COLLEGE OF HEALTH SCIENCES, SCHOOL OF MEDICINE, DEPARTMENT OF INTERNAL MEDICINE.

Title: Inpatient Prevalence of Symptomatic Venous Thromboembolism and Associated factors in Tuberculosis Patients, In Two Major Referral Hospitals, Addis Ababa, Ethiopia.

By: Dr. Assefa Dessalegn Tenkire(MD, internal medicine resident)

Jun/2025

Addis Ababa, Ethiopia

ADDIS ABABA UNIVERSITY, COLLEGE OF HEALTH SCIENCES, SCHOOL OF MEDICINE, DEPARTMENT OF INTERNAL MEDICINE.

Title: Inpatient Prevalence of Symptomatic Venous Thromboembolism and Associated factors in Tuberculosis Patients, In Two Major Referral Hospitals, Addis Ababa, Ethiopia.

By: Dr. Assefa Dessalegn Tenkire(MD, internal medicine resident)

Advisor: Dr. Hanan Yusuf, MD, consultant internist and pulmonologist.

A thesis to be submitted to the Department Of Internal Medicine, College of Health Sciences, Addis Ababa University in Partial fulfillment Of The Requirements of Specialty in Internal Medicine.

Jun/2025

Addis Ababa, Ethiopia

Declaration

I, the undersigned, declare that this research manuscript is a result of the works of my own, has never been submitted for any prior academic award or qualification in any Institution. I also declare that all sources of the materials for the thesis have been duly acknowledged.

Full Name of candidate: Assefa Dessalegn Tenkire

Signature _____

Institution ; Addis Ababa university

Date of submission: Jun/2025

Email: asseabush21@gmail.com

Phone: 0912240887

Approval of thesis submission

I hereby certify that I have read this thesis, titled "**Inpatient Prevalence of Venous Thromboembolism and Associated factors In Tuberculosis Patients, In Two Major Referral Hospitals, Addis Ababa, Ethiopia.**" submitted by Dr. Assefa Dessalegn with registration number GSR/2841/14 a candidate for the internal medicine residency program and it is worthy of acceptance.

Name of Thesis Advisor	Signature	Date
_____	_____	_____
Name of Head of Department	Signature	Date
_____	_____	_____

Research summary information

Name of the principal investigator	Dr. Assefa Dessalegn Tenkire(MD, IMR3)
Supervisor:	Dr. Hanan Yusuf, MD, consultant internist and pulmonologist.
Full title of the project	Inpatient Prevalence of Symptomatic Venous Thromboembolism and Associated factors in Tuberculosis Patients, In Two Major Referral Hospitals, Addis Ababa, Ethiopia.
Study setting	TASH and St. peter referral hospital
Study period	January 1 to December 30/ 2024
Total cost of the project	ETB 37000.50
Address of the PI	Email: asseabush21@gmail.com Phone: 0912240887

Acknowledgments

First of all, I would like to praise the almighty God for all the unconditional blessings throughout my life. I am grateful to express my thanks and appreciation to my advisor Dr. Hanan Yesuf for her constructive comments, unreserved advices and supports starting from the very beginning of this proposal development.

I am also very thankful to have a friend and a brother, Dr. Yonas Birhanu, who have been on my side throughout this work.

My sincere gratitude would also extend to my wife, friends and colleagues who have always been willing to give constructive comments and continuous supports.

List of abbreviations/acronyms

APS–Anti-phospholipid syndrome

ATT- Anti-tuberculosis

COVID–Corona virus disease

DVT–Deep Venous thrombosis

HA-VTE–Hospital acquired venous thromboembolism

IBD–Inflammatory bowel diseases

MOH–Minster of Health

PE- pulmonary embolism

PTB–Pulmonary tuberculosis

SLE–Systemic lupus erythematous

TB–Tuberculosis

TASH–Tikur anbesa specialized hospital

VTE–Venous thromboembolism

WHO–World Health organization

Table of contents

Contents pages

List of tables

List of figure

Abstract

Introduction: Background: Tuberculosis (TB) is a significant risk factor for venous thromboembolism (VTE), yet data on VTE prevalence and predictors in TB-endemic, resource-limited settings including in Ethiopia remain scarce.

Objective: To assess the inpatient prevalence of VTE and associated factors in TB patients in Tikur Anbesa Specialized Hospital(TASH) and St. Peter Hospital, in Addis Ababa, Ethiopia from January to December 2024.

Methods: A hospital-based study was conducted among selected referral hospitals, enrolling 122 TB patients. Data on socio-demographics, clinical profiles, radiological findings, and VTE diagnosis were collected. Multivariable logistic regression identified predictors of VTE.

Results: A total of 122 (93 from St. Petros Hospital and 29 from TAS) patients were hospitalized with a diagnosis of TB during the study period. They were predominantly male (60.7%) and aged 18–39 years (56.6%). The prevalence of VTE was (15/122) 12.3% (95%CI, 7.0-19.5%), with 93.3% of cases diagnosed after anti-TB treatment initiation and 50.0% (7/14) of the cases occurring after 4 weeks of anti-TB treatment. Only 41% of patients received VTE prophylaxis. Anemia (64.6% females, 78.4% males) and thrombocytopenia (34.4%) were common hematologic abnormalities. HIV is the most prevalent (23.0%) among comorbidities. Extrapulmonary TB was independently associated with VTE (adjusted odds ratio [AOR] = 5.35, 95% CI: 1.04–27.41, p = 0.04). Cavitary pulmonary TB (AOR = 6.65, p = 0.08) and female sex (AOR = 5.29, p = 0.09) showed elevated but non-significant odds.

Conclusion: VTE is prevalent among hospitalized TB patients in Ethiopia, particularly those with extrapulmonary involvement. Routine screening, targeted thromboprophylaxis for high-risk subgroups (e.g., EPTB), and standardized protocols are urgently needed to mitigate morbidity in TB-endemic regions.

Keywords: Tuberculosis, VTE, PE, DVT, Ethiopia

2. Introduction

1.1 Statement of the problem

Venous thromboembolism (VTE), which encompasses DVT and PTE, is the third leading cause of vascular death after heart attack and stroke. It is also the most common preventable cause of death in hospitalized patients. The age-standardized mortality rate from atherosclerotic, heart attack and stroke, decreased over the past two decades but deaths from VTE, had been stable since 2008, which increased with the COVID-19 pandemic(1). The burden of VTE is persistently high because of the systemic underuse of thromboprophylaxis in hospitalized patients and the mounting evidence that VTE is often a chronic disease associated with a high risk of recurrence and chronic sequel(1).

Though preventable, Hospital-acquired venous thromboembolism (HA-VTE) in medical patients remains the most common hospital-associated complication, increased mortality and readmission. A retrospective study done from 2013 to 2023 G.C. in 21 hospitals in Northern California shows the rate of HA-VTE ranges from 1.1% to 1.6% in hospitalized medical patients and with increasing incidence over time. Most (2/3rd) of HA-VTE events occurred after discharge, while 1/3rd events occurred during the index admission (2).

A cross-sectional study conducted among 219 patients admitted to Tibebe Ghion Specialized Hospital, Bahr Dar, Ethiopia, from December 2018 to May 2019 shows 6.84% incidence of VTE events, and 80% of them were from high VTE risk groups (>=4 based on Padua risk score stratification) and it occurred in patients who stayed in the hospital for more than 7 days[3]. Most patients with prophylaxis indication, among those who developed VTE, none receive thrombo-prophylaxis against VTE. In the same study, the risk factors associated with VTE were Reduced mobility (adjusted odds ratio=10.00; 95% confidence interval: 1.70–58.70), < 1 month trauma and/or surgery (adjusted odds ratio=18.93; 95% confidence interval: 2.30–155.56), active cancer (adjusted odds ratio=6.00; 95% confidence interval: 1.05–34.27), chronic kidney diseases (adjusted odds ratio=61.790; 95% confidence interval: 2.627–1453.602), and hypertension (adjusted odds ratio=7.270; 95% confidence interval: 1.105–47.835) were significantly associated with the risk of developing venous thromboembolism (3).

VTE risk assessment is an important step to prevent VTE in hospitalized patients. The risk factors for VTE usually are hereditable or acquired. Some of the acquired risk factors are modifiable; including pregnancy and the puerperium, estrogens, obesity, major surgery, immobilization, cancer, and chronic inflammatory disorders such as SLE, IBD, and APS(1-3).

Tuberculosis is a communicable, preventable, and curable disease. More than 10 million people are infected with TB worldwide, every year. The reported global number of people newly diagnosed with TB was 7.5 million in 2022, but an estimated 10.6 million people (95% UI: 9.9–11.4 million) developed TB in 2022(4).

Globally in 2022, TB caused an estimated 1.30 million deaths (95% UI: 1.18–1.43 million), accounting for the world's second leading cause of death from a single infectious agent, after coronavirus disease (COVID-19), and caused almost twice as many deaths as Human Immunodeficiency Virus (HIV)/AIDS(4). There are case reports, case series, and studies that show that tuberculosis and VTE have an association (5-7).

1.2. Justification of the study

There are many established risk factors for VTE so far, among these;- major surgery, heart attack or congestive heart failure, chronic conditions including high blood pressure, diabetes and kidney disease, lower-extremity paralysis due to spinal cord injury, fracture of the pelvis, hip or long bones, infections such as COVID-19, and active cancer.

Hospital-acquired VTE in medical patients remains one of the most serious hospital-associated complications and causes of readmission and prolonged hospital stay. Furthermore, among the recognized causes of post-TB sequelae is pulmonary hypertension which can be partly explained by the occurrence of VTE. Many case reports and case series indicate these associations between TB and VTE.

Ethiopia is among the 30 high TB burden countries worldwide. Moreover, the study site namely TASH is the largest referral hospital in Ethiopia with the first pulmonary and critical care fellowship program in the country where patients are referred for better care while St. Peter Hospital is the first TB treatment site. With the high prevalence of TB in these two hospitals, we plan to assess the prevalence and the association of these two diseases for the first time in Ethiopia.

1.3. Significance of the study

This study is aimed to provide input on the burden of VTE among hospitalized TB patients. This input is especially vital to generate evidence on the need for VTE prophylaxis as a means of prevention in this group of patients. As VTE is one of the leading causes of in-hospital mortality, identifying high-risk groups with subsequent prevention will avert the loss of human life. Furthermore, identifying and characterization these patients will help us quantify and understand one of the neglected but disabling post-TB sequelae including post-TB pulmonary hypertension. The result of the study will be disseminated to St. Peter Hospital which is a national tuberculosis treatment center, minister of Health (MOH), and Tikur Anbessa Specialized Hospital (TASH), and will also be summited for publication. This study will benefit this large group of patients who are admitted with TB and physicians treating them.

2. Literature Review

According to a retrospective study done in the United States, the prevalence of VTE among patients with active tuberculosis was 2.07% (95% confidence interval [CI], 1.62%–2.59%)[8]. Based on this study adults with active tuberculosis had a greater risk of VTE than those without (odds ratio, 1.55 [95% CI, 1.23–1.97], P <.001). VTE in a patient with active TB increases in-hospital mortality compared to patients with only active tuberculosis (92/3413 [2.7%]) or only VTE (5062/199 480 [2.5%]) (P <.001)(8).

A 15-year retrospective data of patients who were diagnosed with tuberculosis, from January 2000 through March 2015, analyzed at Seoul National University, Boramae Medical Center, shows a 0.6% prevalence of PTE, DVT, or both at or after the time of tuberculosis diagnosis. Of those nearly half of the patients (44.7%) had thrombosis at the time of tuberculosis diagnosis(9).

Of 1,801 cases of TB who were admitted at the INMI hospital, in Italy, From January 2016 to December 2021, 1.61% of patients exhibited PTE at admission or during the hospital stay, and 10% of them also had concomitant DVT. The median age at diagnosis of PTE was 50, and all patients with PTE were microbiologically confirmed. Nearly 2/3rd (69%) of patients had single or multiple comorbidities and 37.9% had one or more predisposing factors for PTE at the time of hospital admission. The majority of patients (65.5%) had extensive TB disease(10).

In a chart review of 750 patients with TB discharged from BTBC, Netherlands, between 2000 and 2010, 18 (2.4%) suffered a venous thrombotic event, of these VTEs, 17 were diagnosed before admission to BTBC(11). Most (13/18) VTEs occurred in the time window of two weeks before starting TB medication. Only HIV infection had a strong association with VTE (adjusted Odds ratio 8.2 (95% CI: 2.9–22.7)) in the studied population. The median age at VTE diagnosis was 42 years (range 21–57). Hospitalization was an associated risk factor in 14 of the 18 VTEs. Other classic risk factors were present in five of the 18 VTEs.

A study done at a tertiary hospital, in Portugal, between 2007 and 2011 on adult patients hospitalized for TB shows a 7.2% prevalence of VTE (mean age 56 years, male: 67%): Five patients had pulmonary embolism (PE), seven limb DVT, two cervical vessels DVT, and one had PE, cervical vessel DVT and right atrium thrombus. VTE occurred less than 1 month after starting ant-tuberculosis drugs, except in one patient (3 months) (12). All were treated with rifampicin

containing anti-TB drugs. Rifampicin and other uncharted factors were considered as risks for VTE in TB patients. Most patients (73%) didn't receive thromboprophylaxis. Of those patients, two patients died (13%).

In 2021G.C a case report was published from Malaysia; two bacteriologically confirmed cases of tuberculosis patients who develop VTE (PTE and portal venous thrombosis) (5). Both patients had no risk factors for VTE. Another, case report of a middle-aged man, who had bacteriologic confirmed PTB, also developed VTE (both PTE and bilateral DVT) without any attributable risk factor(6). A case series of three cases (25 years male, 16 years female and 80 years male) of smear-positive PTB patients, who developed DVT were also reported from India, all had no risk factor for VTE(7).

During a prospective multicenter study done between January 2016 and January 2018, in Algeria, 17 cases of VTE associated with bacteriologic confirmed pulmonary tuberculosis were found. The thromboembolic events were DVT, PTE, and both DVT and PTE. The median age was 44.88 years, with a sex ratio of two women to 15 men. In seven patients, the thromboembolic event occurred on the fourth day and 10 days respectively after initiation of anti-tuberculosis treatment. The diagnosis of thromboembolic disease preceded that of tuberculosis in only two cases(13).

In a retrospective study, at the Yaounde Jamot Hospital, Cameroon, of the 100% (n = 3872) patients hospitalized for TB, 31 had VTE, giving a prevalence (95% CI) of 0.8% (0.5%–1.1%). Most (58.1%) of the patients were males and the median [interquartile range (IQR)] age was 40 (33–56) years. Isolated DVT was found in 77.4% (n = 24) of the patients, and 16.1% (n = 5) had isolated PE. Among the known risk factors for VTE, immobility (51.6%), history of VTE (12.9%), and HIV infection 61.2% were found. The diagnosis of VTE was made after they had started anti-TB treatment, with a median delay (IQR) of 13 (7 - 38) days. Among the 31 TB patients with VTE, three died during hospitalization, resulting in an in-hospital mortality rate of 9.7%(14).

A cross-sectional study conducted from December 2018 to May 2019, among 219 patients admitted to Tibebe Ghion Specialized Hospital, Ethiopia, shows a 6.84%(15) prevalence of VTE during their stay at the hospital, and 80% of them were from the high-risk group. Among the study group based on Padua's prediction score, 48.4% of patients were at high risk of developing VTE. VTE prophylaxis was given only for 55 (25.1%) patients and 15 of them were at low risk of

developing VTE (<4 Padua score) and were ineligible for thromboprophylaxis. Reduced mobility, recent trauma and/or surgery, heart and/or respiratory failure, and active cancer were the frequently identified VTE risk factors. Being Female is associated with an increased risk of VTE (adjusted odds ratio=14.51; 95% CI: 2.52–83.39, p=0.003) compared to males(3).

Another intuition-based retrospective study conducted in Hawassa University Compressive Specialized Hospital, Hawassa city, Ethiopia from July 1-August 30, 2022 GC shows a higher overall incidence of DVT 10.6% [95% CI: 8.5%, 13.1%]. In the same study; orthopedic trauma; AOR = 2.6 (95% CI (1.2–5.4), corona virus; AOR = 2.5 (95%CI (1.07–5.1), and hospital stay > 15 days; AOR = 2.2 (95% CI (1.25–3.94) were significantly associated with DVT(5).

3. Objectives

3.1. General Objective

- To assess the prevalence of symptomatic venous thromboembolism (VTE) and its determinants among patients hospitalized for tuberculosis at selected referral hospitals in Addis Ababa, Ethiopia, in 2024.

3.2. Specific Objectives

- To determine the prevalence of symptomatic venous thromboembolism in patients hospitalized for tuberculosis at TASH and St.Peter hospitals in Addis Ababa, Ethiopia, from January to December 2024.

- To identify factors associated with venous thromboembolism in patients hospitalized for tuberculosis at TASH and St. Peter hospitals in Addis Ababa, Ethiopia, from January to December 2024.

4. Methods and Materials

4.1. Study setting

This study was done at two major hospitals in Addis Ababa; Tikur Anbesa Specialized Hospital/TASH and St. Peter Hospital. TASH is the largest referral hospital in the country and St. Peter Hospital is a TB referral hospital in Addis Ababa, where TB patients are treated as an inpatient and outpatient.

4.2. Source population

Patients who are infected with tuberculosis.

4.3. Study population

Patients who are hospitalized for any indication with concomitant diagnosis of tuberculosis made by physicians based on clinical, bacteriologic, and/or imaging means.

4.4. Study design

Institution-based multi-centered retrospective cross-sectional study was conducted from January to December 2024.

4.5. Inclusion and exclusion criteria

- **Inclusion criteria**: All patients who are age >= 18 years old and hospitalized with tuberculosis in the study period.
- **Exclusion criteria**: Patients who have a hereditary cause of venous embolism and whose whole or important part of the data lost was excluded from the study

4.6. Operational definition

A tuberculosis/TB disease is an infectious disease, caused by mycobacteria tuberculosis that most often affects the lungs. The diagnosis of TB can be made bacteriologically (Acid-fast bacilli/AFB smear and nucleic acid amplification/NAA testing and culture), radiological, and sometimes clinically by the physician.

4.7. Sample size determination and sampling procedure

The sample size for this quantitative study is determined using a single population proportion formula with the following assumption: A 10.6% prevalence of VTE in hospitalized patients was taken, from a study done in Hawasa(15), the margin of sampling error tolerated–5% (0.05), critical value at 95% CI of certainty (1.96), calculated as follows: By sample size formula of the single population proportion.

$$Ni = \frac{(Z_{\alpha/2})^2 p(1-P)}{d^2}$$

Where

n = sample size (the desired sample size)

$Z_{\alpha/2}^2$ = standard

P = population Prevalence

D = Margin of error = 5% = 0.05

$$n = \frac{(1.96)^2 \times 0.106(1-0.106)}{(0.05)^2} = 145$$

The source population (N) is 4256[16]

Since the source population (N) is ≤10,000 sample size is corrected as

$$n / (1 + (n / N))$$

$$145 / (1 + (145/4256)) = 140$$

And 10% for non-response/incomplete data making the final sample size of **=154**.

However the calculated sample size was not achieved, so all the TB patients, who fulfill the inclusion criteria, who were admitted to the selected hospitals during the one-year study period were included in the study.

4.8. Variables

Dependent variables

Prevalence of VTE among hospitalized TB patients

Independent variables

Age, sex, BMI/weight, cigarette smoking, contraceptive use for females, HIV, Active cancer, duration of hospitalization/immobilization, major surgery, imaging finding, echocardiography features of pulmonary hypertension, DM, Type of TB diseases(location), previous TB treatment, polycythemia vera(PV), essential thrombocytosis(ET), antiphospholipid syndrome(APS).

4.9. Data collection and materials

Data was collected from secondary sources/patient charts using a standardized tool.

4.10. Data quality assurance

A standardized and structured data collection tool was used. The collected data was confirmed by the principal investigator. The pilot study was conducted before the main study.

4.11. Data analysis

The data collected using the KoboToolbox and exported to Excel, then imported into SPSS version 27.1 for analysis. Descriptive statistics were performed to calculate the mean, median, range, and percentages. Binary logistic regression was conducted to identify predictors of venous thromboembolism (VTE) among tuberculosis (TB) patients. Variables with a p-value < 0.25 in univariate logistic regression were considered eligible for inclusion in the multivariable logistic regression model. Statistical significance was set at a p-value < 0.05, with a 95% CI.

4.12. Ethical consideration

Ethical clearance was taken from Addis Ababa University, College of Health Science, Internal medicine department, institutional review board, and St. Peter Hospital research review committee. Permission was taken from the university administrative bodies. Confidentiality of all the data gathered was maintained throughout the course of the study and after.

4.13. Dissemination of the result

The result of this study was submitted to Addis Ababa University, college of health sciences, school of medicine, and department of internal medicine. The copy of this result also was submitted to St. Peter Hospital management to use the outcome for optimization of patient care and resource allocation. Publication in scientific journals and online dissemination was in due be considered.

5. Results

5.1. Sociodemographic, Comorbidities, and admission diagnosis of TB patients

A total of 122 TB patients (93 from St. Petros Hospital and 29 from TASH) were admitted to the selected hospitals during one-year period. The data shows that tuberculosis (TB) predominantly affects males (60.7%), with the highest proportion of cases occurring in the 18-39 age groups (56.6%). Pulmonary TB(48.4%) is the most common form, followed closely by disseminated TB (44.3%). The majority of the patients had bacteriologic evidence (52.5%), while imaging supported diagnosis in 33.6% of cases. Among comorbidities, HIV is the most prevalent (23.0%). Most patients were admitted for respiratory support (66.4%), while 18.9% stayed in the hospital for less than seven days.

Table 1: *Demographic and Clinical Characteristics of Tuberculosis Patients in Selected Hospitals in Addis Ababa, Ethiopia, from January to December 2024.*

Variables		**Count**	**Frequency**
Sex	Female	48	39.3
	Male	74	60.7
Age group	18-39	69	56.6
	40-59	39	32.0
	≥ 60	14	11.4
Type of TB	Pulmonary	59	48.4
	Disseminated	54	44.3
	Extrapulmonary	9	7.4
	Bacteriologic	64	52.5

Method of diagnosis	Imaging	41	33.6
	Clinical	17	13.9
Comorbidities	Human immune deficiency virus	28	23.0
	Cancer	5	4.1
	Diabetes mellitus	7	5.7
	Hypertensions	6	4.9
	Chronic liver disease	4	3.3
	Chronic kidney disease	5	4.1
	Known Heart failure	5	4.1
Reason for admission	Respiratory failure	81	66.4
	For workup	23	18.9
	Retroviral infection	5	4.1
	Heart failure	13	10.7
Hospital length of stay	⩽7 days	23	18.9
	8–15 days	39	32.0
	16–30 days	31	25.4
	31–90 days	26	21.3
	⩾91 days	3	2.5

5.2. Radiological and Hematologic Profile

Among the total pulmonary tuberculosis patients, radiologically, the majority had segmental involvement (35.2%), with a smaller proportion presenting with cavitary TB (8.2%) and multilobar involvement (military) TB (4.9%). In terms of laboratory findings, the median WBC count was 7,200 (IQR: 4,825-10,000), with 18.9% exhibiting leukocytosis and 18.0% having leukopenia. The median hemoglobin level was 10.1 g/dL (IQR: 8.1-12.7), with 64.6% of females and 78.4% of males having low hemoglobin levels. Anemia severity among patients showed that 11.5% had severe anemia (hemoglobin <7 g/dL), while 32.8% had moderate anemia (hemoglobin between 7-10 g/dL). The median platelet count was 191,000 (IQR: 150,000-341,750). More than one-third(34.4%) of patients showing thrombocytopenia (platelet count <150 x 10^3/mcL) and 17.2 % had thrombocytosis (platelet count >451x103/ mcL). In addition, out of the total 122 patients, 29 (23.8%) underwent echocardiography. Among them, 37.9% had normal findings, 31.0% had

systolic or diastolic dysfunction, 27.6% had pulmonary hypertension, and 3.4% had valvular heart disease.

***Table 2**: Radiologic and hematologic profile of TB patients hospitalized in selected referral hospital in Addis Ababa, Ethiopia, from January to December 2024.*

Variables		**Count**	**Percentage**
Radiologic findings PTB (N=59)			
	Segmental involvement	43	35.2
	Cavitary	10	8.2
	Multilobar involvement(military TB)	6	4.9
Laboratory (N=112)			
White blood cell	Leukoepnia($<4*10^3$/mcL)	22	18.0
	Normal (4-10^3/mcL)	77	63.1
	Leukocytosis ($>10^3$/mcL)	23	18.9

Hemoglobin			
Female(48)	Low(<12g/dl)	31	64.6
	Normal(12-15g/dl)	14	29.2
	High(>15g/dl)	3	6.3
Male(n=74)	Low(<13g/dl)	58	78.4
	Normal(13-17/dl	14	18.9
	High(>17)	2	2.7
Platelet (n=112)			
	Low(<150x10^3/ mcL)	42	34.4
	Normal(150-450x10^3/ mcL)	59	48.4
	High(>451x10^3/ mcL)	21	17.2

5.3. Prevalence of VTE

A total of 15/122 patients (12.3%) were diagnosed with VTE, majority has DVT with only two patients (1.6%) having pulmonary embolism(PE). The majority of VTE diagnoses occurred during hospitalization for TB (12/15, 80.0%). Most diagnoses were made after the initiation of anti-TB treatment (14/15, 93.3%), and 50.0% (7/14) of the cases occurred after 4 weeks of anti-TB treatment. Less than one-third of the patients (27.86%) underwent diagnostic imaging for suspected VTE, with Doppler ultrasound being performed in 67.6% of those cases. Additionally, 50/122 (41.0%) patients were on DVT prophylaxis.

***Table 3**: Prevalence of VTE, occurrence, and screening of TB patients hospitalized in selected referral hospitals in Addis Ababa, Ethiopia, from January to December 2024.*

Variables	**Count**	**Percentage**
Diagnostic test done based on clinical manifestation		
PE diagnosed via Chest CT Angiography (CTA)	11	32.4
DVT diagnosed via Doppler u/s of the extremities	23	67.6
Diagnosis VTE (n=34)	15	12.3

Time of VTE diagnosis		
During hospitalization for TB	12	80.0
After discharge	2	13.3
Before admission	1	6.7
VTE diagnosis relative to anti-TB treament initiation		
After initiation	14	93.3
Before initiation	1	6.7
Occurrence after ATT (n=14)		
Within 2 weeks	5	35.7
2 to 4 weeks	2	14.3
After 4 weeks	7	50.0

5.4. VTE based on the site of Tuberculosis

VTE is prevalent among patients with extrapulmonary TB (44.4%), followed by those with disseminated TB (9.3%), and is least common in pulmonary TB cases (10.2%) (Figure 1).

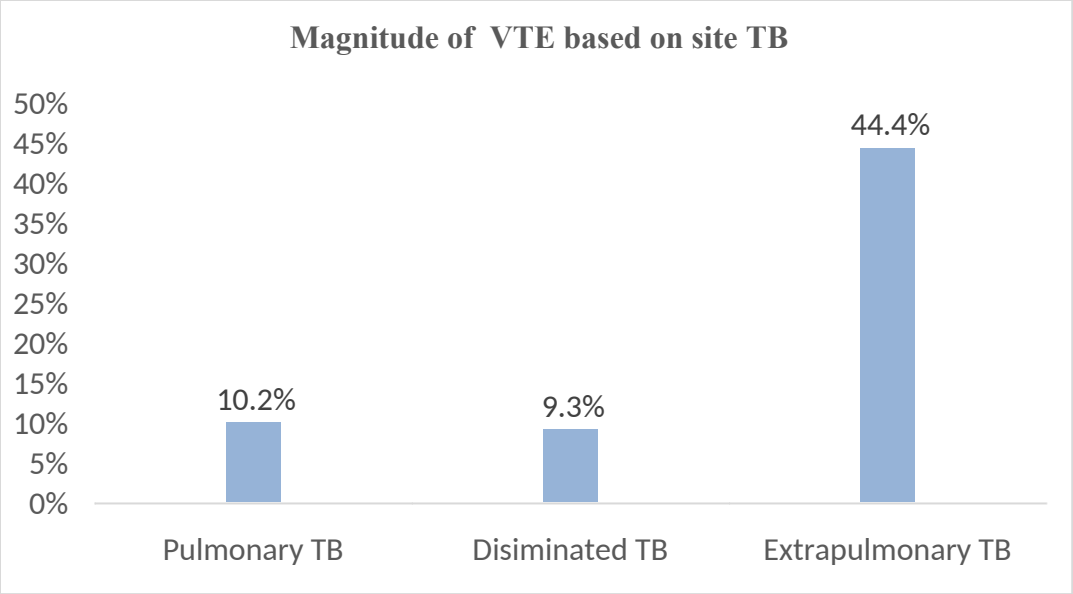

Figure 1: *Magnitude of VTE Based on the type of TB among Hospitalized Patients in Selected Hospitals in Addis Ababa, Ethiopia, from January to December 2024.*

5.5. Factors Associated with VTE Among Hospitalized TB Patients

Binary logistic regression was conducted to identify the predictors of VTE among patients with tuberculosis (TB). Initially, a bivariate (crude) binary logistic regression analysis was performed for all candidate variables including sociodemographic variables, comorbidities, and clinical and imaging findings included in the study. Variables with a p-value less than 0.25 in the bivariate analysis were considered eligible for inclusion in the multivariable logistic regression model. These include sex (Female) (p-value = 0.08), EPTB (p-value = 0.01), Cavitary PTB (p-value = 0.03), and no DVT prophylaxis (p-value = 0.23). These variables are considered for further analysis to assess their potential role as predictors of VTE in TB patients.

The multivariable logistic regression analysis revealed that extrapulmonary TB (AOR = 5.35, 95% CI: 1.04, 27.41, p = 0.04) had higher odds of being associated with an increased risk of DVT, with patients having more than five times higher odds of developing VTE compared to those with pulmonary TB. However, being female (AOR = 5.29, 95% CI: 0.77, 36.68, p = 0.09), cavitary PTB (AOR = 6.65, 95% CI: 0.80, 55.18, p = 0.08), and absences of VTE prophylaxis AOR = 2.45, 95% CI: 0.23, 25.98, p = 0.47) had higher odds with a p-value slightly failing to reach significance.

***Table 4**: Multivariable Logistic Regression Analysis of Factors Associated with VTE Among TB Patients*

Variables	**COR(95%CI)**	**P-value**	AOR (95%)	P-value
Sex				
Female	2.62(0.87,7.90)	0.08	5.29(0.77,36.68)	0.09
Male				
Type of TB				
Pulmonary	1			
DSTT	0.90(0.26,3.14)	0.87	0.77(0.21, 2.79)	0.69
EPTB	7.07(1.48,33.71)	0.01	5.35(1.04,27.41)	0.04
PTB types				
Segmental				
Cavitary	8.78(1.24,62.41)	0.03	6.65(0.80, 55.18)	0.08
Multilobar	4.10(0.31,53.78)	0.28	3.68(0.251,54.11)	0.34
DVT prophylaxis				
No	2.07(0.62,6.93)	0.23	2.45(0.23,25.98)	0.47
Yes	1		1	

6. Discussions

This study aimed to assess the prevalence and predictors of symptomatic VTE among hospitalized TB patients in selected hospitals in Ethiopia**.** The prevalence of VTE was 12.3% among hospitalized TB patients. Female patients made up 60.7%, with the highest proportion in the 18-

39 age group (56.6%). VTE was most common in patients with extrapulmonary TB (44.4%), followed by disseminated TB (9.3%). Extrapulmonary TB was significantly associated with an increased risk of VTE among TB patients.

The prevalence of VTE in TB patients in our study (12.3%) is notably higher than reported in several studies from both developing and developed countries. For instance, studies in Portugal (7.2% VTE prevalence) and Cameroon (0.8% VTE prevalence) observed lower rates [12.14]. In South Korea, a 15-year retrospective analysis found a 0.6% prevalence of VTE or PE among TB patients, with 44.7% of cases diagnosed concurrently with TB [9]. Similarly, a U.S. study reported a 2.07% VTE prevalence in TB patients, with a 1.55-fold increased risk compared to non-TB individuals [8]. The elevated VTE prevalence in our study may stem from delayed diagnosis/treatment prolonging inflammation, comorbidities (e.g., HIV [23%], anemia [64.6–78.4%]), and under used thromboprophylaxis (41%). Prolonged hospitalization (25.4% >16 days) and respiratory failure (66.4%) exacerbated immobility-related stasis. Post-Anti-TB immune changes (VTE >4 weeks post-treatment) and residual inflammation might further amplified risk in our patients.

Hospitalized TB patients exhibit higher VTE prevalence (12.3%) than non-TB patients (5–10%) (12.15). This disparity reflects TB-specific risks: chronic inflammation (e.g., TNF-α, IL-6-driven endothelial damage, granuloma-induced vascular compression, and delayed diagnosis. Unlike the general population, where age or obesity dominates risk, TB patients often lack traditional triggers, as shown in cases from Malaysia and India where DVT occurred without classic risk factors [5–7].

We also identified a significant association between extrapulmonary tuberculosis (EPTB) and a markedly higher rate of DVT in our patient cohort. In a study conducted in Italy, 65.5% of tuberculosis patients with PE had extensive or disseminated disease, suggesting that widespread inflammation and granuloma formation are key contributors [10]. Disseminated tuberculosis (e.g., miliary TB) exacerbates cytokine release, particularly tumor necrosis factor-alpha (TNF-α) and interleukin-1 beta (IL-1β), thereby promoting a hypercoagulable state. Additionally, anatomical involvement in EPTB, such as abdominal or meningeal tuberculosis, may lead to venous compression or prolonged immobilization, further increasing the risk of thromboembolism [5–7]. However, the specific site of involvement was not collected in our study.

7. Limitations and strength

This study has several limitations. The sample size was underpowered to identify multiple risk factors and to conduct subgroup analyses. Additionally, referral bias was present, as the study was conducted in a referral center, where more severe cases with multiple comorbidities were included, potentially affecting the generalizability of findings. The study included only symptomatic VTE patients diagnosed by treating physicians retrospectively to assess the prevalence of VTE. The retrospective nature of the study also limited the ability to include some variables, including malnutrition, genetic thrombophilia, and socioeconomic factors, which were difficult to assess in detail. However, our study targeted a high-risk population by focusing on hospitalized tuberculosis (TB) patients in a high-burden setting (Ethiopia), allowing for the capture of clinically relevant data on VTE prevalence and associated risk factors. Finally, the study incorporated comprehensive clinical profile, integrating radiological and echocardiographic findings, thereby enhancing pathophysiological insights.

8. Conclusion and recommendations

8.1. Conclusions

This study underscores the high burden of DVT among hospitalized tuberculosis (TB) patients in Ethiopia, with a prevalence of 12.3%**,** driven significantly by extrapulmonary TB (EPTB). EPTB emerged as a critical predictor, aligning with global evidence linking disseminated disease and inflammation to hypercoagulability.

8.2. Recommendations

Targeted prophylaxis should be prioritized for high-risk subgroups, particularly patients with extrapulmonary tuberculosis (EPTB) and those with prolonged hospitalization given their heightened risk of VTE, thromboprophylaxis should be considered during hospitalization to reduce the likelihood of thromboembolic complications.

Standardized screening protocols should be implemented to enhance early detection of VTE. Routine doppler ultrasound screening at the time of TB diagnosis and during follow-up, especially after initiating treatment, may improve timely intervention and reduce morbidity.

Integrating DVT risk assessment into national TB management guidelines is essential. Tools such as the Padua score can aid in identifying high-risk patients. Additionally, the development of TB-

specific prophylaxis guidelines, including recommendations on the timing and duration of thromboprophylaxis is necessary to optimize patient outcomes.

Further research is needed to refine thromboprophylaxis strategies in TB patients. Multicenter prospective studies screening all TB patients, especially those requiring hospitalization need to be conducted to validate and further broaden the inclusion of predictors. This study will help optimize the development of prophylaxis protocols which is especially important in countries with high TB burden like Ethiopia.

Annex

References

1. Wendelboe, Aaron. Weitz, Jeffrey I. Global Health Burden of Venous Thromboembolism. Arterioscler Thromb Vasc Biol. 2024;44:1007–1011. https://doi.org/10.1161/ATVBAHA.124.320151
2. Neeman E, Liu V, Mishra P, et al. Trends and Risk Factors for Venous Thromboembolism Among Hospitalized Medical Patients. *JAMA Netw Open.* 2022;5(11):e2240373. https://doi.org/10.1001/jamanetworkopen.2022.40373
3. Asmamaw M, Hungnaw W, Motbainor A, Kedir HM, Tadesse TA. Incidence of thromboembolism and thromboprophylaxis in medical patients admitted to a specialized hospital in Ethiopia using Padua prediction score. SAGE Open medicine. 2022;10. https://doi.org/10.1177/20503121221079488
4. Global tuberculosis report 2023. Geneva: World Health Organization; 2023. License: CC BY-NC-SA 3.0 IGO.
5. Hau Ng B. et al. clots in tuberculosis. Med J Malaysia. 2021, Vol 76 No 6.
6. Gubta R. et al. Venous Thromboembolism in tuberculosis: A Rare Entity. Chest infections. 2015;148(4_MeetingAbstracts):170A. https://doi.org/10.1378/chest.2276841
7. Gupta A, Mrigpuri P, Faye A, Bandyopadhyay D, Singla R. Pulmonary tuberculosis–An emerging risk factor for venous thromboembolism: A case series and review of literature. Lung India 2017;34:65-9.
8. Dentan C. et al. Active tuberculosis and Venous Thromboembolism: Association According to International Classification of Diseases, Ninth Revision Hospital Discharge Diagnosis Codes. Clinical Infectious Diseases 2014;58(4):495–501.
9. Ha H. et al. Thromboembolism in Mycobacterium tuberculosis Infection: Analysis and Literature Review. Infect Chemother. 2019 Jun;51(2):142-149.
10. Di Bari, V.; Gualano, G.; Musso, M.; Libertone, R.; Nisii, C.; Ianniello, S.; Mosti, S.; Mastrobattista, A.; Cerva, C.; Bevilacqua, N.; et al. Increased Association of Pulmonary Thromboembolism and Tuberculosis during COVID-19 Pandemic: Data from an Italian Infectious Disease Referral Hospital. Antibiotics 2022, 11, 398. https://doi.org/10.3390/antibiotics11030398

11. Borjas-Howard J. et al. Venous thrombotic events in patients admitted to a tuberculosis centre. QJM: An International Journal of Medicine, 2017, Vol. 110, No. 4 https://doi://10.1093/qjmed/hcw152
12. European Respiratory Society Annual Congress. 2013. Venous thromboembolic events in tuberculosis.
13. Kambouche F., El Habib L. Pulmonary tuberculosis and venous thromboembolism. International Journal of Medicine, 12 (1) (202) 1-3.
14. Abdou Wouoliyou Nsounfon et al. Prevalence of venous thromboembolism in patients hospitalized for tuberculosis at Yaounde Jamot Hospital (Cameroon), 2010-2019: a cross-sectional study. PAMJ Clinical Medicine. 2022;8(38). https://doi.org/10.11604/pamj-cm.2022.8.38.34174 also Available online at: https://www.clinical-medicine.panafrican-med-journal.com/content/article/8/38/full
15. T. Alemu et al. Incidence and factors associated with DVT among hospitalized adult patients at Hawassa university comprehensive specialized hospital Hawassa city, Sidama, Ethiopia: retrospective cohort study. Journal of Thrombosis and Thrombolysis (2024) 57:164–174. https://doi.org/10.1007/s11239-023-02889-5.
16. Alene KA, Python A, Weiss DJ, Elagali A, Wagaw ZA, Kumsa A, Gething PW, Clements ACA. Mapping tuberculosis prevalence in Ethiopia using geospatial meta-analysis. Int J Epidemiol. 2023 Aug 2;52(4):1124-1136. https://doi/10.1093/ije/dyad052. PMID: 37164625.

Data collection tool

A. Socio demographic Characteristics

1. Age (in years)
    a. 18–39
    b. 40–59
    c. 60–74
    d. ⩾75
2. Sex
    a. Male
    b. Female

B. Clinical characteristics of patients.

1. Type of TB patient is diagnosed with
    a. Pulmonary
    b. Extrapulmonary(Specify specific type)
2. Extent of TB diseases(radiologic)
    a. Segmental involvement
    b. Cavitary
    c. Miliary
    d. Disseminated
3. How diagnosis of TB made?
    a. Clinical
    b. Imaging
    c. Bacteriologic
        i. Gn xpert
        ii. Sputum AFB
        iii. Culture
4. Was the patients screened for VTE?
    a. Yes
    b. No
5. If the answer to above question is yes, what modalities used?
    a. Doppler u/s of the extremities
    b. Chest CT Angiography (CTA)
    c. D dimer

6. Was the patient diagnosed with VTE?
    a. Yes
    b. No
7. If yes, to the above question, what type of VTE?
    a. DVT
    b. PTE
    c. both
8. When was the diagnosis of VTE made?
    a. Prior to admission
    b. During hospitalization for TB
    c. After discharge
        i. Within 30days of discharge
        ii. 30-90days of discharge
        iii. After 90 days of discharge
9. When was the diagnosis of VTE made in relation to anti TB initiation?
    a. Before initiation
    b. After initiation (after how many days of initiation?)
        i. Before 2 weeks
        ii. 2 to 4 weeks
        iii. After 4 weeks
10. Was the patient on DVT prophylaxis?
    a. Yes
    b. No
11. Reason for Current admission?
    a. Heart Failure
    b. Respiratory failure
    c. Ischemic stroke
    d. Acute infection
    e. Retroviral infection
    f. Other–---
12. Complete blood count (CBC) parameters.

a. WBC

b. HGB

c. PLT

13. Did the patient have Echocardiography?

    a. No

    b. Yes

14. If yes what was the finding?

    i. Normal

    ii. Diastolic dysfunction

    iii. Valvular heart diseases

    iv. Mild pulmonary HTN

    v. Moderate pulmonary HTN

    vi. Severe pulmonary HTN

C. Risk assessment/Risk Factors associated With Hospital acquired-VTE

1. Did the patient have bed rest or immobilization for more than 3 days?
    a. Yes
    b. No
2. Duration of hospital stay (in days)
    a. ⩽7
    b. 8–15
    c. 16–30
    d. 31–90
    e. ⩾91
3. Previous history of VTE
    a. Yes
    b. No
4. Recent major trauma or surgery
    a. Yes
    b. No
5. Body mass index in kg/m^2
    a. < 24.9

b. 25-29.9
c. >30

6. Smoking
    a. No
    b. Yes
        i. An active tobacco smoker
        ii. Used to smoke

7. Comorbidities (you can select more than one answer?).
    a. Active cancer
    b. DM (If patient is diabetic, recent hemoglobin A1c?)
        1. >10%
        2. <10%
    c. Retroviral infection
    d. Hypertension
    e. Polycythemia Vera/Essential thrombocytosis
    f. Chronic liver diseases (CLD)
    g. Chronic kidney diseases (CKD)
    h. Nephrotic range proteinuria
    i. Ant phospholipid syndrome (APS)
8. Drug history other than anti TB and anticoagulant?
    a. Ongoing hormonal treatment/hormonal contraceptives
    b. L-Aspargenase
    c. Other medications–-