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Factors Contributing to the Development of Venous Thromboembolism in Patients Admitted to Selected Hospitals of Iran University of Medical Sciences

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Abstract

Background and Aim: Venous thromboembolism (VTE) ranks among the top three cardiovascular causes of hospital mortality, often presenting as pulmonary embolism. Identifying risk factors associated with VTE is crucial for its effective prevention. This study aimed to determine factors associated with the development of VTE in hospitalized patients.

Materials and Methods: This descriptive cross-sectional study was conducted on 200 patients admitted to selected hospitals of Iran University of Medical Sciences between November 2023 and February 2024. Participants were selected by census and progressive method based on inclusion criteria (age over 18, physician-confirmed VTE). Data were collected by a demographic form and a 28-item questionnaire assessing VTE-related factors, and were analyzed by logistic regression through SPSS-22 software.

Results: We found that factors associated with the increased risk of VTE in this study included diabetes (P< 0.001, OR=61.26), bone fractures (P<0.001, OR=56.11), underlying diseases (P<0.001, OR=41.06), hospitalization (P<0.001, OR=31.86), catheterization (P<0.001, OR=31.86), cancer (P<0.001, OR=30.97), age (P<0.001, OR=29.23), surgery (P< 0.001, OR=16.47), family history of cancer (P<0.001, OR=10.49), statin use (P< 0.001, OR=6.54), miscarriage (P=0.017, OR=5.68), high-risk pregnancy (P=0.017, OR=5.68), hyperlipidemia (P<0.001, OR=5.01), and immobility (P<0.001, OR=4.63). All patients also referred to long distance travel as a potential risk factor for VTE.

Conclusion: Clinical, individual, and pharmacological factors contribute to VTE, with clinical factors showing higher prevalence and odds ratios, necessitating a more focused attention. Nurses can use these findings to conduct risk assessment and contribute to the prevention of VTE.

Keywords: Venous thromboembolism, pharmacological factors, individual factors, clinical factors.

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Introduction

Venous thromboembolism (VTE), encompassing deep vein thrombosis (DVT) and its major complication, pulmonary embolism (PE), is a leading cause of hospital mortality [1]. PE, characterized by a blood clot migrating to the pulmonary circulation, carries an estimated mortality rate of 31% and contributes to over 15% of in-hospital deaths [2]. This study focuses on identifying risk factors for VTE, including both DVT and PE, to enhance prevention strategies in hospitalized patients. Approximately, 6% of DVT cases and 12% of PE cases prove fatal within one month of diagnosis [3]. Despite its severe impact, particularly among critically ill patients in intensive care units, venous thromboembolism (VTE) often remains underdiagnosed [4]. Diagnosing VTE typically requires a combination of physical examination, laboratory tests, and imaging techniques, with the Wells score serving as the most reliable diagnostic algorithm [5]. This approach integrates medical history, clinical symptoms and D-dimer testing, with lower D-dimer levels paradoxically increases VTE suspicion [6]. VTE is a recurrent condition, often presenting as a chronic and spontaneously recurring disease, with about one-third of patients experiencing recurrence within 10 years [2]. The peak risk of VTE occurs within 6 to 12 months of initial episode and then gradually declines but persists indefinitely [7]. In roughly 25% of sudden deaths, PE marks the first clinical sign, with the post- PE survival rates of lower than DVT alone [8]. Although the precise mechanisms of VTE remain unclear, Virchow's triad (stasis, endothelial injury, and hypercoagulability) plays a key role in its development [9]. VTE's risk factors fall into genetic and acquired categories. Genetic factors, such as enhanced coagulation activity and factor VII mutations, elevate the risk of VTE compared to those without such mutations [10]. Acquired factors encompass age, obesity, prolonged immobility, smoking, recent surgery, major trauma, acute illnesses, antiphospholipid syndrome, stroke, heart or respiratory failure, prior VTE, congenital venous anomalies, central venous catheters, vena cava filters, pregnancy, childbirth, oral contraceptive use, and certain inflammatory conditions [11]. Approximately half of VTE cases stem from provoking factors, while the rest are idiopathic, with causes yet to be fully elucidated [12, 13].

Preventive strategies target at-risk individuals based on disease severity [14]. Recommended prophylaxis include mobilization, anticoagulation, intermittent pneumatic compression, graduated compression stockings, or a combination of them [15]. During the COVID-19 pandemic, international guidelines advocated prophylactic anticoagulants for all hospitalized patients [16], as coronavirus infection elevated PE risk despite standard thromboprophylaxis [17].

Given VTE's nonspecific symptoms and potential for rapid fatality, identifying its risk factors and implementing prophylaxis are critical. Data on VTE's incidence, risk factors, and thromboprophylaxis use remain scarce in some regions [18]. Recognizing contributing factors is vital for risk stratification, prevention, treatment, and reduction of thrombosis burden [18]. Moreover, limited research fil to elucidate why prophylactic anticoagulants sometimes fail to prevent VTE, with many cases remaining asymptomatic until detected via venography [19]. While some VTE risk factors are known, others remain unidentified [20]. Given regional variations in VTE's prevalence and risk factors, comprehensive data analysis offers valuable insights into DVT prevention. Thus, this study aimed to identify factors contributing to VTE development among patients admitted to

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selected hospitals affiliated with Iran University of Medical Sciences in 2023.

Methods

This descriptive cross-sectional study included all patients admitted to selected hospitals affiliated with Iran University of Medical Sciences between November 2023 and February 2024.The minimum sample size for estimating venous thromboembolism (VTE)'s prevalence, with 95% confidence and a precision of d=0.07, was calculated to be n=195 using a standard formula, based on a 45% DVT prevalence reported by Fariba et al. [21]. From a list of all affiliated hospitals, three hospitals (Firouzgar, Shahid Rajaee Heart, and Hazrat Rasoul Akram Hospitals) were randomly selected by lottery. A total of 200 patients admitted to these hospitals between November 2023 and February 2024 were enrolled using a stratified random sampling method. Inclusion criteria were age of over 18 years and physician-confirmed thromboembolism diagnosis. Exclusion criteria comprised of withdrawal from the study and partial compilation of the questionnaires.

Data were collected by a demographic information form (capturing details such as age, gender, marital status, education level, occupation, body mass index, place of residence, tobacco use, alcohol consumption, and narcotic abuse), and a researcher-designed questionnaire to evaluate pharmacological and clinical factors associated with venous thromboembolism (VTE). The researcher-designed questionnaire, which was developed specifically for this study, comprised of 35 dichotomous (yes/no) items assessing risk factors, such as chronic conditions (e.g., underlying diseases, diabetes, hypertension, heart disease, spinal cord disease), medical interventions (e.g., hospitalization, surgery, catheterization, blood transfusion), lifestyle and immobility factors (e.g., immobility, prolonged travel, lack of exercise), reproductive health (e.g., pregnancy, miscarriage, high-risk pregnancy, oral contraceptive use), cancer-related factors (e.g., cancer, family history of cancer), and other factors (e.g., COVID-19 infection, COVID-19 vaccination, blood type, family history of thrombosis, prior thrombosis, statin use, hyperlipidemia). Narcotic abuse was defined as the non-prescribed or excessive use of narcotic substances, assessed via patient self-reporting during interviews. Catheterization referred to the use of central venous catheters (CVCs) or other indwelling catheters, as reported by patients or confirmed through medical records during hospitalization. Each item received a score of 1 for yes (indicating the presence of risk factor) or 0 (indicating lack of risk factor) For blood type, a score of 1 was assigned to non-O blood groups (A, B, or AB) due to their association with increased VTE risk, while O blood group was scored as 0. For age, a score of 1 was assigned to patients aged 50 years or older, reflecting their increased VTE risk based on prior studies. For gender, female was coded as 1 (yes) and male as 0 (no) due to the higher VTE risk observed in females, potentially linked to reproductive factors such as pregnancy and miscarriage .The total score of this questionnaire ranged from 0 to 35, with higher scores indicating a greater number of VTE risk factors. Content validity for this tool was established through iterative refinements based on feedback from five faculty members with expertise in nursing and clinical practice, ensuring item relevance and clarity experts, ensuring item relevance and clarity. Internal consistency was evaluated using Cronbach's alpha, yielding a coefficient of 0.82, indicating acceptable reliability. Despite the dichotomous (yes/no) nature of the questionnaire items, Cronbach's alpha was deemed appropriate due to the large number of items and consistency with

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similar studies employing dichotomous scales [21,22]

This approach aligns with methodologies in prior VTE research, in which researcher-designed tools were validated through expert review and pilot testing [21].

After proposal approval and ethics clearance (IR.IAU.TMU.REC.1402.108) from the Ethics Committee of the Islamic Azad University, Tehran Medical Sciences Branch, the first author conducted daily ward visits for sampling. Data collection involved questionnaires completed through patient interviews at the selected hospitals. Within each hospital, patients meeting the inclusion criteria were selected using simple random sampling with a random number generator. The first author consulted nursing offices to determine the number of confirmed VTE cases per hospital, and the sample was allocated proportionally to each hospital based on the number of confirmed cases, with the guidance of a statistical consultant. Ethical compliance was maintained by securing approval, explaining study objectives to participants, and ensuring voluntary participation and confidentiality. Descriptive statistics were presented in charts and tables, while analytical statistics were conducted through SPSS-22 software.

Results

This study included 200 participants, all of whom completed the questionnaires. Fifty-six percent of patients were 51 to 60 years old, with majority of them being male (56.5%), married (80 .5%), self-employed (25.5%) and educated at under diploma level (46.5%). Nearly half of the patients (49%) were residing in the provincial capital, 81% had health insurance, and 50% held supplementary insurance coverage (Table 1).

Table 1. Frequency distribution of demographic characteristics of patients

Variable	Category	Number	Percentage (%)
Age (Years)	20–30	11	5.5
	31–40	18	9.0
	41–50	36	18.0
	51–60	112	56.0
	61–70	23	11.5
	Total	**200**	**100.0**
Gender	Male	113	56.5
	Female	87	43.5
	Total	**200**	**100.0**
Marital Status	Married	161	80.5
	Single	17	8.5
	Divorced	12	6.0
	Widowed	10	5.0
	Total	**200**	**100.0**
Education Level	Under Diploma	93	46.5
	Diploma	44	22.0
	University	63	31.5
	Total	**200**	**100.0**
Occupation	Housewife	28	14.0
	Self-employed	51	25.5
	Employee	47	23.5
	Retired	25	12.5

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	Unemployed	49	24.5
	Total	**200**	**100.0**
Place of Residence	Provincial Capital	98	49.0
	City	71	35.5
	Suburbs	15	7.5
	Village	16	8.0
	Total	**200**	**100.0**

Factors most strongly associated with an increased risk of venous thromboembolism (VTE), ranked by odds ratio (OR), included diabetes (P<0.001, OR=61.26), bone fractures (P<0.001, OR=56.11), underlying diseases (P<0.001, OR=41.06), hospitalization (P<0.001, OR=31.86), catheterization (P<0.001, OR=31.86), cancer (P<0.001, OR=30.97), age (P<0.001, OR=29.23), surgery (P<0.001, OR=16.47), family history of cancer (P<0.001, OR=10.49), statin use (P<0.001, OR=6.54), miscarriage (P=0.017, OR=5.68), high-risk pregnancy (P=0.017, OR=5.68), hyperlipidemia (P<0.001, OR=5.01), immobility (P<0.001, OR=4.63), body mass index (P=0.027, OR=4.17), pregnancy (P<0.001, OR=3.27), female gender (P=0.004, OR=2.35), myocardial infarction (P<0.001, OR=0.44), congestive heart failure (P<0.001, OR=0.41), and hypertension (P<0.001, OR=0.41). Notably, all patients referred to long distance travel as a potential risk factor for VTE (Table 2).

Table 2. Frequency distribution of risk factors among patients

Risk Factor	Category	Yes		No		P-Value	Odds Ratio (OR)
		N	%	N	%		
Age	≥50 years	22	11.0	1	0.5	<0.001	29.23
	<50 years	76	38.0	101	50.5		
Gender	Female	53	26.5	34	17.0	0.004	2.35
	Male	45	22.5	68	34.0		
Body Mass Index (BMI)	Yes	11	5.5	3	1.5	0.027	4.17
	No	87	43.5	99	49.5		
Occupation Type	Yes	22	11.0	16	8.0	0.28	1.55
	No	76	38.0	86	43.0		
Underlying Disease	Yes	88	44.0	18	9.0	<0.001	41.06
	No	10	5.0	84	42.0		
Diabetes	Yes	37	18.5	1	0.5	<0.001	61.26
	No	61	30.5	101	50.5		
Hypertension	Yes	42	21.0	0	0.0	<0.001	0.35
	No	56	28.0	102	51.0		
Heart Disease	Yes	27	13.5	0	0.0	<0.001	0.41
	No	71	35.5	102	51.0		
Spinal Disease	Yes	4	2.0	0	0.0	0.056	0.48
	No	94	47.0	102	51.0		
History of Hospitalization	Yes	74	37.0	9	4.5	<0.001	31.86
	No	24	12.0	93	46.5		
History of Surgery	Yes	45	22.5	5	2.5	<0.001	16.47
	No	53	26.5	97	48.5		
History of Fracture	Yes	35	17.5	1	0.5	<0.001	56.11

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	No	63	31.5	101	50.5		
History of Immobility	Yes	52	26.0	20	10.0	<0.001	4.63
	No	46	23.0	82	41.0		
COVID-19 Infection	Yes	80	40.0	81	40.5	0.72	1.15
	No	18	9.0	21	10.5		
COVID-19 Vaccine	Yes	1	0.5	1	0.5	1.0	1.04
	No	97	48.5	101	50.5		
Blood Type Non-O (A,B,AB)		74	37.0	71	35.5	0.42	1.34
	O	24	12.0	31	15.5		
History of Blood Transfusion	Yes	23	11.5	23	11.5	1.0	1.05
	No	75	37.5	79	39.5		
Oral Contraceptive Use	Yes	29	14.5	24	12.0	0.34	1.36
	No	69	34.5	78	39.0		
Family History of Thrombosis	Yes	8	4.0	5	2.5	0.40	1.72
	No	90	45.0	97	48.5		
Previous Thrombosis	Yes	14	7.0	13	6.5	0.83	1.14
	No	84	42.0	89	44.5		
History of Tobacco Use	Yes	25	12.5	21	10.5	0.50	1.32
	No	73	36.5	81	40.5		
History of Narcotic Abuse	Yes	4	2.0	2	1.0	0.43	2.12
	No	94	47.0	100	50.0		
History of Alcohol Use	Yes	7	3.5	9	4.5	0.79	0.79
	No	91	45.5	93	46.5		
History of Statin Use	Yes	38	19.0	9	4.5	<0.001	6.54
	No	60	30.0	93	46.5		

Discussion

This study aimed to identify factors contributing to the development of venous thromboembolism (VTE) among patients admitted to selected hospitals of Iran University of Medical Sciences. Among 35 factors examined, 10 individual factors (age, gender, marital status, education level, occupation, body mass index (BMI), residence, tobacco use, alcohol consumption, and narcotic use) were assessed in this study. These factors are widely recognized as individual or sociodemographic determinants in health-related research, consistent with prior studies (e.g., National Health Interview Survey [NHIS], 2010; Ogden et al., 2014). Their selection was based on their established associations with health outcomes, such as obesity, chronic diseases, and substance use behaviors, as supported by the literature (Kumanyika et al., 2008; Dawson et al., 2013). Age, BMI, and female gender emerged as the most significant predictors of VTE risk. Notably, all participants reported long distance travel as a potential risk factor for VTE.

Supporting these findings, Mousa and colleagues in Egypt identified obesity and tobacco use as significant individual factors in VTE [22]. Similarly, Alamri et al. (2023) in Saudi Arabia highlighted obesity (OR=17.9) as a critical factor in VTE [23]. In China, Tian and Li (2021) found age of over 50 (OR=4.24) to be a key predictor of VTE [24]. Cushman et al. (2016) reported higher DVT risk in men and increased BMI as potential risk factors of VTE[25]. Fariba et al. (2019) noted smoking (16.8 percent) as a risk factor of VTE [21]. Cohen and colleagues in a retrospective cohort study linked age of over 60 and BMI of above 35 to elevated

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VTE risk [26]. Nagler et al. (2021) in the Netherlands identified male gender and immobility as top predictors of VTE [27]. Ren et al. (2021) cited age and tobacco use [28], while Miri et al. (2017) reported duration of ICU stay as VTE risk factors [29]. Lawall et al. (2014) in Germany underscored smoking and immobility as the risk factors of VTE [30].

The role of gender in VTE development and recurrence is notable. While the overall incidence of first VTE shows no consistent differences between sexes, women of childbearing age exhibit a higher incidence due to hormonal factors and pregnancy [31]. However, men generally face a higher risk of VTE recurrence. A large population study found that men had a 13% higher risk of recurrence compared to women [32]. Some studies also link the Factor V Leiden mutation to recurrent VTE in men [33]. The impact of smoking on VTE remains debated although it is known as a risk factor for atherosclerosis, but its association with VTE is less clear. A meta-analysis of participants without prior cardiovascular disease or VTE found that smoking is linked to increased VTE risk, persisting even after excluding cancer patients—contradicting earlier ties to smoking-related hospitalizations. A recent meta-analysis showed that smoking is significantly tied to VTE in case-control studies, but not cohorts [10].

Of the 35 factors, 25 clinical factors were assessed in this study, including chronic conditions (e.g., diabetes, hypertension, hyperlipidemia), medical interventions (e.g., hospitalization, surgery, catheterization), reproductive factors (e.g., pregnancy, miscarriage, high-risk pregnancy), cancer-related factors (e.g., cancer, family history of cancer), and other factors (e.g., immobility, BMI), all of which showed the highest VTE odds. Mousa and colleagues reported immobility, bone fractures, malignancy, and chemotherapy as key clinical factors associated with VTE [22]. Alamri and colleagues also identified ischemic heart disease (OR=4.5), hypertension (OR=0.3), and bone fractures (OR=0.1) as the risk factors of VTE [23]. Tian and Li noted hypertension (OR=2.21) and prolonged bed rest (OR=1.56) as the risk factors of VTE [24]. Meanwhile, Fariba et al. (2019) listed hypertension (37.2%), recent hospitalization (29.6%), cardiovascular issues (27.5%), surgery (16.8%), prior VTE (16.8%), hyperlipidemia (13.7%), and catheterization (13.7%) as the risk factors of VTE [21]. Cohen and colleagues linked heart failure and cerebrovascular disease to VTE [26], while Nagler and colleagues cited immobility, elevated Factor VIII, and inflammation as the risk factors of VTE [27]. Miri et al. emphasized on the duration of ICU stay as a factor that contributes to VTE [29].

Among four pharmacological factors (statin use, vaccination, oral contraceptive use, and miscellaneous drugs), only statin use was found to significantly increase VTE's odds. Fariba et al. (2019) also referred to statin use (15.5%) as the risk factors of VTE [21], while Cohen and colleagues linked steroids use, antirheumatic drugs, and hydroxychloroquine to increased VTE risk [26].

The innovation of present study lies in its unique setting (previously unstudied referral hospitals with nationwide reach—offering broader generalizability), its extensive review of patient records assessing 35 factors, and its focus on confirmed VTE cases. This is while other studies only target specific groups (e.g., Mousa et al. [22], Alamri et al. [23], and Miri et al. [29]). Nurses, as the largest healthcare workforce with constant bedside presence, are pivotal in VTE's prevention and care. By assessing VTE's risk during admission—akin to evaluating pressure ulcers or falls—nurses

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can inform patients and physicians about these risk factors, making this study's findings especially valuable for participating hospitals. This study had several limitations. For instance data were sourced from existing patient records, which may include inaccuracies beyond the researcher's control. Additionally, despite its diagnostic significance, D-dimer test results were not recorded.

Conclusion

Three factors—clinical, individual, and pharmacological—contribute to venous thromboembolism (VTE). While all of these factors merit attention, clinical factors, with their higher prevalence and odds ratios, require particular attention. Nurses across all wards, especially in intensive care and post-surgical units, should know these factors and implement interventions to mitigate VTE's risk in patients. Implementing standardized VTE risk assessment checklists can enhance nursing interventions.

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Conflict of Interest

The authors report no conflicts of interest in preparing this article.

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