

**Research Article** 

# Venous Thromboembolism Risk, Prophylaxis and Outcome in Hospitalized Patients to Medical Wards of University Teaching Hospital

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#### Abstract

**Background:** In patients with venous thromboembolism (VTE), deep vein thrombosis and pulmonary embolism are important causes of disability and death in hospitalized patient. This study aimed at assessing venous VTE risks and prophylaxis and outcome in hospitalized patients to medical wards of Tikur Anbessa Specialized Hospital (TASH).

**Material and methods:** A retrospective cross sectional study involving 200 patients' chart review in those who admitted to medical wards of TASH was conducted using the instrument from TASH guideline on VTE prophylaxis and treatment. Data was entered by EPI Info 7 and then exported to SPSS 21 version software database for analysis.

**Results:** Out of 200 medically admitted patients, 186 (93%) of them had at least two risk factors for VTE development. Only 75 (40%) patients received thromboprophylaxis and VTE was prevented in 61 (32.8%) patients who received prophylaxis. However, 11 (5.5%) of high and highest risk categories study population, developed VTE during their stay at hospital. In 128/200 (64%) study participants, the status of VTE outcome was not known since such information was not documented on patents' charts. Among 14 variables associated with occurrence of VTE, multivariable logistic regression analysis revealed that patients aged  $\geq$  60 years, AOR=6.55 (95% CI [1.40-30.74]), AMI, AOR=83.22 (95% CI [3.07-225.90]), lung diseases including pneumonia, AOR=9.55 (95% CI [11.62-56.40]) and having stroke within one last month, AOR=1.61 (95% CI [9.16-16.8]) were independent predictors for development of VTE events.

**Conclusion:** In this study, all patients have at least one risk factor for VTE. Only 37.5% of patients received TP. There is a need for implementation of existing evidence based guidelines proposed by TASH.

**Keywords:** VTE risk assessment; Thromboprophylaxis; Tikur Anbessa Specialized Hospital; Ethiopia

#### Introduction

Venous thromboembolism (VTE) results from clot formation in the venous circulation and is manifested as deep vein thrombosis (DVT) and pulmonary embolism (PE) [1]. It is a common and potentially preventable disease in hospitalized patients [2,3]. About 25% of all cases of VTE are associated with hospitalization and 50 to 75% of cases of VTE in hospitalized patients occur in those on the medical service [3].

Multitudes of risk factors have been identified in causation of VTE in both hospitalized medical and surgical patients as well as nonhospitalized general population. The common risk factors proposed are advancing age, obesity, surgery, general anesthesia, trauma, immobility, malignancy, neurologic disease, central venous catheter, and prior superficial vein thrombosis, and varicose veins, congenital or acquired thrombophilia [4].

Several risk assessment models that stratify patients according to their risk for VTE have been published, the most notable being those developed by Cohen and Kucher [2,5]. Caprini and the Padua prediction scores are also other VTE risk assessment models [6,7] in many clinical settings. These risk assessment models consist of a list of exposing risk factors (presenting illness or procedures) and predisposing risk factors (genetic and clinical characteristics), each with an assigned relative risk score. The scores are summed to produce a cumulative score, which is used to classify the patient to low, moderate, high or highest risk levels and determine the onset, intensity, type, and duration of prophylaxis [7].

The rationale for providing thromboprophylaxis is that prevention is clinically and financially beneficial compared with treatment of a thromboembolic event once it has occurred [8]. Large prospective studies continue to demonstrate that these preventive methods are significantly underutilized; often with only 30% to 50% eligible patients were receiving prophylaxis [9-12]. The reasons for this underutilization include, underestimation of VTE risk, concern over risk of bleeding, and the perception that the guidelines are resourceintensive or difficult to implement in a practical fashion [9,13-15].

# Material and Methods

## Study area

The study was carried out in Tikur Anbessa Specialized Hospital (TASH), Addis Ababa, Ethiopia. It is a tertiary university teaching hospital with 600 bed capacity out of which 100 are occupied by medical adult patients.

#### Study design and period

A retrospective cross sectional study involving patients' chart review was conducted from April 28 to May 3, 2017 in patients admitted to medical wards of TASH from July 1, 2016 to December 31, 2016 (6 months). All adult patients admitted to the medical wards in the year 2016 were the source population. Medical patients who were admitted in the hospital in the year 2016 from July 1, 2016 to December 31, 2016 were the study population.

#### Inclusion and exclusion criteria

All patients who were admitted to medical wards of TASH from July1, 2016 to December 31, 2016 which meet the study criteria and charts were reviewed till the sample size reaches. Nevertheless, patient's age less than 18 years, those admitted with established DVT and on DVT treatment were excluded from our study.

### Sampling size and sampling technique

The sample size was determined by using the single population proportion formula with p value of 0.5 since there is no study which reported risk of VTE in medical patients in Ethiopia. Since the study population (1069) during six months admission is less than 10,000, the finite population correction formula is used to calculate the actual sample size. Accordingly, 283 patients' charts were included for retrospective review by systematic random sampling method. Finally, we reviewed 200 patients' charts as many charts were excluded as they fall in exclusion criteria.

#### Data collection instrument

Structured data abstraction format (DAF) was used to collect data on patient's socio-demographic characteristics, VTE risk assessment, contraindication, thromboprophylaxis and VTE related patient outcome. The total risk score for each and every patient was calculated and risk stratification was determined by adding all VTE risks seen in each patient. Accordingly, patients with a total risk score of 0-1, 2, 3-4, and  $\geq$  5 were classified under low, moderate, high and highest VTE risk categories respectively. The instrument was prepared based on the guideline used in TASH for prophylaxis and treatment of VTE [16].

#### Data collectors and quality control

The data was collected by four clinical pharmacists after training was given for half day on how to extract the required information from patients' charts. The structured DAF was pre-tested on 5% study population prior to actual data collection for checking its clarity, simplicity, understandability and modification was made based on feedback from the pre-test abstraction format.

#### Data processing and analysis

The principal investigator checked the collected data and any incomplete documents were cleaned prior to data entry. Data was entered by EPI Info 7and then exported to SPSS 21 version software for analysis.

#### **Ethical approval**

Ethical clearance was secured from the ethical review committee of School of Pharmacy Addis Ababa University and also permission was obtained from the hospital. Data obtained in the course of study was only handled by the research team.

#### Results

#### Socio demographic and clinical characteristics

Out of 200 study participants, 119 were male and the mean age was  $41.2 \pm 16.1$  with range of 18-80 years. Almost half of patients were adults with age range of 18-39 years old. Major reasons for hospital admission were due to different hematological malignancies (31.5%) and congestive heart failure (20.5%). Other reasons are shown in Table 1.

Socio demographic profil	N (%)	
Sex	Male	119 (59.5)
	Female	81 (40.5)
Age (in Years)	18-39	98 (49)
	40-59	65 (32.5)
	60-74	31 (15.5)
	≥ 75	6 (3)
Duration of hospital stay	≤ 7	32 (16)
	15-Aug	46 (23)
	16-30	57 (28.5)
	31-90	52 (26.0)
	≥ 91	13 (6.5)
Reason for admission to	Hematologic malignancies	63 (31.5)
	Congestive heart failure	41 (20.5)
	Hypertension	23 (11.5)
	Retroviral Infection	20 (10)
	Diabetes Mellitus	19 (9.5)
	Stroke	18 (9)
	Anemia	7 (3.5)
	Others*	9 (4.5)

**Table 1:** Socio demographic and clinical characteristics of patients admitted to medical wards of TASH (N=200) (Others\* include breast cancer, trauma, acute kidney injury, chronic kidney disease, leshmaniasis, etc.).

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# VTE related risk factors

There were some commonly found VTE risk factors as shown in Table 2. Acute infection, history of blood transfusion, congestive heart failure, serious lung diseases including pneumonia (<1 month), and current cancer or on chemotherapy were VTE risk factors which frequently identified in study population (Table 2).

VTE Risk factors	N (%)
Age 40-59 years	65 (32.5)
Age 60-74 years	31 (15.5)
Age ≥ 75years	6 (3)
Varicose veins	1 (0.5)
History of inflammatory bowel disease	3 (1.5)
Acute infection	75 (37.5)
Rheumatologic disorders	5 (2.5)
Swollen legs(current)	17 (8.5)
Acute myocardial infarction (<1month)	3 (1.5)
Congestive heart failure (<1month)	41 (20.5)
Sepsis(<1month)	29 (14.5)
Serious lung including diseases pneumonia (<1month)	78 (39)
Stroke(<1month)	19 (9.5)
History of DVT/PE	4 (2)
Family history	1 (0.5)
Leg plaster caster or brace	1 (0.5)
Blood transfusion (<1month)	55 (27.5)
Previous malignancy	9 (4.5%)
Present cancer and or chemotherapy	70 (35)
Heparin induced thrombocytopenia	1 (0.5)
Multiple trauma (<1month)	3 (1.5)
Acute spinal cord injury(paralysis)(<1month)	2 (1)
Oral contraceptive or hormonal replacement therapy use	4 (2)
Pregnancy or postpartum(<1month)	5 (2.5)
History of unexplained still born infant recurrent spontaneous abortion	2 (1)

**Table 2:** VTE factors in patients admitted to the medical ward of TASH (N=200) (The percentage couldn't add up to hundred as more than one risk factor may exist in one patient).

#### VTE risk stratification and thromboprophylaxis utilization

Slightly more than half of patients (51%) were in highest risk category for VTE incident. The mean VTE risk score was 4.6 (SD=2.7)

with maximum and minimum of 19 and 1 scores, respectively. VTE prophylaxis was given only for 75 (37.5%) patients and 4 of them were from low risk stratum even if they are ineligible for thromboprophylaxis. In the remaining study participants 125 (62.5%), thromboprophylaxis were not prescribed. Heparin 7500 IU SC BID/day was the most widely used prophylaxis regimen in the studied population (Table 3).

Total risk scor e	Risk stratification	N (%)	VTE Prophylaxis N (%)	VTE prevented N (%)	VTE Develope d N (%)
0-1	Low risk	14 (7)	4 (2)	3 (1.5)	0
2	Moderate risk	39 (19.5)	15 (7.5)	8 (4)	1
3-4	High risk	45 (22.5)	14 (7)	11 (5.5)	3
≥ 5	Highest risk	102 (51)	42 (21)	39 (19.5)	7
Total		200 (100)	75 (37.5)	61 (30.5)	11 (5.5)
Regimen used		N (%)			
Heparin 5000 IU bid/day		9 (4.5)			
Heparin 5000IUor 7500 IU SC bid/day		52 (26)			
Enoxaparin (40 mg or 60 mg SC/ day)		3 (1.5)			
Heparin40mg SC bid plus Warfarin 2.5mg po/day		4 (2.0)			
Warfarin (2.5 mg, 5 mg/day)		7 (3.5)			
No Prophylaxis		125 (62.5)			

 Table 3: VTE risk stratification and thromboprophylaxis provision in patients admitted to medical wards of TASH (N=200).

#### **VTE outcome**

In our study, 11 (5.5%) patients developed VTE events during their stay at hospital and nearly two third of them were from those at highest VTE risk (Table 2) and it was occurred in patients who stayed hospital more than 15 days. In the remaining participants 61 (30.5%) didn't develop VTE during their hospital stay.

# Factors associated with development of VTE development studied participants

On bivariate logistic regression model fourteen variables were associated with the occurrence VTE in our study. For example, male patients are 1.874 more likely to develop VTE when compared with females [1.874 (0.482-7.287)]. Furthermore, being  $\geq$  60 years old [4.089 (1.176-14.216)] exposes patients to develop VTE four times than those less than 60 years old. Study participants who had rheumatogical disorders [4.625 (0.472-45.300)], lung diseases including pneumonia [7.826 (1.644-37.263)], acute myocardial infarction [41.778 (3.457-504.840)] and stroke <1 month 2.403 (. 478-12.087) were 4.625, 7.826, 41.778 and 2.403 more likely to develop VTE than who haven't these diseases respectively. Multivariable logistic regression analysis revealed that patients aged  $\geq$  60 years, AOR=6.553 (95% CI [1.397-30.736]), acute myocardial infarction,

AOR= 83.22 (95% CI [3.066-225.9]), lung diseases including pneumonia, AOR=9.549 (95% CI [11.617-56.393]) and having stroke within one last month, AOR=1.611 (95% CI [9.156-16.579]) were independent predictors for VTE incidents in this study (Table 4).

Variable	VTE incidents		COR , 95% CI	AOR , 95% CI	
5	Yes	No			
	N (%) 11 (5.5)	N (%) 189 (84.5)			
Gender					
Male	3	78	1.874 (0.482-7.287)	1.090 (0.290-4.094)	
Female	8	111	1		
Duration	of hospita	al stay			
≥ 7days	10	168	1.250 (0.152-10.260)	2.780 (.263- 29.434)	
<7days	1	21	1		
Age in ye	ars				
≥ 60	5	32	4.089 (1.176-14.216)	6.553 (1.397-30.736)	
<60	6	157	1		
Total VTE	risk sco	re			
≥ 3	10	137	3.796 (0.474-30.390)	2.752 (.310-24.444)	
<3	1	52	1		
Prophyla	cis provis	sion			
No	8	113	1.794 (0.461-6.977)	4.816 (0.950-24.419)	
Yes	3	76	1		
Acute infe	ection				
Yes	2	73	2.832 (0.595-13.475)	0.527 (0.099-2.819)	
No	9	116	1		
Rheumate	ogical dis	order			
Yes	11	189	4.625 (0.472-45.300)	5.464 (0.404-73.924)	
No	0	0	1		
Swollen le	∋g				
Yes	2	15	2.578 (0.510-13.0310	5.607 (0.708-44.409)	
No	9	174	1		
Acute my	Acute myocardial infarction				
Yes	2	188	41.778 (3.457-504.840)	83.224 (3.066-225.9)	
No	9	1	1		
Congestive heart failure					
Yes	3	38	1.490 (0.377-5.886)	1.511 (0.262-8.713)	
No	8	151	1		
Sepsis					

Yes	10	161	0.575 (0.071-4.669)	0.795 (0.080-7.853)	
No	1	28	1		
Lung dise	Lung diseases including pneumonia				
Yes	9	69	7.826 (1.644-37.263)	9.549 (1.617-56.393)	
No	2	120	1		
Stroke <1month					
Yes	2	16	2.403 (.478-12.087)	1.611 (9.156-16.579)	
No	9	173	1		
Present cancer/on chemotherapy					
Yes	4	66	1.065 (.301-3.771)	3.530 (0.662-18.823)	
No	7	123	1		

 Table 4: Factors associated with development of VTE in hospitalized patients (N=200).

# Discussion

In our study, the most common risk factors found for VTE development were longer hospital stay (39.5%), age  $\geq$  40 years (48%), having lung diseases including pneumonia (39%), acute infection (37.5%), congestive heart failure (20.5%) and present cancer and/or chemotherapy (Additional file 1). A study conducted in Pakistan also reported immobility was identified the most common risk factor for occurrence of VT [4]. Similarly, Rocha et al. [17] described most of these risk factors are risks for VTE. In present study, the risk of developing VTE increases as one stayed longer in a hospital since all patients except one who developed VTE were stayed in the at least for seven days (Table 3). Moreover, in Brazilian studies among the different medical groups, all patients hospitalized for acute heart failure, acute non-infectious respiratory disease, or pulmonary infection, cardiac diseases were considered at higher risk for VTE occurrence [17,18].

From the total population, 93% were prone for the development of VTE (Table 2) which is much higher than report from Saudi Arabia study [19]. Slightly more than half of patients (51%) were in highest risk (having  $\geq$  risk factors) and it is comparable to report from Sub Saharan Africa (46.5%) and Bahl et al. (52.1%) studies [7]. Furthermore, in our study percentage of patients at moderate risk for VTE (19.5%) were almost similar to Pakistan study (20%) [4] but two times higher than USA study [7]. However, a Tunisian survey showed that only 46% of all hospitalized patients are at risk for VTE development.

In our study, thromboprophylaxis was given to only 37.5% of patient and four of them received it without having risk. This result is contrary to Tunisian study where almost all of patients (41% from 46%) at risk received an ACCP (29) recommended prophylaxis. Underutilization prophylaxis was also reported in Saudi Arabia (55.7%) [19], IMPROVE 60% and CURVE (16%) [20] studies. Although VTE risk varied according to individual patient diagnosis, ACCP-recommended prophylaxis was consistently underused in the global ENDORSE medical patient population [12,18].

In present study, the incidence of VTE event was 5.5% which was higher than the reports of other various studies conducted elsewhere

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[6,7,21-24,]. Different reasons for high incidence in studied hospital could be failure to assess risk factors, underutilization of thromboprophylaxis for patients in need at studied setting, fear of risk of bleeding upon provision of prophylaxis. However, the same incidence rate was reported in a single tertiary referral centre, Tasmania, Australia [25]. In our study, being age  $\geq$  60years, having AMI, chronic lung disease including pneumonia and stroke with one last month were independent predictor for VTE development in studied population (Table 4).

Since the study is retrospective chart review, other VTE risk factors may exist which were not written in patients' charts. While reviewing patients' charts, we faced continuous challenge to extract necessary information due to poor organization in clerking patients' history chronologically, illegible physician handwriting and absence of a large number of charts which might have important information. Taking other alternatives like non pharmacological approaches (advising patients on the importance of leg elevation, early ambulation) by physicians to prevent VTE was not assessed in this study since they were not documented in patients' charts. This might affect our finding like risk assessment and stratification; and prophylaxis given to the patients.

# Conclusion

In this study all patients have at least one risk factor for VTE. Only 37.5% of patients received thromboprophylaxis. Among identified risk factors, being age  $\geq$  60years, having AMI, chronic lung disease including pneumonia and stroke with one last month were independent predictor for VTE events. Appropriate risk stratification and provision of prophylaxis for medically admitted patients lead to a better VTE prevention and in providing the best care for the patients who are admitted in the hospital due to many different reasons of admission. There is a need for implementation of existing evidence based guidelines proposed by ACCP and TASH.

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