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A Retrospective Case Review and Risk Factor Analysis of Venous Thromboembolism Patients in High-Altitude Areas

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Abstract

The incidence of venous thromboembolism (VTE), a leading cause of morbidity and mortality worldwide, exhibits considerable geographical variability. Although studies have extensively documented VTE in low-altitude settings, the impact of high-altitude (HA) environments remains underexplored. This study aimed to fill this knowledge gap by examining the incidence and risk factors for VTE in the HA of the Tibetan Autonomous Region, offering a unique perspective on how altitude influences VTE risk. In this retrospective analysis, we reviewed the medical records from the Tibet Autonomous Region People's Hospital between January 2018 and December 2023. We included patients diagnosed with VTE and performed a comprehensive analysis of demographic data, clinical outcomes, and anticoagulant treatment patterns. Statistical methods, including logistic regression, were used to identify potential risk factors and explore the relationship between HA and VTE incidence. 1,084 patients were included in the quantitative synthesis. Based on the information gathered, the prevalence of VTE in the Tibet Autonomous Region People's Hospital between 2013 to 2023 annually increased from 0.74% to 1.12%. Additionally, VTE was mainly associated with the 18 to 64 years age group, low haemoglobin levels, hypertension at HAs. Residents of HA areas had a higher prevalence of VTE than the existing literature on lower-altitude populations. This study highlights the critical influence of HA environments on the incidence of VTE, contributing to tailored healthcare approaches for HA regions. The unique patterns of anticoagulant therapy after discharge highlight the need for personalised treatment plans. Our findings contribute to the global understanding of VTE. The study can contribute to the understanding of VTE at HAs, which aids in the development of tailored treatment for HA residents with VTE.

Keywords: Venous Thromboembolism, High Altitude, Risk Factors, Incidence Rate, Antithrombotic

List of Abbreviations: ALT, alanine aminotransferase; AMI, acute myocardial infarction; APTT, activated partial thromboplastin time; AST, aspartate aminotransferase; DOACs, direct oral anticoagulants; DVT, deep vein thrombosis; FDP, fibrin degradation product; HA, high altitude; PE, pulmonary embolism; VTE, venous thromboembolism

Introduction

Venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE), is a substantial public health concern owing to its widespread prevalence [1], potential for severe complications, and risk of recurrence. VTE is the third leading cause of vascular mortality worldwide [2]. Epidemiological data reveal a geographic variation in the incidence of VTE, with estimated rates typically between 1–2 per 1,000 person-years in Western countries and lower than 1 per 1,000 person-years in Eastern countries [3].

Numerous risk factors have been implicated in the development of VTE, including prolonged immobility (such as during lengthy flights or extended bed rest), surgical interventions, cancer, hormonal therapy, pregnancy, and familial predisposition to blood clots [4, 5]. Although numerous risk factors for VTE have been identified, the specific contribution of each factor to thrombotic risk and underlying pathogenetic mechanisms remain unclear. Lifestyle factors, such as smoking and obesity [6], also increase the risk of VTE. High altitudes (HAs) are associated with a hypercoagulable state [7, 8], potentially escalating the risk of thrombotic events. An increased incidence of VTE is associated with populations residing at elevated altitudes [9, 10], some studies suggest that reduced oxygen availability at high altitudes could lead to hypercoagulability [11, 12]. However, the effect of high-altitude exposure remains poorly understood, potentially increasing the risk of thrombosis. Other studies, however, have found no significant change in thrombotic risk [13, 14]. This inconsistency highlights the need for real-world studies to clarify the impact of high-altitude exposure on venous thromboembolism and to determine whether specific populations (e.g., older adults or individuals with cardiovascular conditions) are more affected.

The People's Hospital of Tibet Autonomous Region, located in Lhasa at an altitude of 3,650 meters, is the largest hospital in Tibet. The unique geographical, cultural, and healthcare context of Tibet enriches the study’s findings and provides insights not typically available from other regions. The region’s residents are genetically adapted to living in hypoxic conditions due to the thin air at high altitudes. This unique demographic factor can influence a wide range of health issues, including cardiovascular health and blood clotting disorders, both closely related to VTE.

This study aimed to analyse the incidence of VTE in HA areas of the Tibetan Autonomous Region by statistically comparing the occurrence and risk factors of VTE between residents of HA and plain areas. Through this comparison, we sought to gain a detailed understanding of how HA environments influence the risk of VTE, thereby facilitating the development of targeted prevention and treatment strategies against these risk factors. Additionally, this study aims to explore VTE treatment and management strategies suitable for HA areas, providing specific clinical guidance.

Materials and Methods

Data Source and Selection

Medical records of patients diagnosed with VTE at the Tibet Autonomous Region People's Hospital between January 2018 and December 2023 were used. The Hospital informtion system was utilized for patient identification and selection. A comprehensive statistical analysis focusing on variables, such as sex, age, pertinent laboratory parameters, comorbidities, duration of hospitalisation, efficacy of therapeutic interventions, and principal pharmacological treatments was performed.

Discharge diagnoses were ascertained using the International Classification of Diseases, 10th Revision (ICD-10) coding system [15]. Our exclusion criteria included: centred on patients with a primary discharge diagnosis of "embolism"， such as discharge diagnosis of pulmonary embolism, venous thrombosis lower limb, portal vein embolism, mesenteric venous embolism . Our exclusion criteria included: patients with less than hospital days 3 days, discharge diagnosis of arterial thrombosis, thrombotic microvascular disease, acute cerebral infarction, thrombotic hemorrhoids, thrombotic thrombocytopenic purpura, spinal cord

tethered syndrome, abdominal pain to check, multiple organ failure, cerumen embolism, hypokalemia and other venous thrombosis discharge diagnosis of patients. To investigate the potential impact of HA exposure on platelet and coagulation function activation in the cohort of patients with VTE, we assessed liver and kidney function, complete blood counts, eight specific coagulation-related assays, and homocysteine levels in 1,084 patients. In addtion, our collect the dosage, frequency and duration of antithrombotic drugs of these patients during hospitalization, and the usage and dosage of antithrombotic drugs and the combined medication in discharge.

Statistical Analysis

Data were analysed utilising SPSS version 21.0 (IBM, Armonk, NY, USA) and GraphPad Prism version 9.0 (GraphPad software, San Diego, CA, USA). The distribution of age categories and types of VTE manifestations is depicted as the absolute number and percentage of the total population within each group. Following patient identification, inclusion, and cohort segmentation, one-to-one matching was performed based on the patient's age and sex. Subsequently, analyses were conducted on the matched cohorts. Initial disparities in baseline characteristics and comorbid conditions between the cohorts were investigated through univariate analysis using Student's *t*-test and chi-squared test accordingly. To elucidate the impact of altitude after adjusting for comorbidities and demographic factors, binomial multivariate logistic regression analysis was performed. Outcomes were expressed as odds ratios with 95% confidence intervals (CI), and a $p < 0.05$ was deemed statistically significant [16].

Results

The Annual Prevalence Rate Distribution of VTE

Figure 1 illustrates the annual number of diagnosed thrombosis cases relative to the total number of patients discharged from 2018 to 2023. Based on the information gathered, the prevalence of VTE in the Tibet Autonomous Region People's Hospital between 2018 to 2023 annually increased from 0.74% to 1.12%.

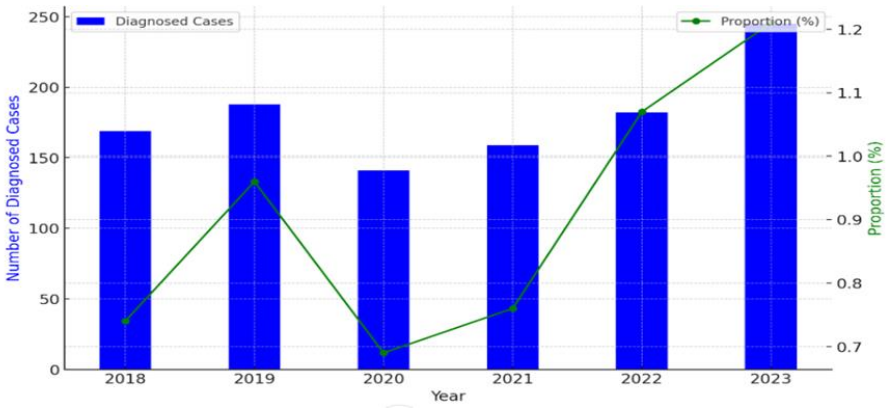

Figure 1: Diagnosed embolism cases and proportion of total discharged patients (2018–2023). The bars depict the number of diagnosed cases for each year, while the green line represents the proportion of these cases in comparison to the aggregate number of discharged patients.

Baseline Characteristics and Comorbidities

A total of 1,084 patients were analysed. The prevalence of VTEs was marginally higher prevalence among women (53.69%) than in men (46.31%). The majority of patients were within the 18–64 age group (63.10%), with a notable decline in cases as age increased. Most patients (72.32%) experienced hospital stays of 14 days or fewer, with the frequency of longer stays diminishing as the duration increased. A substantial proportion of patients exhibited clinical improvement (80.44%); the cure rate was 9.87% and the mortality rate was comparatively low at 1.75%. Lower-limb venous thrombosis was the most prevalent type

of thrombosis (35.70%) and various subtypes of PE were observed, with low-risk PE being the predominant subtype (14.76%). Rarer manifestations included mesenteric venous, portal vein, and intracranial venous sinus thrombosis. The Respiratory Medicine Department recorded the highest number of patients with VTE (37.73%), followed by the Hepatobiliary Surgery Department (29.34%). Other departments, such as Neurology, Mountain Disease, Cardiovascular, Obstetrics and Gynaecology have reported lower incidences of VTE. The The full list of comorbidities and their differences are shown in Table 1. Our findings indicate that in HA areas with the highest incidence observed among individuals aged 45 to 64 years (35.89%). The mean age is 55.17 years (17.74, 95% CI 54.12–56.23).

Table 1: Basic demographic and clinical characteristics and medical history of the study population

Characteristics	Reports, No. (%)
Patient sex	
Women	582 (53.69%)
Men	502 (46.31)
Nation	
Ethnic Han	77 (7.10)
Tibetan	1007 (92.90)
Patient age group (years)	
＜18	10 (0.92)
18–44	295 (27.21)
45–64	389 (35.89)
65–74	234 (21.59)
75–84	139 (12.82)
＞85	17 (1.57)
Length of stay (days)	
≤14	784 (72.32)
14–30	262 (24.17)
30–60	29 (2.67)
＞60	7 (0.65)
Disease outcomes	
Cure	107 (9.87)
Improve	872 (80.44)
Healed	41 (3.78)
Death	19 (1.75)
Other	45 (4.15)
Venous thrombosis type	
Venous thrombosis lower limb	387 (35.70)
Mesenteric venous thrombosis	54 (4.98)
Portal vein thrombosis	24 (2.21)

Portal and intestinal venous thrombosis	18 (1.66)
Intracranial venous thrombus sinus	49 (4.52)
Pulmonary embolism low risk	160 (14.76)
Pulmonary embolism middle risk	107 (9.87)
Pulmonary embolism high risk	75 (6.92)
Pulmonary embolism middle-low risk	36 (3.32)
Pulmonary embolism middle-high risk	28 (2.58)
Pulmonary embolism unstratified	146 (13.47)
Department visited	
Blood Rheumatology ward	11 (1.01)
ICU Intensive Care Unit	11 (1.01)
Mountain disease cardiovascular	73 (6.73)
Respiratory Medicine	409 (37.73)
Internal Medicine	14 (1.29)
Neurology department	128 (11.81)
Nephrology department	18 (1.66)
Gastroenterology department	9 (0.83)
Oncology department	4 (0.37)
Hepatobiliary Surgery	318 (29.34)
Orthopaedic Surgery	19 (1.75)
Urological surgery	2 (0.18)
Neurosurgery	28 (2.58)
Ophthalmology	1 (0.09)
Paediatric	2 (0.18)
Otolaryngology	2 (0.18)
Obstetrics and Gynaecology	35 (3.23)

The Test Indicators of the Patients

The results of the patient-related tests collected showed that most participants (68.79%) exhibited normal alanine aminotransferase levels, whereas a significant portion (26.56%) presented levels above the upper normal limit, possibly indicating liver damage or inflammation. Most individuals (59.37%) had normal aspartate aminotransferase levels; however, 24.97% surpassed the upper range, suggesting potential liver or muscle tissue damage. Approximately half of the patients (44.68%) had creatinine levels below the normal range, which could be associated with reduced muscle mass or physiological normalcy in certain instances [17]. Approximately half of the patients (50.47%) had haemoglobin values within the normal levels. A significant portion (71.90%) of patients exhibited an activated partial thromboplastin time above the upper limit, suggesting potential bleeding disorders or the effect of anticoagulant therapy. A considerable proportion (86.89%) of patients demonstrated elevated D-dimer levels, indicative of an abnormal clotting process, although elevated D-dimer levels can also occur under various conditions, including infection, inflammation, or postoperative states[18,19]. Furthermore, the majority (66.03%) of patients had fib-

rin degradation product levels that exceeded the reference value, potentially indicating abnormal clotting or fibrinolysis. Approximately one-third (30.94%) of the patients had elevated homocysteine levels, which may be linked to vitamin B12 or folate deficiencies and is a known risk factor for cardiovascular diseases[20]. Hypoxic conditions at HAs may increase blood viscosity, thereby increasing the risk of thrombosis [21, 22].

A comprehensive list of the test parameters is presented in Table 2. After excluding 192 cases of wheelchair use, 159 cases of bed rest, and 134 cases with missing body mass index (BMI) data, statistical analysis was conducted on the remaining 599 medical records with recorded BMI. The analysis revealed that the minimum BMI was 16.02, the maximum BMI was 41.00. The mean BMI was 24.87 (SD 4.72), and the median BMI (50% percentile) was 24.39.

Table 2: Clinical laboratory test results distribution among participants

Indicator	Reference Value	Total Number of Samples	Number and Percentage of Patients Within Normal Range	Number and Percentage of Patients Exceeding Upper Reference Limit	Number and Percentage of Patients Below the Lower Reference Limit
ALT (U/L)	9–50	817	562 (68.79%)	217 (26.56%)	38 (4.65%)
AST ((U/L))	15–40	817	485 (59.37%)	204 (24.97%)	128 (15.67%)
Creatinine (μmol/L)	57–97	817	383 (46.88%)	69 (8.45%)	365 (44.68%)
Haemoglobin (g/L)	130–175	951	479 (50.47%)	180 (18.91%)	292 (30.70%)
APTT (S)	28–44	839	272 (32.42%)	540 (71.90%)	27 (3.22%)
D-Dimer (mg/L)	＜0.5	839	110 (13.11%)	729 (86.89%)	N/A
FDP (mg/L)	＜5	839	263 (31.35%)	554 (66.03%)	N/A
Homocysteine (μmol/L)	15–20	181	39 (21.55%)	56 (30.94%)	86 (47.51%)

ALT, alanine aminotransferase; APTT, activated partial thromboplastin time; AST, aspartate aminotransferase; FDP, fibrin degradation product

Comorbidities

Table 3 enumerates various comorbidities, detailing the number of cases and their respective percentages within the population under study for VTE. The statistical results show that at HAs VTE was mainly associated with hypertension (33.12%)， the second is acute myocardial infarction or ischemic stroke (12.36%).The chi-square test results indicated no statistically significant association between discharge diagnosis and hypertension (p=0.480). Patients with VTE frequently experience serious cardiovascular events, such as acute myocardial infarction (AMI) or ischaemic stroke, indicative of the interconnection of these conditions [23].

Table 3: Prevalence of comorbidities among patients with VTE

Comorbidities	Number of Cases (Percentage)
Cancer	93 (8.58%)
Hypertension	459 (33.12%)
Diabetes	68 (6.27%)
Heart failure or respiratory failure	69 (6.36%)

Acute myocardial infarction or ischemic stroke	134 (12.36%)
History of VTE (excluding superficial vein thrombosis)	72 (6.64%)
Known thrombophilia	2 (0.18%)
Long-term bedridden	31 (2.86%)
Recent surgical history	60 (5.54%)
None	196 (18.08%)

VTE, venous thromboembolism

Selection of Anticoagulant Drugs for Hospitalised Patients with Embolism

Upon diagnosis of VTE, immediate anticoagulation therapy was initiated to prevent clot progression and embolism. Anticoagulant selection is guided by patient-specific factors, including renal function, bleeding risks, preferences, drug interactions, and thrombus characteristics. The primary treatment goal is clot stabilisation and minimisation of the risk of embolism, which often requires elevated anticoagulant dosages. Upon hospital admission, VTE risk assessment accounts for immobilisation, surgical history, and comorbidities to determine thromboprophylaxis and treatment levels[24]. Upon diagnosis of VTE, immediate anticoagulation therapy was initiated to prevent clot progression and embolism. Anticoagulant selection is guided by patient-specific factors, including renal function, bleeding risks, preferences, drug interactions, and thrombus characteristics. The primary treatment goal is clot stabilisation and minimisation of the risk of embolism, which often requires elevated anticoagulant dosages [25]. Upon hospital admission, VTE risk assessment accounts for immobilisation, surgical history, and comorbidities to determine thromboprophylaxis and treatment levels. Most patients received either monotherapy (40.68%) or dual antithrombotic therapy (37.08%), reflecting standard regimens. Acute VTE management typically involves parenteral anticoagulants, such as unfractionated heparin or low-molecular-weight heparin. Specifically, 53.06% of the 441 patients who received monotherapy during hospitalisation received sodium heparin or enoxaparin sodium injections.

Discharge with Medications

We compiled data on the antithrombotic medication status at discharge for 1084 patients with venous thrombosis. The details are provided in Table 4. The results showed that the majority of the patients were discharged with oral antithrombotics for continued treatment, in 43.54% of the patients with VTE were treated with rivaroxaban tablets alone after discharge, and 32.29% were not given antithrombotic medication.

Table 4: Anticoagulant medications and their case numbers after discharge

Discharge Medication	Reports, No. (%)
Dalteparin sodium injection	3 (0.28)
Low molecular weight heparin sodium	2 (0.18)
Enoxaparin sodium injection	3 (0.28)
Low molecular weight heparin sodium/dalteparin sodium injection	1 (0.09)
Heparin sodium injection/enoxaparin sodium injection	2 (0.18)
Aspirin enteric-coated tablets	63 (5.81)
Clopidogrel hydrogen sulphate tablets	4 (0.37)
Dabigatran etexilate capsules	9 (0.83)
Warfarin sodium tablets	137 (12.64)

Rivaroxaban tablets	472 (43.54)
Aspirin enteric-coated tablets/rivaroxaban tablets	22 (2.03)
Aspirin enteric-coated tablets/clopidogrel hydrogen sulphate tablets	15 (1.38)
Clopidogrel hydrogen sulphate tablets/rivaroxaban tablets	1 (0.09)
None	350 (32.29)

The chi-squared test demonstrated a significant association between discharge diagnosis and medication use upon discharge ($p < 0.05$).

Discussion

Between 2018 and 2023, the prevalence of VTE in the Tibet Autonomous Region People's Hospital exhibited an increasing annual trend, from 0.74% to 1.12%. This surge may correlate with novel coronavirus infections, as studies have shown a higher incidence of VTE in patients with COVID-19, especially those with severe disease [26, 27]. Viral infections may elevate thrombosis risk by inducing inflammatory responses and increasing blood viscosity [28], alongside vascular endothelial dysfunction. Additionally, lifestyle modifications during the pandemic, such as decreased physical activity and prolonged home isolation, may have contributed to the increasing incidence of VTE[29].Conditions, such as cancer, hypertension, and diabetes, can affect the risk of VTE development, as well as influence its management and outcomes [30, 31].

The incidences of DVT and PE significantly increase with age [32], specifically, after approximately 55 years old. However, by the age of 80, the incidence rates are approximately 1 in 100 per year, which is approximately 1000 times higher than that for those aged 45 years or younger. Furthermore, rates of PE quickly increase compared to those of DVT in older adult populations [33]. Environmental factors could also lead to heightened DVT and PE incidence in younger demographics. The altered daily activities in HA regions, encompassing occupational and recreational pursuits, could affect blood flow and thrombosis risk. The scarcity of medical resources in these areas may impede early diagnosis and treatment of DVT and PE, possibly resulting in a higher incidence among younger individuals.

A notable observation was that approximately 30.70% of patients with thrombosis had haemoglobin levels below the normal range, suggesting a prevalent incidence of anaemia. This contradicts the common perception that HAs lead to polycythaemia [34]. Approximately half of the patients had creatinine levels below the lower limit, indicating potential renal insufficiency. Moreover, a significant number of the samples (78.45%) were outside the reference range for homocysteine, with a particularly high percentage (47.51%) being below the lower limit, indicating potential metabolic anomalies associated with an increased risk of cardiovascular diseases.

The co-occurrence of hypertension was the most prevalent among patients with VTE (33.12 %). Although hypertension is a recognised risk factor for arterial thrombosis [35], its direct role in VTE risk remains unclear. However, patients with hypertension should be carefully monitored because of their elevated risk for cardiovascular complications. Post-AMI or stroke, immobility, particularly paralysis, can predispose patients to VTE. The shared risk factors among AMI, stroke, and VTE emphasise the possibility of concurrent susceptibility [36]. While AMI and stroke involve arterial thrombosis and venous thromboembolism, common underlying mechanisms, such as inflammation and hypercoagulability, may also contribute to both [37].

In the management of VTE, anticoagulant therapies are fundamental to prevent the formation or enlargement of blood clots.This indicates significant differences in the types and conditions of medications prescribed at discharge, depending on the different discharge diagnoses [38]. Rivaroxaban, a selective Factor Xa inhibitor, plays a pivotal role in the coagulation cascade, mitigating blood clot formation. The benefits include predictable pharmacokinetic profiles, obviation of routine monitoring,

and minimal dietary interactions. Rivaroxaban dosing is contingent upon clinical indications and treatment phase, necessitating adjustments for renal function, potential drug interactions, and bleeding risks. Reduced doses are recommended in cases of renal impairment or heightened susceptibility to bleeding. For example, a regimen of 15 mg once daily may be appropriate in patients with moderate renal dysfunction after the initial treatment phase. For initial DVT and PE management, 15 mg twice daily with meals is recommended for the first 21 days, followed by a maintenance dose of 20 mg once daily [39]. In our study, patients administered rivaroxaban typically received conventional treatment regimens, with only one case involving an outpatient medication regimen of rivaroxaban at a dosage of 30 mg once daily and another involving a 2-year-old administered a dose of 2 mg once daily for venous sinus thrombosis.

Anticoagulation therapy duration ranges from a minimum of three months to potentially lifelong treatment, contingent on reversible risk factors, recurrence risk, and the patient's bleeding risk. Post-discharge long-term management plans for VTE were tailored according to individual patient variables, including VTE type, risk factors, renal function, and drug interaction potential. Direct oral anticoagulants (DOACs) were frequently preferred for long-term VTE management because of their ease of administration and minimal monitoring requirements. In contrast to conventional warfarin therapy, DOACs include agents, such as rivaroxaban, apixaban, dabigatran, and edoxaban. One of the key challenges in high-altitude populations is that standard anticoagulants such as warfarin, heparin, or direct oral anticoagulants (DOACs) may have different pharmacokinetics or pharmacodynamics due to the altered vascular environment and reduced oxygen levels. Additionally, altered coagulation function, possibly caused by the plateau environment, may require adjustments in anticoagulant dosing or treatment strategies. These unique environmental factors suggest that standard protocols may not be applicable in high-altitude settings. Real-world insights into anticoagulant therapy outcomes at discharge have profound implications for healthcare providers, potentially leading to innovative strategies for remote monitoring, personalized care, and improved patient education. Ultimately, this could contribute to more effective VTE management in challenging environments.

Conclusion

The main finding of the current cross-sectional study is that the prevalence of VTE in the Tibet Autonomous Region People's Hospital between 2013 to 2023 annually increased from 0.74% to 1.12%. Additionally, VTE was mainly associated with the 18 to 64 years age group, low haemoglobin levels, hypertension at HAs.Our findings provide a better understanding of the effects of HA environments on the occurrence and treatment of VTE, thereby offering more effective prevention and treatment measures for patients with VTE in these regions. Further statistical analyses, including multivariate models, could elucidate the relative contributions of these factors to the thrombotic risk in this patient population. Additionally, this analysis could be augmented with qualitative data on patient history, medication regimens, and other clinical variables to gain a comprehensive understanding of the underlying pathogenic mechanisms. The study can contribute to the understanding of VTE at HAs, which aids in the development of tailored treatment for HA residents with VTE.

Long-term observations continue to explore HA environment influence on the risk factors for VTE, including hypoxaemia, changes in blood viscosity, and lifestyle factors. Studying the differences in VTE incidence between residents of HA and low-altitude areas, along with the underlying physiological mechanisms, can provide targeted strategies for the prevention and treatment of VTE in HA regions. Longitudinal studies and databases should be established for patients with VTE in HA areas to analyse the impact of HA on VTE recurrence and treatment outcomes. Using large data analytics, in conjunction with genetic, epidemiological, and clinical data can reveal the characteristics and patterns of VTE occurrence in HA regions, providing a basis for developing prevention strategies and improving treatment efficacy. However, we recognize that this study has certain limitations. Firstly, relying on data from a single hospital, even one with a significant catchment area, may not fully represent the broader population. Secondly, the lifestyle of Tibetan patients, including dietary habits, physical activity, and cultural practices, could significantly influence the outcomes of anticoagulant therapy. Traditional Tibetan medicine, such as herbal treat-

ments or acupuncture, may also interact with conventional anticoagulant therapy. Additionally, genetic predispositions affecting clotting mechanisms in the Tibetan population could bias conclusions regarding anticoagulant effectiveness. Lastly, unaccounted factors such as climate-related stress and social determinants of health (e.g., social support, education level) may skew the analysis and limit the validity of our findings. Further research is necessary to define protocols that are safe and effective for patients in similar conditions.

Authors' Contribution

Conceptualization – XS, YtW; Design – XS, YtW, BZ; Data collection – LMBM, LMQN; Manuscript preparation – XS, YtW, LPW; Editing – XS.

Availability of Data and Materials

Not applicable

Code Availability

Not applicable

Declarations

Ethics Approval

Not applicable

Consent to Participate

Not applicable

Consent to Publish

All authors have read the journal's authorship agreement and policy on disclosure of potential conficts of interest.

Competing Interest

All the authors have read the manuscript and declare no conflict of interest. No writing assistance was utilized in the production of this manuscript.

References

1. Prabhakar A, Chatterjee T, Bajaj N, et al. (2019) Venous thrombosis at altitude presents with distinct biochemical profiles: a comparative study from the Himalayas to the plains. Blood Adv, 3: 3713-23.

2. Srivastava S, Kumari B, Garg I, et al. (2020) Targeted gene expression study using TaqMan low density array to gain insights into venous thrombo-embolism (VTE) pathogenesis at high altitude. Blood Cells Mol Dis, 82: 102421.

3. Tritschler T, Kraaijpoel N, Le Gal G, Wells PS. Venous Thromboembolism: Advances in Diagnosis and Treatment [published correction appears in JAMA. 2018 Dec 18;320(23):2486. doi: 10.1001/jama.2018.19142]. JAMA, 320: 1583-94.

4. Lowe GD, Haverkate F, Thompson SG, et al. (1999) Prediction of deep vein thrombosis after elective hip replacement surgery by preoperative clinical and haemostatic variables: the ECAT DVT Study. European Concerted Action on Thrombosis. Thromb Haemost, 81: 879-86.

5. Dicks AB, Moussallem E, Stanbro M, Walls J, Gandhi S, Gray BH (2024) A Comprehensive Review of Risk Factors and Thrombophilia Evaluation in Venous Thromboembolism. J Clin Med, 13: 362.

6. Cheng YJ, Liu ZH, Yao FJ, et al. (2013) Current and former smoking and risk for venous thromboembolism: a systematic review and meta-analysis. PLoS Med, 10: e1001515.

7. Jones CA, Broggi MS, Holmes JS, et al. (2022) High Altitude as a Risk Factor for Venous Thromboembolism in Tibial Plateau Fractures. Cureus, 14: e24388.

8. Broggi MS, Yoon CJ, Allen J, et al. (2021) Higher altitude leads to increased risk of venous thromboembolism after acetabular and pelvic ring injury. J Clin Orthop Trauma, 19: 192-5.

9. Pelouch V, Kolár F, Ost'ádal B, Milerová M, Cihák R, Widimský J (1997) Regression of chronic hypoxia-induced pulmonary hypertension, right ventricular hypertrophy, and fibrosis: effect of enalapril. Cardiovasc Drugs Ther, 11(2): 177-85.

10. Shah NM, Hussain S, Cooke M, O'Hara JP, Mellor A (2015) Wilderness medicine at high altitude: recent developments in the field. Open Access J Sports Med, 6: 319-28.

11. Trunk AD, Rondina MT, Kaplan DA (2019) Venous Thromboembolism at High Altitude: Our Approach to Patients at Risk. High Alt Med Biol, 20: 331-6.

12. Agostoni P, Cattadori G, Guazzi M, et al. (2000) Effects of simulated altitude-induced hypoxia on exercise capacity in patients with chronic heart failure. Am J Med, 109: 450-5.

13. Fung KP, Chan KH, Ng V, Tsui PT, You JHS (2019) Health Economic Analysis of Rivaroxaban and Warfarin for Venous Thromboembolism Management in Chinese Patients. Cardiovasc Drugs Ther, 33: 331-7.

14. Jha PK, Sahu A, Prabhakar A, et al. Genome-Wide Expression Analysis Suggests Hypoxia-Triggered Hyper-Coagulation Leading to Venous Thrombosis at High Altitude. Thromb Haemost, 118: 1279-95.

15. Zhou L, Cheng C, Ou D, Huang H (2002) Construction of a semi-automatic ICD-10 coding system. BMC Med Inform Decis Mak, 20: 67.

16. Von Falck C, Orgel M, Wacker F, Aschoff HH, Krettek C, Ringe KI (2022) Icing the Pain-Ultrasound-Guided Cryoablation of Symptomatic Post-Amputation Stump Neuroma. Cardiovasc Intervent Radiol, 45: 223-7.

17. Gustafsson L, Appelgren L, Myrvold HE (1981) Blood flow and in vivo apparent viscosity in working and non-working skeletal muscle of the dog after high and low molecular weight dextran. Circ Res, 48: 465-9.

18. Rostami M, Mansouritorghabeh H. D-dimer level in COVID-19 infection: a systematic review. Expert Rev Hematol. 2020;13(11):1265-1275.

19. Kumaran MS, Singh S, Mehta H, Parsad D (2024) Decoding the variability in clinical and laboratory profiles of Chronic Inducible Urticaria vs. Chronic Spontaneous Urticaria - a retrospective study from a tertiary care center. Arch Dermatol Res, 316: 703.

20. Mallikarjun DN, Malo PK, Mensegere A, et al. (2024) Comparison of homocysteine, vitamin B12 and folic acid between rural and urban ageing Indians and its association with mild cognitive impairment and cardiovascular risk factors: a cross-sectional analysis. Brain Commun, 6: fcae343.

21. Burns P, Lipman GS, Warner K, et al. (2019) Altitude Sickness Prevention with Ibuprofen Relative to Acetazolamide. Am J Med, 132: 247-251.

22. Hudson JG, Bowen AL, Navia P, et al. (1999) The effect of high altitude on platelet counts, thrombopoietin and erythropoietin levels in young Bolivian airmen visiting the Andes. Int J Biometeorol, 43: 85-90.

23. Sławek-Szmyt S, Araszkiewicz A, Jankiewicz S, Grygier M, Mularek-Kubzdela T, Lesiak M (2024) Outcomes With Hybrid Catheter-Directed Therapy Compared With Aspiration Thrombectomy for Patients With Intermediate-High Risk Pulmonary Embolism. Cardiovasc Drugs Ther.

24. Lutfi A, O'Rourke E, Crowley M, et al. (2024) VTE risk assessment, prevention and diagnosis in pregnancy. Thromb Res, 235: 164-174.

25. Prandoni P, Noventa F, Ghirarduzzi A, et al. (2007) The risk of recurrent venous thromboembolism after discontinuing anticoagulation in patients with acute proximal deep vein thrombosis or pulmonary embolism. A prospective cohort study in 1,626 patients. Haematologica, 92: 199-205.

26. Poor HD. Pulmonary Thrombosis and Thromboembolism in COVID-19. Chest, 160:1471-80.

27. Spyropoulos AC, Goldin M, Giannis D, et al. (2021) Efficacy and Safety of Therapeutic-Dose Heparin vs Standard Prophylactic or Intermediate-Dose Heparins for Thromboprophylaxis in High-risk Hospitalized Patients With COVID-19: The HEP--COVID Randomized Clinical Trial [published correction appears in JAMA Intern Med, 182: 239.

28. Dix C, Zeller J, Stevens H, et al. (2022) C-reactive protein, immunothrombosis and venous thromboembolism. Front Immunol, 13: 1002652.

29. Al-Kuraishy HM, Al-Gareeb AI, Al-Hamash SM, et al. (2022) Changes in the Blood Viscosity in Patients With SARS-CoV--2 Infection. Front Med (Lausanne), 9: 876017.

30. Steiner D, Ay C (2022) Risk assessment and primary prevention of VTE in patients with cancer: Advances, challenges, and evidence gaps. Best Pract Res Clin Haematol, 35: 101347.

31. Darzi AJ, Repp AB, Spencer FA, et al. (2020) Risk-assessment models for VTE and bleeding in hospitalized medical patients: an overview of systematic reviews. Blood Adv, 4: 4929-44.

32. Patel H, Sun H, Hussain AN, Vakde T (2020) Advances in the Diagnosis of Venous Thromboembolism: A Literature Review. Diagnostics (Basel), 10: 365.

33. Silverstein RL, Bauer KA, Cushman M, Esmon CT, Ershler WB, Tracy RP (2010) Venous thrombosis in the elderly: more questions than answers. Blood, 110: 3097-3101.

34. Gatterer H, Villafuerte FC, Ulrich S, Bhandari SS, Keyes LE, Burtscher M (2024) Altitude illnesses. Nat Rev Dis Primers, 10: 43.

35. Miraclin T A, Bal D, Sebastian I, Shanmugasundaram S, Aaron S, Pandian JD (2024) Cerebral venous sinus thrombosis - Current updates in the Asian context. Cerebrovasc Dis Extra.

36. Anderson FA Jr, Spencer FA (2013) Risk factors for venous thromboembolism. Circulation, 107: I9-I16.

37. Gregson J, Kaptoge S, Bolton T, et al. (2019) Cardiovascular Risk Factors Associated With Venous Thromboembolism. JAMA Cardiol, 4: 163-73.

38. O. Cohen, S. Levy-Mendelovich, W Ageno (2020) Rivaroxaban for the treatment of venous thromboembolism in pediatric patients, Expert Rev. Cardiovasc. Ther, 18: 733–741. https://doi.org/https://doi.org/10.1080/14779072.2020.1823218.

39. Y. Gao, H. Jin (2021) Rivaroxaban for treatment of livedoid vasculopathy: a systematic review, Dermatol. Ther, 34: e15051.