
	No	29(85.3)	77(81.0)				
Prolonged immobilization	yes	27(79.4)	86(90.5)	1.834 (0.771, 4.360)	0.170	2.392 (0.818, 7.00)	0.111
	No	7(20.6	9(9.5)	1		1	
Heart failure	Yes	5(14.7)	15(15.8)	2.162 (0.808, 5.786)	0.125	0.440 (0.081, 2.379)	0.340
	No	29(85.3)	80(84.2)	1		1	
Prior history of Trauma	Yes	3(8.8)	12(12.6)	1.109 (0.328, 3.746)	0.868		
	No	31(92.2)	83(87.4)	1			
Neurologic disease	Yes	3(8.8)	6(6.3)	0.432 (0.127, 1.465)	0.178	2.504 (0.515, 48.504)	0.255
	No	31(92.2)	89(93.7)	1		1	
History of major bleeding	Yes	13(38.2)	19(20.0)	1.884 (0.440, 1.776)	0.729		
	No	21(61.8)	76(80.0)	1		1	
OCP use	Yes	8(23.5)	16(16.8)	1.965 (0.874, 4.416)	0.102	0.493 (0.177, 1.375)	0.176
	No	26(76.5)	79(83.2)	1			
HRT	Yes	1(2.9)	1(1.1)	3.152 (0.399, 24.899)	0.276		
	No	33(97.1)	94(98.9)	1			
Previous DVT history	Yes	18(52.9)	0	1.302 (0.659, 2.572)	0.447		
	No	16(47.1)	95(100.0)	1			
Other comorbidity *****	Yes	16(47.1)	58(61.1)	1.054 (0.534, 2.079)	0.880		
	No	18(52.9)	37(38.9)	1			
Antithrombotic drug prior to admission	Yes	14(41.2)	11(11.6)	1.374 (0.684, 2.758)	0.372		
	No	20(58.8)	84(88.4)	1			
Diabetes Mellitus	Yes	4(11.8)	3(3.2)	3.869 (1.295, 11.558)	0.015	8.048 (2.494, 25.966)	P<0.001
	No	30(88.2)	92(96.8)	1		1	
Hypertension	Yes	3(8.8)	9(9.5)	0.077 (0.017, 0.358)	0.001	0.518 (0.046, 5.782)	0.593
	No	31(91.2)	86(90.5)	1		1	
Chronic Liver Disease	Yes	2(5.9)	5(5.3)	3.236 (0.733, 14.294)	0.121	3.33 (0.371, 29.930)	0.283
	No	32(94.1)	90(94.7)	1		1	

Renal Failure	Yes	5(14.7)	14(14.7)	1.330 (0.503, 3.514)	0.565		
	No	29(85.3)	81(85.3)	1			
HIV/AIDS	Yes	14(41.2)	4(4.2)	1.182 (0.280, 4.991)	0.820		
	No	20(58.2)	91(95.8)	1			
Cancer	Yes	5(14.7)	9(9.5)	1.568 (0.594, 4.145)	0.364		
	No	29(85.3)	86(90.5)	1			
Others (Anaemia, TB)	Yes	5(14.7)	47(49.5)	1.109 (0.558, 2.202)	0.768		
	No	29(85.3)	48(50.5)	1			
Type of DVT	Unilateral	32(94.1)	85(89.5)	2.215 (0.298, 16,462)	0.437		
	Bilateral	2(5.9)	10(10.5)	1			
Lower extremity DVT	Proximal DVT	30(88.2)	73(80.2)	2.258 (0.670, 7.614)	0.189	5.937 (1.300, 27.110)	0.022
	Distal DVT	3(8.8)	18(19.8)	1		1	
Patient receive UFH	Yes	32(94.1)	95(100.0)	1		1	
	No	2(5.9)	0	2.207 (0.720, 14.281)	0.106	0.521 (0.096, 2.833)	0.451
Don't received warfarin	Yes	28(82.4)	87(91.6)	2.797 (1.087, 7.213)	0.051	1.453 (0.187, 1.100)	0.080
within 24 hrs of heparin	No	6(17.6)	8(8.4)				
Ancillary medications	Yes	24(70.6)	78(82.1)	1			
	No	10(29.4)	17(17.9)	0.837 (0.399, 1.756)	0.633		
Risk factors	Single risk factor	2(5.9)	15(15.8)	1	0.312	1	
	Two risk factors	8(23.5)	38(40.0)	2.188 (0.488. 10.680)	0.130	1.658 (0.322, 8.543)	0.546
	Multiple risk factors	24(70.6)	42(44.2)	1.169 (0.272, 5.020)	0.312	1.026 (0.230, 4.582)	0.973
Parenteral AG for ≥5 days	Yes	29(85.3)	86(90.5)	1			
	No	5(14.7)	9(9.5)	0.895 (0.334, 2.398)	0.824		
INR≥2.0 for ≥24hrs before	Yes	2(5.9)	16(16.8)	1			
	No	32(94.1)	79(83.2)	0.852 (0.201, 3.618)	0.832		
Early start VKA within	Yes	23(67.6)	75(78.9)	1			
24hrs	No	11(32.6)	20(21.1)	1.167 (0.558, 2.441)	0.682		
Initial with SC heparin	Yes	32(94.1)	95(100.0)	1		1	
	No	2(5.9)	0	3.207 (0.720, 14.281)	0.184	1.918 (0.353, 10.424)	0.451
aPTT targeted within 24hrs	Yes	2(5.9)	7(7.4)	1		1	
	No	32(94.1)	88(92.6)	1.108 (0.020, 0.600)	0.032	1.129 (1.020, 10.600)	0.011

¥¥ active infection, metabolic, endocrine or respiratory pathologies, inflammatory conditions, varicose veins with phlebitis

6. 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 (13). Therefore, this study was conducted at two tertiary teaching hospitals setting using prospective cohort study design in order to determine risk factor associated with DVT recurrence, its risk predictors and management practice in accordance with ACCP treatment protocol. Hospitalized patients were carefully assessed for valuable information needed for this particular research and participants' clinical data were consciously recorded and study participants were strictly followed for about 3 months during the 6 months study period.

During this six months study period, about 713 medical cases at JUMC and 893 at SPHMMC were admitted; with a total of 1,606 patients at both settings. From the study, it was found that the prevalence of DVT was 9.96% and 6.5% at JUMC and SPHMMC, respectively; with the overall prevalence of 8.1%. This result was comparable with study done at surgical department of Thailand (42), which was 10.5% and Mulago Hospital in Uganda (52), 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%. This finding was comparable to study done in USA (45) which showed DVT recurrence rate of 22%. But, study done in France (53) showed DVT recurrence rate of 5.5%. This variation may be related to larger sample size (n=1804) and the retrospective study design.

This current study showed that, out of the 129 patients with proven DVT, majority were females, which accounted for 84(65.1%) of the total. This was found to be in line with a study done in Addis Ababa (27, 28). However, study done in Azadi Hospital in Duhok (54) showed, majority of the participants were males. This variation could be explained by the fact that, more females were admitted in both our hospitals than male patients and large numbers of sample size and long term follow up in Duhok hospital.

In our study, the highest DVT incidents were found in the age greater than 35 years. Similar result was found in Addis Ababa (28, 54, 55). But the highest incidence of DVT was varied from different studies, most of the study identified DVT occurrence was high at a mean ± SD age of 63±19.4 and 66±17 (45, 56). And also on the cox regression analysis age increased the hazard of DVT recurrence. Patient with age between 35 to 50 years had more than three 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 in comparable with two studies from Minnesota & Netherland (45, 57), which showed increased risk per additional decade. This is explained by older age linked with sedentary life style, restricted movement, and biology of aging rather than simply an increased exposure to DVT risk factors.

About 2/3rd of participants had left lower extremity involvement and majority of them had involved proximal sites as proved by doppler ultrasonography examination. On multivariate cox regression analysis proximal extension of DVT had strong risk predictors, nearly six times, of DVT recurrence. This is strongly supported by different studies (38, 40, 50, 56). This is may be explained by anatomy of deep venous thrombosis of the lower extremity, showing highly involved site for DVT cases. And also multiple studies showed as if resolution of proximal DVT is slow and less than half had complete lysis after 6 months of anticoagulation.

Among the study participants pregnancy accounted for 32(47.8%) of risk factors associated with deep venous thrombosis from female of child bearing age. From adjusted HR proportional model pregnancy was significantly associated with development of DVT recurrence, which is similar to reports from Arizona hospital(45, 58), 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 utero placental 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 (59).

Regarding gender, our study finding shows that being female were not statistically associated but it increasing less likely the hazard of DVT recurrence [CHR, 1.799; 95% CI, 0.828, 3.905; P=0.138]. This finding in line with study done at Minnesota (45) and another one prospective cohort study done at (60) that follow large number of patients for approximately 2 years failed to support this observation, the result found that being male were significant risk predictor for increasing DVT recurrence and another finding from 11 year prospective cohort study at hematology department of Switzerland university (57), showed as if male sex increased risk of DVT recurrence. This difference is most probably reflected by, the latter two studies were used nearly 2 years observational cohort with large sample and also few male participants were included in this current study and naturally females at productive age are more susceptible, due to the hormonal influences.

In this current prospective cohort study, having prior history of surgery was independent predictor of increased risk of DVT recurrence [AHR, 6.218; 95%CI: 1.54, 25.104; P=0.010]. This finding is in line with the data from Minnesota (57, 60). This may explained 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 (61).

Diabetes mellitus comorbidity was an independent predictor DVT recurrence. Hazards on developing recurrent DVT was eight times more among patients living with DM [AHR, 8.048; 95% CI, 2.494, 25.966; P<0.001]. a similar finding was reported from Canada (43) and also similar data from previous study found that diabetes mellitus was associated with a threefold 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 towards a procoagulant state (62). In addition due to vascular complication from diabetes,

decreased peripheral circulation will result distal ischemia, which have an effect on DVT occurrence.

Another remarkable finding in this present study was inability to achieve target aPTT within 24hrs of parenteral anticoagulant medications was 93%. In this study, it was independent predictor for the development of recurrent DVT [AHR, 1.129; 95% CI, 0.120, 10.600; p=0.011). Failure to rapidly achieve a target aPTT appears to reflect heparin dosing.

Furthermore, we found that unspecified amount of regular alcohol consumption were linked with increased in the development of DVT recurrence, approximately two times. Similar results were found from San Diego, California, USA(39), where high maximum alcohol use is the behavior most linked to increased risk of DVT recurrence. It is evidenced that alcohol promoting oxidative stress and mitochondrial toxicity are associated with tissue injury and cell death. This triggers coagulation activation, via exposure at the cell surface of phosphatidyl serine (63).

Strengths and Limitations of the study

The main strength of this study was being the first original research that reporting the treatment outcomes of DVT in the two large centers. The study also uses more robust study design, prospective cohort study, which will control some of the confounders. However, the study has several limitations; Small sample size, involving only two studies setting in the country so it cannot represent the magnitude of problem in the nation.

7. Conclusions

In general, deep venous thrombosis recurrence rate was higher than most previously reported results. Completes resolution of DVT was seen for small number of patients within the currently recommended duration of anticoagulation, indicating poor inpatient treatment adequacy. Older age, prior history of surgery, pregnancy, diabetes mellitus comorbidity, failure to achieve target aPTT within 24 hrs. of heparin initiation, proximal site involvement and unquantifed regular alcohol consumption were independent predictors of DVT recurrence.

8. Recommendations

A. For patients

- Patients who have any of the risk factors for DVT recurrence should be told to come to hospital if they develop any of the signs or symptoms, so that early diagnosis and management is made to reduce the complications
- Appropriate compression practice on the disease involvement site during the treatment period should be exercised.
- Based on the results from the present study, increased physical activity is recommended to individuals with long periods of immobilization.

B. For health care professionals

- Efforts are needed to prevent DVT and to reduce complications such as recurrences and PTE.
- Better individual risk stratification is needed in order to modify exposures and target primary and secondary prophylaxis to the person who would benefit most.
- Physicians should be encouraged to carry out a Wells score pretest for DVT in all medical patients admitted for at least 7 days.
- Should strictly follow and monitor each patient with DVT for treatment adequacy in hospital as well as on follow up.
- Physicians should stratify patients based on recurrence risk and target long-term anticoagulant therapy to those patients at highest risk for DVT recurrence.

C. Researchers

- Since this current study only focused on the short term outcome of DVT, it is recommended to assess the long-term outcome of DVT

References

1. Goldhaber SZ, Bounameaux H. Pulmonary embolism and deep vein thrombosis. The Lancet. 2012;379(9828):1835-46.

2. Geerts WH, Bergqvist D, Pineo GF, Heit JA, Samama CM, Lassen MR, et al. Prevention of venous thromboembolism: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2008;133(6):381S-453S.

3. Spencer FA, Emery C, Joffe SW, Pacifico L, Lessard D, Reed G, et al. Incidence rates, clinical profile, and outcomes of patients with venous thromboembolism. The Worcester VTE study. Journal of thrombosis and thrombolysis. 2009;28(4):401.

4. Cohen AT, Agnelli G, Anderson FA, Arcelus JI, Bergqvist D, Brecht JG, et al. Venous thromboembolism (VTE) in Europe. Thrombosis and haemostasis. 2007;98(04):756-64.

5. Kahn SR, Ducruet T, Lamping DL, Arsenault L, Miron MJ, Roussin A, et al. Prospective evaluation of health-related quality of life in patients with deep venous thrombosis. Archives of Internal Medicine. 2005;165(10):1173-8.

6. Prandoni P, Lensing AW, Piccioli A, Bernardi E, Simioni P, Girolami B, et al. Recurrent venous thromboembolism and bleeding complications during anticoagulant treatment in patients with cancer and venous thrombosis. Blood. 2002;100(10):3484-8.

7. Hirsh J, Lee AY. How we diagnose and treat deep vein thrombosis. Blood. 2002;99(9):3102-10.

8. Fuji T, Akagi M, Abe Y, Oda E, Matsubayashi D, Ota K, et al. Incidence of venous thromboembolism and bleeding events in patients with lower extremity orthopedic surgery: a retrospective analysis of a Japanese healthcare database. Journal of orthopaedic surgery and research. 2017;12(1):55.

9. Gader AA, Haggaz AED, Adam I. Epidemiology of deep venous thrombosis during pregnancy and puerperium in Sudanese women. Vascular health and risk management. 2009;5:85.

10. Zöller B, Ohlsson H, Sundquist J, Sundquist K. Family history of venous thromboembolism is a risk factor for venous thromboembolism in combined oral contraceptive users: a nationwide case-control study. Thrombosis journal. 2015;13(1):34.

11. Mangeni F, Kawooya M, Kiguli-Malwadde E, Ssali F. Sonography and risk factors for lower limb deep venous thrombosis at Mulago hospital, Uganda. East African medical journal. 2006;83(8):443-9.

12. Amitrano L, Brancaccio V, Guardascione MA, Margaglione M, Iannaccone L, D'Andrea G, et al. Inherited coagulation disorders in cirrhotic patients with portal vein thrombosis. Hepatology. 2000;31(2):345-8.

13. Nicolaides A, Fareed J, Kakkar A, Breddin H. Prevention and treatment of venous thromboembolism International Consensus Statement (guidelines according to scientific evidence). International Angiology. 2006;25(2):101.

14. Cushman M. Treating acute venous thromboembolism: shift with care. N Engl J Med. 2013;369(9):865-6.

15. Conklin P, Soares GM, Dubel GJ, Ahn SH, Murphy TP. Acute deep vein thrombosis (DVT): evolving treatment strategies and endovascular therapy. Rhode Island Medical Journal. 2009;92(12):394.

16. Elsharawy M, Elzayat E. Early results of thrombolysis vs anticoagulation in iliofemoral venous thrombosis. A randomised clinical trial. European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery. 2002;24(3):209-14.

17. Hirsch J. Management of deep vein thrombosis and pulmonary embolism. A statement for healthcare professionals. Council on Thrombosis (in consultation with the Council on Cardiovascular Radiology). American Heart Association, Circulation. 1996;93:2212-45.

18. Geerts WH, Heit JA, Clagett GP, Pineo GF, Colwell CW, Anderson FA, et al. Prevention of venous thromboembolism. Chest. 2001;119(1):132S-75S.

19. Næss IA, Christiansen S, Romundstad P, Cannegieter S, Rosendaal FR, Hammerstrøm J. Incidence and mortality of venous thrombosis: a population-based study. Journal of thrombosis and haemostasis. 2007;5(4):692-9.

20. Flordal PA, Bergqvist D, Ljungström K-G, Törngren S. Clinical relevance of the fibrinogen uptake test in patients undergoing elective general abdominal surgery—relation to major thromboembolism and mortality. Thrombosis research. 1995;80(6):491-7.

21. Yusuf HR, Reyes N, Zhang QC, Okoroh EM, Siddiqi A-E-A, Tsai J. Hospitalizations of adults≥ 60 years of age with venous thromboembolism. Clinical and Applied Thrombosis/Hemostasis. 2014;20(2):136-42.

22. Kröger K, Küpper-Nybelen J, Moerchel C, Moysidis T, Kienitz C, Schubert I. Prevalence and economic burden of pulmonary embolism in Germany. Vascular Medicine. 2012;17(5):303-9.

23. Prandoni P, Lensing AW, Cogo A, Cuppini S, Villalta S, Carta M, et al. The long-term clinical course of acute deep venous thrombosis. Annals of internal medicine. 1996;125(1):1-7.

24. McRae S, Tran H, Schulman S, Ginsberg J, Kearon C. Effect of patient's sex on risk of recurrent venous thromboembolism: a meta-analysis. The Lancet. 2006;368(9533):371-8.

25. Martinez C, Cohen AT, Bamber L, Rietbrock S. Epidemiology of first and recurrent venous thromboembolism: a population-based cohort study in patients without active cancer. Thrombosis and haemostasis. 2014;112(02):255-63.

26. Kearon C, Akl EA, Comerota AJ, Prandoni P, Bounameaux H, Goldhaber SZ, et al. Antithrombotic therapy for VTE disease: antithrombotic therapy and prevention of thrombosis: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2012;141(2):e419S-e96S.

27. Gebremedhin A, Shamebo M. Deep venous thrombosis in a university teaching hospital, Addis Ababa, Ethiopia. East African medical journal. 1998;75(7):432-5.

28. Haile L, Hawaz Y, Assefa G. Risk Factors of Deep Venous Thrombosis in Duplex and Colour Doppler Ultrasound at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia. East and Central African Journal of Surgery. 2013;18(2):61-9.

29. Palareti G. Recurrent venous thromboembolism: what is the risk and how to prevent it. Scientifica. 2012;2012.

30. Lindner DJ, Edwards JM, Phinney ES, Taylor Jr LM, Porter JM. Long-term hemodynamic and clinical sequelae of lower extremity deep vein thrombosis. Journal of vascular surgery. 1986;4(5):436-42.

31. Arcelus JI, Caprini JA, Hoffman KN, Fink N, Size GP, Fareed J, et al. Laboratory assays and duplex scanning outcomes after symptomatic deep vein thrombosis: preliminary results. Journal of vascular surgery. 1996;23(4):616-21.

32. Caprini J, Tapson VF. Treatment of venous thromboembolism: adherence to guidelines and impact of physician knowledge, attitudes, and beliefs. Journal of Vascular and Interventional Radiology. 2006;17(2):406.

33. Bose SC, Kar R, Shamanna SB. A Prospective Study of Adequacy of Anticoagulation with Fixed Dose Weight Adjusted Unfractionated Heparin in Patients with Deep Vein Thrombosis. Indian Journal of Hematology and Blood Transfusion. 2016;32(1):83-6.

34. Linkins L-A, Choi PT, Douketis JD. Clinical impact of bleeding in patients taking oral anticoagulant therapy for venous thromboembolism: a meta-analysis. Annals of internal medicine. 2003;139(11):893-900.

35. Nendaz M, Perrier A. Clinical impact of bleeding in patients taking oral anticoagulant therapy for venous thromboembolism: a meta-analysis, LA Linkins, PT Choi, JD Douketis, in: Ann Intern Med, 139.(2003), 893. Elsevier Masson; 2004.

36. Linkins LA, Choi PT, Douketis JD. Clinical impact of bleeding in patients taking oral anticoagulant therapy for venous thromboembolism: a meta-analysis. Ann Intern Med. 2003;139(11):893-900.

37. Cohen AT. Prevention of postoperative venous thromboembolism. BMJ: British Medical Journal (Online). 2009;339.

38. Ouriel K, Green RM, Greenberg RK, Clair DG. The anatomy of deep venous thrombosis of the lower extremity. Journal of vascular surgery. 2000;31(5):895-900.

39. Golomb BA, Chan VT, Denenberg JO, Koperski S, Criqui MH. Risk marker associations with venous thrombotic events: a cross-sectional analysis. BMJ open. 2014;4(3):e003208.

40. Kyrle PA, Kammer M, Eischer L, Weltermann A, Minar E, Hirschl M, et al. The long-term recurrence risk of patients with unprovoked venous thromboembolism: an observational cohort study. Journal of Thrombosis and Haemostasis. 2016;14(12):2402-9.

41. Andersen B, Steffensen F, Sørensen H, Nielsen G, Olsen J. The cumulative incidence of venous thromboembolism during pregnancy and puerperium. Acta obstetricia et gynecologica Scandinavica. 1998;77(2):170-3.

42. Wilasrusmee C, Kiranantawat K, Horsirimanont S, Lertsithichai P, Reodecha P, Soonthonkit Y, et al. Deep venous thrombosis in surgical intensive care unit: prevalence and risk factors. Asian Journal of Surgery. 2009;32(2):85-8.

43. Piazza G, Goldhaber SZ, Kroll A, Goldberg RJ, Emery C, Spencer FA. Venous thromboembolism in patients with diabetes mellitus. The American journal of medicine. 2012;125(7):709-16.

44. Chee CE, Ashrani AA, Marks RS, Petterson TM, Bailey KR, Melton LJ, et al. Predictors of venous thromboembolism recurrence and bleeding among active cancer patients: a population-based cohort study. Blood. 2014:blood-2014-01-549733.
45. Heit JA, Lahr BD, Petterson TM, Bailey KR, Ashrani AA, Melton LJ. Heparin and warfarin anticoagulation intensity as predictors of recurrence after deep vein thrombosis or pulmonary embolism: a population-based cohort study. Blood. 2011:blood-2011-05-357343.
46. Mwandama C, Andrews B, Lakhi S. Prevalence of deep vein thrombosis and associated factors in adult medical patients admitted to the University Teaching Hospital, Lusaka, Zambia. Medical Journal of Zambia. 2016;43(4):224-30.
47. Prins MH, Lensing AW, Prandoni P, Wells PS, Verhamme P, Beyer-Westendorf J, et al. Risk of recurrent venous thromboembolism according to baseline risk factor profiles. Blood advances. 2018;2(7):788-96.
48. Jiménez D, Aujesky D, Díaz G, Monreal M, Otero R, Martí D, et al. Prognostic significance of deep vein thrombosis in patients presenting with acute symptomatic pulmonary embolism. American journal of respiratory and critical care medicine. 2010;181(9):983-91.
49. Heit JA, Mohr DN, Silverstein MD, Petterson TM, O'fallon WM, Melton LJ. Predictors of recurrence after deep vein thrombosis and pulmonary embolism: a population-based cohort study. Archives of internal medicine. 2000;160(6):761-8.
50. Farzamnia H, Rabiei K, Sadeghi M, Roghani F. The predictive factors of recurrent deep vein thrombosis. ARYA atherosclerosis. 2011;7(3):123.
51. Mehran R, Rao SV, Bhatt DL, Gibson CM, Caixeta A, Eikelboom J, et al. Standardized bleeding definitions for cardiovascular clinical trials: a consensus report from the Bleeding Academic Research Consortium. Circulation. 2011;123(23):2736-47.
52. Vululi ST, Bugeza S, Zeridah M, Ddungu H, Openy AB, Frank M, et al. Prevalence of lower limb deep venous thrombosis among adult HIV positive patients attending an outpatient clinic at Mulago Hospital. AIDS research and therapy. 2018;15(1):3.
53. Bouée S, Emery C, Samson A, Gourmelen J, Bailly C, Cotté F-E. Incidence of venous thromboembolism in France: a retrospective analysis of a national insurance claims database. Thrombosis journal. 2016;14(1):4.
54. Goran A. Deep vein thrombosis of the lower limbs in Duhok: A descriptive study using Doppler ultrasound. Duhok Med J. 2009;3:64-72.

55. Daba FB, Tadesse F, Engidawork E. Drug-related problems and potential contributing factors in the management of deep vein thrombosis. BMC hematology. 2016;16(1):2.

56. Arcelus JI, Caprini JA, Monreal M, Suárez C, González-Fajardo J. The management and outcome of acute venous thromboembolism: a prospective registry including 4011 patients. Journal of vascular surgery. 2003;38(5):916-22.

57. Nagler M, ten Cate H, Prins MH, ten Cate-Hoek AJ. Risk factors for recurrence in deep vein thrombosis patients following a tailored anticoagulant treatment incorporating residual vein obstruction. Research and Practice in Thrombosis and Haemostasis. 2018;2(2):299-309.

58. Devis P, Knuttinen MG. Deep venous thrombosis in pregnancy: incidence, pathogenesis and endovascular management. Cardiovascular diagnosis and therapy. 2017;7(Suppl 3):S309.

59. Kujovich JL. Hormones and pregnancy: thromboembolic risks for women. British journal of haematology. 2004;126(4):443-54.

60. Moreno AF, Navarro MG, Sánchez JO, Díaz RM, Cerezo EM, de Ancos Aracil CL, et al. A risk score for prediction of recurrence in patients with unprovoked venous thromboembolism (DAMOVES). European journal of internal medicine. 2016;29:59-64.

61. Cohen AT. Prevention of postoperative venous thromboembolism. BMJ. 2009;339.

62. Lemkes BA, Hermanides J, DeVries JH, Holleman F, Meijers JC, Hoekstra JB. Hyperglycemia: a prothrombotic factor? Journal of Thrombosis and Haemostasis. 2010;8(8):1663-9.

63. Hansen-Krone IJ, Brækkan SK, Enga KF, Wilsgaard T, Hansen J-B. Alcohol consumption, types of alcoholic beverages and risk of venous thromboembolism: the Tromsø Study: Universitetet i Tromsø; 2011.

APPENDIXI I: Patient Information Sheet

JIMMA UNIVERSITY

INSTITUTE OF HEALTH SCIENCE

SCHOOL OF PHARMACY

Patient information sheet

Name of the principal investigator: Abera Mulatu

Name of study area: Jimma University Medical Center, Jimma and St. Paul's Hospital Millennium Medical College, Addis Ababa/ 'Finfinnee'

Research budget covered by: Amanuel Mental Specialised Hospital, Addis Ababa

Research objective: To determine burden and identifying risk factor and treatment outcomes of Deep Vein Thrombosis in hospitalized patients at JUMC and St. Paul's Hospital Millennium Medical College.

Significance of the study: This study will explore up to date information on the status of Deep Vein Thrombosis among hospitalized patients at inpatient medical and surgical ward of JUMC and St. Paulo's Hospital Millennium Medical College, it may help the prevalence and risk factors of the diseases and describes treatment outcomes, thus facilitate a future assessment of their burden and impact. In turn, this should enable valuable suggestions that may initiate interventions and appropriate community-based health promotion strategies to encourage healthy lifestyles among this groups and as whole population and provide base line information that may be helpful for further investigation and study on the topic.

Study procedure: Information was collected about patients' socio-demographic and clinical characteristics, diagnostic test results and treatment practice at two tertiary hospitals.

Risk on study participant: no risk on study participant

Beneficial: The study participant were benefited by getting valuable information on the identification of risk factors, which is related with DVT progression and it was also helpful for inpatient practitioner at practice site in providing anticoagulant medication information during the management of DVT.

Incentives: Participants were not provided any specific incentive for taking part in the research other than acknowledgment.

Confidentialities: Your participation is voluntary and the information you provide will be made anonymous once you hand in this questionnaire. This means that your name or other form of identification will be deleted from the questionnaire after you hand it in and will not be included in any records we will have.

Whom to contact: If there is any inconvenience or doubt about the study, please contact: Abera Mulatu: Phone No: +251913384290, e-mail address**:** ***mulatua84@gmail.com***

Guca walii-galtee Afaan Oromootin

Kabajamaa/ttuu Haadha/Abbaa hirmaataa/ttuu qorannoo kanaa. Ani maqaan koo barataa Abarrraa Mulaatuu yunivarsitii Jimmaatti barataa kilinikaal faarmaasii waggaa lammaffaa yoon ta'u, yeroo ammaa kana qorannoo waa'ee rakkoolee yaala keesso walqabatan yaalii dhukkuboota keessoo (internal Medicine) keessa jiru irratti gaggeessuuf kan qophaa'ee dha. Kanaafuu galma gallinsa qorannoo kanaatif deebii afanii isin waa'ee yaala keesssanii nuuf kennitan fi Odeeffannoo kaardii yaala keessanii irra jiru baay'ee barbaachisaa dha. Garuu, rakkoolee mul'ateef furmaata kennamu irra ni fayyadamtuu. Odeeffannoon isinirraa argamu maqaas ta'ee mallattoo eenyummaa keessanii kan hin qabnee fi iccitiidhaan kan qabatamudha. Hirmaachuu yookiin hirmaachuu dhabuun keessanii yalii argattan irratti dhiibbaa hin qabu. Garuu qulqullina yaalaa gara fulduraatti hospitaalichaan kennamu fooyyeesuuf ni fayyada. Kanaafuu yaada keessan iftoominaan akka nuuf laattan afferamtaniirtu.

Dabalataanis, hirmaannaan kun guutumaan guututti fedhii iratti kan hundaa'eedha. Gaaffii deebisu hin barbaanne yoo jiraate, irra darbuu yookiin gaafachuu ni dandeessu. Yoo hirmaachuuf eeyyamamaa taatan guca kanarratti mallateesun mirkaneessa. **Eeyyee … lakki……..** yoo gaafii qabaatan bilbila kanaan naaf bilbilaa Abarraa Mulaatuu (+251913384290).

Mallattoo gaafataa_____

Mallattoo deebii kennaa_____

Guyyaa_____(guyyaa/ji'a/bara)

Abarrraa Mulaatuu; Jimma University, IHS, School of Pharmacy, Department of Clinical Pharmacy

Email: *mulatua84@gmail.com*

የመረጃ መስጫና የስምምነት ቅፅ

ስሜ አበራ ሙላቱ በጅማ ዩንቨርስቲ የሁሊተኛ ድግሪ የክሉንካሌ ፋርማሲ ተማሪ ስሆን በኣሁኑ ግዜ ድህረ ምረቃ ጽሁፍ የምሆን ጥናት የውስጥደዌ እና ተያያ¡ ጉዳዮችን በማስመለከት ችግሮቸን ለማጥናት የተዘጋጀ'' በዚህ ሆስፒታል ምርምርን እያደረኩ ስለሆነ ከዕርሶ ጋር ዕንዳደርግ እንድሁም ካርዶ መረጃ ንእንድወስድ እንድፈቅዱሌኝ በትህትና እጠይቆታሇዉ። በዚህ ምርምር ዉስጥ በመሳተፎ በእርሶ ለይ የምደርስቦት ጉዳት ወይም በመሳተፍዎ በፊት ከምያገኙ የህክምና አገሌግልት የምጎሌቦት የለም። ሆኖም ግን በምርምሩ ዉሰወጥ ከተሳተፉ ምናሌባት ከመዳንት ጋር የተያያዘ የህክምና ችግር ከለ ከምደረገዉ ማስተካከያ ሌጠቀሙ ይችሊለ እንድሁም ወደፊቱ የህክምና እንክብካቤ እንደግባት ይጠቅማል። እርስዎ የሰጡን መረጃ ሁለም በምስጢር ይያዛል። እንድሁም የግላዎ መረጃ አይፃፍም። በተጨማሪም በዚህ ምርምር ዉስጥ መሳታፍዎ ሙለ በሙለ በፍሊጎትዎ ላይ የተመሰረተ ነዉ። በምርምሩም ላይ ያሌገባዎት ነገር ካለ በማንኛዉም ግዜ ዋናዉን ተመራማሪ መጠየቅ ይችሊሉ።

የተሳታፊዉ ፊርማ፡ _____

የመረጃ ሰብሳቢ ፊርማ፡ _____

የዋናዉ ተመራማሪ መረጃ፡-

ስም. አበራ ሙላቱ

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Jimma University, IHS, School of Pharmacy, Department of Clinical Pharmacy

ANNEX II: Data collection check list

Dear study participant

This is an invitation for you to participate in a research study to be conducted with the objective of determining and identifying burden, risk factor and treatment outcomes of DVT among Hospitalized patients at Jimma University Medical Center of inpatient medical, surgical, and Gynecology-obstetric ward and St. Paul's Hospital Millennium Medical College of internal medicine, surgical, and gynecology-obstetric ward. As the study is directly related to describing prevalence and incidence of DVT and identifying the risk factors association with the disease and its treatment outcomes. Therefore, you are kindly requested to participate in this study and provide the information required from you.

Many thanks for *considering taking* part in this study.

Instructions for data collectors

A. Select your answer for the questions by marking "√" in the box provided (data collectors)

B. If your answer is out of the choice provided; write it in the space provided

Data collection tool

Jimma University

School of Pharmacy

<table>
<tr><td colspan="3">PART I: Socio-demographic characteristics of patients</td></tr>
<tr><td>1. Card Number_____
2. Admission date_____</td><td>3. Age (yrs):_____</td><td>4. Phone No._____</td></tr>
<tr><td colspan="3">5. Gender: Male_____ Female_____
6. Weight (kg)_____ height(cm)_____</td></tr>
<tr><td>7. BMI (m^2)_____</td><td colspan="2">8. Marital status: Single___Married___Divorced___Widowed_</td></tr>
<tr><td rowspan="2">9. Educational status:
▪ Cannot read & write_____
▪ Primary school_____
▪ Secondary school_____
▪ College and above ____</td><td colspan="2">10. Residence: Rural_____Urban_____</td></tr>
<tr><td colspan="2">11. Monthly Income(ETB): _____</td></tr>
<tr><td>12. Job/Occupation
▪ Office work_____
▪ Farmer _____
▪ Merchant_____
▪ Student_____
▪ Daily laborer, _____
▪ Others, specify_____</td><td colspan="2">13. Living Situation:
▪ Living with immediate family_____
▪ Living with Extended family_____
▪ Living alone_____
▪ If other, specify_____</td></tr>
<tr><td colspan="3">Part II: Behavioural Measurements and Clinical data</td></tr>
<tr><td rowspan="2">14. Alcohol use:
Never___Occasionally___Regularly___</td><td colspan="2">15. Smoker: Current smoker _____ Ex-smoker___non-smoker___</td></tr>
<tr><td colspan="2">16. Chat chewer: Yes_____ No_____</td></tr>
<tr><td colspan="3">17. Herbal medicine use: Yes_____ No_____</td></tr>
<tr><td colspan="2">18. Site of DVT:
▪ Upper Extremity DVT
a. Proximal DVT
b. Distal DVT
▪ Lower Extremity
a. Proximal DVT (Popliteal, superficial femoral, common femoral, or iliac veins)
a. Distal DVT (calf veins (posterior tibial, gastrocnemius, soleil, peroneal, and anterior tibial))</td><td>19. DVT types
▪ Unilateral_____
▪ Bilateral _____</td></tr>
<tr><td colspan="2">21. Common Sign and symptoms present:
▪ Pain_____
▪ Swelling_____
▪ Local Tenderness_____
▪ Pitting edema _____
▪ Skin discoloration _____
▪ Other specify_____</td><td>20. Comorbidity:
▪ Cancer_____
▪ Atrial Fibrillation_____
▪ Diabetes_____
▪ Hypertension_____
▪ Previous stroke_____
▪ Heart failure_____
▪ Chronic Liver disease_____
▪ Renal failure_____
▪ Coronary artery disease_____
▪ HIV/AIDS_____
▪ Other, specify_____</td></tr>
</table>

22. Risk factors:

- *Pregnancy_____*
- *Active cancer_____*
- *Obesity (BMI >30 kg/m^2)_____*
- *Chronic lung disease_____*
- *Recent immobilization≥3 days_____*
- *Heart failure_____*
- Prior history of trauma_____
- *Neurologic disease with hemiparesis, hemiplegia, or paraplegia_____*
- *History of major bleeding_____*
- *Use of estrogen-containing oral contraceptive pill_____*
- *Use of Hormone Replacement Therapy_____*
- *Previous VTE_____*
- *Family history of VTE_____*
- *One or more significant medical comorbidities:*
  - *Heart disease_____*
  - *Metabolic, endocrine or respiratory pathologies_____*
  - *Acute infectious disease_____*
  - *Inflammatory conditions(arthritis)_____*
  - *Varicose veins with phlebitis_____*

23. Diagnosed /type of cancer

- *Colorectal_____*
- *Rectal _____*
- *Breast_____*
- *Brain _____*
- *Lung_____*
- *Liver _____*
- *Other _____*

24. Current chemotherapy

_____
_____
_____

25. Prior history of surgery: *Yes____ No._____*

26. If' 'Yes'' type of surgery

- *Orthopedic*
  - *Hip fracture surgery (HFS)____*
  - *Total hip arthroplasty (THA)____*
  - *Total knee arthroplasty (TKA)____*
- *Simple fracture of lower extremities____*
- *Abdominal surgery____*
- *Cardiac surgery____*

Other specify_____

27. Vital Sign: BP_____ RR_____PR_____O2 sat._____ calf circumference (cm)_____

28. If the patient was on antithrombotic on/prior to admission: mention them with dose

- *Aspirin (dose)_____*
- *Warfarin (dose)_____*
- *Clopidogrel (dose)_____*
- *Other specify(dose)_____*

29. Prior DVT history: *Yes_____ No_____*

Part-IV: 8-item Morisky Medication Adherence Scale- (MMAS-8)			
Items		Yes	No
1. Do you sometimes forget to take your prescribed medication?			
2. In the last two weeks, was there any day when you did not take your medication?			
3. Have you ever stopped taking your medications or decreased the dose without first warning your doctor because you felt worse when you took them?			
4. When you travel or leave the home, do you sometimes forget to take your medications?			
5. Did you take all of your medication yesterday?			
6. When you feel your symptoms are controlled, do you sometimes stop taking your medications?			
7. Have you ever felt distressed for strictly following your treatment plan?			
8. How often do you have difficulty to remember taking your medications?	Never		
	Rarely		
	Sometimes		
	Frequently		
	Always		

Work-Up and procedures	Interpretation	Date (dd/mm/yyyy)
Ultrasound/Doppler		
Echocardiography		
Electrocardiography		
x-ray		

DVT outcome follow up tool

30. Time since in hospital_____

31. Date of discharge_____

32. DVT Admission status:
- *first admission/episode____*
- *second times____*
- *more than 2 times____*

33. Is patient admitted/come with recurrent DVT: *Yes__ No___*

34. If'' Yes'' mention recurrence diagnosis:
- *PE_____*
- *DVT_____*
- *PE and DVT_____*

35. Current DVT status:
- *Worsened_____*
- *No change_____*
- *Improved_____*
- *Complete resolution. _____*

36. Time to event(count from admission date) (in days)
- *Bleeding _____*
- *Recurrence_____*
- *Death _____*
- *INR ≥ 2_____*
- *aPTT ≥ 2-2.5 above the baseline_____*

37. HIT assessment :
- *Platelets < 150,000 mm^3_____*
- *Drop in platelet count > 50% from baseline*
- *Skin necrosis_____*
- *Venous limb gangrene_____*
- *Anaphylactic-type reactions after UFH IV bolus_____*

Anticoagulation management practices recommended by the ACCP guidelines

38. Administration of parenteral anticoagulation for ≥5 days: *Yes_____ No._____*

39. Achievement of an INR ≥2.0 for ≥24 hours before stopping parenteral anticoagulation: *Yes____ No._____*

40. Early start with oral vitamin K antagonists (VKA) : within 24 hrs.: *Yes_____ No._____*

41. Initial treatment with subcutaneous heparin: *Yes_____ No._____*

42. Target aPTT within 24 hours:*Yes_____No_____*

43. *Does the patient have bleeding during his follow up? Yes_____ No_____*

44. If ''yes'' check for these risk assessment for Bleeding on anticoagulant therapy:
- *Uncontrolled HTN_____*
- *Anemia_____*
- *Age >75 years_____*
- *Recent major bleeding_____*
- *Epistaxis_____*
- *Ecchymosis or menorrhagia_____*
- *Upper or lower GI bleeding_____*

45. Admitted to hospital after discharge: *Yes____ No.____*

46. *If 'Yes' for*
- *DVT_____*
- *PE_____*
- *Both PE and DVT_____*
- *Other specify_____*

List of medications patient was taking, including ancillary medications; please include OTC medica tion(s) in the list if available (within a month)

S.No	Name of drug(s)	Dosage regimen at start(dose, frequency, route)	Indication	Date	
				Start	stop
1.					
2.					
3.					
4.					
5.					
6.					
7.					
8.					
9.					
10.					
11.					

Serial coagulation profile starting from admission													
Parameter	Inpatient/in hospital										Follow up		
	Day												
	1	2	3	4	5	6	7	8	9	10	1	2	3
INR													
PT													
aPTT													

Pertinent laboratory values					
S.No	Parameters	Follow up months			
		Baseline	A	B	C
	FBS/RBS				
	Blood pressure				
Lipid panel (mg/dL)					
	LDL-C				
	HDL-C				
	TC				
	TG				
Renal function test and others					
	Scr				
	BUN				
	CrCL				
	Urinary RBC				
	Occult blood (guac test)				
	Serum albumin				
	CD_4 value				
Complete blood count(CBC), Please if there is anemia mention type of anemia:					
	RBC Count				
	Platelet Count				
	Hemoglobin				
	Hematocrit				
Liver Function test (LFT)					
	AST				
	ALT				
	ALP				
	Bilirubin(total)				
	Direct bilirubin				
	Indirect bilirubin				
Cardiac biomarkers					
	Troponins				
	CK-MB				

Research paper final endorsement form to be filled before final submission to the school of pharmacy

Here with my signature, I declare that this research paper is done under my advisor ship and I have approved that this draft is the final draft thesis for submission to the school of pharmacy, Student Research Project office of Jimma University.

NAME_____ Signature _____

Here with my signature, I declare that this research paper has been examined by me and I have checked that the student has corrected the comment that I forwarded before final submission.

NAME_____ Signature _____

Here with my signature, I declare that this research paper is done by me as a principal researcher and I assure that this research paper is the final draft for submission to the school of pharmacy, Student Research Project (SRP) office of Jimma University.

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